No difference in outcomes of liver transplantation using elderly donor grafts versus young donor grafts in the setting of short cold ischemia times

Bezjak, Miran; Jadrijević, Stipislav; Kocman, Branislav; Anna, Mrzljak; Miro, Antonijević; Dalbelo Bašić, Bojana; Mikulić, Danko

Source / Izvornik: **Transplant International,Special Issue:Abstracts of the 20th Biennial European Society for Organ Transplantation (ESOT) Congress, 2021, 34, 316 - 316**

Conference paper / Rad u zborniku

Publication status / Verzija rada: **Published version / Objavljena verzija rada (izdavačev PDF)**

https://doi.org/10.1111/tri.13944

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:264:444449

ESOT LEONARDO DA VINCI TRANSPLANT RESEARCH INNOVATION AWARD

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LDV01 IL-21 DRIVEN EXPANSION AND REPROGRAMMING OF T-BET EXPRESSING B CELLS DURING ANTIBODY-MEDIATED REJECTION OF KIDNEY TRANSPLANTS

Kevin Louis[1], Elodie Bailly[2,3], Camila Macedo[3], Bala Ramaswami[3], Parmjeet Randhawa[3], Geetha Chalasani[3], Adriana Zeevi[3], Carmen Lefaucheur[2], Diana Metes[3]

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Background: Donor-specific antibodies (DSAs) and ensuing development of antibody-mediated rejection (ABMR) are detrimental to organ transplants. Yet, the cellular states underlying alloreactive B-cell responses and the molecular components controlling them remain unclear.
Methods: In a cohort of 96 kidney transplant recipients, we performed 22-color spectral flow cytometry, RNA-seq and *in vitro* assays to profile circulating B cells, as well as multiplex immunofluorescence and RNA-seq to profile infiltrating B cells in allograft biopsies. There were 48 patients without DSAs; of those with DSAs, ABMR emerged in 20 patients, but not in 28 patients.
Results: We identified expanded numbers of $CD27^{+}CD21^{-}$ activated memory (AM) B cells that expressed the transcription factor T-bet in blood of patients who developed DSAs and progressed to ABMR. AM cells were less frequent in DSA+ABMR patients and at baseline levels in DSA patients ($p < 0.001$). AM cells in patients undergoing ABMR markedly upregulated IL-21R, and the downstream transcription factors, IRF4 and Blimp1, displayed a plasma cell precursor transcriptional profile and expressed more restricted *IGHV* sequences, reflective of clonal expansion, when compared to other memory B-cell subsets ($p < 0.001$). IL-21 was a potent inducer of AM cells, their upregulation of T-bet and IL-21R, and promoted their differentiation into DSA-producing plasma cells. AM cells preferentially accumulated in blood of patients with severe ABMR manifestations including late-onset of rejection post-transplant, presence of IgG3 DSAs, and increased vascular inflammation in kidney allografts. Importantly, AM B cells were detected within kidney allografts along with their restricted *IGHV* sequences.
Conclusions: This study delineates a pivotal role for AM B cells in promoting humoral responses and ABMR in organ transplantation, and identifies the IL-21/T-bet axis as an important therapeutic target.

LDV02 SPECIFIC ELIMINATION OF ANTI-HLA ANTIBODY-PRODUCING B CELLS IN AN IN VIVO MOUSE MODEL BY USING CHIMERIC HLA ANTIBODY RECEPTOR (CHAR) T CELLS

Sergi Betriu Méndez[1], Jordi Rovira[2], Elisenda Bañón-Maneus[2], Sandra Sancho[1], Arend Mulder[3], Frans Claas[3], Manel Juan[1], Fritz Diekmann[4], Eduard Palou[1]

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Background: Immunotherapy with genetically modified T cells that express chimeric antigen receptors (CARs) is offering excellent results in various clinical trials in oncology. Furthermore, the development of T-cell expressing chimeric autoantibody receptors (CAARs) has recently been postulated for targeted therapy in autoimmune diseases. On the other hand, one of the main problems in solid organ transplantation is the presence, or de novo generation, of donor-specific alloantibodies, which are associated with a high risk of antibody-mediated rejection. Our group has previously shown that a chimeric receptor composed of an HLA-A2 molecule as the extracellular domain (chimeric HLA antibody receptor or CHAR) can be expressed in T lymphocytes, which then are – *in vitro* – capable of specifically eliminating B cells that produce HLA-A2 alloantibodies.
Methods: In the present study, GFP-Luciferase HLA-A2 antibody-producing hybridome B cells were injected into irradiated NSG mice. These cells rapidly grew located in mice bone marrow. Afterward, CHAR-A2-transduced T cells were additionally injected at days +1 and +7. Monitoring of the persistence of HLA-A2 antibody-producing B cells was performed by GFP expression detection.
Results: In this mouse model, CHAR-A2 transduced T cells were able to eliminate the HLA-A2 antibody-producing B cells. Complete clearance was observed when the T cell: B cell ratio was less than 1:5 and the CHAR-A2 T-cell infusion was performed on the first day after B-cell injection.
Conclusions: Our results demonstrate that CHAR cytotoxic T cells specifically eliminate alloreactive B cells that produce anti-HLA antibodies, being these cells crucial for transplant recipient sensitization and development of antibody-mediated rejection. Our approach could be used to specifically desensitize the highly sensitized recipients in order to offer them an opportunity to be transplanted or to treat antibody-mediated rejection.

LDV03 ENHANCED DELIVERY OF NANOMEDICINE TO KIDNEY GRAFT ENDOTHELIAL CELLS DURING EX VIVO PERFUSION

Claire Albert[1], Laura Bracaglia[1], Akiko Koide[2], Jenna Dirito[3], Taras Lysyy[3], Christopher Edwards[3], John Langford[3], Danielle Haakinson[3], Jordan Pober[4], W. Mark Saltzman[1], Shohei Koide[2], Gregory Tietjen[1,3]

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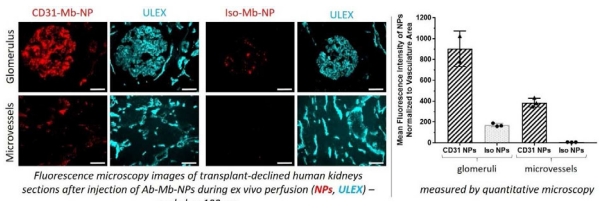
Background: Endothelial cells (ECs) are targets and active participants for multiple pathologies. Efficient delivery of therapeutic agents to graft EC prior to transplantation could render organs more resistant to injury, improving clinical outcomes, and increasing the number of transplantable organs. Targeted nanoparticles (NPs) delivered during ex vivo perfusion can allow specific and sustained delivery as well as increased local concentration of an encapsulated therapeutic. Even though ECs are readily accessible, an efficient retention of therapeutic NPs by ECs remains to be achieved. Here, we describe a new and extremely efficient targeting approach using an engineered synthetic binding protein, a "monobody" (Mb), as linker.
Methods: We have developed a Mb that potently and selectively binds to the Fc region of an antibody isotype. A unique cysteine that enables site-specific conjugation to NPs was introduced. Together, the Mb linker enables the formation of Ab-Mb-NP conjugates. Flow cytometry and quantitative fluorescence microscopy of dye-loaded NPs were used to measure efficiency of binding to ECs.
Results: Ab-Mb-NPs showed significant enhancement of binding in vitro compared with commonly used EDC-NHS conjugated Ab-NPs. This is likely due to a higher number of Ab attached and a better control of Ab orientation leading to high retention of antibody function. The Mb approach also has the advantage of being readily adaptable to different NP compositions and different Abs of the same species/isotype without re-engineering as is necessary with EDC-NHS conjugation. For example, we easily changed the polymer used to formulate the NPs (PLA-PEG or PACE), the targeted molecule (CD31 or ICAM2), and the species of the targeted molecule (human or pig) without having to alter the conditions for conjugation. When administered during ex vivo normothermic perfusion in six transplant-declined human kidneys, the targeted Ab-Mb-NPs bound specifically to the endothelial cells covering ~46% of the microvessels and ~72% of the glomeruli vasculature area compared to ~1% and ~7%, respectively, with the Isotype-targeted NPs.
Conclusions: Mb-coupled conjugation can both simplify and enhance the use of nanomaterials to target graft ECs, opening opportunities to efficiently deliver therapeutics prior to transplantation.



Fluorescence microscopy images of transplant-declined human kidneys sections after injection of Ab-Mb-NPs during ex vivo perfusion (NPs, ULEX) – scale bar 100 um

measured by quantitative microscopy

LDV04 EXTRACELLULAR VESICLES FROM HUMAN LIVER STEM CELLS REDUCE INJURY IN A MODEL OF NORMOTHERMIC PERFUSION OF RAT ISCHEMIC LIVERS

Nicola De Stefano[1], Victor Navarro-Tableros[2], Dorotea Roggio[3], Alberto Calleri[3], Federica Rigo[1], Ezio David[4], Alessandro Gambella[4], Daniela Bassino[5], Antonio Amoroso[6], Damiano Patrono[1], Giovanni Camussi[7], Renato Romagnoli[1]

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Background: Livers from donors after circulatory death (DCD) are one of the most promising options to satisfy donor's request, but there is still a high burden of complications correlated with their use in clinics. Normothermic machine perfusion (NMP) is an extracorporeal circuit that keeps the graft at physiological temperature, providing nutrients and oxygen supply. Human liver stem cell-derived extracellular vesicles (HLSC-EV) are able to reduce liver injury and promote regeneration by transferring specific subsets of mRNA and miRNA to the target cells. We investigated the feasibility and the efficacy of a reconditioning strategy with HLSC-EV in an experimental model of NMP.
Methods: Following total hepatectomy, rat livers were divided into 4 groups: (a) healthy livers (no injury group), (b) livers exposed to 60 min of warm ischemia (WI group), (c) WI livers treated with 5×10^8 HLSC-EV/g of liver (WI+EV1), and (d) WI livers treated with 25×10^8 HLSC-EV/g of liver (WI+EV2 group). The livers were perfused for 6 hours and HLSC-EV, provided by Unicyte AG, and administered within the first 15 min.
Results: Biochemical and morphological analyses confirmed the organ damage derived from WI, and epifluorescence microscopy showed the presence of HLSC-EV within the treated livers. Compared with the WI controls, the HLSC-EV treatment significantly reduced the AST and ALT release and enhanced liver metabolism by promoting bile production, phosphate utilization, and pH self-regulation. Moreover, the higher dose of HLSC-EV (25×10^8 HLSC-EV/g of liver) was able to reduce the intrahepatic resistance, to stimulate liver regeneration, and to limit necrosis extension.
Conclusions: HLSC-EV treatment during NMP was feasible and effective in protecting DCD livers. Both HLSC-EV doses were associated with better metabolism and less transaminase release, while only the higher one was able to ameliorate hemodynamics, promote proliferation, and reduce necrosis.

LDV05 PERIPHERAL BLOOD INFLAMMATORY CHEMOKINES UNCOVER ALLO-IMMUNE INFLAMMATION IN THE ABSENCE OF HISTOLOGICAL LESIONS

Elisabet Van Loon[1], Thomas Barba[2], Baptiste Lamarthée[1], Aleksandar Senev[1], Olivier Thaunat[2], Dominique Schols[3], Maarten Naesens[1]

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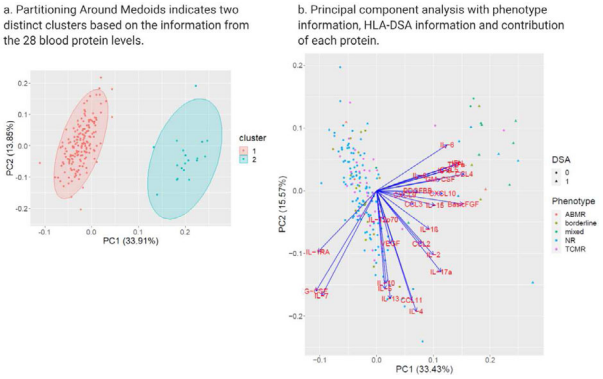
Background: Cytokines and chemokines play a critical role in the pathophysiology of allograft rejection, but the relation of peripheral blood cytokine expression profiles to clinical kidney transplant rejection is insufficiently investigated.
Methods: Levels of 28 cytokines, chemokines, and growth factors were assessed using multiplexed Luminex magnetic bead testing in 293 peripheral blood samples. Blood samples were collected between 2012 and 2016, at time of a kidney allograft biopsy for graft dysfunction within the first year after transplantation in a cohort of 192 consecutive transplants at a single kidney transplant center.
Results: Principal component analysis and hierarchical clustering uncovered two clusters, distinct in their pro-inflammatory cytokine levels (Figure a). Patients in Cluster I ($n = 20$) had higher pro-inflammatory protein expression compared with patients in Cluster II ($n = 172$). Cluster I was hallmarked by a higher prevalence of donor-specific anti-HLA antibodies (HLA-DSA) (75%) (Figure b), and higher incidence of histopathological rejection (70%) compared with Cluster II (HLA-DSA in 1.7% and rejection in 33.7%). Serum C-reactive protein and polyomavirus and/or CMV viremia did not differ between the two clusters. In 30% of biopsies in Cluster I, there was no histological evidence of rejection. Cluster I had a worse graft survival independent of clinical confounders and histological evidence of ongoing rejection (adjusted hazard ratio 3.31, 95% CI 1.09 -10.03, $p = 0.03$). *In silico* analysis of publicly available single-cell RNA-seq data from kidney transplant biopsies demonstrated expression of the observed cytokines in endothelial cells, monocytes, and NK cells. Furthermore, we evaluated the cytokine profiles in *in vitro* models of DSA-mediated NK cell and/or monocyte activation.
Conclusions: The expression of pro-inflammatory cytokines is increased in peripheral blood of kidney transplant patients with circulating HLA-DSA, even in the absence of histopathology of rejection. These results challenge the vision that kidney transplant histology is the gold standard for identification of ongoing allo-immune processes.



LDV06 SCREENING FOR SARS-CoV-2 NEUTRALIZING ANTIBODIES IN CIRRHOTIC PATIENTS WAITING FOR LIVER TRANSPLANTATION: IMPACT ON DONOR POOL EXPANSION

Margherita Saracco[1], Silvia Martini[1], Francesco Tandoi[2,3], Fabrizia Pittaluga[4], Antonio Ottobrelli[1], Antonio Amoroso[5], Rossana Cavallo[4], Roberto Balagna[6], Renato Romagnoli[2]

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Background: The COVID-19 pandemic affected every aspect of health care and threatened the availability of liver donors. To limit this phenomenon, the Italian National Transplant Centre allowed liver transplantation (LT) from SARS-CoV-2 positive donors to patients with severe liver disease who are SARS-CoV-2 positive or with a previous history of COVID-19. We aimed to assess the prevalence of neutralizing antibodies against SARS-CoV-2 in all our cirrhotic patients on LT waiting list in order to increase the chances of donor-recipient match.
Methods: From November 25, 2020 to February 12, 2021, each patient on the LT waiting list was tested for SARS-CoV-2 neutralizing antibodies with LIAISON® SARS-CoV-2 S1/S2 IgG test (quantitative assay for the detection of IgG antibodies against S1/S2 antigens of SARS-CoV-2: >= 15 UA/mL positive). IgG antibodies were retested within 2 months after the first evaluation. COVID-19 asymptomatic patients with positive IgG test underwent immediate SARS-CoV-2 molecular testing using nasopharyngeal swab (NPS, with Simplexa® COVID-19 Direct, DiaSorin Molecular).
Results: At the beginning and at the end of the enrollment period, 61 and 75 patients, respectively, were actively on the LT waiting list. During the study period, 27 first adult LTs were performed in our Centre. 98 patients underwent SARS-CoV-2 IgG test, and 22 (22.4%) of them tested positive. 8/22 (36.4%) had a previous documented history of COVID-19; the remaining 14 (63.6%) were asymptomatic and tested negative at NPS. 5 out of those 22 IgG-positive cirrhotics (22.7%) received a graft from a positive SARS-CoV-2 RNA donor. After a median post-LT follow-up of 8.5 weeks, no SARS-CoV-2-related complications occurred. Only 1 patient showed intermittent NPS positivity without clinical or radiological sign of disease.

Conclusion: In our cohort, 22.4% of cirrhotic patients on the LT waiting list tested positive for SARS-CoV-2 neutralizing antibodies and 63.6% of them did not show a history of COVID-19. This screening allowed a precious expansion of the donor pool by allocating 5 SARS-CoV-2 RNA-positive donors to 5 IgG-positive recipients.

LDV07 DYNAMIC PREDICTION OF KIDNEY GRAFT SURVIVAL WITH ARTIFICIAL INTELLIGENCE: AN INTERNATIONAL STUDY OF DEEP COHORTS OF KIDNEY RECIPIENTS

Marc Raynaud[1], Olivier Aubert[1], Peter Reese[2], Nassim Kamar[3], Chen-Shan Chin[4], Élodie Bailly[5], Marc Ladriere[6], Moglie Le Quintrec[7], Michel Delahousse[8], Ivana Juric[9], Nikolina Basic-Jukic[9], Marta Crespo[10], Helio Tedesco Silva Junior[11], Kamilla Linhares[11], Maria Cristina Ribeiro de Castro[12], Soler Pujol Gervacio[13], Daniel Yoo[1], Jean-Philippe Empana[1], Camilo Ulloa[14], Enver Akalin[15], Georg Böhmig[16], Edmund Huang[17], Denis Glotz[18], Stanley Jordan[17], Andrew Bentall[19], Robert Montgomery[20], Rainer Oberbauer[21], Dorry Segev[22], John Friedewald[23], Christophe Legendre[24], Xavier Jouven[1], Carmen Lefaucheur[1], Alexandre Loupy[1]
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Background: Providing kidney recipients with a dynamic risk assessment of their graft survival is an unmet need. We aimed at developing a dynamic system that generates continuously refined predictions that rely on updates of clinical data.
Methods: International study involving 18 transplant centers from Europe, the US, South-America, and 6 randomized controlled trials (RCT). Patients were divided into a derivation cohort from the Paris Transplant Group, and multiple external validation cohorts. Recipients underwent assessment of clinical, functional, histological, and immunological parameters, together with serial measures of eGFR and proteinuria. We used joint modeling to integrate parameters measured at single time points with parameters repeatedly assessed.
Results: A total of 13,608 patients were included (3,774 patients in the derivation cohort, 834 in the external validation cohorts), and 416,510 eGFR and proteinuria measurements were assessed. The median follow-up post-transplantation was 6.56 years (IQR 4.27-9.54). Joint models revealed that recipient immunological profile, graft scarring, allograft inflammation, and repeated measurements of eGFR, and proteinuria were risk factors of graft survival. The final dynamic system (Fig 1) demonstrated very accurate calibration and discrimination in the derivation cohort (AUC=0.857). The performances were confirmed in the 14 validation cohorts from Europe (overall AUC=0.845), the USA (overall AUC=0.820), South-America (overall AUC = 0.868), and the RCTs (overall AUC = 0.857).
Conclusions: We developed a dynamic, integrative prediction system that accurately predicts the risk of long-term graft failure and outperforms any current prediction models in kidney transplantation based on traditional approaches. This system may help to refine the prognostic judgments of clinicians in everyday practice.

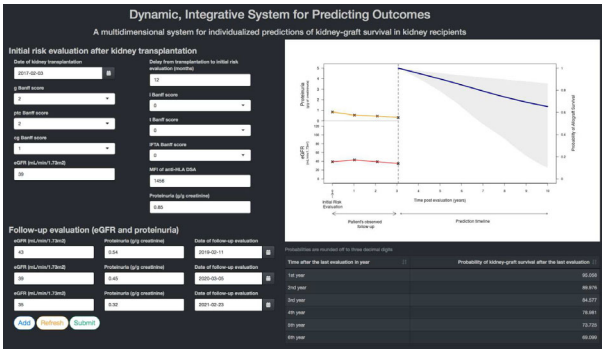

Figure 1 Graft-survival dynamic prediction system: online application

LDV08 REGULAR PHYSICAL ACTIVITY IN THE PREVENTION OF POST-TRANSPLANT DIABETES MELLITUS AND ASSOCIATED METABOLIC CONDITIONS IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Post-transplant diabetes mellitus (PTDM) is a significant risk factor for the survival of graft recipients and occurs in 10-30% of patients after kidney transplant (KT). PTDM is associated with premature cardiovascular morbidity and mortality. Weight gain, obesity, and dyslipidemia are strong predictors of PTDM and by modifying them with active lifestyle it is possible to reduce the incidence of PTDM and affect the long-term survival of patients and grafts. The aim of this work was to determine the effect of regular physical activity on the development of PTDM and its risk factors in patients after KT.
Methods: The primary goal was to complete at least 150 minutes of moderate-intensity physical exertion per week. Study group ($n = 22$) performed aerobic or combined (aerobic + strength) type of sports activity. Monitoring was provided by sports tracker (Xiaomi Mi Band 4 compatible with Mi Fit mobile application). Control group was consisted of 22 stable patients after KT. Each patient underwent oral glucose tolerance test (oGTT) at the end of follow-up. Patients in both groups have the same immunosuppressive protocol. The duration of follow-up was 6 months.
Results: There were significantly fewer patients with normal oGTT in the control group compared with the study group at 6 months ($p < 0.0001$). In the control group, there were significantly more patients diagnosed with PTDM ($p = 0.0212$) and with prediabetic condition (impaired plasma glucose, impaired glucose tolerance) at 6 months ($p = 0.0078$). Significantly lower waist circumference at 3 and 6 months ($p = 0.0437$, $p = 0.0372$) and low-density lipoprotein at 6 months ($p = 0.0444$) were found in the study group compared with the control group. In the study group, the subgroup performing intensive training achieved a significant additional effect on the reduction in waist circumference ($p = 0.0173$). Patients practicing only aerobic activity achieved significant decrease in triglycerides compared with those practicing combined activity ($p = 0.046$).
Conclusion: Regular physical activity after KT provides significant prevention against development of prediabetic conditions and PTDM.

KIDNEY TRANSPLANTATION: BEYOND HISTOLOGY

OP001 MISSING SELF INDUCED MICROVASCULAR REJECTION OF KIDNEY ALLOGRAFTS: A POPULATION-BASED STUDY

Jasper Callemeyn[1], Aleksandar Senev[1], Maarten Coemans[1], Evelyne Lerut[2], Ben Sprangers[3], Dirk Kuypers[1], Alice Koenig[4], Olivier Thaunat[4], Marie-Paule Emonds[5], Maarten Naesens[1]

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Background: Circulating anti-HLA donor-specific antibodies (HLA-DSA) are often absent in kidney transplant recipients with microvascular inflammation (MVI). Missing self, the inability of donor endothelial cells to provide HLA I-mediated signals to inhibitory KIR receptors on recipient NK cells, can cause endothelial damage in vitro, and has been associated with HLA-DSA negative MVI. However, the clinical importance of missing self as a non-humoral trigger of allograft rejection remains unclear.
Methods: In a population-based study of 924 consecutive kidney transplantations between 2004 and 2013, high-resolution donor and recipient HLA typing and recipient KIR genotyping was performed. Missing self was defined as absence of A3/A11, Bw4, C1 or C2 donor genotype, with presence of the corresponding educated recipient inhibitory KIR gene.
Results: Overall, missing self was identified in 399/924 transplantations. Co-occurrence of missing self types additively increased the risk of MVI, with a threshold at 2 concurrent types (HR 1.78, 95% CI 1.26-2.53), independent from HLA-DSA (HR 5.65, 4.01-7.96) (Figure). There was no association between missing self and lesions of cellular rejection. In 145/222 recipients with MVI, no HLA-DSA were detectable, of whom 28/145 had at least 2 missing self types. Missing self associated with transplant glomerulopathy after MVI (HR 2.51, 1.12-5.62), although allograft survival was better than HLA-DSA associated MVI.
Conclusions: Missing self specifically and cumulatively increases the risk for MVI after kidney transplantation, independent from HLA-DSA. Systematic evaluation of missing self improves our understanding of HLA-DSA-negative MVI and could be relevant for improved diagnostic classification and patient risk stratification.

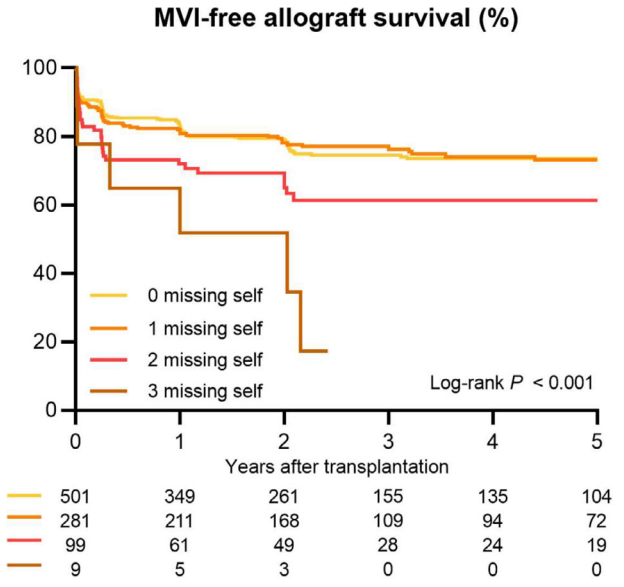

Figure: Kaplan-Meier survival curves for incidence of MVI, censored for recipient death and allograft failure, with groups stratified according to the number of missing self types present within one donor-recipient pair

OP002 THE EFFECT OF THE DIFFERENT DONOR-DERIVED HLA T-CELL TARGETS ON THE DEVELOPMENT OF T CELL-MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

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Background: Many kidney allografts fail due to rejections caused by the donor and recipient HLA incompatibility. Recent studies have shown that HLA-DR and DQ mismatches are particularly harmful by inducing donor-specific HLA antibodies and causing antibody-mediated rejection. However, due to the absence of HLA-specific biomarkers, it remains unknown which HLA mismatches contribute the most to the development of T-cell mediated rejection (TCMR). In this study, we aimed to investigate the associations of the different donor-HLA-derived T-cell epitope targets and the occurrence of TCMR after kidney transplantation.
Methods: Patients who underwent kidney transplantation between 2004 and 2013 were included in this study ($N = 926$ with 3515 biopsies). These patients and donors were genotyped at high-resolution HLA level. We used the PIRCHE-II algorithm to calculate the different donor-HLA-derived T-cell epitope scores for all HLA loci.
Results: The median PIRCHE-II score of our cohort was 311.5 (IQR 205-453). 277 patients (29.9%) developed TCMR and 134 (14.5%) developed only borderline changes on at least one allograft biopsy. In a multivariable analysis adjusted for confounders (Figure 1), the total PIRCHE-II score was independently associated with an increased risk for developing TCMR (per 10, HR = 1.007; 95%CI 1.001-1.013; $P = 0.03$), mainly explained by the PIRCHE-II scores for HLA-DRB1 (HR = 1.071; 95%CI 1.028-1.116; $P = 0.001$) and HLA-DQA1B1 molecules (HR = 1.013; 95%CI 1.002-1.025; $P = 0.02$). The same associations with PIRCHE-II scores for HLA-DRB1 and DQA1B1 were found when borderline changes are counted as TCMR. In a sensitivity analysis restricted to HLA-DSA negative patients, again, only the T-cell epitope targets originating from the donor's HLA-DRB1 and HLA-DQA1B1 molecules were associated with TCMR. Finally, the same PIRCHE-II scores for HLA-DRB1 (HR = 1.042; 95%CI 1.005-1.081; $P = 0.02$) and HLA-DQA1B1 molecules (HR = 1.015; 95%CI 1.005-1.026; $P = 0.0035$) were risk factors for all-cause graft failure, independent of HLA-DSA antibodies.
Conclusions: PIRCHE-II scores for HLA-DRB1 and HLA-DQA1B1 are independent predictors for TCMR development and independent risk factors for all-cause graft failure after kidney transplantation and could be used for improved risk stratification.

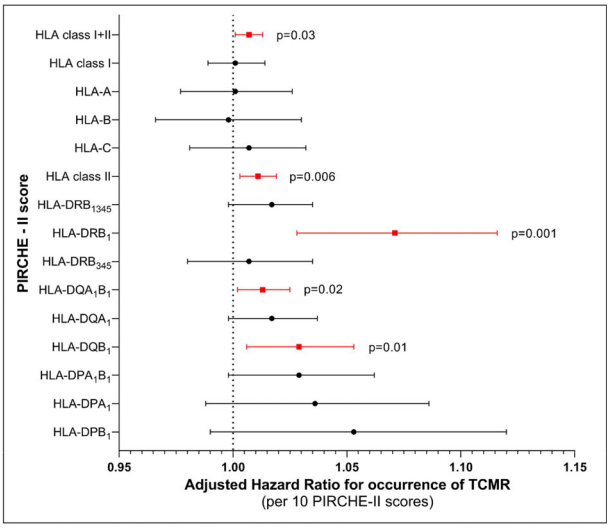

Figure 1. Multivariable Cox hazard ratios for the occurrence of TCMR after kidney transplantation stratified by the different PIRCHE-II scores. Each multivariable Cox model was corrected for donor and recipient age, donor type, cold ischemia time, repeat transplantation, and presence of pretransplant anti-HLA antibodies.

OP003 CRISPR-CAS9 HLA-DELETED GLOMERULAR ENDOTHELIAL CELLS AS A TOOL TO DETECT PATHOGENIC NON-HLA ANTIBODIES IN KIDNEY TRANSPLANT RECIPIENTS

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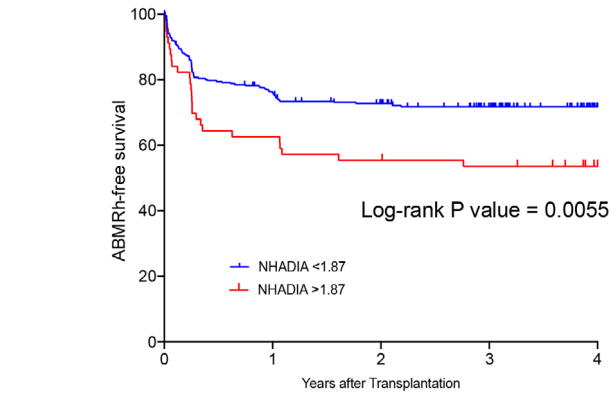
Background: In kidney transplantation recipients (KTRs), donor-specific antibodies directed against Human Leucocyte Antigens (HLA-DSA) are thought to drive antibody-mediated rejection (ABMR) and are associated with poor transplant outcome. However, evidence of microvascular inflammation (MVI), the histological hallmark of ABMR, is increasingly reported in patients without HLA-DSA, strongly supporting the implication of non-HLA antibodies (Abs). In KTRs displaying a severe vascular rejection without HLA-DSA, we previously showed that their pretransplant sera contain Abs specifically targeting conditionally immortalized human glomerular endothelial cells (CiGEnC). To date, assessment of the global non-HLA Abs burden remains limited by the absence of available test.
Methods: We designed a Non-HLA Antibodies DetectIon Assay (NHADIA) to specifically evaluate the presence of non-HLA Abs, usable even in patients with HLA-DSA. To this end, CRISPR-Cas9 technology was used to genetically modify CiGEnC by deleting B2M and CIITA genes to suppress the expression of class I and II HLA antigens, respectively. We next evaluated the association between NHADIA and histology of ABMR (ABMRh).
Results: A two-step process of gene-editing and selection of a CiGEnCΔHLA clone was performed. After thorough validation of the preservation of endothelial phenotype, the produced CiGEnCΔHLA clone was used as target cell for non-HLA Abs. The reactivity against CiGEnCΔHLA cells of serum samples collected immediately before transplantation in 389 KTRs was assessed by flow cytometry and normalized mean fluorescence intensity of NHADIA was tested as a prognostic tool for acute rejection occurrence, MVI severity and graft outcome. Univariate regression showed that NHADIA was associated with retransplantation status. Moreover, NHADIA was correlated with glomerulitis and MVI score at Month 3 and Month 12 and in a multivariate Cox model, NHADIA was significantly associated with ABMRh independently of presence of HLA-DSA. Finally, a NHADIA threshold of 1.87 strongly associated with ABMRh-free survival (Log-rank *P* value = 0.0055, Figure 1).
Conclusion: Altogether, these results support the link between the presence of non-HLA Abs, the severity of endothelial injury and eventually graft failure independently from HLA-DSA.



Number at risk:

NHADIA<1.87	332	256	245	242	242
NHADIA>1.87	57	36	32	31	31

OP004 THE BIATHLETE'S DILEMMA: UNRAVELLING THE MOLECULAR MECHANISMS OF THE IMMUNE PRIVILEGE OF GRAFT ENDOTHELIUM DURING TCMR.

Thomas Barba[1,2], Martin Heinrich Oberbarnscheidt[3], Maud Rabeyrin[4], Candice Roufosse[5], Linda Moran[5], Alice Koenig[1,2], Virginie Mathias[6], Carole Saison[6], Valérie Dubois[6], Emmanuel Morelon[1], Yi-Chun Xu-Dubois[7], Fadi Lakkis[3], Olivier Thaunat[1,2]

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Background: While graft endothelial cells express donor alloantigens and are traversed by cytotoxic T lymphocytes (CTL), the vasculature is usually spared during T cell-mediated rejection (TCMR), which principally targets the epithelial structures. The molecular mechanism responsible for this vascular immune privilege are not known.
Methods and results: Transcriptomic analysis and scorings of endothelial-mesenchymal transition (EndMT) – a validated marker of damages – on kidney rejection biopsies confirmed the relative preservation of graft endothelium during TCMR. However, co-culture experiments with alloreactive CTL showed that endothelial cells were equally sensitive to lysis as epithelial targets, ruling out a cell-intrinsic mechanism of protection.
Intravital microscopy analyzes of murine kidney grafts instead revealed that CTL interactions with endothelial cells were shorter than with epithelial cells. Single cell RNAseq analysis of human renal allograft biopsies and experimental models demonstrated that this was due to the fact that alloreactive CTL were responding to a CXCL12 gradient produced by graft's stromal cells when migrating from the circulation to epithelial cells. In vitro models confirmed that chemotaxis overrides TCR-induced killing response in alloreactive CTL, providing protection to graft endothelial cells.
Conclusion: Challenging the traditional cell-intrinsic view of immune privilege, we propose that CTL are like a biathlete who has to choose whether he uses his muscles to ski or to shoot. When migrating inside the graft, CTL mobilize their cytoskeleton that is no longer available to establish efficient cytotoxic synapse. This original (cell-extrinsic) mechanism might be at stake in other conditions in which maintenance of vascular integrity is crucial.

OP005 TRANSPLANT GLOMERULOPATHY AFTER KIDNEY TRANSPLANTATION: RISK FACTORS, HISTOPATHOLOGICAL FEATURES AND GRAFT OUTCOME

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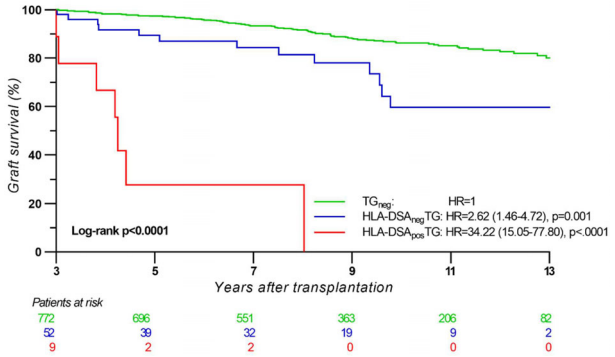
Background: Transplant glomerulopathy (TG) is established as a hallmark of chronic antibody-mediated rejection in kidney transplant patients with donor-specific HLA antibodies (HLA-DSA). The clinical importance of TG in the absence of HLA-DSA is not well established.
Methods: Patients who underwent kidney transplantation between 2004 and 2013 were included in this study ($N = 954$ with 3744 biopsies). We investigated the risk factors, histopathological appearance and prognosis of cases with TG in the absence of HLA-DSA, compared to cases of TG with HLA-DSA, and we evaluated the impact of the PIRCHE-II score and eplet mismatches, determined using high-resolution HLA genotyping, on TG development.
Results: In this cohort, 98 patients (10.3%) developed TG, on average at 3.2 years posttransplant. At the time of TG, 23 patients (23.5%) had persistent pretransplant or de novo HLA-DSA (HLA-DSAposTG group), while 75 patients (76.5%) were HLA-DSA negative (HLA-DSAnegTG). Only HLA-DSA were identified as risk factor for TG development; HLA molecular mismatches, eplet mismatches and PIRCHE-II scores did not associate with TG. The HLA-DSAnegTG biopsies had less interstitial inflammation, less glomerulitis and less C4d deposition in peritubular capillaries compared to the HLA-DSAposTG biopsies. While graft function was comparable between the two groups, HLA-DSAposTG was associated with a higher risk of graft failure compared to HLA-DSAnegTG (HR = 3.84; 95%CI 1.94-7.59; $P = 0.0001$). Landmark analysis at 3-year post-transplant showed that HLA-DSAnegTG patients still had an increased risk of graft failure compared to TG-negative patients (HR = 2.62; 95%CI 1.46-4.72; $P = 0.001$).
Conclusions: In conclusion, TG often occurs in the absence of HLA-DSA, independently of HLA molecular mismatches, and represents a different phenotype with less concomitant inflammation and better graft survival compared to TG developed in the presence of HLA-DSA.

Figure 1. Landmark survival analysis of the patients with TG.



OP006 TERMINAL COMPLEMENT ACTIVATION MAY NOT CONTRIBUTE TO ORGAN DAMAGE IN ANTIBODY-MEDIATED REJECTION

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Background: Antibody-mediated rejection (AMR) is a major cause for graft failure in kidney transplant recipients (KTR). However, its etiology is still poorly understood. Recent Banff classifications point towards an ambiguous involvement of the complement system in AMR, acknowledging heterogenous AMR subtypes. Additionally, disappointing long-term effectiveness of complement inhibitors suggests that terminal complement activation is an insufficient explanatory model for AMR pathogenesis. This study aimed to clarify the role of local and systemic complement activation in AMR.
Methods: We measured systemic complement cascade activation markers, C3, C3d, C5b-9 in a retrospective KTR cohort. Local complement activation was analyzed as C3d, C4d, and C5b-9 deposition in biopsies. In vitro, we examined classical complement activation via anti-HLA-antibodies and complement regulator expression CD59 on conditionally immortalized endothelial cells (CiGEnCs).
Results: We included 53 KTR, which were pathologically classified as AMR ($n = 20$), non-AMR patients ($n = 18$), and as normal controls patients ($n = 15$). No evidence of increased complement activation was detected in plasma of AMR patients. Deposition of C3d and C4d was increased in AMR patients, without concomitant C5b-9 expression. Glomeruli tended to show stronger complement deposition than peritubular capillaries. Congruently, in vitro experiments showed C3 and C4d without C5b-9 co-deposition on CiGEnCs. CD59 was continuously expressed on CiGEnCs.
Conclusion: We provide evidence in vivo and in vitro, that local, linear activation of proximal complement system is central in AMR pathogenesis. In contrast, terminal C5b-9 might play an inferior role in AMR, possibly accounting for the inefficacy of terminal complement inhibitors. CD59 is a possible protection mechanism against terminal complement activation, especially in peritubular capillaries. Additional complement-independent mechanisms could contribute to AMR pathogenesis.

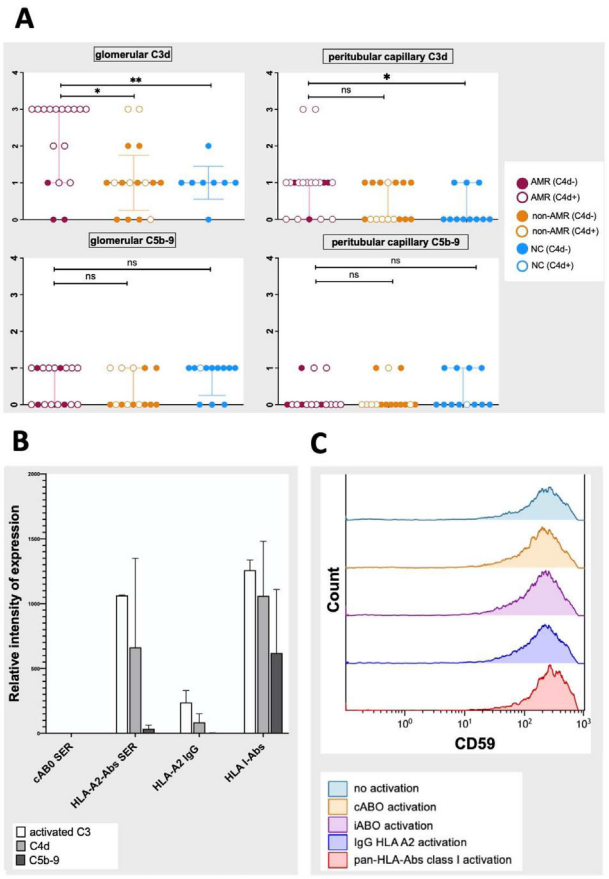

Figure *Terminal Complement Activation May Not Contribute to Organ Damage in Antibody Mediated Rejection.* Complement factor deposition in vivo and in vitro. Immunohistochemical staining for complement factors C3d, C5b-9 in glomerular and peritubular structures in renal biopsies of KTR (A). Complement factors C3 (activated), C4d and C5b-9 on conditionally immortalized glomerular endothelial cells *in vitro* in flow cytometric analysis, under four different incubation conditions (B). Deposition of complement regulator, CD59, was measured in flow-cytometry under five different incubation conditions (C). Semiquantitative scores of C3d and C5b-9 deposits were determined for KTR patients classified as AMR, non-AMR and NC. (A): *p <0.05; **p <0.001; ns, not signficant; KTR, kidney transplant recipients; AMR, antibody-mediated rejection; NC, normal transplant patient controls; C4d+, C4d-positive; C4d-, C4d-negative; cABO, ABO-bloodgroup-compatible; SER, serum; HLA, Human Leucocyte Antigen; Abs, Antibodies; IgG, Immunoglobulin G; FITC, Fluorescein isothiocyanate; iABO, ABO-bloodgroup-incompatible.

OP007 CD56DIM CD16BRIGHT NK CELLS DURING ANTIBODY-MEDIATED REJECTION DISPLAY INCREASED PROLIFERATION, ACTIVATION AND TYPE-1 INFLAMMATORY CYTOTOXIC PROFILES

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Background: $CD56^{dim}$ $CD16^{bright}$ NK cells are highly potent for cell-mediated cytotoxicity (CMC), antibody-dependent cell-mediated cytotoxicity (ADCC) and IFN-γ production. The contribution of NK cells to antibody-mediated rejection (ABMR) injuries has been highlighted through transcriptomic analysis. However, description of circulating NK cells profiles during ABMR is lacking.
Methods: Deep phenotypic analysis of circulating $CD56^{dim}$ $CD16^{bright}$ NK cells using 25-color spectral flow cytometry was implemented in 67 kidney transplant recipients: (i) 17 donor-specific anti-HLA antibody (DSA) free of ABMR, (ii) 17 DSA+ biopsy-proven mixed ABMR, (iii) 17 stable free of DSA/rejection, (iv) 16 T-cell mediated rejection and (v) 17 healthy controls. Samples were analysed at the time of rejection, or DSA occurrence, or at matching time points in stable patients. Functional assays were performed in 8 patients from each group, consisting of 6-h coculture of PBMC with T2 lymphoblastic cells (TAP-deficient, HLA-A2 expressor) with or without anti-HLA-A2 positive serum.
Results: $CD56^{dim}$ $CD16^{bright}$ NK cells from ABMR patients, when compared to the other groups, significantly proliferated (Ki67+) and selectively up-regulated IL-2R/-15Rβ chain and IL-21R, suggesting their higher responsiveness to common γ chain cytokines that support NK cell survival, proliferation and cytotoxicity. Moreover, they co-expressed elevated levels of EOMES and T-bet, as well as of CD16a/FcγRIIIa-inducible CD160 and CD161/NK1.1, cytotoxicity markers that reflect their higher Type-1 activation status. Indeed, $CD56^{dim}$ $CD16^{bright}$ NK cells from ABMR patients displayed increased Type-1 inflammatory cytokine release (high IFN-γ and TNF-α to IL-10 ratios) in ADCC and CMC assays.
Conclusions: Significant $CD56^{dim}$ $CD16^{bright}$ NK cell phenotypic and functional changes occur during ABMR with potential involvement to allograft injury. Early detection of proliferating, activated, inflammatory cytotoxic $CD56^{dim}$ $CD16^{bright}$ NK cells in the blood of ABMR patients could help for timely therapeutic intervention.

OP008 SPARSE INTRAGRAFT MOLECULAR CLASSIFIERS FOR ANTIBODY-MEDIATED AND T-CELL MEDIATED KIDNEY TRANSPLANT REJECTION: DEVELOPMENT AND VALIDATION

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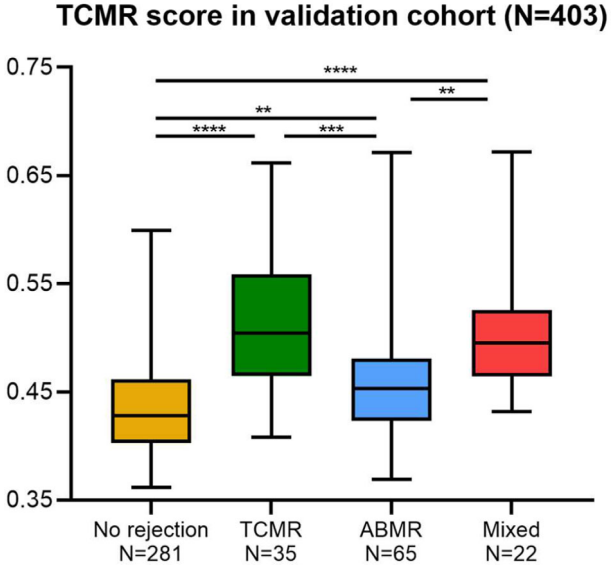
Background: Although the distinct transcriptional landscapes of antibody-mediated rejection (ABMR) and T-cell mediated rejection (TCMR) have been largely elucidated, applying these gene expression signatures in transplant clinics is hampered by the large number of features, unclear cut-off values and difficult integration with histological findings. We aimed to develop and validate a sparse molecular classifier for ABMR and TCMR.
Methods: In a discovery cohort of 224 prospectively collected kidney transplant biopsies, microarray gene expression was used to build two separate prediction models for presence of ABMR or TCMR, as assessed according to the Banff classification. Class imbalance was addressed by SMOTE, and variable selection for logistic regression was performed by lasso regularization. The diagnostic accuracy and prognostic value of the obtained ABMR and TCMR classifiers were assessed in two external validation cohorts.
Results: From the discovery cohort, a 2-gene ABMR classifier and 3-gene TCMR classifier were derived. In the first validation cohort ($N = 403$ biopsies), very good diagnostic accuracy was retained for ABMR (ROC-AUC 0.80, 95% CI 0.75-0.85) and TCMR (ROC-AUC 0.84, 95% CI 0.79-0.90), also allowing discrimination between pure and mixed phenotypes (Figure). In the second validation cohort ($N = 282$ biopsies), ABMR and TCMR scores predicted graft failure (respective time-integrated AUC of 0.82 and 0.80) and identified a group of biopsies at risk without proven histological rejection.
Conclusions: We identified and validated an intragraft 2-gene ABMR classifier and 3-gene TCMR classifier that can be used as diagnostic, discriminatory and prognostic tools. The clinical value of the classifiers was most apparent in the prediction of outcome beyond the histological diagnosis of rejection. Robust variable selection models can yield parsimonious molecular classifiers for kidney transplant rejection with preserved accuracy, which may facilitate their interpretation and clinical implementation.



SHOULD I INCLUDE MY CANCER PATIENTS IN THE LIVER TRANSPLANT LIST? FROM GIST TO HCC

OP023 OUTCOME OF LIVER TRANSPLANTATION FOR NON-HCC MALIGNANCIES – A COLLABORATIVE TRANSPLANT STUDY REPORT

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[1]Heidelberg University Hospital, General, Visceral and Transplant Surgery, Heidelberg, Germany; [2]Heidelberg University Hospital, Institute of Immunology, Heidelberg, Germany

Background: Malignancies other than hepatocellular carcinoma (HCC) are relatively uncommon indications for liver transplantation (LT). Cholangiocellular carcinoma (CCC), metastases from neuroendocrine tumors (NET), and sarcomas of the liver (LSAR) are generally accepted indications for LT, but the reported results differ widely and are dominated by reports from single specialized centers. Therefore, the outcome of LT for these tumors is a matter of ongoing debate.
Methods: Graft and patient survival of 14,623 LTs that were performed during 1988–2017 in HCC, CCC, NET, and LSAR patients and reported to the Collaborative Transplant Study were analyzed.
Results: 13,862 recipients with HCC (94.8%), 498 with CCC (3.4%), 100 with NET (0.7%), and 163 with LSAR (1.1%) were identified. The 32.1% 5-year graft survival rate observed in CCC recipients was notably inferior compared to the 63.2% rate in HCC, 51.6% rate in NET, and 64.5% rate in LSAR recipients ($P < 0.001$ for all versus CCC). In the multivariable Cox regression analysis, CCC patients exhibited, compared to HCC patients, besides a higher risk of graft loss, also a significantly higher mortality risk due to cancer during the first five post-transplant years (HR 1.77 and 2.56, respectively; $P < 0.001$ for both). A somewhat higher but statistically not significantly increased risk of graft loss and mortality due to cancer was also found in NET patients (compared to HCC, HR 1.20 and 1.37; $P = 0.25$ and 0.29, respectively).
Conclusions: Patient and graft survival of CCC recipients was reduced compared to HCC recipients. Based on our results, which were derived from 127 transplant centers of various grades of specialization from 27 countries, LT in CCC does not appear to offer satisfying results outside highly

specialized programs. However, considerations for LT in non-HCC malignancies need to factor in individual circumstances, since universal routines might not be applicable to these cases.

OP024 LIVER TRANSPLANTATION SURVIVAL BENEFIT OVER LIVER RESECTION FOR COLORECTAL LIVER METASTASIS IN A SELECTED COHORT OF PATIENTS WITH HIGH TUMOR LOAD

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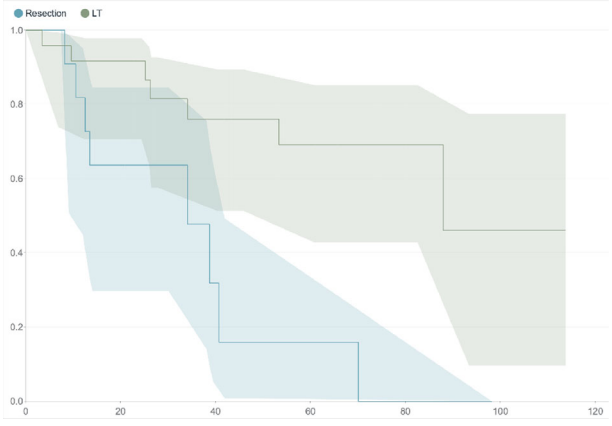
Backgroud: Liver transplantation (LT) for unresectable colorectal liver metastasis (CRLM) was investigated in the SECA trials that identified the risk factors for poor outcome (Oslo criteria) and showed 5-year overall survival (OS) up to 83%. Worldwide, LT for CRLM is limited to unresectable disease. However, resectability is more an anatomic-technical parameter than a biological predictor. Hence, we tested the hypothesis that LT could offer better survival than technically resectable patients when hepatic tumor load is above a threshold (tumor burden score TBS $\geq$ 9), in patients that satisfy the inclusion criteria for transplant according to the SECA-I study.
Methods: Liver resection (LR) performed at HBP Unit Padua University Hospital in CRLM patients between 2010 and 2019, were compared with LT for unresectable CRLM performed both by Department of Transplantation Medicine Oslo University Hospital, and HBP Unit Padua University Hospital between 2006 and 2019. Exclusion criteria were age $\geq$70 years, liver first approach, extra-hepatic tumor, neoadjuvant chemotherapy < 6 weeks, standard contraindications to LT, other malignancy, weight loss < 10%, ECOG score > 1, follow-up < 6 months.
Results: 364 CRLM patients underwent 441 LR and 56 LT. 184 patients were eligible: 128 underwent LR and 56 LT. 5-year OS after LR and LT was 40.5% and 54.7% ($P = 0.102$).
In LR group, 101 (80.2%) patients had low TBS (<9) and 25 (19.8%) high ($\geq$9); among LT, 19 (34.5%) patients had low TBS and 36 (65.5%) high ($P < 0.001$). In the high TBS cohort, 5-year OS after LR and LT was 22.7% and 52.2% ($P = 0.055$).
In the group of patients with both Oslo score $\leq$ 2 and high TBS (13 LR; 24 LT) at 5 years: OS after LR and LT was 13.6% and 69.1% ($P = 0.002$); DFS after LR and LT was 0% and 23.9% ($P = 0.005$); and survival after relapse after LR and LT was 16% and 57.9% ($P = 0.060$).
Conclusions: Selected CRLM patients with low Oslo score and high TBS could benefit from LT with survival outcomes that are far better than what is achieved by LR.



OP025 DIFFERENT PATTERNS OF RECURRENCE AFTER LIVER RESECTION AND TRANSPLANTATION FOR METASTATIC NEUROENDOCRINE TUMORS

Jorgelina Coppa, Marianna Maspero, Roberta Elisa Rossi, Carlo Sposito, Sherrie Bhoori, Michele Droz Dit Busset, Maria Flores, Marco Bongini, Ugo Giustizieri, Vincenzo Mazzaferro
Fondazione IRCCS Istituto nazionale dei tumori, Milano, Italy

Background: The liver is the most frequent site of metastases in neuroendocrine tumors and represents a negative prognostic factor. When feasible, curative liver resection (LR) and liver transplantation (LT) offer the best long-term outcomes for neuroendocrine liver metastases (NELM). LR is often not feasible due to bilobar disease and, in selected cases, LT might be considered. The risk of tumor recurrence is considerable after both approaches; however, studies comparing the different patterns of recurrence for these two groups are scarce.
Methods: Data from all consecutive patients who underwent curative liver surgery for NELM (either LT or LR) at our center between 1984 and 2019 were retrospectively analyzed.
Results: Patients were 96 in the LR group and 53 in the LT group. LR patients were older than LT patients (median 57 versus 46, $P < 0.001$), with no differences in primary tumor site, liver involvement, grading, serum chromogranin level at liver surgery, and Ki67%. The 5-and 10-year survival rates were 92% and 84% for LT, and 85% and 69% for LR, respectively ($P = 0.02$). The 5 and 10-year disease-free survival rates were 68% and 45% for LT, and 33% and 19% for LR, respectively ($P < 0.0001$). The median time between liver surgery and first recurrence was 21 months for LR and 62 months for LT ($P < 0.001$). Liver recurrence was most common in LR (64/69, vs 3/30 in LT, $P < 0.001$); interestingly, LT tended to have more multifocal recurrences (15/30 vs 7/69 in LR, $P = 0.01$) and recur most often outside the liver, most commonly in distant lymph nodes (15/30, vs 5/69 in LR, $P = 0.001$), locoregional lymph nodes (10/30 vs 3/69, $P < 0.001$), and bone (10/30, vs 4/69 in LR, $P < 0.001$).
Conclusion: NELM exhibit different patterns of recurrence after LT and LR, with LR recurring most often to the liver and LT to the distant lymph nodes. LT confirms better disease-free intervals among selected patients. The different patterns of recurrence may serve as a basis for future studies.

OP026 LONG TERM OUTCOMES AFTER LIVER TRANSPLANTATION VERSUS RESECTION FOR MILAN-IN NEUROENDOCRINE TUMOR LIVER METASTASES

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Background: The best management of neuroendocrine liver metastases (NELM) is still under debate. Surgical resection with curative intent should be the first choice, being liver tranplantation (LT) reserved to highly selected patients in whom curative surgery is not feasible anymore. The risk of tumor recurrence is high after both LR and LT and the most favorable outcomes after LT are observed when strict selection criteria ("Milan criteria") are applied. Studies comparing long-term outcomes after liver resection (LR) vs LT in the specific setting of Milan-in patients are scanty.
Methods: Data from all consecutive patients who underwent curative liver surgery for metastatic NET (either LR or LT) at our center between 1984 and 2019 were retrospectively analyzed. Only patients meeting Milan Criteria for LT at the pre-surgical staging were included in the analysis.
Results: 53 Milan-in patients underwent LT vs LR that fit Milan criteria were 56 (58%) out of 96. Demographic and preoperative variables were comparable between the two cohorts. The 3-year, 5-year and 10-year survival rates were 98%, 92% and 84% for LT and 92%, 89% and 75% for LR, respectively ($P = 0.047$). The 3-year, 5-year and 10-year disease-free survival rates were 79%, 68% and 45% for LT and 48%, 33% and 18% for LR, respectively ($P < 0.0001$).
Conclusion: Patients with Milan-in NELM who underwent LT had longer overall survival and disease-free survival than patients who underwent LR.

OP027 UNRESECTABLE GASTROINTESTINAL STROMAL TUMOR (GIST) LIVER METASTASES AS A NEW INDICATION FOR LIVER TRANSPLANTATION. HAS ITS TIME ARRIVED?

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Background: Liver metastases from gastrointestinal stromal tumors (GIST) can be found synchronously to a primary tumor and in the medium/long term after resection of a high-risk GIST. In these cases, treatment with tyrosine kinase inhibitors like imatinib has provided good results, but drug resistance is common after two years of treatment. Liver resection of potentially resectable metastases can improve the results of medical treatment. In cases of unresectability, the role of liver transplantation (LT) has not been well-studied.
Methods: A systematic review of the literature was undertaken from January 1995 to December 2020.
Results: Fifteen cases were identified. In eight cases, the LT was carried out before 2000. Mutational status was only studied in seven cases. LT was performed in 12 cases with a deceased donor and in three cases with a living donor. After a mean follow-up of 52.4 months, overall survival was 86.6% with disease-free survival of 53.3%.
Conclusions: LT in the management of unresectable GIST metastases has rarely been performed. Although its application has a solid theoretical basis, its use understood as a radical extension of a standard resection can only be recommended within prospective studies by groups with considerable experience in both GIST and transplantation care.

OP028 LIVER TRANSPLANTATION FOR UNRESECTABLE PERIHILAR CHOLANGIOCARCINOMA: AN ITALIAN SURVEY

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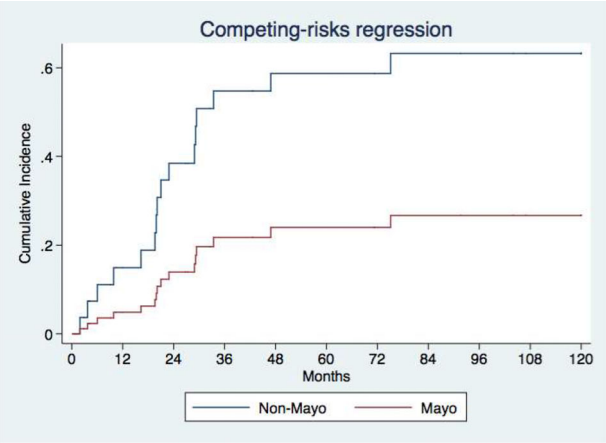
Background: Perihilar Cholangiocarcinoma (pCCA) is a rare, but increasing, tumor of the liver. Liver resection (LR) can offer a 5-year overall survival (OS) rate of 20–40% after R0 resection. Unfortunately, only 20–25% of patients are appropriate candidates for curative resection. Liver Transplantation (LT) was initially curbed by dismal results, until the Mayo Clinic group introduced a novel protocol, with reported 5-year OS after LT of 74%.
Methods: All 22 Italian liver transplant Centers were contacted and asked to participate to a national survey. Eight Centers reported having performed at least one LT for pCCA and provided data. Data analysis was conducted considering the year of LT and if neoadjuvant chemotherapy was performed (Mayo Clinic protocol). Primary endpoint was competing risk of cancer-related-death (other-causes-of death as competing event).
Results: From 1984 to 2019, 37 LT for pCCA were performed in 8 Italian centers; 25 (67.6%) were performed before 2015; 15 (40.5%) met the criteria for inclusion in the Mayo Clinic protocol. Nineteen patients recurred after LT. Sites of recurrence were liver (47.4%), lung (36.8%), lymph nodes (21.1%), peritoneum (21.1%), peri-hilar (10.5%) and bone (10.5%).
Patients complying with the Mayo Clinic protocol (Mayo group) had a 5-Year competing risk of cancer-related death of 22% (Figure 1), while those not complying to the protocol (Non-Mayo) had a 5-Year risk of cancer-related death of 58%. The hazard ratio of Mayo vs. Non-Mayo group was 0.31 (95% CI 0.10-0.98, $P = 0.047$).
Conclusions: With accurate patient selection and neoadjuvant treatment, 5-year cancer-related death after LT for pCCA seems acceptable to justify organ allocation. The introduction of Direct-Acting Antiviral in the treatment of hepatitis C virus (HCV) reduced the need for LT and produced extra donor availability. In the era of transplant oncology, indications for LT should expand on the basis of robust data and specific protocols. In 2015, Italian organ allocation policy changed, indicating LT for pCCA only in the context of controlled prospective studies.
This survey aims to set the basis for a national monitoring of the outcome and to propose an Italian LT program for unresectable pCCA based on the Mayo Clinic protocol.



Transplant Center	N° of LT for pCCA
Padova	9
Milano – Niguarda	8
Milano – Istituto Nazionale Tumori	7
Torino	5
Bologna	4
Ancona	2
Pisa	1
Milano - Policlinico	1

OP029 THE BENEFICIAL INTENTION-TO-TREAT SURVIVAL EFFECT OF LIVING DONATION IN PATIENTS WITH HEPATOCELLULAR CANCER WAITING FOR LIVER TRANSPLANT

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Background: Conflicting data exist about the outcome of hepatocellular cancer (HCC) patients enrolled in a living-donor liver transplantation (LDLT) project. This study aims to evaluate the impact of a potential living donation process on the intention-to-treat survival rates of HCC patients listed for liver transplantation (LT).
Methods: The East-West collaborative HCC-LT effort allowed analyzing data of 3.052 HCC patients listed during the period Jan2000-Dec2017.These patients, belonging to 12 collaborative centers from Europe, the United States, and Asia, formed the Training Set. A Validation Set consisted of 906 HCC patients listed for transplantation during Jan2000-Dec2015 at Toronto General Hospital. The impact of LDLT was tested in the pre-Propensity Score Match (PSM) Training Set, the post-PSM Training Set, and the Validation Set.
Results: Three multivariable Cox regression analyses for intention-to-treat patient death were created on the pre-PSM Training, post-PSM Training and Validation Set populations. In all three settings, LDLT was an independent protective factor, reducing the risk of overall death by 48% (HR = 0.52, 95%CI = 0.45-0.61; $P < 0.001$), 45% (HR = 0.55, 95%CI = 0.50-0.61; $P < 0.001$), and 38% (HR = 0.62, 95%CI = 0.49-0.79; $P < 0.001$), respectively. When LDLT was incorporated in the mathematical models, the model discriminatory ability was further improved in all cases (Figure 1).
Conclusions: The potentiality of a living donor at listing almost halves the intention-to-treat risk of dying in listed HCC patients. This benefit is explained by the almost elimination of the drop-out risk. This beneficial effect is confirmed after "calibration" of the Training Set for tumor characteristics and severity of liver dysfunction and in the Validation Set in which both living- and deceased-donor LT strategies are commonly performed.

Variables	Beta	HR	95%CI		P	Beta	HR	95%CI		P	Beta	HR	95%CI	
			Lower	Upper				Lower	Upper				Lower	Upper
	(A) pre-PSM Training Set population					(B) post-PSM Training Set population					(C) Validation Set popul			
HBV-related cirrhosis	-0.30	0.74	0.63	0.87	<0.001	-0.31	0.73	0.65	0.82	<0.001	-0.52	0.59	0.46	0.76
Alcohol-related cirrhosis	-	-	-	-	-	0.23	1.26	1.11	1.43	<0.001	-	-	-	-
NASH-related cirrhosis	0.31	1.36	1.07	1.73	0.01	0.28	1.32	1.08	1.60	0.006	-	-	-	-
LDLT	-0.65	0.52	0.45	0.61	<0.001	-0.60	0.55	0.50	0.61	<0.001	-0.47	0.62	0.49	0.79
MELD value 30-40	0.69	2.00	1.44	2.78	<0.001	0.59	1.81	1.39	2.37	<0.001	1.13	3.09	1.27	7.52
Diameter of major lesion (cm)	0.06	1.06	1.03	1.09	<0.001	0.07	1.08	1.06	1.10	<0.001	0.06	1.06	1.01	1.10
Log$_{10}$AFP	0.20	1.23	1.13	1.33	<0.001	0.26	1.29	1.22	1.36	<0.001	0.28	1.32	1.18	1.48
AIC Model without LDLT	13,978.46					27,080.49					5,534.05			
AIC Model with LDLT	13,906.01					26,935.41					5,516.86			

Abbreviations: HR, hazard ratio; CI, confidence intervals; PSM, propensity Score Match; HBV, hepatitis B virus; NASH, non-alcoholic steato-
LDLT, living-donor liver transplantation; MELD, model for end-stage liver disease; AFP, alpha-fetoprotein; AIC, Akaike information criterion

OP030 TUMOR RELATED SURVIVAL AFTER LIVER TRANSPLANTANTION OR RESECTION FOR HCC: A COMPETING RISK ANALYSIS WITH AN INTENTION TO TREAT ANALYSIS PERSPECTIVE

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Background: Many patients with Hepatocellular Carcinoma (HCC) present at diagnosis a tumor stage suitable for both Liver Resection (LR) and Liver Transplantation (LT). LR is generally safer, available for all, schedulable at the best timing, but less radical and not able to cure the underlying cirrhosis. Contrarily, LT is much more invasive, unavailable for all the candidates, performed at unpredictable time, but with more extended radicality and able also to cure the underlying cirrhosis. Until now, what is the best candidate for LR or LT upfront is extremely unclear. The aim of the study was to validate a model to predict tumor results after LR or LT for patients eligible for both.
Methods: All the 2640 consecutive cases of LR or LT for HCC at the 4 centers involved into the study were collected. After a propensity score matching (PSM), an homogeneous patient's cohort was selected and compared between LR and LT groups. An intention-to-treat (ITT) analysis with a competing risk model was applied comparing the tumor related deaths of patient groups.
Results: Between 2005 and 2015, 551 LRs and 580 LT candidates (LTc) were selected for the study. Of the 580 LTc, 512 were effectively transplanted, whereas 68 (11.7%) were dropped due to tumor progression. After a PSM, 101 high risk patients were, respectively, selected for each groups: LR and LT. Variables considered for the risk assignment were: alfafetoprotein, tumor size, tumor number, AST, MELD, and age at tumor diagnosis. The 3- and 5-years cumulative incidence of tumor related death was, respectively, 23% and 31% vs 5% and 9% for LR and LT group (*P*-value = .002).
Conclusions: The high risk patients' cohort has significantly better ITT tumor-related survival with a LT rather than a LR upfront. The microvascular invasion or HCC satellitosis may significantly increase the risk of tumor related death even in low and intermediate risk patients who have received LR. The ab-initio LT should be considered in these reconverted risk patients.

MITIGATING DONOR RELATED RISKS

OP031 EVOLUTION OF PATIENTS WITH DEVASTATING BRAIN INJURY ADMITTED IN INTENSIVE CARE UNIT FOR INTENSIVE CARE TO FACILITATE ORGAN DONATION

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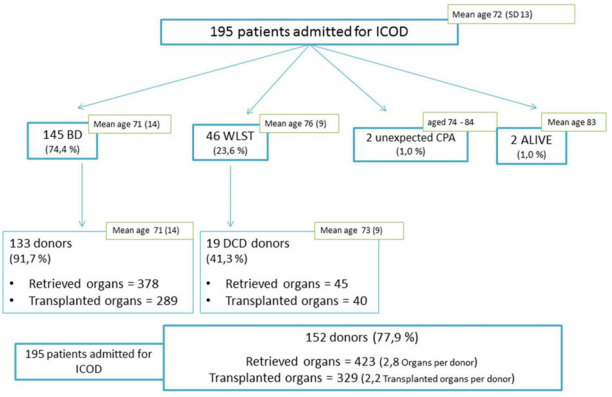
Background: Intensive Care to facilitate Organ Donation (ICOD) is a challenging practice. The aim of this study is to evaluate the outcomes of patients with devastating brain injury (DBI) admitted to the Intensive Care Unit (ICU) for ICOD and to identify clinical and radiographic factors predictive of evolution to brain death (BD).
Methods: Prospective study done in 26 hospitals. Patients with DBI admitted to the ICU for ICOD with no apparent contraindication for donation. Severity Scores measured by the attending physician and signs in the first cerebral computed tomography (CT) were analyzed as predictors of BD in the first 48h. Univariate analyses by x^2 test were undertaken to identify demographic, clinical and radiographic data that might predict transition to BD within the first 48h. A logistic regression model (OR and 95% confidence interval) was used to assess each variable independent predictive capacity.
Results: Of 195 ICOD patients included in the study, 145 evolved to BD, 118 within the first 48h and 135 within 72h from admission Figure 1 Withdrawal of life-sustaining treatment (WLST) $n = 46$ was the main reason for not transitioning to BD; in 45%, WLST occurred during the first 48h. Overall, 133 patients became actual donors after BD and 19 actual donors after circulatory death, with 2.8 organs recovered and 2.2 organs transplanted *per* donor. Two patients were discharged alive with a Glasgow Outcome Score of 3.

Table 1 Predictive factors of BD within the first 48 h

Age	< 75 y $n = 84$	63 (75.0)	0.069	2.389	0.018
	≥75 y $n = 87$	54 (62.1)		[1.161–4.918]	
Scores*	Yes 148	107 (72.3)	0.006	2.704	0.045
				[1.024–7.139]	
Spontaneous Intracranial Hemorrhage	Yes 111	81 (73.0)	0.082	1.774	0.126
	No 60	36 (60.0)		[0.852–3.696]	
Midline shift	< 10 mm 66	37 (56.1)	0.006	2.357	0.017
	≥10 mm 105	80 (76.2)		[1.167–4.760]	

Figure 1 Evolution of ICOD patients and efficiency on transplantation.



Conclusions: ICOD can substantially contribute to increase the availability of organs for transplantation and offer more patients the opportunity of posthumous donation if consistent with their wishes. Severity scores cutoffs applied according to baseline diagnosis, age < 75 years and midline shift ≥10 mm in CT may help to predict early transition to BD in patients with DBI.

OP032 PERCEIVED AND VERIFIED CANCER HISTORY IN POTENTIAL SOLID ORGAN DONORS: AN AUSTRALIAN COHORT STUDY

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Background: Australia has increased organ donation by identifying and considering more potential donors, but donation rates lag other countries. We sought to establish the accuracy of cancer history known at time of donation decisions and to explore any misclassification with potential strategies for improvement.
Methods: Cohort of New South Wales potential donors 2010-2013, linked to health datasets. We compared perceived cancer history (known at referral) to cancer history verified in linked health records. Cancer transmission risk was estimated using clinical guidelines. Potential donors declined due to cancer history but verified low-risk were missed opportunities; those accepted but verified high-risk were excess-risk donors. Proposed improvement strategies were decision support, real-time data-linkage to existing datasets, and increasing risk tolerance.
Results: Among 472 potentially suitable NSW resident donor referrals, 152 (32%) had a perceived cancer history which was verified in 58 (38%), 132 (28%) were declined due to perceived transmission risk, and 340 (72%) became actual donors. Under a low-risk threshold there were 38/132 (29%) missed opportunities and 5/340 (1%) excess-risk donors. With decision support there would have been 5/38 (13%) missed opportunities avoided and 2 (40%) more excess-risk donors, with real-time data-linkage 6/38 (16%) missed opportunities avoided and 2 (40%) fewer excess-risk donors, and with increased risk tolerance 12/43 (28%) missed opportunities avoided and 1 (20%) more excess-risk donor.
Conclusions: Potential donors' cancer history available at referral is lacking and transmission risk misclassification is common. There are missed opportunities where decision support or more accurate cancer history could safely increase organ donors.

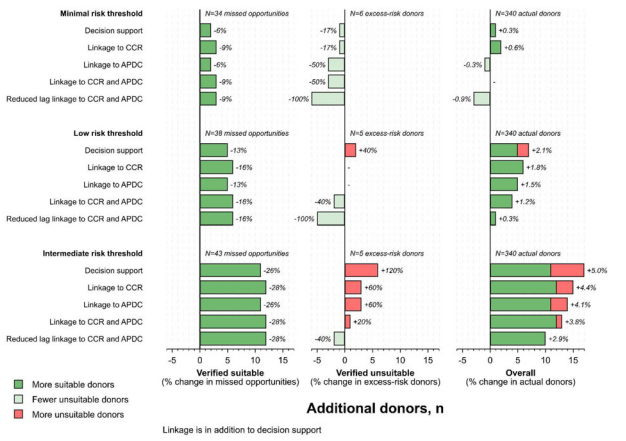

Figure 1 Change in number of verified suitable and unsuitable donors with each potential strategy to reduce missed opportunities and excess-risk donors, under varying risk tolerance thresholds

OP033 KIDNEY TRANSPLANTATION FROM MARGINAL DONORS: AN INCREASED RISK OF URINARY COMPLICATION. STUDY FROM 10,279 PATIENTS.

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Background: Due to the increasing need of kidneys suitable for transplantation, we have expanded the donor population to include marginal donors (Extended criteria donor, controlled and uncontrolled donation after circulatory death). The implication of such a strategy in terms of urinary complications has only been marginally analysed. The objective of this work is to evaluate the impact of marginal donors on urological complications.
Methods: Between January 1, 2002 and January 1, 2018, 10,279 kidney transplants in adult recipients were recorded within the DIVAT network (Computerized and VAlidated Data in Transplantation). Data were extracted in relation to 44 pre- and post-operative variables, ECD status was included, according to United Network for Organ Sharing definition (UNOS). The main analysis focused on associations between the donor ECD/SCD status, donor type (DBD, uncontrolled/controlled DCD) and urinary complications at 1 year.
Results: Overall urological complication rate was 16.26%. The donor's ECD status was significantly associated with an increased risk of urinary complications at 1 year in Multivariate analysis (OR: 1.50 (1.31-1.71), $P < 0.001$). There is no association between donor type and urinary complication. The placement of an endo-ureteric stent was beneficial in preventing urinary complications in all donors and particularly in ECD donors. The presence of an urinary complication in the first year seems to be associated with the occurrence of transplant failure after one year.
Conclusions: The donor's ECD status is associated with stenosis and ureteric fistulas at 1 year. Recipients of grafts from ECD donors should probably be considered for closer urological monitoring and systematic preventive measures. Urological skill and urologists involvement in kidney transplantation could contribute to reduce the associated risk of these complications regarding to these outcomes.

OP034 THE ROLE OF THE SURGICAL CARE PRACTITIONER IN ORGAN RETRIEVAL: A SINGLE-CENTRE EXPERIENCE

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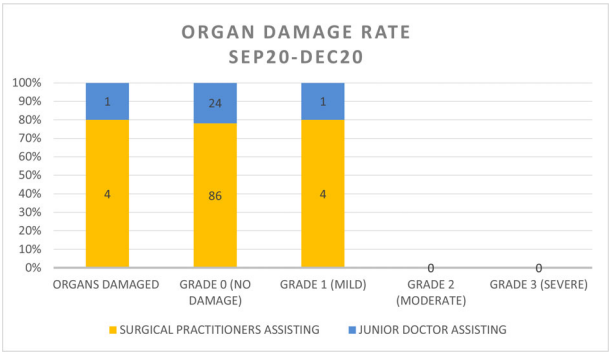
Background: Surgical care practitioners (SCPs) are non-medically qualified personnel competent in many aspects of surgical assistance. With appropriate training and supervision, they can perform procedures relevant to organ retrieval, in particular recovery of the iliac conduits. SCPs were introduced in Newcastle in 2010 as part of the abdominal national organ retrieval service (NORS) team in order to address shortages in the organ retrieval assistant rota. The aim of this study is to evaluate the effectiveness and safety of this model and introduce the role to the wider transplant community.
Methods: Data on retrievals performed by the Newcastle abdominal NORS team were retrospectively collected from local and national sources over a 4-months period from September 2020. Retrievals assisted by the SCPs were compared to those assisted by surgical trainees. The primary outcome measure was organ damage including, damage to iliac conduits, for both groups. National data published by NHSBT regarding organ damage rates were also used as a comparator.
Results: The total number of organ retrievals attended by the Newcastle team in the 4-months period was 45; 80% were assisted by a SCP (20 DBD; 16 DCD). The total number of organs retrieved was 115. The total number of conduits retrieved by the SCPs was 38 (19 Iliac arteries; 19 Iliac veins) compared to 16 by trainee surgeons. No damage to the iliac conduits was reported in either group. The overall rate of organ damage reported was 4%, all with severity grade of 1 (mild). No differences were noted when an SCP was assisting compared to a junior doctor (4% vs 4%); however, the number of organs retrieved with assistance of an SCP was significantly higher (90 vs 25). Retrieved organ damage rates were significantly lower for the Newcastle abdominal team, compared to other abdominal NORS teams in the UK according to NHSBT data.
Conclusion: SCPs are a safe and skilled workforce who provide expert surgical assistance in all types of organ retrievals. Based on this study and national data, they contribute effectively to maintain a highly functional retrieval service with significantly low rates of organ damage. We believe this model can be safely implemented in other organ retrieval centres who wish to address shortages in the assistant rota.



OP035 ASSESSMENT OF DONOR-RECIPIENT SIZE MISMATCH BASED ON BODY SURFACE AREA INDEX AND ITS IMPLICATIONS ON OUTCOMES OF DECEASED-DONOR LIVER TRANSPLANTS

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Background and Aims: Transplanting too small or too big liver grafts for recipient's size has detrimental effects on transplant outcomes. Liver size is correlated with body surface area (BSA). We used the ratio of donor's BSA to recipient's BSA (BSA index) to assess potential donor-recipient size mismatch and define the BSAi cut-off points beyond which liver transplant outcomes are affected.
Methods: We included 12,117 liver-only transplants of whole liver graft from deceased donors performed in adult recipients (January 2000 – June 2020). We divided the included cases into groups according to BSAi and compared them regarding primary-non function (PNF) rates, early hepatic artery thrombosis (HAT), early portal vein thrombosis (PVT), early inferior vena cava (IVC) or hepatic vein (HV) occlusion, graft survival and recipient survival.
Results: There were no differences concerning PNF, early HAT or early IVC/HV occlusion. Cases with BSAi > 1.3 had higher rates of PVT (5.7%) and the risk was higher than size matched transplants (OR: 2.605, 95% CI: 1.233-5.503, $P = 0.012$). Graft survival was worse in cases with BSAi≤0.85 (HR: 1.186, 95% CI: 1.035-1.36, $P = 0.014$) and BSAi > 1.4 (HR: 2.331, 95% CI: 1.365-3.981, $P = 0.002$) when compared with transplants with 0.85 < BSAi≤1.4. Recipient survival was worse in cases with BSAi≤0.75 (HR: 1.452, 95% CI: 1.042-2.024, $P = 0.028$) and BSAi > 1.3 (HR: 1.476, 95% CI: 1.052-2.07, $P = 0.024$) when compared with transplants with 0.75 < BSAi≤1.3.
Conclusions: Donor-recipient size mismatch affects early PVT rates, graft survival and recipient survival in deceased-donor liver transplants. We suggest BSAi > 0.85 and BSAi≤1.3 as the safety margins for deceased-donor liver transplant.

OP036 ASSESSMENT OF HEPATIC STEATOSIS BASED ON NEEDLE BIOPSY IMAGES IN DECEASED DONOR LIVER

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Background: Assessment of hepatic steatosis before transplantation requires graft biopsy for examination by an expert pathologist. The development of a simple method based on evaluation of images taken from tissue samples with a smartphone camera could expedite and facilitate the decision to accept or decline the liver. The aim of our study was to assess the degree of hepatic steatosis by analysing photographic needle biopsy frustule images.
Methods: Pictures of 33 biopsies were acquired with a smartphone in the operating room. Images were taken with a white paper sheet right next to the sample for colour balancing. Image processing was carried out automatically using ImageJ: background subtraction, conversion to the HSB colour space, segmentation of the biopsy area and evaluation of statistical features (mean, mode, median) of Hue (H), Saturation (S), Brightness (B) as well as Red (R), Green (G) and Blue (B) channels on the biopsy area. After having extracted all the features, correlations with the gold standard steatosis percentage were calculated to select candidate features to be used for classification. Moderate correlations were found for H, S, R (mean in particular). Images were then classified on their gold standard steatosis percentage (more or less than 30%) by histology. Thresholds for the 3 selected features were empirically determined to predict the class, and for each feature, sensitivity, specificity and accuracy were calculated. Features were aggregated by majority voting to obtain a classifier able to discriminate suitable (< = 30%) grafts for transplantation.
Results: Correlations were found for H, S, R. The sensitivity, specificity and accuracy of the final classifier were 0.625, 0.960, and 0.879, respectively.
Conclusions: The steatosis assessment based on needle biopsy images, proved to be an effective and promising method. Deep learning approaches could also be experimented with a larger set of images.

OP037 TISSUE DONATION ACTIVITY OF A THIRD LEVEL HOSPITAL ACCORDING TO THE NEW DEFINITIONS ESTABLISHED BY THE CRITICAL PATHWAY

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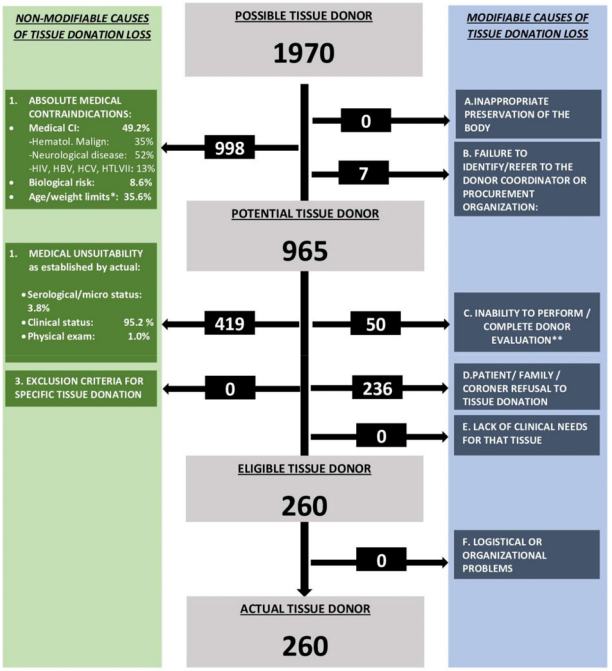
Background and Aims: The European Committee for Organ Transplantation of the Council of Europe recently proposed a "Critical Pathway" with the aim to develop a common systematic approach and lay the foundations to measure efficiency and effectiveness of deceased tissue donation (1). We present the 2020 deceased tissue donation activity of one of the largest tissue procurement centers of Spain classified according to the new pathway.
Methods: Vall d'Hebron (VHUH) is a university, 1100 bed third-level hospital covering an area of 450,000 habitants. The "Critical Pathway" defines the steps of tissue deceased donation process following the definition previously reported for organ donors (2): Possible tissue donor-PTD- (person who has died or is in a situation of imminent death); Potential tissue donor-PTT- (Dead PTD with no apparent absolute contraindication whose body has been preserved according to requirements for tissue procurement); Eligible tissue donor-ETD- (PTT consented donor who is medically suitable and meets specific criteria for the donation for at least one type of tissue) and Actual tissue donor (ATD) (ETD from whom at least one tissue was recovered with the primary intention of clinical application).
Results: A total of 1970 PTD were identified (male 56.8%, median age 76 (min 0–max 103) years old), 965 of whom (48.9%) became PTT. Two hundred and sixty (26.9 %) PTT became ETD, all of whom progress to ATD generating a total of 258 corneal, 42 musculoskeletal, 38 skin, 6 blood vessel and 32 heart valve tissue grafts Figure 1.
Conclusions: Despite an optimized donation process (few modifiable causes of loss), VHUH tissue donation potentiality is hampered by the profile of the possible donor (aged and high percentage of medical contraindications). Training in family approach could be implemented as a measure to increase efficiency.

1. Sandiumenge A, et al. Transpl Int 2021 (in press). 10.1111/tri.13841.
2. Dominguez-Gil B, et al. Transpl Int 2011; 24 (4): 373-8.

FIGURE 1. CRITICAL PATHWAY FOR DECEASED TISSUE DONATION HUVH



CI: Contraindications / HIV: Human immunodeficiency virus/ HBV: Hepatitis B Virus/ HCV: Hepatitis C virus/ HTLV: Human T-lymphotropic virus * Age and weigh limit: corneas 2 and 89 years old. Min weight: 2,5 kg
** includes impossibility to find family to investigate donation will.

OP038 FACING THE CHALLENGE: TRANSPLANT ACCESS FOR THE HIGHEST SENSITIZED PATIENTS (CPRA = 100%). THE SPANISH EXPERIENCE

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Background: The Spanish National Kidney allocation system for highly sensitized patients (PATHI) is based on virtual crossmatch and incorporates a prioritization score that includes blood type, dialysis vintage and donor-recipient age gap. PATHI increased the transplant options of patients with cPRA≥98% with 326 transplants of 1306 candidates (24.9%) registered between 2015 and 2018. However, the transplant rate for patients with cPRA = 100% was only 7.9%.Aiming to prioritize any chance of transplantation to these difficult to transplant patients, 200 extra points were added to the ranking score just for the category cPRA = 100% on June 15th, 2018.
Objective: To evaluate the characteristics of patients with cPRA100% and the impact of the new score on offers for them and their transplantation rate.
Methods: Demographic and clinical characteristics were collected of patients with cPRA = 100% in the program between January 2017-December 2019. Two periods of 18 months were considered in order to compare the number of offers and transplants performed before and after the change in the score.
Results: 539 patients with cPRA = 100% were active in PATHI during the study period. Men accounted for 54.5% and mean age was 54.9 (12.5), median time on dialysis was 83 (IQR54-122) months. The main cause of immunization was a prior transplant (88.7%). The number of offers after the implementation of the new score increased from 104 to 173. One hundred and four patients were transplanted in the whole study period. The transplant rate after the new score almost doubled the previous number, from 7.8% to 14.9% (table 1) with no significant decrease in patients with cPRA = 98-99%

Conclusion: A change in the model of prioritization has increased significantly the transplant rate for patients with cPRA = 100%. However, it still remains low for this difficult to match group. New strategies such as desensitization combined with prioritization in PATHI, as well as a case by case evaluation to check the option of removing some donor specific antibodies (DSA) from the list of unacceptable DSA have now been implemented to increase transplant options.

Table 1. Characteristics of patients with cPRA=100% registered, offers and transplants

Age Mean (SD) years	54.9 (12.5)		
Time on dialysis Median (IQR) months	83 (54-122)		
Gender			
Male	294 (54.5%)		
Female	245 (45.5%)		
Blood type			
O	243 (45.1%)		
A	225 (41.7%)		
B	43 (8%)		
AB	28 (5.2%)		
Previous transplant			
Yes	478 (88.7%)		
No	61 (11.3%)		
	Period 1 (01/01/2017-15/06/2018) (n=435)	**Period 2** (15/06/2018-31/12/2019) (n=477)	**P***
Number of patients active			
New inclusions	373 (85.7%)	104 (21.8%)	
Previously active	62 (14.3%)	373 (78.2%)	
Patients who receive an offer	104 (23.9%)	173 (36.3%)	<0.001
Median prioritization Score (IQR)	78 (62-97)	275 (260-297)	<0.001
Number of transplants performed	34 (7.8%)	71 (14.9%)	0.002
Time on dialysis Median (IQR) months (recipients transplanted)	88 (58-141)	84 (51-109)	0.532

**Chi2 and Mann Whitney when applicable*

PAEDIATRIC KIDNEY TRANSPLANT TECHNIQUE AND POST-OP MANAGEMENT: GOOD SEED MAKES GOOD FRUIT

OP067 THE IMPACT OF DONOR AND RECIPIENT SIZE IN PAEDIATRIC RENAL TRANSPLANTATION

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Introduction: Our aim was to investigate the impact of the recipient size and the mismatch between donor and recipient size in the outcomes of paediatric renal transplantation.
Methods: We included 14,322 single-kidney renal transplants in paediatric recipients (younger than 18 years old) from the UNOS database that were performed within a period of 20 years (01/2000–02/2020) in the USA. We divided the cases into deciles according to recipient weight, recipient body surface area (rBSA) and BSA index (BSAi, donor BSA/recipient BSA) and compared graft survival, delayed graft function (DGF) rates and primary non-function (PNF) rates.
Results: All the three indices were significantly associated with graft survival ($P < 0.001$). There was a gradual decrease in the median graft survival as the recipient weight and rBSA were increasing, whereas there was a gradual increase in the median graft survival as the BSAi was increasing. The difference between the 1st and 10th decile in median graft survival was 2575 days for recipient weight, 2424 days for rBSA, and 2291 days for BSAi. In living-donor renal transplants, DGF rates were increased at both ends of the recipient weight ($P = 0.04$) and rBSA ($P = 0.02$) spectrums (6.1%-7.9%), but there was no association between DGF rates and BSAi ($P = 0.175$). No associations were found between DGF rates and any of the tested indices in deceased-donor renal transplants. There were no associations between PNF rates and any of the tested indices in either living-donor or deceased-donor renal transplants.
Conclusions: Recipient size and weight, and donor size relative to recipient size influence graft survival in paediatric renal transplants. DGF is affected by the recipient size and weight, but not by the donor size relative to recipient size, and only in living-donor renal transplants.

OP068 UK CONSENSUS ON SURGICAL TECHNIQUES IN PAEDIATRIC RENAL TRANSPLANT

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Background: Paediatric renal transplantation is undertaken annually in around 130 children and young people in the UK. At the present time, there is neither evidence nor consensus on the surgical techniques involved such as optimal site of vascular anastomosis. We sought to assess whether there is variation in practice in UK Paediatric Renal Transplant units.
Methods: We circulated a questionnaire to all 10 UK paediatric transplant centres. The questionnaire assesses operative approach, vessel choice, arteriotomy, laterality, ureteric stent use, timing of its removal and post-operative imaging according to recipient weight (<15 kg, 15–30 kg and >30 kg).
Results: Extraperitoneal placement was the preferred approach by 69% of respondents for recipients weighing <15 kg, and by all respondents for recipients weighing >15 kg. Routine use of JJ Stent in all recipients, independent of weight, was reported by 77% of respondents; with removal at 4–6 weeks post-transplant reported by 42% and at 6–8 weeks in 58% of respondents. For the arterial anastomosis, 77% of respondents reporting using aortic punch for all weight categories.
The preferred site of vascular anastomosis, laterality and timing of ultrasound, according to recipient weight, are set out in the Table 1:
Conclusion: Our survey identified a clear preference for the extraperitoneal approach, even for recipients < 15Kg and unanimity in performing the vascular anastomosis on common iliac vessels in recipients between 15 and 30 kg. There was a general preference overall for the use of JJ stent and aortic punch and the use of on-table ultrasound. This data will be used at a platform for the development of standards of care for paediatric recipients in the UK, with further assessment to be done on standards around planning and pre-operative work-up for paediatric transplantation.

Table1 Recipient Weight	Vessel Choice Aorta / IVC	Common iliac	External iliac	Laterality Right into right	Left into right	Post-op Imaging U/S on table	U/S Immediately post-op	U/S Day 1 post-op	U/S Routine pre-discharge (if primary function)
< 15kg	62%	38%	0%	92%	92%	62%	8%	15%	15%
15-30kg	0%	100%	0%	85%	92%	39%	23%	23%	15%
> 30Kg	0%	42%	58%	100%	92%	33%	25%	25%	17%

OP069 IMPACT OF VASCULAR ANOMALIES ON SURGICAL COMPLICATIONS AND OUTCOME IN PEDIATRIC KIDNEY TRANSPLANTATION: A RETROSPECTIVE SINGLE-CENTER ANALYSIS.

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Background: Kidney transplantation (KTx) in pediatric patients remains challenging due to smaller sized recipients, donor- recipient mismatches and congenital anomalies.
The aim of our study was therefore to evaluate the impact of vascular anomalies (VA) on the incidence of perioperative complications after KTx and to analyze the effect on long-term graft outcome.
Methods: We retrospectively reviewed all 421 KTx performed at our institution from 1993 through December 2019. We excluded 118 KTx due to missing data or >18-years of age at transplantation. We included 303 KTx in the analysis, comparing KTx with vascular anomalies (VA) versus KTx without VA (no-VA).
Results: Recipients were predominantly of male gender (58.4%) with a median age of 12.2 (1.6-18.0) years. We identify 21 KTx with VA: seven (33%) arterial, 9 (42%) venous and five (24%) with a combination of arterial and venous anomalies. We found similar demographics characteristics between the two groups and no differences in post-operative complications incidence (Table 1). Farther, in terms of patient survival and graft-survival death-censored, we did not found differences between the two groups (Figure 1, A-B).
Conclusions: With the limitations of a retrospective analysis, our data confirm the good long-term results in pediatric KTx in terms of graft and patients survival. In our experience, recipient VA does not affect graft survival, but shows a tendency for patient survival.

Table 1

	AV (21) Median (range) or *N* (%)	No-VA (282)	*P*
Age at Transplant (years)	10.9 (1.6-16.9)	12.2 (2.1-18)	*.216*
Time on waiting-list (months)	4.4 (0-45)	6.5 (0-78)	*.406*
Living donor	6 (28)	56 (20)	*.242*
Previous KTx	1 (4.7)	7 (2.4)	*.441*
Intraperitoneal graft	1 (4.7)	2 (0.01)	*.197*
Combined Transplants	2 (9.5)	10 (3.5)	*.316*
Nephrectomy intraoperative	5 (24)	64 (23)	*.528*
Surgical Complications	3 (14)	32 (12)	*.476*

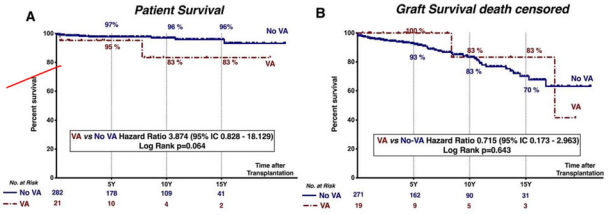

Figure 1 A-B (A: patient survival; B: graft survival death-censored)

OP070 FINAL HEIGHT OF CHILDREN OVER 12 YEARS INITIATED ON A STEROID MINIMISATION IMMUNOSUPPRESSIVE REGIMEN FOLLOWING KIDNEY TRANSPLANTATION

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Background: A large European study has shown that only 55% of adults who started renal replacement therapy in childhood achieved normal height (height SDS ≥-1.88). Children ≥12 years do not demonstrate any catch-up growth following kidney transplantation. No data are available regarding the effect of corticosteroid minimisation (CSM) immunosuppressive regimen on the final height of this group of children. Our aim was to determine the effect of CSM immunosuppressive regimen on final height in children who underwent kidney transplant ≥12 years.
Method: A retrospective review of electronic records was performed on patients who underwent a kidney transplant at ≥12 years and were initiated on a CSM immunosuppressive protocol[2] from 2009 to 2019. Normal height was defined as a height SDS of ≥1.88.
Results: 51 patients were included (mean follow-up 2.6 years, range 0.26–5.49 years). A normal final height SDS was achieved in 36 (71%), with a median final height SDS of -0.86 (median final height was 152.5cm in girls and 173.2cm in boys). The significant factors associated with achieving normal final height were male gender ($P = 0.03$), and shorter duration of dialysis ($P = 0.019$). All boys ($n = 9$) transplanted under the age of 15 years achieved normal final height (final height SDS −1.46 to 1.66). Pre-emptive transplantation was not associated with normal final height ($P = 0.076$). 73% (37) of patients had a normal BMI SDS, 12% (6) were overweight and 12% (6) were obese. 41% (21) were on antihypertensive medication at the last paediatric follow-up.
Conclusion: 71% of children ≥12 initiated on a CSM immunosuppressive protocol achieved normal final height. Boys < 15 years were more likely to achieve a normal final height compared to girls of a similar age.

References:

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OP071 IMPACT OF DONOR HUMAN LEUKOCYTE ANTIGEN SPECIFIC ANTIBODIES DETECTED IN PEDIATRIC KIDNEY TRANSPLANT PATIENTS WITH STABLE OR DECLINED GRAFT FUNCTION

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Background: This retrospective multicenter long-term cohort study investigates the impact of de novo donor specific anti-human leucocyte antigen antibodies (dnDSA) detected in the context of acute allograft dysfunction (AAD) or routine follow-up on long-term allograft survival and function in pediatric kidney transplantation (KTx).
Methods: 70 patients with dnDSA screening in the context of acute allograft dysfunction (AAD) (>50% serum creatinine (sCr) increase) or routine follow-up were enrolled during a 20-year period. Number of dnDSA specificities, longitudinal antibody total mean fluorescence intensity (MFI-sum) and sCr levels were collected.
Results: Median follow-up time was 8.6 years. dnDSA were detected in 22 (31.4%) patients. Compared to dnDSA negative patients, allograft survival was significantly shorter only in patients with detected dnDSA and AAD (8 patients) (log rank $P < 0.001$). Concurrent MFI-sum >10,000 and >1 dnDSA specificities was the most significant risk factor of AAD ($P < 0.001$) in dnDSA positive patients. Long-term significant MFI-sum changes (>12,000 MFI values) were associated with sCr increase > 0.5 mg/dl in dnDSA positive patients with initial stable allograft function ($P = 0.010$).
Conclusions: In pediatric KTx, AAD is the determinate event which shortens expected allograft survival in dnDSA positive patients. Concurrent high MFI-sum and multiple dnDSA specificities strongly predicts AAD in dnDSA positive patients. Long-term dnDSA impact on allograft function occurs with higher MFI-sum changes, indicating the need for systematic MFI monitoring.

OP072 ROLE OF NON-DONOR SPECIFIC ANTIBODIES IN PEDIATRIC KIDNEY TRANSPLANTATION

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Background: Despite advances in immunosuppressive therapy, late allograft failure remains a considerable problem in renal transplantation. While the role of donor specific anti-HLA antibodies (DSA) in the pathogenesis of allograft damage has been largely demonstrated, the role of non-donor specific antibodies (NDSA) is still controversial.
This study was aimed to evaluate the occurrence of NDSA in pediatric renal transplant recipients and their correlation with clinical outcomes (renal function, viral infections, rejection).
Methods: We retrospectively analyzed 52 pediatric renal transplant recipients undergone to anti-HLA antibodies monitoring between 2015 and 2018. Antibodies were measured out 6, 12 and 24 months after transplantation. Protocol biopsies were performed at the same timeline. Collected data included creatinine, eGFR, proteinuria, immunosuppressive therapy, viral infections, number and type of rejections. Patients were divided into 4 groups: without antibodies (NA), with NDSA only (NDSA), with both DSA and NDSA (DSA+NDSA), and with DSA only (DSA).
Results: All groups had similar demographic and clinical characteristics. Occurrence of DSA and NDSA was similar (15% of patients) 6 months after-transplantation (PO), while 8% had both DSA and NDSA. 12 months PO, 19% of patients had DSA, 21% NDSA and 12% both. 24 months PO, 15% had DSA, 11% NDSA and 10% both. Protocol biopsies showed subclinical rejection (acute or chronic) in 23% of patients at 6 months PO (5% antibody mediated rejection (AMR) and 75% T-cell mediated rejection (TCMR), in 25% at 12 months (23% AMR, 77% TMCR) and in 30% at 24 months (25% AMR, 75% TCMR). Statistical analysis showed no significant correlation between NDSA only and rejection, but NDSA seemed to play synergistic action with DSA in AMR. Compared to others, NDSA children had better eGFR, but higher proteinuria ($P = 0.02$), as well as DSA+NDSA group ($P = 0.026$).
Conclusions: NDSA do not seem to cause rejection *per se*; however, they play a synergistic action with DSA in AMR. Proteinuria is significantly higher in patients with NDSA compared to other groups, suggesting a contribution in the pathogenesis of allograft damage. Our results suggest that NDSA should be considered as a wake-up call for graft outcome and their regular monitoring may be a useful tool in clinical practice.

OP073 STANDARDISATION OF IMMUNOSUPPRESSIVE AND ANTI-INFECTIVE DRUG REGIMENS IN UK PAEDIATRIC RENAL TRANSPLANTATION: THE HARMONISATION PROGRAMME

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Background: Current variation in practice of immunosuppressive drug (ISD) therapy and anti-infective (AI) prescribing in children and young people (CYP) undergoing kidney transplantation impairs assessment of outcomes and may disadvantage some CYP. Different regimens employed in the UK vary according to unit preference, levels of immunological risk, primary disease or co-morbidities (obesity/diabetes/bone disease). Early steroid withdrawal has been reported to significantly improve growth at six months post-transplant; however, up to 30% of CYP in early steroid withdrawal regimens switch to steroid maintenance regimens due to intolerance of mycophenolate mofetil (MMF) and/or acute rejection. As a result, steroid maintenance regimens continue to be widely used in the UK. We sought to develop best practice guidance nationally in order to improve quality of care and reduce variation in practice.
Methods: Unit protocols from all UK kidney transplant units were 'pooled' to identify variations in practice. Medline, CINAHL, PsycINFO and EMBASE (all 1980 – 2020) databases were searched for ISD and AI regimens employed for CYP undergoing renal transplantation using PICO methodology. Where evidence was lacking, formal Delphi consensus methodology was employed to develop a national guideline on ISD and AI prescribing.
Results: There was significant variation, particularly within steroid maintenance regimens, with up to tenfold differences in steroid dosing. Prior to standardisation, 7/10 units used anti-CD25 induction. We developed and implemented formal consensus-based guidance for a steroid maintenance and early steroid withdrawal regimen, which precisely define ISD and AI dose and duration, and tacrolimus level target ranges.
Conclusions: To our knowledge, this is the first report of national standardisation of ISD and AI prescribing and monitoring. Outcome data for patient and graft survival and function, acute rejection, infection and drug toxicity will be captured prospectively

OP074 KIDNEY TRANSPLANTED CHILDREN NOT RESPONDING TO ANTI-REJECTION TREATMENT: HOW TO IMPROVE THE OUTCOME

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Background: Despite the significant improvement in immunosuppressive therapy over the years, graft rejection remains the leading cause of graft loss in kidney transplanted children. The aim of this study was to identify which are the acute rejection (AR) at major risk for non-responding to anti-rejection treatment.
Methods: A retrospective analysis of all the AR diagnosed in our Hospital (January 2015-August 2020) in kidney-transplanted children, who completed the anti-rejection treatment and a follow-up biopsy after the AR treatment, was carried out. The immunohistochemical characterization (IC) of the cellular infiltrate with anti-CD3/CD20 antibodies was performed on all the biopsies.
Results: We observed 73 AR (53% subclinical) in 52 children: 33 males, median age 9 years, 19% pre-emptive, 30% living donor, 10% at 2nd kidney transplant. The Banff-17 criteria classified 54% cellular, 38% antibody-mediated and 8% mixed rejections. At the IC 84% had a mixed CD3-CD20 infiltrate. Cellular AR received pulse methylprednisolone (median dose 386 mg/mq, IQR 293-488) and anti-thymocyte globulin in 7 cases. The antibody-mediated AR received: 88% pulse steroid therapy, 94% immunoglobulin, 62% plasmapheresis and 68% Rituximab. After treatment, a follow-up biopsy proved: 32% Banff1, 42% persistent AR and 26% IFTA. At the univariate and multivariate analysis, children at risk for non-responding to AR treatment were those at the 2nd transplant, previously dialyzed (OR 10.51, 1.72-64.28), with a poor graft function at discharge from transplant (OR 0.98, 0.96-0.99), older at the time of AR (OR 1.19, 1.06-1.35). AR, if diagnosed by a protocol biopsy (OR 0.15, 0.04-0.57), or treated with a major pulse methylprednisolone dose (OR 0.98. 0.98-0.99) or switched to Tacrolimus (OR 0.49, 0.25-0.95), had a better outcome. A predominant CD3 infiltrate increased risk of non-responding to treatment (OR 10.11, 1.05-97.00).
Conclusions: The protocol biopsy, the pulse steroid dose and the switch to Tacrolimus are the only modifiable variables that correlate with a better response to the anti-rejection therapy. The implementation of IC of the inflammatory infiltrate could be an additional tool to identify patients most likely to not respond to therapy.

FROM DONOR SELECTION TO OUTCOME PERFECTION IN LUNG TRANSPLANTATION: THE PATH TO PARADISE BEGINS IN HELL

OP075 LONG-TERM OUTCOME AFTER LUNG TRANSPLANTATION FROM DONATION AFTER EUTHANASIA EQUALS DONATION FROM CONTROLLED CIRCULATORY-DEAD AND BRAIN-DEAD DONORS

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Background: Organ transplantation is hampered by lack of suitable organs. In countries with a legal framework for euthanasia, organ donation following euthanasia (donation after circulatory death category V (DCD-V)) could expand the donor pool. However, lung transplantation (LTx) after euthanasia remains relatively unacquainted and long-term outcome has not been reported yet. We describe our single-center experience and evaluate long-term outcome in a propensity-matched comparison to DCD-III (withdrawal from life-sustaining therapy) and donation after brain death (DBD).
Methods: All sequential single-lung transplantations (SSLTx) between 2007 and 2020 were retrospectively analyzed. Propensity matching was performed using recipient age/gender, LTx indication, use of extracorporeal lung support and donor age, which resulted in a 1:2 DCD-III and a 1:3 DBD matching. Chronic lung allograft dysfunction (CLAD)-free and overall recipient survival were the primary endpoints.
Results: 769 SSLTx were performed of which 22 were from DCD-V donors (2.9%). 13 women and 9 men (median age 57 years) expressed their specific wish to become organ donor at the time of euthanasia. Euthanasia request was granted for neuromuscular ($n = 9$) or psychiatric ($n = 8$) disorder or unbearable pain ($n = 5$). Median donor warm ischemia time was 11 min. Indication for LTx was COPD ($n = 11$), pulmonary fibrosis ($n = 5$), cystic fibrosis ($n = 4$) and bronchiolitis obliterans ($n = 2$). CLAD-free 3- and 5-year survival were 86.4% and 58.9%, respectively, being non-inferior to DCD-III (83.7% and 61.1%; $P = 0.82$) and DBD (62.2% and 50.5%; $P = 0.12$). Five-year patient survival was 90.9%, comparable to both DCD-III (84.8%; $P = 0.97$) and DBD (73.9%; $P = 0.25$) cohorts.
Conclusions: This propensity-matched cohort study suggests for the first time that LTx with DCD-V grafts yields similar long-term outcome compared to DCD-III and DBD grafts. Therefore, lungs donated after euthanasia may be a justifiable option to increase the donor pool.

Table: Overview of the recipient outcome

Outcome	Statistic	DCD-V	DCD-III	P-value*	DBD	P-value*
	N	22	44		66	
Days on ventilator				0.49		0.17
	Median IQR	2.0 (1.0; 4.0)	2.0 (1.0; 4.0)		3.0 (1.0; 6.0)	
ICU stay (days)				0.70		0.44
	Median IQR	6.0 (5.0; 10.0)	6.0 (4.0; 12.0)		7.0 (4.0; 11.0)	
Hospital stay (days)				0.55		0.25
	Median IQR	29.0 (27.0; 40.0)	26.0 (20.0; 36.5)		30.0 (23.0; 41.0)	
Reoperation[1]				0.57		0.59
Yes	n/N (%)	5/22 (22.73%)	14/44 (31.82%)		20/66 (30.30%)	
No	n/N (%)	17/22 (77.27%)	30/44 (68.18%)		46/66 (69.70%)	
PGD[2]				0.56		0.42
At least one PGD 3	n/N (%)	5/21 (23.81%)	14/42 (33.33%)		21/59 (35.59%)	
No PGD 3	n/N (%)	16/21 (76.19%)	28/42 (66.67%)		38/59 (64.41%)	
CLAD-free survival				0.82		0.12
3 years		86.4 (63.4; 95.4)	83.7 (68.7; 91.9)		62.2 (49.0; 72.9)	
5 years		58.9 (26.8; 80.8)	61.1 (42.6; 75.3)		50.5 (37.0; 62.5)	
Patient survival				0.97		0.25
3 years		90.9 (68.3; 97.6)	90.7 (77.0; 96.4)		77.8 (65.4; 86.3)	
5 years		90.9 (68.3; 97.6)	84.8 (69.0; 93.0)		73.9 (60.7; 83.2)	

CLAD, chronic lung allograft dysfunction; ICU, intensive care unit; IQR, interquartile range; PGD, primary graft dysfunction
**p-values refer to the comparison with DCD-V*
[1]within first 90 days after lung transplantation
[2]within first 72 hours after lung transplantation

OP076 THE FIRST SPANISH EXPERIENCE USING THE LUNG ALLOCATION SCORE: FIVE YEARS´ EXPERIENCE OF A SINGLE CENTER,LAS AS A PROTECTIVE FACTOR FOR WAITLIST DEATHS

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Background: In May 2005, the policy of lung allocation for transplantation in the USA was changed from a system that allocated donor lungs based primarily on waiting time to a system that allocated lungs based primarily on a Lung Allocation Score (LAS). There are no data on the effect of the LAS on lung transplantation programmes in Spain.
Methods: All patients undergoing first-time lung transplantation during the period from January 1, 2010 through December 31, 2019 were included in the study. The cohort was divided into two cohorts, one before LAS(BLE) era between 01/2010 and 12/2013 and another after LAS(ALE) era between 01/2014 and 12/2019. Waitlist characteristics, transplant procedures and up to 5-year post-transplant outcomes were analysed.
Results: The implementation of the LAS system was associated with a decrease of the median waiting time for transplant from 4.03 (IQR 7.09) to 2.62 month (IQR 5.69) ($P = < 0.001$). The waiting time decreased over ALE era in all indications except COPD. After LAS era, waitlist deaths decreased from 6.3% to 2.7%($P = 0.01$). Death decreased in ILD from 8.2% to 4.4% ($P = 0.16$) and significantly in PPH, from 16.7% to 0% ($P = 0.008$). COPD patients did not increase their mortality in waitlist despite the increase of waiting time (Table 1). On multivariate analysis, the use of LAS was directly associated with decrease waitlist deaths (R^2 0.198, $P = 0.01$). After implementation of the LAS, we observed an improvement in early and late survival (Figure 1).
Conclusions: The implementation of the LAS system in a Spanish lung transplant region is associated with a decrease in waiting list mortality without worsening the short and long-term outcomes.

		BLE	ALE	*P*
Waiting time in month (IQR)	COPD	3.74 (6.61)	4.21 (8.02)	0.73
	ILD	3.31 (5.51)	2.01 (4.43)	< 0.001
	PPH	2.44 (6.11)	1.31 (3.56)	0.18
	BC/CF	8.64 (5.71)	2.49 (13.33)	0.08
	Other	3.05 (4.56)	2.59 (2.85)	0.32
Death in waitlist (%)	COPD	0	1.3	0.41
	ILD	8.2	4.4	0.16
	PPH	0	0	–
	BC/CF	16.7	0	0.008
	Other	7.1	3	0.52
Outcomes (days) (IQR)	LMV	8 (32.25)	7 (32)	0.22
	ICU-LOS	17 (34)	18 (30)	0.31
	HLOS	39 (32.25)	33 (29)	0.01

COPD: *obstructive pulmonary disease/emphysema*; ILD: *interstitial lung disease*; PPH: *primary pulmonary hypertension*; BC/CF*: bronchiectasis/cystic fibrosis;* LMV: Length of mechanical ventilation ICU-LOS: ICU length of stay; HLOS: hospital length of stay

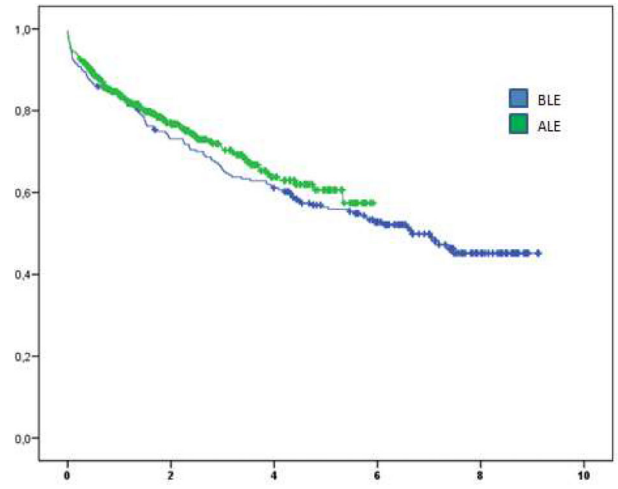

Figure 1. Survival

OP077 LUNG TRANSPLANT FOR PULMONARY FIBROSIS; SMALLER DONOR LUNGS IMPACT SURVIVAL

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Background and aims: Sizing of donor lungs in respect of the potential recipient, in pulmonary transplantation is accepted as an important feature of decision making, allocation and utilisation. However, our understanding of the relationship between lung size and outcomes after transplantation is limited. We aim to assess the impact of size mismatch on post-transplant survival, for patients with pulmonary fibrosis (PF) in the UK.

Methods: Data on all adult, first-time lung transplants for PF, between January 2010 and December 2019, were obtained from the UK Transplant Registry (UKTR). Donor to recipient predicted Total Lung Capacity (pTLC) ratio was used to assign patients to 3 'size' groups: < -20%, -20% to 0% and ≥0%. Unadjusted 90-day, 1- and 5-year, post-transplant survival was assessed using Kaplan-Meier survival curve and log-rank tests.

Results: In total, 318 recipients were identified; 141 (44%) single lung, 234 (73.6%) male, median age 58 years (IQR 52–62), mean donor pTLC 5.7 l (±1), mean recipient pTLC 6.4 l (±1.1), mean pTLC mismatch ratio −10.8% (±13.4).

Kaplan-Meier analysis of size mismatch groups for the total patient cohort, identified a significant difference in 90-day survival ($P = 0.02$), with no difference at 1- ($P = 0.1$) and 5-years ($P = 0.13$).

In the single lung cohort, no significant difference in survival was identified (Figure 1). For double-lung transplant recipients, analysis of size mismatch groups identified a significant difference in 90-day survival ($P = 0.06$). (Figure 2)

Conclusion: We have identified a significant impact of *undersized* lungs on short-term survival after double lung transplant for Pulmonary Fibrosis. Further analysis is required to understand the relationship between lung size-mismatch in this patient population.

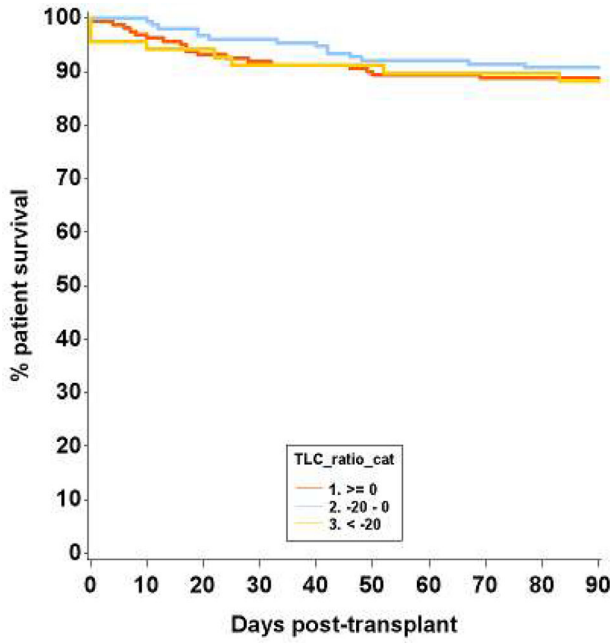

Figure 1. Kaplan Meier 90-day survival analysis, for single lung transplant cohort, by size mismatch group

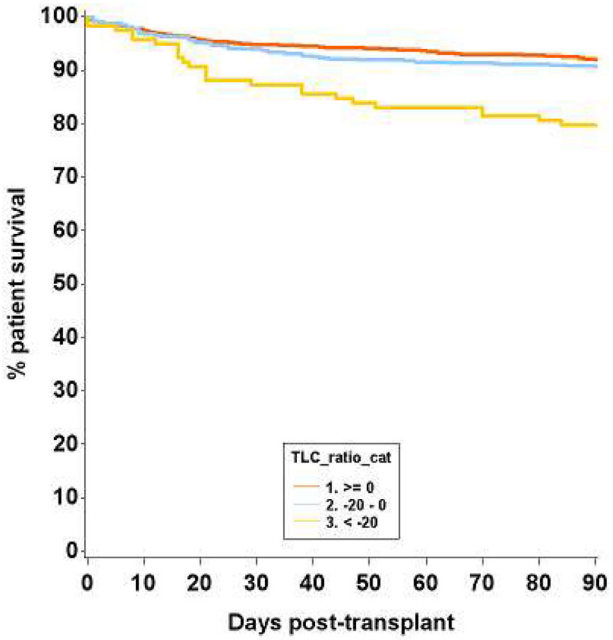

Figure 2. Kaplan Meier 90-day survival analysis, for double lung transplant cohort, by size mismatch group

OP078 LUNG TRANSPLANT FOR LATE REFRACTORY ARDS (LR-ARDS) : PRIMARY EXPERIENCE IN FOCH HOSPITAL

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Background: In some patients with **(LR-ARDS)** on maximal support by ECMO, considering switch from "ECMO to recovery" to bridge to lung transplantation (LTx) could be an option. We report our preliminary experience in such strategy.
Methods: Between 2016 and 2020 patients with **LR-ARDS** on ECMO to recovery strategy failure referred to our center for LTx evaluation were reviewed. Patients with pre-existing lung disease or other severe comorbidities before ARDS onset were not considered for evaluation. In all cases, lung damage irreversibility was established by multidisciplinary staff. Results are expressed in median [min;max]. This study was approved by ethic local committee (CERF).
Results: 13 patients (4F; 9 M) aged of 56y [20;63] were included. The etiologies were Sars-cov-2 ARDS (9), toxic (2), Anti-mda5 AIP (1), and unknown (1). Only 6 patients were transferred in our center. Among 6 patients, 4 were transplanted and 2 died before LT. ECMO duration, MV duration and ICU stay before LT were, respectively, 35 days [20;88], 38 [20;89], 34 [3;94]. All patients had sarcopenia and severe ICU acquired paresis with MRC < 12 and were tracheotomized and none had bedsores. There was no difference between LTx and non LTx patients. Contra-indications for LTx were severe extra-respiratory failure (1/6) and non-controlled infection (1/6). All transplant patients are alive follow-up 445d [95;1790]. Post-operative MV duration was 24 days [9;126]; LOD in ICU was 59 days [29;202]. Every induction protocol included basiliximab then usual post-operative immunosuppression. 2 patients were informed of and accepted LTx surgery and 2 could not. Though, patients graft acceptance and treatment adhesion were good in all cases. Relatives were systematically extensively informed of risks and benefits, and accepted the strategy. All patients were listed in high emergency program after expert panel acceptation.
Conclusion: In our experience**,** LTx seems to be a reasonable option in irreversible LR-ARDS under maximal support therapy in very selected patients in an expert center with a specific task force (transplantationARDS@hopital-foch.com). Incidence of such young potentially eligible patient is increased due to the current COVID-19 pandemic. As further evaluations are needed, we propose to create a national registry to evaluate this new strategy.

OP079 DONORS FROM DONATION AFTER CARDIAC DEATH ARE A RISK FACTOR FOR BRONCHIAL COMPLICATIONS AFTER LUNG TRANSPLANTATION: A RETROSPECTIVE MULTICENTER STUDY

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Background: After lung transplantation, bronchial complications (BC) are one of the major concerns. The etiology of airway complications has been attributed mostly to donor bronchial ischemia. Bronchial blood supply is derived from the pulmonary and bronchial arteries, whom arise from the descending aorta or intercostal arteries. The technique used in lungs retrieved from donation after cardiac death (DCD) implies the cessation of bronchial circulation and may increase the ischemic injury. In this study, we aimed to assess the impact of DCD on BC.
Methods: A retrospective, observational, multicenter cohort study was conducted at 3 Spanish transplant centers from 2015 to 2019. All lung transplantations performed in adults were included. The patients without any information about type of donor or BC were excluded. The patients were divided based on type of donor in DCD group (139) or brain death donor (DBD) group (705). We monitored the incidence of bronchial dehiscence (BD) and bronchial stenosis (BS) classified according the ISHLT grading system. Our objective was to evaluate the role of DCD on the incidence of airway complications. We performed a univariate analysis with chi-square or Fisher's exact test and multivariate analysis. All reported *P*-values are 2-sided. $P < 0.05$ was considered statistically significant.
Results: We performed 845 consecutive adult lung transplantations. Overall incidence of BD was 4.49% (38 patients), and the incidence of BS was 10.9% (93 patients). We did not see differences in incidence of BD (5.1 vs 4.5, $P = 0.74$) according to a type of donor, but we observed greater incidence of BS in DCD group (17.5% vs 10%, $P = 0.01$). On multivariate analysis, BD was directly associated with male gender (R^2 0.152, $P = 0.05$), positive microbiological cultures of donor (R^2 0.71, $P = 0.04$) and interrupted suture technique (R^2 0.34, $P = 0.004$). BS was associated DCD donors (R^2 0.64, $P = 0.01$) and recipient's positive microbiological cultures after transplantation (R^2, $P = 0.012$). We did not see a direct association between warm or cold ischemia and any BC.
Conclusion: The incidence of BS after LT is higher in grafts from DCD than DBD donors. The grafts from DCD donors have an increased risk for BS. The Warm ischemic time could have a role, but more studies are needed to confirm this data.

OP080 CLUSTER ANALYSIS IDENTIFIES DISTINCT PROFILES OF TRANSBRONCHIAL BIOPSIES IN LUNG TRANSPLANT RECIPIENTS ASSOCIATED WITH ALLOGRAFT SURVIVAL

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Background: Diagnoses based on transbronchial biopsies (TBB) after lung transplantation remain challenging due to the heterogeneity of the lesions. The aim of the study was to identify different phenotypes of histological lesions using unsupervised analyses.
Methods: 498 consecutive lung transplant recipients from October 2011 to December 2019 were included. All the biopsies performed after transplantation (protocol and for cause biopsies) were assessed for elementary lesions: cellular rejection (A lesion), peribronchiolar infiltrate (B lesion), cells in capillary, organizing pneumonia, alveolar cell hyperplasia, alveolar fibrin. Comprehensive histological and outcome data were used in unsupervised cluster analysis. Associations between each cluster and outcomes were then assessed using time-dependent Cox regression analysis.
Results: Among the 2561 post-transplant allograft biopsies. 1961 were protocol biopsies and 600 for cause biopsies. An unsupervised hierarchical classification algorithm of the TBB revealed 6 clusters characterized by distinct patterns of lesions (Figure 1A) ranging from biopsies without abnormalities (Cluster #1) to biopsies showing high degree of active lesions (cells in capillary, organizing pneumonia, alveolar cell hyperplasia, alveolar fibrin) (Cluster #6). The 6 clusters displayed distinct allograft and patient survival profiles with incremental risk of graft loss and patients death between clusters (Cluster #4, #5, and #6 associated with the higher risk of graft loss and patient death [$P < 0.001$, $P = 0.046$, and $P < 0.001$, respectively]) (Figure 1B). Two clusters (Cluster #3 and #4) were associated with a higher risk of Chronic Lung allograft Dysfunction ($P = 0.019$ and $P = 0.001$, respectively).

Conclusion This study using a probabilistic data-driven clustering approach applied in a large well-defined cohort identified 6 different phenotypes of TBB associated with distinct risk of graft loss, patient death and CLAD. Reducing the heterogeneity among the TBB can improve disease characterization, enable patient-specific risk stratification, and open new avenues for cluster-based treatment strategies.

OP081 DONOR LYMPHOCYTES IN PERIPHERAL BLOOD OF PATIENTS AFTER LUNG TRANSPLANTATION COMPRISE HIGH FREQUENCIES OF KIR-POSITIVE T AND NK CELL SUBSETS

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Background: For end-stage lung diseases, lung transplantation (LuTx) is the only curative treatment option. Acute and chronic rejections are major limitations and a deeper understanding of the contribution of immune responses early after LuTx is needed. Passenger leukocytes, derived from donor lungs and migrating into the recipients` periphery, are primarily NK and T cells. We characterized the expression of killer cell immunoglobulin-like receptors (KIR), regulating NK and $CD8^+$ T cell activity, on donor and recipient NK and T cells in recipient blood after LuTx.
Methods: Peripheral blood samples at pre, T0hr, T24hrs and 3wks post Tx of $n = 51$ LuTx recipients were analyzed for the presence of HLA-mismatched donor cells and their KIR repertoire as well as activation status using flow cytometry and correlated with clinical parameters, i.e. primary graft dysfunction (PGD) and cold ischemic times (CIT).
Results: Within 3wks after LuTx, donor NK and T cells were detected in $n = 51$ patients with a peak at T0hr. An increase of the $KIR2DL1^+$ subset was detected within the donor NK cell repertoire. Moreover, donor NK cells showed significantly higher frequencies of $KIR2DL1^+$ cells ($P < 0.01$) 3wks post LuTx compared to recipient NK cells. This effect was also observed in donor T cells 3wks after LuTx with higher proportions of $KIR2DL1^+$ ($P < 0.05$) and $KIR3DL1^+$ ($P < 0.01$) T cells. Higher activation levels of donor NK/T cells ($P < 0.001$) were detected as compared to recipient cells via CD25 expression and degranulation capacity. The KIR repertoire on donor NK/T cells in LuTx recipient blood does not correlate with PGD. The frequencies of KIR^+ donor NK cells increased directly after LuTx with longer CIT.
Conclusion: Higher frequencies of donor NK/T cells expressing KIR compared to recipient NK/T cells argue for their origin in the lung as part of a highly specialized immunocompetent compartment. Despite KIR expression, the activation level of donor NK/T cells in the periphery of the recipient may be higher compared to recipient cells. Moreover, a positive correlation was detected for KIR surface expression on NK cells and CIT but not PGD implying extended preservation times have an impact on NK subset composition. Hence, donor NK/T cells might have a regulatory effect in the balance between tolerance and rejection as well as graft survival after LuTx.

OP082 MIR-339 AND GALECTIN-3: DIAGNOSTIC VALUE IN PATIENTS WITH AIRWAY OBSTRUCTION AFTER LUNG TRANSPLANTATION

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Background and Aims: Respiratory complications can be the cause of graft dysfunction after lung transplantation (LTx). Reliable non-invasive diagnostic biomarkers of post-transplant complications are required. MicroRNAs (miR) are small non-coding regulatory molecules; miR-339 high values are associated with respiratory diseases. Galectin-3 (gal-3) is highly expressed in fibrosis of transplanted solid organs. The aim is to evaluate the miR-339 expression and gal-3 concentrations in lung recipients including with airway obstruction after LTx.
Methods: The study included 57 lung recipients (34 men and 23 women aged 10 to 74 (36 ± 18) years) were followed up to 5 years after LTx. The miR-339 plasma expression was detected by real-time PCR (Qiagen, USA); gal-3 levels were measured by ELISA (Bender MedSystems GmbH, Austria).
Results: During follow-up in 30 (52.6%) recipients post-transplant complications were detected: 12 (40.0 %) cases of airway obstruction, 18 (60.0%) – others, including infections. The levels of miR-339 and gal-3 were significantly higher in recipients with airway obstruction to compare with 27 (47.3 %) recipients without any complications ($P = 0.036$ and $P = 0.014$, resp.).
Increasing miR-339 (above the 0.02 fold change of expression) and galectin-3 (above the 11.7 ng/ml) threshold levels is associated with risk of airway obstruction after LTx (Tab.).

Table Diagnostic characteristics of miRNA-339 and gal-3 at airway obstruction after LTx.

Biomarker	RR	95% CI	Sensitivity	Specificity	Diagnostic efficiency
miR-339	2.625	[1.144–6.023]	60.0%	75.9 %	70.4%
gal-3	3.619	[1.165–11.239]	72.7%	72.7 %	78.8%
miR-339 + gal-3	7.141	[1.049–48.601]	83.3%	81.8 %	82.4%

Conclusion: A measurement of miR-339 expression in combination with gal-3 level might be perspective to identify recipients at high risk of airway obstruction after LTx.

IS THERE ROOM FOR IMPROVEMENT IN DONATION?

OP141 IMPACT OF THE CHANGE IN ORGAN DONATION LAW IN ENGLAND ON DONATION RATES IN THE MULTICULTURAL AND ETHNICALLY DIVERSE CITY OF LONDON

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Background: The new law for organ donation in England came into effect on the 20th May 2020. This changed moved consent for organ donation from a system of 'Opt-in' to 'Opt-Out' or 'Deemed' consent. This was during the middle of the first lockdown due to the Coronavirus pandemic in the UK. The London regional organ donation team saw a huge decrease during the same time period of potential eligible organ donors. Additionally, challenges to obtaining consent for donation are linked to the fact that London is the most diversely populated city in the UK with 'White-British' attributing to just 44.9% (2011 UK Census) of the population and over 250 languages are spoken in the city.
Initial National figures collated up until 31st October 2020 showed that 26% of all donations that took place in England during this time period did so after patients' consent was deemed- that being considered as willing to donate as they had not expressed an organ donation decision during their lifetime (NHSBT).
Methods: To understand the impact of the law-change all approaches to donor families in the London region were examined for a six-month period (May –Sept 2020). Data were obtained from the 'Potential donor audit' undertaken in all acute hospital trusts within the London region. The review looked at the following; type of potential donor i.e. DBD or DCD, potential donor demographics, next of kin demographics, demographics of the requesters involved in approaching for donation, use of additional resources in the approach (e.g. video explanations, translation services etc) and the outcome of these approaches.
Results: During this time period there were 147 approaches for donation made to families of potential organ donors (100 potential DBD and 47 potential DCD) in London, resulting in 75 consents. Of these consents 15 were deemed, attributing to 33% of the consents, which is higher than the national average. This was an unexpected outcome due to the complexities of seeking support and consent for donation in a diverse population. There were 9 potential donors during this time period who had registered an 'Opt-Out' decision.
Conclusion: Additional review of all approaches in this timeframe not only shows the complexities of approaching families for donation but doing so during a global pandemic and demonstrates the importance of utilising trained requesters.

OP142 OPT OUT LEGISLATION IN THE UK – PRELIMINARY DATA

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Background: Opt out legislation has been implemented in Wales (2015), England (2020), Scotland (2021) and is being considered for Northern Ireland. Trends in opt in and out registrations on the NHS Organ Donor Register (ODR) and deceased donor consent rates across the four UK nations are presented.
Methods: Data from the ODR and UK Potential Donor Audit (PDA) are included. Consent rates of the four UK nations are compared against the UK consent rate using a funnel plot. The UK rate is dominated by the

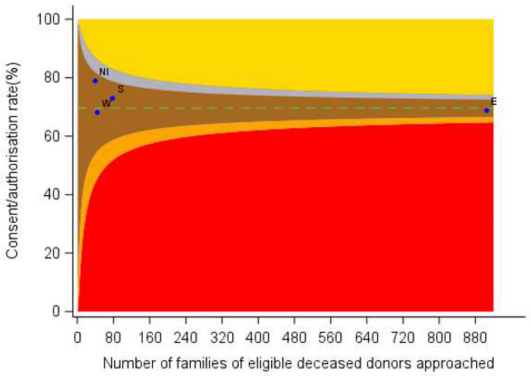
consent rate in England, owing to its much larger population (84%). The graph shows for each nation, the consent rate plotted against the number of donation decision conversations with the UK rate and 95% and 99.8% confidence limits superimposed. Nations that lie outside the confidence limits are statistically different from the UK rate. These are unadjusted funnel plots so any differences in patient mix, between the four nations, have not been accounted for.
Results: Between April and September 2020, Scotland had the highest proportion of opt in registrations on the ODR, 50.1%. Wales had the highest proportion of opt out registrations on the ODR, 6.1%. Opt out registrations remained low in nations without out opt legislation (see **Table 1**). There was a significant fall in the number of donation decision conversations (family approaches), across all nations in 2020/21 due to the COVID pandemic, although consent rates remained consistent. The funnel plot presented in Figure 1, indicates that Northern Ireland and Scotland had the highest consent rates during 2020/21, 78.9% and 73.1%, respectively, but this does not reach statistical significance.
Conclusion: Opt out legislation has been or is planned to be implemented throughout the UK. Whilst it is too early to determine the impact of opt out legislation in England and Scotland, the data provide a preliminary look at the current ODR registrations and consent rate data across the UK.
Data will be updated to include April 2020 to March 2021.

Table 1

	ODR registrations pmp at 30 September 2020			
	Opt in registrations		Opt out registrations	
Nation	*N* (million)	%	*N* (million)	%
England	21.3	38.1	1.6	2.8
Wales	1.3	41.4	0.2	6.1
Scotland	2.7	50.1	0.003	0.5
N. Ireland	0.9	48.1	0.0002	0.1
UK	26.3	39.6	1.8	2.7

*Population estimates are the mid-2018 estimates based on UK Office for National Statistics 2011 Census figures

Figure 1 - All deceased donor consent rates by nation, April 2020 to September 2020



OP143 DISPARITIES IN THE USE OF DONATION AFTER CARDIAC DEATH LIVER ALLOGRAFTS FROM DONORS OVER 60 YEARS OF AGE IN THE UNITED STATES VS. THE UNITED KINGDOM.

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Background & Aims: There is dire need for exploration of novel ways to expand utilization of available liver allograft resources. Such is the use of older (at or >60 years) donation after circulatory death (DCD) donor livers. There seems to be marked variation in DCD practices between the US and the UK. To assess DCD transplant demographics and outcomes using older (at or >60 years) DCD livers in large UK vs. US national cohorts.
Methods: Retrospective cohort study of 1163 DCD UK LT recipients and 3396 from the US. Both cohorts were split into subgroups with donor cut-off age of 60 years (G1, at or >60 years; G2, <60). Study period: 2001–2015; in the UK and the US. Data were retrieved from the National Health Service Blood and Transplant and the Scientific Registry of Transplant Recipients, which included data on all transplant recipients in the UK and the US, respectively.
Results: In the US, G1 represented only 2.4% of total DCD LTs performed, contrary to 23% in the UK. Within both national cohorts, median warm (WIT) and cold ischemia times (CIT) were similar. US waitlist time halved in G1 (56 vs. 102 days; $P = 0.056$). 64.2% of G1 in UK ($P = 0.000$) were transplanted in London and Birmingham; 88.1% ($P = 0.000$) were imported. Contrary to the UK, there was striking inter-regional variation in G1 and overall DCD rates in the US; most allografts were used locally (78.3%, $P = 0.05$). 1-, 3-, and 5- year UK DCD graft survival seemed to be superior. UK 1-,3-, and 5-year survival was comparable between G1&G2 (88%, 80%, and 75% in G1 vs. 88%, 81.3%, and 76.7% for G2, respectively; $P = 0.397$); in the US, it was inferior in G1 (81.9% vs. 77.5%, 72.5% vs.64.3%, and 67.5 vs. 56.3%, respectively; $P = 0.011$).
Conclusions: DCD liver transplant rates remain disappointingly low in the US. Based on the UK experience, expansion of our donor pool through a broader use of DCD allografts including older DCD donors should be encouraged.

OP144 PRIORITIZING DONOR HEPATECTOMY DURING COMBINED LUNG AND LIVER PROCUREMENT IN DCD DONORS IS SAFE AND FEASIBLE: A SINGLE CENTRE EXPERIENCE

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Background: Prolonged donor hepatectomy time (dHT) impairs both short- and long-term outcome after liver transplantation (LiT). Such a negative impact is not observed for lung transplantation (LuT). Since 2/2017, priority is given to procure the liver before the lungs during multi-organ donation after circulatory death (MOD-DCD) procedures in our centre. We evaluated if prioritizing hepatectomy over pneumectomy in MOD-DCD reduced dHT, and whether this affected outcomes after LiT and LuT.
Methods: All MOD-DCD procedures from 2010-2020 where both liver and lungs were procured by our centre were retrospectively reviewed. dHT was defined as the time between the start of cold flush and immersion of the graft in ice-cold preservation solution. We compared dHT before and after 2/2017, as well as one year patient survival, death-censored graft survival, primary graft dysfunction (PGD) after LiT and LuT, and non-anastomotic biliary strictures (NAS) after LiT.
Results: Thirty-two MOD-DCD procedures were performed before 2/2017 (median dHT 39 min [IQR 30-44]) and 19 procedures after 2/2017 (34 min [32-36], $P = 0.06$). In a linear regression model, there was a significant negative correlation between the year of MOD-DCD and dHT (Rho = -0.32, $P = 0.02$) (Figure 1). Patient survival and graft function in LiT and LuT did not differ between era's and are presented in Table 1.
Conclusions: In our center, an increasing awareness to keep dHT as short as possible resulted in gradual but significant decrease of dHT in MOD-DCD from 2010 to 2020. Formalizing the protocol in 2/2017 for MOD-DCD procedures, i.e. prioritizing hepatectomy over pneumectomy, did not further reduce dHT. Importantly, prioritizing hepatectomy in MOD-DCD did not have a negative impact on LuT outcome, suggesting it is not only a feasible, but also a safe strategy to effectively reduce dHT.

Table 1.

	Before Feb 2017	After Feb 2017	*P*-value
Liver transplant outcomes			
One year patient survival	26/27 (96%)	10/11 (91%)	0.50
One year graft survival (death censored)	25/26 (96%)	10/10 (100%)	> 0.99
PGD	5/27 (19%)	3/14 (21%)	> 0.99
NAS within 1 year	6/27 (22%)	2/14 (14%)	0.69
Lung transplant outcomes			
Any PGD 3 within 72 h	12/33 (36%)	4/19 (21%)	0.35
One year patient survival	29/33 (88%)	12/17 (71%)	0.24
One year graft survival (death censored)	29/29 (100%)	12/12 (100%)	> 0.99

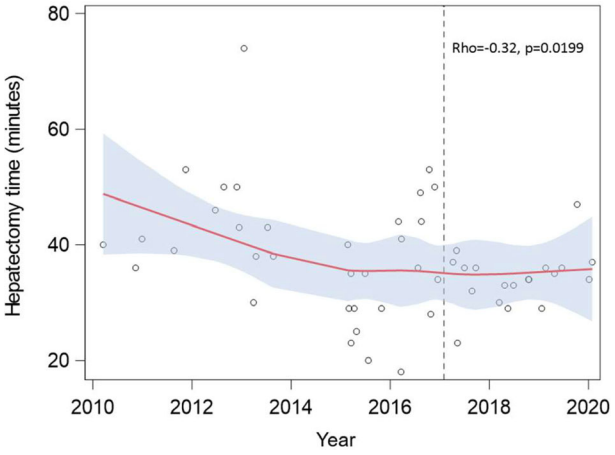

Figure 1.

OP145 COMPUTERISED INTEGRATION OF ALTERNATIVE LIVING DONOR KIDNEY TRANSPLANTATION PROGRAMS: FIRST PROMISING RESULTS FOR DIFFICULT-TO-MATCH PATIENTS

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Background: Computerised Integration of Alternative Transplantation (CIAT) programs was developed to increase the chances of highly immunized (HI) and long waiting (LW) kidney transplant candidates. CIAT integrates AB0-desensitisation, HLA-desensitisation, donor-exchange, altruistic and domino-paired donation. Strict criteria were defined for selected HI (sHI) patients. sHI patients are given priority, and dependent on titers, AB0-incompatible (AB0i) and/or HLA-incompatible matching (HLAi) is allowed. LW candidates (> 2y dialysis) can opt for an AB0i match. In a 1 center simulation of 2015-2016, CIAT matched 8 out of 20 sHI patients. Six matches had a negative CDC cross-match, 2 of them were AB0i. Two matches had a positive CDC cross-match (one was negative in 1:4 dilution).
Methods: From 2017 onwards CIAT algorithm was tested in our center to gain logistic experience, and to optimize the program. Protocols have been created and pathways were developed for recognition of sHI and LW candidates, for logistics and patient information. CIAT runs were performed between national runs.
Results: Between 2017 and 2020, 105 couples, 21 unspecified donors (UD), 47 sHI and 55 LW patients and all waiting list patients were included in CIAT. 58 transplantations were accomplished: 54 compatible, and 4 AB0i transplantations. 9 sHI patients were matched. 1 cross-match was CDC positive (1:4 dilution negative), but HLAi transplantation was cancelled during COVID. 8 couples with negative CDC cross-matches were transplanted, 3 were AB0i. Their median vPRA was 95% (range 91-100), median age 50 years (range 25–73) and median waiting time 4 y (range 1 y–9 y). 13 LW patients were transplanted: 12 compatible and 1 AB0i, median waiting time 3 y (2 y–6 y). 5 UD's donated to the waitlist, 16 initiated chains (10 doublets, 6 triplets). There were 7 kidney-exchange cycles (6 doublets, 1 triplet). In the same period, 11 pairs were transplanted through the national exchange program: one sHI patient was matched.
Conclusions: CIAT yields very promising results for sHI and LW candidates. Negotiations on national implementation, are ongoing. Extrapolation of our results to national size would mean between 16-20 sHI transplants per year. Apart from an enormous health-gain for sHI and LW patients this means a vast reduction of healthcare costs.

OP146 ALTRUISTIC KIDNEY DONATIONS: OPTIMIZING UTILITY AND BENEFICENCE

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Background: Altruistic Donors (AD) do not have any genetic or emotional relationship with recipients. We review trends in characteristics, utilization, and impact of donor-recipient factors on graft survival in the United States.
Methods: All Adult (≥18 years) Living Kidney Donors who were recorded in the UNOS (United Network for Organ Sharing) database as Code 10 (Anonymous) from Oct 1997 through Sep 2017 were reviewed along with Recipients and Transplant Outcomes from ADs. Death censored Kidney Graft Survival (DC-KGS) and overall survival were estimated using Kaplan-Meier (KM) Method. Cox proportional hazards model was used to evaluate the association between risk factors and KGS.
Results: 2174 donor-recipient pairs were reviewed during the study period. Donor, recipient characteristics, transplant outcomes and DC-KGS are shown in Table 1. Controlling for recipient age, race, whether delayed graft function (DGF) occurred, and pre-emptive transplant status, patients who were treated for rejection within one year had an increased hazard of kidney graft failure compared to patients who were not treated for rejection within one year. Controlling for recipient age, race, pre-emptive transplant status, and whether the patient was treated for rejection within one year, patients who had DGF had an increased hazard of kidney graft failure compared to patients who did not have DGF. KM survival analysis showed longer DC-KGS when the Donor was at least 20 years younger than recipient compared to donors who were closer in age to the recipient or older ($P = 0.0087$).
Conclusions: Transplants from Anonymous Living Donors have excellent long term outcomes. Better matching of controllable donor-recipient factors like age and BMI in addition to routine matching algorithms can improve graft survival. Application of this in Paired Kidney Donation particularly compatible sharing can optimize the utility and beneficence from this invaluable donation.

Table1

Donor Characteristics		Recipient Characteristics	
Age, mean ± SD; median (min-max) (years)	44.0 ± 12.2; 45 (18-76)	Age, mean ± SD; median (min-max)(years)	49.4 ± 13.2; 51 (18-79)
Race, n (%) Caucasian African American Other	 2,015 (92.7%) 51 (2.4%) 108 (5.0%)	Race, n (%) Caucasian African American Other	 1,472 (67.7%) 337 (15.5%) 365 (16.8%)
Female Male	1224 (56.3%) 950 (43.7%)	Female Male	883 (40.6%) 1,291 (59.4%)
BMI, mean ± SD; median (min-max)	25.7 ± 3.9; 25.4 (15.7-42.2)	BMI, mean ± SD; median (min-max)	27.9 ± 5.6; 27.5 (11.3-52.1)
History of Hypertension, n (%)	42 (2.1%)	and Pre-emptive, n (%)	486 (22.4%)
Blood Type, n (%) O A B AB	 1,003 (46.1%) 824 (37.9%) 261 (12.0%) 86 (4.0%)	Waiting Time (on List), mean ± SD; median (min-max)	656.8 ± 597.5; 485 (0-4941)
Donor Nephrectomy Side, n (%) Left Right	 1,899 (87.4%) 275 (12.7%)	Most Recent Peak PRA, n (%) <=20 21-80 >80	 2,060 (94.8%) 80 (3.7%) 34 (1.6%)
ABO Match, n (%) Identical Compatible Incompatible	 1940 (89.2%) 217 (10.0%) 17 (0.8%)	Cause of ESRD, n (%) DM HTN PKD FSGS IgA Others	 457 (21.0%) 342 (15.7%) 298 (13.7%) 151 (6.9%) 122 (5.6%) 804 (37.0%)
Transplant Characteristics			
HLA Mismatch Level, n (%) 0 21(1.0%) 1-4 1058 (49.2%) 5-6 1069 (49.8%)		BMI Mismatch (Recipient – Donor), mean ± SD; median (min-max) 2.2 ± 6.6; 2.1 (-19.2-31)	
Age Mismatch (Recipient – Donor), mean ± SD; median (min-max).			5.4 ± 16.0; 4 (-40-51)
Recipient Age Older > 20 years Donor Age, n (%)			413 (19.0%)
Donor Age Older > 20 years Recipient Age, n (%)			141 (6.5%)
Transplant Outcomes			
One Year Acute Rejection Rate, n (%)		166 (7.6%)	
Delayed Graft Function, n (%)		90 (4.1%)	
Recipient Died with Functioning Kidney, n (%)		174 (8.0%)	
Graft Survival (Death as a Censoring Event), n (%)(KM Method) One year Five years Ten years		 1,685 (97.6%) 764 (90.6%) 183 (74.8%)	

Kidney Graft Survival: Death Censored Multivariable Analysis (overall model p value < 0.0001)			
	Hazard ratio	Confidence Interval	p-value
Recipient Age, one-year increase	0.98	0.97 – 0.99	0.0014
Race Black vs Caucasian	1.09	0.78 – 1.54	0.2176
Delayed Graft Function, Yes vs No	5.00	3.40 – 7.35	<.0001
Treated for Rejection within One Year, Yes vs No	1.95	1.36 – 2.78	0.0003
Pre-emptive Transplant, No vs Yes	1.38	0.95 – 2.00	0.0927

OP147 MEASURING THE GAINS OF THE PARTICIPATION OF COMPATIBLE PAIRS TO KIDNEY EXCHANGE PROGRAMS AT A LOCAL LEVEL.

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Background: Kidney paired donation (KPD) enables kidney transplant candidates with willing, but incompatible living donors, to join a registry of other incompatible pairs in order to obtain transplant solutions potentially compatible. A strong correlation between the number of pairs enrolled in a KPD program and the success of the matching runs has been widely demonstrated. Expanding the pool of potential donors is a strategy to increase the probability of finding a compatible match, especially for 0 blood type and high sensitized recipients. The inclusion of compatible pairs in KPD programs has been suggested as a valuable option to provide undeniable benefits for recipients of incompatible pairs, whereas advantages for compatible pairs seem to be more questionable.
Methods: To assess the overall benefit of compatible pair participation (CPP) in a KPD program, a retrospective study on 444 pairs (312 compatible pairs and 132 incompatible pairs) who referred to a Single Transplant Centre for living donor transplantation, was conducted. The matching algorithm of the current study was designed in order to improve the overall quality of the matches by maximizing the number of transplants, avoiding or reducing desensitization treatments and minimizing the Living Kidney Donor Profile Index (LKDPI) of each pair in a maximum of 3-way loop.
Results: Simulation's results showed that, by combining KPD and CPP, a 2% increase in the overall number of transplant ($n = 10$) was recorded. Concurrently, a 50% decrease ($n = 52$) in the desensitization treatments and an improvement in the total score of LKDPI (from 11,556 to 7967) was achieved. Interestingly, in the subgroup of compatible pairs, the overall LDKT score decreased from 4736 to 1694.
Conclusions: Our results suggested that this strategy can potentially benefit not only incompatible pairs but also compatible pairs without being for them a pure altruistic participation. A detailed informed consent about the option of participating to a KPD program for compatible pairs should include the potential gain of improving the quality of the match and the LKDPI.

OP148 OUTCOMES IN CADAVERIC UTERUS TRANSPLANTATION

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Background: Uterus transplantation (UT) is the only treatment for women with uterine factor infertility (UFI). Procurement from dead brain donation (DBD) has proved to be safe for both life-saving organs and graft survival with comparable outcomes to living donation (LD); however, there have been only isolated cases with deceased donors (DD). We present our experience using DD which is the world's largest.
Methods: This is an analysis of prospectively collected data of UTx from DD performed at the Cleveland Clinic. Recipient inclusion criteria were absolute UFI, BMI < 30 kg/m^2, ages 18 to 45 and at least six frozen embryos ready to be implanted. Child-bearing age donors with no uterine abnormalities were considered for donation, prioritizing those who had a previous term pregnancy.
Results: Eight UT from DD have been performed since 2016. No injuries to donor's life-saving organs were reported. Mean procurement time was 249 min (158-367), whereas mean operative time was 537 min (334-870). The average cold ischemia time was 300 min (110-434) and the mean hospital stay was 11 (5-30) days. No death occurred and all recipient are well. Two grafts were lost: one because of arterial pseudoaneurysm due to candida albicans infection on post-operative day (POD) 12 and a second one due to vascular thrombosis on and POD 6. The reinstitution of menstruation occurred on average on POD 22. Three patients became pregnant with the first embryo transfer attempt. Graft rejection was observed and successfully treated in two patients. No hypertension or preeclampsia occurred, whereas one case of gestational diabetes was reported. Renal function remained normal in all recipients with mean creatinine value of 0.81, 0.89 and 0.92 mg/dl, respectively, at 3, 6 and 12 months after UT. Three women had a successful pregnancy and a delivery of a healthy baby on weeks 34+2, 34+6 and 34+2. A fourth patient is pregnant (third trimester) and two patients are currently undergoing embryo transfers.
Conclusions: Our results of UT using DD are comparable to those with LD. The use of DD eliminates the burden of donor complications and many ethical problems. Although it is premature to state that DD grafts are capable of establishing and carrying a pregnancy as a native organ, we do have encouraging findings.
Table: Outcomes

	Postoperative Complications	Pregnancy	Healthy Baby Delivery	Creatinine (md/dL) at post-operative month		
				3	6	12
1	Hysterectomy due to arterial mycotic pseudoaneurysm (POD12)	NA	NA	NA	NA	NA
2	Grade 3 rejection	Grade 2 Rejection: placenta previa and accreta	Yes	0.89	0.90	1.2
3	Re-laparotomy for pelvic hematoma; DVT/PE; hemorrhagic ovarian cyst (POM2)	Subchorionic hematoma	Yes	0.74	0.88	0.81
4	Post-transplant DM and elevated HbA1C	Not yet	NA	0.79	0.67	0.81
5	Hysterectomy due to vascular thrombosis (POD6)	NA	NA	NA	NA	NA
6	Re-laparotomy on POD1 due to poor vascular window US; Grade 4 rejection	Gestational diabetes	Yes	0.80	0.89	0.7
7	Incisional hematoma	Not yet	NA	0.90	1.1	1.2
8	None	Ongoing; abnormal 2nd trimester bleeding	Anticipated March 2021	0.75	0.93	0.82

ABDOMINAL TRANSPLANTATION: BITTERSWEET INTERACTIONS

OP149 BETA-CELL DEATH, RATHER THAN INSULIN RESISTANCE, DRIVES HYPERGLYCAEMIA IN ORGAN DONORS.

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Background: Donor hyperglycaemia following brain death had been attributed to reversible insulin resistance and is treated with insulin therapy. Our islet and pancreas transplant recipient data show that donor insulin therapy is related to lower beta-cell function and survival 3-months post-transplant suggesting that mechanisms other than insulin resistance are predominant. We hypothesized that beta-cell death drives donor hyperglycaemia.
Methods: Clinical data and plasma samples were obtained from brain dead pancreas donors. Glucose, c-peptide and Homeostasis Model Assessment determined glycaemic control, beta-cell function (HOMA-β) and insulin resistance (HOMA-IR). Levels of circulating unmethylated cell-free DNA (uCFDNA) of the insulin (INS1) gene promoter and microRNA-375 assessed beta-cell death, whilst uCFDNA of the REG1A and CUX2 genes represented pancreatic exocrine (PE) cell death. Data were compared between 'insulin-treated' and 'not insulin-treated donors' (IT *vs.* not-IT).
Results: In 92 pancreas donors, 40 (43%) required insulin. Glycaemic control and beta-cell function were poorer in IT donors than in not-IT donors (median [IQR] peak glucose: 8 [7-11] *vs.* 6 [6-8] mmol/l, $P = 0.016$; C-peptide: 3195 [2868-3386] *vs.* 3280 [3159-3386] pmol/l, $P = 0.046$; HOMA-β 69 [45-95] *vs.* 99 [75-116] %, $P = 0.028$). Insulin resistance was similarly elevated regardless of donor insulin status (2.6 [2.3-2.9] vs 2.6 [2.4-2.9], $P = 0.743$). IT donors had higher levels of INS1 (35 [18 = 52] *vs.* 30 [8-51] copies/ml, $P = 0.035$) and miR-375 (1050 [188-1950] *vs.* 725 [315-1100] copies/nl, $P = 0.05$) but similar levels of PE (19 [11-36] *vs.* 17 [7-42] copies/ml, $P = 0.283$). INS1 and miR-375 levels were related to c-peptide levels (β [SE]; INS1: 683 [287], $P = 0.020$; miR-375: 688 [281], $P = 0.017$).
Conclusions: In pancreas donors, hyperglycaemia requiring insulin therapy occurs because of beta-cell death rather than insulin resistance and may explain the relationship with post-transplant beta-cell dysfunction.

OP150 PERIOPERATIVE THROMBOINFLAMMATORY MARKERS DIFFER IN PANCREAS TRANSPLANT ALONE AND SIMULTANEOUS PANCREAS-KIDNEY RECIPIENTS AND PREDICT GRAFT THROMBOSIS

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Background: Pancreas graft survival is lower for pancreas transplant alone (PTA) compared to simultaneous pancreas-kidney (SPK) transplants; the pathophysiology, however, is unknown. Thrombosis is the predominant reason for early graft loss and is more common in PTA recipients. We hypothesized that perioperative differences in thromboinflammatory markers exist between PTA and SPK recipients and between PTA patients with and without a graft thrombosis.
Methods: Preoperative and daily plasma samples during the first postoperative week were obtained for 32 PTA and 35 SPK patients. Coagulation marker thrombin-antithrombin complex (TAT), complement activation products C3bc and terminal complement complex (TCC), and 13 of 27 cytokines, were detected with enzyme-linked immunoassays.
Results: Venous pancreas graft thrombi ($P = 0.003$) and 1-year graft losses ($P = 0.046$) were significantly higher in PTA than SPK recipients. Preoperatively, coagulation and complement markers were similar, while TNF, IP-10, MCP-1, MIP-1α, and IL-4 were significantly higher in SPK compared to PTA recipients. Postoperatively, PTA recipients had higher TAT concentrations on the first postoperative day ($P = 0.008$), while TNF, IL-1ra, MIP1-α and IL-4 were significantly higher overall during the first postoperative week in SPK recipients. PTA recipients with versus without graft thrombosis had higher TCC preoperatively and on postoperative day one ($P = 0.038$ and $P < 0.001$, respectively). TCC increased the risk for graft thrombosis (0.1 TCC increase odds ratio 1.5 [95% CI 1.0-2.2], $P = 0.043$ preoperatively and 1.3 [1.1-1.5], $P = 0.009$ postoperatively).
Conclusions: Early postoperative coagulation activation was higher in PTA than SPK recipients and general inflammation more pronounced in SPK recipients. Pre- and postoperative complement activation was associated with increased risk of graft thrombosis. Activation of thromboinflammatory markers may affect outcome and serve as targets for future interventions.

OP151 DIFFERENTIALLY METHYLATED CELL FREE DNA MONITORING IN PANCREAS TRANSPLANT RECIPIENTS WITH FUNCTIONING GRAFT

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Type 1 diabetes (T1D) is characterized by pancreatic βcells destruction. Pancreas and islet transplantation are an alternative therapeutic approach to revert the situation. Despite of use immunosuppressive therapy, allograft rejection continues being a risk, and cell-free DNA (cfDNA) poses as an attractive biomarker. In T1D patients, differentially methylated DNA encoding preproinsulin (INS) in the plasma correlates with β-cell death. In islet, quantification unmethylated-INS (INS-cfDNA) levels at 24 h correlate with graft outcomes. We aimed at evaluating the dynamic of INS-cfDNA in pancreas transplant recipients with a functioning graft.
We conducted a prospective longitudinal study including all pancreas transplant recipients from 2017 to 2018. Induction immunosuppression protocol in all patients included with thymoglobulin, tacrolimus, mycophenolate, and prednisone. Plasma samples were collected in PAXgene tubes before transplant (D0), 1 h, 24 h and 7 days (D7) post-transplant and at the moment of protocol biopsy (3 weeks and 12 months). Patients with biopsy-proven acute rejection were excluded. cfDNA concentration was determined by Qubit. INS-cfDNA was converted with a bisulfite and quantification performed by digital droplet PCR.
A total of 22 of patients were included in the analysis. Total cfDNA levels increased significantly 1 h post-reperfusion compared to baseline (D0). Afterwards, the evolution of the cfDNA concentration reflected a progressive decrease until B3, and an increment at B12 (D0 (3.72 ± 3.67), 1 h (11.28 ± 10.28), 24 h (5.94 ± 5.18), D7 (5.74 ± 3.90), B3 (3.98 ± 3.44) and B12 (7.04 ± 2.29)). In *de* novo T1D patients, INS-cfDNA was significantly increased compared to baseline (D0) of patients with long-standing T1D (15.63 ± 3.78 vs 0.10 ± 0.12). On longitudinal analysis, there was a tendency towards an increment in cfDNA-INS at 1h (0.93 ± 1) and 24h (2.30 ± 4.51) ($P > 0.05$). Interestingly, at B12 there was a significant increase (8.19 ± 5.39) compared to all previous determinations ($P < 0.001$). We describe a preliminary longitudinal analysis of the dynamic of circulating INS-cfDNA in a cohort of pancreas transplant recipients. The correlation with outcomes should be addressed in a larger cohort to evaluate it ability as a biomarker to predict graft function, acute rejection, or diabetes relapse.

OP152 COMPARABLE OUTCOMES FOR CIRCULATORY DEATH AND BRAIN-STEM DEATH PANCREAS TRANSPLANTATION IRRESPECTIVE OF THE USE OF NORMOTHERMIC REGIONAL PERFUSION

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Background: Simultaneous pancreas and kidney transplantation is the optimum treatment for patients with type 1 diabetes and renal failure, providing survival benefit over deceased donor kidney transplant alone.
Methods: We performed a retrospective analysis of prospectively collected outcomes of the first 10 years of our Donation after Circulatory Death (DCD) pancreas transplant program, including DCD donors undergoing Normothermic Regional Perfusion (NRP).
Results: 211 patients (139 donation after brainstem death (DBD), 72 DCD (59 conventional DCD and 13 NRP retrieval)) were included in the study. Patient survival at 1, 3, 5, and 10 years was 99.0%, 96.6%, 93.4% and 84.3%, respectively, with no significant difference in patient survival between those recipients receiving grafts from DBD or conventional DCD donors. Death-censored pancreas and kidney graft survival at 5 years was 83.9% and 93.2%, respectively, with no significant difference between DCD and DBD cohorts. For those receiving a DCD graft, patient survival, and pancreas and kidney transplant outcomes were comparable, irrespective of whether the organs were procured conventionally or following NRP.
Conclusions
In conclusion, utilisation of DCD pancreases is a safe approach to expanding the donor pool with equivalent results to DBD transplantation. Pancreas transplantation following NRP appears to be feasible, but warrants further study.

OP153 UTILITY OF DONOR-DERIVED CELL-FREE DNA IN PANCREAS-KIDNEY TRANSPLANTATION

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Background: Among solid organ transplants, pancreas transplantation is one of the leading causes of acute rejection within the first 12 months. Graft

biopsy, the gold standard, is risky and often not accessible. Hence, a non-invasive biomarker with good predictive value, such as donor-derived cell free DNA (dd-cfDNA), may be useful in predicting risk of rejection. In this study, we sought to analyze the utility of a dd-cfDNA test in patients with SPK - simultaneous pancreas-kidney transplant, and PAK- sequential pancreas after kidney transplant.
Methods: A retrospective study was conducted from 2017 to 2020 at the Hospital Clínic Barcelona, on patients admitted for a pancreas graft biopsy. Plasma samples were collected on the day of biopsy. Dd-cfDNA fraction was assessed using Prospera™, a SNP-based mmPCR methodology to assess risk of rejection (either T-cell mediated rejection [TCMR] or antibody mediated rejection [ABMR]).
Results: Of the 57 samples (SPK $n = 47$ and PAK $n = 10$), 75% (43/57) had confirmed biopsy (Banff criteria: No rejection $n = 29$; Indeterminate $n = 5$; aTCMR grade 1-3 $n = 8$; aABMR $n = 1$). In SPK recipients, dd-cfDNA levels were elevated in patients with graft rejection (TCMR 0.99 [0.52-3.05] or ABMR 8.24 vs no rejection 0.68 [0.34-1.01]; $P = .0051$) Figure 1. However, no significant difference in dd-cfDNA was observed between stable ($n = 6$) and rejection ($n = 4$) groups in PAK recipients. In stable patients, dd-cfDNA levels were highly elevated in SPK patients (0.65 ± 1.2%) compared to PAK (0.22 ± 0.05%; $P = .019$).
Conclusions: dd-cfDNA assay can differentiate rejection from stable graft in SPK patients. Further analysis would be needed to understand the baseline differences observed in the dd-cfDNA levels between SPK and PAK and between ABMR and TCMR.

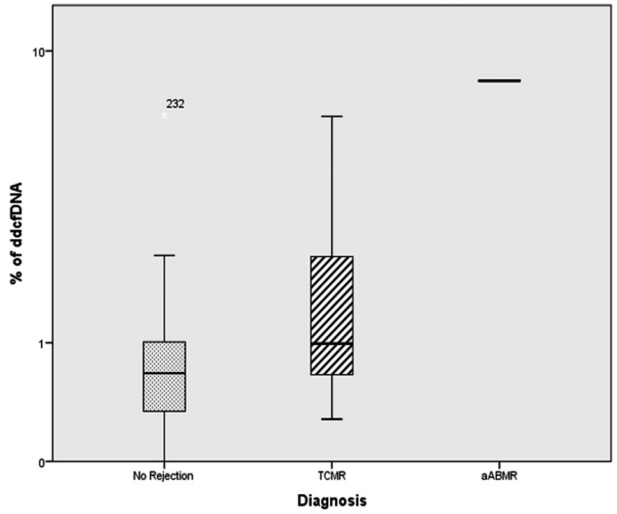

Figure 1 Association between percentage dd-cfDNA in SPK patients and the type of rejection

OP154 EFFICACY AND SAFETY OF PANCREAS TRANSPLANT ALONE (PTA) IN SUBJECTS WITH TYPE 1 DIABETES (T1D): 15 YEAR ACTUAL FOLLOW-UP

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Background: PTA represents the only approach for restoring long-term normoglycemia in diabetic patients by replenishment of beta cell functional mass. However, the long-term safety and efficacy of PTA in T1D is still debated.
Methods: In the present study, we report the outcomes of PTA as performed in our center, after 15 years actual follow-up. Forty-four consecutive patients were studied (re-transplants excluded), having the following clinical characteristics at time of transplant: age, 37.5 ± 8.2 years; 20 males and 24 females; BMI: 23.7 ± 3.1 kg/m^2; duration of diabetes, 24.5 ± 9.6 years; C-peptide values: 0.1 ± 0.2 ng/ml; insulin requirement, 43.5 ± 12.7 IU/day. PTA was performed with the portal-enteric drainage. The anti-rejection induction phase included basiliximab in 84% of cases or ATG in the remaining 16%. Tacrolimus and mycophenolate mofetil were used in the maintenance phase.
Results: After 15 years from the transplant, patient survival was 81.8% (36/44 patients), with a mortality rate per year of 1.2%. Based on the recent Igls criteria, pancreas graft function was excellent or good in 58.3% of cases (excellent: 50%; good: 8.3%). At 15 years since PTA, 8 patients (18.2%) developed stage 4 (4 pts) or 5 ESRD (3 pts), which was mainly associated with lower pre-PTA eGFR. Of them, 3 subjects started dialysis replacement therapy to then received a kidney transplant.
Conclusions: These actual 15-yr results show that PTA is an effective and reasonably safe option to cure diabetes in selected cases of T1D patients.

OP155 PRELIMINARY ITALIAN EXPERIENCE OF COMBINED LIVER TRANSPLANTATION AND SLEEVE GASTRECTOMY

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Background: Obesity currently represents one of the major public health concerns leading to chronic diseases such as non-alcoholic steatohepatitis (NASH) related cirrhosis. During the last years liver transplantation (LT) for NASH cirrhosis was increasingly performed in Europe, accounting for approximately 6% of transplant indications. Unfortunately, post-transplant outcome in obese patient is usually impaired by higher incidence of metabolic and cardiovascular complications and recurrent or de novo NASH. To reduce morbidity and mortality rates, bariatric surgery was proposed at the time of LT.
Methods: From January 2016 to December 2020 five combined LT and sleeve gastrectomy (SG) were performed at Tor Vergata University, Rome. Median recipients age was 48 years (IQR: 45-53). Main indication for LT was NASH cirrhosis ($N = 4$). One patient only suffered from hepatocellular carcinoma (HCC) on hepatitis C virus infection related cirrhosis. At the time of LT, patients had a median biological model for end-stage liver disease (MELD) score of 19 (IQR: 14-29) and median body mass index (BMI) of 47 kg/m^2 (IQR: 42-50). Out of 5 LT/SG recipients, four were insulin-dependent diabetes. Three of them also suffered from arterial hypertension requiring antihypertensive drugs. All LT/SG were performed using brain death donor liver grafts. The SG was performed by an experienced bariatric surgeon following completion of LT.
Results: Median follow-up was 18 months (IQR: 4-37). One patient only experienced multi-organ failure and died 15 days after LT. At the last clinical follow-up, patients had normal liver function tests, median BMI of 35 kg/m^2 (IQR: 30-39) thus achieving 19% of body weight loss. After transplantation, two patients showed arterial hypertension resolution. Among patients with diabetes, 3 of them turned out to be diet-controlled.
Conclusions: Combined LT/SG in selected recipients resulted in an effective and stable weight loss thus reducing metabolic complications.

OP156 LIVER INCLUSION IN INTESTINAL TRANSPLANTATION: SINGLE-CENTER EXPERIENCE

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Methods: Retrospective analysis was performed. Target tacrolimus trough levels were lower in liver-inclusive (4-5 μg/l) versus isolated ITx (7-8 μg/l). Subgroup analysis by Fisher's exact test and Kaplan-Meier analysis for survival estimation were performed.
Results: 24 ITx were performed in 21 patients, between 2000 and 2021. Isolated ITx was performed in 11 patients and liver-inclusive ITx in 13 (8 combined liver-ITx and 5 multivisceral). Living-donor isolated ITx was

performed in 1 patient. Re-ITx was performed in 3 patients for chronic rejection ($n = 1$); acute rejection ($n = 1$); and acute rejection & CMV ($n = 1$) at 14, 1 and 3 years after ITx, respectively. Intensive care unit (ICU) and hospital stay were longer after liver-inclusive ITx (table). Isolated ITx recipients experienced more severe (grade 2-3) late (>3 months) acute and chronic rejection *vs.* liver-inclusive ITx (6 *vs.* 0 ($P = 0.0034$) and 2 *vs.* 0, respectively). In both groups, three recipients died. No Graft versus Host disease (GvHD) was seen and post-ITx lymphoma (PTLD) was diagnosed in one patient post-mortem. All 15 survivors, of which 5 isolated and 10 liver-inclusive ITx, are nutritionally independent and well. After isolated ITx, 1/5/10 years graft & patient survival were 64%/51%/51% and 91%/65%/51%, respectively. After liver-inclusive ITx, 1/5/10 years graft and patient survival were 84%/84%/84%.

Conclusion: Even in a relatively small ITx cohort, the protective effect of liver-inclusion against rejection is clear, despite lower immunosuppression. The protective effect outweighs the risk of major surgery, without effect on GvHD or PTLD, and resulting in superior long-term graft survival after liver-inclusive versus isolated ITx.

	Isolated ITx (N=11)	Liver-inclusive ITx (N= 13)
Re-transplant	1	2
Post-transplant ICU-stay *(median; range)*	11 days (2–60)	14 days (7–70)
Post-transplant hospital stay *(median; range)*	85 days (55–319)	125 days (66–680)
Follow-up *(median; range)*	3.5 years (0.75–16)	6.75 years (0.25–18)
Severe early acute rejection Grade 2 Grade 3	 1 2	 3 1
Severe late acute rejection Grade 2 Grade 3	 1 5	 0 0
Chronic rejection	2	0
Post-transplant lymphoma	0	1
Graft-*vs.*-host disease	0	0
Graft survival: 1/5/10 years	64%/51%/51%	84%/84%/84%
Patient survival: 1/5/10 years	91%/65%/51%	84%/84%/84%

OPTIMISING OUTCOMES AFTER HEART TRANSPLANTATION: FROM A LITTLE SPARK MAY BURST A FLAME

OP157 SHORT-TERM INTERLEUKIN-6 BLOCKADE PREVENTS ALLOGRAFT REJECTION UNDER COSTIMULATION BLOCKADE IN MURINE CARDIAC TRANSPLANTATION

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Background: The costimulation blocker CTLA4-Ig is a non-nephrotoxic alternative to Calcineurin-inhibitors. It has demonstrated superior patient and graft survival in kidney transplantation and also provided improved control of the humoral allo-immune response. However, its widespread use, especially in thoracic transplantation, is still hampered by an unacceptably high rate of acute cellular rejections. A rationally targeted induction regimen might overcome this obstacle.

Methods: C57BL/6 mice were transplanted with a fully mismatched Balb/c cardiac allograft and received anti-thymocyte globulin (ATG; 0.15 mg/day 0, 5), anti-interleukin-6 monoclonal antibodies (αIL6; 0.6mg day -1; 0.3 mg/day 4, 6) and CTLA4-Ig (0.25 mg/day 0, 4, 14, 28, 56, 84) as indicated. Heart allograft survival was followed by palpation for up to 100 days. Flow cytometry of peripheral blood, spleen and graft-infiltrating lymphocytes was performed.

Results: CTLA4-Ig monotherapy prolongs graft survival, but most grafts are rejected by day 45 (MST = 36 days). Adding ATG induction, led to a median survival time of 80 days. Combined induction therapy with ATG and anti-IL6 facilitated long-term (100 days) survival of fully mismatched cardiac allografts under CTLA4-Ig in all individuals (ATG+αIL6+CTLA4-Ig 8/8 vs. ATG+CTLA4-Ig 4/9; $P = 0.0152$). Mechanistically, the additional blockade of interleukin-6 delayed T-cell recovery upon ATG-mediated depletion and further increased the frequency of regulatory T cells (peripheral blood day 8 post HTX; ATG+αIL6+CTLA4-Ig: mean = 12.81%, 95%-CI = 16.21–9.40 vs. ATG+CTLA4-Ig: mean = 6.98%, 95%-CI = 8.42–5.36; $P = 0.0015$). In the long-term, the refined induction regimen disrupted the formation CD8 effector-memory T cells (spleen) and dramatically reduced CD8 T-cell infiltration in the heart allografts at day 100 post-transplant.

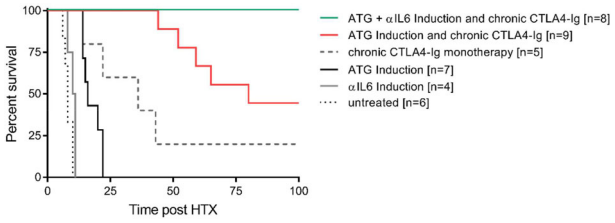

Figure 1 *Cardiac allograft survival*
C57/BL6 mice were transplanted with a fully mismatched Balb/c cardiac allograft and received treatments as indicated. HTX survival is depicted as Kaplan-Meier curve.

Conclusion
ATG and interleukin-6 blockade synergize as induction to prevent rejection under CTLA4-Ig immunosuppression in a clinically relevant experimental setting.

OP158 CD34+ CELL THERAPY IS ASSOCIATED WITH BENEFICIAL CLINICAL OUTCOMES IN ADVANCED CHRONIC HEART FAILURE PATIENTS LISTED FOR HEART TRANSPLANTATION

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Purpose: The impact of cell therapy in advanced heart failure patients listed for heart transplantation (HTX) is poorly defined. We sought to investigate the long-term effects of $CD34^+$ cell therapy in this patient population.

Methods: We enrolled data of all patients listed for heart transplantation at our center between 2007 and 2017. Pediatric patients (<18 years), patients with congenital heart disease, mechanical circulatory support, and patients awaiting multi-organ transplantation were excluded. Of 372 patients included, 33 patients (Group A) received $CD34^+$ cell therapy, and 339 (Group B) received optimal medical management. In Group A, autologous $CD34^+$ cells were obtained with apheresis and immunomagnetic selection, and injected transendocardially. All patients were followed for 1 year; the primary endpoint was the rate of delisting from HTX elective waiting list.

Results: At the time of HTX listing the two groups did not differ in age (56 ± 7 years in Group A vs. 54 ± 10 years in Group B, $P = 0.24$), gender (male: 100% vs. 80%, $P = 0.12$), heart failure etiology (ischemic; 44% vs. 39%; $P = 0.55$), history of hypertension (61% vs. 59%; $P = 0.99$), diabetes (26% vs 24%, $P = 0.80$), left ventricular ejection fraction (LVEF: 22 ± 3% vs. 24 ± 4%, $P = 0.15$) or NT-proBNP levels (3524 ± 3821 pg/ml vs. 4048 ± 3482 pg/ml, $P = 0.64$). Within 1 year after HTX listing patients in both groups did not differ in rates of HTX (48% in Group A vs. 50% in Group B, $P = 0.88$), LVAD implantation (0% in Group A vs. 4% in Group B, $P = 0.25$), or total mortality (3% vs. 10%; $P = 0.16$). However, in Group A, 24% of patients were delisted due to clinical improvement; compared to only 9% of patients in Group B ($P = 0.005$). At the time of HTX listing, the delisted patients displayed similar clinical characteristics than the remaining cohort (LVEF: 22 ± 2% in the delisted vs. 23 ± 4% in the remaining cohort, $P = 0.67$; NT-proBNP: 2822 ± 1198 pg/ml vs. 3983 ± 3927, $P = 0.45$, ishemic heart failure etiology: 43% vs. 39%, $P = 0.77$, history of hypertension: 61% vs. 58%; $P = 0.82$; or diabetes: 20% vs 27%, $P = 0.52$). On multivariate analysis, cell therapy was an independent correlate of delisting ($P = 0.002$).

Conclusion: $CD34^+$ cell therapy appears to be associated with beneficial clinical outcomes and increased rates of delisting in advanced heart failure patients awaiting heart transplantation.

OP159 SURVIVAL AFTER HEART TRANSPLANT VS. SIMULTANEOUS HEART KIDNEY TRANSPLANT BY DEGREES OF RENAL DYSFUNCTION AT TRANSPLANTATION IN THE UNITED STATES

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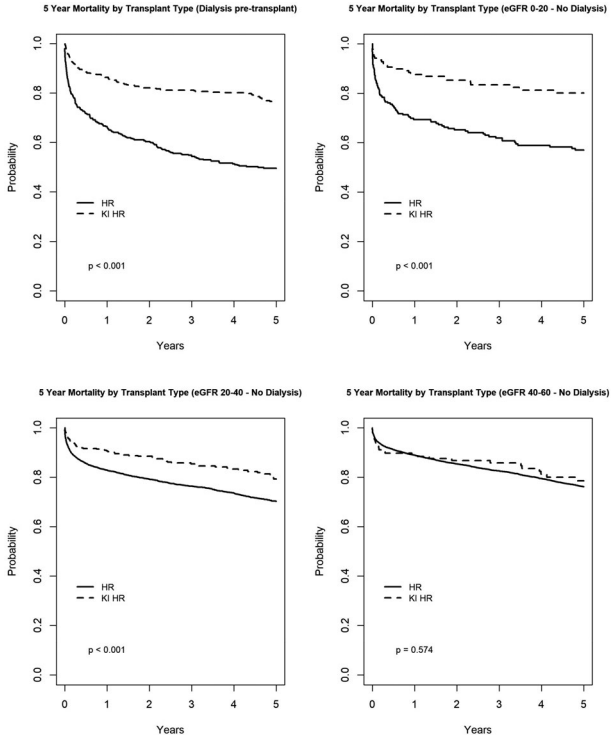
Background and Aims: There has been a rising trend for utilizing kidneys in heart transplant candidates with different renal dysfunction degrees. We sought to assess the impact of SHK in candidates with renal dysfunction.
Methods: We analyzed the SRTR between 1/1/2000 and 9/31/2019. We identified all primary adult heart transplant recipients (HAT) and simultaneous heart kidney transplants (SHK). We sorted the recipients based on the degree of renal dysfunction at the time of transplantation into: dialysis group, eGFR < 20, eGFR 20-40 and eGFR > 40-60 ml/min. Kaplan-Meier curves were generated to compare mortality by transplant type among the four groups. We analyzed predictors of mortality in each of the four groups separately. We used Cox proportional hazard models adjusted for recipient age, gender, race, diabetes status, heart transplant indication, ICU status, waiting time in weeks, transplant year, donor age, local vs. import organs, heart ischemia time and payor type. The transplant center was included as a random effect to account for center variability. Follow-up was censored at five years post-transplant.
Results: 14,728 received (HAT) and 1296 received (SHK). The proportion of SHK increased over the study period. SKH recipients were more likely to be publicly insured, diabetic, male, in ICU before transplant and non-white. The proportion of SHK recipients with reasonably good renal function (>40-60 ml/min) before transplantation was 11.3%. In the multivariable Cox regression model for recipients in the eGFR > 40-60 ml/min group, there was no survival benefit to SHK as compared to HAT (LLCI, **aHR,** ULCI) (0.61, **0.92**, 1.39). In the lower the GFR groups, compared to HAT, SHK was associated with 35% better survival in the eGFR 20-40 ml/min group (0.49, **0.65**, 0.85), 68% improved survival (0.18, **0.32**, 0.57) in the eGFR < 20 ml/min group and 55% improved survival (0.34, **0.45**, 0.58) in the dialysis group.
Conclusion: Compared to HAT, SHK appears to be associated with survival benefit when recipient eGFR is less than 40 ml/min or on dialysis. Utilizing kidneys in heart transplant recipients with eGFR > 40 ml/min at the time of transplantation is an unwarranted use of a scarce resource.



OP161 THE EXPRESSION LEVELS OF CIRCULATING MIR-101 AND MIR-27 ASSOCIATE WITH HEART TRANSPLANT ACUTE REJECTION

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Background and Aims: The acute rejection is a main cause of graft dysfunction in heart transplanted recipients. MicroRNAs (miR) are regulatory molecules that have potential value for post-transplant complications diagnostic. The aim of the study is to determine the diagnostic value of miR levels for acute rejection and to evaluate its relationship with biomarkers: fibrosis (galectin-3), rejection (ST2), neoangiogenesis (placental growth factor, PLGF).
Methods. The study enrolled 72 heart recipients, aged 16 to 70 (48.6 ± 10.9) years and 38 patients with severe chronic heart failure, aged 26 to 70 (48.8 ± 9.9) years. The control group consisted of 12 healthy individuals who did not differ significantly by sex and age. Expression levels of five miRs (-27, -101, -142, -339, -424) were measured by PCR in plasma; concentrations of galectin-3, ST2, PLGF, were measured by ELISA. Graft rejection was verified through morphological analysis of endomyocardial biopsy specimens.
Results: Patients with end-stage chronic heart failure had significantly higher levels of miR-27, -339 and -424 compared with the healthy individuals ($P = 0.02$, $P = 0.0001$, $P = 0.001$, resp.). The levels of miR-101 and miR-27 in recipients with acute graft rejection are significantly lower than in recipients without rejection ($P = 0.04$ and $P = 0.03$, resp.). When the miR-101 expression level is below the determined threshold value (-8.36 fold change), the risk of acute graft rejection is RR = 1.8 [95% CI 1.13–3.01]. When the miR-27 expression level is below -5.07 fold change RR = 1.9 [95% CI 1.12–3.37]. The risk of rejection by simultaneous decrease of miR-101 and -27 below threshold values is RR = 2.0 [95% CI 1.16–3.36]. MiR-27 expression levels in heart recipients correlated with ST2 ($P = 0.02$) and PLGF concentrations ($P = 0.02$).
Conclusion: In heart recipients, miR-101 and -27 have a diagnostic value for acute rejection and correlate with the plasma levels of ST2 and PLGF.

OP162 REAL WORLD DATA OF EVEROLIMUS WITH OR WITHOUT CALCINEURIN-INHIBITORS ON LONGTERM OUTCOME AFTER HEART TRANSPLANTATION

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Background: Despite many clinical studies investigated the effect on everolimus (ERL) on on outcome, the best time point when to start ERL with or without calcineurin-inhibitors (CNIs) in the clincal practice is still under discussion. Thus, we studied the long-term effect of ERL in the clinical routine on outcome after HTx.
Methods: 105 patients were divided into 3 main groups (MG) according to the time of ERL start; MG1: ERL start ≤3 months (mo) after HTx ($n = 46$), MG 2: ERL start 4-12 months after HTx ($n = 33$) and MG 3: ERL start > 12 months after HTx ($n = 26$). Patients of MGs were divided in patients with early CNI withdrawal ≤3 months (sub-group, SG, 1, $n = 25$) or in CNI therapy > 12 months (SG2, $n = 71$) after ERL start. Incidence of BPACR (≥2R) was compared between the groups at 12 and 60 months after HTx. Cardiac allograft vasculopathy (CAV) was assessed with coronary angiography. Glomerular filtration rate (GFR) was calculated (MDRD formula) in relation to baseline value before ERL start, and up to 60 months after ERL start (ΔGFR ml/min).
Results: Patients of MG1 had a higher ΔGFR at 60 months after ERL start compared MG2 and MG3 (MG1: +1.6, G2:-12.7, G3: -6.3, p1vsp2 = 0.035 and p1vsp3 = 0.27). In all MGs, early CNI withdrawal (SG1+2) led to a higher GFR compared to concomitant CNI therapy at 60 months after HTx. Incidence of BPACR at 12 months after HTx showed no differences between the main groups (MG1:15.2%, MG2:19.1%, MG3:19.2%, $P = 0.72$). However, CNI-free patients of MG1 had a higher incidence of BPACR than patients with concomitant CNI therapy of MG1 at 12 months (SG1:33.3% vs. SG2:6.9%, $P = 0.03$) and at 60 months (SG1:22% vs. SG2:0%, $P = 0.049$). All BPACR were without hemodynamic compromise. Regarding CAV, no significant difference was seen at 60 months (MG1:11.8%, MG2:5.6%, MG3:8%, $P = 0.74$). The incidence of CMV infections was significantly lower only at 12 months in patients MG1 compared to MG3 (15.2% vs. 42.3%, p1vs3 = 0.01).
Conclusion: Real-life data show that early ERL start within 3 months after HTx had a long-term beneficial effect on renal function. CNI withdrawal

within 3 months after ERL start further enhanced the nephroprotective effect. While the incidence of BPACR was increased by early CNI-withdrawal, graft function was not impaired. The incidence of CAV was not different among the study groups.

OP163 CLUSTERING ANALYSIS IDENTIFIES DISTINCT PROFILES OF HEART TRANSPLANT RECIPIENTS ASSOCIATED WITH PATIENT SURVIVAL

Guillaume Bonnet[1], Guillaume Coutance[1], Olivier Aubert[1], Marc Raynaud[1], Anouk Asselin[1], Marie Cecile Bories[2], Patrick Bruneval[3], Shaida Varnous[4], Leprince Pascal[4], Xavier Jouven[1], Alexandre Loupy[1]

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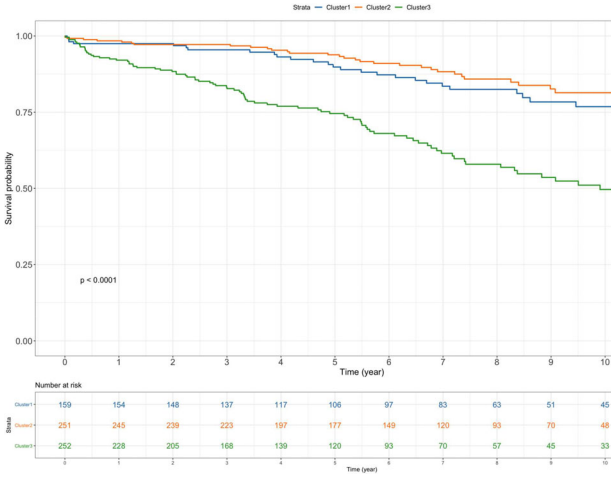
Background: Risk stratification after heart transplantation remains challenging due to the heterogeneity in patient profiles. Unsupervised analysis has already demonstrated its clinical relevance in organ transplantation and can be useful to identify new patient profiles. We aimed at identifying distinct phenotypic subgroups in a highly phenotypic cohort of heart recipients using unsupervised cluster analysis.
Methods: We enrolled consecutive patients underwearing a heart transplant between 2009 and 2017 from two French referral centers. A systematic assessment of clinical, biological, immunological, and outcome data was performed for each patient, including donor characteristics (sex, age), recipient characteristics (sex, age, BMI, ethnicity, diabetes mellitus, hypertension, smoking status, ischemic cardiomyopathy), and transplant characteristic (CMV, HLA mismatches and circulating anti-HLA DSA). An hierarchical clustering on principal components was applied to these parameters to identify patient profiles.
Results: Among the 662 heart recipients included, the median follow-up post-transplantation was 6.3 ± 3.5 years. Three distinct profiles were identified: Profile 1 (n = 159, 24%) was driven by a higher proportion of donor and recipient females, a moderate BMI, and a low cardio-vascular risk. Profile 2 (n = 251, 38%) was driven by a higher proportion of donor and recipient males, low cardio-vascular risk, and low proportion of DSA. Profile 3 (n = 252, 38%) was driven by a higher proportion of donor and recipient males, higher recipient age, higher BMI, and a higher cardio-vascular risk. The three profiles displayed distinct patient survival, ranging from 90% to 65% rates 6 years after heart transplant ($P < 0.001$ by log-rank) (Figure). Based on the findings, we built an application providing the probabilities of belonging to each cluster, according to the individual parameters.
Conclusion: Using an unsupervised method in a well-defined cohort of heart recipients, we identified three distinct patient profiles associated with different outcomes. By predicting the belonging to the cluster, we showed that clustering analyses might improve risk stratification in heart recipients.

Figure. KAPLAN-MEIER representation of the respective three clusters that were identified by unsupervised analysis in heart transplantation.



OP164 LONG TERM FOLLOW-UP OF CARDIAC TRANSPLANTATION WITH SELECTED ORGANS BY PHARMACOLOGICAL STRESS ECHOCARDIOGRAPHY

Sofía Martin-Suarez[1], Mariafrancesca Fiorentino[1], Gregorio Gliozzi[1], Tonino Bombardini[2], Giacomo Murana[1], Marco Masetti[3], Mario Sabatino[3], Antonio Loforte[1], Luciano Potena[3], Davide Pacini[1]

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Background: Cardiac donor's shortage makes a functional cardiac stress testing useful to provide information about the quality of the organ. Since 2004, the ADONHERS project (Aged Donor Heart Rescue by Stress Echo) was applied to rescue initial unsuitable hearts. The aim of this paper is to evaluate the long-term outcome of patients transplanted following this protocol.
Methods: From April 2004 to April 2014, a total of 275 cardiac transplantations were performed in our center: 23 (8.4%) applying the ADONHERS Protocol (AP) evaluation of LV regional kinetics and contractile reserve by baseline echocardiography and after administration of dipyridamole (20 patients) or dobutamine (3 patients). Regional wall motion was graded on a scale from 1 (normal) to 4 (dyskinetic) in each of the 17 segments at rest and after stress. None of the donors had a pre-harvesting coronary angiography.
Results: Recipients were predominantly male in both groups (AP 82.6 % and NON ADONHERS Protocol (NAP) 79%, P 0.17). AP recipients and donors were older (recipients 55.8 vs 51.5 (P 0.08) and donors 54.5 vs 37.8 P 0.001). Urgent transplantation was 8.7% and 14% in AP vs NAP (0.43). Mean ischemic time in AP group was shorter (181.9 min vs 197.2 min, P 0.008). Severe EGF occurred in two (8.7%) patients requiring ECMO in AP vs 21 (8.3%) in NAP (P 0.95). In hospital mortality was 8.7% vs 7.9% in AP vs NAP (P 0.9). Postoperative coronarography showed one case of stenosis treated with PTCA. Mean follow-up time was 74.7 months for AP vs 110.1 in the NAP group (P 0.044). Five years survival for the AP was 68.5% and 79.7% in the NAP (P 0.019)
Conclusions: Our results demonstrate that the ADONHERS protocol allowed to rescue nearly a 10% of donors otherwise discarded. Results were good in the short and in the long term. This protocol might be an extremely useful bedside evaluation tool also in cases of noncritical atherosclerosis in order to induce ischemia or to evidence the contractile reserve in cases of somewhat depressed contractile function.

OP160 DONOR-DERIVED CELL-FREE DNA FOR THE DETECTION OF HEART ALLOGRAFT INJURY: IMPACT OF REJECTION SEVERITY AND TIMING OF THE LIQUID BIOPSY

Jeroen Verhoeven[1,2], Annemiek Peeters[1,2], Evert De Jonge[3], Jan Von der Thüsen[4], Carla Baan[1,2], Ron van Schaik[3], Dennis Hesselink[1,2], Olivier Manintveld[5,6], Karin Boer[1,2]

*[1]Erasmus Medical Center, Internal Medicine, Nephrology and Transplantation, Rotterdam, Netherlands; [2]Erasmus Medical Center, Erasmus MC Transplant Institute, Rotterdam, Netherlands; [3]Erasmus Medical Center, Clinical Chemistry, Rotterdam, Netherlands; [4]Erasmus Medical Center, Pathology, Rotterdam, Netherlands; [5]Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; [6]Erasmus MC, University Medical Center Rotterdam, Cardiology, Rotterdam, Netherlands***Introduction:** Donor-derived cell-free DNA (ddcfDNA) may serve as a biomarker for minimally invasive diagnosis of heart allograft rejection. An endomyocardial biopsy (EMB) is the gold standard for diagnosing allograft rejection but this procedure itself causes injury which may influence ddcfDNA values. In this study, we measured ddcfDNA values after heart transplantation in relation to severity of rejection. Second, the influence of the EMB procedure on ddcfDNA levels was investigated.
Material and methods: A total of 228 plasma samples of 14 heart transplant recipients was studied. DdcfDNA was determined before (n = 114) and immediately after (n = 114) the EMB procedure. Pre-EMB ddcfDNA values were compared between different classes of allograft rejection. The fraction of ddcfDNA from total cfDNA (%) was determined by using the droplet-digital PCR (ddPCR; BioRad) method targeting single-nucleotide polymorphisms (SNPs).
Results: A total of 114 EMB tissue samples was collected. These samples were classified as 0R (no rejection; n = 46), 1R (mild cellular rejection; n = 66) and 2R (moderate cellular rejection; n = 2). The median pre-EMB ddcfDNA fractions were 0.06% (0.00-0.22; interquartile range) for 0R, 0.07% (0.00-0.16) for 1R and 0.24% (0.07-0.42) for 2R. No differences were observed between 0R and 1R, nor for 2R. Second, pre-EMB, the median fraction of ddcfDNA was 0.07% (0.00-0.20) and increased significantly to

0.10% (0.04-0.23) immediately post-EMB ($P < 0.05$). A 1.46-fold increase was observed in ddcfDNA values post-EMB, compared to pre-EMB.
Conclusion: Differences in ddcfDNA between different grades of allograft rejection were small and overlap considerably. Based on this dataset with small numbers of 2R rejections, we did not find that ddcfDNA could serve as biomarker for allograft injury caused by allograft rejection. Moreover, allograft injury resulting from the EMB procedure causes a detectable increase of ddcfDNA in heart transplant recipients. For this reason, it is essential to collect all blood samples for ddcfDNA analysis before the biopsy procedure in heart transplant recipients.

PREDICTIVE MODELS AND TOOLS IN TRANSPLANTATION: LOOKING INTO THE CRYSTAL BALL

OP165 COMPUTER BASED, VS HUMAN BASED ASSESSMENT OF KIDNEY ALLOGRAFT FAILURE PREDICTION AND STRATIFICATION (HUMAN VS IBOX TRIAL)

Gillian Divard[1], Marc Raynaud[1], Elodie Bailly[1], Maureen Assayag[2], Yannick Binois[1], Raphael Cohen[3], Helix Zhang[4], Camilo Ulloa[5], Basmah Abdalla[6], Kamilla Linhares[7], Vasishta Tatapudi[8], Maarten Naesens[9], Magali Giral[10], Nassim Kamar[11], Olivier Thaunat[12], Michel Delahousse[13], Christophe Legendre[1,14], Carmen Lefaucheur[1], Olivier Aubert[1,14], Alexandre Loupy[1,14]
[1]Paris Translational Center for Organ Transplantation, Paris, France; [2]Kidney Transplant Department/ Bicêtre Hospital/Assistance Publique – Hôpitaux de Paris, Le Kremlin-Bicêtre, France; [3]Department of Physiology/ Hôpital Européen Georges Pompidou/Assistance Publique-Hôpitaux de Paris, Paris, France; [4]The first affiliated hospital of Sun Yat-sen University,, Guangzhou, China; [5]Clinica Alemana de Santiago, Santiago, Chile; [6]Department of Medicine, Division of Nephrology/ David Geffen School of Medicine at UCLA , Los Angeles, United States; [7]Universidade Federal de Sao Paulo, Hospital do Rim, Escola Paulista de Medicina, Sao Paulo, Brazil; [8]NYU Langone Health, New York, United States; [9]KU LEUVEN, LEUVEN, Belgium; [10]CHU de Nantes, Nantes, France; [11]Toulouse University Hospital, Saubens, France; [12]Hôpital Edouard Herriot/INSERM, Lyon, France; [13]Department of Transplantation, Nephrology and Clinical Immunology, Foch Hospital, Suresnes, France; [14]Kidney Transplant Department/ Necker Hospital/ Assistance Publique – Hôpitaux de Paris, Paris, France

Background and Aims: Clinical decision-making process after transplantation is mainly driven by patient individual risk of allograft failure prediction assessed by physicians. However, this task remains difficult and uncertain due to the integration of data. We sought to evaluate and compare physician-based risk assessment to a well-trained and validated patient risk prediction algorithm.
Methods: From the iBox derivation set qualified database, patients were randomly selected and constituted the reference set population. We generated an anonymized electronic health record for each patient including a total of 60 classical kidney transplant prognostic parameters related to transplant characteristics, and post-transplant parameters including allograft function, proteinuria, histology, diagnoses, and immunological profile. We enrolled 9 physicians at various stages of their careers (3 residents, 3 fellows and 3 seniors) to assign a graft survival probability based for each patient blinded to outcome and algorithm predictions. We compared the human based predictions to the iBox based prediction as well as the true outcomes (allograft failures) using calibration curves. The relative importance of the parameters that led to each physician's prediction were also determined using Random forest survival model.
Results: Among the 400 patients evaluated, the mean time of risk evaluation was 1.03 ± 0.29 years post-transplant. The iBox predictions were the most reliable to the true graft survival, while physicians tend to overestimate the risk of graft loss at risk evaluation (Figure 1A). The individual graft survival probabilities predicted by physician's showed wide heterogenicity with a poor intraclass correlation of 0.58 95%CI [0.51-0.64], 0.48 95%CI [0.39-0.56] for Residents, 0.61 95%CI [0.39-0.74] for Fellows and 0.59 95%CI [0.45-0.69] for Senior physicians. Except for eGFR, the main determinants of physician's prediction were disparate among the physicians regardless of their career achievement (Figure 1B).
Conclusions: This study demonstrates the overall limited performance of physicians to predict patient individual risk of long-term allograft failure. Computer assistance may help improve physicians prognostic judgement in the clinical care and decision-making process.

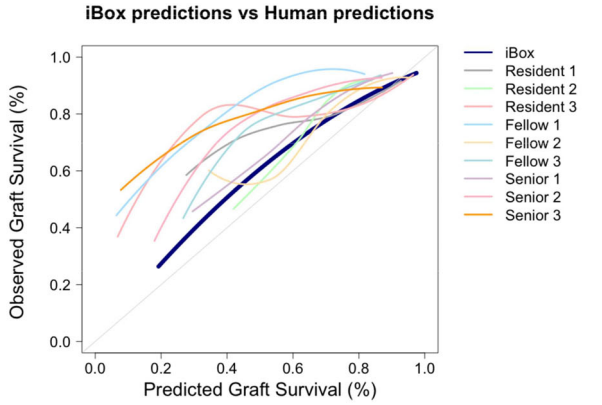

Figure 1A: Smoothed calibration curve comparing the observed graft survival and the predicted graft survival of each physician's and the iBox system.

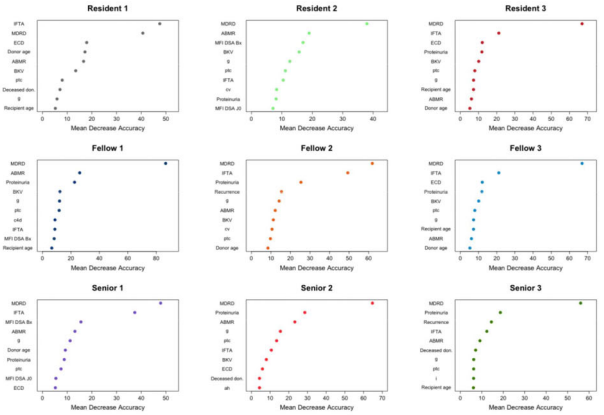

Figure 1B: Importance of the 10 parameters that led to the prediction based on the mean decrease accuracy from each physician's Random Survival Forrest.

OP166 MULTIDIMENSIONAL PROGNOSTICATION TOOL FOR KIDNEY TRANSPLANT PATIENT SURVIVAL : THE MORTALITY MBOX

Charlotte Debiais-Deschamps[1], Olivier Aubert[1], Daniel Yoo[2], Maud Racape[1], Gillian Divard[1], Carmen Lefaucheur[1], Christophe Legendre[3], Alexandre Loupy[1]
[1]Paris Translational Center for Organ Transplantation, Paris, France; [2]Paris Translational Centre for Organ Transplantation, Paris, France, [3]Necker Hospital, Paris, France

Background: Predicting kidney transplant patient mortality has been hampered by registry-based studies and low level phenotyped cohorts without specific design towards mortality prediction. This represents a limitation for decision making and ultimately patient care. We aimed to build a robust patient mortality prognostication system.
Methods: We enrolled 1466 patients transplanted in France between 2004 and 2014 in whom a protocol-based collection including more than 120 parameters from the recipient (past medical history, risk factors) donor and graft, biological and imaging data, was performed on the day of transplantation (TX) and during the first year of transplantation. Multivariable Cox model was used to develop an individual predictive score of mortality, further improved by a Lasso regression in order to retain the strongest predictors of mortality.
Results: Among the1466 kidney transplant recipients, 309 patients died after a median post-TX follow-up time of 7.6 years. Among the 120 parameters 19 predictors were selected using lasso regression. The strongest predictors of patient survival were (1) Baseline recipient factors (age, history of cancer, diabetes mellitus, chronic obstructive pulmonary disease, cardiovascular events: myocardial infarction, stroke or arteritis, supraventricular cardiac rhythm disorder, psychiatric history and VHC status) (2) Post-TX parameters (need for dialysis, cardiovascular complications and cancer in the first year of TX) and (3) biological variables (HbA1c, C-Reactive Protein, Albumin, Gamma-Glutamyl Transferase, Uric acid, Neutrophils and Urinary protein). The mortality score showed accurate calibration and discrimination at 10 years (C-index = 0.81).

Conclusions: We generate the first integrative patient survival score that shows a superior prediction performance when compared to previous prognostic systems, reaching 81% prediction accuracy at 10 years. This score may help therapeutic decision making and provide a surrogate endpoint in clinical trials.

OP167 MORTALITY AFTER EMERGENCY SURGERY COMPARING KIDNEY TRANSPLANT OR DIALYSIS PATIENTS VERSUS THE GENERAL POPULATION: A NATIONAL COHORT STUDY

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Background: Emergency surgery is associated with increased mortality, with pneumonia the leading cause of death according to national audits. Kidney failure patients have higher burden of cardiovascular disease and, especially kidney transplant recipients, susceptibility for infection. Therefore, we hypothesize mortality risk may be higher for kidney failure patients after emergency surgery and causality skewed compared to the general population.
Methodology: We analysed data for every emergency surgery procedure in England between April 2004 and March 2019 (acquired December 22nd 2020). Data were extracted from Hospital Episode Statistics using administrative ICD-10 and OPCS-4 codes, with linkage to the national death registry. We excluded age ≤18, repeat transplants, multi-organ transplant and residence outside England. Kidney failure patients were identified and stratified according to ICD-10 and OPCS-4 codes. We analysed seven procedures that account for 80% of all emergency general surgery procedures and deaths.
Results: In total, 691,064 emergency surgical procedures were undertaken, with 0.16% (n = 1097) performed on kidney transplant recipients and 0.23% (n = 1567) on dialysis patients (see Table). The commonest procedure in the general population was appendectomy (49% of procedures, n = 336,648), with laparotomy the commonest in kidney transplant recipients (46% of procedures, n = 507) and dialysis patients (45% of procedures, n = 704). 30-day and 1-year mortality was highest after laparotomy (13.4% and 26.7%, respectively), and lowest after appendectomy (0.2% and 0.4%, respectively). For every emergency procedure, demographics and comorbidities were significantly different for kidney failure patients versus the general population. 30-day and 1-year mortality was higher for dialysis versus transplant versus the general population, with cardiac deaths significantly more common in 4/7 procedures for kidney failure patents (dialysis > transplant) compared to the general population.
Discussion: Mortality after emergency surgery is higher for kidney failure patients, dialysis worse than kidney transplant patients, with cardiovascular deaths more common than the general population due to a greater burden of underlying diabetes and cardiovascular diseases.

Emergency surgery		Kidney transplant		Dialysis		General		Total
		N	%	N	%	N	%	N
Emergency surgery procedures	1.Partial Colectomy	126	11%	252	16%	63,199	9%	63,577
	2.Small Bowel Resection	137	12%	190	12%	33,994	5%	34,321
	3.Cholecystectomy	128	12%	107	7%	92,499	13%	92,734
	4.Appendectomy	95	9%	84	5%	336,648	49%	336,827
	5.Lysis of Peritoneal Adhesions	14	1%	10	1%	5,214	1%	5,238
	6.Surgery for Peptic Ulcer	90	8%	220	14%	41,748	6%	42,058
	7.Laparotomy	507	46%	704	45%	115,098	17%	116,309
	Total	1,097	0.2%	1,567	0.2%	688,400	99.6%	691,064
Mortality rate	Death within 30-days	131	11.9%	501	32.0%	32,457	4.7%	33,089
	Death within 1-year	262	23.9%	754	48.1%	65,303	9.5%	66,319

OP168 ARE SURVIVAL BENEFITS OF KIDNEY TRANSPLANTATION VERSUS REMAINING ON THE WAITING LIST VALID FOR ALL KIDNEY FAILURE PATIENTS IN THE CONTEMPORARY ERA?

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Background: Multiple studies demonstrate the survival benefit of kidney transplantation versus remaining on the waiting list for kidney failure patients. However, as survival rates for dialysis patients have improved, while donor/recipient marginality has increased, it is unclear if survival benefits remain valid in the contemporary era or translate across different population cohorts. The aim of this study was to replicate these historical analyses in a national cohort study using country-specific demographics for the UK.
Methods: We analysed UK Transplant Registry data for dialysis patients listed from 01/01/2000 to 30/09/2019 (follow up to 31/12/2020). Different statistical models were utilised to explore survival differences. Our primary analysis explored hazard ratios (HR) in a Cox proportional hazards model after adjustment for immortal time bias (comparing time since transplant versus time from listing). However, we included competing models including comparing time from listing for both study cohorts (to avoid selection bias) and weighted Cox regression to account for non-proportional hazards.
Results: Data were available for 42,368 dialysis patients placed on the waiting list during the study period, of whom 31,038 received a kidney transplant (240,908 patient-years follow-up). Significant baseline demographics exist comparing transplant patients versus those remaining on the waiting list. Mortality risk is higher immediately after kidney transplantation, with equal risk reached by 72 days post-transplant and superior survival after 75 days post-transplant. In unadjusted analyses, long-term mortality is lower after transplant versus remaining on the waiting list (19% versus 36%, respectively, $P < 0.001$). In an adjusted Cox model, transplantation was associated with lower HR (0.18, 95% CI 0.17-0.19, $P < 0.001$). In sub-analyses stratified by age (≥60, ≥65 or ≥70), sex, ethnicity or cause of kidney failure, or any alternative survival modelling, kidney transplantation retains significantly lower HR for all-cause mortality versus remaining on the waiting list.
Conclusions: Regardless of patient demographic or statistical model, survival after kidney transplantation remains superior to remaining on the waiting list for kidney failure patients on dialysis in the contemporary era.

OP169 TRENDS OF RENAL FAILURE AFTER NONRENAL SOLID ORGAN TRANSPLANT: A COMPETING RISK ANALYSIS OF THE SRTR

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Background: As the outcomes of solid organ transplant continue to improve, we sought to assess the trends of end stage kidney disease after nonrenal solid organ transplant (NRSOT) in the United States.
Methods: We utilized the SRTR standard analysis file to ascertain the incidence of renal failure after NRSOT with death as a competing risk, conditioned on surviving at least 90 days post-transplant. We defined renal failure as being listed for or receiving a kidney transplant. Between 1987 and 2019, there were 625 intestinal, 127,963 liver, 2109 pancreas, 61,365 heart, 37,246 lung and 1056 heart/lung first time transplant recipients. We compared the trends over three distinct periods before 2000, between 2000-2009 and after 2010. Cumulative incidence curves for renal failure were created for each era, and each transplant type within each era. The patients at risk at 1, 3, 5 and 10 years are displayed (Figure 1). Analysis was performed in R, version 4.0.2.
Results: The 5-year cumulative incidences of renal failure after each transplant type within each era are listed in Table 1. In each era, there was a statistically significant difference in renal failure between transplant types (overall $P < 0.001$), mainly attributable to pancreas and intestine. Other transplant types had similar incidence of renal failure for each era. In the 3rd era, the 1-year post transplant proportion of CKD (eGFR < 30 ml/min) was 2.7% in pancreas, 5.4% in liver, 11.0% in intestine, 8.2%in heart, 10.3% in lung and 9.2% in heart/lung transplants. However, the estimates are limited by missing creatinine data at one year in thoracic transplants before 2015 and do not account for patients who died before one-year post-transplant.
Conclusion: The incidence of renal failure after NRSOT has declined over the years specifically post pancreas and intestinal transplant, while remained similar for all other types to slightly increased in the last era. Estimating the burden of ESRD after nonrenal solid organ transplant is crucial for counseling candidates and future planning.

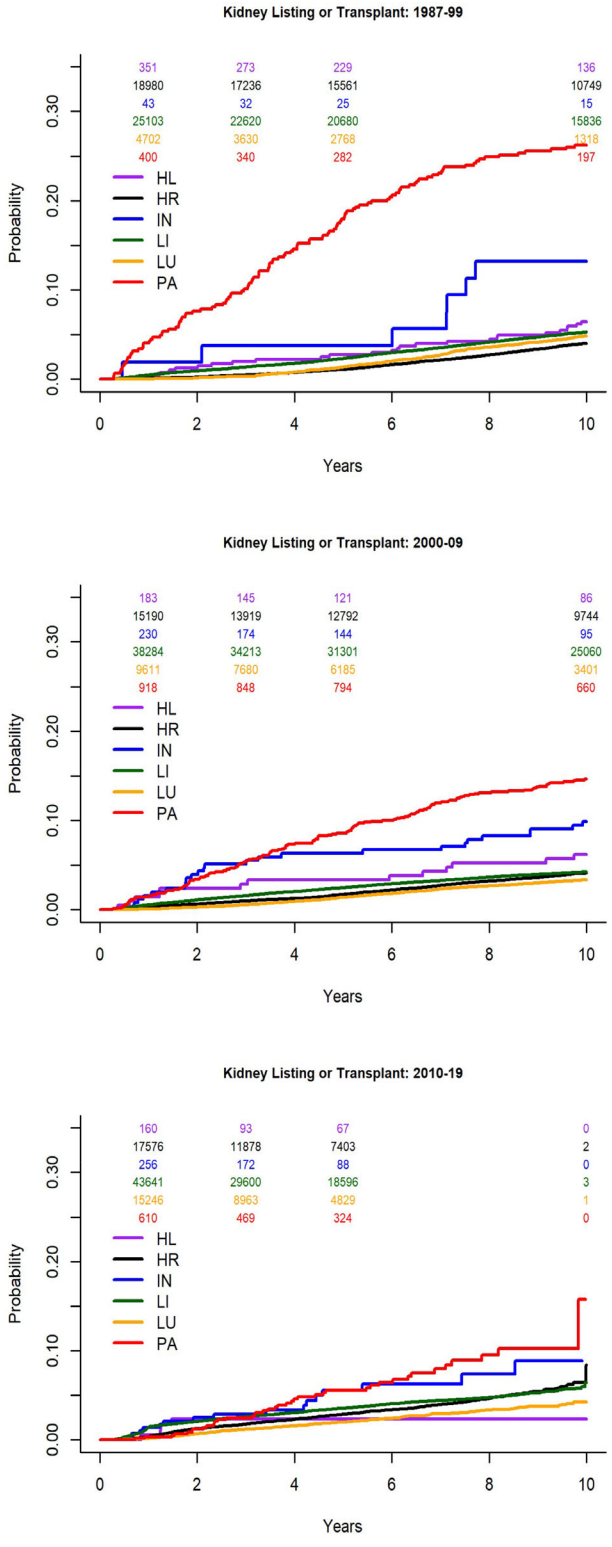

Figure 1. Cumulative Incidence of Renal Failure

Table 1. 5-Year Cumulative Incidence of Renal Failure

	1st Era (Before 2000)	2nd Era (2000-2009)	3rd Era (2010-2019)
Pancreas	17.9%	8.6%	5.5%
Liver	2.3%	2.4%	3.5%
Intestine	3.8%	6.3%	5.6%
Lung	1.3%	1.3%	2.0%
Heart	1.1%	1.7%	2.9%
Heart-Lung	2.7%	3.3%	2.3%

OP170 MEDICATION ADHERENCE AND FEAR OF REJECTION AFTER CONVERSION FROM DUAL TO MONOTHERAPY: A RANDOMIZED CONTROLLED TRIAL

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Introduction: After kidney transplantation, a strict immunosuppressive medication regimen is necessary for graft survival. However, non-adherence to medication has been shown to occur early after transplantation and to increase over time. Weaning the medication regimen in order to lower the immunosuppresive burden, may also be a way to promote adherence, although little is known about the impact of such a regimen on fear of rejection.
Methods: We performed a nested cohort study on medication adherence and fear of rejection in a randomized, investigator-driven, open-label, single centre pilot study. Participants were randomized at 6 months post-transplant to either continue tacrolimus and mycophenolate mofetil (TAC/MMF) or to taper MMF at 6 months and discontinue MMF at 9 months (TAC monotherapy). They completed questionnaires about medication adherence (BAASIS) and fear of rejection (Perceived Threat of the Risk for Graft Rejection (PTGR)) at 6 and 12 months post-transplantation.
Results: The majority of the participants at 6 months ($n = 78$) were male (73.1%), European (65.4%), low educated (52.6%) and had a median age of 61.5 years. More than the half of the participants had a living donor (59.0%). Medication adherence was significantly higher in TAC monotherapy compared to dual TAC/MMF therapy ($\chi 2$ (1) = 4.582; $P = .032$). Despite the fact that the intervention arm discontinued MMF, we found no difference in fear of rejection between the two groups of recipients ($P = .887$).
Conclusions: Tacrolimus monotherapy by discontinuing MMF in immunologically low-risk kidney transplant recipients improves medication adherence and does not have an adverse effect on fear levels. Simplification of the medication regime is a potential tool for increasing adherence in clinical practice.

OP171 THE ASSOCIATION OF TRAJECTORIES OF DEPRESSION AND ANXIETY ON OUTCOMES AT THE LONG TERM AFTER LIVER TRANSPLANTATION

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Background: Previously we identified distinct trajectories of no, resolved, and unresolved symptoms of depression and anxiety among liver transplant recipients (LTRs) within the first two years after transplantation. This study aimed to examine whether the distinct trajectories of depression and anxiety were associated with (graft)survival, psychological functioning and quality of life at the long-term (7-11 years) after liver transplantation.
Methods: Follow-up measurement of the Psychological Aspects of Transplantation-study. Data regarding (graft)survival were retrieved by medical record review. Of the 90 LTRs eligible for follow-up measurement, 72 (80%) filled out the questionnaire collecting data on psychological functioning (STAI6, CES-D) and quality of life (WHOQoL-BREF). Survival analyses, X^2-analyses and ANOVA's were used to analyse data.
Results: Of the 153 participants in the original study, 45 (29%) died and 17 (11%) had graft failure before the follow-up measurement. No significant differences between the distinct trajectories of depression or anxiety were found regarding survival (respectively, $P = 0.39$ and $P = 0.38$,) or graft survival (respectively, $P = 0.20$ and $P = 0.21$). Of the 72 participants in the

follow-up measurement, 15% showed symptoms of depression and 25% symptoms of anxiety. LTRs within the trajectories of unresolved symptoms showed significantly more often symptoms of depression or anxiety compared to LTRs in the trajectories of resolved or no symptoms, respectively, 38% vs. 11% vs. 5% ($P = .02$) for depression and 82% vs. 25% vs. 11%, ($P < .001$) for anxiety. Regarding quality of life, LTRs within the trajectory of unresolved symptoms of both depression and anxiety showed significantly ($P < .001$) lower quality of life scores compared to those with no symptoms or resolved symptoms.
Conclusions: The distinct trajectories of depression and anxiety were not associated with (graft) survival on the long term after transplantation. However, LTRs within the trajectories of unresolved symptoms showed more often high symptom levels of psychological problems and experienced a significantly lower level of quality of life compared to recipients with no or resolved symptoms. This shows that monitoring and treatment of psychological problems remains important in the care of LTRs.

OP172 I-DTI: A SECOND OPINION PLATFORM BETWEEN HEALTHCARE PROFESSIONALS RELATED TO ORGAN DONATION AND TRANSPLANTATION

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Background: Nowadays, 10% of the transplant needs are performed and only 0.05% of worldwide dead population becomes organ donor. Due to COVID pandemic, donation and transplantation rates have significantly decreased worldwide. Social distancing, displacement restriction and safety measures make even more necessary telematic communication tools to face the current crisis.
I-DTI is designed as a second opinion platform allowing to share knowledge between healthcare professionals and internationally distinguished experts related to donation and transplantation.
Objectives: To develop and assess I-DTI second opinion platform, targeting to developing countries during current COVID-19 context.
Methods: I-DTI has been developed based on Medxat® app, accessible via www.i-dti.com and downloadable from digital stores for mobile devices. Database server is encrypted with RAS using cloud technologies. Information is sent through HTTPS (SSL/TLS) codified channels following international data protection laws.
I-DTI main function is 24/7 consultancy area. I-DTI covers the following topics: organ donation, transplantation and follow-up, tissue donation and COVID-19. I-DTI incorporates social network features like profile customisation, finder, and instant messaging service.
The accessibility, contents and service of the tool was evaluated in three geographic areas: Kerala (India), Philippines and Trinidad and Tobago.
Results: From April to December 2020, 60 healthcare professionals from the target areas were invited to join I-DTI pilot program. An average of 5 consultancies/week were received and answered in less than 24 h considering urgency. More than 50% of total consultancies were COVID-19 related and were stored in library cases for academic purposes.
Satisfaction surveys were delivered to study quality indexes, receiving a total score of 9.3/10. (Accessibility 9.3 / Contents: 8.9 / Networking: 9.2 / Applicability: 9.5)
Conclusions: I-DTI proved great value for knowledge sharing, international cooperation and data compilation especially in developing countries. The specialization of I-DTI topics opens a way to develop new contents and introduce artificial intelligence technologies.
So far, more than 600 users from more than 20 countries (65% in developing) joined I-DTI.

IMMUNOLOGICAL MECHANISMS OF ORGAN REJECTION

OP173 DEFECTIVE T REGULATORY CELL RESPONSES IN KIDNEY TRANSPLANT RECIPIENTS DEVELOPING ANTIBODY-MEDIATED REJECTION

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Background: Although T regulatory cells (Tregs) are recognized to be involved in organ transplant tolerance and to prevent T cell-mediated rejection process, their role in controlling humoral alloimmunity has been less appreciated.
Methods: We established *in vitro* cellular models using human Tregs and performed 22-color flow cytometry profiling of circulating Tregs, effector T and B cells in a cohort of 96 kidney transplant recipients.
Results: Human $CD25^{hi}CD127^{-}$ Tregs were capable of direct suppression of T follicular helper (T_{FH}) cell proliferation in a dose-dependent manner ($P = 0.001$) and of T_{FH} cell production of IL-21 ($P = 0.01$). In T_{FH}-B cell co-cultures, $CD25^{hi}CD127^{-}$ Tregs significantly inhibited CD80- and CD86-dependent B cell activation ($P < 0.001$), B cell differentiation into plasma cells ($P < 0.001$) and IgG production ($P = 0.002$). In patients developing donor-specific antibodies (DSAs) post-transplant ($N = 48$), we identified a significant decrease in frequencies of blood $FoxP3^{hi}$ Tregs ($P < 0.001$) and loss of $FoxP3^{hi}$ $CXCR5^{+}$ T follicular regulatory subset ($P < 0.001$). These decreases were more pronounced in DSA-positive patients who progressed to antibody-mediated rejection (ABMR) ($N = 20$). In contrast, blood $FoxP3^{hi}$ Tregs were expanded in stable patients who did not develop DSAs ($N = 48$) and these Tregs manifested an effector memory $CD45RO^{+}ICOS^{+}$ profile in these patients. Interestingly, the loss in frequencies of $FoxP3^{hi}$ Tregs in patients with ABMR was inversely correlated with increased frequencies of blood effector $CD45RO^{+}CD127^{+}CXCR5^{+}$ T_{FH} cells, effector $CD27^{+}CD21^{-}$ B cells and $CD27^{hi}CD38^{hi}$ plasmablasts ($P < 0.001$ for all correlations).
Conclusions: These *in vitro* and *in vivo* analyses exemplify the role of human Tregs in tempering humoral responses and identify a defect in the blood Treg compartment of patients developing ABMR, which may contribute to loss of immune regulation in these patients.

OP174 CD21-CD27+ ACTIVATED MEMORY B CELLS ARE A DELETERIOUS SOURCE OF PLASMA CELLS AND DONOR SPECIFIC ANTIBODIES IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Heterogeneity in human memory B cells (MBCs) is increasingly recognized. However, how functionally distinct MBC subsets may differently impact the magnitude and the quality of donor-specific antibody (DSA) response is unclear.
Methods: Using spectral flow cytometry, RNA-seq and co-culture assays, we evaluated the heterogeneity of circulating MBC subsets, their response to T follicular helper (T_{FH}) cell help, and their relationship with DSA pathogenicity (strength, C1q-binding, IgG subclasses) and antibody-mediated rejection (ABMR) in 96 kidney recipients.
Results: Three distinct circulating MBC subsets were identified in kidney transplant recipients: $CD21^{+}CD27^{+}$ resting memory (RM), $CD21^{-}CD27^{+}$ activated memory (AM) and $CD21^{-}CD27^{-}$ tissue-like memory (TLM). When co-cultured with T_{FH} cells, RM cells displayed the most potent capacity to differentiate into plasma cells and generate polyclonal IgGs; however, only AM cells could generate DSAs *in vitro.* Patients who developed DSAs post-transplant ($N = 48$) displayed significantly higher frequencies of circulating AM cells than patients without DSAs ($N = 48$). Unlike for RM and TLM, frequencies of AM cells strongly correlated with that of circulating plasma cells and DSA MFI levels. Frequencies of AM cells also correlated with the presence of $IgG3^{+}$ DSAs in sera, while TLM cells were predictive of the presence of $IgG2^{+}$ DSAs. Consistently, patients with DSAs who progressed to ABMR ($N = 20$) displayed higher frequencies of AM cells than those with DSAs remaining without ABMR ($N = 28$). Unlike RM and TLM, AM cells were transcriptionally poised for plasma cell differentiation and expressed pathogenic *IGHV* sequences known to be associated with allograft rejection.
Conclusions: This study identifies AM cells as a deleterious source of plasma cells and pathogenic DSAs. Thus, concomitant targeting of AM cells along with their plasma cell progeny represent an optimal means of dampening the humoral response during ABMR.

OP175 ACUTE ANTIBODY MEDIATED REJECTION IN MICE IS ACCOMPANIED BY ELEVATED BASOPHIL LEVELS AND THE DEVELOPMENT OF IGE+ CD23+ B CELLS

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Background and aims: Allograft damage caused by donor-specific antibodies (DSA) is still one of the major causes of graft loss. We have recently demonstrated that MHC-specific DSAs of the IgE subtype occur upon allograft rejection in mice and humans. A potential role for MHC-specific IgE DSAs in the pathology of ABMR remains to be delineated.
Methods: Fully mismatched BALB/c heart allografts were transplanted onto untreated CCR5KO B6 recipients, a model of acute ABMR. MHC-specific IgE and IgG1 was measured using a custom-made ELISA employing MHC class I and II monomers. Levels of IgE effector cells, such as basophils and eosinophils, were measured weekly before and after transplantation using flow cytometry.
Results: Although allograft survival in CCR5KO mice was not significantly different compared to wild type C57BL/6 mice, the production of IgG DSAs occurred much earlier. Levels of MHC-specific IgE after rejection were higher in CCR5KO recipients compared to controls. Furthermore, basophil (CD49b+ FceRI+ IgE+) levels in periphery were significantly elevated at the time of rejection and an increase in basophil-bound IgE was detected. Interestingly, we could also see a formation of IgE+ CD23+ B cells after cardiac allograft rejection with significantly higher levels in CCR5KO recipients than WT recipients.
Conclusion: We could show that MHC-specific IgE develops upon allograft rejection in a murine model of acute ABMR. Furthermore, levels of basophils in periphery and basophil-bound IgE are elevated after rejection. The increase in IgE+ CD23+ B cells after rejection suggests a possible production of IgE immune complexes upon rejection.

OP176 CYTOMEGALOVIRUS SPECIFIC POLYFUNCTIONAL T-CELL RESPONSES EXPRESSING CD107A ASSOCIATED WITH CONTROL OF CMV REACTIVATION AFTER LIVER TRANSPLANTATION

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Background: Cytomegalovirus (CMV) viral load after liver transplantation (LT) is controlled by cell mediated immune responses (CMI). Quantification of CMV-specific T cells may allow identifying patients that achieve spontaneous CMV control, with no need of expensive and potentially toxic antiviral therapies
Methods: Prospective post-LT clinical, virologic and immunological monitoring was carried out up to 1 year in a cohort of adult LT recipients. CMV-specific responses were characterized using flow-cytometry multiparametric analysis.
Results: We analyzed 527 samples from 49 LT recipients-R (79.6% R+, 20.4% R−). CMV reactivation occurred in 24 patients (18 D+/R+ and 6 D+/R−). In pre-LT samples ($n = 43$), 53.5% and 62.8% of the patients had a detectable CMV-pp65 CD8+ or CD4+ T-cell response, respectively (at least one cytokine). In contrast, only 27.9% or 20.9% of patients had detectable CMV-specific CD8+ or CD4+ polyfunctional T cells, respectively. Patients with CMV-specific CD4+ T cells higher than 0.05% of total T cells pre-LT had less CMV reactivation episodes ($P < 0.001$), and less severe CMV events ($P < 0.05$). Only those patients with undetectable CMV-specific CMI pre-LT developed CMV infection and were diagnosed with severe CMV events. According to predictive models, determination of polyfunctional CMV-specific CD4+ T cells expressing CD107a before LT identifies 80% of the patients who will develop a CMV event and 75% of those that will not develop CMV episodes.
Conclusions: The quantitation of CMV-specific CMI, especially that driven by CD4+ T cells, showed good diagnostic performance to predict CMV reactivation. CMV-specific CMI may be a useful marker for spontaneous control of CMV reactivation to tailor antiviral treatment after LT.
Disclosure: This study was supported by competitive grants from the ISCIII, Ministerio de Sanidad (PI13/01770, PI18/01759, PI18/01824), CIBERehd and CIBEResp and co- financed by European Development Regional Fund "A way to achieve Europe".

OP177 IL-10 SIGNALING IN T CELLS IS ESSENTIAL FOR TRANSPLANT TOLERANCE INDUCTION

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Background: Costimulation blockade (CoB)-based immunotherapy is a very promising approach for better management of transplant recipients. Elucidating which factors impact the efficacy of CoB is a necessary step to maximize its clinical applicability. Pro- and anti-inflammatory cytokines are being recognized as having an impact on T cell activation beyond effector differentiation. We then aimed at elucidating the role that direct IL-10 signaling in T cells has on the outcome of CoB therapy.
Methods: Balb/c skin was transplanted to wt C57BL/6 (B6) mice or to B6 with T cell-restricted expression of a dominant negative IL-10 receptor (10R-DN). Recipients received peri-transplant donor specific infusion and three weekly anti-CD154 mAb doses. Ex vivo flow cytometric analysis, mixed leucocyte reaction (MLR), and ELISpot assays were used characterize the behavior of wt and 10R-DN T cells.
Results: Unmanipulated 10R-DN recipients rejected their transplant with dynamics identical to wt B6. However, differently from wt B6, graft survival in 10R-DN could not be promoted by CoB (MST 105 days vs 30 days in the latter) revealing a novel and important effect of IL-10 on T cells. This accelerated rejection correlated with increased production of TNF-α, IFN-γ and IL-17 by T cells in spleen and draining lymphoid tissues. MLR experiments indicated that despite IL-10 signaling is not involved in the ability of anti-CD154 to modulate alloreactive T cell proliferation, absence of this pathway impaired induction of Tregs. We also tested if IL-10 could impact costimulation-independent T cell activation (a phenomenon recognized to afflict the efficacy of CoB). In vitro experiments clearly showed that IL-10 neutralizes the poorly investigated effect of TLR-mediated costimulation of naïve, effector, and memory T cells. We are currently investigating the mechanisms behind such an important regulation.
Conclusions: Overall, these results reveal a previously unappreciated role of IL-10 signaling in T cells as pre-requisite for the therapeutic efficacy of CoB. Merged with the recognized plasticity of IL-10 signaling, this observation opens a novel area of investigation that could reveal new "Achille's Heels" in the successful implementation of CoB and suggest complementary interventions for the actuation of robust immunoregulation.

OP178 ROLE OF ALLOREACTIVE CD8+ T CELLS IN TREG MEDIATED SKIN GRAFT SURVIVAL

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Background: The selective in vivo expansion and activation of regulatory T cells via administration of interleukin-2 (IL-2) coupled to a specific antibody against IL-2 (IL-2 cplx) was successfully used to induce tolerance towards islet allografts; however, survival of fully mismatched skin grafts could not be significantly prolonged. Here we investigate whether depletion of alloreactive CD8+ T cells has a positive impact on Treg mediated skin graft survival.
Methods: Recipient C57BL/6 mice received fully mismatched BALB/c or single MHCII mismatched BM12 skin grafts in combination with IL-2 cplx, Rapamycin and a short term treatment of anti-IL-6 mAb. To analyze the role of CD8+ T cells experimental settings devoid of alloreactive CD8+ T cells were created by using an anti-CD8 antibody or the single MHCII mismatched mouse model. To study the mechanisms of skin graft rejection, development of donor-specific antibodies, formation of T cell memory as well as graft infiltrating leucocytes were investigated.
Results: The combination of IL-2 cplx with Rapamycin and an IL-6 neutralizing antibody leads to significantly prolonged survival of fully mismatched (MST = 34 days) as well as single MHCII mismatched (MST = 77.5 days) skin grafts. Furthermore, analysis of sera showed a significant decrease of donor reactive IgG1 ($P < 0.05$) and IgG2a/b ($P < 0.01$) in this settings. Interestingly, depletion of CD8+ cells, did not lead to further prolongation of

skin graft survival but a significant increase of donor specific IgG1, which was detectable by d28 post skin graft rejection.
Conclusion: Combined treatment with IL-2 cplx, Rapamycin and anti-IL-6 leads to significantly prolonged skin allograft survival. Particularly noteworthy, humoral response and sensitization are impeded in this setting. Depletion of CD8+ cells results in - albeit delayed - formation of donor-reactive antibodies suggesting that a CD8+ cell population is needed for sustainable prevention of sensitization.

OP179 INVESTIGATING THE ALLOIMMUNE BACKGROUND OF THE HISTOLOGICAL CHANGES SUGGESTIVE OF ANTIBODY-MEDIATED INJURY IN THE ABSENCE OF HLA-DSA ANTIBODIES

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Background: The histology of antibody-mediated rejection ($ABMR_h$) is observed frequently after kidney transplantation, but a significant percentage of the patients do not have detectable donor-specific anti-HLA antibodies ($DSA_{neg}ABMR_h$). While there is an active interest in non-HLA autoantibodies' role to $DSA_{neg}ABMR_h$ phenotype, it remains crucial to exclude the possible contribution of the HLA incompatibility to this phenotype. We aimed to investigate the associations between the HLA molecular mismatches and the occurrence of the $DSA_{neg}ABMR_h$ phenotype.
Methods: All consecutive adult kidney recipients transplanted at a single center between 2004 and 2013 were eligible for this study. *HLAMatchmaker*, *PIRCHE-II* and *HLA-EMMA* tools were used to determine the number of HLA molecular mismatches (MM) for all HLA loci together.
Results: Patients with pretransplant HLA-DSA were excluded from this study. Of the remaining 798 kidney transplant recipients with available biopsy follow-up, 123 (15.4%) developed $ABMR_h$ in the absence of *de novo* HLA-DSA. In adjusted multivariable Cox analysis (Table 1), HLA antigen (HR = 1.30 per 1; 95%CI 1.15-1.46; $P < .0001$), HLA allele (HR = 1.10 per 1; 95%CI 1.03-1.16; $P = 0.002$) and HLA amino acid mismatches (HR = 1.09 per 10; 95%CI 1.03-1.15; $P = 0.002$) were identified as risk factors for developing $DSA_{neg}ABMR_h$. Similarly, all the different HLA molecular mismatches, *HLA-EMMA* (HR = 1.11 per 10; 95%CI 1.04-1.20; $P = 0.003$), eplet MM (HR = 1.24 per 10; 95%CI 1.08-1.41; $P = 0.002$) and *PIRCHE-II* (HR = 1.15 per 100; 95%CI 1.05-1.25; $P = 0.002$) associated with $DSA_{negABMRh}$. The subsequent multivariate Cox model, censored for cases with DSAnegABMRh and C4d deposition (ABMR according to Banff 2019), confirmed that HLA incompatibility is a risk factor for developing $DSA_{neg}ABMR_h$. Finally, in a sensitivity analysis restricted to anti-HLA antibody-negative patients ($n = 660$), again, all different levels of HLA mismatches were independently associated with the $DSA_{neg}ABMR_h$ rejection phenotype.
Conclusions: HLA mismatches associate with $DSA_{neg}ABMR_h$, also in patients without any sign of circulating HLA antibodies. This indicates that the donor-recipient HLA-incompatibility at least partially explains the development of the histological features of ABMR, in an HLA antibody-independent process.

Table 1. *Multivariable Cox analysis in patients without* HLA-DSA (N=798).

HLA mismatch approach	*Events*	*Cox models*		
		HR	*95% CI*	*p-value*
$DSA_{neg}ABMR_h$ (censored for dnDSA)				
ABDRDQ antigen MM (per 1)	123	1.30	1.15 – 1.46	**<.0001**
HLA allele MM (per 1)	123	1.10	1.03 – 1.16	**0.002**
HLA amino acids MM (per 10)	123	1.09	1.03 – 1.15	**0.002**
HLA-EMMA (per 10)	123	1.11	1.04 – 1.20	**0.003**
HLA eplet MM v3.1 (per 10)	123	1.24	1.08 – 1.41	**0.002**
PIRCHE-II score (per 100)	123	1.15	1.05 – 1.25	**0.002**
$DSA_{neg}ABMR_h$ (censored for dnDSA and $DSA_{neg}ABMR_hC4d+$)				
ABDRDQ antigen MM (per 1)	101	1.27	1.12 – 1.44	**0.0002**
HLA allele MM (per 1)	101	1.09	1.03 – 1.17	**0.007**
HLA amino acids MM (per 10)	101	1.08	1.02 – 1.15	**0.01**
HLA-EMMA (per 10)	101	1.10	1.01 – 1.19	**0.02**
HLA eplet MM v3.1 (per 10)	101	1.20	1.04 – 1.40	**0.01**
PIRCHE-II score (per 100)	101	1.14	1.04 – 1.26	**0.007**

Each multivariable analysis per row was corrected for donor and recipient age, donor type, cold ischemia time and repeat transplantation.

OP180 RECIPIENT SEX AND ESTRADIOL LEVELS AFFECT TRANSPLANT OUTCOMES IN AN AGE-SPECIFIC FASHION

Ryoichi Maenosono[1,2], Jasper Iske[1], Yeqi Nian[1,3], Yang Liu[1], Koichiro Minami[2], Haruhito Azuma[2], Hao Zhou[1], Edgar Milford[1], Abdallah Elkhal[1], Stefan G. Tullius[1]
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Background: In diseases outside of transplantation, sex has been shown to impact immune responses. Effects of donor/recipient sex and hormonal changes over a life-time on alloimmunity and transplant outcomes have not been delineated.
Methods: Using clinical data from more than 335,000 kidney transplant recipients collected in the SRTR, we examined the impact of recipient sex on graft survival stratified by multivariable cox proportional hazards regression. To delineate mechanistic aspects, we made use of skin and cardiac transplant models under controlled hormonal changes assessing alloimmune responses.
Results: Young female recipients (15-34 years) demonstrated significantly reduced 5-year graft survival rates (Log-rank, $P < 0.0001$). The impact of recipient sex on graft survival demonstrated an age-specific pattern with an improvement of graft survival in female recipients with increasing age ($P < 0.0001$). Multivariable hazard ratios for graft survival were 1.14 (95% CI, 1.03 to 1.25) in young (15-34 years) and 0.81 (95% CI, 0.72 to 0.89) in old female recipients (55-74 years).
Experimentally, skin and cardiac transplants demonstrated a prolonged survival in young male compared to female recipients (12 vs. 9 days, $P = 0.002$). Graft survival in female recipients had been linked to hormonal levels with prolonged graft survival observed in female young ovariectomized recipients (9 vs. 11 days, $P = 0.0094$). Age prolonged graft survival in both old male and female transplant recipients while ovariectomies in old mice did not alter graft survival. Notably, equitable results were obtained under CLTA4-Ig immunosuppression. Mechanistically, alloimmunity had been linked to hormonal levels with T cells of ovariectomized female mice demonstrating a compromised proliferation and reduced IFN-γ production. Consistently, $CD4^+$ T cells displayed an augmented Th1 polarization in vitro in presence of 17β-estradiol at levels reflective of a normal estrus cycle (10^{-10}M) that decreased at estrogen levels reflective of pregnancy (10^{-8}M).
Conclusion: This is the first study linking donor/recipient sex mismatches and hormonal levels to transplant outcomes. Experimental studies delineate the capacity of hormones in shaping alloimmune responses and demonstrate sex-specific effects independent of immunosuppression.

COVID-19 IN DONORS AND RECIPIENTS: SURFING THE WAVES OF PANDEMIC

OP227 IMPACT OF THE COVID-19 PANDEMIC ON WORLDWIDE ORGAN DONATION AND TRANSPLANTATION

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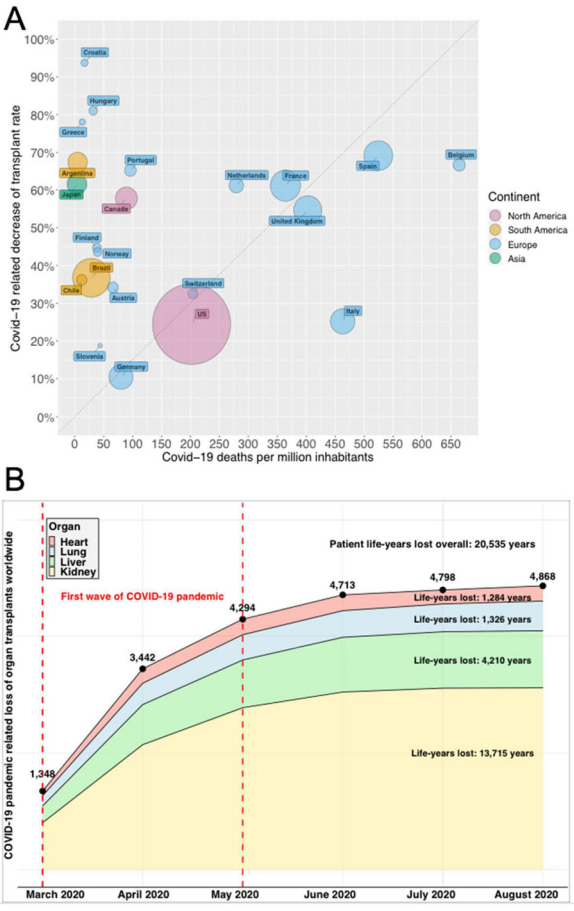
Background: COVID-19 has caused substantial reductions in solid organ transplantation. However, only limited reports are available concerning the effects of the pandemic on transplant rates worldwide.
Methods: Consecutive data on organ transplants were collected including kidney, liver, lung, and heart since the beginning of the COVID-19 outbreak in 2020 along with data from the same period in 2019 for 22 countries: 16 European, 2 North American, 3 South American, and Japan. The primary outcome was the COVID-19 pandemic effect on global transplant activity. The secondary outcome was the disparity of transplant activity within each country.
Results: Among the 22 participating countries, the overall decrease transplant activity was 31%. Three patterns of COVID-19 mortality rate and related transplant activity were identified: 1) sharp decrease in transplantations despite a low rate of deaths; 2) moderate decrease in transplantations with a high number of deaths; 3) slight decrease in transplantations with a moderate to high death rate (Figure 1A). The nation level analysis revealed 3 distinct profiles within countries: (i) nationwide reduction regardless of the low incidence of COVID cases in some regions; (ii) stable rate regardless of COVID incidence; and (iii) a decrease only in regions with a high rate of COVID cases. Finally, while the number of organ transplant rapidly dropped during the first 3 months of the pandemic, it stabilized after June 2020. Simulation models revealed that the potential organ loss corresponds to more than 20,000 patient life-years lost (Figure 1B). Given the dynamics of transplant activity across the 22 countries over time, we created an open-access dashboard, which will be updated (https://covidtransplants.org).
Conclusions: This study illustrates how the COVID-19 pandemic has been associated with an heterogeneous adaptation in terms of organ transplantation both at national levels and within countries with substantial effect on waitlisted patient mortality.

Figure 1: A) Diminution of total transplants between 2020 and 2019 according to the number COVID-19-related deaths per million in each country. B) Number of organ transplants and life-years lost during the COVID-19 pandemic in 2020 compared to 2019 by month and by organ



OP228 MAINTENANCE OF A DECEASED-DONOR KIDNEY TRANSPLANTATION PROGRAM DURING PANDEMIC SARS-COV-2

Richard Dumbill[1], Zeeshan Akhtar[2], Sushma Shankar[1], Venkatesha Udupa[2], James Gilbert[2], Isabel Quiroga-Giraldez[2], Ben Storey[2], Thomas Connor[2], Edward Sharples[2], Paul Harden[2], Philip Mason[2], Andrea Devaney[2], Martin Barnardo[2], Simon Knight[1], Rutger Ploeg[1], Peter Friend[1], Sanjay Sinha[2], Udaya Udayaraj[2], Srikanth Reddy[2]
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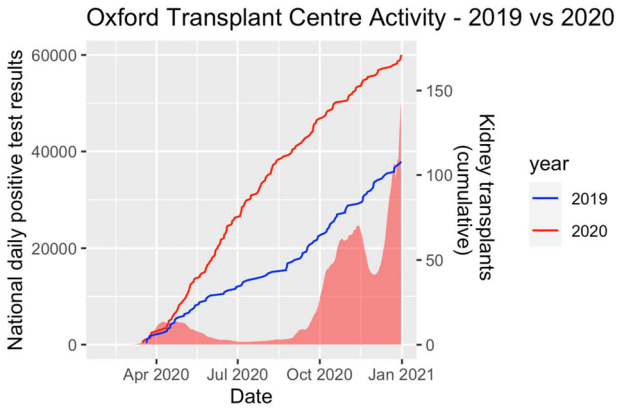
Background: SARS-CoV-2 has profoundly affected transplantation worldwide. Oxford has continued to conduct a transplant program throughout the pandemic. It is not known a) whether transplant programs should be continued or suspended in such circumstances; or b) if they are continued, what changes are necessary.
Methods: Changes made to transplant practice in Oxford and detailed clinical data were prospectively recorded during the pandemic. Data from a historical cohort (transplanted 12 months earlier) were collected retrospectively. Data for the prevalent Oxford transplant (OT) and dialysis (OD) cohorts, and England dialysis (ED) and transplant (ET) cohorts were provided by the UK Renal Association.
Results: Renal transplantation occurred in Oxford at a higher rate during the pandemic than 12 months prior (Figure 1). In the pandemic transplant cohort (operated 16/3/20 - 1/1/21, $n = 171$), there were 6 positive PCR results (3.5% vs 0/108 0% historical cohort, ns) and 2 deaths (1.2% vs 4/108 3.7% historical cohort, ns). The effects of changes to transplant practice during the first wave could be seen in longer cold ischaemia times (14 h 20 vs 11 h 45, $P < 0.05$), lower DRI (1.02 vs 1.029, $P < 0.01$), and a switch from universal Alemtuzumab induction to Basiliximab. DGF incidence (29% vs 41% historical), and complications leading to early readmission (21% vs 20% historical) remained similar.
At 1/3/20 the OD cohort consisted of 503 patients, and the OT cohort 1396. By 2/1/21 there had been 81 (OD) vs 32 (OT) positive PCR results (16% vs 2%, $P < 0.01$). There were 18 OD vs 6 OT deaths with a positive test (3.6% vs 0.4%, $P < 0.01$). We identified an additional 16 OD and 25 OT patients who were PCR −/ IgG +.
At 1/3/20 the ED cohort consisted of 23,668 patients; the ET cohort of 31,127 patients. By 2/1/21 there had been 3960 positive tests in the ED cohort vs 1018 in the ET cohort (16.7% vs 3.3%, $P < 0.01$). There were 1054 ED vs 211 ET deaths with a positive test (4.5% vs 0.7%, $P < 0.01$).
Conclusions: These results are consistent with the peri-transplant period posing an intermediate COVID-specific risk between that seen by dialysis patients, and that seen by patients with historic renal transplants. Continuation of a renal transplant program with careful donor and recipient selection therefore minimises COVID-specific risk for eligible patients on dialysis.



OP229 SAFE USE OF SARS-COV-2 POSITIVE DONORS IN LIVER TRANSPLANTATION

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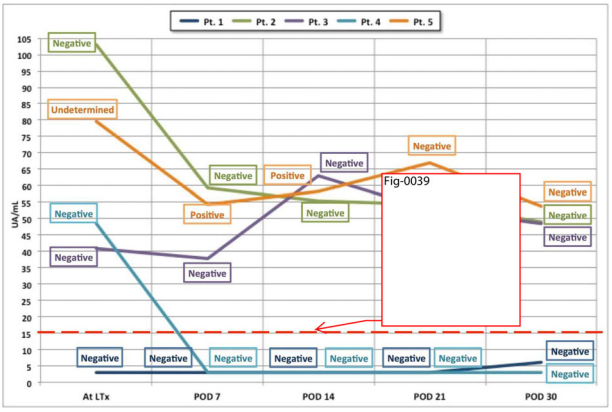
Background: In 2020, the transplant scenario has radically changed due to the COVID-19 pandemic. From November 2020, the Italian National Transplant Centre established that organs from SARS-CoV-2 positive deceased donors, can be offered to patients listed for heart or liver transplantation (LTx), who are SARS-CoV-2 positive or with a previous COVID19 infection, in serious clinical conditions, for whom the risk of death or evolution of clinical condition during the waiting list, balance the risk of a potential donor-derived infection.
Methods: From 21/11/20 to 11/12/20, 5 donors who tested SARS-CoV-2 positive at nasopharyngeal swab (NPS) or bronchoalveolar fluid (BAL) were considered suitable for LTx. During organ procurements, protective equipment such as face masks (NK-92 and FFP3), eye goggles and standard gloves and gowns were used. A liver donor biopsy was always performed to detect SARS-CoV-2. A direct real-time (RT)-PCR assay was carried out to detect SARS-CoV-2 nucleic acid in BAL or NPS, or liver biopsy specimens using a DiaSorin Simplexa® COVID-19 Direct or a Cepheid Xpert® Xpress SARS-CoV-2. Serum samples of donors and recipients (before and after LTx on post-operative day (POD) 7, 14, 21, 30) were tested for antibodies against SARS-CoV-2 with the DiaSorin Liaison® SARS CoV-2 S1/S2 IgG.
Results: Table shows donor's and recipient's features. All donors tested SARS CoV-2 S1/S2 IgG negative and SARS-CoV-2 BAL positive at harvesting; SARS-COV-2 was negative in all liver biopsies. All but one recipients experienced a pre-LTx NPS positivity and were admitted to a COVID ward with mild COVID-19. Only one patient with a previously positive NPS, was SARS-CoV-2 IgG negative: she is a baby with Wiedemann-Steiner syndrome and combined immunodeficiency needing immunoglobulin replacement therapy. The trend of SARS-CoV-2 IgG and NPS at the LTx and in the PODs are depicted in the figure. After a follow-up of two months, all the recipients and the grafts are alive, without any SARS-CoV-2-related complications.
Conclusions: A cautious use of liver grafts from SARS-CoV-2 positive donors was safe and, until now, no donor-derived infection was observed.

TABLE: Donor's and recipient's features

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
DONOR					
Age	17	51	62	51	66
Gender	M	M	F	M	F
Blood type	B	0	A	A	0
Body Mass Index (Kg/m2)	21	25	25	24	29
Cause of brain death	Trauma	Cerebrovascular	Cerebrovascular	Cerebrovascular	Meningitis
Donor Risk Index	1,70	1,57	2,28	1,90	2,16
SARS-CoV-2 symptoms before harvesting	No	No	Pneumonia	No	No
RECIPIENT					
Age	1	51	70	60	64
Gender	F	F	M	M	M
Blood type	AB	A	A	A	A
Weight (Kg)	6.4	74	73	77	52
Body Mass Index (Kg/m2)	16	28	25	26	21
Liver disease	Sclerosing cholangitis	Biliary cirrhosis	NASH	Alcohol	Alcohol
Hepatocellular carcinoma	No	No	Yes	Yes	Yes
Waiting list times (days)	10	0	19	81	57
At LTx SARS-CoV-2 IgG (UA/mL)	<3.80	103.00	40.90	48.50	79.70
MELD-Na at LTx	29	25	12	9	12

FIGURE: Trend of SARS-CoV-2 IgG at LTx and in the post-operative days (POD) 7, 14, 21 and 30; in the colored boxes the nasopharyngeal swabs (NPS) at the same intervals.



OP230 IS IT SAFE TO RECEIVE KIDNEYS FROM DECEASED KIDNEY DONORS WHO TESTED POSITIVE FOR COVID-19 INFECTION?

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Introduction: Our modern world is facing extraordinary circumstances while passing through a serious pandemic caused by the novel coronavirus (COVID-19) which may lead to multi-organ system failure & death. COVID-19 deaths may provide a potential source for kidneys available for transplantation. In our study, we are discussing the safety of receiving kidneys from donors who tested positive for the novel coronavirus.
Methodology: All renal transplant recipients registered in UNOS database who had their transplants during the 1st wave of COVID-19 pandemic between 1st of March 2020 and 4th of September 2020 were retrospectively reviewed. Patients who received kidney transplants from a deceased donor with positive COVID-19 test were included in our study. Patients were followed up till 4th of December 2020. Data about recipient factors (age, sex, ethnicity, diabetes, hypertension, body mass index, cause of renal failure, number of previous transplants, date of renal transplant), transplant factors (type of induction therapy, maintenance immunosuppressive therapy, delayed graft functions, early post-operative rejection episodes, HLA mismatch, PRA level, cold ischemia time) and donor factors (age, sex, ethnicity, diabetes, hypertension, date of COVID-19 test, type of COVID-19 test) were collected. Outcome measured were patient and graft survival till the end of the follow-up.
Results: Five renal transplant patients received kidneys from deceased donors who tested positive for COVID-19 infection. The timing of COVID-19 test ranged between one day and 12 days pre-transplant. Two donors tested positive for COVID-19 infection using nucleic acid testing one day before the transplant operation. One donor tested positive for COVID-19 infection using antibody testing two days before the transplant operation. Two donors tested positive for COVID-19 infection using antibody testing 12 days before the transplant operation. Follow-up time was six months for one patient and four months for the rest. None of the transplant recipients acute rejection episodes, graft or patient loss till the time of follow-up.
Conclusion: Receiving kidneys from deceased donors who tested positive for COVID-19 infection is considered safe and does not affect acute rejection rates, graft or patient survival.

OP231 A NATIONAL RESPONSE TO COVID PRIORITISING LIVER TRANSPLANT RECIPIENTS WITH THE HIGHEST NEED PROVIDED EXCELLENT OUTCOMES IN THE UK

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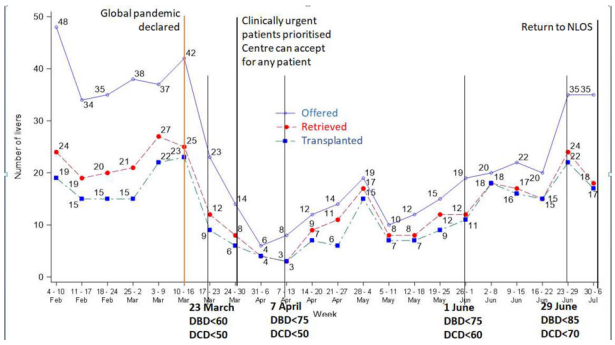
Background: The UK has been severely affected by COVID-19, with specific challenges in organ transplantation. Here, we describe the co-ordinated response to, and outcomes from, the 'first wave', across all 7 adult and 3 paediatric UK liver transplant (LT) centres.
Methods: Changes to the transplant process were agreed. These included liver donor age restrictions and changes to offering. A 'high-urgent' category was established (27th Mar–9th Jul), prioritising for LT only those with UKELD > 60, HCC reaching transplant criteria, and others deemed likely to die within 90 days. Outcomes were compared with the same time period in 2018 & 2019 when the system of national liver offering by transplant benefit had been introduced.
Results: There was a significant fall in the number of weekly LT (11 from 18), with an initial drop 84%, before gradual recovery (Figure 1). The retrieval rate for deceased donors (71%; $P < 0.0001$) and, in particular DCD (35%; $P = 0.008$) but not DBD (89%; $P = 0.2$), was higher in 2020, though subsequent transplant rate was similar.
In total, 188 LT (157 adults and 31 paediatric) were undertaken. Compared to previous 5 years, paediatric LT was maintained (mean 29); but significant reduction in adult (37%) and total (32%) LT. Almost all adult LT (148) were super urgent ($n = 15$) or high urgent ($n = 133$). We successfully prioritised those with highest illness severity (Table 1) with no prolongation of ITU or hospital stay and no reduction in 90 days patient survival ($P = 0.84$). There was a small (5% vs 3%) but significant ($P = 0.0012$) increase in deaths or removals from the UK LT waitlist, during this time which occurred predominantly in the priortised high urgency patients.
Conclusions: During the 'first wave' a nationally coordinated response mitigated against a significant fall in LT activity. LT recipients with highest need were prioritised; waitlist mortality was only marginally increased. Transplant outcomes remained excellent without a significant increase in hospital resource utilisation.
Figure 1 Number of livers from UK deceased donors offered, retrieved and transplanted, showing time points in changes to donor age restrictions and the liver offering scheme (4 Feb -9 Jul 2020)



	Median (IQR)			
Variable	2018 (N=156)	2019 (N=159)	2020 (N=97)	p value
Recipient age	57.5 (48.5 - 63.5)	55 (46 - 63)	53 (45 - 59)	0.02
Bilirubin	62 (33.5 - 121)	62 (33 - 118)	88 (46.5 - 206.5)	0.0030
INR	1.5 (1.3 - 1.8)	1.4 (1.3 - 1.7)	1.6 (1.4 - 1.9)	0.04
Sodium	136 (132 - 139)	136 (133 - 139)	136 (132 - 139)	0.6
Albumin	30 (26 - 35)	31 (27 - 36)	28.5 (26 - 34)	0.04
UKELD	56 (53 - 60)	56 (53 - 59)	58 (55 - 60)	0.01
MELD	18 (13 - 22)	16 (12.5 - 20)	18 (15 - 22)	0.01
Wait time	23.5 (8 - 92.5)	25 (7 - 96)	73 (19 - 150)	0.0030
Donor age	53.5 (39 - 64)	52 (41 - 63)	47 (35 - 59)	0.04
Donor BMI	25.95 (23.31 - 29.03)	25.95 (23.12 - 28.89)	25.75 (23.12 - 29.67)	0.91

Table 1 Recipient, donor and transplant characteristics for UK first adult elective CLD deceased donor liver transplants (27 Mar – 9 July) by year

OP232 COVID-19 IN LIVER TRANSPLANT CANDIDATES: WAIT-LIST OUTCOMES AND POST-TRANSPLANT COURSE

Giovanni Perricone[1], Christophe Duvoux[2], Chiara Mazzarelli[1], Raffaella Vigano[1], Rita Facchetti[3], Paolo Cortesi[3], Speranta Iacob[4], Sylvie Radenne[5], Damiano Patrono[6], Gabriela A. Berlakovich[7], Angus Hann[8], Luisa Pasulo[9], Lluis Castel[10], Francois Faitot[11], Olivier Detry[12], Federica Invernizzi[13], Giulia Magini[14], Paolo De Simone[15], Ilias Kounis[16], Maria Cristina Morelli[17], Fernando Diaz[18], Bo Goran Erczon[19], Carmelo Loinaz[20], Chris Johnston[21], Laure Elkrief[22], Constantino Fondevila[23], Wojciech Polak[24], Luca Belli[1]

[1]ASST GOM Niguarda , Hepatology , Milan , Italy; [2]Hôpital Henri-Mondor Ap-Hp, Créteil, France; [3]Building U8 - University of Milan Bicocca, Monza, Italy; [4]Fundeni Clinical Institute, Bucureşti, Romania; [5]Hospital La Croix-Rousse - HCL, Lyon, France; [6]Ospedale Molinette, Torino, Italy; [7]Vienna General Hospital, Wien, Austria; [8]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom; [9]Papa Giovanni XXIII hospital, Bergamo, Italy; [10]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [11]Hôpital de Hautepierre - Hôpitaux Universitaires de Strasbourg, Strasbourg, France; [12]University of Liege Hospital (ULiege CHU), Dpt of Abdominal Surgery and Transplantation, Liege, Belgium; [13]Policlinico of Milan, Milano, Italy; [14]Hôpitaux Universitaires de Genève (HUG), Genève, Switzerland; [15]Azienda Ospedaliero Universitaria Pisana - Stabilimento di Santa Chiara, Pisa, Italy; [16]Hôpital Paul-Brousse Ap-Hp, Villejuif, France; [17]S. Orsola-Malpighi Polyclinic, Bologna, Italy; [18]Gregorio Marañón Hospital, Madrid, Spain; [19]Nya Karolinska, stockolm, Sweden; [20]University Hospital 12 de Octubre, Madrid, Spain; [21]Royal Infirmary of Edinburgh, Edinbourgh, United Kingdom; [22]Hopital Trousseau, Chambray-lès-Tours, France; [23]Hospital Clínic de Barcelona, Barcelona, Spain; [24]Erasmus MC, Rotterdam, Netherlands

Background: The impact of prior SARS-CoV-2 infection on patients on the waiting list for liver transplantation (LT) and on their post-LT course is presently unknown.
Methods: Data from adult LT candidates with laboratory confirmed SARS-CoV-2 infection was collected across Europe and all consecutive patients with symptomatic COVID-19 were included in the analysis.
Results: From February 21st to November 20th, 2020, 136 adult cases with laboratory-confirmed SARS-CoV-2 infection from 33 centers in 10 European countries were collected, with 113 having symptomatic COVID-19. Thirty-three (29.2%) were managed as outpatients, 80 (70.8%) required hospitalization including admission to the intensive care unit (28/80, 35%). Thirty-seven (37/113, 32.7%) patients died after a median of 18 (10-30) days, respiratory failure being the major cause (33/37, 89.2%). The 60-day mortality risk did not change between first (35.3%, 95% CI 23.9-50.0) and second wave (26.0%, 95% CI 16.2-40.2). Multivariable Cox regression analysis showed MELD score ≥15 (MELD15-19:HR 6.09 95%CI 2.01-18.44; MELD ≥ 20:HR 5.21, 95%CI 1.76-15.45) and dyspnea on presentation (HR:4.1, 95%CI 2.09-8.06) being the two negative independent factors for mortality. Twenty-six patient received a LT after a median time of 78.5 (IQR:44-102) days and 25 are alive after a median follow-up of 118 days (IQR:31-170).
Conclusions: Mortality of LT candidates with symptomatic COVID-19 was high (32.7%) peaking at 45% in decompensated cirrhotic with MELD > 15 and did not significantly differ between the 2 waves of the pandemic, respiratory failure being the major cause of death thus supporting high priority for vaccination. Prior SARS-CoV-2 infection did not affect early post-transplant survival (96%).

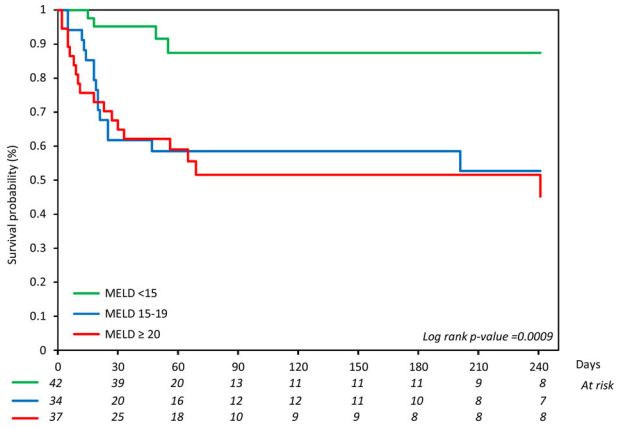


Figure 1. Kaplan-Meyer survival from the date of COVID-19 symptoms stratified by MELD

OP233 PANCREAS TRANSPLANTATION IN THE TIME OF COVID. A SINGLE CENTRE'S EXPERIENCE

Ann Etohan Ogbemudia[1,2], Fungai Dengu[1,2], Richard Dumbill[1,2], Simon Knight[1,2], Faysal El-Gilani[1,2], Srikanth Reddy[2], Isabel Quiroga-Giraldez[2], James Gilbert[2], Venkatesha Udupa[2], Paul Harden[2], Philip Mason[2], Andrea Devaney[2], Paul Johnson[1,2], Edward Sharples[2], Rutger Ploeg[1,2], Peter Friend[1,2], Sanjay Sinha[1,2]

[1]University of Oxford, Nuffield department of Surgical Sciences, Oxford, United Kingdom; [2]Oxford Transplant Centre, Oxford, United Kingdom

Background: The ongoing COVID-19 pandemic has led to significant reduction in pancreas transplantation (PT) activity worldwide. On 9th March 2020, we suspended 64 patients on our PT waiting list, excluding 4 highly sensitized patients who remained eligible for kidney transplantation. The primary reasons for suspension were the perceived risk with the use of alemtuzumab (lymphocyte depleting immunosuppression) and constrained access to intensive care.

Our PT program successfully resumed on 4th August 2020 through the adoption of new strategies and creative resource management to enable resumption of PT activity to fit into competing hospital resources and logistics.

We share our experience as well as the clinical outcomes of the first cohort of 20 discharged patients transplanted during the pandemic.

Methods: We capitalised on our strengths namely being situated in "Covid-19 free" hospital site and were able to predict a seamless resumption due to the ongoing operational infrastructure maintained by the kidney transplantation program

A. Patients were updated regularly and encouraged to continue sending monthly blood samples for tissue typing

B. Enhanced Recovery (ER) was created to ease demands on ICU capacity. This is a dedicated bed in the theatre recovery suite supported by both recovery and transplant nurses to provide level 2 (HDU) care

C. Using outcomes from pre-COVID-19 PT data, we were able to select recipients suitable for ER and define a PT acceptance process (Figure 1)

D. We revised our donor and recipient characteristics criteria to improve accepted organ offers proceeding to transplantation and also to reduce perioperative morbidity.

E. We gained support from microbiology to provide 24 h rapid COVID-19 PCR access (CEPHEID GeneXpert)

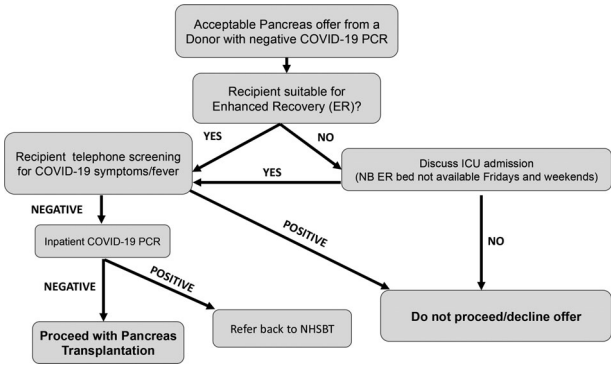


Figure 1 Pancreas transplantation acceptance process during the pandemic

Results: Our donor and transplant recipient demographics and outcomes are summarised in table 1.

Parameter (mean ± STD)	20 transplants
Donor Age, years	40.15 ± 12.4
Donor Type (DBD/DCD)	16/4
Donor BMI	21.4 ± 3.7
Recipient Age, years	43.8 ± 9.2
Recipient Sex (M/F)	10/10
Recipient BMI	24.5 ± 3.2
RRT HD/PD/Predialysis	9/4/7
Cold ischaemia time, hours	11.02 ± 1.75
Length of hospital stay, days (median)	10.5
Readmission in 30 days	5/20 (25%)
Complications	6/20 (30%)
SARS-CoV-2 positive recipients to date	1

Conclusions

Our early results following our rigorously revised PT program provides evidence that with a cautious and considered approach we can continue pancreas transplantation into the second, COVID-19 wave with alemtuzumab induction without exposing our patients to additional or new risks.

OP234 A CASE SERIES OF PAEDIATRIC KIDNEY TRANSPLANTS DURING THE ONGOING COVID-19 PANDEMIC

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Background: During the COVID-19 pandemic, multiple lockdowns and a high incidence of cases impacted European transplant programs. During the first wave, there was a need to stop both the living donor (LD) and deceased donor (DD) paediatric kidney transplant (KT) programs in our centres, subsequently reopening them fully. Increased confidence in our processes and outcomes led us to keep our deceased donor paediatric programme open during the UK's second wave. We report our experience with 25 children who received a KT.

Methods: From May 2020 to February 2021, all paediatric KT recipients were recorded and followed up in Evelina London Children's Hospital, Southampton Children's Hospital and Great Ormond Street Hospital. We prospectively recorded outcomes and instances of SARS-CoV-2 infection in KT recipients.

Results: There was 100% patient and 100% renal allograft survival in all 25 (12 (48%) female) KT recipients aged 2 to 17 (median 11) years of whom 18

were from LD (72%) and 7 from DD (28% [5 KT from donors after brain death and 2 after cardiac death]). Two patients (8%) developed COVID-19; one of them 5 weeks post-KT presenting with low grade fever and high CRP for one week without acute kidney injury during admission for surgical complication. The second one 4 months post-KT, presenting with low grade fever without any further complication. Four (16%) transplants were intraperitoneal, with 21 (84%)extraperitoneal, including an en-bloc KT. No vascular complications and two ureteric complications requiring surgical intervention were recorded. All of the patients shielded as per local guidelines.
Conclusion: During the pandemic, different strategies had to be taken to enable paediatric KT programmes to continue. This enabled safe and effective transplantation options from both living and DD. In our experience, two transplant recipients acquired COVID-19 post-transplant without renal allograft dysfunction and did not require any changes to the immunosuppression.

TACKLING SOLID ORGAN INJURY VIA DRUGS OR CELLS

OP275 THE GENETIC DELETION OF THE DUAL SPECIFICITY PHOSPHATASE 3 (DUSP3) ATTENUATES KIDNEY DAMAGE FOLLOWING ISCHEMIA/REPERFUSION IN MOUSE

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Background: DUSP3 is a positive regulator of the innate immune response in case of sepsis, but its role in the ischemic damage is unknown. We study (i) whether and where DUSP3 is expressed in the renal parenchyma, and (ii) whether its genetic deletion in mice (Dusp3−/−) attenuates the ischemic injury.
Methods: Exp1: Ten C57BL/6 male WT and Dusp3−/− mice underwent right nephrectomy and left renal ischemia (30 min)/reperfusion (48 h) (I/R). Renal function was assessed upon I/R biomarkers: serum levels of urea (BUN) and creatinine (SCr). The expression of inflammatory markers was quantified at both mRNA and protein levels in ischemic vs. non-ischemic kidneys in WT vs Dusp3−/−.
Exp2: Renal resistivity index (RRI) was measured by Doppler ultrasound ($n = 10$ mice). The expression of CD31 and VEGF vascular markers was quantified by qPCR and immuno-staining.
Results: Exp1: An immuno-reactive signal for DUSP3 was detected in nephrin-positive glomeruli and in Meca-32-positive endothelial cells in both outer and inner medulla, with no immunoreactivity in Dusp3−/− kidneys. Following I/R, the mRNA level of DUSP3 was increased 1.8-fold compared to baseline. Immunoblotting showed a 77-fold increased expression of DUSP3 post I/R. Serum levels of I/R biomarkers were significantly lower in Dusp3−/− compared to WT mice following renal I/R (BUN: 78.4 ± 33.7 vs. 258.9 ± 162.9 mg/dl; SCr: 0.1 ± 0.07 vs. 0.8 ± 0.9 mg/dl; $P < 0.01$). At mRNA levels, Dusp3−/− ischemic kidneys showed a significantly decreased expression level of TNF-α, KIM-1, IL-6, IL-1β and caspase-3 compared to WT. PCNA-, F4-80- and CD11b-positive cells were significantly reduced in Dusp3−/− versus WT renal parenchyma post I/R.
Exp2: The RRI was lower in Dusp3−/− compared to WT (0.56 ± 0.03 vs. 0.66 ± 0.02; $P < 0.001$). The Dusp3−/− kidneys were characterized by a 1.8-fold increased expression of CD31 compared to WT. At mRNA levels, the Dusp3−/− kidneys showed increased basal levels of CD31 and VEGF compared to WT.
Conclusions: The genetic deletion of DUSP3 is associated with (i) increased renal vascular density, (ii) decreased RRI and (iii) nephroprotection against renal I/R injury.

OP276 H2S ENRICHED FLUSH-OUT IN DBD AND NON-DBD PORCINE KIDNEYS

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Background: Kidney extraction time has a detrimental effect on post-transplantation outcome. We previously found that prolonged extraction time increases the risk of delayed graft function and can also lead to an elevated risk of graft failure rate in recipients. The hypothesis is that this results from a temperature increase of the kidney when extraction takes longer, which subsequently results in a higher metabolic rate. Lowering temperature or metabolic rate could potentially be protective. Therefore, this study aims to improve the flush-out and potentially decrease ischemic injury by addition of hydrogen sulphide (H_2S). H_2S is a gasotransmitter capable of inducing a hypometabolic state and its addition during abdominal flush could therefore help to reduce injury and improve organ quality.
Methods: 22 porcine kidneys (female Danish domestic pigs, +/− 62 kg) were extracted during organ recovery surgery. 4 groups were formed: living control, living H_2S, donation after brain death (DBD) control, and DBD H_2S. Directly after the abdominal flush, kidneys were extracted and flushed with or without H_2S. Next, all kidneys endured 90 min of room temperature ischemic time to simulate the increase in temperature during a deceased donor procedure before the kidneys were preserved via static cold storage for 13 h. The next day, normothermic machine perfusion was applied to test kidneys on metabolism, renal function, injury markers, and histology.
Results: No difference was seen between all four groups in metabolism, measured by oxygen consumption and ATP. Fractional sodium excretion was the best in the living control kidneys and worst in the DBD control ($P = 0.0196$). The living kidneys with H_2S show superiority in creatinine clearance compared to the DBD control group ($P = 0.0243$). No difference was seen between all four groups in perfusion parameters, injury markers (lactate, LDH, ASAT, MDA and NGAL), urine production and total protein in urine. Histology and cytokines levels still need to be performed.
Conclusion: We found an overall trend of better function in the living kidneys compared to the DBD kidneys. The addition of H_2S during the flush out had no beneficial effect in both living and DBD kidneys on the parameters studied. Further studies are needed to determine the effect of H_2S on transplant outcome.

OP277 PATTERNS AND INHIBITION OF CELL DEATH DURING STATIC COLD STORAGE OF HUMAN KIDNEYS

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Background: Estimates suggest that more than 40% of kidneys from extended criteria donors are discarded annually because they are viewed as likely to fail. However, the basis of post-transplant failure is unclear and as a result, we lack appropriate strategies to treat these organs. We hypothesized that failure will result from regulated cell death during cold ischemia and that this could be minimized by inhibiting key apoptotic pathways.
Methods: To better appreciate how kidneys respond to cold ischemia, we biopsied a series of nine kidneys at times from 12 to 72 h of cold storage and quantified cell death by means of TUNEL staining. To evaluate whether cell death was mediated by the intrinsic pathway of apoptosis, we tested the effects of a Bax inhibitor, BAI1, in a human organ culture model.
Results: We found that kidneys from older, marginal donors (70-74 y/o) had significantly more cell death visualized via TUNEL staining (Figure 1B) than younger donors (39-52 y/o) in this series (Figure 1A). Cell death increased over time and became apparent in older donors between 30-36 h of cold storage (Figure 1B). Preliminary data suggest that tubular epithelial cells are the predominate cell type positive for TUNEL staining as cold time increases. BAI1 significantly decreased cell death in human organ culture, inhibiting cell death both during cold storage and after a period of warm injury (Figure 1, C and D).
Conclusions: These data suggest that cell death throughout the course of cold storage is more extensive in marginal kidneys and can be reduced by pharmacological intervention. We speculate that inhibition of cell death in marginal organs may improve clinical outcomes.

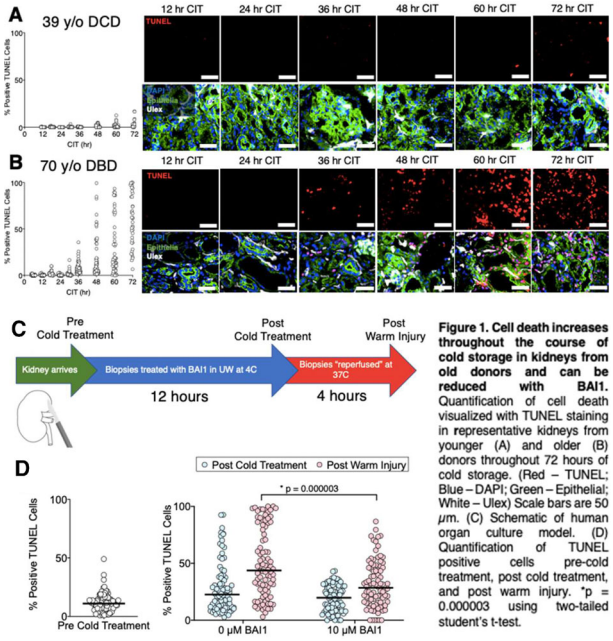

Figure 1. Cell death increases throughout the course of cold storage in kidneys from old donors and can be reduced with BAI1. Quantification of cell death visualized with TUNEL staining in representative kidneys from younger (A) and older (B) donors throughout 72 hours of cold storage. (Red – TUNEL; Blue – DAPI; Green – Epithelial; White – Ulex) Scale bars are 50 µm. (C) Schematic of human organ culture model. (D) Quantification of TUNEL positive cells pre-cold treatment, post cold treatment, and post warm injury. *p = 0.000003 using two-tailed student's t-test.

OP278 COMBINED DRUGS APPROACH TO PREVENT ISCHEMIA-REPERFUSION INJURY DURING TRANSPLANTATION OF LIVERS (CAPITL): RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Background: Ischemia-reperfusion injury (IRI) impairs outcomes after liver transplantation (LT). In a porcine LT model, a combined drugs approach (CDA) targeting several steps of the IRI-cascade reduced IRI-severity and eliminated primary graft non-function *(Monbaliu et al. Ann Surg 2009)*. We hypothesized that perioperative administration of CDA would reduce IRI after LT in humans.
Methods: A single-center, randomized controlled trial was designed to investigate efficacy of CDA with peak aspartate aminotransferase (AST) –a surrogate for IRI- as primary endpoint (NCT02251041). The CDA consisted of ex-situ portal infusion of epoprostenol, a dose of melatonin and vitamin E before recipient anesthesia and intravenous infusion during the anhepatic and reperfusion phase of antithrombin-III, infliximab, apotransferrine, EPO-β, complement-inhibitor and glutathione. Secondary endpoints were early allograft dysfunction (EAD), acute kidney injury (AKI), ischemic cholangiopathy (IC), IRI histological score and 1-year patient/graft survival. All adults receiving a first full-size LT were eligible if inclusion criteria were met.
Results: 72 patients were included (36/group). Peak AST was similar between CDA and control group (1263 ± 217 IU/l *vs.* 1451 ± 364 IU/l; $P = 0.50$). There was no difference between CDA and placebo groups in EAD (36% *vs.* 47%, $P = 0.47$), AKI (20.6% *vs.* 11.5%, $P = 0.37$), IC (12.5% *vs.* 6%, $P = 0.43$) and IRI score (3 ± 1.66 *vs.* 2.6 ± 1.64, $P = 0.35$). One-year patient and graft survival were 89% and 91% in CDA *vs.* 92% and 100% in placebo group ($P = 0.65$ and 0.07, respectively).
Conclusions: In human LT, this peri-operative CDA-approach did not reduce IRI by targeting different steps in the IRI-cascade. This is an important finding since such a pleiotropic approach has been often advocated but never been clinically evaluated. These data suggest that therapies targeting IRI alone may not necessarily suffice to ameliorate the preceding and already established preservation injury.

OP279 DONOR SIMVASTATIN TREATMENT IS SAFE AND IMPROVES OUTCOMES AFTER LIVER TRANSPLANTATION: A RANDOMIZED DOUBLE-BLIND CLINICAL TRIAL.

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[1]*IRCCS ISMETT, Palermo, Italy*; [2]*Bern University Hospital, University of Bern, Department of Biomedical Research _ Hepatology, UVCM, Inselspital, , Bern , Switzerland*; [3]*Indiana University School of Medicine, Division of Transplant Surgery, Department of Surgery, Indianapolis, United States*; [4]*University of Verona, Department of Diagnostics and Public Health , Verona, Italy*

Background: Liver transplantation (LT) is currently the only curative therapy for end stage liver disease (ESLD). However, there is a shortage in donors and there is no effective treatment for preventing short-term graft loss and ischemia-reperfusion injury (IRI) after deceased donor LT. We aimed to determine the safety and clinical benefits of treating donors with simvastatin compared with placebo at 90 and 180 days post-transplant, with special focus on the graft loss.
Methods: The SIMVAstatin donor treatment before Liver Transplants (SIMVALT) study is a monocentric, prospective, double-blinded, randomized phase 2 trial of 2 parallel groups of eligible adult patients conducted between June 30, 2018, and April 30, 2020. The trial enrolled 57 adult patients (18-65 years-old) with ESLD and/or liver tumor who were randomized to undergo LT from donors treated with simvastatin or placebo. The minimum follow-up was 6-month (last follow-up, November 30, 2020). Intention-to-treat-based population analyses was done. Simvastatin treatment was given as a single intra-gastric administration of 80 mg to donors after brain-death in the Experimental Group. In the Control Group, donors received placebo.
Results: Patient and graft survival rates at 90-day and 180-day were 100% in the Experimental Group ($n = 28$). In the Control Group ($n = 29$), the 90-day and 180-day graft and patient survivals were significantly lower, being, respectively, 89.66% ($P = 0.0804$) and 86.21% ($P = 0.0415$), and 93.1% ($P = 0.1572$) and 86.21% ($P = 0.0415$). The percentage of patients with severe Clavien-Dindo complications (≥IIIb) was higher in the Control Group 55.2% Vs 25.0% in the Experimental Group ($P = 0.0307$). There only significant changes in the LFTs' trends throughout the study between two groups, were a significant increase in gamma-glutamyl transferase (POD15 $P = 0.0174$ and POD30 $P = 0.0375$) and alkaline phosphatase levels (POD15 $P = 0.0152$), in the Experimental Group. Hospital stay were similar in both groups.
Conclusions: This study showed that donor simvastatin treatment before LT was safe has and significantly improved early graft and patient survival after LT. ISRCTN27083228.

OP280 MODIFIED IMMUNE CELL (MIC) INFUSION IN KIDNEY TRANSPLANTATION

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Background: We have recently shown that donor blood cells, modified *in vitro* by an alkylating agent (MIC, modified immune cells), induced specific immunosuppression against the allogeneic donor when administered prior to transplantation (Morath C et al., *J Clin Invest* 2020). An additional important finding was an up to 68-fold increase in the frequency of immunosuppressive $CD19^{+}CD24^{hi}CD38^{hi}$ transitional B lymphocytes compared to the frequency in transplanted controls without MIC infusions. The question arises whether donor-specific immunosuppression and increased regulatory B lymphocytes (Breg) are permanently detectable in MIC-treated patients.
Methods: Four patients from a phase-I clinical trial who had received 1.5×10^8 MIC per kg b.w. on day -7 before living donor kidney transplantation and who were on low immunosuppression during follow-up were compared to 12 transplanted control patients.
Results: MIC-treated patients showed an excellent clinical course with no donor-specific human leukocyte antigen antibodies or rejection episodes. On day 1080 after transplantation, graft function was stable with a median

serum creatinine of 1.59 mg/dl and a median urinary protein excretion of 17 g/moL creatinine. Patients had absent *in vitro* lymphocyte reactivity against stimulatory donor blood cells while reactivity against third party cells was preserved as an indication of continued donor-specific unresponsiveness. $CD19^+CD24^{hi}CD38^{hi}$ and $IL10^+CD19^+CD24^{hi}CD38^{hi}$ Breg were with 2.2/μl and 1.0/μl, respectively, strikingly higher than the 0.0/μl ($P < 0.001$) and 0.0/μl ($P < 0.001$) in transplanted controls and in the range of the numbers of healthy individuals ($N = 34$: 2.4/μl, $P = 0.73$, and 0.8/μl, $P = 0.60$). In addition, significantly higher Breg numbers were found for $CD1d^+$ ($P = 0.0071$), $CD19^+CD38^+CD147^+CD1d^+$ ($P = 0.0071$), $CD19^+CD25^+$ ($P = 0.0077$), $CD19^+CD25^+CD73^+CD71^+$ ($P = 0.013$), $CD19^+CD25^+CD73^-CD71^+$ ($P = 0.0011$), $CD19^+CD24^{hi}CD27^+$ memory ($P = 0.029$), and $IL10^+CD19^+CD24^{hi}CD27^+$ memory Breg ($P = 0.042$).
Conclusion: Donor-specific immunosuppression after MIC infusion is long-lasting and is associated with a striking increase in Breg at various stages of B cell development, including memory Breg.

OP281 CHARACTERISATION OF DISTINCT GRAFT INFILTRATES FOLLOWING REGULATORY T CELL THERAPY IN KIDNEY TRANSPLANT RECIPIENTS

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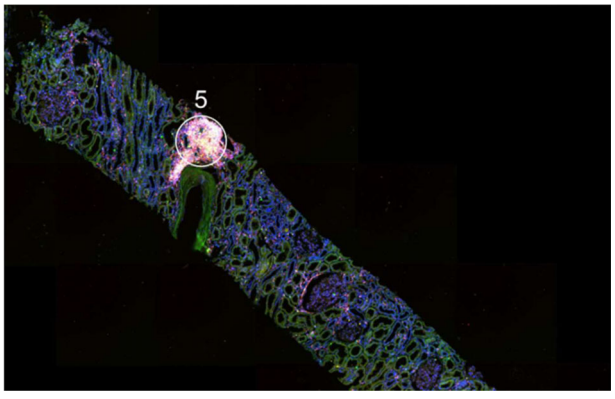
Background: Regulatory T cell therapy is an emerging treatment in the field of clinical transplantation with the potential to improve short and long-term transplant outcomes. A critical aspect of these studies is generating an understanding of how infused regulatory T cells impact on the recipient immune response to alloantigen including within the graft.
Methods: 8 Patients receiving regulatory T cell infusion as part of a phase 1 clinical trial underwent a protocol biopsy at 8 months post-transplant. Observed immune infiltrates were compared with those from patients experiencing an acute cell mediated rejection episode and infiltrates seen in routine surveillance biopsies from patients with clinically stable graft function. Biopsies were analysed by routine immunohistochemistry. NanoString GeoMX digital spatial profiling of protein and mRNA expression was performed to greater characterise immune infiltrates.
Results: Routine histology demonstrated the presence of unique cellular infiltrates in all patients treated with regulatory T cells that were dense and remarkably focal in nature. 4 colour immunofluorescence (figure) demonstrated such infiltrates contain a greater proportion of CD4+ FOXP3+ cells than infiltrates seen in patients experiencing a rejection episode (4.45% Vs 1.6%, $P < 0.001$). Principle component analysis revealed that protein expression and RNA expression patterns clearly demonstrate distinct infiltrates in rejection Vs cell therapy biopsies. Further interrogation revealed significantly different expression of cell markers such as CD3, CD45, CD14, CD68 and CD20 as well as functional markers such as Ki67, Granzyme B, CXCL9 and CXCL10 in infiltrates noted in biopsies from patients receiving cell therapy compared to those from patients experiencing a rejection episode and surveillance biopsies in patients with stable graft function.
Conclusions: Infiltrates from patients treated with cell therapy demonstrate elevated FOXP3 expression and a more quiescent or tolerant microenvironment than seen in infiltrates associated with rejection raising the possibility of regulatory T cells mediating intra-graft immune regulation. We demonstrate that infiltrates in all three clinical scenarios demonstrate unique properties and represent distinct cell populations.



OP282 LONG TERM FOLLOW-UP OF LIVER TRANSPLANT RECIPIENTS AFTER ALLOGENEIC MESENCHYMAL STROMAL CELL INFUSION

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Background: Some properties of mesenchymal stromal cells (MSCs) might be particularly of interest after organ transplantation. The authors aimed to report herein the long-term results of their first-in man, prospective, controlled, phase-1 study evaluating the safety of a single third-party MSC infusion after liver transplantation (LT).
Methods: Ten liver transplant recipients under standard immunosuppression received 1.5–3 $\times$ 10^6/kg unrelated third-party MSCs on post-operative day 3 $\pm$ 2 and were prospectively compared to a control group of 10 liver transplant recipients. Primary endpoints were set to prospectively detect potential delayed side effects of MSC infusion, and particularly occurrence of infections and cancers. As secondary endpoints, liver graft- and patient survivals, graft rejection and function, occurrence of bile duct complications, and development of anti-HLA antibodies against liver- or MSC-donors were studied.
Results: There was no difference in overall rates of infection or cancer at 5 years of follow-up between the two groups. There was also no difference in liver graft- and patient survivals, graft rejection, blood liver tests or occurrence of bile duct complications. The prevalence of de novo liver DSA related to HLA-mismatches was two times higher in the MSC group compared to the control group. Three patients of the MSC group (30%) developed at least 1 de novo HLA antibody against MSC-donor. All the de novo class II HLA antibodies against MSC were linked to a shared HLA mismatch between the liver and MSC donors and 75% of HLA class II shared-mismatches led to de novo HLA antibodies.
Conclusions: This long-term follow-up confirms the safety of one single MSC infusion after LT. The potential interesting effects of MSC need to be confirmed by prospective studies. The development of anti-HLA antibodies against MSC donor should be further evaluated especially in case of shared HLAmismatchesbetween graft- and MSC-donors, despite the fact that no deleterious effect could be detected.

REDUCING THE THREAT OF INFECTIOUS AND CARDIOVASCULAR DISEASE AFTER TRANSPLANTATION

OP323 MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE) AFTER KIDNEY TRANSPLANTATION: A POPULATION-COHORT ANALYSIS OF ENGLISH TRANSPLANT CENTRES

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Background: MACE rates within the first year after kidney transplantation in North American centres are reported at between 7.0% and 8.7% but data from European cohorts are lacking. The aim of this population-cohort analysis was to determine MACE rates within the first year after kidney transplantation in England.
Methodology: We obtained data for kidney transplant procedures performed in England between 1st April 2002 and 31st March 2018. Data were extracted from Hospital Episode Statistics using administrative ICD-10 and OPCS-4 codes, with linkage to the national death registry. We excluded age ≤18, repeat transplant in same period, multi-organ transplant and residence outside England. MACE was defined as any hospital admissions with myocardial infarction, stroke, unstable angina, heart failure, any coronary revascularisation procedure and/or any cardiovascular-related death. Univariable/multivariable logistical regression analyses were conducted to investigate the odds for MACE after kidney transplantation.
Results: Our study cohort comprised of 30,325 kidney transplant recipients. MACE events occurred in 781 patients within the first-year post-transplantation (2.6% of all kidney transplant procedures). Of these events, 201 occurred during the index admission for surgery (representing 25.7% of first-year MACE events and 0.7% of all kidney transplant procedures). Predictors of long-term mortality were age, non-White ethnicity, socio-economic deprivation, deceased donor, pre-existing diabetes, increased Charlson score, previous cardiac history and MACE within the first year (HR 2.59; 95% CI 2.34-2.88, $P < 0.001$). Patients who suffered a non-fatal MACE within the first year had 1-, 3-, 5- and 10-year patient survival of 80.5%,

70.2%, 54.5% and 38.6%, compared to 97.4%, 94.4%, 90.7% and 78.4% for patients not developing MACE ($P < 0.001$). Patients having MACE events during the index admission compared to subsequent admissions were differentiated by age, sex and previous cardiac history but had similar patient survival ($P = 0.283$).
Discussion: MACE events within the first year after kidney transplantation are associated with increased mortality risk in England but incidence is significantly lower at 2.6% than those reported in North America despite similar cardiac screening strategies.

OP324 IMPACT OF EVEROLIMUS-TACROLIMUS COMBINATION ON CARDIOVASCULAR PARAMETERS EVALUATED BY CARDIAC-MRI. RESULTS FROM A PILOT RANDOMIZED CLINICAL TRIAL

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Background: Left ventricular mass hypertrophy (LVH) is a common echocardiographic finding in patients in dialysis or waiting list. Although renal transplantation improves LVH, data on the effect of mTORI in combination with an CNI are conflictive. ENHVIE study (ClinicalTrials.gov Identifier: NCT03415750) is an exploratory RCT evaluating the impact of a CNI-iMtor combination on LVH in kidney transplant recipient through Cardiac-MRI.
Methods: Patients were recruited if LVH was confirmed by Cardiac-MRI. Other inclusion criteria were: +12 months from transplantation, eGFR-CKD EPI > 30 ml/min, and no contraindication to mTORI. At study entry all patients received immunosuppression with tacrolimus (TAC) plus mycophenolate mophetil (MMF), and they were randomized either to continue with TAC+MMF, or to shift to TAC+EVR. Primary endpoint was reduction in Left Ventricular Mass (LVM, 10 gr/m^2) after 12 months from randomization. Secondary endpoints were: change in aortic distensibility, blood pressure (measured by ABPM), and change in Global Longitudinal Strain (software Qstrain 2.0)
Results: 20 out of 56 screened patients presented LVH at Cardiac-MRI and were randomized 1:1 either to continue with MMF-TAC or to switch to EVR/TAC. The two study groups were similar for baseline characteristics. 85% of patients had a no dipper status at ABPM.
At the end of the study, no significant difference was observed in reduction in LVM (ΔLVM 1.75 [-3.4-+9.4] gr/m^2 vs 4.4 [-6.5-+7.9] gr/m^2 control vs study group, respectively. *P.* 0.65. Figure 1). Secondary endpoints for control vs study group were not different.
Three patients reached the primary outcome: 2 in control group, 1 in study group. Use of ARBs/ACEi was the only variable to be related to a reduction of LVM (ΔLVM 11[4.5-13] gr/m^2 vs 0.8 [-3-+7.5] gr/m^2 for users vs not users *P.* 0.03).
Conclusions: Conversion from MMF to mTORI in kidney transplant recipients showed no impact on cardiac and vascular (aortic) parameters measured by gold-standard technique (cardiac-MRI). To reduce LVH of kidney transplant, use of ARBs/ACEi seems to be effective.

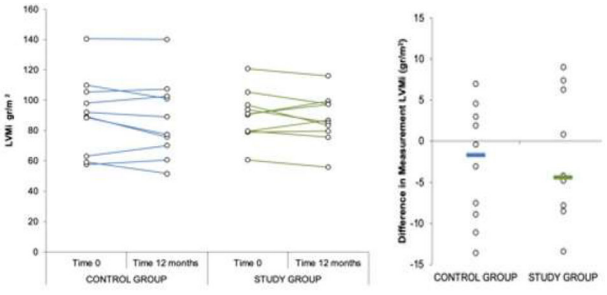

FIGURE1. A. Evolution of Left Ventricular Mass indexed for BSA for each patient in control and study group.
B. Difference in measurement for each patients. Box represent median values for each group.

OP325 PHASE 3 OPEN-LABEL STUDY OF MARIBAVIR FOR REFRACTORY/RESISTANT CYTOMEGALOVIRUS INFECTION IN TRANSPLANT RECIPIENTS: SUBGROUP ANALYSES BY ORGAN TYPE

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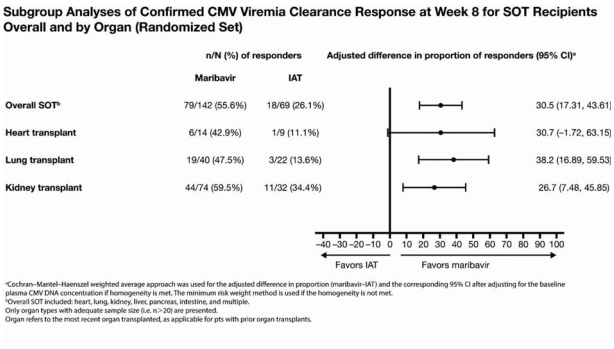
Background: Treatments (Tmt) for refractory with/without resistance (R/R) cytomegalovirus (CMV) infections are limited. We report subgroup analyses by SOT type from a multicenter randomized trial that assessed the efficacy of maribavir (MBV) vs investigator-assigned therapy (IAT) in pts with R/R CMV infection.
Methods: Transplant recipients (≥12 yrs) with CMV infection (viral load [VL] ≥2730 IU/ml/≥910 IU/ml CMV DNA [blood/plasma]) refractory to recent Tmt (failure to achieve > 1 $\log_{10}$ decrease in CMV DNA after ≥14 days) were eligible (NCT02931539). Stratified (HCT/SOT + screening CMV VL) pts were randomized 2:1 to MBV 400 mg BID or IAT (val/ganciclovir, foscarnet, cidofovir, foscarnet+val/ganciclovir) for 8 wk Tmt period + 12 wks follow-up. Primary endpoint: confirmed CMV clearance (plasma CMV DNA < 137 IU/ml in 2 consecutive tests ≥5 days apart) at end of Wk 8. Key secondary endpoint: CMV clearance and symptom control at end of Wk 8 and maintained through Wk 16. Tmt group differences, adjusted for baseline CMV DNA (< 9100/≥9100 IU/ml) + SOT/HCT were compared (Cochran–Mantel–Haenszel tests). Subgroup analyses by SOT type were conducted.
Results: 352 pts were randomized (235 MBV, 117 IAT; median age 55 yrs [range 19–79]). Significantly more pts (MBV vs IAT) achieved the primary (55.7% vs 23.9%; difference, 95% CI: 32.8%, 22.8–42.7; $P < 0.001$) and key secondary endpoint (18.7% vs 10.3%; difference, 95% CI: 9.5%, 2.0–16.9; $P = 0.013$). 211 pts (59.9%) were SOT recipients (kidney, 50.2%; lung, 29.4%; heart, 10.9%; liver, 3.3%; pancreas, 0.9%; intestine, 0.5%; multiple, 4.7%). No SOT pts lost grafts. A benefit trend for MBV vs IAT in kidney, lung, and heart transplants (subgroups with adequate sample size) was seen (Figure). Overall population: Tmt-emergent AEs (TEAEs) occurred in 97.4% MBV vs 91.4% IAT pts; 2 Tmt-related serious TEAEs led to death (1 pt/arm). Acute kidney injury (TEAE) was lower with MBV vs foscarnet (8.5% vs 21.3%) as was Tmt-related acute kidney injury (1.7% vs 19.1%). Neutropenia (TEAE) was lower with MBV vs val/ganciclovir (9.4% vs 33.9%) as was Tmt-related neutropenia (1.7% vs 25.0%).
Conclusions: MBV had superior efficacy vs IAT in clearing CMV in transplant recipients with R/R CMV infection, with consistent trends across organ types. Overall, MBV exhibited lower rates of Tmt limiting toxicities common with IAT.



OP326 SURVEILLANCE AND TREATMENT OF HUMAN HERPESVIRUS 8 IN TRANSPLANT RECIPIENTS: A STRICT PROTOCOL TO BRING MORTALITY TOWARD ZERO

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Background: Human Herpesvirus 8 (HHV8) has been associated to a broad spectrum of diseases in solid organ transplantation (SOT) recipients. Donor derived infection (DDI) has been associated with rapidly fatal cytokine storm (KICS: Kaposi Sarcoma Associated Herpes Virus Cytokine Syndrome). ISMETT has developed a protocol aiming to promptly detect and treat HHV8 DDI in D+/R−.
Methods: HHV8 serology (IFA lytic and latent) was performed on 771 donors and 1171 recipients (liver 574; kidney 386, heart 88; lung 92; pancreas 1, combined 30) between 2011 and 2019 to determine risk of HHV8 DDI. HHV8DNA strict monitoring by real-time polymerase chain reaction was performed after SOT. Since 2017 we established a protocol of early treatment of patient with detectable HHV8DNA with early switch to m-TOR inhibitor, patients with KICS received rituximab. We studied rate of HHV8 DDI transmission and outcome in the pre- and post- intervention period.
Results: 28 donors (3.7%) and 88 recipients (7.5%) were HHV8-seropositive. Among 2 heart, 1 lung and 7 kidney recipients with mismatch none developed DDI. Among 23 liver recipients with mismatch, 15 (65%) had a HHV8 donor derived infection: 11 patients developed non neoplastic disease of them 7 were KICS. In the era pre-intervention (2011-2016) among 5 patients who developed disease 3 (60%) had a rapid fatal outcome. In the post-intervention period (2017-2019), 6 patients developed disease and were promptly treated, none of them died and they had complete resolution of HHV8 disease.
Conclusions: Primary DDI HHV8 can cause a severe nonmalignant illness. Donor screening for HHV8 Ab to identify recipients at risk is strongly advised; however, lack of a standardized serology is the major limiting factor to support this recommendation. In the high-risk group strict HHV8DNA monitoring, clinical surveillance, early introduction of mTOR inhibitor and use of rituximab in case of KICS may bring mortality to zero.

OP327 MTOR INHIBITORS PREVENT CMV INFECTION THROUGH THE RESTORATION OF FUNCTIONAL AB AND ΓΔ T CELLS IN KIDNEY TRANSPLANTATION

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[1]CNRS UMR 5164 , Immunoconcept, Bordeaux, France; [2]CHU Bordeaux, Nephrology Transplantation Dialysis Apheresis, Bordeaux, France; [3]INSERM , U1218, IECB, Talence, France; [4]University of Bordeaux, CNRS UMS 3427, Bordeaux, France; [5]CHU Bordeaux, Department of Virology, Bordeaux, France; [6]INSERM , ACTION, U1218, IECB, Talence, France; [7]University of Bordeaux, IBGC UMR5095, Bordeaux, France; [8]CHU Bordeaux, Department of Immunology, Bordeaux, France; [9]University of Bordeaux, INSERM U1219 , Bordeaux, France; [10]CNRS UMR 5164 , Immunoconcept, Bordeaux, France

Background: The reported association of mTOR-inhibitors (mTORi) treatment with a lower incidence of cytomegalovirus (CMV) infection in CMV-seropositive (R+) kidney transplant recipients (KTR) remains unexplained.
Methods: The incidence of CMV infection and T-cell profile was compared between mTORi-treated and mycophenolic acid (MPA)-treated KTR, and we analyzed mTORi effects in vitro on T cell phenotype and functions.
Results: In MPA-treated R+ KTR, we showed that both alpha-beta and gamma-delta T cells displayed a more dysfunctional phenotype (PD-1+, CD85j+) at day 0 of transplantation in the 16 KTR with severe CMV infection when compared to the 17 KTR without or with spontaneously resolving CMV infection. In mTORi-treated patients ($n = 27$), the proportion of PD-1+ and CD85j alpha-beta and gamma-delta T cells decreased when compared to MPA-treated patients ($n = 44$), as well as the frequency and severity of CMV infections. mTORi treatment also led to higher proportions of late-differentiated and cytotoxic gamma-delta T cells, and IFNgamma-producing and cytotoxic alpha-beta T cells. In vitro, mTORi (i) increased proliferation, viability and CMV-induced IFNgamma production of T cells, (ii) decreased PD-1 and CD85j expression in T cells that shifted to a more efficient EOME-S^{low} HOBIT^{high} profile. In gamma-delta T cells, mTORi effect was related to increased TCR signaling.
Conclusion: Our results reveal (i) that severe CMV replication is associated with a dysfunctional T-cell profile and (ii) that mTORi improve T-cell fitness in association with a better control of CMV. Dysfunctional T cell phenotype could represent a new biomarker to predict post-transplantation infection and to stratify patients who should benefit from mTORi treatment.

OP328 PRECISION MEDICINE IN TRANSPLANTATION: MAGNITUDE, DURATION, AND IMPACT OF CMV VIREMIA ON GRAFT AND MORTALITY OUTCOMES

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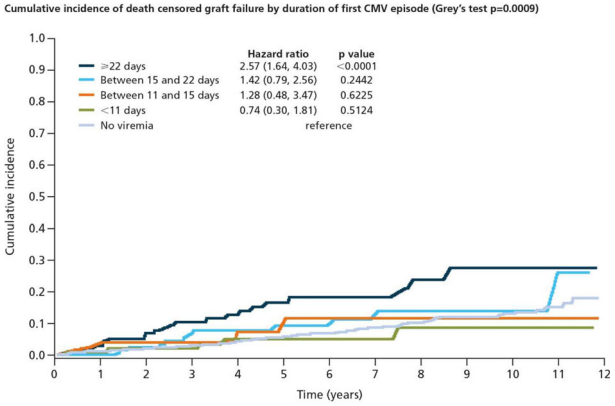
Background: The Genome Canada Precision Medicine Program mapped a large transplant cohort with uniform management for prognostic implications of cytomegalovirus (CMV) viremia, immune suppression, and antiviral therapy to define the impact of viremia on graft and patient outcomes.
Methods: A retrospective database analysis of patients who received a renal transplant at University of British Columbia Jan 1, 2008–Dec 31, 2018 were followed until Dec 31, 2019 and stratified by donor source, graft number, donor/recipient (D/R) CMV status (+/−) and viral episode for analysis of quantitative viremia, clearance, recurrence, and graft and patient outcomes. Kaplan–Meier plots (survival probability log-rank test for death, and cumulative incidence Gray's test for graft failure) were used to compare CMV viremia outcomes. Unadjusted hazard ratios (HR) were calculated with a Cox proportional model.
Results: This analysis included 2466 patients; 60% white, 63% male, mean age ± SD 52 ± 15 years; and CMV strata were D+/R+ (36%), D+/R− (18%), D−/R+ (28%), and D−/R− (18%). 434 patients developed CMV viremia (viral titer ≥830 IU/ml) with cumulative frequency: D+/R− (34%), D+/R+ (22%), D−/R+ (12%), D−/R− (1%). Patients had 1–4 episodes of viremia (mean ± SD 1.2 ± 0.5 episodes). Median time to first viremia was 120 days; this was shortest in D+/R+ (81 days), followed by D−/R+ (91 days), then D+/R− (236 days) reflecting routine prophylaxis strategies, and D−/R− (1794 days). Viremia episodes ranged by 2–114 days (mean ± SD 19 ± 13 days), with a significant linear relationship between maximum viral load and viremia duration ($P < 0.0001$). Patient mortality (15% vs 11%, $P = 0.005$) and death-censored graft failure (10% vs 7%, $P = 0.007$) were more frequent in patients with CMV viremia vs no viremia. Death-censored graft failure was greatest in patients with viremia episodes ≥22 days (graft failure HR: 2.57, 95% CI: 1.64, 4.03; Figure).
Conclusion: Magnitude and duration of CMV viremia are significantly correlated, with duration a prognostic risk for graft loss and death. Timing, magnitude, and duration of CMV viremia are heterogeneous within the D/R CMV status risk strata despite uniform treatment strategies. Detailed monitoring and rapid, effective therapy are therefore important to maximize transplant graft success and patient survival.



Episode durations were stratified by quartiles and hazard ratios were calculated relative to no viremia (p=0.0001).

OP329 POST-HOC ANALYSIS OF THE CAVIAR STUDY: DO SHORT-TERM BENEFITS OF LIFESTYLE INTERVENTION TRANSLATE TO LONG-TERM BEHAVIOUR CHANGE AT 3-YEARS?

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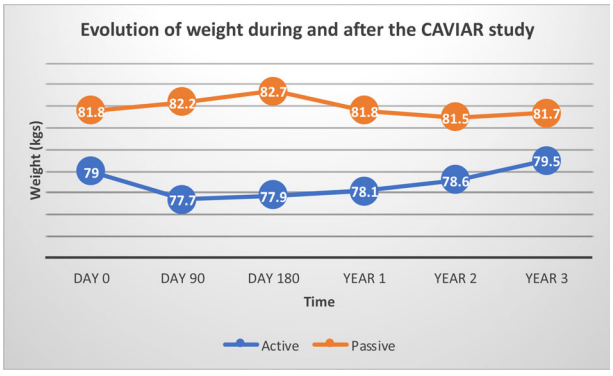
Background: The CAVIAR study (*Transplantation 2020;104(7):1491-1499*) was a randomised controlled trial comparing benefits of active (renal dietitian using behaviour change techniques) versus passive (leaflet advice) lifestyle intervention in kidney transplant recipients. Active versus passive lifestyle intervention reduced the incidence of post-transplantation diabetes (PTDM) (7.6% versus 15.6%, respectively, $P = 0.123$) and lowered weight (mean difference −2.47 kg, $P = 0.002$) over the 6-month study duration. However, poor long-term adherence to behaviour change may attenuate short-term clinical benefits. In this planned post-hoc analysis, CAVIAR study participants were analysed 3-years after study recruitment (2.5 years after study completion) to see how they fared.
Methods: Between August 17th 2015 and December 18th 2017, 130 individuals were recruited and gave informed consent for electronic data linkage beyond 6-month study completion. Data were extracted from electronic patient records at 3-years for: weight, creatinine, total cholesterol, PTDM, cardio-metabolic medications, cardiovascular events, death-censored graft and patient survival. Data with regard to weight were captured at six timepoints: during study (baseline, day 90, day 180) and post study (1-year, 2-years, 3-years). Data were analysed using R Studio (Version 1.3.959) as an intention-to-treat analysis.
Results: From 130 study participants, 9 were lost to follow-up leaving 121 patients records for review. Compared to study completion, active study participants gained weight (+1.6 kg) while passive study participants lost weight (-1.0 kg). Weights returned to baseline for both groups (see Figure). Comparing active versus passive groups, there was no difference in PTDM rates (16.1% versus 13.6%, respectively, $P = 0.691$), patient survival (100.0% versus 96.7%, respectively, $P = 0.147$) or death-censored graft survival (96.8% versus 98.3%, respectively, $P = 0.578$). There was no difference in creatinine, cardiovascular events or use of cardio-metabolic medications between groups.
Conclusions: Our post-hoc analysis of the CAVIAR study suggests behaviour change intervention requires incorporation into routine clinical care for short-term clinical improvement to translate into sustainable long-term benefits.



OP330 BARIATRIC SURGERY COMPROMISES MACROPHAGE DRIVEN ALLOIMMUNITY IN OBESE TRANSPLANT RECIPIENTS

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Background: Obesity initiates a chronic inflammatory network linked to more frequent perioperative complications and increased acute rejection rates after organ transplantation. Clinically, obese transplant candidates have undergone bariatric surgery facilitating transplantation. The effects of obesity on alloimmunity and transplant outcomes have not been defined.
Methods: We delineated the effects of obesity and bariatric surgery on alloimmunity and transplant outcomes in diet induced obese (DIO) mice. Performing allogeneic skin transplants in DIO recipient mice that underwent sleeve gastrectomies (SGx), we defined the interplay of innate and adaptive immune responses; quantitative metabolomic profiling in lean, DIO and DIO mice undergoing SGx delineated the effects of metabolic changes on alloimmunity.
Results: Skin transplants were rejected significantly earlier in mismatched DIO mice ($P < 0.01$). DIO recipients that underwent SGx prior to transplantation, in contrast, demonstrated significantly prolonged graft survival times ($P = 0.05$) with reduced Th1 and Th17 frequencies ($P < 0.001$). This observation was further confirmed in vitro with compromised IFN-γ expression in MLR ($P < 0.01$) while IL-10 production had been increased ($P = 0.05$). Through metabolomic profiling, we identified restored TDCA/Valine levels following SGx comparable to those in lean controls that had been depleted in DIO mice. Mechanistically, we delineated restrained macrophage polarization through TDCA/valine via TGR5 signaling to inhibit $CD4^+$ T cell activation leading to a decreased production of IL-17 and IFN-γ in vitro and in vivo.
Conclusions: We provide novel insights into obesity induced inflammation and its impact on allo-immunity and transplant outcomes. SGx initiated anti-inflammatory capacities on $CD4^+$ T cell driven allo-immune responses through compromised macrophage polarization. Restored TDCA/Valine levels simulated the effects of SGx, suggesting those metabolites as novel treatments ameliorating obesity augmented alloimmune responses.

FRONTIERS IN KIDNEY IMMUNOSUPPRESSION

OP363 IMMUNE RESPONSES FOLLOWING TOCILIZUMAB THERAPY TO DESENSITIZE HLA-SENSITIZED KIDNEY-TRANSPLANT CANDIDATES

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Background and Aims: Kidney-transplant candidates (KTCs) who are HLA highly sensitized (calculated panel-reactive alloantibodies > 95%) have poor access to deceased-kidney transplantation unless desensitization is attempted.
Methods: In this single-center prospective study, 13 highly sensitized desensitization-naïve KTCs received IV tocilizumab (8 mg/kg) every 4 weeks. We evaluated tolerability as well as immune responses, i.e., T-cell-, B-cell-, T-follicular helper [Tfh]-subsets, blood cytokines (IL-6, soluble IL-6 receptor -sIL-6R-, IL-21), blood chemokines (CXCL10, CXCL13), and anti-HLA alloantibodies.
Findings: Over the tocilizumab treatment course, six patients presented with mild leucopenia, four presented with mild thrombopenia, and four had a slight increase in aminotransferase levels. Only one patient presented with an infectious complication, i.e., spondylodiscitis. Regarding immune parameters, there were no significant changes of percentages of lymphocyte subsets, i.e., CD3+, CD3+/CD4+, CD3+/CD8+ T cells, and NK cells. This was also the case for Tfh-cell subsets, B cells, mature B cells, plasma cells, pre-GC B cells, and post-GC B cells, whereas we observed a significant increase in naïve B cells ($P = 0.02$) and a significant decrease in plasmablasts ($P = 0.046$) over the tocilizumab treatment course. CXCL10, CXCL13, IL-21, total IgG, IgA, and IgM levels did not significantly change during tocilizumab therapy; conversely, there was a significant increase in IL-6 levels [44 (1Q 6.2; 3Q 246) vs. 197 (1Q 180; 3Q 219) pg/ml); $P = 0.03$] and a huge increase in sIL-6R [63,815 (1Q 57,475; 3Q 88,828) vs. 358,271 (1Q 330,740; 3Q 396,376) pg/ml; $P = 0.00004$]. There was a marginal effect on anti-HLA alloantibodies (class-I and class-II).
Conclusions: In highly sensitized KTCs, tocilizumab as a monotherapy was well tolerated and associated with a significant decrease in plasmablasts; however, it had almost no effect on anti-HLA alloantibodies.

OP364 TOCILIZUMAB AS FIRST-LINE THERAPY FOR CHRONIC/ACTIVE ANTIBODY MEDIATED REJACTION IN KIDNEY TRANSPLANT RECIPIENT: 12 MONTHS MONOCENTRIC EXPERIENCE

Marco Busutti, Alessandra Cingolani, Valeria Grandinetti, Federica Maritati, Claudia Bini, Francesca Iacovella, Valeria Corradetti, Simona Barbuto, Giorgia Comai, Gaetano La Manna

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Introduction: Kidney transplant is the gold standard treatment for end-stage renal disease (ESRD). One of the major causes of long term graft loss is represented by chronic-active antibody mediated rejection (cAMR), an entity whose diagnosis is based on laboratoristic and histologic elements. Treatment of cAMR is an open field of debate. Tocilizumab, an anti-IL6 monoclonal antibody has been recently proposed as a first line treatment for cAMR showing encouranging results.
Methods: We describe our monocentric experience using Tocilizumab as first-line therapy for cAMR; graft function and proteinuria has been checked monthly, DSA and histology have been evaluated every 6 months.
Results: 12 KTx recipients reached a follow-up of 12 months. We excluded from analysis patient with concomitant relapse of nephropathy and/or diagnosis of other types of rejection. Mean graft age at baseline was 14 $\pm$ 6.6 years. Mean DSA MFI was 7500 $\pm$ 1800 for Class I and 19,300 $\pm$ 3600 for Class II HLA. Kidney function showed a progressive worsening during follow-up that reaches statistical significance at 12 months (eGFR 30 $\pm$ 9 ml/min at baseline; 27 $\pm$ 7 ml/min at 6 months; 23 $\pm$ 14 ml/min at 12 months), conversely proteinuria remained stable during follow-up period. 3 patients shown graft failure during follow-up requiring RRT. We did not observed any statically significant variation in DSA MFI levels.
From a histological point of view, we observed a significant improvement in active cAMR lesions (C4d deposition and Acute tissue injury (MTA, g > 0/ ptc > 0, v > 0)) and no progression among chronic lesions (Transplant glomerulopathy, PTC multilayering and arterial intimal fibrosis). No adverse effects has been observed.
Conclusions: Tocilizumab shown encouraging results, reducing kidney inflammation and active lesions in kidney biopsy and not allowing progression of chronic lesions. Although we observed a progressive worsening of kidney function, our population was burdened by severe graft disfunction and advanced chronic lesions at baseline. We can reasonably suppose that significant improvement in long term kidney function can be achieved starting Tocilizumab in earlier stage of graft dysfunction.

OP365 CLINICAL TRANSLATION OF CD40-CD154 PATHWAY CO-STIMULATION BLOCKADE IN SOLID ORGAN TRANSPLANTATION

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Novartis Institutes for Biomedical Research, Basel, Switzerland

Background: Transformative improvements for the prevention of allograft rejection have been a result of development of medicines like calcineurin inhibitors (CNIs). Yet long-term allograft survival and function remains a high unmet need, emphasizing the importance of development of new therapeutics. Blocking CD28-CD80/CD86 interactions resulted in prolongation of allograft survival, spurring interest in development of therapies that target other costimulatory pathways like CD40-CD154 interactions. The primary aim of our research was clinical translation of the CD40-CD154 blockade in transplantation (Tx) with the anti-CD40 antibody iscalimab, including delineation of its mechanism of action, as well as how it differentiates from other medications used in Tx.
Methods: We compared the effects of iscalimab to CNIs in a non-human primate (NHP) model of kidney Tx. Subsequently we performed a 12-month multicenter RCT evaluating efficacy, safety, and tolerability of iscalimab in combination with mycophenolate mofetil (MMF) and corticosteroids (CS) compared with tacrolimus (TAC), MMF and CS, in de novo kidney Tx recipients (NCT02217410). All patients received basiliximab induction.
Results: Iscalimab prolonged kidney allograft survival and function in NHP. Blinded analyses indicated that iscalimab treatment resulted in statistically significant improvements in allograft histology and transcriptomics in comparison to CsA. In the clinic, close to normal histology was maintained with iscalimab in contrast to TAC, albeit in a limited number of patients. These data were consistent with superior renal function observed with iscalimab vs. TAC after 6 months (53.0 vs 44.0 ml/min), comparable composite endpoint of treated BPAR, graft loss and death (iscalimab 21.2 vs TAC 22.2%), less serious AEs, and a lower rate of new-onset diabetes mellitus with iscalimab vs TAC.
Conclusions: We describe key findings in the translation of CD40-CD154 blockade into the clinic, highlighting the positive preclinical and clinical proof-of-concept data that support further clinical development of iscalimab. Additionally, differentiating histological and molecular features following iscalimab treatment in kidney TX could enable this therapeutic approach to address long-term allograft survival and function.

OP366 IMPAIRED FLU-SPECIFIC MEMORY B CELL RESPONSE AFTER INFLUENZA VACCINATION IN BELATACEPT-TREATED KIDNEY TRANSPLANT RECIPIENTS

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Background and aims: Costimulation blockade with Belatacept (BELA) is known to modulate directly B-cell function and at the B cell-T follicular helper (Tfh) cell interaction, ultimately inhibiting the production of *de novo* DSA. However, whether this effect is exclusively mediated on alloantigen-specific B-cell responses or if it has a broader effect in other non-HLA-antigen B-cell responses it has not been elucidated yet. The objective of this work was to compare the kinetics and function of circulating Tfh and memory B cells specific against influenza antigen ($H1N1^+$mBC), in kidney transplant (KT) recipients receiving a BELA-based or a tacrolimus (TAC)-based regimen after influenza vaccination.
Methods: Twenty-three consecutives KT patients ($n = 9$ on BELA and $n = 14$ on TAC), receiving the influenza vaccine covering the H1N1 antigen, were included in this study. $H1N1^+$mBC ($CD19^+CD27^+H1N1^+$) and Tfh ($CD4^+CD45RA^+CXCR5^+$) cells were assessed using flow cytometry both prior and at different time-points during the first 3 months after vaccination (10 days, 1 month, 3 months). All patients displayed no DSA and a stable graft function at time of study.
Results: Circulating Tfh were significantly lower in the BELA group than TAC patients at baseline (6.9% vs 12.8% of CD4+ T cells, $P = 0.02$) and remained stable after vaccination at all time points in both groups. While the median percentage of $H1N1^+$mBC was similar prior to vaccination (0.18% vs 0.13% of CD19+ cells, in BELA and CNI, respectively, $P = 0.64$), significantly lower frequencies in the BELA group were observed at month 3 (0.15% vs 0.27%, respectively, $P = 0.05$). Interestingly, among patients with very low frequencies of $H1N1^+$mBC at baseline, suggesting to have no baseline mBC response, a high increase of $H1N1^+$mBC at M3 was only observed within the TAC group whereas the frequencies remained unchanged as compared to baseline in the BELA group (Ratio % $H1N1^+$mBC M3/Baseline = 5.1 $\pm$ 5.9 vs 0.7 $\pm$ 0.1 in TAC and BELA, respectively, $P = 0.02$).
Conclusion: BELA-treated KT patients seem to be less capable to generate and maintain a flu-specific mBC response after vaccination compared to those receiving a TAC-based regimen, especially in absence or low $H1N1^+$mBC prior to immunization, thus suggesting an impaired capacity to produce *de novo* antigen-specific mBC under co-stimulation blockade

OP367 BRINGING A PHARMACOKINETIC POPULATION MODEL INCLUDING PHARMACOGENETICS INTO CLINICAL PRACTICE TO OPTIMIZE TACROLIMUS DOSAGE IN RENAL TRANSPLANTATION

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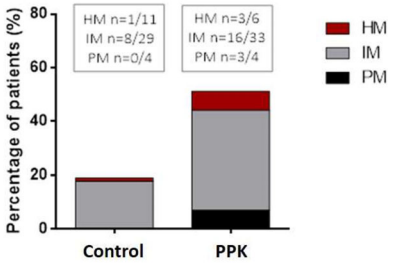
Background: Tacrolimus (Tac) dosage in renal transplant according to the manufacture's labelling considering patient body weight results in higher percentage of patients out of postulated targets. A population pharmacokinetic model (PPK) may help to optimize Tac adjustment. Our group previously developed a PPK model including pharmacogenetics (cluster *CYP3A4* and *CYP3A5* enzymes), age and hematocrit.
Methods: we conducted a prospective two-arm, randomized clinical trial to determine Tac starting dose and subsequent dose adjustments in renal transplant recipients. Patients were randomized as control group with Tac dosage according to the manufacturer's labelling or PPK group adjusted

CYP phenotype:	PM			IM			HM		
Group:	Control $n = 4$	PPK $n = 4$	*P*	Control $n = 29$	PPK $n = 31$	*P*	Control $n = 10$	PPK $n = 6$	*P*
Dose modifications to get target	3.3 ± 1.7	0.3 ± 0.5	*0.022**	1.8 ± 1.5	0.6 ± 0.8	*0.0002****	1.5 ± 0.5	0.5 ± 0.6	*0.008***
Times under-exposure (90 days) C_0 < 6 ng/ml	3.5 ± 1.7	0.3 ± 0.5	*0.017**	1.8 ± 1.5	1.0 ± 1.2	*0.048**	2.1 ± 1.5	1.0 ± 1.1	*0.177*
Times over-exposure (90 days) C_0 > 10 ng/ml	1.3 ± 1.5	0.3 ± 0.5	*0.321*	1.7 ± 1.3	0.5 ± 0.8	*0.000****	0.6 ± 0.7	0.3 ± 0.5	*0.459*

Figure 1



Percentage of patients that achieved Tac C_0 target after the first steady-state. Each column represents the percentage of kidney-transplanted patients that achieved Tac C_0 target (6-10 ng/ml) after receiving the first dose. Columns are stratified in colors considering the CYP phenotype of patients in each group [poor (PM) (*CYP3A4*22* carriers with *CYP3A5*3/*3*), intermediate (IM) (*CYP3A4*1/*1* with *CYP3A5*3/*3* or *CYP3A4*22* carriers with *CYP3A5*1* carriers) and high metabolizers (HM) (*CYP3A4*1/*1* and *CYP3A5*1* carriers)].

based on target C_0 exposures using a Bayesian prediction model. Primary endpoint: Percentage of patients that achieved Tac C_0 target (6-10 ng/ml) after first Tac dose with a 30% of superiority margin. Secondary aims: days needed to achieve target, dose adjustment fluctuations and benefits for different CYP3A clusters: poor (PM), intermediate (IM) and high metabolizers (HM).
Results: Patients were recruited (45 control group and 45 PPK group). 51.2% of the PPK group patients and 20% in the control group reached target C_0 at the first steady-state ($P < 0.001$) (Figure 1). PPK patients reached faster Tac C_0 target (7.5 days) compared to control group (25 days) ($P < 0.001$). PPK group showed fewer dose modifications (1.02 PPK vs 2.60 control, $P < 0.001$) within 90 days after renal transplant. Table 1 shows Tac C_0 infra and over-exposure and dose modifications according to groups and cluster phenotypes.
Conclusions: The integration of CYP3A4 and CYP3A5 SNPs, age, and hematocrit in a PPK model allows individualization of the Tac doses in the immediate follow-up (90 days) after renal transplant showing remarkable results compared with conventional Tac dose adjustment.
NUMBER OF TAC DOSE MODIFICATIONS AND TIMES OUT OF C_0 TARGET

OP368 TOCILIZUMAB EVALUATION IN DESENSITIZATION BEFORE KIDNEY TRANSPLANTATION AS AN ADD-ON TO APHERESIS: THE TETRA STUDY

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Background and Aims: Allo-sensitized patients represent a rising challenge for kidney transplantation. Desensitization strategies are developed to restore access to transplantation in otherwise non-transplantable patients. Tocilizumab is a recent addition to the desensitization armament. We investigated the effect of tocilizumab as an add-on to our standard of care (SoC) desensitization strategy based on rituximab and apheresis.
Methods: We prospectively included highly sensitized patients to receive monthly tocilizumab infusions for 6 months before our SoC regimen (Toci+-SoC group, as compared to the SoC group). We compared the effect of these two strategies in terms of reduction in mean fluorescent intensities (MFI), MFI rebound, and transplant outcomes at 1-year post-transplantation (kidney function, graft loss). The SoC was based on apheresis sessions (number and frequency adjusted to the achieved MFI decrease) and two rituximab doses (375 mg/m^2). Three HLA Luminex evaluations were considered for each patient: at baseline (before desensitization), on the day of transplantation (D0), and at one-year post-transplantation.
Results: 25 patients were included in the SoC group and 7 in the Toci+SoC group. There were initial medians of 23 and 52 detectable class 1 antibodies in the SoC and Toci+SoC groups, respectively, and 13 and 32 for class 2. Pre-transplantation MFI reductions were similar between groups. There was a tendency toward a higher reduction of positive antibodies (3000-MFI threshold) for the Toci+SoC group. At 1-year post-transplantation, there was no absolute difference in overall MFI rebounds, but Toci+SoC helped lower the rebound of antibodies with high baseline MFIs. Graft function and survival rates were similar at one-year post-transplantation (median eGFR 62.8 vs. 65.6 ml/min/1.73 m^2 for SoC and Toci+SoC, resp.).
Conclusion: Tocilizumab as an add-on to SoC desensitization may help control the post-transplantation rebound of antibodies with high baseline MFIs. We found access to transplantation was similar with or without tocilizumab.

OP369 OUTCOMES OF RABBIT ANTI-THYMOCYTE GLOBULIN VERSUS IL-2 RA INDUCTION THERAPIES IN 2DR MISMATCH RENAL TRANSPLANT RECIPIENTS

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Introduction: 2DR HLA mismatch indicates high immunological risk renal transplant. Induction therapy with rabbit Anti-thymocyte Globulin (r-ATG) and IL-2 Receptor Antagonist (IL-2RA) resulted in marked reduction of acute allograft rejection rate and improved graft survival. However, the outcomes in 2DR (HLA-DR) mismatched renal transplant recipients (RTRs) in the era tacrolimus-mycophenolate mofetil maintenance immunosuppression remains understudied.
Methods: This was a retrospective cohort study using data from the United States Organ Procurement and Transplantation Network, all 2 DR mismatched RTRs who were maintained on tacrolimus and mycophenolate mofetil immunotherapy between 2005 and 2015 were included. Follow-up data were until September 2020. Patients who received transplants from living donors were included in the study. Instrumental variable regression models were used to assess effect of induction therapy on acute rejection episodes at 6 months post-transplant and on graft survival. Type of induction therapy was instrumented for the transplant centre to reduce the centre effect on the choice of the induction therapy. Cox proportional hazard regression analysis was performed to assess the effect of induction therapy on graft survival. The regression models were adjusted for collected recipient, donor and transplant factors.
Results: 3052 patients received IL2-RA while 5143 patients received R-ATG induction. Using instrumental variables regression models, there were no significant differences between IL2-RA versus R-ATG induction in acute rejection episodes (OR = 1.49, 95% CI ranges from 0.73 to 3.05, $P = 0.27$), or graft survival (coefficient = 0.95, 95% CI: -0.18 to 2.10, $P = 0.10$). Using Cox proportional hazards regression, there was no significant difference in graft survival between either induction therapies (HR = 0.90, 95% CI: 0.74 to 1.09, $P = 0.29$).
Discussion: This study showed no significant difference in acute rejection episodes or graft survival when using ATG or IL-2RA in 2DR HLA mismatched renal transplant recipients in the current tacrolimus-based maintenance immunosuppression era. Therefore, IL2-RA is a safe induction therapy in this group of patients and non-inferior to R–ATG induction therapy.

OP370 HAEMATOLOGICAL AUTOIMMUNE DISORDERS FOLLOWING ALEMTUZUMAB INDUCTION FOR KIDNEY TRANSPLANT

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Background: Haematological Autoimmune Disorders (HAD) have been associated with Alemtuzumab (Az); namely immune thrombocytopenia (ITP), autoimmune haemolytic anaemia (AIHA), Evans syndrome (ES) and Red Cell Aplasia (RCA). We describe the largest cohort to date of patients developing HAD associated with a single dose of alemtuzumab induction for kidney transplant (KT) or Simultaneous Pancreas and Kidney transplant (SPK).
Methods: Records of 2156 RT or SPK recipients with Az-induction during 2005-2020 were retrospectively studied for the occurrence of HAD, excluding recipients with < 6 month follow-up. Patients received a single dose of Az perioperatively, followed by tacrolimus monotherapy with a steroid sparing protocol. MMF and steroids were added only for biopsy-proven rejection. Secondary ITP/AIHA and PTLD were excluded.
Results: 66 of 2156 patients (2.5%) developed HAD over a mean follow-up of 5.9 ± 4.5 years. 38/66 developed ITP, 14/66 AIHA, 13/40 ES, 1 RCA. Mean time from Az exposure to HAD diagnosis was 6.5 ± 0.1 year (median 2.5 year). Most patients were asymptomatic at diagnosis. Prednisolone ± IVIG was the first-line treatment, followed by Rituximab for AIHA and Rituximab or Thrombopoeitin-receptor-agonists for ITP. 61/66 achieved complete remission (CR) and 1 patient remains in partial remission (PR). Recurrence was observed in 22/64 patients. Mean time-to-recurrence was 8.9 ± 0.8 m. 7/66 patients had refractory HADS requiring multiple agents (10 in one case). 12/66 had a major consequence of HADS (e.g. intracranial haemorrhage, gastrointestinal bleed)
Conclusions: HAD post Az induction are characterized by asymptomatic presentation, delayed onset post exposure and responsiveness to treatment. Although the incidence is low, they are associated with significant morbidity and mortality. Increased awareness, early diagnosis and prompt treatment are essential for improved outcome.

ORGAN PERFUSION, CURRENT AND FUTURE OUTCOMES

OP371 NORMOTHERMIC REGIONAL PERFUSION OR NORMOTHERMIC MACHINE PERFUSION IN LIVER TRANSPLANTATION FROM DONATION AFTER CIRCULATORY DEATH

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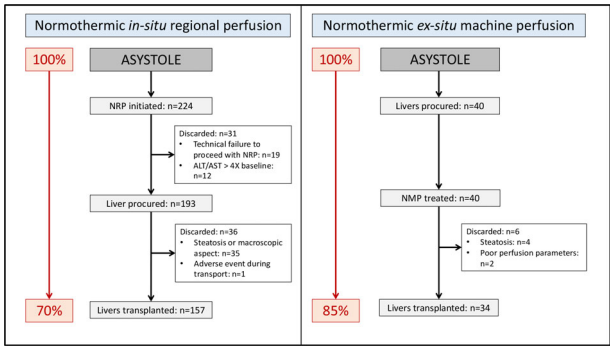
Background: In-situ normothermic regional perfusion (NRP) and ex-situ normothermic machine perfusion (NMP) aim to improve outcomes of liver transplantation (LT) using donors after circulatory death (DCD). However, these two dynamic preservation strategies have not been compared yet. The aim of this study was to compare outcomes of DCD grafts exposed to NRP with subsequent static cold storage (SCS) versus continuous NMP commenced at the donor centre after a short period of SCS.
Methods: This international multicentre retrospective study included DCD donor livers that had been subjected to either NRP or NMP. The NRP cohort was transplanted in six French centres participating in the national NRP organ retrieval programme. The NMP cohort was enrolled by four UK and one Belgian centres as part of a multinational randomised controlled trial (COPE). Study endpoints were liver utilisation rate, 2-year patient and graft survival, 30-day graft loss, incidence of clinically manifest biliary strictures, early allograft dysfunction and peak aspartate aminotransferase (AST) levels.
Results: Overall, 157 NRP and 34 NMP livers were transplanted, resulting in organ utilisation rates of 70% vs 85% ($P = 0.056$). The donor and recipient characteristics were similar, including the donor functional warm ischemic time (22 vs 20 min; $P = 0.170$), UK-DCD risk score (6 vs 5 points; $P = 0.15$) and lab-MELD scores (12 vs 12 points; $P = 0.99$). NRP livers were more frequently allocated to recipients suffering from hepatocellular carcinoma (62 vs 21%; $P < 0.001$). HCC-censored 2-year graft and patient survival were 89% vs 88% ($P = 0.78$) and 93% vs 94% ($P = 0.865$) after NRP and NMP, respectively, with similar 30-day graft loss (5% vs 9%; $P = 0.416$). The incidence of non-anastomotic biliary strictures (1% vs 3%; $P = 0.357$) and early allograft dysfunction (20% vs 9%; $P = 0.139$) were also similar, although peak post-transplant AST levels were lower in the NMP cohort (865 vs 344 IU/l; $P < 0.001$).
Conclusions: Outcomes for both in-situ NRP and continuous ex-situ NMP of DCD grafts appear to match benchmarks expected for DBD livers. This study may inform the appropriate design of a prospective randomised trial comparing the efficacy of both preservation strategies in DCD liver transplantation.

Outcomes	NMP (n=34)	NRP (n=157)	*P*
30-day graft loss	3 (8.8)	8 (5.1)	0.416
30-day patient death	2 (5.9)	4 (2.5)	0.290
Early allograft dysfunction	3 (8.8)	32 (20.4)	0.114
AST peak 7 days (IU/L)	344 (216-701)	847 (532-1422)	<0.001
INR level day 7	1.1 (1.0-1.2)	1.1 (1.0-1.2)	0.779
Total bilirubin day 7 (mmol/l)	29 (16-57)	21 (12-40)	0.122
Non-anastomotic biliary strictures	1 (2.9)	2 (1.3)	0.447
Anastomotic stricture	6 (17.6)	14 (8.9)	0.134
Hepatic artery thrombosis	1 (2.9)	4 (2.6)	1.000



OP372 ADMINISTRATION OF GALINISERTIB DURING NORMOTHERMIC MACHINE PERFUSION POTENTIALLY PROTECTS DONATION AFTER CIRCULATORY DEATH DONOR KIDNEYS

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Current strategies to assess donor kidney quality are based on clinical scores or require biopsy for histological assessment. Non-invasive strategies to identify and predict graft outcome at an early stage are therefore needed. Hypothermic machine perfusion (HMP) provides the opportunity to observe secreted biomarkers that reflect kidney function pre-transplantation. Our aim was to evaluate the renal secretome in the perfusate of donation after brain death (DBD) kidneys preserved using HMP by comparing proteomic profiles of good and suboptimal outcome one-year post transplantation.
HMP perfusate samples were collected during an international randomized controlled trial. Samples were divided into two groups ($n = 22$ per group) based on one-year post transplantation kidney function defined by estimated glomerular filtration rate (eGFR) (good outcome (GO) ≥ 60 ml/min/1.73 m^2; suboptimal outcome (SO) ≤ 30 ml/min/1.73 m^2). Perfusate samples were obtained at two time points: 15 min after start of HMP (T1) and before termination of HMP (T2). Protein profiles of samples were analysed using liquid chromatography tandem mass spectrometry.

In total, 1255 proteins were identified and quantified. Hierarchical clustering of the top 100 most abundant proteins at T1 showed discrimination between grafts with a GO and SO at 1-year post transplantation (Figure 1A). KEGG pathway enrichment analysis of these proteins showed enrichment of complement and coagulation cascades (Figure 1B). Analyses of the differentially abundant proteins revealed consistent significant upregulated expression of proteins involved in classical complement activation in the GO group vs. the SO group at both T1 (Figure 1C,D) and T2. Furthermore, secreted C1CQ and FABP5 (T1) and IGHV2-26 and DSP (T2) can predict transplantation outcome with a predictive value of 85% and receiver-operated curve (ROC) with an area under the curve (AUC) of 0.95, and 100% and ROC with an AUC of 1.00, respectively.
This study shows that the secretome of DBD kidneys after 15 min of HMP distinguishes donor kidneys with GO and SO 1-year post transplantation. The upregulation of proteins involved in activation of complement and coagulation pathways was consistent in our analyses of both time points.

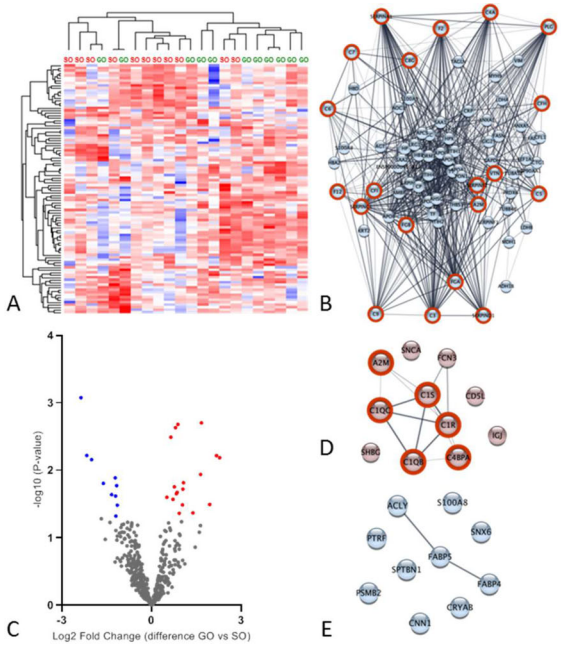

Figure 1. Quantitative proteomic analysis of perfusate samples after 15 minutes of hypothermic machine perfusion (T1). A. Heat map and hierarchical clustering of 100 most abundant proteins at T1. B. String analysis of 100 most abundant proteins. Nodes circled with red represent functional enrichment of the KEGG complement and coagulation pathway (FDR 7.73e-28). C. Volcano plot showing differential protein expression at T1 between good outcome (GO) and suboptimal outcome (SO) at one-year post-transplantation. X-axis demonstrates protein level difference indicated by log2 fold change, Y-axis demonstrates statistical significance indicated by -log10 (p-value). A -log10 (p-value) of > 1.3, and a fold change of > 0 was considered significant. Blue dots represent significant downregulated proteins. Red dots represent significantly upregulated proteins. D. String pathway analysis of significantly upregulated proteins proteins at T1. Nodes circled with red represent functional enrichment of the KEGG complement and coagulation pathway (FDR 2.13e-11). E. String analysis of significantly downregulated proteins at T1. FDR; false discovery rate.

OP373 GRAFT UTILIZATION AFTER NORMOTHERMIC REGIONAL PERFUSION IN CONTROLLED DONATION AFTER CIRCULATORY DEATH - 5-YEAR EXPERIENCE FROM FRANCE

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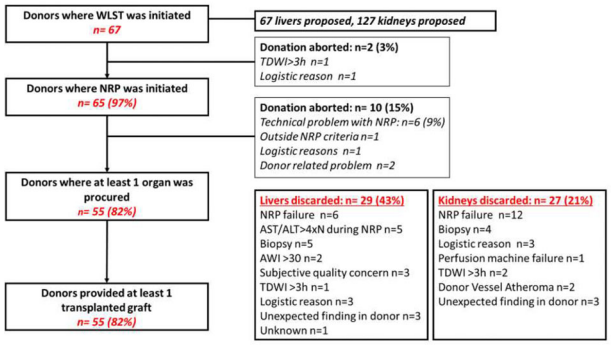
Background: The use of normothermic regional perfusion (NRP) in controlled donation after circulatory death (cDCD) has been suggested to improve posttransplant outcomes. However, data on why organs are not procured or transplanted after NRP in cDCD are still lacking. Thus, this study aims at performing a detailed analysis of graft utilization after NRP in cDCD.
Methods: This retrospective study included all cDCD donors proposed for procurement of at least one abdominal organ in the south-east donor region of France from 2015-2020. In France, strict national selection criteria are applied to all cDCD donor including donor age and limited warm ischemia times (Table 1). Prior to initiation of NRP, donors undergo standardized post-mortem femoral vessel cannulation over pre-placed guide-wires. Organ specific utilization rates were defined as the proportion of transplanted grafts from donors in which withdrawal of life sustaining therapies (WLST) was initiated.
Results: Sixty-seven donors underwent WLST during the study period (Table 1). NRP was initiated in 65 (97%) donors and was aborted in 6 (9%) donors due to technical problems, predominantly cannulation failures. Procurement proceeded in 55 (82%) donors after 213 min (195-229) of NRP. The graft utilization rate for kidneys and livers was 78% (n = 100) and 57% (n = 38), respectively. In detail, 55% (n = 16) of all discarded liver grafts were outside the required quality criteria including: pathological biopsy (macrosteatosis > 20% and fibrosis > F2; n = 5), transaminases increase during NRP (> 4 × N; n = 5) and AWI > 30 min (n = 2) (Figure 1).
Conclusions: While the majority of cDCD donors successfully completed WLST, a significant number of grafts, especially liver grafts, were discarded due to quality concerns after initiation of NRP. These results highlight that besides mastering the technical challenges of NRP, further analysis of ischemia-reperfusion injury in abdominal organs during NRP are warranted to expand transplantation of cDCD grafts.

Table 1: Donor and procurement characteristics

	Proposed cDCD Donors (n=67)	*French cDCD Selection Criteria*
Donor Age, year	54 (43-61)	*< 71 years*
Donor BMI, kg/m2	24 (22-27)	
Cardiac arrest prior to ICU admission, n (%)	42 (63)	
Cause of Admission, n (%)		
Cerebrovascular accident	12 (18)	
Hypoxic brain injury	40 (60)	
Trauma	15 (22)	
Donor ICU stay, days	8 (6-15)	
*Warm ischemia times**		
Total Donor Warm Ischemia, min	33 (29-41)	*≤3h*
Functional Donor Warm Ischemia, min	23 (20-28)	*≤45min*
Asystolic Donor Warm Ischemia, min	17 (15-22)	*≤30min for livers, ≤45min for kidneys*
Donor vessel cannulation duration, min	12 (10-17)	

**After cardiac arrest of the donor, a "no-touch" period of 5min is observed prior to declaration of brain death*
Continuous values are shown as medians and interquartile range

Figure 1: Study flowchart and reasons for graft discard



WLST: withdrawal of life sustaining therapy; TDWI: total donor warm ischemia; NRP: normothermic regional perfusion; AST/ALT: transaminases; AWI: asystolic warm ischemia time

OP374 HYPOTHERMIC OXYGENATED MACHINE PERFUSION (HOPE) IN LIVER TRANSPLANTATION FOR EXPANDED CRITERIA DONOR GRAFT: SINGLE CENTER EXPERIENCE

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Background: Hypothermic Oxygenated Machine Perfusion (HOPE) is widely used in Liver Transplantation (LT) to assess and improve organ function in Expanded Criteria Donor (ECD) liver grafts. However, there is no consensus within transplant community concerning indications on its use in LT. The aim of this study is to evaluate the impact of Machine Perfusion (MP) Reconditioning in ECD Liver grafts.
Methods: ECD grafts were defined according to Fisher-Frohlich *et al*. From January 2016 to February 2021, 51 ECD *grafts* were perfused with HOPE after *cold storage (CS)* according to an "end-ischemic model" of MP before LT (study group). We tracked for the first 7 days the main markers of liver and kidney function after LT. Outcome within first 90-days after LT were compared to those ECD *grafts* (191) preserved only with *CS (control group)* during the same study period. To balance baseline donor and recipient characteristics of the two groups, we used the inverse probability of treatment weighting method (IPTW). The primary end-point was early patient mortality ($\leq$ 3 months) after LT.
Results: Liver Grafts in the study group had a macro steatosis > 30% reported in 33% of the cases. Median Perfusion Time in HOPE was 212.5 min, preceded by a median CS time of 232.5 min. We discarded 4 of the 51 *grafts* due to unsatisfying hemodynamic parameters or too high lactate concentration. In reconditioned grafts we reported 2 PNF (4.26%) and 12 EAD (25.5%) after LT. One patient who developed PNF received a retransplant in 5 PDO. One patient underwent re-LT after 3 months due to Ischemic Cholangiopathy (2%). Five patients died due to sepsis or cardiovascular events. In 34 cases, post-operative course was free from major vascular or biliary complications. The control group was significantly different from the study group for the following variables: donor transaminases peak, sodium peak, macro steatosis, and recipient MELD score. Using IPTW we perfectly balanced the two populations. IPTW adjusted post-LT early mortality was 8.1% in the study group vs. 14.6% in the control group (P = 0.04).
Conclusions: Our preliminary data suggest a protective effect of HOPE on early patient mortality after LT with ECD grafts. To understand the pathophysiological meaning of this result, a complete revision of all pre and post-operative data of enrolled patients is ongoing.

OP375 A RANDOMIZED CONTROLLED TRIAL OF DUAL HYPOTHERMIC OXYGENATED MACHINE PERFUSION IN DONATION AFTER CIRCULATORY DEATH LIVER TRANSPLANTATION

Rianne van Rijn[1], Ivo Schurink[2], Miriam Cortes Cerisuelo[3], Robbert J. de Haas[1], Nigel Heaton[3], Bart van Hoek[4], Volkert Huurman[4], Ina Jochmans[5], Otto B. van Leeuwen[1], Vincent E. de Meijer[1], Diethard Monbaliu[6], Roberto Troisi[7], Aude Vanlander[7], Jeroen de Jonge[2], Robert J. Porte[1]

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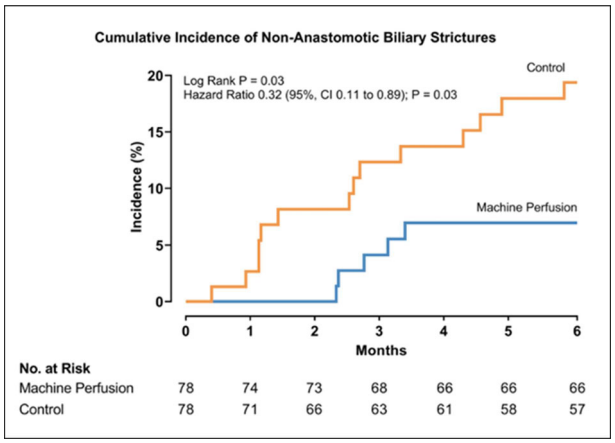
Background: Transplantation of livers from donation after circulatory death (DCD) donors is associated with an increased risk of non-anastomotic biliary strictures. Hypothermic oxygenated machine perfusion of livers may reduce the incidence of biliary complications, but data from prospective controlled studies are lacking.
Methods: In this multicenter, controlled trial we randomly assigned patients undergoing transplantation of a DCD liver to receive that liver after dual hypothermic oxygenated machine perfusion or conventional static cold storage alone (control group). The primary end point was the occurrence of non-anastomotic biliary strictures within 6 months after transplantation. Secondary end points included other graft-related and general complications.
Results: A total of 156 patients were enrolled; 78 participants received a machine perfused liver and 78 received a liver after static cold storage only. Non-anastomotic biliary strictures occurred in 6% of the patients in the machine perfusion group and 18% of the controls (risk ratio, 0.36; 95%CI, 0.14 to 0.94; P = 0.03). Post-reperfusion syndrome occurred in 13% of the recipients of a machine perfused liver and in 27% of the controls (risk ratio, 0.43; 95%CI, 0.20 to 0.91; P = 0.03). Early allograft dysfunction occurred in 26% of machine perfused livers vs. 40% of controls (risk ratio 0.61; 95%CI, 0.39 to 0.96; P = 0.03). Cumulative number of treatments for non-anastomotic biliary strictures was 4-fold lower after machine perfusion, compared to controls. There were no significant differences in adverse events.
Conclusions: Hypothermic oxygenated machine perfusion reduced the risk of non-anastomotic biliary strictures after DCD liver transplantation by two-third.



Cumulative Incidence of Symptomatic Non-anastomotic Biliary Strictures: Shown are the time-to-event Kaplan–Meier curves. Hazard ratio was adjusted for stratification factors (transplant center and primary sclerosing cholangitis) and prespecified, established donor risk factors (donor warm ischemia time and donor risk index).

OP376 VIABILITY TESTING DURING EX VIVO NORMOTHERMIC MACHINE PERFUSION OF THE PORCINE LIVER BY ANALYSIS OF MITOCHONDRIAL RESPIRATION

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Background: Normothermic machine perfusion (NMP) enables organ viability testing prior to transplantation. However, reliable parameters are lacking. Since mitochondria are key-players in cellular bioenergetics, they may provide direct information on hepatic function. Thus, we aimed to identify sensitive parameters using high-resolution respirometry (HRR) to assess mitochondrial function of the porcine liver during NMP.
Methods: Porcine livers were machine perfused under normothermic conditions for 4 days. Biopsy samples were taken every 24 h and analysed for mitochondrial respiration. Oxidative phosphorylation (OXPHOS) for succinate, nicotineamide adenine dinucleotide (NADH), and fatty acid oxidation (FAO) pathways were assessed, and OXPHOS-coupling efficiencies (OCE) were calculated. Capacity of the electron transfer (ET) system and outer membrane integrity were evaluated. Flux control ratios (FCR) were calculated. Perfusate samples were analysed for lactate levels.
Results: Generally, OXPHOS capacity of the succinate pathway was 4-times higher compared to NADH and FAO pathways. This is in line with the FCRs, where the proportions of the different respiratory control states have been determined. However, the calculated OCE for NADH and FAO pathways were the highest. Over NMP-time, an overall decline for all pathways was observed, indicating an impairment of the bioenergetic function. The changes were detectable at first in the OCE of the succinate pathway, which correlated with increased perfusate lactate levels, a well-established marker indicative for liver injury. Simultaneously, the ET excess capacity and cytochrome c control factor increased, indicating damage to the phosphorylation system and loss of the outer membrane integrity, respectively.
Conclusion: Assessment of the mitochondrial respiration and their dynamics during NMP provide reliable information on the quality of the *ex vivo* perfused porcine liver, whereby the succinate pathway seems to be the most sensitive.

OP377 DISCARDED LIVERS TRANSPLANTED AFTER NORMOTHERMIC PERFUSION: A NEW FRONTIER TO REDUCE WAITLIST MORTALITY

Cristiano Quintini[1], Luca Del Prete[1,2], Giuseppe D'amico[1], Teresa Diago Uso[1], Koji Hashimoto[1], Federico Aucejo[1], Masato Fujiki[1], Bijan Eghtesad[1], Kazunari Sasaki[1], Choon Hyuck David Kwon[1], Charles Miller[1], Liu Qiang[1]

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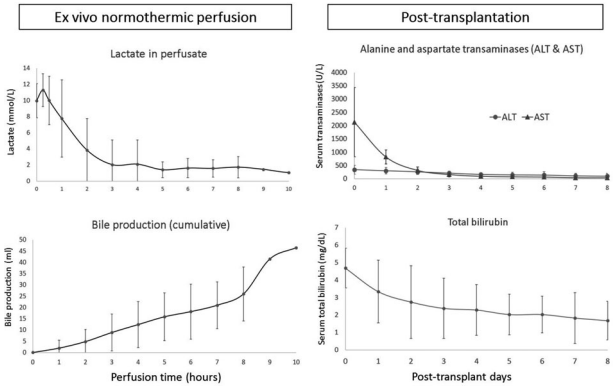
Background: Despite efforts to increase organ donation, waitlist mortality due to liver shortage is still a reality. Normothermic machine perfusion (NMP) holds the potential to enhance graft preservation, extend viability and allows liver function evaluation in organs previously discarded because considered too high risk for transplant.
Methods: We report our preliminary result of a single center prospective cohort pilot study (NCT03456284). Discarded livers from other transplant centers were transplanted after assessment and reconditioning with our institutional developed NMP device.
Results: Seventeen human livers declined for transplantation were enrolled for assessment with NMP. Discard reasons were high warm ischemia time in donors after circulatory death (DCD), steatosis, hyperbilirubinemia and hypertransaminasemia. Viability criteria included bile production rate, perfusate lactate clearance rate, hemodynamics and liver morphology during NMP. Five livers (29%) were ultimately discarded after NMP because of insufficient lactate clearance ($>$ 4.1 mmol/l after 4 h), limited bile production ($<$ 0.5 ml/h) or moderate macrosteatosis, whereas twelve (71%) were considered suitable for transplantation. They included eight DCD livers with 13–46 min of donor warm ischemia time and 3 h 41 min–7 h 42 min of cold ischemia time. NMP duration time was 3 h 49 min–10 h 29 min without technical problems or adverse events. Liver recipients had a model for end-stage liver disease score of 15-23 before transplantation. No intraoperative or major early postoperative complications as well as no primary non-function occurred in all transplanted recipients. All patients are alive. Five livers had early allograft dysfunction with fast recovery and one patient developed ischemic cholangiopathy after four months successfully treated with biliary stents. All other patients had good liver function with a follow-up time of two weeks to nine months.
Conclusions: Liver ex-vivo NMP permitted transplantation of 71% of discarded livers that otherwise would have been lost, with good graft and recipient's outcomes. The definition of even more selective viability criteria represents a challenge for future studies and a key factor to further reduce the discard rate and waitlist mortality.



OP378 SELECTIVE USE OF EX-SITU MACHINE PERFUSION AFTER NORMOTHERMIC REGIONAL PERFUSION IN LIVER TRANSPLANTATION FROM DONATION AFTER CIRCULATORY DEATH

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Background: Ex-situ dynamic preservation of liver grafts from donation after circulatory death (DCD) is diffuse. In Italy, the use of normothermic regional perfusion (NRP) in the setting of DCD is systematic. The clinical utility of the sequential use of NRP and ex-situ machine perfusion (MP) is not evidence-based. We reviewed our experience with liver transplantation (LT) from DCD with the aim of identifying possible selection criteria for NRP alone versus NRP plus ex-situ MP.
Methods: We retrospectively analyzed the outcome of 18 patients transplanted with grafts from type 3 DCD from October 2017 to June 2020. NRP was followed by ex-situ MP only when the vascular flow and lactate clearance were deemed inadequate. Magnetic resonance for detection of ischemic type biliary lesions (ITBL) was routinely performed 6 months after LT.
Results: A 16/18 (89%) grafts were preserved by static cold storage after NRP. The mean functional warm ischemia time (fWIT) was 41 $\pm$ 7 min. During NRP, the mean flow was 120 $\pm$ 27% of the ideal flow and the mean lactate clearance was 61 $\pm$ 10%. The rate of primary non-function (PNF) and early allograft dysfunction (EAD) were 0 and 13% (2/16 patients), respectively. The incidence of ITBL was 0%. No patients underwent retransplantation. To date, 15/16 (94%) patients are alive, with a mean follow-up of 24 $\pm$ 10 months; 1/16 (6%) patient died 29 days after LT due to a cerebrovascular accident.
A 2/18 (11%) grafts underwent dynamic preservation after NRP. In the former case, the fWIT was 55 min. During NRP, the mean flow was 46% of the ideal flow and the lactate clearance was 43%. In the latter case, the fWIT was 32 min. During NRP, which was early discontinued due to untreatable bleeding, the lactate clearance was 8%. One patient developed EAD. No PNF, nor ITBL, nor graft loss were registered. Both patient are alive 21 and 10 months after LT, respectively.

Conclusions: Our results suggest that, when its quality and effectiveness appear adequate, NRP alone may overcome the detrimental effects of warm ischemia, with reasonably no need for subsequent ex-situ MP unless logistics require that ex-vivo time duration is prolonged. We believe that the assessment of NRP quality and efficacy may help select which grafts can be safely directly implanted, which ones may deserve subsequent ex-situ MP and which ones should be discarded.

MOLECULAR PREDICTORS OF OUTCOMES

OP379 PROTEOMIC ANALYSIS OF MACHINE PERFUSION SOLUTION FROM BRAIN DEAD DONOR KIDNEYS REVEALS THAT COMPLEMENT ACTIVATION IS ASSOCIATED WITH 1-YEAR OUTCOME

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[1]University Medical Centre Groningen, Department of Surgery, Groningen, Netherlands; [2]University Medical Centre Groningen, Department of Anesthesiology, Groningen, Netherlands; [3]University of Oxford, Target Discovery Institute, Nuffield Department of Medicine, Oxford, United Kingdom; [4]University Medical Centre Utrecht, Department of Nephrology and Hypertension, Utrecht, Netherlands

Current strategies to assess donor kidney quality are based on clinical scores or require biopsy for histological assessment. Non-invasive strategies to identify and predict graft outcome at an early stage are therefore needed. Hypothermic machine perfusion (HMP) provides the opportunity to observe secreted biomarkers that reflect kidney function pre-transplantation. Our aim was to evaluate the renal secretome in the perfusate of donation after brain death (DBD) kidneys preserved using HMP by comparing proteomic profiles of good and suboptimal outcome one-year post transplantation.
HMP perfusate samples were collected during an international randomized controlled trial. Samples were divided into two groups ($n = 22$ per group) based on one-year post transplantation kidney function defined by estimated glomerular filtration rate (eGFR) (good outcome (GO) $\geq$ 60 ml/min/1.73 m^2; suboptimal outcome (SO) $\leq$ 30 ml/min/1.73 m^2). Perfusate samples were obtained at two time points: 15 min after start of HMP (T1) and before termination of HMP (T2). Protein profiles of samples were analysed using liquid chromatography tandem mass spectrometry.
In total, 1255 proteins were identified and quantified. Hierarchical clustering of the top 100 most abundant proteins at T1 showed discrimination between grafts with a GO and SO at 1-year post transplantation (Figure 1A). KEGG pathway enrichment analysis of these proteins showed enrichment of complement and coagulation cascades (Figure 1B). Analyses of the differentially abundant proteins revealed consistent significant upregulated expression of proteins involved in classical complement activation in the GO group vs. the SO group at both T1 (Figure 1C,D) and T2. Furthermore, secreted C1CQ and FABP5 (T1) and IGHV2-26 and DSP (T2) can predict transplantation outcome with a predictive value of 85% and receiver-operated curve (ROC) with an area under the curve (AUC) of 0.95, and 100% and ROC with an AUC of 1.00, respectively.
This study shows that the secretome of DBD kidneys after 15 min of HMP distinguishes donor kidneys with GO and SO 1-year post transplantation. The upregulation of proteins involved in activation of complement and coagulation pathways was consistent in our analyses of both time points.

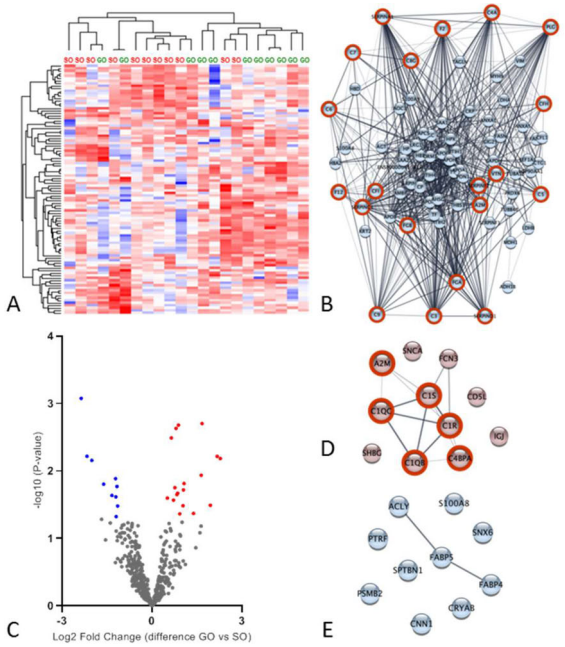

Figure 1. Quantitative proteomic analysis of perfusate samples after 15 minutes of hypothermic machine perfusion (T1). A. Heat map and hierarchical clustering of 100 most abundant proteins at T1. B. String analysis of 100 most abundant proteins. Nodes circled with red represent functional enrichment of the KEGG complement and coagulation pathway (FDR 7.73e-28). C. Volcano plot showing differential protein expression at T1 between good outcome (GO) and suboptimal outcome (SO) at one-year post-transplantation. X-axis demonstrates protein level difference indicated by log2 fold change, Y-axis demonstrates statistical significance indicated by -log10 (p-value). A -log10 (p-value) of > 1.3, and a fold change of > 0 was considered significant. Blue dots represent significant downregulated proteins. Red dots represent significantly upregulated proteins. D. String pathway analysis of significantly upregulated proteins proteins at T1. Nodes circled with red represent functional enrichment of the KEGG complement and coagulation pathway (FDR 2.13e-11). E. String analysis of significantly downregulated proteins at T1. FDR; false discovery rate.

OP380 OPERATIONAL TOLERANCE-RELATED GENES ALLOW NON-INVASIVE DETECTION OF SUBCLINICAL REJECTION AT ONE YEAR AFTER RENAL TRANSPLANTATION

Richard Danger[1], Ludmilla Le Berre[1], Marion Cadoux[1], Clarisse Kerleau[1], Pierrick Guérif[1], Karine Renaudin[1,2], Magali Giral[1], Sophie Brouard[1]
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Background: We previously identified a score measured in peripheral blood composed of 6 genes and two clinical parameters able to discriminate operational tolerant patients, who are rare patients keeping a functional renal transplant in absence of immunosuppression for years.
Methods: We tested this score in a large multicentric cohort of 600 renal transplanted patients with paired biopsies and blood samples at 1-year post-transplantation, by quantitative PCR and the enzyme-free method NanoString.
Results: We first showed that this score may be refined and improved by the use of only two of these genes, AKR1C3 and TCL1A and 3 clinical parameters. Second, we showed that this score was able to discriminate patients with subclinical rejection (SCR) with evidences of antibody (sABMR) or T cell (sTCMR), a major threat affecting up to 25% of patients and associated with negative allograft outcomes. This score is applicable as soon as one year after transplantation with an AUC of 0.84.
Conclusions: While further validations are needed to increment this score in routine use, these data show that this composite score may not only help reducing unnecessary biopsies in absence of allograft function decline but may also be an indication for biopsy or treatment modulation when SCR is identified.

OP381 URINE PROTEOME PROFILING TO IDENTIFY THE MOLECULAR SIGNATURE OF PRIMARY NON FUNCTION PRIOR TO TRANSPLANT IN DECEASED DONOR KIDNEYS

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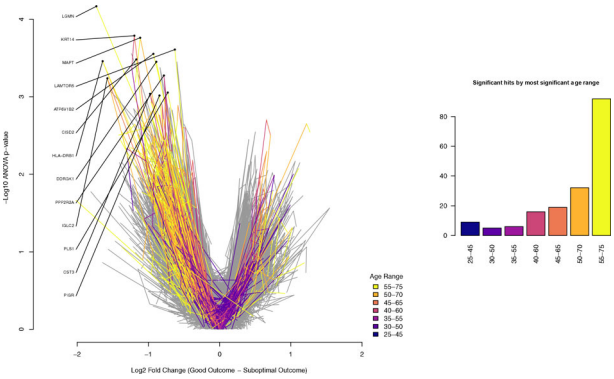
Background: Primary Non Function (PNF) after kidney transplantation is a devastating event leading to graft failure and a significant impact on the prognosis of the patient. To be able to predict PNF will not only avoid an unsuccessful procedure and return to dialysis but may also prevent sensitisation that could affect the patient's transplantability in the future. To date, a molecular profile in the donor kidney to anticipate PNF and help the clinical decision making whether to accept or decline a potential graft is lacking. Urine produced by a deceased donor prior to organ retrieval and allocation provides a rich source of kidney-enriched proteins that may be informative as regard the quality of the donor kidney. In this study, we evaluated whether the urinary proteome can help to identify a clinically relevant molecular signature for imminent PNF using the urine of higher-risk donation after circulatory death (DCD) donors.
Methods: 30 donor urine samples were selected from the UK Quality in Organ Donation (QUOD) biobank following propensity score matching. Selected samples were grouped into one of three different outcomes; primary non function (PNF), delayed graft function (DGF) or immediate function (IF). An equal quantity of protein from each sample was subject to shotgun proteomics: 1D liquid chromatography, and analysis by high resolution mass spectrometry using a label-free quantitative strategy.
Results: A total of 3956 different gene products were identified; empirical bayes moderated t-statistics was used to define the molecular signatures of PNF, DGF and IF groups. The expression of 202 proteins significantly changed between PNF, DGF and IF groups. 44 targets were identified, with some of them previously found to be associated with kidney failure; i.e. galactosidase alpha (GLA) was high in urine samples collected from the PNF group whilst the expression of CST3, as a biomarker for rapid kidney function decline, was high in DGF group.
Conclusions: This explorative study shows that proteome profiling of urine samples collected in DCD donors may provide a clinically relevant urinary signature associated with short-term outcomes in kidney transplantation. Following these promising first findings, further validation in a separate cohort is currently performed.

OP382 AGE-RELATED PROTEOMIC DIFFERENCES IN DECEASED DONOR KIDNEYS ASSOCIATE WITH 12-MONTH POSTTRANSPLANTATION OUTCOME

Philip Charles[1], Rebecca Vaughan[2], Simon Davis[1], Iolanda Vendrell[1], Roman Fischer[1], Edward Sharples[3], Benedikt Kessler[1], Alberto Santos Delgado[1,4], Rutger Ploeg[5], Maria Kaisar[2,5]
[1]University of Oxford, Nuffield Department of Medicine, Oxford, United Kingdom; [2]NHS Blood and Transplant, Bristol, United Kingdom; [3]Oxford University Hospitals, Oxford, United Kingdom; [4]University of Copenhagen, Center for Health Data Science, Copenhagen, Denmark; [5]Nuffield Department of Surgical Science, University of Oxford, Oxford, United Kingdom

Background: Currently, clinical factors such as donor age aid decisions on which donor kidneys to transplant. These have limited predictive value; older donors with potentially good function are not utilised, while inferior organs are transplanted with suboptimal outcomes. Robust markers to assess donor kidney quality as predictors of posttransplant function are urgently needed to evaluate candidates and to improve understanding of mechanisms leading to chronic graft dysfunction.
Methods: Kidney biopsies ($n = 186$; Donors after Brain Death $n = 100$, Donors after Cardiac Death $n = 86$) were provided by the UK QUOD biobank, selected from donors where both kidneys were transplanted and had similar posttransplantation outcomes. Proteomic analysis of the biopsies was performed using a high-sensitivity spectral-library based mass spectrometry approach (SWATH; Sequential Window Acquisition of all THeoretical spectra). Protein data were analysed in an integrative model combining donor and recipient demographic and clinical measurements, and histological features identified by image analysis of corresponding PAS-stained slides, against 12-month posttransplantation outcome (eGFR).
Results: We quantified 2984 protein groups (< 50% missing values). Naive analysis showed a dominant effect of donor age on outcome. Deeper analysis of the data with a Prediction Rule Ensemble machine learning method revealed strong proteomic alterations associated to outcome. We shortlisted 179 proteins (FDR < = 0.1) that were donor age-dependent and correlated to outcome, 51% of which were most significant in the oldest (55-75) age subgroup; several have previously been associated with renal dysfunction including PIGR ($P < 0.001$), DDRGK1 ($P < 0.0005$) and LGMN ($P < 0.0001$).
Conclusions: We have used a novel integrative approach to improve donor kidney risk stratification and prediction of posttransplant function. Preimplantation proteomic signatures offer potential predictive power within donor age subgroups. Biological changes associated to fibrosis, inflammation and cell damage suggest novel targets to recondition donor organs.

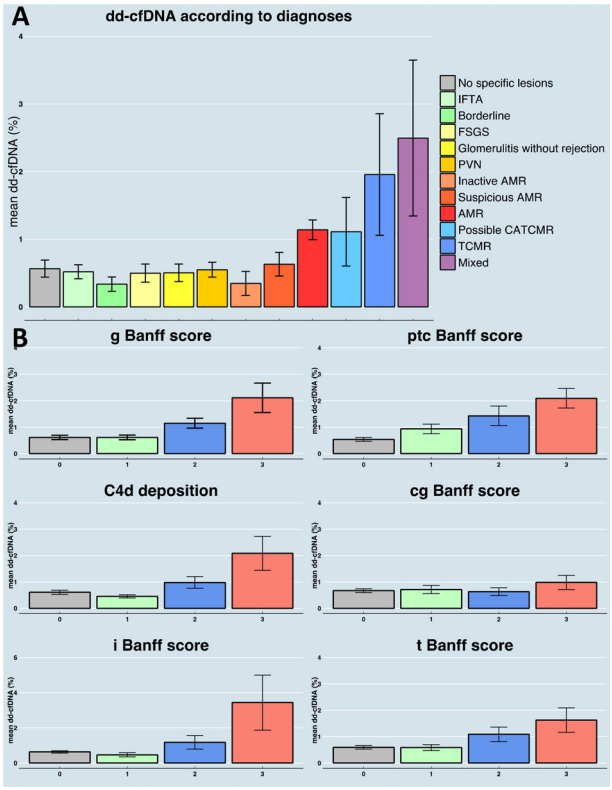


OP383 DEVELOPMENT AND VALIDATION OF AN INTEGRATIVE DD-CFDNA SYSTEM TO PREDICT ALLOGRAFT REJECTION : A POPULATION BASED STUDY

Olivier Aubert[1], Romain Brousse[1], Juliette Gueguen[1], Maud Racape[1], Daniel Yoo[1], Christophe Legendre[1,2], Dany Anglicheau[1,2], Carmen Lefaucheur[1], Alexandre Loupy[1]
[1]Paris Translational Center for Organ Transplantation, Paris, France; [2]Necker Hospital, Paris, France

Background: Post-transplantation patient care requires development and validation of non-invasive biomarkers to improve allograft monitoring and prevention from unnecessary biopsies. Preliminary reports have suggested the association of donor derived cell-free DNA (dd-cfDNA) with allograft rejection. However, there is no proof of its added value beyond standard of care patient management in large and deep phenotyped cohort.
Methods: We enrolled 1196 kidney transplant recipients having concomitant evaluation of allograft histology, anti-HLA DSA and functional parameters between 2013 and 2018 (582 patients [637 biopsies]) in the derivation cohort and 614 in the validation cohort. dd-cfDNA was measured in plasma at the time of the biopsy. Diagnoses were assessed using Banff 2019 criteria. Parameters associated with rejection were assessed using uni- and multivariable logistic regression. We developed a risk model using independently associated variables.
Results: Higher levels of dd-cfDNA were observed for AMR and TCMR or both compared to other diagnoses (Figure 1A). We found an incremental dd-cfDNA levels with increasing Banff lesion scores for g, ptc, i, t, cg and C4d .There was no association of dd-cfDNA levels with allograft inactive lesions (Figure 1B). In multivariable analysis, dd-cfDNA ($P < 0.001$) showed predictive capability independently of DSA ($P < 0.001$), eGFR ($P = 0.019$) and occurrence of recent clinical or immunological event (acute kidney injury and/or new onset or worsening proteinuria and/or de novo DSA) ($P = 0.008$). Based on these parameters, we built an integrative idd-cfDNA model that showed good discrimination (C-index: 0.83) and added value beyond a model without dd-cfDNA. We confirmed our results in the validation cohort.
Conclusions: We demonstrate the independent and added value of dd-cfDNA in addition to conventional features to predict rejection. This first integrative system shows improved performance for patient monitoring and could help physicians in decision-making process.

Figure 1 : dd-cfDNA results according to the diagnoses (Panel A) and according to the Banff scores (Panel B)



OP384 SUBOPTIMAL RECIPIENT OUTCOMES CORRELATE TO INCREASED INFLAMMATORY MARKERS IN DECEASED AFTER BRAIN DEATH DONORS

Rebecca Vaughan[1], Priyanka Joshi[2], Sadr Shaheed[2], Rutger Ploeg[1,2], Maria Kaisar[2]

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Background and Aims: Cerebral injury during Donation after Brain Death (DBD) will induce a systemic inflammatory response affecting immediate kidney function and survival posttransplantation. Assessment methods of donor organ quality prior to transplant that can predict transplantation outcomes will improve donor organ utilisation and provide monitoring tools for novel targeted interventions.
Methods: DBD plasma samples obtained prior to retrieval (n = 160) were provided by the UK QUOD biobank. Plasma samples were selected from donors from whom both kidneys were transplanted and had the same post-transplantation outcomes; either suboptimal (SO) or good (GO). Kidneys with SO (n = 80) had a mean 1 year eGFR = 29 ± 6 ml/min. Kidneys with GO (n = 80) had a mean 1 year eGFR = 81 ± 14 ml/min. We examined 92 circulating inflammatory proteins using Luminex technologies. Key circulating cytokines that were significantly altered between donors with extreme post-transplant outcomes were further validated using an in-vivo model of immortalised human kidney podocytes and proximal tubular cells (PTECs) to detect the impact on the cytoskeleton and glomerular basement membrane.
Results: We identified that Transforming Growth factor -β (TGF-β) and Interferon-γ (IFN-γ) were significantly increased in DBD plasma samples with suboptimal transplant function. Association of both signalling mediators with changes to protease expression, apoptosis and fibrosis was confirmed using an in-vitro human kidney cell model, suggesting that circulating signatures of inflammation are indicative of subclinical changes in donor kidneys, and that these factors may contribute to the development of graft dysfunction.
Conclusions: This probative study highlights circulating markers associated with inflammation and injury in plasma samples from DBD donors that maybe indicative of inflammation and injury in donor organs prior to retrieval. Increased expression of inflammatory markers is well established in ischaemic reperfusion injury and graft dysfunction, whilst the results in this study suggests injury to organs may start in the donor, and upregulation of markers in donor plasma maybe predictive of injury.

OP385 PROTEOMIC ANALYSIS OF URINARY EXTRACELLULAR VESICLES REVEALS SPECIFIC BK VIRUS-RELATED BIOLOGICAL FINGERPRINTS.

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Background: Nephropathy from BK virus (BKV) infection is an evolving challenge in kidney transplantation. It is the consequence of the current immunosuppressive pharmacological strategy aimed at reducing acute rejection and improving allograft survival. However, although the clinical/histological characteristics of this infection are well defined, the biological machinery associated to this condition is still partially defined.
Methods: We enrolled 45 kidney transplant recipients and, subsequently, the protein content of microvesicles/exosomes isolated from urine of 8 randomly selected patients with only viruria, 8 with both viruria and viremia and 8 matched controls with normal renal function (CTR) was investigated by mass spectrometry, followed by weighted gene co-expression network analysis, SVM learning, and PLS-DA to select the most discriminative proteins.
Results: Bionformatic analysis (including Z-score normalization, heatmap visualization, k-means analysis associated to PLS-DA) identified a core panel of 70 proteins able to discriminate the 3 study groups ($P < 0.001$). In particular, out of 49 and 21 proteins were the most promising biomarkers for BKV viremia-viruria or BKV viruria groups, respectively. Additionally, to better assess the degree of discrimination, we performed GO enrichment analysis based on annotation extracted from various databases. A total of 42 signature were enriched. Processes were clustered in three main groups in function of their GO annotation (infection, kidney disease and fibrosis). Notably, in a subsequent extensive functional analysis, among the proteins enriched in exosome or microvesicles of BKV samples, we identified a total of 959, 452, 113, 134 and 164 proteins associated, respectively, with infectious, chronic kidney disease, tubule disease, renal fibrosis/EMT and Complement.
Conclusions: Our data identified specific extracellular vesicles proteomic fingerprints in kidney transplant recipients affected by BKV infection and identified novel potential urinary biomarkers of this disease.

OP386 NOVEL AVENUE OF ALLOGRAFT MONITORING: DIRECT MEASUREMENT OF DONOR-SPECIFIC EXTRACELLULAR VESICLES IN HUMAN PLASMA SAMPLES

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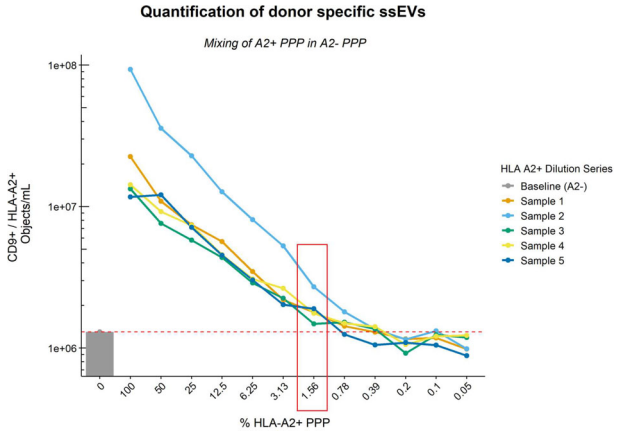
Background: Extracellular Vesicles (EVs) are tissue-specific, nanosized particles that facilitate cell to cell communication, regulate protein expression and even affect antigen presentation. Recently, we developed a protocol to identify single small EVs (ssEVs) in complex samples such as plasma *without* prior isolation of the EVs. Here, we adapted this protocol to identify ssEVs based on their HLA phenotype as a first step to detect allograft specific ssEVs in the circulation of kidney transplant recipients.
Materials & Methods: EDTA blood samples from kidney transplant donors (HLA-A2+, n = 21) and recipients (HLA-A2-, n = 33) were collected before transplantation. Platelet-poor plasma (PPP) was generated and samples were diluted in PBS, stained with a donor-specific HLA antibody (HLA-A2) in combination with a common EV marker (tetraspanin CD9) and measured using standardized Imaging Flow Cytometry (IFCM).
Results: Quantification and comparison of CD9+/HLA-A2+ double-positive ssEVs showed a significant difference between both groups ($1.1E^7 \pm 8.9E^6$ vs $3.5E^5 \pm 2.5E^5$ objects/ml, A2+ vs A2-, respectively, $P = 6.5E^{-5}$) with A2- concentrations representing background level of the machine. CV values for inter- and intra-assay variability were 16% and 11%, respectively. Serial dilution of A2+ PPP in A2- PPP (n = 5) showed a linear reduction in the numbers of CD9+/HLA-A2+ ssEVs according to the dilution rate whilst total CD9+ ssEVs levels remained unchanged. The lower limit of detection of IFCM was defined as the dilution at which point CD9+/HLA-A2+ ssEVs dropped below baseline (A2- PPP) and was determined to be 1.5% (Figure).
Conclusion: Here we demonstrate for the first time the discriminatory capabilities and lower detection limit of IFCM for identification of specific ssEV subsets in unprocessed human plasma. Identification, quantification and characterization of donor specific ssEVs opens up the possibility to monitor these EVs over time after transplantation, and may prove to be a minimally invasive biomarker.



THE NON-SELF RESPONSES AND ITS CONSEQUENCES

OP471 DIAGNOSTIC VALUE OF DONOR-DERIVED CELL-FREE DNA TO PREDICT ANTIBODY-MEDIATED REJECTION IN DONOR-SPECIFIC ANTIBODY-POSITIVE RENAL ALLOGRAFT RECIPIENTS

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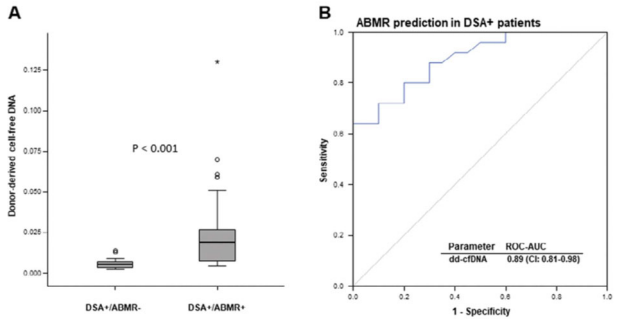
Background: Donor-specific antibody (DSA) detection is associated with an increased risk of antibody-mediated rejection (ABMR). Risk stratification via DSA monitoring, however, remains imprecise and a positive DSA result may not necessarily implicate an active rejection process. Accordingly, there is a need for novel non-invasive biomarkers to improve ABMR prediction. Here, we investigated the diagnostic accuracy of donor-derived cell-free DNA (dd-cfDNA) in a defined cohort of DSA-positive patients.
Methods: The study included 45 HLA class I and/or II DSA-positive kidney allograft recipients, who were recruited upon cross-sectional antibody/ABMR screening in the context of a randomized controlled trial to evaluate the therapeutic efficiency of proteasome inhibition in late silent ABMR (BORTEJECT study; ClinicalTrials.gov, NCT01873157). cfDNA was extracted retrospectively from biobanked EDTA-plasma samples, and dd-cfDNA was analyzed by CareDx AlloSeq cfDNA assay.
Results: Out of forty-five DSA+ kidney allograft recipients, 25 (56%) were diagnosed with ABMR. DSA-positive recipients with ABMR showed significantly higher levels of dd-cfDNA compared to DSA-positive recipients without rejection: median dd-cfDNA of 1.90% (IQR: 0.78-3.90) vs. 0.52% (IQR: 0.35-0.72); $P < 0.001$ (Figure 1A). Receiver operating characteristic (ROC) analysis revealed an area under the curve (AUC) of 0.89 (CI: 0.81-0.98) (Figure 1B). The ROC-AUC calculated for dd-cfDNA levels was thereby comparable to that calculated for mean fluorescence intensity of immunodominant DSA (0.88; CI: 0.78-0.99). A combination of dd-cfDNA and immunodominant DSA further increased predictive accuracy (ROC-AUC: 0.94; CI: 0.88-1.00).
Conclusions: dd-cfDNA monitoring may be a useful surveillance tool in renal transplantation. Together with serologic DSA monitoring, this innovative test principle may considerably improve non-invasive detection of ongoing ABMR late after transplantation, even in subclinical settings.

Figure 1



OP472 DEVELOPMENT AND VALIDATION OF A MACHINE LEARNING BASED VIRTUAL BIOPSY SYSTEM IN KIDNEY TRANSPLANT PATIENTS

Daniel Yoo[1], Gillian Divard[1], Maarten Naesens[2], Marion Rabant[1], Nikolina Basic-Jukic[3], Oriol Bestard[4], Carmen Lefaucheur[1], Olivier Aubert[1], Alexandre Loupy[1]

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Background: In kidney TX, day-zero biopsies are used to assess organ quality and discriminate lesions inherited from the donor or acquired after transplantation. However, many centers worldwide do not perform those biopsies which remain invasive, costly and may delay the transplant procedure. We aimed to develop and validate a non-invasive virtual biopsy system.
Methods: 17 centers were included from Europe, North America, and Australia from 2000 to 2019. Candidate predictors were assessed following a pre-specified protocol. Outcome measures were the day-zero biopsy lesions (Banff classification) including cv, ah, IFTA scores and % of sclerotic glomeruli. 6 machine learning models were developed and their performances were assessed.
Results: A total of 12,992 day-zero biopsies were included. 11 parameters were used to build the classifiers including donor age, kidney function, hypertension, BMI, proteinuria, diabetes, sex, donor type, cause of death, and Hep-C status. The ensemble models (random forests, neural networks, gradient boosting, extreme gradient boosting tree, linear discriminant analysis, and naive Bayes) showed multi-AUC of 0.738, 0.817, and 0.788 for prediction of cv, ah, and IFTA scores, and a good performance for predicting glomerulosclerosis (mean absolute error, MAE = 4.766). We confirmed the robustness and generalizability in multiple clinical scenarios and subpopulations and built an online interface for clinicians https://transplant-pred/Virtual_Biopsy.
Conclusions: We developed and validated the first virtual biopsy system that enables the prediction of day-zero biopsy, based on routinely collected parameters. This can assist clinicians in assessing allograft quality, discrimination of donor derived vs acquired lesions after transplantation and prevent overdiagnosis of calcineurin inhibitor (CNI) toxicity.

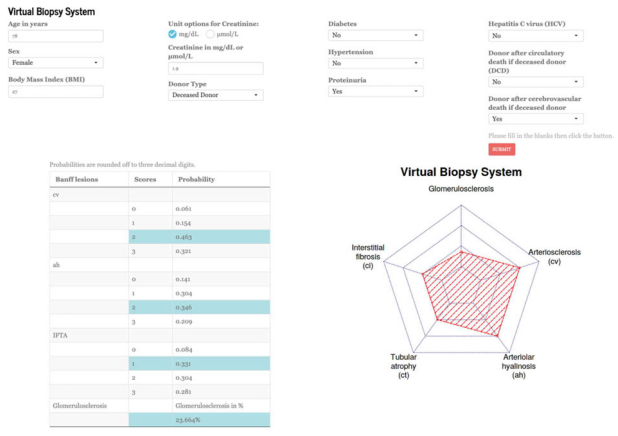

Figure 1 Virtual Biopsy ready-to-use online application

OP473 DEVELOPMENT OF A COMPREHENSIVE BANFF AUTOMATION SYSTEM FOR KIDNEY ALLOGRAFT PRECISION DIAGNOSTICS

Daniel Yoo[1], Juliette Gueguen[1], Gillian Divard[1], Marc Raynaud[1], Marion Rabant[1], Mark Haas[2], Michael Mengel[3], Valentin Goutaudier[1], Olivier Aubert[1], Alexandre Loupy[1]

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Background: Since 1991, the Banff classification has been the gold standard for kidney allograft rejection diagnostics. However, with time, the classification has become complex with many rules and possible scenarios, leading to possible errors and misclassifications. The 2019 Banff report appealed for a systematization and automation of Banff classification.
Methods: We built a consortium comprising data scientists, clinicians, and pathologists. We collected all published Banff rules and integrated them into complex algorithms covering all possible scenarios to generate and automatize Banff classification. We converted the algorithms into an application to assign diagnoses as well as recommendations. We deployed the system in real life for 6 months and collected feedback including usability, consistency, and refinement for complex cases. We last compared the assessments of 5030 contemporary biopsies assessed by pathologists with those provided by Banff automation.
Findings: We encoded all Banff rules and related scenarios (44 quadrillion combinations) and translated them into 45 effective diagnoses and 25 additional Banff recommendations. We devised a software that generates automated Banff reports with the biopsy corresponding diagnosis and nearest neighbour projection (Figure). Among the 5030 biopsies, we found that the Banff automation reclassified 42.9% of AMR cases, 43.2% of TCMR, while 42.7% of biopsies labelled as borderline were reclassified as normal (Table). Finally, the Banff automation-based diagnostics (AMR, TCMR) outperformed the stratification of long-term allograft failure as compared with the pathologist-based diagnostics.
Conclusion: We built the first comprehensive, user-friendly, and fully integrated Banff automation system. This open access tool might improve reproducibility, consistency, thereby reducing misdiagnoses. Lastly, this system may show great benefits to standardize clinical trials and post-transplant patient management and treatment.

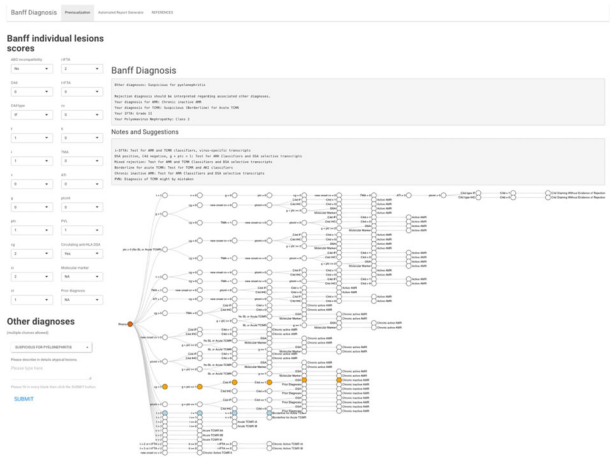

Figure 1 Online application to automatize Banff rules

Table 1. Comparison of biopsy assessments between pathologists and the Banff automation

Pathologist diagnosis	n	Application diagnosis								Discrepancies (=% of row)
		Active AMR	Chronic AMR	Suspicious AMR	Acute TCMR	Borderline infiltrate	Chronic active TCMR	Mixed rejection	Other diagnoses*	No specific lesion	
Active AMR, n (%)	174	109 (62.64%)	6 (3.47%)	33 (19.08%)	2 (1.16%)	0 (0%)	0 (0%)	15 (8.67%)	0 (0%)	9 (5.2%)	65/174 (37.3%)
Chronic AMR, n (%)	120	26 (21.67%)	59 (49.17%)	20 (16.67%)	2 (1.67%)	1 (0.83%)	0 (0%)	8 (6.67%)	0 (0%)	4 (3.33%)	61/120 (50.83%)
Suspicious AMR, n (%)	48	20 (41.67%)	3 (6.25%)	9 (18.75%)	0 (0%)	1 (2.08%)	0 (0%)	6 (12.5%)	0 (0%)	9 (18.75%)	39/48 (81.25%)
Acute TCMR, n (%)	120	1 (0.83%)	0 (0%)	9 (7.5%)	68 (56.67%)	17 (14.17%)	10 (8.33%)	13 (10.83%)	0 (0%)	2 (1.67%)	52/120 (43.3%)
Suspicious acute TCMR, n (%)	6	0 (0%)	0 (0%)	0 (0%)	2 (33.33%)	1 (16.67%)	2 (33.33%)	0 (0%)	0 (0%)	1 (1.67%)	6/6 (100%)
Borderline infiltrate, n (%)	349	7 (2.01%)	1 (0.29%)	17 (4.87%)	2 (0.57%)	148 (42.41%)	21 (6.02%)	4 (1.15%)	0 (0%)	149 (42.69%)	201/349 (57.6%)
Chronic active TCMR, n (%)	28	1 (3.57%)	0 (0%)	3 (10.71%)	2 (7.14%)	3 (10.71%)	16 (57.14%)	0 (0%)	0 (0%)	3 (10.71%)	12/28 (42.86%)
Mixed rejection, n (%)	42	8 (19.05%)	0 (0%)	4 (9.52%)	2 (4.76%)	1 (2.38%)	0 (0%)	26 (61.9%)	0 (0%)	1 (2.38%)	16/42 (38.1%)
Other diagnosis*, n (%)	130	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	130 (100%)	0 (0%)	0/130 (0%)
No specific lesion, n (%)	3329	57 (1.71%)	25 (0.75%)	69 (2.07%)	37 (1.11%)	49 (1.47%)	35 (1.05%)	7 (0.21%)	0 (0%)	3050 (91.62%)	279/3329 (8.4%)
Missing data, n (%)	684	11 (1.61%)	2 (0.29%)	4 (0.58%)	3 (0.44%)	1 (0.15%)	2 (0.29%)	0 (0%)	0 (0%)	661 (96.64%)	not applicable
Total	5030	240	96	168	120	222	86	79	130	3889	731/4346** (16.82%)

* Other diagnoses: recurrent nephropathy, *de novo* glomerulonephritis, BK virus nephropathy, other viral nephropathy, pyelonephritis
** total n of biopsies with a diagnosis assigned by a pathologist

OP474 ASSESSMENT OF THE IBOX PREDICTION SYSTEM IN REAL LIFE SETTING AND DIFFERENT MEDICO-ECONOMIC TRANSPLANT SYSTEMS: THE IBOXEXT TRIAL

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Background: The iBox (NCT03474003) is a prognostication system assessing long-term kidney allograft failure, which recently received regulatory endorsement for surrogate endpoint for clinical trials. However, the iBox system which was primarily built using a deep phenotyped cohort needs proof of validity in extended clinical scenarios and various medico-economic systems is lacking.
Methods: 9159 transplant recipients were included from 16 academic medical centers from Europe (France, Belgium, Spain, $n = 6846$), the United States ($n = 1537$) and South America (Brazil, Argentina, $n = 776$). The iBox score integrates eight independent prognostic factors including the time from transplantation to evaluation, functional factors (eGFR, urine protein creatinine ratio (UPCR)), histologic results (IFTA, g+ptc, i+t, cg Banff scores), and anti-HLA DSA. The performance of the iBox system was assessed in each scenario for its discrimination capability (C-index) and calibration.
Results: We found that the iBox system performance and transportability was conserved (1) in the 16 centers from Europe, US and south America (C-index = 0.82); (2) in the distinct populations treated by CNI, mTORi or Belatacept (C-index = 0.81, 0.87 and 0.81, respectively); (3) Using different eGFR formulas ($MDRD_{186}$, $MDRD_{175}$ and CKD-epi formulas, C-index = 0.81); (4) using urinary dipstick instead of UPCR (C-index = 0.79). We also extended and confirmed the accurate prediction capability of the iBox up to 10 years post evaluation (C-index = 0.79) with an adequate calibration. Finally, we demonstrated that competition with patient death did not affect the overall iBox predictive performance.
Conclusions: The $iBox^{ext}$ trial confirms in various medico-economic systems and additional scenarios its transportability and context of use further supporting its use as a surrogate end point for clinical trials.

OP475 EARLY INFLAMMATION AFTER KIDNEY TRANSPLANTATION IS ASSOCIATED WITH LONG-TERM ALL-CAUSE MORTALITY

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Background: Low-grade inflammation has been established as a risk factor for all-cause mortality in the non-transplant population; however, the role of inflammation among kidney transplant recipients (KTRs) is still uncertain. As the level of inflammation normalize around two months after transplantation, we hypothesized that patients with extensive inflammation at this point would have increased mortality.

Method: 1046 patients were included in this cohort study. Median follow-up time was 10.3 years. 20 inflammatory biomarkers were collected 8-10 weeks after transplantation. Patients with any sign of acute inflammation and/or early graft rejection were excluded. Low-grade inflammation was measured as a composite inflammation scores; one main score for an overall proinflammatory milieu consisting of the values of 10 different biomarkers, and, additionally, composite scores for innate activity, extracellular matrix (ECM) remodeling, vascular inflammation, and endothelial dysfunction. These scores were tested in cox regression models adjusted for traditional risk factors.
Results: A total of 312 (29.8%) patients died during the follow-up-period. When testing the biomarkers independently, eight of twenty biomarkers were significantly associated with all-cause mortality. In the analyses including the overall proinflammatory score, the patients in the upper three quartiles had a progressive hazard ratio (HR), and the ones in the upper quartile had a HR of 5.348 (3.218-8.890) compared to the reference group (see Table and Figure). For the subgroups of inflammation, innate immune system activity, ECM remodeling, and vascular inflammation showed the same pattern (Table).
Conclusion: It appears to be a strong association between subclinical inflammation in the early phase after kidney transplantation and all-cause mortality
Table 1: Association between the different grades of inflammation av long term all-cause mortality with the 1st quartile as reference category (adjusted for traditional risk factors)

	Quartiles of Inflammation Score			
	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile
Hazard Ratios (95% CI)				
Proinflammatory score	1.00 (ref)	1.989 (1.153-3.431)	2.756 (1.632-4.656)	5.348 (3.218-8.890)
Innate immune system activity	1.00 (ref)	1.553 (0.995-2.423)	2.109 (1.374-3.237)	3.830 (2.486-5.901)
ECM remodeling activity	1.00 (ref)	1.789 (1.134-2.821)	2.567 (1.669-3.946)	2.854 (1.803-4.519)
Vascular inflammation	1.00 (ref)	1.865 (1.247-2.790)	2.338 (1.572-3.479)	3.018 (1.992-4.573)
Endothelial dysfunction	1.00 (ref)	1.181 (0.759-1.837)	1.444 (1.025-2.034)	1.391 (0.979-1.975)

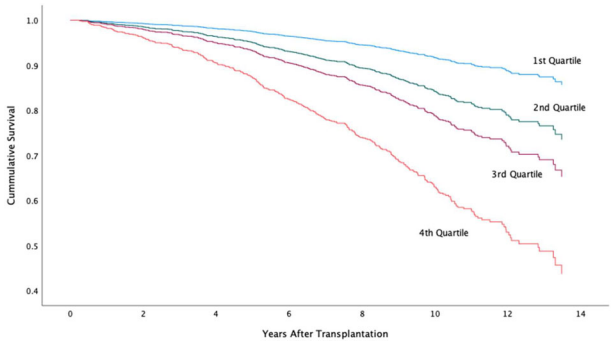

Figure 1: Cox regression survival plot for overall proinflammatory score based on quartiles and all-cause mortality.

OP476 LOSS OF CD24HICD38HI TRANSITIONAL B CELLS IN ANTIBODY-MEDIATED REJECTION OF KIDNEY TRANSPLANTS

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Background: Transitional B cells (TrBs) have regulatory properties and play an important role in limiting alloreactive T-cell mediated responses. However, their role in controlling humoral alloimmunity has been less appreciated.
Methods: We established *in vitro* cellular models using human TrBs and performed 22-color flow cytometry profiling of circulating TrBs, effector T and B cells in a cohort of 96 kidney transplant recipients.
Results: Human $CD24^{hi}CD38^{hi}$ TrBs were capable of direct suppression of T follicular helper (T_{FH}) cell proliferation in a dose-dependent manner ($P = 0.004$) and of T_{FH} cell production of IL-21 ($P = 0.02$). In T_{FH}-B cell co-cultures, $CD24^{hi}CD38^{hi}$ TrBs significantly inhibited CD80- and CD86-dependent B cell activation ($P < 0.001$), B cell differentiation into plasma cells ($P < 0.001$) and IgG production ($P = 0.002$). These mechanisms of suppression were IL-10 dependent. In patients developing donor-specific antibodies (DSAs) post-transplant ($N = 48$), we identified a marked decrease in frequencies of blood $CD24^{hi}CD38^{hi}$ TrBs ($P < 0.001$) with a loss of both T1 and T2 TrB subsets ($P < 0.001$). These decreases were more pronounced in DSA-positive patients who progressed to antibody-mediated rejection (ABMR) ($N = 20$). In contrast, blood $CD24^{hi}CD38^{hi}$ TrBs were maintained in stable patients who did not develop DSAs ($N = 48$) and manifested a $CD21^{-}CD11c^{+}PD\text{-}1^{+}$ expression profile in these patients. Interestingly, the loss in frequencies of $CD24^{hi}CD38^{hi}$ TrBs in patients with ABMR was inversely correlated with increased frequencies of blood effector $Ki\text{-}67^{+}CD45RO^{+}CXCR5^{+}$ T_{FH} cells, effector $CD21^{-}CD11c^{+}CD27^{+}$ B cells and of $CD27^{hi}CD38^{hi}$ plasmablasts ($P < 0.001$ for all correlations).
Conclusions: These *in vitro* and *in vivo* analyses exemplify the role of human $CD24^{hi}CD38^{hi}$ TrBs in tempering antibody responses and reveal a defect in the blood TrB compartment of patients undergoing ABMR that may contribute to loss of immune control in these patients.

OP477 CIRCULATING AND INTRAGRAFT DONOR (HLA)-SPECIFIC B CELLS DRIVE ANTIBODY-MEDIATED REJECTION IN HEART AND KIDNEY TRANSPLANT PATIENTS

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[1]IDIBELL, Experimental Nephrology Laboratory, Barcelona, Spain; [2]Bellvitge University Hospital, Kidney Transplant Unit, Barcelona , Spain; [3]Bellvitge University Hospital, Anatomical Pathology, Barcelona, Spain; [4]Montpellier University hospital, Nephrology, dialysis and transplantation, Montpellier, France; [5]Pure MHC, Oklahoma city, United States

Background: Humoral alloimmune memory is the main barrier for successful transplantation and is generated by a complex compartmentalized B-cell immune response. Besides donor-specific antibodies (DSA), circulating donor (HLA) memory B cells (mBc) have been show to play an active role predicting and during antibody-mediated rejection (ABMR) in kidney transplant patients. Here we aimed to characterize the kinetics and role of donor (HLA)-specific B cells in different immune compartments such as peripheral blood, bone marrow as well as within cellular infiltrates of rejecting grafts in both kidney and heart transplant recipients undergoing acute antibody-mediated rejection (ABMR).
Methods: In order to characterize the presence and kinetics of the humoral alloimmune response of distinct B-cell counterparts, we evaluated B-cell subsets in a donor (HLA)-specific manner in main lymphoid compartments including bone marrow and peripheral blood, as well as in cardiac and kidney allograft biopsies at the time of ABMR. Analyses of circulating DSA, donor (HLA)-specific IgG-secreting mBc in peripheral blood as well as long-lived plasma cell responses in bone marrow were tracked using solid phase assays and a novel HLA-specific B-cell fluorospot assay. Intragraft donor (HLA)-specific B cells were assessed in OCT-embedded frozen biopsies using fluorophore-conjugated HLA-tetramers.
Results: High frequencies of donor (HLA)-specific IgG-secreting long-lived plasma cells and mBCs were detected in the BM and peripheral blood, respectively. Notably, mBCs showed higher donor (HLA)-specific B-cell specificities than circulating DSA. Interestingly, B-cell graft infiltrates were observed in the majority of ABMR samples, which included donor (HLA)-specific B cells harboring the same HLA repertoire as those found in the periphery.
Conclusions: Our study highlights the important role of HLA-specific alloreactive B cells during acute ABMR both in kidney and heart transplant patients, which may be found in distinct biological compartments to maintain DSA formation, and ultimately driving allograft rejection.

OP478 ANTIBODY-MEDIATED REJECTION OF KIDNEY ALLOGRAFT IS ASSOCIATED WITH AN INCREASE IN DIFFERENTIATED CD28-CD8+ T CELLS IN THE PERIPHERAL BLOOD

Hoa Mai[1], Sabine Le Bot[2], Marie Rimbert[3], Karine Autain-Renaudin[4], Richard Danger[5], Florent Leborgne[6], Clarisse Kerleau[7], Nicolas Degauque[5], Florent Delbos[8], Magali Giral[5], Sophie Brouard[5]

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Background: CD28-CD8+ T cells represent a differentiated CD8+ T cell subset that is found to be increased in various conditions associated with chronic antigenic stimulation such as aging, chronic viral infections, autoimmune diseases, cancers, and transplantation. In the transplant setting, we previously showed that patients with chronic kidney graft rejection had higher percentage of CD28-CD8+ T cells in the peripheral blood but those findings need to be confirmed in large cohorts of patients.

Methods: Using multivariate statistical models, we analyzed a large cohort of 1032 kidney transplant patients in whom 1495 kidney graft biopsies were performed concomitant with a peripheral blood leukocyte phenotyping by flow cytometry to investigate whether there was an association between the level of CD28-CD8 T cells in the blood and the diagnosis of graft rejection according to the recent Banff classification of renal allograft pathology.

Results: The histological diagnoses of kidney graft biopsies were divided into 5 groups: normal/sub-normal ($n = 1060$), grade 2 or 3 interstitial fibrosis/tubular atrophy ($n = 90$), antibody-mediated rejection (ABMR) ($n = 211$), T cell-mediated rejection ($n = 51$), and borderline rejection ($n = 83$). We found that ABMR was associated with a significant increase in the percentage as well as the absolute number of CD28-CD8+ T cells in the peripheral blood at the time of biopsy. The confounder-adjusted mean difference in the log percentage and the log absolute number between the ABMR group and the normal/sub-normal group were 0.29 ($P = 0.0004$) and 0.38 ($P = 0.0004$), respectively. It means that the percentage and absolute number of peripheral CD28-CD8+ T cells were 38% and 46% higher, respectively, in patients with ABMR compared to those with normal/sub-normal biopsies.

Conclusions: Those data suggest that differentiated CD28-CD8+ T cells participate in ABMR and that the quantification of peripheral CD28-CD8+ T cells may help to refine the diagnosis of ABMR. Further studies are warranted to clarify the immunological role of this T cell subset in kidney graft rejection.

PRECISION IN MONITORING

OP083 BILE LACTATE AS A MARKER OF BALLOONING AND POTENTIAL CRITERIA FOR CHOOSING A PRESERVATION STRATEGY OF LIVER GRAFTS

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Background: For several decades, the shortage of donor organs has been one of the main problems of transplantation all over the world. The aim of the research was to determine the diagnostic value of donor's bile as a marker that can give an additional assessment and objectify the condition of the liver graft, assess the need for machine perfusion, and predict the course of the early postoperative period.
Methods: From July 2017 to November 2019 during the organ retrieval, bile from the common bile duct and a liver parenchyma biopsy have been taken. All grafts were divided into two groups. The first group consisted of organs that were transplanted and group 2 consisted of organs that were found unsuitable for transplantation. Morphological evaluation and bile BOC analysis were carried out.
Results: A reliable relationship was determined between the level of bile lactate from both groups of donors and the level of hepatocyte ballooning ($R = 0.50$, $P = 0.001$). In those cases where severe ballooning was observed, significantly higher levels of lactate in the bile of donors 1.9 mmol/l were determined [1.2; 2.55], in comparison with those samples where it was not expressed 0.6 [0.3; 1.7] ($P = 0.006$). The performed ROC analysis allowed to determine the level of bile lactate at 1 mmol/l as a cut-off at which the probability liver cells ballooning is maximal (AUC = 0.830). At group 1, a reliable association was obtained between the level of donor bile lactate and ALT at the peak value ($R = 0.56$, $P = 0.004$) and on the 7th postoperative day ($R = 0.53$, $P = 0.01$), as well as with the INR level at the peak value ($R = 0.63$, $P = 0.001$).
Conclusion: Bile lactate reliably reflects the degree of hepatocytes ballooning and objectifies the condition of donor livers, as well as predicts the course of the early postoperative period. Bile lactate levels greater than 1 mmol/l are a potential criterion for oxygenated machine perfusion.

OP084 TISSUE VIABILITY AND MITOCHONDRIAL RESPIRATION DURING STATIC COLD STORAGE PREDICTS LIVER TRANSPLANTATION OUTCOME

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Background: Donor and organ parameters with strong predictive value in liver transplantation are lacking. We herein evaluate the potential of in-depth liver viability and bioenergetics testing in static cold stored (SCS) grafts for their predictive value towards the outcome in liver transplantation.
Methods: In a prospective, single arm trial, we enrolled 43 patients undergoing liver transplantation. Liver wedge biopsy samples were taken upon arrival. Histology and real-time confocal imaging (RTCA) of SYTO®16/PI und WGA were employed. Mitochondrial respiration was assessed by high-resolution respirometry (HRR; O2k, Oroboros Instruments) with a focus on OXPHOS capacity and coupling efficiency (*L/P* coupling-control ratio) of the succinate-linked respiration. Early allograft dysfunction (EAD) served as primary endpoint, MEAF and L-GrAFT, graft and patient survival, length of stay and biliary complications served as secondary endpoints. Data were analysed using parametric and non-parametric tests (including Spearman rank correlation). RTCA score and OXPHOS coupling efficiency were evaluated in uni- and multivariate logistic regression analyses.
Results: Twenty-two recipients (22/43, 51.2%) experienced EAD. Pre-transplant histology results were not significantly different between EAD and non-EAD. EAD correlated well with MEAF score ($P < 0.01$) and L-GrAFT ($P = 0.02$, Spearman's ρ 0.574 for MEAF and 0.357 for L-GrAFT). The mean RTCA score was predictive for EAD (-0.75 ± 2.27) vs non-EAD; (0.70 ± 2.08; $P = 0.01$). The OXPHOS coupling efficiency correlated with EAD (0.8 in non-EAD compared to 0.7 in EAD-livers; $P = 0.02$) and was congruent with the RTCA result ($P = 0.005$, Spearman's ρ 0.493). The MEAF score correlated negatively with the RTCA readout ($P = 0.01$, Spearman's ρ −0.407). The occurrence of biliary complications and the overall length of stay were comparable between recipients with EAD and non-EAD.
Conclusions: Both RTCA and HRR are valuable tools for tissue viability and bioenergetics function assessment with predictive value towards EAD in liver transplantation.

OP085 DYNAMIC FORECASTING OF PATIENT-SPECIFIC KIDNEY TRANSPLANT FUNCTION WITH A SEQUENCE-TO-SEQUENCE DEEP-LEARNING MODEL

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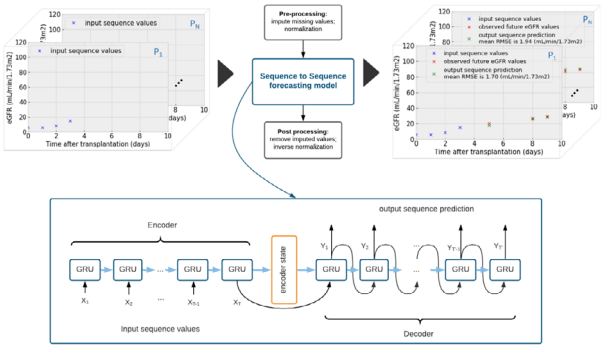
Background: Alike other clinical biomarkers, trajectories of estimated glomerular filtration rate (eGFR) are characterized by intra-individual variability. These fluctuations hamper the distinction between alarming graft functional deterioration or harmless fluctuation within the patient-specific expected normal range of eGFR. We postulated that a deep learning approach could forecast future eGFR sequences and alarm clinicians on deviations of measured values from the patient-specific predicted range.
Methods: The data consisted of 140 866 eGFR measurements from 2103 transplantations, divided into a derivation cohort of 933 kidney transplant patients with 100 867 eGFR measurements, and two independent validation cohorts with 39 999 eGFR measurements from 1170 patients. We used deep learning with Gated Recurrent Unit-based Sequence-to-Sequence (GRU-Seq2Seq) modelling to predict patient-specific eGFR trajectories.
Results: Both in the training and in the independent validation sets, the GRU-Seq2Seq models accurately predicted future patient-specific eGFR trajectories in the first 3 months after transplantation, based on the grafts' previous eGFR values (root mean square error [RMSE] 6.4–8.9 ml/min/1.73 m^2). Accuracy increased with increasing numbers of eGFR values as input and more adjacent timeframe predictions as output. The GRU-Seq2-Seq model predictions outperformed the more conventional autoregressive integrated moving average (ARIMA) prediction model, at all input/output number of eGFR values. When applying the short-term GRU-Seq2Seq architecture for building models to predict eGFR sequences beyond 3 months post-transplant, overall error remained low.
Conclusions: We developed and validated a sequence-to-sequence deep learning model for individual forecasting of kidney transplant function. The patient-specific sequence predictions could be used in clinical practice to guide physicians on deviations from the expected intra-individual variability.

Figure 1. Schematic overview of the GRU Seq2Seq models for forecasting patient-specific kidney transplant function. The top panel shows the pipeline of the proposed model. The lower panel schematically illustrates the sequence-to-sequence model encoder-decoder architecture. First, N different patients' (P_1 to P_N) continuous eGFR values (input sequence values, X_1–X_5, blue crosses) were pre-processed and then analyzed by the sequence-to-sequence model. The predictions from the model (Y_1–$Y_{T'}$, green crosses) were post-processed and then evaluated by comparison with the observed eGFR values (red crosses) using the root mean square error (RMSE).



OP086 MONITORING OF ANTIVIRAL IMMUNE RESPONSE AS AN INDICATOR OF IMMUNOSUPPRESSION INTENSITY AND OUTCOME AFTER KIDNEY TRANSPLANTATION: THE VIRENO STUDY

Veronica Di Cristanziano[1], Patrick Affeldt[2], Katharina Burkert[2], Georg Dieplinger[3], Martin Kann[2], Franziska Grundmann[2], Thomas Benzing[2], Adams Ortwin[4], Rolf Kaiser[1], Dirk Stippel[3], Christine Kurschat[2], Florian Klein[1], Roman-Ulrich Müller[2]

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Background and aims: The VIRENO study is an interdisciplinary, multicenter, and non-interventional project aimed to identify immunological parameters able to predict the occurrence of major complications after kidney transplantation (KTX), including viral infections and rejections.
Methods: The viro-immunological monitoring of our cohort was performed pre-KTX, 3 weeks and 6 months post-KTX. It included assessment of anti-BKPyV IgG in both living donor and recipient and of TTV (torque teno virus) viremia in recipients. The cellular immunity to CMV was assessed by QuantiFERON-CMV (Qiagen) and T-SPOT®.CMV by Oxford Immunotec. The viro-immunological status was correlated with clinical information focusing on major immunological and infectious events in the first year after KTX.
Results: Overall, 64 patients were monitored for one year following KTX. In a first step, we compared the median of reactive ELISPOT results in all CMV serostatus positive recipients (R+) who had a CMV reactivation within the first year to those who had not. Differences in median spot number for pp65 pre-KTX (CMV-reactivation: 223 spots vs. No CMV-reactivation: 506 spots) in those groups were significant ($P = 0.04$). Furthermore, we found a significant correlation between ELISPOT IE1 after 3 weeks > 100 spots and a CMV-reinfection within the first year (two tailed fisher exact $P = 0.042$). BKPyV IgG after 6 months was significantly associated with the risk of BKPyV-Infection within the next 6 months ($P = 0.016$). In the group of patients with BKPyV-infection median IgG level was 91 IU/ml compared to 65 IU/ml in the group without BKPyV-infection. Lower TTV-DNA load baseline (in plasma and whole blood) was associated with higher risk of organ rejection within the first year (whole blood $P = 0.031$, plasma= $P = 0.021$). Comparing both groups, the median TTV-DNA load in those patients without event of acute rejection (50 patients) was 1.6E+04 cop/ml (whole blood) and 1.4E+03 cop/ml (plasma). In 11 patients, acute rejection was observed. In this group, median level of TTV viremia was 1.5E+03 cop/ml (whole blood) and 9.5E+02 cop/ml (plasma).
Conclusions: Overall, these first data provide a preliminary overview on the ability of the viro-immunological monitoring to measure the individual changes in the functionality of immune system pre- and post-Tx.

OP087 LUMINAL ACTIVATION OF COMPLEMENT WITH APICAL DEPOSITION OF C3DG AND C5B-9 IN THE PROXIMAL TUBULES IN KIDNEY TRANSPLANT RECIPIENTS

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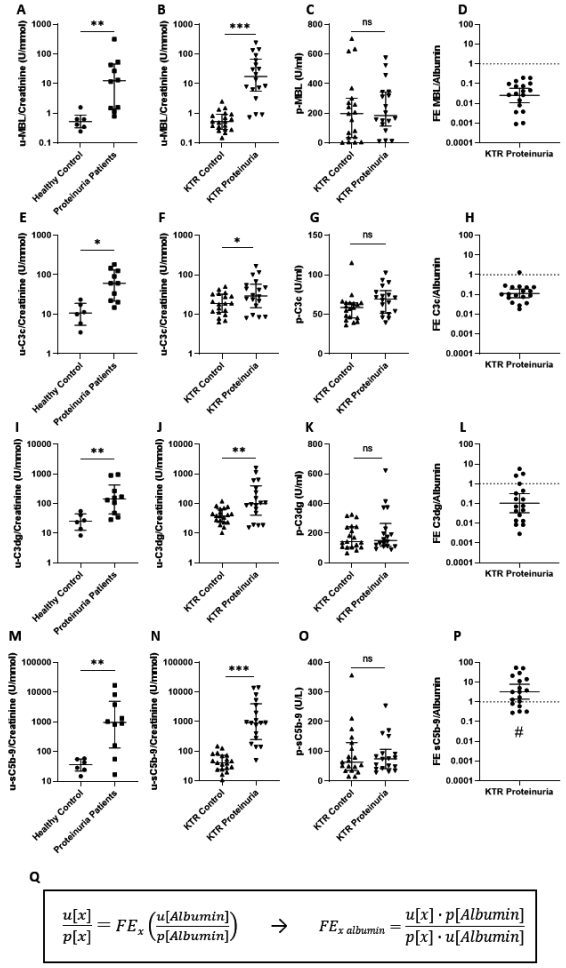
Background: In kidney transplant recipients (KTRs), proteinuria predicts decline in kidney function and graft failure. We hypothesized that circulating complement factors are aberrantly filtered to the tubular fluid, followed by activation and apical membrane attack in proteinuria.
Methods: C3 activation split products (C3c, C3dg), sC5b-9 and MBL were analyzed by ELISA in controls ($n = 6$) and KTRs ($n = 19$) with albumin/creatinine (ACR) < 30 mg/g and patients ($n = 10$) and KTRs ($n = 19$) with ACR ≥ 300 mg/g. A 1-year prospective cohort of KTRs was divided in no-proteinuria ($n = 11$), ≥30% ACR increase ($n = 12$) and ≥30% ACR decrease ($n = 11$). Urinary extracellular vesicles (uEVs) from KTRs were analyzed by western blotting for sC3c, C3dg, C5b-9 and SGLT2.
Results: Urine complement activation split products and MBL increased significantly in patients with proteinuria and KTRs with ACR ≥300 mg/g compared to their respective controls; MBL ($P < 0.01$ both) C3c ($P < 0.05$ both), C3dg ($P < 0.01$ both) and sC5b-9 ($P < 0.01$ both). sC5b-9 fractional excretion ratio (FE) normalized to albumin was 3.3[CI95 1.4–7.8], indicating local generation. Urine C3dg and sC5b-9 increased from 3 to 12 months in KTRs with increase in proteinuria while sC5b-9 decreased when ACR decreased. Plasma levels were similar. C5b-9 was detected in uEVs in 6/9 KTRs with proteinuria and in no uEVs from KTR controls. Lectin affinity isolation of uEVs from proximal tubules enriched for C5b-9 and SGLT2. C3dg co-immunoprecipitated C5b-9 and SGLT2, but not soluble C3c, and signal was maintained after centrifugation at 10 000 G, documenting association with larger uEVs.
Conclusions: Proteinuria is associated with aberrant filtration and intratubular activation of complement, deposition of C3dg and C5b-9 on proximal tubular apical membranes in kidney allograft transplant patients. In perspective, pharmacological inhibitors of complement that reach the luminal compartment may have therapeutic potential.

Fig. 1



OP088 THE UPTAKE OF THE PET RADIOTRACER 18-FLUORODEOXYGLUCOSE BY THE RENAL ALLOGRAFT CORRELATES WITH THE ACUTE BANFF SCORES OF CORTEX INFLAMMATION

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Background and Aims: Acute T-cell mediated rejection (TCMR) is associated with the recruitment of mononuclear leukocytes into the renal transplant, which is the core of Banff classification. The boosted metabolism of inflammatory cells can be assessed by [^{18}F]FDG-derived positron emission tomography (PET). The correlation of Banff *versus* PET scores of acute inflammation in the renal transplant is unknown.
Methods: We prospectively performed 114 [^{18}F]FDG PET in 105 adult kidney transplant recipients who underwent a *per cause* transplant biopsy. Biopsy-proven polyoma-BK nephropathies ($n = 7$) and uninterpretable PET images ($n = 2$) were excluded. The mean standardized [^{18}F]FDG uptake value (SUV_{mean}) was measured in 4 regions of the renal cortex. The acute Banff score was defined as the sum (0–15) of g (glomerulitis), ptc (peritubular capillaritis), t (tubulitis), i (inflammation in non-scarred cortex) and v (endarteritis). The Banff "total i" score (0-3) corresponded to the total cortical inflammation, including scarred and non-scarred cortex. Regression of the mean of the 4 SUV_{mean} ($mSUV_{mean}$) against the acute Banff score was done. The distribution of $mSUV_{mean}$ between "total i" groups was assessed by non-parametric Kruskal-Wallis test followed by Dunn's *post hoc* test.
Results: The mean age of the cohort was 51.5 ± 14.3 years, with M/F ratio of 67/38. The prevalence of biopsy-proven TCMR and borderline was 20.9% and 16.2%, respectively. The mean of $mSUV_{mean}$ was 1.82 ± 0.45. The highest value of acute Banff score was 12, while 55.2% of biopsies were scored as 0. The distribution of "total i" score was: 0 (58.8%); 1 (20.6%); 2 (8.8%); 3 (11.8%). A significant correlation between $mSUV_{mean}$ and acute Banff score was found, with adjusted R^2 of 0.38. The $mSUV_{mean}$ was significantly different between "total i" groups, with 2.33 ± 0.76 in score 3 *versus* 1.68 ± 0.24 in score 1.
Conclusion: [^{18}F]FDG PET may help noninvasively assess the degree of allograft inflammation in *per cause* clinical settings.

DOES ORGAN PERFUSION BUY US TIME?

OP089 METABOLISM-REGULATED SUB-NORMOTHERMIC CULTURE SYSTEM OF HUMAN KIDNEYS RETAINS EX VIVO VIABILITY FOR 4 DAYS

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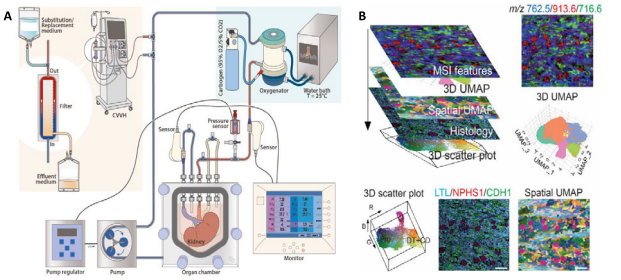
The limit of kidney viability within an ex-vivo setting is currently set at 24 h while accurate assessment tools for kidney function in those conditions are lacking. Here, we describe a novel platform that enables prolonged donor kidney culture with controlled metabolism at sub-normothermic temperature, which could serve as alternative strategy for organ preservation and resuscitation. We developed and optimized a kidney culture system using porcine kidneys after which we cultured 5 human donor kidneys that were discarded for various medical reasons. Through lowering the culture temperature to sub-normothermic conditions and the incorporation of a clinical veno-venous hemofiltration (CVVH) apparatus, we succeeded in preserving physiological levels of electrolytes, metabolites and waste products. By metabolically steering the culture medium we were able to extend (tubular) cell viability up to four days. After culture, we used single cell resolution mass spec imaging to assess viability and confirm conservation of cellular composition of the organs. In addition, kidneys were assessed for glomerular filtration barrier integrity and energy metabolism by nuclear magnetic resonance (NMR) spectroscopy. This novel platform can be explored to ensure and preserve kidney function after procurement.



A Set up of the culture system. Kidneys were cultured in a custom-made air-tight culture chamber providing single sampling ports for kidney artery, venous and ureter. The CVVH was driven by an independent integrated pump (20 ml/min), resulting in an effective continuous overall 5% perfusate substitution rate. **B Workflow of MSI based spatial segmentation platform**. A spatial segmentation of the lipid species detected by MSI was performed using a two-dimensional uniform manifold approximation and projection (2D UMAP) analysis, which was able to identify clusters of composite renal cells. Combining the MSI-derived spatial segmentation information with post-MSI immunofluorescent staining of the renal tissues (LTL: proximal tubule, NPHS1: glomeruli, CDH1: distal tubule) allowed for direct mapping of the cell identity to its location in the tissue.

OP090 FEASIBILITY OF PROLONGED NORMOTHERMIC MACHINE PERFUSION OF DISCARDED DECEASED DONOR KIDNEYS TO BETTER ASSESS AND ENHANCE ORGAN UTILISATION

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Background: To better assess viability and stimulate the regenerative potential in deceased donor kidneys prolonged normothermic machine perfusion (NMP) beyond 1 h may be required. The aim of this study was to develop and test feasibility and safety of a 6-h NMP protocol using discarded donor kidneys.
Methods: Seventeen discarded kidney (9 DCD, 8 DBD) were perfused for 6 h at 37°C following prior cold preservation. The clinically applied 1-h protocol, as previously published by Hosgood et al., was adapted to allow a stable and prolonged NMP. Key adjustments included washing red blood cells (RBC) prior to perfusion, addition of albumin to increase colloid osmotic pressure and recirculating urine to avoid loss of sodium and maintain a physiological pH. A pulsatile pressure of 75 mmHg and a RBC based perfusion solution oxygenated with 95%O_2/5%CO_2 was used. Throughout NMP renal haemodynamics was monitored whilst perfusate, urine and biopsy samples were collected to assess the effect of NMP on the quality of the kidney.
Results: Throughout NMP a stable temperature, renal arterial flow (T0h: 48.7 ± 27.7; T6h: 59. 7 ± 20.7 ml/min/100 g), arterial resistance (T0h: 2.4 ± 2.2; T6h: 1.4 ± 0.6 mmHg) and pH (T0: 7.2 ± 0.20; T6h: 7.3 ± 0.05) were achieved. The majority of donor kidneys ($n = 11$) produced urine during NMP. Histological characteristics of acute injury (dilatation, edema, vacuolization, casts) showed no increase as a result of NMP. Kidneys were divided in two groups based the reason of discard with A: surgical problems; B: insufficient clearance/high donor risk factors. At the end of NMP (T6h) kidney injury molecule-1 (KIM-1) levels were significantly higher in group B vs A (A: 273 ± 92; B: 582 ± 111 pg/mL; $P = 0.01$) in perfusate. LDH, ASAT and neutrophil gelatinase-associated lipocalin (NGAL) were also higher in group B but differences did not reach significance.
Conclusions: Prolonged NMP mandates adjustments to the perfusate including the addition of a colloid, defined electrolyte concentrations and urine-recirculation whilst using fresh washed RBCs is also paramount. This study shows that end-ischaemic prolonged NMP is feasible and appears to

be safe in maintaining stable perfusion parameters and structural kidney integrity.

OP091 OBSERVATIONS ON 24-HOUR EX SITU NORMOTHERMIC LIVER PERFUSION

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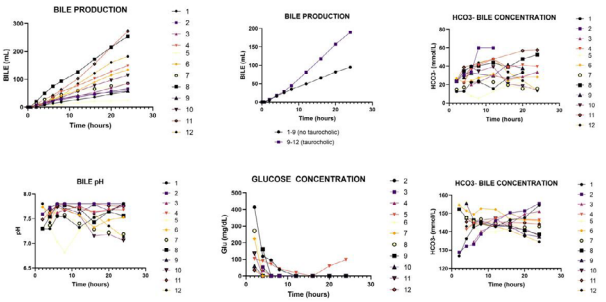
Background: In human liver transplantation, normothermic machine perfusion is being applied with increasing frequency, though little has been published regarding its extended application (≥24 h). In this study, we aimed to perfuse livers 24 h to optimize technique of extended *ex situ* liver perfusion in a pre-clinical model.
Methods: Following donor exsanguination, pig livers (N = 12) are recovered; prepared; and connected to the NMP device (Devocean-Liver2000, Devocean Medical Instrument, Ltd., Guangdong, China) via the portal vein, hepatic artery, and common bile duct. The caval vein is left open, and perfusate flows from graft to receptacle, where it is recovered, reoxygenated, reheated, and returned to the hepatic artery as pulsatile flow and the portal vein as continuous low-pressure flow. Perfusion commences with blood mixed with calcium and antibiotics. Parenteral nutrition, insulin, heparin, multivitamins, trace elements, and bile salts are infused continuously. Hemodynamic, gasometric, and biochemical parameters are monitored, as are bile production and composition. In the first six experiments, one liter of perfusate is removed at 12 h and replaced with fresh blood.
Results: All livers were perfused for 24 h. After 1 h, hemodynamic parameters remained stable, without need for exogenous vasoactive substances. In the perfusate, glucose and lactate levels decreased progressively. Transaminase levels remained stable throughout 24 h, while urea levels increased progressively, even in spite of partial perfusate exchange. Bile production commenced immediately and was constant. In bile, glucose levels declined to undetectable, while pH, bicarbonate, and sodium levels were increased (FIGURE).
Conclusions: The strategy of NMP adequately maintains livers for 24 h, though longer perfusions might require addition of a dialysis filter to avoid adverse effects of increasing urea levels on hepatic metabolic function.



OP092 IMPROVEMENT OF A RAT MODEL OF PROLONGED LIVER NORMOTHERMIC MACHINE PERFUSION

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Background: Liver normothermic machine perfusion (NMP) is a promising platform for ex-situ organ treatment. NMP therapeutic potential can be further enhanced. In particular, extension of perfusion time could allow improving efficacy of pharmacological and antimicrobial treatments. The aim of our study was to implement a rat model of prolonged NMP.
Methods: A first series of experiments included the following study groups ($n = 5$): (1) Native; (2) static cold storage (SCS), livers were procured and stored at 4°C for 30 min; (3) NMP-DMEM, SCS followed by 150 min NMP with DMEM as perfusate; (4) NMP-RBC, as NMP-DMEM with human red blood cells (RBCs) added to the perfusate (Ht 15%); (5) NMP-OXY, as NMP-RBC, but RBCs were replaced with non-cellular hemoglobin (Oxyglobin). Next, we set up a procedure for 12 h-NMP (NMP-OXY12, $n = 5$). Perfusate samples were collected to evaluate cell injury markers and metabolites, while tissue biopsies were taken to assess liver morphology and ATP content.
Results: Compared to NMP-DMEM, NMP-RBC and NMP-OXY groups showed increased oxygen delivery ($P < 0.001$) and consumption ($P = 0.001$) and greater bile production ($P = 0.001$). Enhanced clearance of lactates ($P = 0.006$), potassium ($P = 0.016$), and glucose ($P = 0.029$) was observed in NMP-OXY relative to NMP-DMEM and NMP-BLOOD. ATP content of livers from the NMP-OXY group was higher than NMP-DMEM and NMP-RBC, while it was comparable to that of the SCS group (Figure 1). Based on these data, we elected to perform 12 h-NMP using Oxyglobin-based protocol. Bile output was maintained over 12 h. At the end of the procedure, lactates were 1.1 ± 0.3 mmol/l and ATP content resulted similar to that of NMP-DMEM (Figure 1). Markers of cell injury and liver morphology were similar across experimental groups.
Conclusions: The use of non-cellular hemoglobin enabled to safely perfuse livers over 12 h, preserving hepatocellular metabolism. Prolonged rat liver NMP is feasible and offers the opportunity to test different strategies for graft ex-situ treatment.

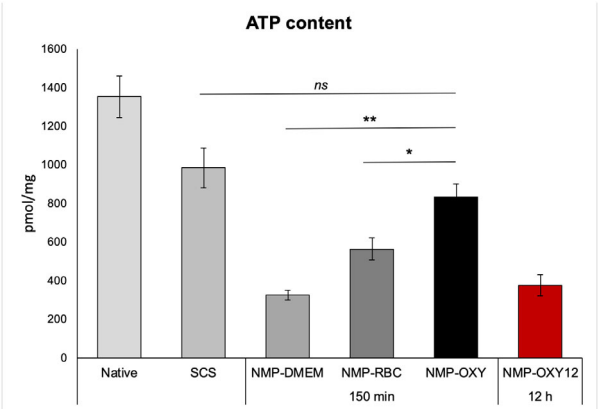

Figure 1 *ATP content in liver biopsies subjected to 150 min- and 12h-normothermic machine perfusion (NMP) compared to native and static cold storage (SCS) groups.*

OP093 SUCCESSFUL EX-VIVO RECONDITIONING OF KIDNEYS RETRIEVED 4.5 HOURS AFTER CIRCULATORY DEATH

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Background: Organ shortage is a major limiting factor in organ transplantation. Most patients receive their kidneys from brain-dead-donors (DBD) although the use of kidneys from cardiac death donors (DCD) has increased. Many preservation solutions have been tested to include DCD kidneys in the donor pool; however, none so far have proven to give acceptable results in warm ischemia times (WIT) beyond 2 h after circulatory arrest. We present a novel *ex-vivo* perfusion strategy, using an albumin-based preservation solution to salvage kidneys from porcine donors in an uncontrolled DCD model.
Methods: Two hours after circulatory death, ice slush was added in the pig abdomen. Organs were procured after a total of 4.5 h of ischemia. The study group kidneys ($n = 21$) were injected on back-table with anti-thrombolytic agents (Lys-Plasminogen, Anti-thrombin-III and alteplase) through

the renal artery. Thereafter, kidneys were machine-perfused for three hours with an albumin-rich cell free solution at a temperature of 15°C and pressure of 20 mmHg. Washed erythrocytes were added to the solution and the perfusion continued for another 3 h at 32°C and 30 mmHg. The control group consisted of kidneys ($n = 7$) with the same perfusion protocol except for the anti-thrombolytic treatments. The vascular resistance and arterial flow were continuously monitored along blood gases of the solution and urinary output. At the end, the kidneys were examined macroscopically and samples collected for histological evaluation.
Results: The vascular resistance in study kidneys decreased to <200 mmHg/ml/min, significantly lower ($P < 0.0022$) and arterial flow increased to >100 ml/100 g/min, significantly higher ($P < 0.00018$) than control kidneys. Minor reversible damages to the tubules and no changes to the glomeruli were seen.
Conclusion: Our findings suggested that even after 4.5 h of WIT in a uDCD kidney, it is possible to salvage organs for subsequent transplantation.

OP094 A CLINICAL COMPARISON OF TWO DIFFERENT OXYGEN CARRIERS FOR COMBINED HYPOTHERMIC AND NORMOTHERMIC MACHINE PERFUSION OF HIGH-RISK DONOR LIVERS

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Background and Aims: Ex-situ normothermic machine perfusion (NMP) is increasingly used for pretransplant viability assessment of high-risk donor livers. When applied after static cold storage ('back-to-base'), a short period of hypothermic oxygenated machine perfusion (HMP) prior to NMP reduces ischemia-reperfusion injury during NMP. Excellent results have been reported after combined HMP and NMP, using a single perfusion solution containing an hemoglobin-based oxygen carrier (HBOC). We aimed to determine whether similar results can be obtained with a perfusion solution containing red blood cells (RBC) instead of HBOC.
Methods: In a prospective observational cohort study, sequential HMP and NMP was applied in 50 nationwide discarded donor livers in the Netherlands. The first 18 procedures were part of a prospective clinical trial with a HBOC-based perfusion solution for both HMP and NMP (www.trialregister.nl; NTR5972). The subsequent 32 procedures were performed using Belzer Machine Perfusion Solution (MPS) for HMP, followed by an RBC-based perfusion solution for NMP.
Results: A total of 50 consecutive HMP-NMP procedures were included. All but two livers were derived from donation after circulatory death donors, with a median donor risk index of 2.83 (IQR 2.51–3.09) and median donor age of 63 years (IQR 53–71). After viability assessment during NMP, 12 livers in the HBOC-group were transplanted versus 18 in the RBC-group (utilization rate 67% vs. 55%, $P = 0.42$). One-year graft and patient survival were 92% and 100% in the HBOC-group versus 94% and 100% in the RBC-group, resp. ($P = 0.96$ and $P = 1.00$). Post-transplant cholangiopathy occurred in one patient (3%). There were no differences in other post-transplant outcomes among the two groups.
Conclusions: Ex-situ machine perfusion using sequential HMP-NMP for resuscitation and viability assessment of high-risk human donor livers results in excellent transplant outcomes, irrespective of the type of oxygen carrier used.

OUTCOME OPTIMISATION IN PAEDIATRIC ORGAN TRANSPLANTATION: ALL ROADS LEAD TO...MILAN

OP123 UK DECEASED DONATION AND TRANSPLANT ACTIVITY IN PAEDIATRICS FOR 2019 – 2020

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Background: We present data on organ donation and transplantation in children for 2019–2020, following the launch the National Strategic Plan for Paediatric and Neonatal Organ Donation in early 2019.
Methods: A standardised dataset collected by Specialist Nurses for Organ Donation (SN-ODs) on paediatric ICU deaths, was analysed by NHSBT Statistics department. Further data were extracted from the UK Transplant Registry.
Results: Of 1125 paediatric deaths, 290 met referral criteria and 98% potential Donation after Brain Death (DBD) and 83% potential Donation after Circulatory Death (DCD) patients were referred to a SN-OD. Failure to identify potential DCD donors, was the commonest reason for non-referral. Neurological testing rate was 74% with 65 eligible for DBD patients. Of 180 eligible DCD patients, 112 were not approached with general medical condition and Coroner/Procurator Fiscal (C/PF) refusal accounting for 55%. Consent/authorisation was given for 68% and 46% DBD and DCD donors, respectively, and 89% and 58% became actual donors. No families overruled their child's known wish to be an organ donor. The five-year neurological testing rate is static around 73%. SNOD presence for both DBD and DCD donation and consent rates have improved. At year-end, the transplant list comprised 198 paediatric patients, an increase of 18 compared to 2018-2019 with 18 more waiting for a kidney. In 2019-20, 230 paediatric patients received a transplant, 40 fewer compared with 2018/2019, with 18 fewer deceased donor kidney transplants.
Conclusions: Paediatric OD referral rates are continuing to improve, especially for DBD. SNOD presence for both DBD and DCD is also at an all-time high. Opportunities exist to improve DCD referral, neurological testing and DCD approach rates. Improved collaboration between SNODs, PICU staff and the C/PF and other professionals, may explain the reduction in refusal rates by C/PF. Consent rates also show a rising trend, but are significantly lower for ethnic minority families. Delivery workstreams as part of the National Strategic Plan implementation aim to achieve further improvements. The transplant waiting list has increased by 10% with a concurrent 15% fall in overall transplant activity. This is likely related to the introduction of the new kidney offering scheme and its impact will be monitored.

OP124 THE END STAGE RENAL DISEASE (ESRD) IN ANORECTAL MALFORMATION (ARM) PATIENTS: RISK FACTORS AND OUTCOME

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While in adults the leading causes of KT are hypertension and diabetes, in children congenital anomalies of the kidney are the most frequent causes of ESDR. End Stage Renal Disease (ESRD) requiring Kidney Transplant (KT) remains an important cause of morbidity in patients with AnoRectal Malformation (ARM).Differently from other categories, few information is available regarding the risk factors and the outcome in this selected population. This study aimed to identify risk factors for kidney transplant (KT) in ARM patients (ARM-KT) and compare the outcome of KT in ARM-KT vs. patients with urological anomalies but no ARM (URO-KT). A prospectively ARM and KT maintained database were queried to identify patients with ARM who underwent a KT (cases) and those with urological anomalies no ARM undergoing KT (controls) between 2000 and 2016. Data regarding type of ARM, gender, urological anomalies (UA), age at KT and possible interventions that could have delayed KT, follow-up length were considered. Bivariate analysis was performed. Out of 117 ARM patients in the study period (62 complex, 55 less complex), 8 (7%) underwent KT (all complex ARM). Associated urological anomalies were significantly more common in ARM-KT compared to other ARM patients, 100% vs. 52%, $P = 0.001$. The urological malformation was clearly severe from the outset (bilateral small kidney, single dilated kidney, and/or severe lower urinary tract malformation). During the same period 23 patients with urological conditions (mainly primary vesico-ureteral reflux and posterior urethral valves), but no ARM, underwent KT (Uro-KT group). Comparing ARM-KT with Uro-KT, there was no difference in the age at transplant and type of donor ($P = 1$ and 0.6, respectively). ARM-KT patients required more often hemodialysis before KT (50% vs. 8.7%, $P = 0.05$), required more often an aorto-caval anastomosis at KT (75% vs. 30%, $P = 0.04$), and, despite a significantly shorter follow-up (median 3 vs. 6.3 years, $P = 0.02$), required more frequently a second KT (50% vs. 8.6%, $P = 0.02$). Patients with high ARM and urological anomalies were at increased risk of KT compared to other ARM patients. The outcome was poorer compared to patients with urological anomalies but no ARM. This information might help selecting cases requiring closer follow-up in order to prevent a second kidney transplant.

	Uro -KT 23	ARM-KT 8	P Value
Sex F (%)/M (%)	1 (4.3)/ 22(95.7)	3 (37.5) /5 (62.5)	0.04
Age at KT median (min-max)	5.5 (2-15)	5.5 (2-15)	1
Peritoneal Dialysis / Haemodialysis n (%)	16(69.5)/2(8.7)	4(50)/4(50)	0.05
Cadaver Donor /Living-related Donor N (%)	17(73.9)/6(26)	5(62.5)/3(37.5)	0.6
Aorto-caval anastomos /Iliac anastomosis N (%)	7 (30)/ 16(69.5)	6(75)/2(25)	0.04
Warm ischemia (min-max)	55.28 (35-90)	49.3 (30-70)	0.2
Patch N(%)	5(4.6)	1(12.5)	1
Rejection N(%)	6(26)	5 (62.5)	0.07
Rejection Timing median (min-max)	22 (6-77)	15.8 (1-36)	0.63
Second KT N (%)	2(8.6)	4(50)	0.02
Follow-up median (min-max)	6.3 (1-12)	3 (1-4)	0.02

OP125 PREEMPTIVE KIDNEY TRANSPLANTATION VERSUS NON-PREEMPTIVE KIDNEY TRANSPLANTATION IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Preemptive kidney transplantation (PKT) is performed before initiating dialysis to avoid dialysis-related morbidity and mortality. However, whether PKT is also associated with better clinical outcomes in children and adolescents compared to kidney transplantation after a period of dialysis (nPKT) is unclear as studies report mixed findings. This systematic review aimed to compare clinical outcomes of PKT versus nPKT in paediatric patients.
Methods: A bibliographic search was conducted on multiple databases. Studies that compared first or subsequent, living or deceased donor PKT versus nPKT in paediatric patients were included. Study selection, quality assessment and data extraction were carried out by two independent reviewers. The Downs and Black Checklist was used for assessing the methodological quality. Where possible, data were meta-analysed using the random-effects model. The I^2 statistic was calculated to assess heterogeneity. The review was registered with PROSPERO [CRD42014010565].
Results: Twenty-two studies met the inclusion criteria. Of the total 22 622 paediatric patients, 5583 (24.7%) received PKT and 8987 (39.7%) had a living donor transplant. The methodological quality scores ranged from 10 to 19 out of a maximum score of 28. The meta-analyses comparing PKT versus nPKT revealed that PKT patients had a significantly lower risk of overall graft loss (16 studies; RR 0.57; 95% confidence interval (CI) 0.49–0.66; I^2 = 51.2%) and acute rejection (7 studies; RR 0.81; CI 0.75–0.88; I^2 = 0%). Moreover, PKT patients with living donor transplants had a significantly lower risk of patient death (three studies; RR 0.53; CI 0.34–0.83; I^2 = 0%) and overall graft loss (five studies; RR 0.57; CI 0.46–0.69; I^2 = 0%). No differences were observed between PKT and nPKT in terms of overall patient death and the incidence of delayed graft function.
Conclusions: PKT in paediatric patients reduces the risk of graft loss and acute rejection compared to nPKT.

OP126 DOES EXTRAPERITONEAL APPROACH INCREASE THE RISK OF COMPLICATIONS AFTER KIDNEY TRANSPLANT IN LOW-WEIGTH CHILDREN? EXPERIENCE FROM A SINGLE INSTITUTION

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Background: The caliber of the vessels and the disproportion between the graft and the recipient are major challenges in kidney transplantation (KT) in low-weight patients (LW). For this reason, a transperitoneal approach is sometimes recommended. We hypothesized that the extra-peritoneal approach might be as successful as in normal patients.
Methods: Data of all consecutive KTs performed between 2013 and 2019 were reviewed. Early outcomes and surgical complications (such as bleeding, graft thrombosis, difficult wound closure) were compared between children weighing ≤15 kg (LW Group) and those weighing >15 kg (NW Group).
Results: All the 108 KTs were performed through an extraperitoneal approach. Thirty-one (mean age 3.5–1.4 years) weighted ≤15 kg (mean 11.1 ± 2.0 kg). In the other group mean age was 13.1 ± 4.2 years and mean weight was 36 ± 16 kg. Patients from LW Group experienced one case of primary graft non-function (PNGF) (3.2%), no cases of delayed graft function (DGF), nine surgical complications occurred (29%), with four venous thrombosis., whilst patients from NW Group encountered one case of PNGF (11.3%), eight cases of DGF (10), 11 complications (14%) with only one case of venous thrombosis. In both groups no need for patch during wound closure and no wound dehiscence were reported.
Conclusions: Our results demonstrated that the extraperitoneal approach can be used and be as effective in low-weight children to older patients. No differences were observed in the overall complication rate (P = 0.10), except for the occurrence of venous thrombosis (P = 0.02), that might be related to the characteristics of these patients.

OP128 PEDIATRIC LIVER TRANSPLANTATION WITH DCD GRAFTS: SINGLE CENTER EXPERIENCE

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Background: Liver grafts from DCD donors are increasingly accepted as extension of the organ pool for transplant. There is little data on the outcome of liver transplant with DCD grafts in children.
Methods: Liver transplants performed in recipients < 16 years were included. Patient and graft survival and complication rates were compared between DCD and DBD recipients.
Results: Between 2001 and 2018, 677 liver transplants were performed in children. Of these, 118 patients with a minimum follow-up of 24 months were selected: 44 DCD and 74 DBD. The median follow-up was 93 months for the DCD group and 103 months for DBD. The median DWIT of DCD grafts was 23 minutes. DCD recipients were more likely to receive whole grafts while DBD recipients were transplanted predominantly with LLS. The total CIT was lower for DCD, and DCD grafts had higher AST levels postoperatively while DBD had higher bilirubin. All other variables were comparable in the 2 groups. Patient survival rate was similar for recipients of DCD and DBD grafts at 6-months (93.1% DCD). At 5- and 10-years DCD outcomes were better than DBD (P 0.0016). Graft survival rate was 91% at 1-year in DCD, compared to 93% in DBD. At 10-years, graft survival was 89% in recipients of DCD and 85% in DBD (P 0.015). Graft loss occurred in 10% recipients of DCD grafts and in 13.5% recipients of DBD grafts. In DCD recipients 1 case of graft failure occurred within 3months due to HAT, another developed late HAT, 1 patient had cholangiopathy and the fourth had graft dysfunction. All 4 patients underwent retransplantation and are all still alive. In the DCD group, the DWIT exceeded 30 min in 4 patients and half of these lost their grafts. The rate of complications in the first year after transplantation was similar in the 2 groups. PNF did not occur in this series. Arterial thrombosis occurred in 4.5% of DCD grafts and 6.7% of DBD. DBD recipients had higher rate of PTLD and de novo AIH. The rate of retransplantation was lower in the DCD group (9.1% vs. 13.5%). 6.8% recipients of DCD grafts and 17.6% DBD recipients died.
Conclusion: DCD grafts transplanted in children showed excellent graft and patient outcomes with a low incidence of complications. Liver reduction with DCD grafts is feasible and associated with good long-term outcomes. Splitting should be considered if CIT for both grafts can be kept < 8 h.

REGENERATION FOR TRANSPLANTATION

OP209 IDENTIFICATION OF PREDICTIVE MARKERS FOR THE GENERATION OF WELL-DIFFERENTIATED IPSC-DERIVED KIDNEY ORGANOIDS

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Background: Human-induced pluripotent stem cell (iPSC) derived kidney organoids have the potential to advance studies to kidney development and disease. However, the differentiation from iPSC to kidney organoids is a complex procedure with unpredictable results. Off-target cell populations in kidney organoids cause variable outcomes of differentiation.
Method: We evaluated the differentiation of human iPSC from five different lines, three different donors, in four different experiment batches into kidney organoids. To associate the quality of kidney organoid differentiation with predictive molecular markers, a ranking system for organoids was developed based on the ratio between nephron structure area and stromal tissue area determined by histological examination. Well-differentiated organoids were defined as organoids with more than 30% nephron structure area and expressed high levels of glomerular and/or tubular markers. Subsequently, correlations were made with expression profiles of iPSC markers, early kidney development markers and stromal markers.
Results: A large variability in the percentage of nephron structures and the expression of kidney specific genes was observed between organoids, showing no association with iPSC lines or batches. High expression of the pluripotency marker SOX2 in kidney organoids and in undifferentiated iPSC was associated with poorly-differentiated kidney organoid. Furthermore, early secretion of FGF2 predicted poorly-differentiated kidney organoid. Interestingly, while cadherin-1 (CDH1) expression in kidney organoids indicates distal tubular cell formation, high CDH1 expression in iPSC predicted poor kidney organoid development. High expression of the nephron progenitor marker FOXD1 and significantly increased TGFβ levels were found in well-differentiated kidney organoids.
Conclusion: This study demonstrates that early expression profiles predict the outcome of kidney organoid formation. This finding contributes to a better understanding of kidney organoid formation and helps to improve the robustness of kidney organoid protocols and thereby their use for research on kidney disease and repair.

OP210 PRE-VASCULARIZED ORGANOID GENERATED FROM DECELLULARIZED HUMAN PLACENTA SUPPORT PANCREATIC TISSUES IN TYPE-1 DIABETES TREATMENT

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Background: Replacing damaged organs with biological substitutes capable of protecting the islets and facilitating vascularization is a great objective in the field of islet transplantation. A decellularized placenta includes a large number of cotyledons with a conserved vessel structure of the native organ. Our goal is to obtain a perfect decellularization protocol to generate pre-vascularized organoids by recellularizing this ECM with HUVECs and pancreatic islets.
Methods: After blood removal, cotyledons were dissected from the placentas and decellularized using a bioreactor. Cell removal was assessed by histology and quantification of residual DNA. Presence of structural proteins and ECM structure were analyzed using SEM, CT scan and mass spectrometry. Recellularization protocols were conducted, with HUVECs or BOECs as endothelial cell sources, and with Ins-1E cells or rat islets as insulin secreting cell sources. Function of recellularized cotyledons was assessed in vitro with glucose stimulated insulin secretion tests (GSIS). To assess in vivo biocompatibility and function of the scaffolds, we transplanted in diabetic NSG mice. Glycaemia was measured every day to monitor normalization of blood glucose levels.
Results: Our protocol led to successful decellularization, as evidenced by the absence of cells and the preserved ECM structure. Moreover, DNA quantification did not reveal any residual DNA. Quantification of GAG and hydroxyproline, and mass spectrometry analysis show that structural proteins are conserved. SEM and CT scan images revealed that the ECM structure was preserved after the decellularization protocol. Cells after recellularization showed a good vascularization after 7 days. The GSIS test shows a perfect organ response in the production of insulin.
Conclusions: The decellularized cotyledon is the perfect scaffold to reproduce a prevascularized insulin-producing organ, which allows transplanted cells to survive during the peri-transplantation period.

OP211 PORTAL VENOUS REPOPULATION OF DECELLULARISED RAT LIVER SCAFFOLDS WITH SYNGENEIC BONE MARROW STEM CELLS

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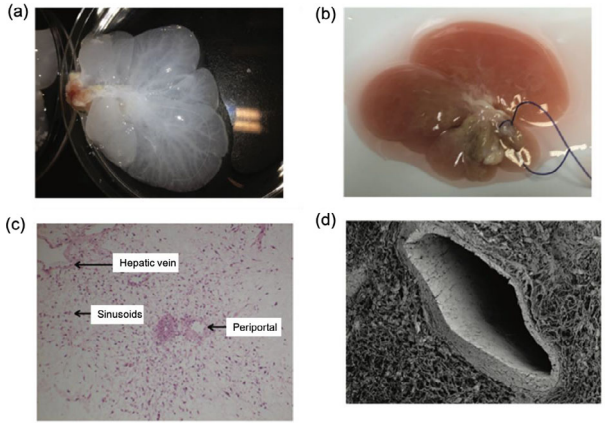
Background: Liver transplantation is the only life-saving treatment for end-stage liver failure but is limited by the organ shortage and consequences of immunosuppression. Repopulation of decellularised scaffolds with recipient cells provides a theoretical solution, allowing reliable and timely organ sourcing without immunosuppression. Recellularisation of the vasculature of decellularised liver scaffolds was investigated as an essential prerequisite to the survival of other parenchymal components.
Methods: Liver decellularisation was carried out by portal vein (PV) perfusion using a detergent-based solution within an organ chamber at 37°C. Scaffolds were perfused via the PV with culture medium and infused with 10^7 primary bone marrow (BM) stem cells selected by plastic adherence. BM stem cells were assessed for key marker expression using fluorescence-activated cell sorting (FACS), and recellularised scaffolds analysed by light (LM), electron (EM) and immunofluorescence (IF) microscopy.
Results: Recellularised scaffolds changed in macroscopic appearance from a translucent (a) to an opaque (b) structure by day 30. Stem cells engrafted in portal, sinusoidal and hepatic vein compartments on LM (c) with cell alignment reminiscent of endothelium on EM (d). Engrafted cells expressed sinusoidal endothelial endocytic receptors (mannose, Fc and stabilin); and cell surface marker expression altered following engraftment from a haematopoietic ($CD31^-$ $CD45^+$) to an endothelial phenotype ($CD31^+$ $CD45^-$) on FACS and IF.
Conclusions: To our knowledge this is the first report of BM stem cells used to repopulate decellularised liver vasculature. This approach is potentially clinically relevant as the cells are recipient specific, sourceable in relevant numbers, and not subject to oncogenic concerns that relate to cell lines or induced pluripotent stem cells. These results represent one step towards complete recellularisation of liver vasculature and progress in generation of transplantable neo-organs.



OP212 THE MATRIX RELOADED: USING INTRAHEPATIC CHOLANGIOCYTE ORGANOIDS AND DECELLULARIZED HUMAN LIVER EXTRACELLULAR MATRIX TO CREATE FUNCTIONAL LIVER TISSUE

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Background: Liver transplantation is the only durable treatment for end-stage liver disease, but shortage of donor organs remains a limiting factor. Tissue engineered liver constructs could aid in decreasing donor shortage. A particularly promising approach is to repopulate decellularized human liver extracellular matrix (ECM) with patient-derived hepatobiliary stem cells. Intrahepatic cholangiocyte organoids (ICO) are an interesting cell source, as they can differentiate towards hepatocytes and cholangiocytes. Our aim is to determine the repopulation potential of ICO in decellularized liver ECM.
Methods: Human livers deemed unsuitable for transplantation (N = 3) were decellularized using a standardized protocol by pressure-controlled machine perfusion with 4% Triton-X-100 + 1% ammonia. No cells were found in the remaining extracellular matrix (ECM). Circular sections (Ø8 mm, thickness: 200 μm) were cut. ICO were initiated from healthy liver biopsies (N = 8) and expanded. The organoids were dissociated and added to the ECM sections as single cell suspension ($25{\cdot}10^4$ cells/section). The constructs were cultured in expansion medium or in hepatocyte differentiation medium. Cultures were terminated after 21 days and analyzed.
Results: ICO (N = 4) efficiently repopulated the liver ECM sections. It took 4–7 days for the cells to grow confluent layers on top of the ECM. During the following days, the cells self-organized into columnar shaped cells as shown by histological analysis. KRT-7 (cholangiocyte) and albumin (hepatocyte) markers increased 4-fold (SD: ±7) and 17-fold (SD: ±26) respectively compared to controls. Albumin expression increased 35-fold (SD: ±36) and LGR5 (stem cell marker) decreased 8-fold (SD: ±4) after differentiation. Albumin and KRT-7 were also detectable with immunofluorescence.
Conclusion: ICO are capable of repopulating decellularized human liver ECM segments *in vitro*. The ECM appears to drive self-differentiation of the ICO towards cholangiocytes and hepatocytes as marker increase when cultured in expansion or hepatocyte differentiation medium. These results encourage upscaling towards larger-scale perfusion based recellularization experiments where patient-derived ICO can be used to engineer functional and clinically relevant hepatic tissue *in vitro*.

OP213 PERFUSION-DECELLULARIZATION OF VASCULARIZED BONE MATRIX: APPLICATION TO THE PORCINE FORELIMB

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Background: Large bone defects still remain a challenge for the surgeon, and available reimplanted bone substitutes can't properly restore optimal function along with long term osteointegration and full survival of the bone graft. We present in this study a new animal model of bone substitute based on the perfusion-decellularization technique, applied on vascularized porcine bone shafts xenografts.
Methods: 11 porcine bone forelimbs including the radius and the ulna were harvested with their vasculature based on an interosseous artery and perfusion-decellularized. Characterization of the obtained matrices was performed through histological analyses, DNA and ECM proteins dosages, density acquisitions and biomechanical testing. The quality and preservation of the vasculature was assessed through barium-sulfate injected CBCT acquisitions. The potential for in vivo reimplantation was assessed through fibroblast static cell seeding, adipose mesenchymal stem (AMS) cells seeding and evaluated with classic histological staining and immunohistochemistry.
Results: Decellularization was successful for all grafts with excellent preservation of the ECM and global structure. DNA and ECM proteins measurements revealed optimal clearing of the cellular compartment and preservation of major proteins. Density acquisitions revealed a slight decrease of density whereas biomechanical testing was unmodified. The vasculature was entirely preserved throughout the whole graft and all seeded cells were viable in all samples, with the initiating of new bone formation and osteogenic differentiation of AMS-cells.
Conclusions: Fully vascularized decellularized and transplantable bone shafts xenografts were obtained with true potential for in-vivo reimplantation. Thereby, they may offer in a close future new perspective for large bone defects repair, and in global bone tissue engineering.

OP214 ANTI-FIBROTIC EFFECTS OF MEMBRANE PARTICLES FROM MESENCHYMAL STROMAL CELLS IN A RENAL ISCHEMIA REPERFUSION INJURY MOUSE MODEL

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Background: Membrane particles (MP) are nanovesicles artificially generated by extrusion of the Mesenchymal Stromal Cell (MSC) membranes. MP were designed to circumvent the risks of MSC therapy such as a poor biodistribution due to their large size and unknown behaviour after infusion, while keeping the reparative properties of MSC. We demonstrated earlier that MP have endothelial regenerative capacity, and antifibrotic effect on lung fibroblasts. In this study, the aim is to explore whether MP have antifibrotic effect on a renal ischemia reperfusion injury (IRI) mouse model.
Methods: IRI was performed by clamping the right kidney of the mice for 37 min. The MP were intravenously infused 3–5 h after ischemia. The kidneys were harvested 3 days after renal IRI. Four groups of mice were analysed: Sham, IRI, IRI + MP derived from 1 million of MSC, and IRI + MP derived from half million of MSC. Gene expression of proinflammatory cytokines was measured in the kidneys such as IL6, and TNFα; and kidney injury marker KIM-1; and profibrotic molecules such as TGFβ, PAI-1, fibronectin, collagen I, and III. Sirius red for collagen staining was performed to evaluate fibrosis in the histological analysis of the kidneys.
Results: We found no difference between IRI mice treated with MP and IRI untreated mice with respect to the proinflammatory markers. IRI induced an upregulation of the mRNA expression of profibrotic genes such as TGFβ and PAI-1, and proteins from the extracellular matrix, including fibronectin, collagen I, and III. Interestingly, the higher doses of MP significantly decreased the expression of TGFβ, PAI-1 and the main extracellular matrix proteins involved in fibrogenesis. The percentage of fibrosis area in the histological analysis of the kidneys were in line with the results observed in the gene expression of profibrotic markers.
Conclusions: Our findings show that MP have early antifibrotic effects on renal IRI. Future research will address questions including mechanisms of action and anti-fibrotic effects in long term with the goal of using MP as a new approach to combat renal fibrosis.

BIOMARKERS: WHAT'S CIRCULATING?

OP215 IMPACT OF DELAYED GRAFT FUNCTION ON BASELINE DONOR DERIVED CELL-FREE DNA (DD-CFDNA) IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Donor derived-cell free DNA (dd-cfDNA) is a serum biomarker now available to predict acute rejection in renal allografts. The technology utilizes targeted next generation sequencing and does not require donor genotyping. A level ≥1% suggests allograft injury usually from acute rejection. Delayed graft function (DGF) can be associated with ongoing allograft inflammation. We aimed to evaluate the impact of DGF on baseline dd-cfDNA levels in kidney transplant recipients (KTRs).
Methods: Our center has been checking dd-cfDNA levels (AlloSure, CareDx, Brisbane, CA) as for-cause and surveillance in high immunological risk KTRs since 2018. We identified patients who underwent deceased donor kidney transplantation at our center between April 2018 and June 2020 who

had dd-cfDNA measured between 4 and 12 weeks post-transplant. A dd-cfDNA value ≥1.0% prompted allograft biopsy. Patients with biopsy evidence of rejection were excluded from the analysis since the aim was to compare baseline values. Patients were divided into 2 groups based on the presence or absence of DGF (defined as need for dialysis during the first post-transplant week). The 4–12 week average and week 8 dd-cfDNA values were compared between the DGF and no- DGF groups using t-test.
Results: There were 80 deceased donor KTRs included in the analysis (DGF, $n = 23$; no-DGF = 57) with 189 dd-cfDNAA levels including 56 in DGF and 123 in no-DGF groups. Average 4–12 week baseline dd-cfDNA levels were similar between DGF and no-DGF groups (0.39 ± 0.21 vs. 0.49 ± 0.44, $P = 0.17$). Similarly, there was no significant difference of 8-week baseline dd-cfDNA levels between DGF and no-DGF groups (0.30 ± 0.18 vs. 0.43 ± 0.45, $P = 0.07$).
Conclusions: Despite the possibility of higher levels of ongoing intra-graft inflammation associated with DGF in KTRs, we did not observe higher baseline dd-cfDNA levels in these patients compared to KTRs who did not experience DGF. Our findings indicate that the development of DGF following kidney transplantation does not adversely impact the reliability of dd-cfDNA as a biomarker in predicting allograft rejection.

OP216 COMPARING METHODS FOR DONOR-DERIVED CELL-FREE DNA QUANTIFICATION IN PLASMA AND URINE FROM KIDNEY AND LIVER TRANSPLANT RECIPIENTS

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Background: In the area of solid organ transplantation, there is an unmet need for diagnostic methods providing improved performance for allograft monitoring and being less costly and invasive than tissue biopsies. Liquid biopsy has emerged as a novel approach using quantification of cell-free DNA (cfDNA) originating from the allograft (donor-derived, dd-cfDNA).
Methods: Different approaches were compared for the quantification of dd-cfDNA in urine and plasma of kidney and liver allograft recipients: (A) Droplet digital PCR (ddPCR) using allele-specific detection of seven common HLA-DRB1 alleles and the Y chromosome; (B) high-throughput sequencing (HTS) using a custom QIAseq DNA panel targeting 117 common polymorphisms; and (C) a commercially available kit (AlloSeq® cfDNA, CareDx). Dd-cfDNA was quantified as fractional abundance (FA), and for ddPCR and HTS also as donor copies, utilizing Unique Molecular Identifiers (UMIs).
Results: A total of 99 urine and plasma samples from kidney and liver recipients showed a strong linear correlation between ddPCR and HTS for the FA of dd-cfDNA ($r = 0.97$), donor copies/ml ($r = 0.97$) and total copies/ml ($r = 0.73$). In a subset of 20 kidney and liver plasma samples, dd-cfDNA FA also showed a strong correlation of ddPCR ($r = 0.95$) and HTS ($r = 0.99$) with AlloSeq® cfDNA. All correlations had an intercept of −0.13 to 0.15 (total copies/ml: 22.95) and a slope of 0.96 to 1.13.
Conclusions: This first direct comparison of different dd-cfDNA quantification methods yielded comparable results with no indication of systematic bias. Additionally, the strong correlation with ddPCR based measurements indicates the suitability of the presented custom HTS method for absolute dd-cfDNA quantification (copies/ml). These findings suggest that the definition of method-independent diagnostic cutoffs may be feasible in the further evaluation of dd-cfDNA for minimally invasive graft monitoring.

OP217 PITFALLS IN THE DETECTION OF DONOR-DERIVED CELL-FREE DNA IN TRANSPLANT RECIPIENTS

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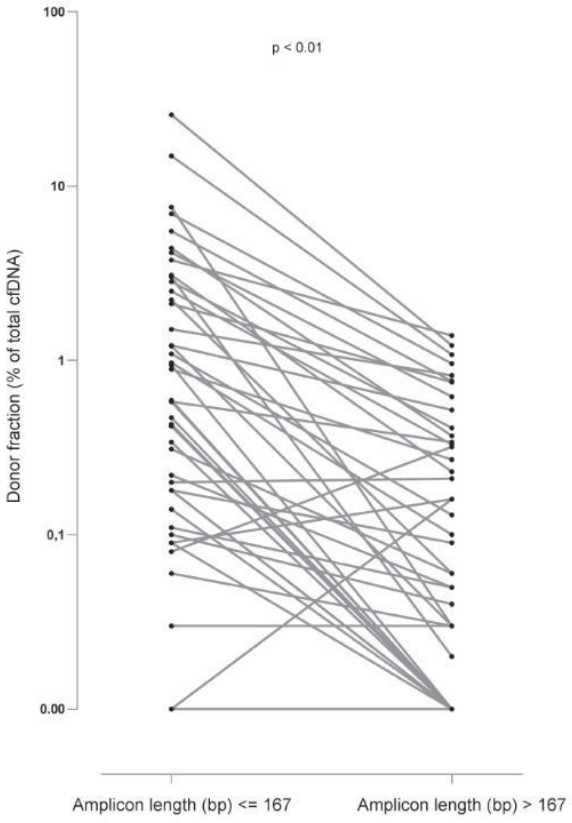
[1]Erasmus Medical Center, Internal Medicine, Nephrology and Transplantation, Rotterdam, Netherlands, [2]Erasmus Medical Center, Erasmus MC Transplant Institute, Rotterdam, Netherlands, [1]Erasmus Medical Center, Internal Medicine, Nephrology and Transplantation, Rotterdam, Netherlands

Introduction: Donor-derived cell-free DNA (ddcfDNA) are small fragments (<167 basepairs (bp)) in the circulation of transplant recipients and is proposed as potential biomarker to detect allograft rejection. Genetic differences between donor and recipient allows quantification of ddcfDNA using PCR-based methods targeting insertion/deletion polymorphisms (InDels). Pitfalls of these detection methods that need to be considered are (1) PCR efficiency differences due to different amplicon lengths and (2) correction for either heterozygous (in theory 50% of genomic fraction) or homozygous (in theory 100% of genomic fraction) donor genotype.
Material and methods: cfDNA was isolated from 162 kidney transplant recipients plasma samples (day 3 after transplantation). ddcfDNA was quantified by targeting one or two donor-specific InDels with assays ranging from 56 to 225 bp in length. Total cfDNA was quantified by Ribonuclease P. ddcfDNA was expressed as fraction (%) of total cfDNA. Hetero- or homozygous genotype was determined on genomic donor DNA with the same donor-specific (InDels) as for ddcfDNA quantification. Quantification was performed by a droplet digital PCR (ddPCR).
Results: In cfDNA samples, an inverse correlation was observed between ddcfDNA and amplicon length ($r = -0.22$, $P < 0.01$). Pairwise comparison of ddcfDNA in 46 patients of which ddcfDNA was determined using both short (≤167 bp) and large (>167 bp) amplicons showed that median (IQR) donor fraction was 0.54% (0.18–2.30) for short amplicons and decreased to 0.05% (0.00–0.32) for large amplicons ($P < 0.01$) (Figure 1). Genomic InDel fraction for hetero- and homozygous genotype ranged from 9.1%–68.2% and 79.8%–147.2%, respectively.
Conclusions: Quantification of ddcfDNA is less efficient using InDels with large amplicons (>167 bp) and thus the use of short (≤167 bp) InDel amplicon assays is necessary for accurate quantification of ddcfDNA. The genomic InDel fraction was neither 50% nor 100% indicating that correction for hetero/homozygous genetic variants with a factor 2 is undesirable as it may introduce extra variety in the results.

Figure 1



OP218 CIRCULATING ENDOTHELIAL CELL LEVELS TRANSIENTLY INCREASE IN PERIPHERAL BLOOD AFTER KIDNEY TRANSPLANTATION

Hector Tejeda Mora, Jeroen Verhoeven, Wenda Verschoor, Karin Boer, Dennis Hesselink, Martijn van den Hoogen, Luc van der Laan, Carla Baan, Robert Minnee, Martin Hoogduijn
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Background: The diagnosis of kidney transplant rejection is based on late biochemical markers and invasive histological and clinical markers. Early, specific and minimally-invasive biomarkers may improve rejection diagnosis. Endothelial cells (EC) are one of the earliest targets in kidney transplant rejection and may be released into circulation upon injury. We investigated whether circulating EC (cEC) could serve as an earlier and less invasive biomarker for allograft rejection.
Methods: In the present study, blood was collected from a cohort of 51 kidney transplant recipients before and at multiple timepoints after transplantation (day-3, day-7, month-6), including the morning of a for cause biopsy. The number and phenotype of cEC was assessed by flow-cytometric analysis, by staining for CD31, CD34, CD45, CD105, CD133, CD146 and kidney injury molecule (KIM-1). Unbiased selection of EC was done using a non-linear generalization of principal component analysis (PCA) and unsupervised clustering for unbiased selection of cEC.
Results: Paired analysis revealed a transient cEC increase of 2.1-fold on the third day post-transplantation, recovering to preoperative levels at seventh day post-transplant and onwards ($P < 0.001$). Analysis of HLA subtype demonstrated that cEC mainly originate from the recipient (0.9–18.9% of donor derived cEC). cEC levels and expression of the progenitor marker (CD133) were related to recipient age ($P < 0.05$), but not with allograft rejection, allograft function or other allograft pathologies. However, cEC in patients with allograft rejection and increased levels of cEC showed elevated levels of KIM-1.
Conclusions: These findings indicate that both the donor and recipient endothelium are affected during early stages of transplantation and cEC levels in transplant patients show a strong association with recipient age. Contrary to other reported vascular damage pathologies, injury derived from acute rejection episodes did not influence cEC levels. cEC numbers may not improve rejection diagnosis.

OP219 PERIPHERAL BLOOD TRANSCRIPTOMICS DEMONSTRATE GREAT POTENTIAL IN UNRAVELING PATHOPHYSIOLOGICAL PATHWAYS OF KIDNEY ALLOGRAFT PATHOLOGY

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Background: Molecular changes in kidney allografts during inflammatory pathology can be reflected by changes in circulating immune cells. Peripheral blood signals could aid in non-invasively unraveling the underlying pathways, to improve our pathophysiological knowledge of these diseases, facilitate their diagnosis, and identify new targets for therapy.
Methods: We performed RNA-sequencing on 384 peripheral blood samples, paired with a concomitant kidney allograft biopsy, selected for their histopathological phenotype from biobanked samples from four centers. We performed differential expression and pathway analysis per phenotype and the abundance of involved cell types was quantified by xCell. Finally, we integrated our results with publicly available micro-array data from 224 kidney allograft biopsies.
Results: Differentially expressed genes (DEG) in any rejection vs. no rejection (N = 72, FDR *P*-value < 0.05) demonstrated upregulation of glucocorticoid receptor signaling and NOD-like receptor signaling. The upregulated pathways identified for histology of antibody-mediated rejection were strongly immune-specific, in contrast to less specific pathways for T cell-mediated rejection. DEG in polyomavirus viremia and nephropathy were comparable and demonstrated upregulation of mitochondrial dysfunction and interferon signaling. Presence of donor-specific antibodies was accompanied by activation of the calcineurin/NFAT-pathway. Upon integration of biopsy and blood transcriptomic data, DEG in rejection phenotypes were highly consistent across both tissues and transcriptomic platforms, further strengthening our findings. Cell enrichment analysis demonstrated only minor differences in cell type enrichment scores between rejection phenotypes in the blood, despite major differences in cell enrichment scores between rejection phenotypes in the biopsy transcriptomic data.
Conclusions: The biologically plausible immune-specific pathways uncovered in this study demonstrate that peripheral blood signals mirror molecular changes in the graft, thereby non-invasively providing novel pathophysiological insights.

OP220 DIFFERENTIALLY EXPRESSED TISSUE MICRORNAS DISTINGUISH SPECIFIC DISEASE PHENOTYPES FOLLOWING KIDNEY TRANSPLANTATION

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Background and Aims: Recently, many microRNAs (miRNAs), small non-coding regulatory RNAs, have been found to be involved in pathological processes after kidney transplantation. In recent years, the focus has been on circulating miRNAs, and data on miRNA expression in tissues are sparse. The aim of the current study was to investigate the association between selected miRNAs in kidney transplant biopsy specimens and pathological phenotypes after transplantation.
Methods: Forty-five kidney transplant recipients with performed kidney graft biopsy were divided into 4 groups: (i) control group, CTRL ($n = 12$), patients who had a surveillance biopsy showing minor nonspecific changes; (ii) nonspecific group, NS ($n = 6$), who had an indication graft biopsy showing only nonspecific chronic changes; (iii) antibody-mediated rejection group, AMR ($n = 12$), patients with histologically proven AMR and (iv) recurrent glomerulonephritis group, rGN ($n = 15$), patients with histologically proven rGN. The expression of 6 selected miRNAs (miR-29c, miR-126, miR-146a, miR-150, miR-155, miR-223) in kidney transplant biopsy specimens was determined by qPCR using let-7a, miR-16, miR-103a-3p and miR-191 as reference genes and compared with the respective disease phenotype.
Results: Selected candidate miRNAs miR-29c ($P = 0.044$), miR-150 (P 0.001) and miR-155 (P 0.001) distinguished AMR and rGN from the other patient groups. MiR-29c and miR-150 also differentiated between AMR and rGN ($P = 0.005$ and $P = 0.001$, respectively). In addition, all but miR-146a distinguished ABMR from the control group (Figure 1).
Conclusion: Our results show that expression profiles of selected miRNAs in kidney transplant biopsy specimens can distinguish AMR and rGN compared to the control group and patients with non-specific changes. MiR-29c and miR-150 may also be useful for distinguishing AMR and rGN. Tissue expression of selected miRNAs could be used as an additional diagnostic biomarker of kidney transplant injury phenotype.

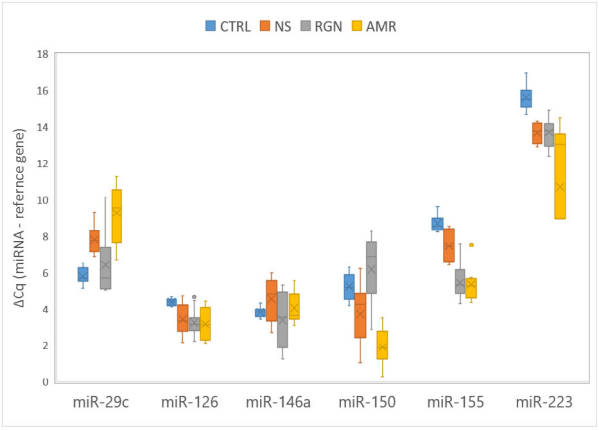

Figure 1. Box plots for differential expression of selected microRNAs (miRNAs) in kidney transplant biopsy specimens in the control group (CTRL), nonspecific patient group (NS), antibody-mediated rejection (AMR), and recurrent glomerulonephritis (rGN) group.

AVAILABLE TECHNOLOGIES IN KIDNEY TRANSPLANTATION: MAKE GOOD USE OF IT, IF YOU WANT TO WIN THE RACE

OP221 ROBOT-ASSISTED SURGERY AS A MINIMALLY INVASIVE APPROACH FOR KIDNEY TRANSPLANTATION RECIPIENTS: A SYSTEMATIC REVIEW AND META-ANALYSES

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Background and Aims: Kidney transplantation is the preferred treatment for patients with end-stage renal disease (ESRD). Over the decades, little

has changed regarding the technique, as open kidney transplantation (OKT) remains the gold standard. Recently, robot-assisted kidney transplantation (RAKT) has emerged as an interesting alternative, possibly adding the benefits of minimally invasive surgery for kidney transplant recipients. The aim of this systematic review and meta-analysis is to give an overview of the current literature and to compare the clinical outcomes of RAKT with OKT.
Methods: The MEDLINE, Embase, Web of Science and Cochrane databases were systematically searched. Baseline characteristics, intraoperative and postoperative outcomes were collected, as well as long-term renal function and data on graft and patient survival.
Results: Fifteen studies were included for the qualitative analysis and nine studies were included for the quantitative analysis. Overall, RAKT leads to a decreased risk of surgical site infection (Risk ratio (RR) = 0.12, $P = 0.007$) and a decreased risk of developing a symptomatic lymphocele (RR = 0.17, $P = 0.04$), less postoperative pain (Mean difference (MD) = −1.3 points, $P < 0.001$) smaller incision length (MD = −9.13 cm, $P < 0.001$) and shorter hospital stay (MD = −1.61 days, $P = 0.04$) when compared to OKT. No difference was found in renal function, graft, and patient survival.
Conclusions: Current evidence shows that RAKT is a safe and feasible alternative to conventional OKT with the benefits of minimally invasive surgery and without compromising the long-term renal function and graft and patient survival.

OP222 ROBOTIC VS. LAPAROSCOPIC DONOR NEPHRECTOMY: A RETROSPECTIVE BI-CENTRIC COMPARISON OF SURGICAL OUTCOMES FROM TWO HIGH VOLUME CENTERS

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Background: Minimally invasive surgery represents the gold standard for living-donor kidney procurement. Several studies focused on robot-assisted (RDN) and laparoscopic donor nephrectomy (LDN), in order to assess their safety, feasibility and outcomes. We sought to compare the results of LDN and RDN performed in two high-volume transplant centers, focusing on patient selection, learning curves and postoperative outcomes.
Methods: The study enrolled all minimally invasive nephrectomies consecutively performed by two senior surgeons since the beginning of their experience with LDN and RDN. We retrospectively compared donor characteristics and intra- and postoperative outcomes for each technique.
Results: A total of 328 (114 RDN and 214 LDN) procurement were performed from 2010 to 2017: we depicted higher frequency of right nephrectomies in LDN (21.5 vs. 12.3%; $P = 0.04$), while RDN showed higher prevalence of arterial variations (36.8 vs. 18.8%; $P < 0.001$). No open conversions were reported; operative time did not significantly differ between RDN and LDN (220 vs. 214 minutes; $P = 0.11$), though intraoperative blood loss (11.4% vs. 0.0% >100ml; $P < 0.001$), and warm ischemia time (220 vs. 165 sec; $P < 0.001$) were significantly higher in RDN. Comparison of the first 114 cases for both techniques documented higher decrease in operative time (OT) in RDN group ($P = 0.0002$), expressing a faster learning curve. Looking for determinants for longer surgeries, we identified higher BMI as a risk factor for longer OT in both RDN and LDN; multiple arteries significantly prolonged OT in LDN, while did not affect RDN; both procedures were equally shortened by growing surgical volume. Postoperative complications did not significantly differ between RDN and LDN (10.5% vs. 11.2%; $P = 1.00$), and RDN resulted in shorter hospital stay (4 vs. 5 days; $P < 0.001$).
Conclusions: This is the largest European comparative study between RDN and LDN that has been reported so far. Despite our results could be influenced by selection, indication and management biases due to bicentric enrollment, RDN seems to improve multiple vessels handling, determining a faster learning curve and shorter hospital stay despite higher intraoperative blood loss; considering the low incidence of postoperative complications both techniques should be considered as equally safe.

OP223 INDICATIONS FOR AND TECHNIQUES OF NATIVE NEPHRECTOMY IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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Background: We review the clinical indications, timing and surgical techniques for native nephrectomy (NN), together with the associated pathological findings in transplant patients with autosomal dominant polycystic kidney disease (ADPKD) at our institute over a period of 20 years.
Methods: A retrospective review of patients with ADPKD who had both kidney transplantation and NN was performed. NN was performed via a midline or rooftop open incision or hand assisted laparoscopic nephrectomy with an 8 to 10cm infra-umbilical incision.
Results: 348 kidney transplants were performed for ADPKD from 1998 to 2018; 184 (52.9%) were male and 89 (55%) were deceased donor transplants. NN was performed on 93 (26%) patients of whom 51 (54%) were male. Mean age at time of NN was 49 ± 9 yrs; significantly younger than age at transplantation 52 ± 12 ($P = 0.043$). Unilateral NN was performed in 37 (39%) patients of whom 11 (30%) went on to have a staged contralateral NN. NN timing was pretransplant ($n = 47$, 50.5%), simultaneous ($n = 3$, 3.3%) and post-transplant ($n = 43$, 46.3%). Indication for NN was pain ($n = 36$, 38.7%), infections ($n = 33$, 35.4%), haematuria ($n = 11$, 11.8%), space ($n = 4$, 4.3%) and tumour suspicion ($n = 3$, 3.3%). Histology revealed renal cell carcinoma in 6 specimens from 4 (4.3%) patients and benign tumours in 11 specimens. Benign findings were from smaller (22.4 ± 5 cm) kidneys compared to malignant (24.2 ± 4 cm); however, this was not significant ($P = 0.28$). NNs were performed via open surgery in 44 (47.3%) and laparoscopic-assisted in 49 (52.7%) patient. The length of hospital stay post-NN was significantly longer with open compared with laparoscopic techniques (12 ± 6 v 5 ± 5 days; $P = 0.003$). NN did not influence patient survival or graft survival when compared to non-NN ADPKD patients ($P = 0.17$ and $P = 0.54$ respectively)
Conclusions: In our experience, 26% of ADPKD patients required NN that was approximately equally performed pre and posttransplant. There has been a shift from bilateral to unilateral NN in ADPKD. Hand-assisted laparoscopic NN is feasible and safe in these large kidneys with decreased morbidity and shorter length of hospital stay than open surgery.

OP224 A LARGE SERIES OF LAPAROSCOPIC NEPHRECTOMIES FOR POLYCYSTIC KIDNEYS PRE, POST AND SIMULTANEOUS WITH KIDNEY TRANSPLANTATION: ANALYSIS OF OUTCOME.

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Background: Native nephrectomy (NN) is often necessary in patients presenting with Autosomal Dominant Polycystic Disease (ADPKD). Need for gaining space in case of future transplant is among the most common reason for NN but need for post-transplantation NN is also reported due to the occurrence of complications in native polycystic kidneys after transplant. The ideal timing of NN in relation to transplant is controversial and no consensus exists on performing the intervention prior to, during or after kidney transplantation (KT). The laparotomic open approach has been considered for many years as the safest surgical approach despite being an extensive surgical operation with significant tissue manipulation and morbidity. The laparoscopic native nephrectomy (LNN) has been showing optimal results worldwide by decreasing morbidity rate.
Methods: In this study we report a Single-Centre experience with LNNs in patients with ADPKD. Feasibility and benefits of the laparoscopic approach were evaluated and a comparison with the traditional open surgery was carried out. Data related to 52 patients who underwent LNN, both unilateral and bilateral, between February 2018 and September 2020 were retrospectively reviewed. Results were compared with those of 32 patients who underwent open NN between October 2015 and April 2020.
Results: Thirty-nine nephrectomies were performed pre-KT, 11 post-KT and 2 simultaneous with KT. Operative time was longer for LNN, both in unilateral (230 ± 53.7 vs. 178.3 ± 97 min, *P value* < 0.01) and bilateral cases (367 ± 78.5 vs. 180.9 ± 54.5 min, *P value* < 0.001). No difference was observed in kidney's size between the two groups (*P value* 0.49). The laparoscopic technique provided a shorter hospital stay (median length of stay was 6 days, ranging from 3 to 19 days vs. 7 days in the open cohort, ranging from 5 to 14 days, *P value* < 0.01), as well as less surgical complications such as incisional hernias, compared with the open technique (1.9% vs. 15.6%, *P value 0.003*), independently from the timing related to KT.

Conclusions: LNN is a safe and feasible alternative to open NN, regardless of kidney's size. This technique provides all the benefits of minimally invasive surgery, offering less surgical trauma as well as better esthetical outcome and it can be safely performed pre or post KT.

OP225 ROBOT ASSISTED KIDNEY TRANSPLANTATION: A SAFE APPROACH FOR COMPLEX LIVING TRANSPLANT SITUATIONS.

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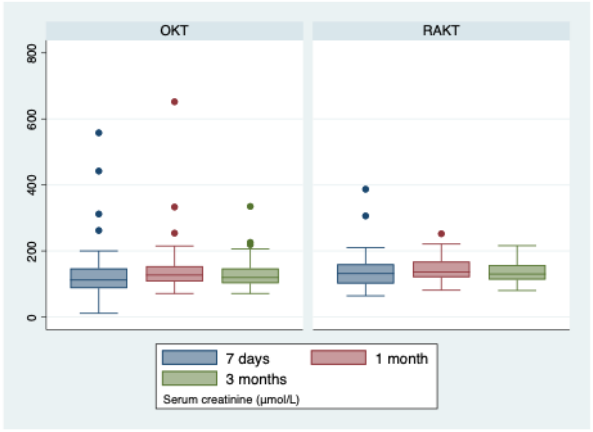
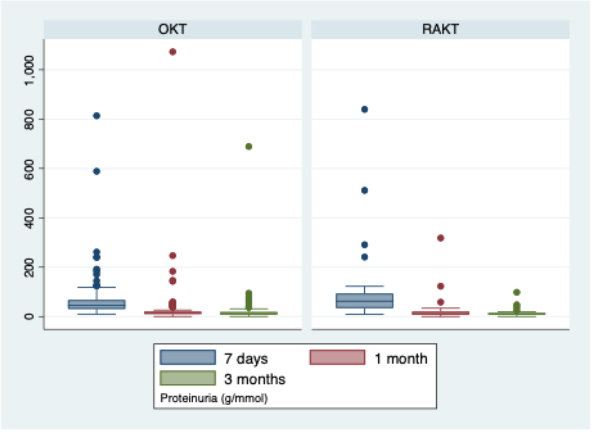
Background: Robot-assisted Kidney Transplantation (RAKT) offers advantages in comparison with open approaches (OKT) in terms of infection reduction and recovery, and is even superior in intricate situations like complex vascular anatomy. Also, the development of lymphocele and wound healing disorders appear to decrease. The aim of this study is to compare a single-centre cohort of living kidney transplants of OKT versus RAKT, in terms of surgical parameters, as well as specific allograft outcomes.
Methods: This is a single-centre retrospective study were all living transplant are included from 2015, with OKT (n = 111) and RAKT (n = 34) recipients. A comparative recipient analysis was performed, without differences in baseline characteristics. All surgical, clinical, analytical and histological data was collected.
Results: Baseline variables are described in Table, with no significant differences except for cold ischemia time. No significant differences were obtained in graft function in OKT vs RAKT based on creatinine at 7 days (124 μmol/l (CI 111–137.5) vs 140 (117.8–163)), 1 m (138 μmol/l (CI 125.9–151.2) vs. 148 (135.3–160.7)) and 3 months (128 μmol/l (CI 120.5-135.9) vs 135 (123.4–147.5)) and proteinuria (Figure). Right kidney was regularly considered in RAKT conferring a significant difference to OKT. In RAKT group, complications were artery thrombosis (n = 1), paralytic ileum (n = 1), anterior abdominal wall bleeding (n = 1) and pre-bladder hemorrhage (n = 1). Complex vascular anatomy was present in 17.7% of RAKT cases (n = 5 double artery, n = 1 double vein systems).
Conclusions: RAKT is not inferior to the open approach in terms of immediate and mid-term graft survival, with limited complications. An optimal kidney selection is allowed in RAKT considering the potential use of the right kidney, as well as almost 20% of vascular complex allografts availability, representing a favorable technique to overcome significant limitations in living transplantation.

Table

Characteristics	OKT (n=106)	RAKT (n=34)	significance (p<0.05)
Donor (man, y)	35.29%, 51.48	33.96%, 54.84	no
Recipient (man, y)	79.59%, 49.3	73.63%, 51.41	no
Donor hypertension	14.15%	8.82%	no
Recipient hypertension	89.62%	88.24%	no
Donor diabetes	0%	0%	no
Recipient diabetes	12.26%	5.88%	no
Donor body mass index (mean, sd)	1.76 (.0173604 .1787361)	1.802344 .0301422 .1757574	no
Recipient body surface area	1.817 (.019 -.198)	1.85 (.036-.21)	no
HLA missmatch	1.85(.0361-.21)	4.2 (.337-1.96)	no
pre-transplant cPRA (%)	14 (8.51-19.48)	14.65 (4.93-24.36)	no
Kidney donor laterality (% Right)	23.08	41.18	yes
Induction treatment (w/o ind/BSX/rATG)	3.85% /79.81%/ 16.35%	8.82 %/ 67.65 % 23.53%	no
Donor SCr pretransplant (median/min/max/iqr)	66/ 45/ 100 /17	66.5/45/107/ 24	no
Cold ischemia time (mean/ CI 95%)	58.23 (52.4 - 64.02)	86.06 (77.04 - 95.07)	yes

Figure





OP226 FULL ROBOTIC DONOR NEPHRECTOMY FOR LIVING DONOR KIDNEY TRANSPLANT

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Background: Robotic approach for donor nephrectomy has several advantages over conventional open and laparoscopic techniques, thanks to the use of articulated instruments, 3D view, and image stability, allowing for a safe and reproducible procedure.
Methods: We report our early experience of full robotic donor nephrectomy for living donor kidney transplant, with 11 cases from November 2019 to February 2021. All the procedures were performed with daVinci Si platform, docking 2 robotic arms plus the camera arm.
Results: Four right nephrectomies and 7 left nephrectomies were performed in the study period: the side of nephrectomy is determined according to functional and anatomical evaluations. Median operative time was 245 min including docking, with median estimated blood loss of 10 ml. Median warm ischemia time, from arterial clamping to reperfusion at back table, was 188 s while median cold ischemia time was 90 min. No intra-operative or post-operative complications occurred among the donors, with a median post-operative stay of 3 days. Of note, no vascular thrombosis occurred after kidney transplant.
Conclusions: With the limits of a preliminary experience, our results confirm that robotic approach is safe, effective and reproducible, even at the beginning of the learning curve of this procedure. However, is crucial to approach donor nephrectomy after having gained adequate proficiency with the robot and having completed a general learning curve.

ETHICAL AND LEGAL ASPECTS OF DONATION AND TRANSPLANTATION

OP269 ETHICS SUPPORT FOR PAEDIATRIC CARDIAC DCD

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Background: The first heart transplant in 1967 was effectively cardiac-DCD (cDCD), but ethical concerns meant cDCD was abandoned, especially once the Harvard criteria permitted DBD, considered superior due to lack of donated-organ ischaemic damage. In 2008, infant cDCD was reported using 75-s from cardiac arrest to organ retrieval, rather than the usual 5-min, to reduce cardiac ischaemia. This proved controversial with concerns about safe death-verification and heart transplant following a death verified by 'cardiac' criteria. Despite sporadic attempts, other centres did not report the same success.
Methods: The UK Donation Ethics Committee considered the subject, determining several fundamental principles: (i) Human death is a single entity, verifiable by either neurological or circulatory criteria. (ii) After death, any organ can be donated and used for transplantation, whichever method was used. (iii) No change to standard criteria should occur to facilitate donation, reinforcing the required 5 min continuous circulatory arrest before death verification. In 2014, an Australian team reported successful cDCD using the Organ Care System (OCS-Transmedics) and standard death verification. Subsequently, the UK Papworth team reported similar success and, given paediatric heart transplant death rates, met with the GOSH heart transplant team (HTT) to explore cDCD in children.
Results: HTT brought cDCD to the GOSH-Bioethics team for discussion sequentially:
• 2014: UKDEC principles considered equally applicable to children.
• 2018: Ethical aspects of OCS cDCD in children - Primary ethical determinants: Appropriate recipient & parent consent to innovative cDCD transplant vs established, but uncertain, chance of DBD transplant; equity with listed adults and financial aspects.
• 2019: Reviewed consent forms & process and multidisciplinary team support.
• Late 2020: strong ethical imperative to develop & trial small donor (<30 kg) systems to permit younger recipients agreed; equity & children of any size's right to benefit vital considerations.
Conclusions: Six children underwent successful cDCD in 2020; smaller sized devices in development – but financial considerations significant. We describe how an ethics team can help development of a novel cDCD process in a children's hospital.

OP270 ARE WE READY TO START WITH THE PEDIATRIC DONATION AFTER CARDIOCIRCULATORY DETERMINATION OF DEATH IN ITALY?A SINGLE-CENTRE SURVEY ON PICU ATTITUDE

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Background: in Italy we don't have a program of pediatric donation after cardiocirculatory determination of death (pDCDD)even if we know that an active program could increase the number of eligible donors in PICU (1). Many centres around the world investigated the PICU staff attitude before launching the program to avoid the potentially negative reactions and to determine the acceptance of a new practise of donation.
Methods: we conducted an electronic and anonymous survey about perspective and opinions towards pDCDD among the 65 PICU health care providers (nurses, doctors, psychologists, healthcare assistants) of an Italian tertiary-care Children Hospital. The survey was divided in 3 parts: (I)questions about general demographic data; (II) 18 statements about personal wish to donate, experience of discussing donation, knowledge about donation; (III)attitudinal statements regarding 2 pediatric Maastricht III scenarios of organ donation.
Results: The response rate was more than 70% and respondents were predominantly nurses. All respondents declared to be in favor of pDCDD; more than 60% stated that they would feel comfortable proposing organ donation to the family of a dying patient on whom the withdrawal of therapies has been agreed; half of respondents stated that the pDCDD could improve the bereavement of the family. About the scenarios, more than 60% would consider that they would have acted in the best interest of the patient in organizing the donation after the withdrawal of therapies. The majority of respondents declared that they would like to receive a specific training on pDCDD.
Conclusions: This study provides the first insights into the opinions of the PICU staff towards pDCDD at an Italian Hospital. It shows a very good general attitude on this topic and provides a crucial first step towards implementation of the program.
1. Giugni C. et al Is donation after circulatory determination of death feasible for pediatric patients in italy? *Pediatric Transplantation*. 2021;00:e13977"

OP271 INEQUITABLE ACCESS TO TRANSPLANTS: PERSONS WITH IMPAIRED DECISION-MAKING CAPACITY

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Background: Inequitable access to organ transplantation has received considerable scrutiny in recent years. Published evidence suggests a significant proportion of patients with impaired decision-making capacity face inequitable access to transplantation.
Methods: The ESOT 'Ethical and Legal Issues' working group reviewed published clinical and ethics literature relating to transplantation in persons with impaired decision-making capacity. An expert consensus process was undertaken.
Results: We identified four patient groups potentially affected by impaired decision-making capacity and four themes of empirical evidence. These are set out in Table 1.

Table 1

	Common Themes			
	Medication adherence	Graft outcomes	Patient outcomes	Quality of life (QoL)
Group potentially affected by impaired decision-making capacity				
Intellectual disability	Limited evidence suggests no concern	Outcomes comparable	Outcomes comparable	QoL improved
Severe mental health conditions	Increased non adherence in depression but not in other conditions	Conflicting evidence	Poorer outcomes in pre-existing psychological diagnosis. Causation not addressed.	QoL improved
Cognitive impairment	Possible reduced adherence	Increased graft loss Causation unclear	Increased mortality Causation not addressed	QoL improved
Permanent disorders of consciousness	Not applicable	No evidence	No evidence	Theoretical reason to believe QoL would be different

Conclusions: Impaired decision-making capacity should not in and of itself be considered as a barrier to registration on the transplant waiting list or allocation of an organ. In order to reduce unintended inequity and inadvertent discrimination, transplant pathways should focus on ensuring the eligibility of persons with impaired decision-making capacity for transplantation is based upon sound evidence and outcomes without reference to non-medical criteria. Where a patient with impaired decision-making capacity is judged to be unsuitable for transplantation, the basis for this decision should be clearly documented and communicated to them and their family/carers. We call upon transplanting centres and national bodies to include data on decision-making capacity in routine transplant reporting schedules in order to improve the evidence base upon which such decisions are made.

OP272 FRIEND OR FOE: LAW, REGULATION AND THE PSYCHOSOCIAL ASSESSMENT OF LIVING KIDNEY DONORS

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Background: Living kidney donation's greatest conundrum is found within the assumption that it violates a cornerstone of the Hippocratic oath – *above all, do no harm*. Due to this, a nephrectomy has become synonymous with an assessment of physical harm. In the United Kingdom, legal and clinical guidance is aimed at inflicting minimum physical harm when assessing living kidney donors (LKD). The emphasis on physical harm has potentially led to an oversight of psychosocial harm and benefit. The Regulator (Human Tissue Authority) does not deem a mental health assessment (MHA) by a mental health professional *mandatory* for LKD. The National Health Services, and British Transplant Society, do, however, recommend that non-directed altruistic LKDs should undergo a MHA, albeit with sparse guidance on the matter. This has led to inconsistency and variability regarding who is referred for a MHA, the professional association of the assessor, and the nature of the MHA.
Methods: A review of the UK legislative and regulatory donation and transplantation framework (legislation; case law; statutory and non-statutory bodies guidance) was undertaken to determine the extent of MHA guidance. As well as a study of regulatory theory based on Prosser's framework of *Regulation as Collaborative Enterprise* to determine the role regulation might play in an area such as kidney donation that is filled with social conflict based on moral and religious beliefs.
Results: I argue that MHAs should be routinely included as part of the psychosocial assessment to ensure that all LKD receive optimal care, pre-and posttransplant. The role regulation might play to implement the MHA should not be overlooked. Firstly, regulation has the potential to promote the efficiency of the psychosocial assessment by ensuring a clear and consistent approach to the MHA. Secondly, it allows for the protection of basic human rights. Finally, it allows a forum for participation and deliberation which will contribute to enhancing public trust in the decision-making process of including or excluding potential LKD.
Conclusion: Regulatory action to routinely include the MHA of LKD has the potential to ensure a consistent and clear approach which also allows for the protection of basic human rights. As a whole, it might contribute to ensure the efficient operation of the LKD assessment.

OP273 FAMILY'S LEGAL ROLE IN DECEASED ORGAN PROCUREMENT. AN EUROPEAN AND COMPARATIVE LAW STUDY

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Background: Several European countries are approving legislative reforms moving to a presumed consent system in order to increase organ donation rates. Nevertheless, irrespective of the consent system in force, family's decisional capacity probably causes a greater impact on such rates.
Methods: We have developed a systematic methodology in order to analyse and compare European organ procurement laws. We have designed a framework that includes, for each country: the consent policy (opt-in, opt-out); the possibility for individuals to register their wills regarding OP (the existence of registries to express a consent, a refusal, both, or to designate a representative to deal with the issue); the decisional capacity allowed or required from the family depending on the deceased's wishes (unknown, expressed consent, expressed refusal); and the family's right to be informed about organ procurement decisions.
Results: With our results we clarify the weight given by each European law to relatives' decisional capacity over individual's preferences, expressed or not while alive, regarding the destination of his or her organs after death.
Conclusion: This study constitutes the first comprehensive and comparative legislative mapping on European transplantation laws. The results could be useful for drawing trends in legislative changes in Europe and provide a better understanding of the impact of the law on deceased organ policies.

OP274 WITHDRAWING LIFE SUSTAINING TREATMENT AND ORGAN DONATION OF BRAIN DEATH PATIENTS

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Background: According to the statistics of the National Agency for Management of Life-Sustaining Treatment, over 3 years, 134 945 (28 256 in 2018, 51 747 in 2019, 54 942 in 2020) patients who were enlisted for life sustaining treatment had withdrawn treatment since the implementation of law in February 2018. However, Korea Organ Donation Agency (KODA) reported that a number of patients among the referred potential brain deaths requested for withdraw life sustaining treatment. Their family consent rate of organ donation was lower than that of the family, who did not receive any mention about interruption of the end of life care.
Methods: The study was designed using the referred cases of potential brain death of KODA from 2018 to 2020. We analyzed the request cases of withdrawing life sustaining treatment and the result of donation progress in each step.
Results: Within the research period, there were a total of 7085 cases (2426 in 2018, 2484 in 2019, 2175 in 2020) of brain death, and among them, 949 (193 in 2018, 376 in 2019, 380 in 2020) people requested for withdraw life sustaining treatment. In terms of gender, 63.4% of the cases were male, and the most common age group was the fifties (24.2%). Cases in neurosurgery department (545, 57.4%) was most frequently reported among other

medical fields, followed by emergency department (125, 13.2%) and others. When it comes to cause of death, 564 (59.4%) died from disease and 380 (40.1%) died because of accidents. Among 949 who requested withdrawal of life sustaining treatment, 792 (83.5%) were appropriate for organ donation, and 675 (85.2%) cases were able to confirm the intention to donate. Among 792 cases, 86 families agreed for organ donation but only 59 cases (7.4%) were succeeded in organ procurement.
Conclusion: We estimated that more families will wish to withdraw life sustaining treatment of potential brain death even though they receive precise information about organ donation. Therefore, in order to activate organ donations, system revision that introduces information about organ donation as well as withdrawing life sustaining treatment is necessary. Also, in the application form of withdrawing life sustaining treatment, there should be information about organ donation in the application form of withdrawing life sustaining treatment.

HOT ISSUES IN LIVING KIDNEY DONATION

OP303 DONATING A KIDNEY TO A STRANGER: ARE HEALTHCARE PROFESSIONALS FACILITATING THE JOURNEY? RESULTS FROM THE BOUND STUDY

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Background: Despite their positive impact on the United Kingdom (UK) kidney transplant programme, unspecified kidney donors (UKDs) are approached with a degree of caution and suspicion by some transplant clinicians. The aims of this study were to identify transplant professionals' views, attitudes and experiences of unspecified kidney donation (UKD) and to assess whether these differed between members of the multidisciplinary team, and between high and low volume centres.
Methods: A purposely designed questionnaire was validated, piloted and then distributed to transplant professionals within each of the 23 UK transplant centres.
Results: 153 responses were obtained, with representation from all UK centres. UKD was considered a virtuous act, however, concerns regarding psychopathological motivations, regret and outcomes were prevalent. Some transplant professionals felt that their programme was under-resourced and that they would benefit from additional training. Those less supportive of UKD held more negative attitudes towards UKDs' mental health, risk taking, and motivations ($P < 0.003$). Those less accepting of UKD were less experienced and held more negative attitudes towards perceived resource use and decision making ($P < 0.003$). High volume centres were less supportive and less accepting of UKD than low volume centres ($P < 0.001$).
Conclusions: This is the first study to quantitatively explore the views of UK transplant professionals towards the UK UKD programme. A significant number of participants highlighted a need for more training and resources. A small but significant number of transplant professionals held negative views, who in turn were less supportive of UKD. This correlates with data from previous studies stating that potential donors detect negative attitudes during encounters with staff. Surprisingly, higher volume centres were less supportive of UKD than lower volume centres.

OP304 HOW GOOD IS A LIVING DONOR? THE EFFECT OF DONOR DEMOGRAPHICS ON POST KIDNEY TRANSPLANT OUTCOMES

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Background and Aims: Living donor kidney transplantation is associated with better transplant outcomes. In the attempt to expand the donor pool, the donor's age, gender and body mass index (BMI) might be considered as potential determinants of the kidney transplant outcomes, and thus for potential recipient selection. We aimed to investigate the effects of donor demographics on kidney function, graft and recipient survival, delayed graft function (DGF) and acute rejection (AR).
Methods: Systematic review and meta-analysis. EMBASE, MEDLINE, Web of Science, BIOSIS, CABI, SciELO and Cochrane were searched using algorithms. NHBLI tools were used for risk of bias assessment. Mean difference (MD), standardized mean difference (SMD) and risk ratio (RR) were calculated in Revman 5.4.
Results: 5129 studies were identified by the search algorithm; 37 studies met the inclusion criteria and were analyzed. No significant difference in recipient 1-year survivals was found between recipients of donors aged < 50 vs donors aged > 50 (RR = 0.65 95 CI: 0.1–4.1) and recipients of donors aged < 60 vs donors aged > 60 (RR = 0.81 95 CI:0.3–2.3). Graft survival was significantly higher in recipients of grafts from donors aged < 60 (Figure 1). AR (RR = 0.62 95 CI: 0.5–0.8) and DGF (RR = 0.28 95 CI: 0.1–0.9) were significantly higher in recipients of donors aged > 60 compared to donors < 60. 1-year serum creatinine was significantly lower in recipients from donors aged < 60 compared to donors aged > 60 (MD = 0.3 mg/dl 95 CI: 0.1–0.9). Recipients of grafts from male donors had a lower 1-year serum creatinine compared to recipients of female donors (MD = 0.12 mg/dl 95 CI: 0.2–0.1), but with high heterogeneity. There was no significant difference in graft survival between recipients of male and female donors. Donor obesity of did not have a significant effect on incidence of DGF (RR = 0.66 95 CI: 0.32–1.34) or AR (RR = 0.73 95 CI: 0.6–0.9).
Conclusions: Older donor age was associated with worse recipient post-transplantation outcomes. Recipients of male kidneys had better renal-function 1-year post transplantation. Donor obesity did not significantly affect DGF or AR in recipients.

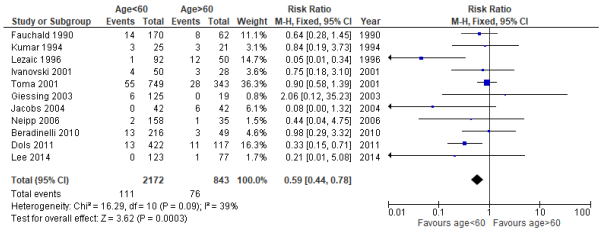

Figure 1 Comparison of 1-year graft survival between renal transplant recipients from donors aged less than 60 years and donors older than 60 years.

OP305 IMPACT OF MEASURED VERSUS ESTIMATED GFR ON LIVING KIDNEY DONOR SELECTION: A MULTICENTER COHORT STUDY

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Background: Most transplant centers use estimated glomerular filtration rate (eGFR) for evaluation of potential living kidney donors. Measured GFR (mGFR) allows more precise kidney function assessment, and therefore holds potential to increase the living donor pool. We aimed to address the impact of the mGFR method on donor selection and long-term safety.
Methods: In this longitudinal cohort study, we compared eGFR (CKD-EPI) before and at five years after donation in donors from one center using mGFR-based donor screening (Groningen, $n = 250$) with two centers using eGFR-based screening (Rotterdam, $n = 647$ and Nijmegen, $n = 169$). Follow-up was complete in all donors.
Results: Donor age was similar among the cohorts (Groningen 53 ± 10 years, Rotterdam 52 ± 13 years and Nijmegen 53 ± 9 years) with small differences in sex distribution (Groningen 54%, Rotterdam 58%, and Nijmegen 47% female, $P < 0.05$ vs. Groningen). Before donation, eGFR was lower in Groningen (91 ± 13 ml/min/1.73 m^2) than in Rotterdam (93 ± 15 ml/min/1.73 m^2, $P < 0.05$ vs. Groningen) and Nijmegen (94 ± 12 ml/min/1.73 m^2, $P < 0.05$ vs. Groningen). Pre-donation 24-h creatinine clearance was 127 ± 33 ml/min in Groningen and 128 ± 38 ml/min in Nijmegen ($P = 0.86$). Pre-donation mGFR was 115 ± 22 ml/min/1.73 m^2 in Groningen. At five years post-donation, eGFR was similar among the centers (Groningen 62 ± 12 ml/min/1.73 m^2, Rotterdam 61 ± 14 mL/min/1.73 m^2, Nijmegen 62 ± 11 ml/min/1.73 m^2, P = NS). The 5-year decline in eGFR was smaller in Groningen (−29 ± 10 ml/min/1.73 m^2), compared with Rotterdam (−32 ± 10, $P < 0.05$ ml/min/1.73 m^2 vs. Groningen, $P < 0.05$ vs.

Groningen) and Nijmegen (-33 ± 8 ml/min/1.73 m^2, $P < 0.05$ vs. Groningen). The % of donors with eGFR < 45 ml/min at 5 years was similarly low between the centers (Groningen 5%, Rotterdam 11%, Nijmegen 4%, P not significant)
Conclusion: mGFR-based donor screening may facilitate acceptance of more donors with marginal eGFR without adverse effects on long-term kidney function, providing potential for a safe expansion of living donor pool.

OP306 PREDICTION OF RENAL OUTCOMES IN LIVING KIDNEY DONORS USING CROSS-VALIDATED LOGISTIC REGRESSION

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Background: Living kidney donation (LD) represents a unique opportunity in the treatment of end-stage renal disease, offering better organ quality and shorter waiting times for patients. However, the healthcare professionals involved have a responsibility to ensure the safety and health of the donor. Although numerous examinations are performed prior to kidney donation to identify medical risks, some donors develop poor renal outcomes.
Methods: Renal outcomes three years after LD ($n = 193$) were retrospectively analysed in a single-center study cohort from 2007 to 2018. Poor renal outcome was defined as eGFR < 60 ml/min/1.73 m^2. A logistic regression model with forward stepwise feature selection using 10-fold cross validation was employed. The regression coefficients were used to generate a predictive score. The independent variables studied were age, sex, smoking, hypertension, therapy with ACE inhibitors or angiotensin receptor blockers, BMI, eGFR, haemoglobin, creatinine, urea, calcium, and phosphate.
Results: Of 193 donors, 123 had an eGFR $\geq$ 60 ml/min/1.73 m^2 three years after LD. Cross validation was used to identify the variables relevant for logistic regression: eGFR, age, BMI, and haemoglobin at LD. The developed score correctly predicted good renal function (eGFR $\geq$ 60 ml/min/1.73 m^2) after LD in 106 donors (sensitivity of 86%). The development of worse renal function was correctly predicted in 52 donors (specificity of 74%).
Conclusions: Important influencing variables at the time of LD for the development of the donor's renal function are baseline eGFR, age, BMI and Hb level. Our newly developed score is a useful tool for stratifying kidney risk and counseling a potential kidney donor.

OP307 CHANGES IN KIDNEY FUNCTION AFTER LIVING DONOR NEPHRECTOMY: A TWO-DECADE SINGLE CENTER EXPERIENCE

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Background: Living-donor kidney transplantation (LDKT) is currently the best option for patients with end stage renal disease (ESRD). Better understanding of changes in renal function after nephrectomy for donation and how it differs by donor characteristics might help clinicians in wider patient selection, counselling, and follow-up care.
Methods: A retrospective analysis was performed in a single-center LDKT activity between 2000 and 2020. The following donor characteristics were evaluated before donation (T0), at 6 months (T1), at one year (T2) and at the last follow-up (T3): GFR, BMI, comorbidities such as arterial hypertension, diabetes mellitus type II, dyslipidemia, cardiovascular diseases. The eGFR was estimated using the CKD-EPI equation.
Results: 199 living voluntary kidney donors were evaluated for a median follow-up of 9 years. The median age of the cohort was 50 years. 70% were women. T0-eGFR was 96 ml/min/1.73 m^2. Average T1-eGFR was slightly reduced, while at T2 was increased with a constant maintenance until the last follow-up. The mean Delta eGFR (Δ-GFR) = -25.50 ± 19.01, with a mean BMI change (Δ-BMI) = 0.92 ± 2.25. Placing the Δ-GFR as a dependent variable, on linear regression analysis, this correlated positively with T0-BMI and T0-eGFR ($P < 0.001$).
Conclusions: The T0-eGFR, estimated using the CKD-EPI formula, was confirmed as a highly reliable method to reflect the variation in GFR after kidney donation and to predict the risk of ESRD. Our experience suggests that the living donors with higher initial BMI have a reduced eGFR at T3 compared to those with lower pre-donation BMI, stressing that the risk of developing kidney disease is attributable to the onset of metabolic disorders which are certainly factors of independent risk.

OP308 A DYNAMIC MARKOV MODEL TO ASSESS THE COST-EFFECTIVENESS OF THE KIDNEY TEAM AT HOME INTERVENTION IN THE NETHERLANDS

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Background: The Kidney Team at Home program is an educational intervention aimed at patients with chronic kidney disease to assist them in their choice for kidney replacement therapy. Previous studies have shown that the intervention results in an increase in knowledge and communication on kidney replacement therapy, and eventually in an increase in the number of living donor kidney transplantations. The study assesses the cost-effectiveness of the intervention compared to standard care.
Methods: A dynamic probabilistic Markov model was used to estimate the monetary and health benefits of the intervention in the Netherlands over 10 years. Data on costs and health-related quality of life were derived from the literature. Transition probabilities, prevalence and incidence rates were calculated using a large national database. An optimistic and a pessimistic implementation scenario were compared to a base case scenario with standard care.
Results: In both the optimistic and pessimistic scenario, the intervention is cost-effective and dominant compared to standard-care: savings were €108,681,985 and €51,770,060 and the benefits were 1382 and 695 QALYs respectively.
Conclusions: The superior cost-effectiveness of the intervention is caused by the superior health effects and the reduction of costs associated with transplantation, and the relatively small incremental costs of the intervention. The favourable findings of this implementation project resulted in national uptake of the intervention in the Netherlands as of 2021. This is the first time a psychosocial intervention has been implemented as part of standard care in a kidney replacement therapy program worldwide.

NAVIGATING FOLLOW-UP AFTER HEART TRANSPLANTATION: MY COURSE IS SET FOR AN UNCHARTED SEA

OP297 MULTICENTER ITALIAN STUDY ON DURABLE RADIAL MECHANICALLY ASSISTED CIRCULATORY SUPPORT (MIRAMACS): ENCOURAGING LONG-TERM OUTCOMES

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Background: The Multicenter Italian study on RAdial Mechanically Assisted Circulatory Support (MIRAMACS) represent the first Italian observational analysis, gathering continuous-flow (CF) left ventricular (LVAD) and biventricular assist device (BiVAD) implantation performed in adult patients.
Methods: Eight participating hospitals contributed pre-, peri- and long-term postoperative data on LVAD implants to the registry. Data for all implants in adult patients performed between January 2000 and September 2020 were analysed. BiVADs were excluded.
Results: A total of 515 patients received a CF-LVAD. Mean age of LVAD recipients was 60 ± 10 years (mostly, male, 89.3%). The adopted systems were: HeartWare HVAD ($n = 213$), HeartMate III ($n = 140$), HeartMate II ($n = 89$), Jarvik 2000 ($n = 50$), Berlin Heart Incor ($n = 19$) and other brands ($n = 4$). Less invasive surgery was adopted in 6.6% of patients. Thirty-day mortality was 6.1%. Mean follow-up time was 57 ± 15 months. Ninety-nine patients (19.2%) were transplanted. Survival at 1-year, 3-years, 5-years of bridge to transplantation (BTT) and destination therapy (DT) cohorts was 82.1%, 60.4%, 41.8%, and 69.8%, 45.6%, 30.1%, respectively. Bleeding, infection, neurological and device malfunction events were reported in 7.7%, 27.7%, 18.8% and 6.9% of patients, respectively. INTERMACS profile 1–2, patients age >64-year-old, DT intention for treatment, and old-generation axial-flow pump adoption resulted to be independent risk factors for early death ($P < 0.001$). Fully-magnetically centrifugal pumps performed better.
Conclusions: This initial MIRAMACS report shows results comparable with other registries. CF-LVAD therapy success rate has been, herein, confirmed satisfactory. Detailed prospective data collection, additional participating centres and further analyses need to be set.

OP298 DEVELOPMENT AND VALIDATION OF SPECIFIC POST-HEART TRANSPLANT RISK SCORES ACCORDING TO THE CIRCULATORY SUPPORT STATUS AT TRANSPLANT

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Background: The clinical use of post-transplant risk scores is limited by their poor statistical performance. We hypothesized that developing specific prognostic models for each type of circulatory support at transplant may improve risk stratification.
Methods: We analyzed the UNOS database including contemporary, first, non-combined heart transplantations (2013–2018). The endpoint was death or retransplantation during the first year post-transplant. Three different circulatory support statuses at transplant were considered: no support, durable mechanical support and temporary support (inotropes, temporary mechanical support). We generated 1,000 bootstrap samples that we randomly split into derivation and test sets. In each sample, we derived an overall model and three specific models (one for each type of circulatory support) using Cox regressions, and compared, in the test set, their statistical performance for each type of circulatory support.
Results: A total of 13 729 patients were included; 1220 patients (8.9%) met the composite endpoint. Circulatory support status at transplant was associated with important differences in baseline characteristics and distinct prognosis ($P = 0.01$), interacted significantly with important predictive variables included in the overall model, and had a major impact on post-transplant predictive models (type of variables included and their corresponding hazard ratios, Figure). However, specific models significantly improved risk stratification (discrimination, reclassification indices, calibration) compared to overall models in a very limited proportion of bootstrap samples (<15%). These results were consistent across several sensitivity analyzes.
Conclusions: Circulatory support status at transplant reflected different disease states that influenced predictive models. However, developing specific models for each circulatory support status did not significantly improve risk stratification.
FIGURE. Most selected predictive variables according to the circulatory support status at transplant (% of bootstrap samples). Opaque bars: variable among the 10 most selected for this model. Transparent bars: variable not among the 10 most selected for this model.

OP299 CORE SIGNATURE OF REJECTION-SPECIFIC CYTOKINES AND CHEMOKINES IN HEART BIOPSIES AFTER TRANSPLANTATION

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Background: Allograft rejection remains limiting for survival after HTX. The aim of the project was to characterize the cytokine/chemokine network in heart biopsies and peripheral blood plasma after TX. The quantified cytokine/chemokine concentrations could reflect the ischemia/reperfusion response as well as rejection status of the allograft. We hypothesize that in heart biopsies with histopathological proven rejection the microenvironment is significantly altered and potentially specific cytokine/chemokine patterns could indicate allograft rejection.

Methods: Heart biopsies (N = 181 biopsies; 52 patients) and peripheral blood samples (N = 35 patients) were obtained at different time points after HTX. Using luminex-based multiplex assays 50 cytokines/chemokines in tissue lysates and peripheral blood plasma were quantified. Concentrations of samples with rejection and no-rejection were compared. Moreover correlation of tissue and plasma levels were performed.
Results: With regard to the rejection status we identified significant differences in lysate concentrations. Especially CXCL9, CXCL4 and CXCL10 showed significantly elevated concentrations in biopsies with rejection ($P < 0.001$). In addition, we identified individual long-term changes of single patients after HTX and significant differences comparing tissue lysates with plasma concentrations. Interestingly, we found no strong correlation between plasma and lysate concentrations. Moreover significantly elevated concentrations of MIF, M-CSF, FGF basic and ICAM-1 ($P < 0.05$) in the first biopsies after HTX were found by comparing cold static preservation and normothermic machine perfusion.
Conclusion: We could detect a core signature for biopsies with pathologically secured rejection consisting of increased concentrations of the chemokines CXCL9, CXCL3, CXCL4and CXCL10. This signature is clearly distinguished from the pattern of the ischemia/reperfusion response (i.e. elevated levels of IL-6, CXCL8, IL-10) suggesting differences in the underlying inflammatory mechanisms. Importantly, since there was no correlation between the measured protein concentrations in plasma and tissue lysates, biopsies remain indispensable for the diagnosis of heart rejection.

OP300 ECHOCARDIOGRAPHIC ASSESSMENT OF THE LEFT ATRIUM FOR CATEGORIZATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION IN HEART TRANSPLANT RECIPIENTS

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Background: Evaluation of left ventricular (LV) diastolic function with echocardiography in heart transplant (HTx) recipients is of particular importance as diastolic dysfunction (DD) may reveal allograft rejection or vasculopathy early, but it is challenging due to the complex morphology and function of left atrium (LA). Left atrial strain (LAS) is a promising tool in categorizing diastolic function in non-HTx population. We aimed to evaluate the structural and functional characteristics of LA in determining LV diastolic function in HTx recipients.
Methods: Transthoracic echocardiograms of 27 patients 1 and 4 months following HTx was obtained to measure mitral inflow and annular velocities (v), E/e' ratio, peak velocity of tricuspid regurgitation (TRv_{max}) and LA volume index (LAVi). LA function was measured by speckle tracking-derived LAS. Serum NT-proBNP levels were analysed as well. Data values were given as mean ± standard deviation. Statistical analysis was performed using *t*-test and Spearman test.
Results: Average E/e' (11.9 ± 4.3 vs. 8.7 ± 2.1; $P < 0.05$), septal e' v (6.6 ± 1.9 cm/s vs. 7.7 ± 1.8 cm/s; $P < 0.05$), lateral e' v (11.2 ± 2.8 cm/s vs. 13.7 ± 3.1 cm/s; $P < 0.01$) and TRv_{max} (2.7 ± 0.3 m/s vs. 2.5 ± 0.3 m/s; $P < 0.001$) improved significantly over time. LAVi and LAS did not change significantly. LAS was reduced compared to normal values from the literature. NT-proBNP levels decreased significantly (8543 ± 8413 pg/ml vs. 1000 ± 846 pg/ml; $P < 0.001$). There were no correlations between LAS or LAVi and TR v_{max}, septal or lateral e' v, E/e' or NT-proBNP.
Conclusions: The guideline-recommended diastolic parameters independent of LA significantly improves over time in HTx population. Hence, in this cohort, LA structural and functional impairment cannot be assessed exclusively as a consequence of DD and elevated LV filling pressure but might be characteristics related to surgical techniques. Relevance of LAVi and LAS in determining LV diastolic function is limited after HTx.

OP301 CARDIAC COMPUTED TOMOGRAPHY ANGIOGRAPHY FOR THE SCREENING OF CARDIAC ALLOGRAFT VASCULOPATHY, TWO YEARS OF EXPERIENCE

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Background: Cardiac allograft vasculopathy (CAV) is an accelerated form of coronary artery disease affecting heart transplantation (HT) recipients with high morbidity and mortality rates. Annual screening for CAV is warranted according to the International Society for Heart and Lung Transplantation (ISHLT) guidelines. The golden standard for CAV screening is coronary angiography. In this study, we evaluated the feasibility and safety of cardiac computed tomography angiography (CCTA) for the screening of CAV.
Methods: From Feb 2018 – Jan 2020 all patients >4 years post-HT were actively converted from myocardial perfusion imaging to CCTA for CAV screening. Contra-indications were iodine allergy or glomerular filtration rate < 30 ml/min/1.73 m^2. All first scans are included. CAV grades (from 0 to 3) on CT were determined similar to the ISHLT guidelines. Scans were scored on image quality (non-diagnostic, moderate, good, excellent), Agatston calcium score (CACS) and coronary stenosis (0%, <50%, >50%). Major adverse cardiovascular events (MACE) were scored 1-year post-CCTA.
Results: In total, 160 patients were included. In one patient, no CT with contrast was performed due to IV access issues. Median age was 55 [43–64] years, 55 (34%) were female and median time between HT and CCTA was 11 [8–16] years. Mean heart rate during the CCTA was 74 ± 11 beats per minute. Image quality was good/excellent in 140 (88%). Median radiation dose was 2.1 [1.6–2.9] mSv. Agatston CACS was available in 135 (84%) patients with a median of 1 [0–61]. CAV scores were 0, 1, 2 and 3 in 90 (57%), 34 (21%), 15 (9%) and 20 (13%) patients respectively. Additional tests were performed in 24 (15%) patients of whom 22 had a coronary angiography. A significant stenosis was seen in 14/160 (9%) patients of whom 12/14 (86%) underwent percutaneous coronary intervention. One year post-CCTA, MACE occurred in 8 (5%) patients, none of whom were related to significant coronary stenosis (see Table).
Conclusions: CCTA is a safe and feasible tool to screen for CAV post-HT with a low radiation dose, good image quality and good sensitivity. We believe CCTA can act as a gate keeper for coronary angiography in HT patients.

Patient	MACE one year post-CCTA
1	Cerebrovascular accident (CVA) and malignancy resulting in non-cardiac death
2	Sudden cardiac death most probably due to rejection (no CAV on CCTA)
3	Type 4 myocardial infarction
4	CVA 4 months post-CCTA
5	CVA after PCI
6	CVA 6 months post-CCTA
7	Transient ischemic attack 3 weeks post-CCTA
8	Non-ST elevation myocardial infarction in a patient with known severe CAV

OP302 SUDDEN CARDIAC DEATH AFTER HEART TRANSPLANTATION: A POPULATION BASED STUDY

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Background: The epidemiology and natural history of sudden cardiac death (SCD) after heart transplantation (HTx) remain imprecisely described. We aimed to assess the incidence and determinants of SCD in a large cohort of HTx recipients, compared to the general population.
Methods: Consecutive HTx recipients ($n = 1246$) between 2004 and 2016 in two referral centers were included. Clinical, biological, pathologic, immunologic and functional parameters were assessed. The SCD incidence was compared to the incidence of SCD observed in the general population from the Paris Sudden Death Expertise Center registry ($n = 19\,706$ SCD, 2011–2017). A competing risk multivariable Cox analysis was used to identify the independent determinants of SCD after HTx.
Results: 1246 HTx recipients were included with a median follow-up time post-transplantation of 4.3 years (IQR 0.9–7.1). The annual incidence of SCD was 12.5 per 1000 person-years (95% CI: 9.7–15.9) in the HTx recipients, compared to 0.54 per 1000 person-years (95% CI: 0.53–0.55) in the general population ($P < 0.001$). The risk of SCD was particularly elevated among the youngest (<30 years) HTx recipients, with an annual incidence of 38.6 per 1000 person-years, compared to the general population of the same age, with a standardized mortality ratio for SCD up to 837.6. Beyond the first year, SCD was the leading cause of death, contributing to 22.0% of the overall mortality. In a competing risk multivariable analysis, five

independent variables were associated with the occurrence of SCD: donor age ($P = 0.003$), recipient age ($P = 0.001$) and ethnicity ($P = 0.034$), preexisting DSA ($P = 0.009$) and last left ventricular ejection fraction ($P = 0.048$).
Conclusions: HTx recipients are at very high risk of SCD compared to the general population. The consideration of specific risk factors may help identify high-risk subgroups that should benefit from more aggressive preventive strategies in order to improve long-term survival.

Figure 1: Annual incidence of sudden cardiac death according to patient's age in the Paris general population (SDEC) and in the heart transplant cohort.

The annual incidence of sudden death was represented by 10-year age groups in the Paris general population through the Sudden Death Expertise Center registry (SDEC) and in the heart transplant patients in the same geographical area over the same period. The incidences were represented with a logarithmic transformation.

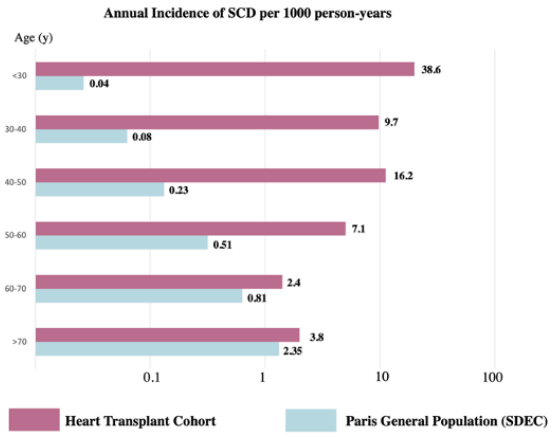

Table Factors associated with sudden cardiac death in the multivariable Cox analysis with the competitive risk model.

This table shows the association of clinical, immunological, functional and structural parameters associated with sudden cardiac death in the multivariable Cox analysis, with competitive risks taking into account all other known causes of death.

	n=885	HR	p value
Donor characteristics			
Age (10-year increment)		1.44 [1.13;1.83]	0.003
Recipient characteristics			
Age (10-year increment)		0.71 [0.57;0.87]	0.001
Non-Caucasian ethnicity			
No		1	-
Yes		1.88 [1.05;3.38]	0.034
Immunology			
Pre-formed DSA			
No		1	-
Yes		2.28 [1.22;4.26]	0.009
Echocardiography parameters			
Last LVEF (10-percent increment)		0.76 [0.59;0.99]	0.048

DSA: donor-specific antibodies; LVEF: left ventricular ejection fraction

PSYCHOSOCIAL ASPECTS OF TRANSPLANTATION

OP345 POSTTRAUMATIC GROWTH IN LIVER TRANSPLANT RECIPIENTS: RESULT OF A PROSPECTIVE COHORT STUDY

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Background: Next to psychological problems, liver transplant recipients (LTRs) also report positive psychological changes after transplantation. This is often referred to as post-traumatic growth (PTG). Because little is known about PTG in LTRs, this study aimed to examine: (1) the extent to which PTG occurs, (2) the presence of distinct trajectories of PTG, and (3) demographic, clinical, and personal variables of influence on trajectories of PTG.
Methods: A prospective cohort study among adult LTRs ($n = 104$) from three transplant centers in the Netherlands. Data regarding demographic, psychosocial, and personal variables were retrieved by self-report questionnaire before transplantation and at 3 (T1), 6 (T2), 12 (T3) and 24 (T4) months after transplantation. PTG was assessed by the Post Traumatic Growth Inventory (PTGI). Clinical data were retrieved by medical record review. Trajectories were based on 0.5 SD of the difference in PTGI-score between T0 and T1. Kruskal-Wallis tests were used to compare groups.
Results: Overall, the mean PTGI-score increased significantly from 43.0 (±23.8) at T0 to 50.4 (±24.1) at T1, but did not change significantly afterwards (T2-T4). Three distinct trajectories of PTG were identified: a group with an increase in PTGI-score (51.9%), a group with a stable PTGI-score (27.9%), and a group with a decrease in PTGI-scores (20.2%). Compared to LTRs with a stable or increased PTGI-score, those within the trajectory of decreased PTGI-score were younger ($P = 0.02$), more often single ($P = 0.01$), longer hospitalized after the transplant ($P = 0.01$), showed higher anxiety ($P = 0.04$) and depression ($P < 0.01$) scores, a lower score on personal control ($P = 0.03$) and a higher discrepancy between expected and observed quality of life score on all domains on T1 ($P < 0.03$).
Conclusions: A subset of liver transplant recipients experienced PTG after transplantation. Interventions aimed at regaining control may be helpful to enhance PTG in this patient group.

OP346 VIEWS AND EXPERIENCES OF PATIENTS AWAITING A TRANSPLANT AND OF TRANSPLANTED PATIENTS: A NATIONAL SURVEY TO UNDERSTAND THEIR NEEDS

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Background: The knowledge of the needs of waitlisted and transplanted patients is essential for taking initiatives and adopting proper behaviors. This is the purpose of a research project, funded by the Italian National Transplant Center, in collaboration with the Italian National Heart Transplant Association (ATCOM).
Methods: Two online questionnaires were developed: one addressed to waitlisted patients, the other to transplant recipients. Each questionnaire includes 19 questions, mostly closed-ended and multiple-choice questions, some of which are aimed at understanding their needs, which have been subsequently analysed. 1138 waitlisted patients and 1936 transplanted patients supplied their feedback.
Results: Among waitlisted patients, a sense of discouragement and distrust prevails (46.7%) due to their clinical conditions and, above all, to the long waiting times. 28.7% are afraid they will not make it and only 22% feel trust and hope. In already transplanted patients, feelings of gratitude prevail (62.3%), although anxiety (42.7%) and fear (19.7%) testify a state of anguish shared by 62.4% of survey participants. Rejection and complications concern both transplant recipients (54.9%) and patients awaiting transplant (41.6%). Waitlisted patients consider transplant as the main opportunity for help (78.4%), followed by psychological support (40.9%) and knowledge of care pathway (26.8%). Psychological support is also indicated by 25.8% of transplant recipients, together with continuous treatment (29.2%) and knowledge of care pathway and reference persons (28.8%). 23.5% of interviewed transplant recipients also expressed their sadness for not being allowed to have news about the donors and their families. Another common feeling in both surveys is great concern about the SARS-CoV-2 pandemic, for the risk of being infected and for the current state of difficulty in which hospitals are working, that is making treatments and care less accessible for waitlisted patients as well as for routine visits for transplant recipients.
Conclusions: Focusing on the patients' main needs and, above all, working to meet them means not only putting the patient at the center of the care pathway, but increasing the chances of a better life quality, despite suffering or worries.

OP347 PSYCHOLOGICAL FACTORS ASSOCIATED WITH MEDICATION NONADHERENCE IN KIDNEY TRANSPLANT PATIENTS

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Background: Immunosuppression nonadherence is high within kidney transplant recipients (KTR), with rates estimated to be between 36% and 55%. This is important because medication nonadherence is known to be a major risk factor for poor patient and graft outcomes. This study explored associations between patient perceptions of their graft, beliefs about medication and nonadherence, and whether these psychological factors predict nonadherence.
Methods: We conducted a cross-sectional analysis (N = 220) from a longitudinal cohort of long-term kidney transplant recipients followed-up between 2013 and 2020. Patients completed questionnaires including (i) Medicines Adherence Report Scale (MARS), (ii) Brief Illness Perception Questionnaire (BIPQ) and (iii) Beliefs about Medicines Questionnaire (BMQ).
Results: N = 220 completed questionnaires in 2019. Of these 139 (63.2%) were male and 81 (36.8%) were female with mean age 53.24 (range 20–79 years, *SD* = 12.84). Univariate analyses revealed nonadherent patients were significantly younger ($P = 0.038$), had lower perceived treatment control ($P = 0.006$), poorer understanding of risk of graft failure ($P < 0.001$) and greater concerns about medication ($P = 0.007$). This is set out in Table 1. Hierarchical logistic regression found understanding of risk of graft failure to be a significant predictor of medication adherence, with a one score increase in understanding reducing the odds of being adherent by a factor of 0.79 ($P = 0.002$, CI 0.68, 0.92).
Conclusion: Our findings highlight the importance of tailoring interventions to increase understanding of risk of graft failure among kidney transplant patients. Treatment control and concerns surrounding medication could be considered as targets for interventions. In addition, since younger patients appear at risk for nonadherent behaviour, adherence support should be provided for younger patients in adult nephrology services.

Table 1 Univariate analyses of variables between groups

Variable	Sample Mean (*SD*) (N = 220)	Group Mean (*SD*) Adherent (*n* = 95)	Nonadherent (*n* = 125)	*P* value
Age	53.2 (12.84)	55.29 (12.15)	51.67 (13.17)	.038*
Treatment Control	8.45 (2.02)	8.69 (2.13)	8.26 (1.91)	.006**
Understanding	7.94 (2.12)	8.53 (1.74)	7.50 (2.28)	<.001**
Concerns	11.67 (3.80)	10.88 (3.91)	12.27 (3.63)	.007**

Note. *$P < .05$. **$P < .01$.

OP348 PSYCHOLOGICAL EVALUATION OF DIALYSIS PATIENTS AND KIDNEY TRANSPLANT RECIPIENTS DURING COVID-19

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The status of having received a kidney and being on dialysis have been shown to increase morbidity and mortality related to COVID-19 infection. The aim of this study was to evaluate the traumatic stress anxiety and depression parameters in this group to explore the impacts of pandemic. Study was conducted at Ankara Dışkapı Research and Training Hospital Nephrology Clinic between October 2020- January 2021. Patients receiving dialysis and kidney transplant recipients were invited to complete a sociodemographic form, the Impact of Events Scale (IES-R) and the Hospital Anxiety and Depression Scale. Their laboratory workup results at the last clinic visit were also recorded. Patients receiving hemodialysis (N = 89), and who underwent kidney transplantation (N = 36) were recruited. Anxiety and depression levels of patients on dialysis were higher than the transplant group, while the traumatic stress score of the transplant group was elevated compared to the dialysis patients ($P < 0.05$). A statistically significant positive correlation was found between IES-R and anxiety and depression scores ($r = 0.605$ and $r = 0.482$, respectively, $P < 0.001$). In terms of biochemical parameters, creatinine, urea, phosphorus, parathyroid hormone, calcium levels were found to be lower and albumin and hemoglobin values were higher in the transplantation group compared to the HD group ($P < 0.05$). It is observed that patients receiving hemodialysis and transplant recipients experience different psychosocial difficulties during the COVID-19 outbreak, and determining their psychological needs and planning appropriate psychosocial interventions would be beneficial considering the higher risk of developing COVID-19 infection and increased complications.

OP349 PSYCHOLOGICAL MORBIDITY AMONG LONG-TERM KIDNEY TRANSPLANT RECIPIENTS: A SINGLE CENTRE STUDY

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Background: Depression and anxiety among kidney transplant recipients have been associated with lower quality of life and graft rejection. However, the literature on long-term kidney transplant recipients (LTR) is limited. This study investigated the relationship between depression and anxiety in LTR (≥7 years) with work/social functionality and Glomerular Filtration Rate (GFR).
Methods: Between 04/01/2019-09/12/2019 N = 275 LTR were screened using Generalised Anxiety Disorder (GAD-7), Patient Health Questionnaire (PHQ-9), and Work and Social Adjustment (WSA) Scale. Demographic characteristics (age, gender and ethnicity) and GFR were also catalogued. PHQ-9 and GAD-7 scales were transformed into binary variables. PHQ-9 and GAD-7 scores ≤10 catalogued 'depressive symptoms'. Univariate and logistic regression analyses were performed to investigate differences and determine odds ratio of variables associated with depression or anxiety.
Results: N = 139 (63.18%) were male. Mean age was 53.2 years (range 20–79 years). Mean GFR was 49.4 ml/min (range 16–92 ml/min). N = 15 (7%) had depression and N = 13 (6%) had anxiety. WSA was significantly associated with depression ($U = 316$, $P \leq 0.001$) and anxiety ($U = 412.5$, $P \leq 0.001$). LTR GFR was associated with anxiety. The 'no anxiety' group had a higher GFR $P = 0.045$. In the 'anxiety' group there was a statistically significant greater proportion of female (11.1%, $P = 0.017$), and non-white patients (12.8%, $P = 0.036$). Logistic regression adjusting for the other variables showed higher work and social difficulties were significantly associated with depression ($OR = 1.194$) (95% CI 1.106, 1.290, $P \leq 0.001$) and anxiety ($OR = 1.141$) (95% CI 1.065, 1.222, $P \leq 0.001$). This is in Table 1.

Table 1 Mann-Whitney *U* for WSA and Psychological Morbidities

Psychological morbidity	WSA Scores; Median (Interquartile range)	*U*	*P*
Depression (No Depression group; depression group)	0 (4); 27 (23)	316	≤0.001
Anxiety (No Anxiety group; anxiety group)	0 (4); 27 (23)	412.5	≤0.001

Conclusion: There was a low prevalence of depression and anxiety in our LTR cohort. However, WSA and GFR are predictive of psychological morbidity in LTR. WSA functionality was significantly associated with anxiety and depression. This should be factored during assessments and we recommend that WSA scores should be routinely collated for LTR.

OP350 PSYCHOLOGICAL MORBIDITY ACROSS THREE KIDNEY TRANSPLANT PATIENT GROUPS: A SINGLE CENTRE COMPARATIVE STUDY

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Background: Depression and anxiety in transplant patients are associated with increased mortality and co-morbidity. However, guidance on identifying those at risk is limited. We investigated psychological morbidity across three transplant patient groups (i) Long-term kidney transplant (LKT) >7 years post-transplant; (ii) 12–18 months post-transplant (PT); (iii) Failing grafts (GFR < 20 ml/min) attending Transplant Support Clinic (TSC).

Methods: Between 04/01/2019-11/03/2020 N = 427 were screened using (i) Patient Health Questionnaire (PHQ9) and (ii) Generalised Anxiety Disorder (GAD7). Scores were transformed into binary variable. Scores >10 catalogued 'depression/anxiety'. Fisher's Exact Test, Pearson's Chi-Square analysis and logistic regression modelling were performed to determine significant proportion differences between groups and identify associations between group and psychological morbidity.
Results: N = 357 completed questionnaires were analysed. N = 247 LKT of which N = 96(38.9%) were female (mean age 52.6 years). N = 51 PT of which N = 23(45.1%) were female (mean age 48.1 years). N = 59 TSC of which N = 32(54.2%) were female (mean age 49.19 years). Pearson's Chi-Square statistic was statistically significant. TSC had a greater proportion of depressive symptoms (33.9%) than PT (15.7%) and LKT (6.9%). LKT had the greatest proportion with no depressive symptoms (93.1%) (Table 1).

Table 1 Proportions across three groups based on PHQ-9 score. (N = 357)

	Patient Groups		
PHQ-9 Score Category	LKT (n = 247)	PT (n = 51)	TSC (n = 59)
No Depressive Symptoms (scores ≤10)	230 (93.1%)	43 (84.3%)	39 (66.1%)
Depressive Symptoms (scores >10)	17 (6.9%)	8 (15.7%)	20 (33.9%)

Pearson Chi-Square statistical significance was $P \leq 0.001$.
In a logistic regression model controlling for age and gender, TSC patients had 6.2 times higher odds of having PHQ-9 > 10 (95% CI 3.0, 13.1, $P < 0.01$) compared to LKT. Fisher's Exact Test revealed statistically non-significant differences between GAD7 categories across groups.
Conclusion: We have identified statistically significant differences in psychological well-being between three transplant groups. In particular, TSC patients are at greater odds of having depressive symptoms. Further interrogation is needed to determine factors contributing to psychological wellbeing.

IMPROVING TECHNIQUES IN LIVER TRANSPLANTATION: CHEF'S RULES FOR BETTER OUTCOME

OP351 RESULTS OF NON-ANATOMICAL REDUCTION COMPARED TO STANDARD LEFT LATERAL SECTION IN PEDIATRIC LIVER TRANSPLANTATION

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Background: Non-anatomical reduction of the left lateral liver section (LLS) and creation of monosegmental graft are the main options to address the challenge of large-for-size grafts in pediatric liver transplantation (LT). Any reduction of LLS, in turn, increases the risk of biliary and infectious complications due to the extended resection surface and. We compared the results of non-anatomical (NAR) reduction and standard LLS in pediatric LT recipients.
Methods: 90 (11%) of 790 LTs were performed in pediatric recipients. The reduction criteria were the size of the recipient's abdomen, shape of graft and thickness more than 7 cm, GW/RW > 4%. The technique of reduction was adopted from M. Kasahara [J.Pediatr Surg. 2008] with addition of oblique plane of III seg. transsection for thickness reduction when needed.
NAR was used in 24 patients (LDLT–18, SPLIT–2, DBD–4) with a median age of 8 [7;12] months, graft weight (GW) 214 [204; 256]g, GW/RW – 3 [2.5; 3.3]%. Urgent indications were in 2 LTs (9%). Standard LLS was used in 40 patients (LDLT–29, SPLIT–3, DBD–8) with a median age of 14 [7; 24] months, median GW 262 [216; 297] g, GW/RW 2.8[2.2; 3.4]%. Urgent indications were in 10 LTs (26%).
Results: GW/RW (P = 0.5), proportion of LDLT (71%–LLS and 72%–NAR, P = 0.5), the rate of relaparotomies (39%–LLS and 36 %–NAR, P = 0.5) and the incidence of infection (44%–LLS and 50%–NAR, P = 0.44) were comparable. The median GW was significantly lower in the reduction group (P = 0.048). GW correlated to AST (ρ = 0.42; P = 0.003) and ALT (ρ = 0.49; P = 0.0004) after 48h, as well as GW/RW to AST (ρ = 0.37; P = 0.008) and ALT (ρ = 0.45; P = 0.001). There was a trend towards a lower median age (P = 0.09), the frequency of all (31%, P = 0.4) and severe forms of EAD (18%, P = 0.3) in the NAR compared to the LLS group (42% and 28%, respectively), and hospital mortality (23%–LLS and 9%–NAR, P = 0.14). The rate of urgent indications (P = 0.09) and more complex graft revascularizations (P = 0.07) was higher in the standard LLS group.
Conclusions: Non-anatomical reduction of the LLS is a reliable way to overcome the risk of large-for-size graft when adapted to patient and graft and is associated with lower incidence of early graft dysfunction and hospital mortality compared with standard LLS transplantation.

OP352 BILIARY RECONSTRUCTION USING HIGH BILIARY RADICAL IS SAFE OPTION FOR MULTIPLE GRAFT BILE DUCT IN RIGHT LOBE LIVING DONOR LIVER TRANSPLANTATION

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Background: Multiple graft bile ducts (BDs) are related to higher incidence of biliary complications (BCs) and biliary reconstruction for multiple BDs still remains a technical challenge during living donor liver transplantation (LDLT). Especially, biliary reconstruction using high biliary radicals (right or left hepatic duct) of recipients for multiple BDs has very high probability of BCs secondary to devacularization and ischemia. Therefore, hepaticojejunostomy has been performed instead in cases with multiple BDs which are not close to each other although duct to duct anastomosis (DDA) has more physiological advantages.
Methods: Herein, we analyzed clinical outcomes through retrospective reviews 227 patients receiving DDA for right lobe grafts LDLT from January 2013 to September 2018. 87 LDLT using grafts with multiple BDs have been performed and among them, 39 patients received DDA using high biliary radicals with minimal hilar dissection, external biliary stents and mucosal eversion technique to reduce BCs. We compared clinical outcomes between these 39 patients and those receiving DDA using common hepatic duct of recipients for multiple graft BDs (CHD group).
Results: The incidence of biliary leakage and stricture were 10.3% and 12.8% and these outcomes were not different to those in CHD group. Neither overall patient survival nor graft survival differed significantly between the two groups. Moreover, these results were comparable to those in groups using graft with single graft BD during the same periods.
Conclusions: The choice of high biliary radicals as the recipient BDs for multiple graft BDs was not associated with higher incidence of BCs and furthermore, it could be a safe option for biliary reconstruction during LDLT.

OP353 RE-THINKING OF T-TUBE USE AT WHOLE LIVER TRANSPLANTATION: AN ANALYSIS ON THE RISK OF DELAYED GRAFT FUNCTION

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Background: In whole liver transplantation (LT), functional regeneration is essential for the graft to recover from the ischemia-reperfusion injury, and for the recipient to recover from the pre-LT cirrhosis-related complications. The failure of this process is clinically diagnosed as early allograft dysfunction (EAD). Bile acids have been identified as crucial trigger of liver regeneration, while persistent biliary inflammation has been associated with a detrimental effect. Thus, the use of a T-tube, an indwelling catheter in the biliary tract which interrupts the enterohepatic cycle of bile acids, might increase the risk of EAD after LT.
Methods: Retrospective study on a cohort of 257 LT recipients during the period 2010–2018. Exclusion criteria were split grafts, biliary or vascular complications, graft loss or patient's death, within postoperative day 14. EAD was defined according to the criteria of Olthoff et al, and graded according to the Model for Early Allograft Function (MEAF) score.
Results: EAD developed in 24.5% of recipients and the median MEAF score was 3.8 [interquartile range 2.8–5.6]. Both MEAF and EAD predicted 90-days post-LT mortality. A T-tube was used in 47.5% of cases. Recipients with a T-tube, compared to those without it, showed an higher MELD score at LT and received a graft from a older donor and with a longer total ischemia time. After propensity score matching of the two groups for these characteristics, the T-tube group showed a significantly higher prevalence of EAD and value of MEAF (T-tube vs no-T-tube, EAD: 29.4% vs. 17.8%, P = 0.039; MEAF: 4.3 [3.3–5.7] vs. 3.6 [2.5–4.6], P = 0.007).
Conclusions: In LT, T-tube use is an independent risk factor for EAD and predictor of MEAF, irrespective of graft quality and severity of pre-LT liver disease.

OP354 POST-LIVER TRANSPLANT INFERIOR VENA CAVA STENOSIS IN A LARGE VOLUME UK CENTRE.

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Background: Inferior vena cava stenosis (IVCS) is a rare complication of liver transplantation with a reported incidence rate of 3%. Limited clinical consensus exists on the management of IVCS. We report the management and outcomes of patients with IVCS at our transplant centre.
Methods: Relevant data were collected from adult patients who underwent liver transplantation at our centre between October 2014 and August 2020. These included demographics, investigation and management details with regards to IVCS. Values presented as % of total and median with interquartile range (IQR).
Results: Out of 636 liver transplants during the study period, 48 (7.6%) patients were investigated for possible IVCS. Of those, 14 (2.2% of total) were found to have IVCS, 85.7% (n = 12) were female. Only 2/14 were re-transplants and pre-transplant portal vein thrombus was present in 3 cases (21.4%). 10 livers (71.4%) were DBD donors. Normothermic machine perfusion was used in 4/14 patients. All 14 recipients found to have IVCS had had an implantation using a modified piggyback cavocavostomy technique. The IVCS was identified at a median of 25.5 days (19.7–30.8 days) following transplantation within the suprahepatic IVC in 92.9% (n = 13). Hemi-azygos collateralisation was seen in 4 cases (28.6%). 8 of the 14 recipients underwent intervention for IVCS, 6 patients were managed with balloon venoplasty, 1 patient required an IVC stent and 1 was managed surgically. Six of the recipients with IVCS died, 4 of whom had an intervention for their stenosis and 3 of these were within 90 days of their transplant. Pressures measured at the anastomotic stricture were higher in those who succumbed (median of 21 vs 12.5 mmHg; P = 0.017).
Conclusions: At our centre, cava-replacement technique was not associated with IVCS. Patients with more significant strictures (as evidenced by higher pressures at the anastomotic stenosis) may have an increased mortality risk.

OP355 PRE-LIVER TRANSPLANT MANAGEMENT OF NON-NEOPLASTIC PORTAL VEIN THROMBOSIS: A LONG TERM MONOCENTRIC EXPERIENCE

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Background: Non-neoplastic portal vein thrombosis (PVT) is a frequent complication of liver cirrhosis, and it was widely considered as a relative-contraindication to liver transplantation (LTx), in the past.
Methods: From April 2004 to October 2018, 1699 first adult LTx from deceased donors were performed in our LT centre. Among these, we managed 165 (10%) recipients with pre-LTx PVT. We aimed to describe: challenging management of PVT in cirrhotics, Yerdel classification before and after LTx, modality and timing of treatments, intra-operative findings, type of portal vein reconstruction, and PVT relapse.
Results: Recipients' median [IQR] age was 56.1 [51.0–61.3] years with a median [IQR] MELD score at LTx of 15 [12–18]. Underlying liver disease was: HCV = 39.4%, HBV = 26.6%, Alcohol = 15.2%, Other = 18.8%. Cirrhosis was complicated by hepatocellular carcinoma in 42% of cases, 75% of whom staged as Milano IN. Pre-LTx PVT Yerdel classification was: 1 = 46%, 2 = 41%, 3 = 13%. 39% of patients underwent radiological porto-systemic shunt (TIPS) placement; 40% was treated by anticoagulants alone and 21% received no treatment. Pre-LT downstaging of PVT was observed in 99(60%) recipients. PVT Yerdel classification at transplantation was respectively: 0 = 31.5%, 1 = 45.5%, 2 = 22%, 3 = 1%. Despite pre-LTx management, surgical portal vein thrombectomy was necessary in 64 (39%) patients, 3 (2%) venous patches were used and 1 (0.6%) cavo-portal transposition was performed. 1-, 3-, 5-, and 10-year grafts and recipients survival was 91%, 86%, 84%, 73% and 95%, 90%, 87%, 78%, respectively. All patients underwent anticoagulant prophylaxis after LTx; PVT relapse was observed in 6.6% of the cases, without compromising graft and patient survival.
Conclusion: A patient-tailored pre-LT PVT management can lead to a safe and feasible LTx. Extensive use of TIPS and anticoagulant therapy allowed LTx also in patients with extensive PVT with a direct portal vein anastomosis in the majority of patient.

OP356 PHYSIOLOGICAL RECONSTRUCTIONS IN LIVER TRANSPLANTATION WITH NON-TUMORAL EXTENDED PORTAL VEIN THROMBOSIS: RESULTS AT TWO LARGE VOLUME CENTRES

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Background: Although not representing an absolute contraindication, non-tumoral portal vein thrombosis (PVT) may increase the risk and technical complexity of liver transplantation (LT). Different types of physiological reconstructions are available to ensure an optimal blood flow into the liver from the splanchnic venous system.
Methods: Data of two large volume Transplant Centers collected consecutively (2000–2019) were retrospectively analyzed. Among 283 LT with PVT (n = 180 Bologna; n = 103 Bergamo), we selected 84 patients with PVT extended into mesenteric vein (MV) (Yerdel grade III–IV). Fifty one patients (61%) underwent a thrombectomy and T-T porto-portal anastomosis (TTA Group). In 33 cases (39%) a thrombectomy was not feasible and more complex physiological reconstructions were performed (Bypass Group): n = 10 mesenterico-portal by-pass, n = 14 anastomosis on splanchnic varix (gastric or choledochal) and n = 9 reno-portal anastomosis. Patient/graft survival and morbidity (complications within 90 POD) were evaluated.
Results: The clinical and surgical characteristics of the overall population and of the two subgroups (TTA vs Bypass) are shown in Table 1. The two groups were comparable except for the extension of PVT. As expected Yerdel grade IV was more frequent in Bypass (45.4%) than in TTA (11.7%) (P = 0.0005). The time of surgery, the need of PRBC transfusions and the median ICU stay were also similar. The rate of re-thrombosis was 5.8% in TTA vs 6% in Bypass (P = 0.97). The incidence of early complications was slightly higher in the latter (93.9%) although not significantly (P = 0.18); moreover, the severity was overlapping. Overall, the in-hospital mortality rate was 9.5%; of the 7 patients who died only three had surgery-related complications. Graft survival at 5 years was 67.9% TTA Group vs. 68.9% Bypass Group; log rank = 0.83. Five-year overall survival did not differ between the two groups (69.5% TTA Group vs. 71.7% Bypass Group; log rank = 0.93).
Conclusion: Physiological reconstructions are effective in the demanding surgical scenario of LT with extended PVT. Both TTA and Bypass procedures achieved remarkable rate of patient and graft survival at 5 years. The incidence of complications after surgery is high, but in most of cases they are manageable and do not require ICU admission.

Tab-1 Clinical and Surgical Characteristics	Descriptive Data	Overall n=84	TTA Group n=51	Bypass Group n=33	P
Recipient Age	median; [IC]	56 [53-58]	57 [54-60]	52 [48-59]	0.13
Male sex	(n-%)	56- 66.6	33- 64.7	23-69.6	0.67
BMI	median; [IC]	25 [24-26]	25.4[24.2-27.4]	24.5 [23.4-25.9]	0.49
Donor Age	median; [IC]	64 [57-70]	62 [56-67]	72 [62-74]	0.13
MELD at LT	median; [IC]	19 [18-21]	20 [18-22]	17 [15-22]	0.18
Upper abdomen Surgery	n-%	16- 19.2	11-21.5	5-15.1	0.36
HCC	n-%	58-69	37-72.5	21-63.6	0.38
Viral Etiology	n-%	50- 62.5%	33 – 64.7%	17 – 51.5	0.08
Esophageal varices	n-%	81 – 97.6	49-96.1	32- 96.9	0.76
TIPS at LT	n-%	7- 8.4	6 –11.7	1 – 3	0.15
Ascites	n-%	55-65.5	35- 68.6	20 – 60.6	0.45
Time of surgery (min)	median; [IC]	450 [420-480]	435 [420-480]	450 [405-510]	0.38
Blood Trasfusions PRBC (ml)	median; [IC]	1120 [850-1250]	1120 [840-1500]	1120 [750-1680]	0.97
Cold Ischemic Time (min)	median; [IC]	405 [390-435]	415 [395-440]	400 [360-436]	0.87
ICU stay (days)	median; [IC]	5 [4-6]	5[3-6]	5[4-7]	0.92
90 days Complications Rate	n-%	74-88	43-84.3	31-93.9	0.18
90 days Complications Severity Grade 3 Dindo-Clavien Grade 4 Dindo-Clavien	n-% n-%	34-40.4 13-15.4	22-43.1 10-19.6	12-36.3 3-9	0.14
Re-Thrombosis	n-%	5-5.9	3-5.8	2-6	0.97
In-hospital Mortality	n-%	8-9.5	4-7.8	4-12.1	0.51

RECIPIENT CHALLENGES IN LIVER TRANSPLANTATION: MAY THE FORCE BE WITH YOU

OP357 EFFECT OF PRE-TRANSPLANT SARCOPENIA ON THE ESTIMATION OF STANDARD LIVER VOLUME IN LIVING-DONOR LIVER TRANSPLANT CANDIDATES

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Background: The estimation of the standard liver volume (SLV) in living-donor liver transplantation (LDLT) candidates is of pivotal importance. The most commonly used formula are body weight (BW)-based. However end-

stage liver disease causes a significant modification of the body mass composition, making BW an unreliable anthropometric parameter. The aim of the study was to investigate whether LT candidates with sarcopenia are at an increased risk of receiving an inappropriate SLV estimation by standard BW-SLV formula.
Methods: Non-BW-SLV estimation formulas were tested in 262 LDLT donors, and compared to a standard BW-SLV formula. The anthropometric parameters used were the thoracic width (TW-SLV) and thoracoabdominal circumference (TAC-SLV). Subsequently, sarcopenic and non-sarcopenic LDLT candidates (total, 217 patients) were compared in terms of estimated BW-SLV (routine method) and non BW-SLV.
Results: In donors, TW-SLV showed comparable concordance with CT scan measured total liver volume as BW-SLV. The performance of TAC-SLV was low. In recipients, the prevalence of pre-LT sarcopenia was 30.4%. Sarcopenic patients were attributed a significantly lower BW-SLV than non-sarcopenic (sarcopenia versus no-sarcopenia, 1063.8 ml [1004.1–1118.4] vs. 1220.7 ml [1115.0–1306.6], $P < 0.001$), despite comparable TW-SLV, age, body high and gender prevalence. As a result, sarcopenic patients received a graft with a statistically lower weight at organ procurement, and developed more frequently a small for size syndrome(SFSS) according to the Dahm et al. (27.7% vs 6.8%, $P < 0.01$) and Kyushu (28.7% vs. 9.2%, $P < 0.01$) definition.
Conclusions: In sarcopenic patients, BW-SLV formulas are affected by an high risk of SLV underestimation, thus exposing them to an increased risk of post-LT SFSS.

OP358 A PROSPECTIVE ANALYSIS OF CLINICAL FRAILTY ASSESSMENT AND TELOMERE LENGTH IN A NATIONAL COHORT OF LIVER TRANSPLANT CANDIDATES

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Background: Frailty is a clinical condition characterised by loss of physiologic reserve and increased susceptibility to stressors. Incidence of frailty is increased in patients with cirrhosis compared to healthy elderly adults and has been associated with adverse outcomes in liver transplant candidates. This study aimed to assess multiple clinical frailty assessments and biomarkers of cellular ageing as predictors of decompensation-related hospitalisations, time on the waiting-list and post-transplant outcomes.
Methods: 80 patients were prospectively evaluated while undergoing liver transplant assessment. Clinical assessments included Liver Frailty Index (LFI), Fried Frailty Index (FFI), and Rockwood Frailty Score (RFS). Assessments were repeated at 3-monthly intervals whilst wait-listed and post-transplant. Relative telomere length (RTL) was measured in a subset of patients using qPCR. Outcomes included decompensation-related hospitalisations, time on the waiting-list and post-transplant outcomes.
Results: The prevalence of clinical frailty ranged from 20% to 37%, depending on the frailty score. Clinical frailty scores were highly correlated (LFI and FFI $r_s = 0.601$, $P < 0.005$, LFI and RFS $r_s = 0.513$, $P < 0.005$). MELD-Na was associated with increased RFS ($r_s = 0.244$, $P = 0.032$). Median FFI and RFS were significantly increased in patients with Child-Pugh C (FFI = 3. RFS = 4) compared to A and B (FFI = 1, U = 819 $P = 0.002$, RFS = 3 U = 766.5 $P = 0.035$). FFI was significantly higher in patients admitted with hepatic encephalopathy (mean rank = 18.56), compared to those without admission (mean rank 29.80, U = 134, $P = 0.039$). There was no significant association between RTL and MELD-Na or Child-Pugh. There was no significant associated between RTL and frailty measure or age, but there was a trend towards reduced RTL and both increased age ($r_s = -0.244$, $P = 0.088$) and increased frailty (LFI $r_s = -0.2$, $P = 0.164$, FFI $r_s = -0.131$, $P = 0.368$, RFI $r_s = -0.112$, $P = 0.438$).
Conclusions: Frailty was associated with both increased MELD-Na and Child-Pugh score. Frailty was also increased in patients admitted to hospital with HE. This is the first time telomere length has been investigated in this cohort of patients in regards to frailty, and demonstrates a negative correlation between the two.

OP359 FAST-TRACK LIVER TRANSPLANTATION: 100 MONTHS OF A FULL-FLEDGED ERAS PROTOCOL

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Background: Enhanced recovery after surgery (ERAS) has been shown to facilitate discharge, decrease length of stay (LOS), improve outcomes and reduce costs. We used this concept to design a comprehensive fast-track pathway (OR-to- discharge) before starting our liver transplant activity and then applied this protocol prospectively to every single patient undergoing liver transplantation at our institution, monitoring the results periodically. We now report our results after 100 months of activity.
Methods: Prospective cohort study of all the liver transplants performed since we started our program 100 months ago. Balanced general anesthesia, fluid restriction, thromboelastometry, inferior vena cava preservation and temporary portocaval shunt were strategies common to all cases. Our standard protocol for immunosuppression included steroids, tacrolimus (delayed in the setting of renal impairment, with basiliximab induction added) and mycophenolate mofetil. Tacrolimus dosing was adjusted using a Bayesian estimation methodology. Oral intake and ambulation were started very early.
Results: A total of 316 liver transplants were performed in 302 patients (241M/61F) over 100 months, mean age 57.1 ± 9.4 years, raw MELD score 15.2 ± 7.8 (MELD-Na 17.2 ± 8). Predominant etiologies were alcohol ($n = 178$) and HCV ($n = 99$), with hepatocellular carcinoma present in 166 (55%). Twenty-two of the 316 transplants were URGENT (7%) and thirteen of them were performed for Fulminant Hepatic Failure. Fourteen patients underwent combined liver and kidney transplants. The median operating time was 309 min (range 167–546) with median cold ischemia time of 267 min (130–628). We transfused PRBCs in the OR in 45 cases (14.2%) at an average of 2.4 ± 1.2 units per case. Median ICU LOS was 12.7 h, and median post-transplant hospital LOS was 4 days (2–82) with 43 patients (15.1%) going home by the 2nd posttransplant day, 115 (40.5%) by the 3rd, and 167 (58.8%) by the 4th, which defines the LOS of our fast-track group (2–4 days). Overall thirty-day-readmission rate was 35.6%, and it was significantly lower (28.7% vs. 45.3% $P = 0.0041$) in the fast-track group. Patient survival was 87.5% at 1 year and 78.9% at 5 years for the entire series.
Conclusions: Fast-Tracking of Liver Transplant patients is feasible and can be applied as the standard of care.

OP360 ARE WE READY FOR BARIATRIC SURGERY IN A LIVER TRANSPLANT PROGRAM? A META-ANALYSIS

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Background: Obesity-related non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) are two main causes of end-stage liver disease requiring a liver transplantation. Studies exploring bariatric surgery in the liver transplantation setting have increased in recent years; however, a systematic analysis of the topic is lacking to date. There are several factors to take into account in order to establish bariatric surgery in the transplantation, such as the indications and selection of patients, the time of bariatric surgery, the most appropriate weight reduction surgery technique, possible complications and immunosuppression that the patient will receive once the transplant has been performed. This meta-analysis was conducted to explore the perioperative and long-term outcomes of bariatric surgery in obese patients undergoing liver transplantation.
Methods: Electronic databases were systematically searched for studies reporting bariatric surgery in patients undergoing liver transplantation. The primary outcomes were postoperative complications and mortality. We also extracted data about excess weight loss, body mass index, and improvement of comorbidities after bariatric surgery.

Results: A total of 96 patients from 8 articles were included. Bariatric surgery-related morbidity and mortality rates were 37% (95% CI 0.27–0.47) and 0.6% (95% CI 0.02–0.13), respectively. Body mass index at 24 months was 31.02 (95% CI 25.96–36.09) with a percentage excess weight loss at 12 and 24 months of 44.08 (95% CI 27.90–60.26) and 49.2 (95% CI 31.89–66.66), respectively. After bariatric surgery, rates of improvement of arterial hypertension and diabetes mellitus were 61% (95% CI 0.45–0.75) and 45% (95% CI 0.25–0.66), respectively. In most patients, bariatric surgery was performed after liver transplant and the most frequent technique was sleeve gastrectomy.
Conclusions: Bariatric surgery can be performed safely in the setting of liver transplantation resulting in improvement of obesity-related comorbidities. The optimal timing and technique require further studies.

OP361 RISKS FACTORS FOR CHRONIC RENAL DYSFUNCTION IN LIVER TRANSPLANTED PATIENTS WITH DONOR AFTER CIRCULATORY DEATH: GENEVA SINGLE CENTER EXPERIENCE

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Background: Donation after circulatory death (DCD) is a growing source of liver transplantation (LT) and has come to represent almost 30% of all donation activity in Geneva. DCD LT are associated with an increased incidence of acute kidney injury (AKI) as well as chronic kidney disease (CKD) compared with donation after brain death, leading to a reduced patient and graft survival. We aimed to identify risk factors for chronic renal injury in a cohort of DCD recipients at the Geneva Transplantation Centre in order to optimise the donor-recipient match and to tailor immunosuppressive regimens in higher risk patients.
Methods: This is a retrospective single-center study of 20 consecutive patients who underwent a controlled (Maastricht III) DCD liver transplantation between January 2018 and September 2020. In an univariate analysis, we tested the correlation between the occurrence of AKI and CKD with following variables: donor, recipient age and BMI, model for end-stage liver disease, pre-LT kidney injury, recipient cardiovascular risk factors (rCVRF), need for renal replacement therapy (RRT), aspartate aminotransferase peak, intraoperative red cell concentrate requirement, functional warm and cold ischemia time, UK risk score.
Results: The incidence of perioperative AKIN 3 in DCD liver recipients was 40% (8 out of 20), with 37% requiring RRT (3 out of 8). 75% of the recipients with AKI progressed to CKD. We found a significant correlation between rCVRF (>1) and/or high rBMI (>27 Kg/m^2) and AKI ($P = 0.006$)/CKD ($P = 0.028$); however, no correlation was observed between pre-LT renal dysfunction and CKD. The UK risk score is able to predict AKI ($P = 0.035$) but not CKD.
Conclusions: In our monocentric study, we showed that recipient presenting more than 1 CVRF and/or a high BMI are at higher risk to develop CKD. A donor-risk score including rBMI could better predict CKD. A renal sparing immunosuppression protocol should be considered in these patients.

OP362 THE IMPACT OF HEPATIS-C VIRUS DIRECT ACTING AGENTS IN LIVER TRANSPLANTATION USING VERY OLD DONOR GRAFTS: A SINGLE CENTER ANALYSIS

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Background: Aim of our research is to evaluate the impact of new anti-hepatitis C-virus direct acting agents (DAA) treatment in the pre- or perioperative period in liver transplantation (LT) when very old grafts are used, by comparing the outcomes of this population to different control groups.
Methods: we retrospectively analyzed the results of a study group composed by HCV+ recipients who were treated with DAA in the pre- or peri-operative period with DAA and received a graft aged 70 or older. This group was compared to three different control groups: an historical untreated HCV positive population receiving an old donor graft (Group noDAA-HCV-OLD); an HCV negative population receiving an old donor graft during the same time period (Group noHCV-OLD); an HCV negative population receiving a younger donor graft (aged 18–69 years) during the same time period (Group noHCV-YOUNG).
Results: In the period 2015-2018 (DAA era), 511 LT were performed at our institution: 164 were performed on HCV+ recipients using donor grafts aged 70 or older, and 263 on HCV- recipients. Among these latter, 143 were performed using grafts older than 70, and 120 using donor whose age was between 18 and 69. The noDAA-HCV-OLD group was of 101 LT from 2007 to 2011 (pre-DAA era). Graft survival rates at 1 and 3 years were 88% and 81% in the DAA-HCV-OLD group and 82% and 68% in the noDAA-HCV-OLD group ($P = 0.007$). At multivariate Cox regression analysis for the risk of graft loss the use of DAA was the only protective factor (HR 0.35, $P < 0.001$). Graft survival rates was similar: in the DAA-HCV-OLD group and in the noHCV-OLD group ($P = 0.76$). At multivariate Cox regression analysis for the risk of graft loss no specific factor was significantly associated to a better graft survival. Graft survival rates at 1 and 3 years was 88% and 81% in the DAA-HCV-OLD group and 94% and 92% in the noHCV-YOUNG group ($P = 0.02$). The multivariate Cox regression in the post PSM population found HCV was the only detrimental factor (ß = 1.54, HR 4.64, $P = 0.04$).
Conclusions: DAA were able to zero HCV-recurrence related graft loss, and 3-years graft survival improved of 20.6%. Moreover, the outcomes of older graft recipients became equal irrespectively of their HCV-serological status. HCV-negative recipients of younger livers still enjoy better results if compared to those receiving an older graft.

MANAGING THE DIFFICULT PAEDIATRIC LIVER RECIPIENTS: ALL IS WELL THATS ENDS WELL

OP415 MANAGEMENT OF CONGENITAL PORTOSYSTEMIC SHUNTS

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Background: Congenital portosystemic shunts (CPSS) are rare vascular disorders causing encephalopathy, liver tumors and pulmonary complications. It has historically been treated by liver transplantation when developing complications. Today, treatment consists of endovascular or surgical closure to restore portal flow. Here, we present a single center experience using an anatomical/surgical classification.
Methods: A retrospective study was performed of pediatric patients with CPSS from 2000 to 2021 at Karolinska University Hospital (Sweden). Clinical features, association with pulmonary or liver failure, type of shunt, treatment and outcomes were reviewed. Blanc et al. classification was used to categorize CPSS.
Results: A total of 14 patients were identified. Median age at presentation was 1 month after birth. 9/14 were male. Associated syndromes were: hepatopulmonary syndrome (2/14) and clinically evident portal hypertension (3/14). The most common clinical symptom was neurological alterations (7/14) ranging from tiredness (5/14), lack of attention (6/14), development delay (4/14) to chronic encephalopathy (1/14). Type of shunt: 3/14 patients had extra-hepatic shunts, 6/14 had portocaval pattern shunt (PC) (5 end-to-side (ESPC) and 1 H-shaped PC), 2/14 had a persistent ductus venosus pattern and 3/14 had intra-hepatic shunts. In 3 patients, CPSS closed spontaneously (2 had small intrahepatic shunts and 1 H-shaped PC). Six patients were treated by endovascular technique and 5 with open surgery (2 meso-Rex by-pass, 1 one-step closure and 2 two-step closure). Surgery was performed when there was too high portal pressure after balloon occlusion test or due to anatomical characteristics of the shunt. Failure of treatment occurred in 2 occasions, plug migration and meso-Rex thrombosis. After treatment all patients experienced clinical improvement, in 11/14 patients ammonium levels normalized and 4/5 patients the benign tumors size reduced.
Conclusion: We present the experience with CPSS at our center. By adopting a surgical classification, we have observed that patients with a CT describing an ESPC or side-to-side type CPSS could benefit by a hybrid endovascular-surgical treatment. Intrahepatic portal flow could be re-established in all cases by occlusion of the shunt with clinical improvement.

OP416 HEPATOPORTOENTEROSTOMY VERSUS PRIMARY LIVER TRANSPLANTATION FOR BILIARY ATRESIA

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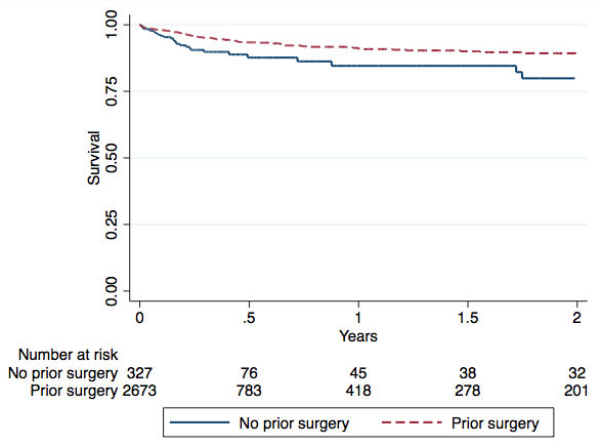
Introduction: Kasai hepatoportoenterostomy (HPE) is the standard of care for children with biliary atresia (BA). Some, however, have advocated for primary liver transplantation (pLT) as a superior treatment approach. The aim of this study was to characterize the rate of pLT in the treatment of BA and compare outcomes of pediatric candidates with BA listed for liver transplantation with and without prior HPE.
Methods: The SRTR/OPTN database was retrospectively reviewed for all children with BA listed for primary liver transplant in the United States between March 2002 and December 2017. Candidates were categorized as pLT if they had not undergone previous abdominal surgery prior to listing.
Results: Three thousand and six patients with BA were listed for LT during the study period. Only 11% of these candidates had not undergone previous abdominal surgery (Table 1). Candidates without prior abdominal surgery had higher risk for waiting list mortality (adjusted HR 0.53, 95% CI 0.34–0.84, $P = 0.007$; Figure 1). Among those that successfully underwent LT, there was no significant difference in patient ($P = 0.9$) or graft survival ($P = 0.6$) by prior surgery status.
Conclusions: Given the waiting list survival benefit of HPE prior to liver transplantation, HPE should remain the gold standard initial surgical treatment for children with BA.

Table 1. Candidate Characteristics at Listing by Previous Abdominal Surgery Status

Mean (SD)/ n (%)	No Previous Abdominal Surgery (n = 327, 11%)	Previous Abdominal Surgery (n = 2,679, 89%)	P-Value
Age, years	1.04 (3.03)	1.72 (3.70)	**0.002**
Weight, Kg	9.73 (10.38)	11.73 (12.45)	**0.005**
Female	215 (66%)	1,587 (59%)	**0.02**
Race/Ethnicity			**0.001**
White	131 (40%)	1,327 (50%)	
Black	77 (24%)	436 (16%)	
Hispanic	65 (20%)	580 (22%)	
Asian	35 (11%)	208 (8%)	
Other	19 (6%)	128 (5%)	
Private insurance	134 (41%)	1,256 (47%)	**0.04**
Calculated MELD/PELD score	14.51 (11.22)	11.55 (10.63)	**< 0.001**
Listing score including exception points			**< 0.001**
< 15	166 (51%)	1,686 (63%)	
16-30	120 (37%)	782 (29%)	
> 30	17 (5%)	81 (3%)	
Status 1	18 (6%)	91 (3%)	
TIPS	2 (1%)	13 (1%)	0.7
Mechanical ventilation	4 (1%)	80 (3%)	0.07
Dialysis	2 (1%)	14 (1%)	0.8

SD = standard deviation; MELD = model for end-stage liver disease; PELD = pediatric end-stage liver disease; TIPS = transjugular intrahepatic portosystemic shunt



OP417 THE ROLE OF VASCULAR ADHESION PROTEIN-1 IN THE PATHOGENESIS OF CHRONIC ALLOGRAFT HEPATITIS AFTER PAEDIATRIC LIVER TRANSPLANTATION

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Background: Whilst the overall survival of paediatric liver transplant (LT) recipients has improved, the long-term graft outcome remains uncertain. Studies of protocol liver allograft biopsies demonstrated a high prevalence of unexplained graft inflammation and graft fibrosis in biopsies obtained >1 year post-LT in children with normal liver biochemistry. The pathogenic mechanisms of this late graft injury remain mostly unknown. Vascular adhesion protein-1 (VAP-1) is a membrane-bound amine oxidase that promotes leukocyte recruitment to the liver and inflammation. This study aims to assess the role of VAP-1 in the pathogenesis of graft inflammation and fibrosis.
Methods: We conducted a single-centre retrospective analysis of patients with a 10-year protocol liver biopsy ($n = 22$) and a clinically indicated biopsy for acute cellular rejection (ACR; $n = 9$). Chromogenic staining and immunofluorescence staining were carried out for assessment of VAP-1 expression and distribution. The expression of VAP-1 was also determined by quantitative RT-PCR of AOC3 mRNA in liver tissue. Statistical analysis included t-test for independent values to assess the PCR results. P - value < 0.05 was judged as statistically significant.
Results: Histopathological evaluation of the 22 protocol biopsies showed normal histology ($n = 4$), graft hepatitis ($n = 9$) and fibrosis without inflammation ($n = 9$). Chromogenic immunostaining showed a sinusoidal and pericentral pattern of VAP-1 expression, especially in patients with graft hepatitis and perivenular fibrosis. In general, however, chromogenic immunostaining did not show a difference between diseased and normal biopsies. Confocal microscopy using CD31 as an endothelial marker and α-smooth muscle antigen (α-SMA) showed a strong co-localisation of VAP-1 and α-SMA in liver biopsies of patients with graft hepatitis. Quantitative RT-PCR of AOC3 mRNA demonstrated significantly greater expression of VAP-1 in patients with chronic graft hepatitis than in patients with normal histology, fibrosis without inflammation or ACR.
Conclusion: Our findings suggest a role of VAP-1 in graft hepatitis in the pathogenesis of graft fibrosis after paediatric LT. We plan a multi-centre study to assess the role of VAP-1 as a biomarker in tissue and sera for chronic graft injury prospectively.

OP418 VEIN OUTFLOW OBSTRUCTION AFTER LEFT LATERAL SEGMENTS TRANSPLANT: EXPERIENCE AT A LARGE PEDIATRIC TRANSPLANTATION CENTER.

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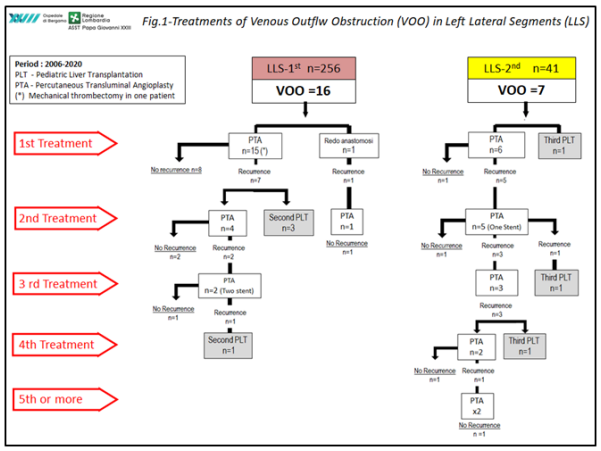
Background: Vein outflow obstruction (VOO) is a known cause of graft and patient loss after pediatric liver transplantation (PLT). The purpose of our study was to address the incidence, diagnosis and therapeutic modalities of VOO in a cohort of left lateral segment (LLS) recipients.
Methods: From 2006 to 2020, 305 LLS were performed and the procedures were stratified according to the progressive number of transplant: LLS-1st ($n = 256$), LLS-2nd ($n = 41$) and LLS-3rd ($n = 8$).
Results: 23 recipients (23/256; 7.5%) experienced VOO. Sixteen VOO were found in LLS-1st grafts (16/256; 6.2%), 7 in LLs-2nd (7/41; 17%) and none in LLS-3rd. The incidence of VOO was higher in LLS-2nd as compared with LLS-1st ($P = 0.01$), however, incidence of variant hepatic vein anatomy with 2 separated segmental veins was not significantly different between LLS-1st (37%) and LLS-2nd (43%) ($P = 0.80$).VOO had been diagnosed from 1 day to 4.31 years after transplantation. The median follow-up time was 3.33 years (range 0.32–13.7 years). Most of them (15/23:65%) occurred during the first year after transplant. In the first 2 months after transplant, the diagnosis was only based on ultrasound finding. In LLS-1st,

out of 16 VOO, one patient was treated with surgical revision while PTA (Percutaneous Transluminal Angioplasty) was performed in 15 children. Eleven patients (11/15:73%) had complete resolution of VOO and out of them 8 children needed just one PTA, while multiple PTA attempts were performed in 3 patients. In 4 cases (4/11:36%) the graft was lost. In LLS-2nd group, one patient with VOO received retransplantation as first treatment; 6 children were treated with PTA with success in 4 cases but 2 patients failed and underwent retransplantation (Figure 1).
Conclusion: VOO after PLT is an unusual but critical complication leading to graft loss in 1/3 of cases. The incidence was significant higher in LLS-2nd as compared with LLS-1st. PTA was a safe and efficient treatment for venous outflow obstruction in most cases.



OP419 LIVER TRANSPLANTATION FOR LANGERHANS CELL HISTIOCYTOSIS: A PROTOCOL BASED APPROACH

Jagadeesh Menon[1], Naresh Shanmugam[1], Joseph Valamparampil[1], Vimal Kumar[2], Mukul Vij[3], Ashwin Rammohan[4], Abdul Rahman Hakeem[5], Mohamed Rela[4]
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Background: Liver involvement in Langerhans cell histiocytosis (LCH) can be spectrum varying from asymptomatic hepatomegaly to secondary sclerosing cholangitis with cirrhosis, with or without decompensation and portal hypertension (PHTN). Modification of conventional approach is required for treating these subset of patients with LCH having advanced liver disease.
Methods: We did a retrospective analysis on patients (n = 8) who had advanced liver disease due to of LCH, referred to our centre. The demographics, clinical profile, chemotherapy protocols, particulars of liver transplant (LT), graft survival and patient survival in follow-up period were analysed.
Results: Five were patients were males and three were females. The median age of diagnosis of LCH was 25 (9–48) months which was confirmed by biopsy of skin 4 (50%), lymph node 3 (37.5%) and nail 1 (12.5%). All patients had PHTN at presentation with 4 (50%) having hepatic decompensation (DCLD). All patients with decompensated cirrhosis 3 (37.5%) except one, was treated with Cytarabine & Prednisolone (modified protocol) and rest with Vinblastine & Prednisolone based chemotherapy (conventional LCH III protocol). 2 (50%) patients in the DLCD group had non-response to chemotherapy with 1 patient dying of septicemia. Rest 6 (75%) underwent LT after a pre transplant PET scan showing disease remission, with indications being DCLD (n = 2) and PHTN (n = 4). Two patients had underwent urgent LT in between chemotherapy, as the liver disease was progressing (after 2 & 6 cycles respectively). The median period of LT form the time of diagnosis was 28 (2–195) months. After a median follow-up of 30.5 (10.5–50) months, all patients are alive with normal graft function and no disease recurrence.
Conclusions: Modified chemotherapy is effective in inducing disease remission in patients with LCH presenting with advanced liver disease without causing hepatic or systemic toxicity. Early LT can be successfully offered in such scenarios once the primary disease is in remission.

OP420 COMPARISON OF CYSTATIN C, CREATININE AND IOHEXOL CLEARANCE IN PEDIATRIC LIVER TRANSPLANTATION - A RETROSPECTIVE COHORT STUDY

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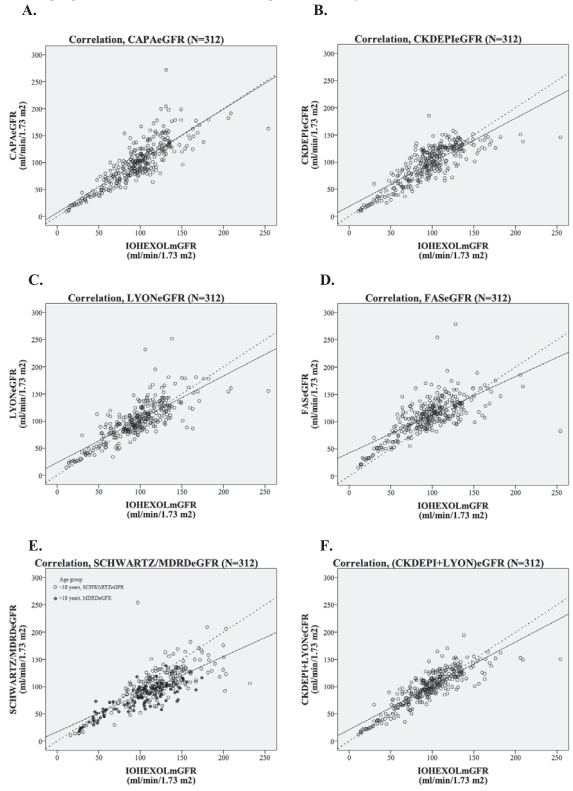
Background: Impaired renal function after pediatric liver transplantation (LT) is a recognized problem. Accurate monitoring of glomerular filtration rate (GFR) is imperative to detect declining renal function. GFR can be estimated via s-creatinine (eGFRcrea) and/or p-cystatin C (eGFRcyst) or measured by inulin and/or iohexol clearances (mGFRinulin/iohex). We retrospectively compared eGFRcrea and eGFRcyst, to mGFRiohex after LT.
Methods: Data from 91 children with 312 concomitant measurements of s-creatinine, p-cystatin C, and iohexol clearance, obtained between 2007 and 2015, were analyzed. eGFR was calculated by using the p-cystatin C-based CAPA (Caucasian, Asian, pediatric and adult cohort) and CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formulas, and the s-creatinine-based Schwartz-LYON, FAS (Full age spectrum), revised Schwartz and MDRD (Modification of Diet in Renal Disease) formulas. Also, the arithmetic means of cystatin C-based and creatinine-based equations were used. Every calculated eGFR was compared to mGFRiohex in statistical correlation, accuracy, precision, bias, and misclassifications.
Results: Among the different equations, p-cystatin C-based formulas (CAPA and CKD-EPI) as well as the s-creatinine-based Schwartz-LYON formula showed the most correct estimates regarding accuracy (84%–87.5%), bias (0.19–4.0 ml/min/1.73 m^2), and misclassification rate (24.7%–25%). In patients with renal function <75 ml/min/1.73 m^2, cystatin C-based formulas were significantly more accurate and less biased than creatinine-based formulas.
Conclusions: In conclusion, s-creatinine could be used in a clinical setting on a regular basis in liver transplanted pediatric patients, with reliable results, if eGFR is calculated by the Schwartz-LYON formula. When suspected renal dysfunction, cystatin C-based eGFR should be calculated, since it gives more accurate and less biased estimates than creatinine-based eGFR, and should be confirmed by mGFR (iohexol).

Figure 1. A-F. Regression diagrams for respective eGFR to mGFR in all ages. Full line indicating regression line. Dotted line indicating line of identity.



T- AND B-CELL RESPONSE TO SARS-COV2 IN SOT

OP427 SARS-COV-2 REACTIVE CELLULAR AND HUMORAL IMMUNITY IN TRANSPLANT POPULATION IS SIMILAR TO THE GENERAL POPULATION DESPITE IMMUNOSUPPRESSION

Constantin Thieme[1], Moritz Anft[2], Krystallenia Paniskaki[3], Arturo Blázquez Navarro[1,2], Adrian-Atila-Nicolas Doevelaar[2], Felix S. Seibert[2], Bodo Hoelzer[2], Margarethe Jusine Konik[3], Toni Luise Meister[3], Stephanie Pfänder[3], Eike Steinmann[3], Marc Moritz Berger[4], Thorsten Brenner[4], Uwe Kölsch[5], Sebastian Dolff[3], Toralf Roch[1,2], Oliver Witzke[3], Peter Schenker[6], Richard Viebahn[6], Ulrik Stervbo[2], Timm H. Westhoff[2], Nina Babel[1,2]

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Background: The ability of transplant (Tx)-patients to generate a protective antiviral response under immunosuppression is pivotal in COVID-19 infection. However, analysis of immunity against SARS-COV-2 is currently lacking.
Methods: Here, we analyzed T cell immunity directed against SARS-CoV-2 spike-, membrane-, and nucleocapsid-protein by flow cytometry and spike-specific neutralizing antibodies in ten Tx in comparison to 26 non-immunosuppressed (non-Tx) COVID-19 patients.
Results: Tx-patients (seven renal, one lung, and two combined pancreas-kidney transplants) were recruited in this study during the acute phase of COVID-19 with a median time after SARS-CoV-2-positivity of 3 and 4 days for non-Tx- and Tx-patients, respectively. Despite immunosuppression, we detected antiviral $CD4^+$ T cell-response in 90% of Tx-patients. SARS-CoV-2-reactive $CD4^+$ T cells produced multiple pro-inflammatory cytokines, indicating their potential protective capacity. Neutralizing antibody-titers did not differ between groups. SARS-CoV-2-reactive $CD8^+$ T cells targeting membrane- and spike-protein were lower in Tx-patients, albeit without statistical significance. However, frequencies of anti-nucleocapsid-protein-reactive, and anti-SARS-CoV-2 polyfunctional $CD8^+$ T cells, were similar between patient cohorts. Tx-patients showed features of a prematurely aged adaptive immune system, but equal frequencies of SARS-CoV-2-reactive memory T cells.
Conclusions: In conclusion, a polyfunctional T cell immunity directed against SARS-CoV-2-proteins as well as neutralizing antibodies can be generated in Tx-patients despite immunosuppression. In comparison to non-immunosuppressed-patients, no differences in humoral and cellular antiviral-immunity were found. Our data presenting the ability to generate SARS-CoV-2-specific immunity in immunosuppressed patients has implications for the handling of SARS-CoV-2-infected Tx patients and raises hopes for effective vaccination in this cohort.

OP428 LONG TERM IMMUNITY TO SARS-COV-2 AMONG SOLID ORGAN TRANSPLANT RECIPIENTS

Alexandre Fava[1], Laura Donadeu[2], Vincent Pernin[3], Maria Meneghini[1], Elena Crespo[2], Núria Sabé[4], Laura Llado[5], José Gonzalez-Costello[6], Edoardo Melilli[1], Nuria Montero Perez[1], Anna Manonelles[1], Josep Cruzado[1], Francesc Moreso[7], Manuel Lopez[8], Carme Facundo[9], Ignacio Revuelta[10], Marta Crespo[11], Carolina Santana[12], Olivier Thaunat[13], Oriol Bestard[1]

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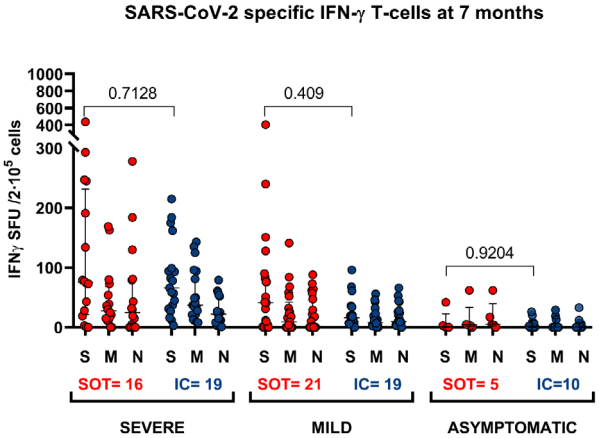
Background: Long-term immunity is key to prevent from pathogen re-infections. Recent reports have described a maintenance of SARS-CoV-2-specific adaptive immunity among immunocompetent (IC) individuals up to 8 months after COVID-19 infection. Nevertheless, whether responses persist among Solid Organ Transplant (SOT) recipients remains unknown.
Methods: SARS-CoV-2-specific serological and functional B and T-cell memory immune responses against main immunogenic antigens (S, M N) were assessed by ELISA and by a FluorSpot assay measuring multiple cytokine producing T cells (IFN-γ, IL2, IFN-γ/IL-2, IL5/IL21) in two groups of COVID-19 convalescent patients: 42 SOT and 48 IC patients, after a median of 211 (IQR, 194-223) days. Patients were stratified according to the severity of COVID-19 infection as: severe hospitalized (n = 35), mild symptoms (n = 40) or asymptomatic (n = 15).
Results: Patients developing a severe disease displayed higher anti-Spike IgG titters than those affected from a milder or asymptomatic infection. However, no differences were found between SOT and IC groups (Table 1). A similar pattern was found regarding SARS-CoV-2-specific cytokine-producing T-cell frequencies, with the highest immune reactivity among patients having developed most severe COVID-19 infection, without differences between SOT and IC patients (Figure 1). A high correlation was found between SARS-CoV-2(spike Ag) IgG-producing memory B cells (mBc) and anti-Spike IgG titters in serum (r = 0.4323, P = 0.0095). Nonetheless, a number of seronegative patients (12/35) did show detectable circulating SARS-CoV-2-specific mBc, especially among the mild/asymptomatic group.
Conclusions: Our data show that SARS-CoV-2 elicits a long-lasting adaptive cellular immune response among SOT patients, similarly to those IC patients. However, the severity of COVID-19 infection seems to drive the strength of adaptive immune responses also during long-term convalescence. The high correlation between SARS-COV-2-specific circulating antibodies and its mBc frequencies, strongly suggests a direct role of peripheral mBc in the maintenance of long-lasting serological memory against the virus.

Table 1

Median IgG titters (UA/ml)	SOT	IC	*P*-value
SEVERE	55.5	80.6	0.2066
MILD	12.8	5.37	0.1585
P-value	**0.0354**	**<0.0001**	



OP429 SARS-COV-2-SPECIFIC SEROLOGICAL AND FUNCTIONAL T-CELL IMMUNE RESPONSES DURING ACUTE COVID-19 IN SOLID ORGAN TRANSPLANT PATIENTS

Alexandre Fava[1], Laura Donadeu[2], Vincent Pernin[3], Maria Meneghini[4], Elena Crespo[5], Núria Sabé[6], Laura Llado[7], José Gonzalez-Costello[8], Edoardo Melilli[4], Nuria Montero Perez[4], Anna Manonelles[9], Josep Cruzado[4], Olivier Thaunat[10], Oriol Bestard[4]

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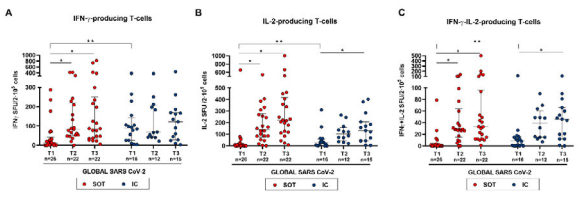
Background: The description of protective humoral and T-cell immune responses specific against SARS-CoV-2 has been reported among immunocompetent (IC) individuals developing COVID-19 infection. However, its characterization and determinants of poorer outcomes among the at-risk Solid Organ Transplant (SOT) patient population has not been thoroughly investigated.
Methods: Cytokine-producing T-cell responses such as IFN-γ, IL-2 and polyfunctional IFN-γ/IL-2 against main immunogenic SARS-CoV-2 antigens (Spike [S], Membrane [M] and Nucleocapsid [N]); along with IgM/IgG serological immunity, were tracked in SOT ($n = 28$) during acute infection and at 2 consecutive time-points over the following 40 days of convalescence. These results were compared to matched IC ($n = 16$) patients admitted with similar moderate/severe COVID-19.
Results: We describe the development of robust serological and functional T-cell immune responses against SARS-CoV-2 among SOT patients, similarly to IC patients up to 40 days after infection. However, at the infection onset (day 7 after diagnosis), despite no differences on IgG titers, SOT displayed lower IgG seroconversion rates (77% vs. 100%; $P = 0.044$) and lower median cytokine-producing T-cell frequencies against three main immunogenic antigens (S,M,N) Figure 1). Interestingly, SOT with the poorest outcomes displayed significantly hampered IL-2-producing T-cell responses, especially against antigen N, than those with a more benign course.
Conclusions: Our data show that SOT achieve comparable functional immune responses than immunocompetent individuals after moderate/severe COVID-19, despite an initial delay, which may entail poorer clinical outcomes among this population.

Figure 1



OP430 TRANSPLANT PATIENTS ARE ABLE TO GENERATE SARS-COV-2 CROSS-REACTIVE MEMORY B AND TFH CELLS DESPITE IMMUNOSUPPRESSION

Krystallenia Paniskaki[1], Moritz Anft[2], Constantin Thieme[3], Sarah Skrzypczyk[2], Margarete Justine Konik[1], Sebastian Dolff[1], Timm H. Westhoff[4], Guido Heine[5], Ulrik Stervbo[2], Oliver Witzke[1], Nina Babel[2,3]

[1]University Hospital Essen, University Duisburg-Essen, Department of Infectious Diseases, West German Centre of Infectious Diseases, Essen, Germany, [2]Marien Hospital Herne, University Hospital of the Ruhr-University Bochum, Center for Translational Medicine and Immune Diagnostics Laboratory, Medical Department I, Herne, Germany, [3]Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin-Brandenburg Center for Regenerative Therapies, and Institute of Medical Immunology, Berlin, Germany, [4]Marien Hospital Herne, University Hospital of the Ruhr-University Bochum, Medical Department I, Herne, Germany, [5]University Hospital Schleswig Holstein, Department of Dermatology and Allergy, Kiel, Germany

Background: Preexisting immune responses to seasonal endemic coronaviruses or other pathogens might have a pivotal role in protection against SARS-CoV-2. While preexisting SARS-CoV-2-reactive T cells were previously described for immunocompetent populations, data on preexisting immunity in transplant population and more importantly its correlation with clinical outcomes is currently lacking.
Methods: In this study, we analyzed the preexisting B and T cell immune responses against SARS-CoV-2 in 26 unexposed kidney transplant recipients (Tx) and non-transplant individuals (non-Tx) in comparison to 22 convalescent Covid-19 patients by flow cytometry.
Results: We detected Spike protein SARS-CoV-2-specific B cells in 64% of unexposed Tx and 33% non-Tx patients, whereas 62% of convalescent patients showed SARS-CoV-2-specific B cells. In both unexposed groups, SARS-CoV-2 IgG antibodies were not detectable. In comparison to convalescent patients, unexposed patients showed lower magnitude of Spike-specific B cells, however, without a statistical difference. Of interest, the magnitude of SARS-CoV-2-specific T cell immunity in Tx patients was comparable to non-Tx patients. In line with detectable SARS-CoV-2-specific memory B cells, we detected SARS-CoV-2-reactive follicular Th cells ($CD4^+CD154^+CD137^+CXCR5^+$) in 61% of the unexposed cohort without statistically significant differences between Tx and non-Tx. Follow-up clinical data of unexposed cohort between 01.03.2020 and 15.01.2021 revealed no clinical history of SARS-CoV-2 infection.
Conclusion: We demonstrate memory B cells and follicular T cell immunity against SARS-CoV-2 in unexposed Tx and non-Tx adults suggesting preexisting immunity. Tx patients present the ability to generate cross-reactive B and T cells despite immunosuppression. Although first data demonstrate no clinical manifestation of COVID-19 in patients with pre-existing immunity, further larger studies are required to demonstrate the antiviral protection.

OP431 SYSTEMATIC SCREENING FOR SARS-COV-2 S1/S2 ANTIBODIES HELPS TO BETTER ASSESS THE REAL INCIDENCE OF COVID-19 IN KIDNEY TRANSPLANT RECIPIENTS

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Aims and Background: Early estimations of COVID-19 incidence in kidney transplant recipients (KTRs) were biased since relying only on PCR-confirmed and/or severe cases. Systematic serological testing allows to a posteriori diagnose COVID-19 in asymptomatic patients. Therefore, combining serological testing with PCR may help to better assess the real incidence of COVID-19.
Methods: This monocentric prospective study focuses on the first wave of the pandemic in Belgium: from 01/03/20 to 30/09/20, all KTRs were asked about symptoms suggestive of COVID-19. From 01/06/20, they were offered a systematic serological screening using the DIASORIN chemiluminescence immunoassay SARS-CoV-2 S1/S2 IgG. Results of all SARS-CoV-2 PCRs performed for any reason during the study period were extracted from medical files. COVID-19 cases were defined as positivity of any of these 2 tests, and further categorized as being symptomatic or not.
Results: The initial cohort included 704 KTRs. During the study period, 17 patients died (independently of COVID-19), 5 returned to dialysis (independently of COVID-19) and 28 new KT were performed: all these cases contributed to the exposed population. From this cohort, 525 (74.6%) accepted to be serologically tested. The number of PCR-proven COVID-19 cases was 14/704 (2.0%), only 1 being asymptomatic (systematic screening). All 14 were screened for antibodies with a seroconversion rate of 78.6%. Another set of 14 KTRs were diagnosed based only on serology, 6 being strictly asymptomatic. Among the 8 symptomatic KTRs, 2 had been falsely tested negative by PCR. No PCR testing had been performed in the remaining 6 cases. Combining information from both PCR and serology suggests a total incidence of COVID-19 of 4.0% (confidence interval 95%: 2.5%–5.4%).
Conclusions: Systematic serological screening doubled the estimated incidence of COVID-19 in our cohort. The seroconversion rate among PCR-proven COVID-19 cases was lower than in the general population.

OP432 COMPARISON OF THE IMMUNE RESPONSES OF RENAL TRANSPLANT RECIPIENTS AFTER COVID-19 VERSUS SARS-COV2 VACCINATION

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Background: Because kidney transplant recipients (KTR) are at very high risk of severe disease and mortality following SARS-Cov2 infection, they have been defined as a priority population to receive RNA-based vaccination. However, KTR were excluded from the pivotal studies, which evaluated the efficiency of these new vaccines. Due to therapeutic immunosuppression, the short and long-term efficiency of anti-SARS-Cov2 vaccination in KTR population remain to be determined.
Methods: In the present study, anti-SARS-Cov2 humoral and cellular specific immune responses will be monitored in KTR after clinically symptomatic infection ($n = 67$, COVID KTR) or RNA vaccination ($n = 100$, Vacc KTR). Results of the 2 cohorts of KTR will be compared between them and with those of 2 cohorts of matched healthy volunteers (HV).
Preliminary results: COVID KTR and HV all developed early anti-SARS-Cov2 IgM. However, while all COVID HV also developed high titers of anti-SARS-Cov2 IgG, only 66% of KTR did the same. Of the remaining COVID KTR, 25% developed low titers (10–20 less) and 10% had no detectable IgG response. This led us to suspect a defective germinal center response in KTR that was confirmed by in vitro functional assay enumerating circulating anti-SARS-Cov2-specific $CD4^+$ T cells. Cytotoxic T cell responses in COVID KTR and HV population are currently under investigation. These data will be confronted with patients' clinical pictures to establish protective correlates. The vaccination campaign of KTR start this week in our transplantation centre and we have already obtained the authorisations to enrol 100 KTR and 30 HV.
Conclusions: In a few months, we expect to be able to provide a precise estimation of the efficiency of mRNA vaccination in KTR. Identification of the variable associated with the response to vaccine will be helpful to clinicians to select the appropriate care for each patient.

LEARNING FROM EACH OTHER TO IMPROVE ORGAN DONATION

OP433 OVERVIEW OF COLLABORATIVE APPROACH TO HELP THE DEVELOPMENT OF ORGAN AND TISSUE DONATION AND TRANSPLANTATION AT EUROPEAN LEVEL.

Martí Manyalich[1,2,3], Chloe Balleste[2,3], Maria Gomez[3], Estephan Arredondo[3], Entela Kondi[3]

[1]Hospital Clinic of Barcelona, Transplant Consulting, Barcelona, Spain, [2]University of Barcelona , Barcelona, Spain, [3]Donation and Transplantation Institute, Barcelona, Spain

Background: In Europe yearly are performed around 34 500 transplants. But nevertheless, much more are needed to satisfy the needs of the patients in waiting list for a transplant. The distribution of the performed transplants among the European countries is very heterogeneous attributed to the very different donation and transplantation (D&T) systems. Cooperation and exchanging experience and knowledge are mandatory to improve the activity and to unify the procedures. Therefore, several European initiatives supported by the EU Commission have been carried out to address this issue.
Methods: Since 2004 different EU consortiums have joint efforts to design and implement actions through projects (Figure 1) in the following identified levels of cooperation:
-Education of health care professionals and general population in organ and tissue D&T
-Create quality system of tissue banking and in hospital performance of the D&T practice.
-Establish legislative, organizational, and institutional recommendations to develop D&T programs.
Results: 7 consortiums have been created with the participation of 19 EU countries. More than 9000 health care professionals and more others from general public have been trained so far and educational tools have been created. Guide of recommendation and models for EU tissue banking Accreditation have been established as well as a methodology to evaluate the organ D&T performance at hospital level with 131 Quality Criteria and 31 Quality Indicators.
Conclusions: The cooperation between the countries has proved to be essential to the development of D&T programmes among the European countries. Exchange of experience and identification of best practices facilitate the role model systems that could be adapted to the less developed countries. Successful training programs reaching different profiles of population have produced significant improvements in D&T.

OP434 INCREASE ORGANS PROCURED AND TRANSPLANTED VIA A COMPREHENSIVE, INTEROPERABLE, AND SECURE DIGITAL DONOR AND TRANSPLANT MANAGEMENT PLATFORM

Jonathan Baldanza, John Piano
Transplant Connect, Los Angeles, United States

Background: One of the barriers to increasing the number of donors and transplants is the lack of an integrated, real-time clinical workflow platform. It is well understood that costly inefficiencies exist in the current fragmented donation and transplantation ecosystem: systems operate in silos without seamless sharing of key data. A modern, interoperable digital system can directly increase the number of life-saving organs procured and transplanted.
Methods: We hypothesize that the use of the comprehensive iTransplant™ platform increases the number of organs procured and transplanted. The platform is a modern web-based system which provides advanced communication tools and securely interfaces with external systems such as hospital EMRs and laboratory LIS systems: referrals, hospital charts and test results are received in real-time in the platform via secure web-service interfaces.
Results: The use of iTransplant™ has led to a significant increase in referrals and organs transplanted: over a period of 19 months in 1 hospital system implementation during which the only major process change was the adoption of this electronic interface, the annualized average shows a 49% increase in vented referrals (173–258), a 125% increase in organ donors (6.7–15) and a 78% increase in organs transplanted (25.3–45). Over the same time period, the integration with lab systems saved over 1400 hours of staff time and increased patient safety by eliminating manual transcription of lab results.
Conclusions: Continued successful results are achieved internationally in increasing the number of procured and transplanted life-saving organs as a result of: (1) the automated, seamless and electronic receipt of referrals and donor data by Organ Procurement Organizations in their iTransplant™ Platform, (2) the elimination of manual data transcription, and (3) the increase in the quality and timeliness of patients' data being available to donation and transplantation professionals.

Figure 1:

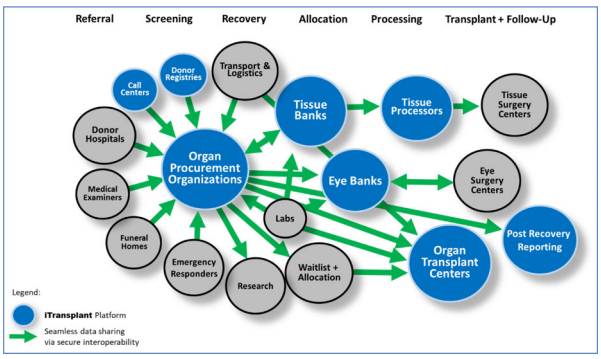
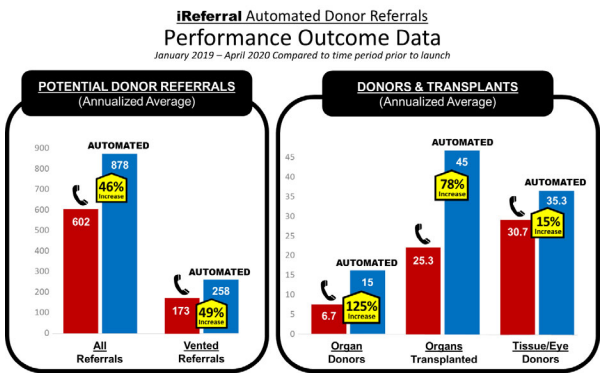


Table 1:



OP435 IMPACT ON DONOR DETECTION AFTER THE IMPLEMENTATION OF QUALITY INDICATORS AND TPM TRAINING PROGRAM IN THE KINGDOM OF SAUDI ARABIA

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Background: World Health Organization is advocating for the development of self-sufficiency in donation and transplantation (D&T) worldwide. Since 2017, the Ministry of Health of the Kingdom of Saudi Arabia (KSA) launched a program coordinated by DTI Foundation (DTI) with the support of the Saudi Center for Organ Transplantation (SCOT) aiming to improve the deceased donation rates by implementing educational programs and quality management systems. The present study summaries the effect of the implementation of a quality indicators pilot program in the KSA's critical pathway for organ donation.
Methods: The DTI-SCOT collaboration has included: (a) diagnosis study to achieve a comprehensive vision of donation system (2017); (b) implementation of a pilot program to maximize the donor referral in 6 centers; (c) monthly follow-up to analyze the data collected leaded by international experts, (d) external audits and e) implementation of an intermediate TPM online training at national level (2020).
Results: The collaboration allowed to identify the organizational, structural, and educational needs. At the pilot program hospitals, the donation alerts increased from 100 to 298 during the first year of the project (250 of these were potential, 101 eligible and 26 were actual donors). This represented near 200% increase in potential donor detection and referral and a final 44% increase in the donation rate. So far, more than 200 ICU doctors, and nurses from more than 30 different hospitals has been training through this program. KSA critical pathway (2017–2020) evolution is summarized at the Figure 1.
Conclusions: The collaboration with DTI made possible to stablish new donor detection and audit methodologies. In-hospital protocols were reviewed and redefined, specifically those related to brain death diagnosis and donor maintenance. In 2019 in KSA, 113 deceased donors were reported. Therefore, 342 deceased organ transplantations were performed.

Year	Possible	Potential	Eligible (family Approached)	Consented	Actual	Utilized
2017	637	415	329	124	110	109
2018	643	441	379	110	96	94
2019	585	411	354	126	114	113
2020	408	286	230	74	65	63

Figure 1. Critical pathway for Organ Donation in KSA (2017-2020)

OP436 THE DONOR ACTION PROGRAM IN THE EMILIA-ROMAGNA REGION FROM 1998 TO 2019: RESULTS

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Background: To establish high quality levels in organ donation, the Emilia-Romagna region (ERR), a northern Italy region of 4 459 477 inhabitants, has supported the "Donor Action" program (DA) since 1998. The question was: are all brain deaths diagnosed, reported and assessed?
Methods: The program started in July 1998 in 28 ERR Intensive Care Units (ICUs, 253 beds in all), 7 belonging to hospitals with neurosurgical departments (81 beds in all). DA analyzes potential donor identification by reviewing the records of deceased patients. This is done by transplant hospital coordinators utilizing a regional computer network, then data are collected and analysed by the ER Transplant Reference Centre.
Results: Over the years the total deaths in ICUSs (649 vs. 1940), but the percentage of severe brain damage decreased (43.9% vs. 25.6%). In spite of this, the number of brain death assessments increased (86 vs. 246) (Table 1), such as organ donors. Organ donors increased from 24.1 per million population (p.m.p.) to 38.7 p.m.p. with a consequent rise in transplantation activity. Refusals keep on representing a big issue (24.6%).
Conclusion: These data show that in ERR, DA contributed to improving the efficiency of the regional transplantation system.

Table 1 DA results

	1998 2nd sem	2012	2013	2014	2015	2016	2017	2018	2019
ICUs Total Deaths	649	1764	1638	1636	1832	1767	1883	1874	1940
Severe Brain Damage (SBD)	285	414	363	371	429	399	432	447	497
SBD/Total Deaths %	43.9	23.5	22.2	22.7	23.4	22.6	22.9	23.9	25.6
Brain Death Assessments	86	198	188	186	228	229	237	241	246
Organ Donors	55	114	111	101	124	143	136	123	173
Refusals (N° / %)	26/33	50/ 26	43/ 23	56/33	63/30	61/27	67/29	76/31.4	63/24.6

Table 2 Donation and Transplantation activity in the ERR.

	1998 2nd sem	2012	2013	2014	2015	2016	2017	2018	2019
Organ donors per million population	24.1	26.3	27.4	23.1	26.5	33.3	30.7	29.0	38.7
Heart Transplantations	24	20	20	17	18	28	20	17	27
Kidney Transplantations	139	128	147	131	174	187	181	183	195
Liver Transplantations	76	116	115	110	115	140	132	111	171

OP437 ORGAN DONATION AND TRANSPLANT IN THE ENGLISH-SPEAKING CARIBBEAN REGION: 10 YEARS OF INTERNATIONAL COOPERATION

Maria Gomez[1], Hassina Mohammed[2], Adedamola Soyibo[3], Entela Kondi[1], Marián Irazábal[1], Chloe Balleste[1], Estephan Arredondo[1], Bridgit Elcock-Straker[4,5], José García-Buitrón[1], Martí Manyalich[1]

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Background: 1266 persons were reported to be suffering ESRD in six Caribbean community (CARICOM) countries in 2006. In contrast, only 21 kidney transplant patients were reported. The Trinidad and Tobago Ministry of Health in association with Donation and Transplantation Institute (DTI Foundation) of Spain established a collaboration in January 2010 towards the development of their deceased donation program for transplant. Last year, 2020, the University Hospital of the West Indies and the Ministry of Health and Wellness of Jamaica also joined a collaboration with DTI.
Method: The collaboration applies the SEUSA program. A compendium of standardized tools that combine best practices in organ donation from 3 main models: Spain- Europe and USA. Phase (PH) 1. Diagnosis study. PH2. Establishment of the Structure as a Transplant Procurement Managers (TPM). PH3.Deceased Alert System (DAS) implementation for reporting 100% of potential Donor. PH4. Conversion rate improvement. PH5. Awareness and Training for Health Care Professionals applying the "Essentials in Organ Donation" (EODs) and PH6. Hospital audits. The SEUSA program have been applied in three main hospitals in T&T for the last 10 years; also phase 1 was implemented in Jamaica in 2020.
Results: Trinidad and Tobago accounts with their TPM's Network inside of each of the main public hospitals and deceased organ donation for transplant procedures have been established. 139 organs have been transplanted in Trinidad and Tobago from both living and deceased donors. After PH1, Jamaica has identified their donor potentiality and defined a roadmap for its national deceased organ donation program.
Conclusion: The collaboration between regional and international organization at the Caribbean countries has demonstrated an effectiveness for the establishment of organ donation for transplant program. The success of the SEUSA Methodology is that of adapting the methodology to the needs of each country.

OP438 QUALITY MANAGEMENT SYSTEM APPLIED TO ORGAN DONATION: UNITED ARAB EMIRATES EXPERIENCE

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Background: The 3rd Global Consultation on Organ Donation and Transplantation stated that every nation should achieve self-sufficiency in organ donation. In the Middle East the deceased organ donation (DD) average rate is 2.29 donors/pmp. The United Arab Emirates (UAE) started their DD program in 2017 approving brain death declaration. UAE National Transplant Committee started an international collaboration with Donation and Transplantation Institute (DTI Foundation) in 2017 for the development of the DD program. In 2019, 4 hospital-based organ donation unit (H-ODU) were established in Abu Dhabi. The aim of this study was to combine the ISO 9001:2015 quality management system (QMS) and the Organ Donation European Quality System (ODEQUS) to improve DD.
Method: SEUSA is based on the Spanish, European and USA models tailored to the local needs. The QMS used was a combination of the ISO with ODEQUS methodology. The Abu Dhabi hospitals were selected according to their DD potentiality. Monthly follow-up between H-ODU's staff and DTI team were performed to monitor SOPs development and ODEQUS KIPs measurement. After a 6 months implementation period, an internal audit was performed by a DTI experts in DD/ISO QMS. Finally, an external audit was performed and ISO 9001:2015 quality certification was granted.
Results: 10 SOPs regarding DD were developed per unit and 4 ODEQUS key indicators (KPI) were selected (Table 1). After completed the internal audits, 1 H-ODU applied for the external audit and quality certification. As a result of the measures implemented, UAE moved from 0 donors to 1.1 donors/pmp in 2019. Lastly, in 2020 the Abu Dhabi Department of Health released the KPIs as a mandate for all hospitals to improve DD performance.
Conclusion: The collaboration between local and international organization supports the successful implementation of DD best practices in new regions.

DIABETES AND VIRAL INFECTIONS AFTER TRANSPLANTATION: OUT OF THE FRYING PAN AND INTO THE FIRE

OP453 THE PRESENCE OF METABOLIC SYNDROME BEFORE TRANSPLANTATION INCREASE THE RISK OF CARDIOVASCULAR EVENTS FOLLOWING LIVER TRANSPLANTATION

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Background: Metabolic syndrome (MS) is common in liver transplant (LT) recipients. Its association with cardiovascular (CV) disease, malignancies in the adult population is well established. If this association occurs in LT candidates is unknown.
Aims: The aim of this study was to assess the prevalence of pre-LT MS and its evolution over time and if MS pre-LT was associated with a higher risk of post-LT cardiovascular events (CVE), *de novo* tumours or survival. Variables associated with those outcomes were also analysed.

Methods: Retrospective, single center study that included LT recipients from January 2012 to December 2017 followed-up since January 2020. Baseline features (MS before LT and at 1 year post-LT) and outcomes (CVE, *de novo* tumors and survival) were recorded.
Results: Among 483 recipients, MS was present pre-LT in 20% with an increasing prevalence over time, from 16% in 2012 to 34% in 2017 ($P = 0.025$). At 1-year post-LT, an additional 12% had developed *de novo* MS. During a 56-months follow-up, 13% developed a CVE and 9% *de novo* tumour. One and 5-yr survival rates were 91% and 83% in those with pre-LT MS and 93% and 85% in those without ($P = 0.94$). MS before LT was independently associated with a higher risk of post-LT CVE (HR: 2.66 IC (95%): 1.6–4.4 $P < 0.001$), but not with *de novo* tumors ($P = 0.94$) nor survival ($P = 0.58$). Other pre-LT variables associated with CVE were men gender, age and obesity: HR 2.4, IC (95%) 2.4 (1.1–5.5), $P = 0.02$, HR 1.1 IC 95% (1.06–1.17) $P = 0.001$, HR 3.3 IC 95% (1.8–5.9), $P = 0.001$ respectively. Renal dysfunction an HCC pre-LT were associated with worse survival HR 2.09 (1.19–3.60) $P = 0.01$ and 1.77(1.07–2.90) $P = 0.02$ respectively. No baseline features were associated with the development of *de novo* tumors.
Conclusions: Pre-LT MS is increasingly in liver transplant recipients and is associated with higher risk of post-LT CVE. Encouraging follow-up of CV risk factors encompassing the pre-LT MS may be a means to improving CV outcomes.

OP454 TREAT-TO-TARGET TRIAL OF CONTINUOUS SUBCUTANEOUS INSULIN-PUMP THERAPY IN NEW-ONSET DIABETES AFTER TRANSPLANTATION (SAPT-NODAT)

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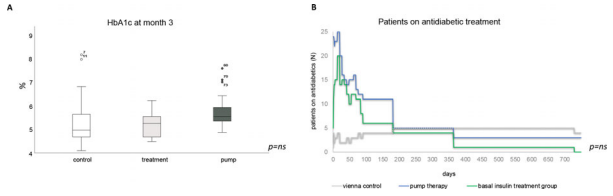
Background and aims: Early basal insulin therapy for postoperative hyperglycemia significantly reduced the odds for overt posttransplant diabetes mellitus (PTDM) in kidney transplant recipients (KTRs). We determined efficacy and safety of continuous insulin infusion (CSII) therapy versus basal insulin (BI) and standard-of-care control (CTR), hypothesizing that glucose control might be more effective with CSII than BI.
Materials and methods: KTRs without previous diabetes were randomized 1:1:1 into CSII (insulin lispro [Humalog], applied with a MiniMed Paradigm Veo pump) versus BI (intermediate-acting insulin isophane [Humulin N]) versus CTR. The CSII and BI groups were both targeting an afternoon glucose of 110mg/dL after patients at least once had capillary glucose ≥140 mg/dl postoperatively. In the CTR group, short-acting insulin was allowed for fasting venous blood glucose ≥200 mg/dl. Primary endpoint: HbA1c at month 3.
Results: Among 85 participants, 69 were still included at month 3 in the ITT population (N = 23 CSII, N = 19 BI, N = 27 CTR), and their median HbA1c was 5.6% (CII), 5.3% (BI) and 5.0% (CTR; all *P* for between-group comparisons non-significant; see Figure panel A). Mean ± standard deviation HbA1c increased by 0.60 ± 0.92% (CII), 0.32 ± 0.53% (BI) and 0.38 ± 1.00% (CTR; all *P* for between-group comparisons non-significant). PTDM rates at month 12, defined by antidiabetic treatment alone, were 14% (CII), 6% (BI) and 21% (CTR; Figure panel B), with odds ratios [95% CIs] for PTDM (treatment-versus-CTR) of 0.78 [0.35–1.70] and 0.25 [0.03–2.41] for CSII and BI, respectively. One hypoglycemic event (>40 mg/dl, clinically not concerning) occurred in one BI patient.
Conclusion: Early postoperative glycemic control using CSII therapy was safe but did not prevent an increase in HbA1c. Development of PTDM at month 12 was similar in all 3 groups, but results from a larger clinical trial (ITP-NODAT, NCT03507829) have previously indicated that BI can prevent PTDM incidence in patients who adhere to the protocol.



OP455 SODIUM/GLUCOSE COTRANSPORTER 2 INHIBITORS IN RENAL TRANSPLANT DIABETIC PATIENTS. SINGLE CENTER PILOT STUDY.

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Background: Preexisting diabetes and post-transplantation diabetes (NODAT) confer reduced patient and graft survival in kidney transplant recipients (Ktx). Added to the general risk factors for NODAT, there are Tx-related factors. There are very few data over the safe use of sodium/glucose cotransporter 2 inhibitors (SGLT2i) in KTx with a need to assess their efficacy and safety.
Methods: Retrospective observational study of a cohort of 57 KTx with diabetes who initiated therapy with a SGLT2i. Transversally we describe baseline clinical data and analyze longitudinally outcomes at 6 and 12 months (m) of follow-up post SGLT2i initiation (N = 57, N = 42 y N = 30 respectively).
Results: From 1st Jan 2019 onwards, SGLT2i therapy was initiated in 57 Ktx. 77.2% were males with a mean age of 62.35 ± 9.7. 66.7% had NODAT and only 5.3% had a steroid-free regimen besides Tacrolimus and MMF. SGLT2i were started a median time of 58 (1–268) m postKTx. Mean duration of SGLT2i was 11.7 ± 7.1 m. 35% of treated patients discontinued SGLT2i, 40% of them due to raising creatinine (Cr). There was a significant increase in mean Cr over time at 6 and 12 m post-initiation (table). Reduction in eGFR was only significant at 12th m. 6 patients were admitted for this reason motivating a renal biopsy in 4. There were 3 reports of TCMR in these. Mean tacrolimus through levels were significantly lower at 6 and 12 m without changes in dosing. There was no change in the number of episodes of urinary tract infections or positive urine cultures ($P > 0.05$). Tolerance to SGLT2i was good overall with only one discontinuation due to intolerance. There were only 3 admissions due to decompensated heart failure during SGLT2i therapy.
Conclusions: In our 57 KTx cohort, SGLT2i appear safe and well tolerated, although they may increase baseline creatinine and lower tacrolimus levels. The number of urinary tract infections did not increase during SGLT2i therapy.

	BASELINE PARAMETERS	6 MONTHS ON TREATMENT (N = 42)		12 MONTHS ON TREATMENT (N = 30)	
Variables	Baseline	Baseline	6 months	Baseline	12 months
Hemoglobin (g/dl)	13.8 ± 1.63	14 ± 1.7	14.4 ± 1.8	14 ± 1.5	14.4 ± 1.6
Serum Creatinine (mg/dl)	1.46 ± 0.43	1.38 ± 0.38	**1.47 ± 0.53***	1.31 ± 0.33	**1.44 ± 0.4***
MDRD4 (ml/min/1.73m²)	54.37 ± 18,77	56.67 ± 18.55	54.84 ± 19.33	57.94 ± 16.86	**53.34 ± 15.07***
Serum sodium (mEq/L)	141 ± 2	141 ± 2	141 ± 3	141 ± 2	**143 ± 3***
Hemoglobin A_{1c} (%)	7.6 ± 1.7	7.5 ± 2	7.3 ± 1.2	7.5 ± 2.3	7.8 ± 2.3
Tacrolimus levels (ng/ml)	7.6 ± 2.15	7.9 ± 2.2	**6.4 ± 1.9****	8.4 ± 2.2	**7.2 ± 1.7***
Tacrolimus dose (mg/24h)	3.5 (0.75 – 10)	3.5 (0.5 – 10)	3.5 (0.5 – 8)	4 (1.5 – 10)	3.5 (1.5 – 8)
Urinary Sodium (mg/dl)	76 ± 34	75 ± 36	71 ± 28	76 ± 37	71 ± 24
Urinary Creatinine (mg/dl)	55 ± 26	58 ± 28	**47 ± 2***	58 ± 30	56 ± 28
Proteinuria (g/dl)	0.1 (0 – 1.4)	0.1 (0 – 1.4)	0.1 (0 – 1.4)	0.1 (0 – 1.4)	0.1 (0 – 2.2)

* p < 0.05
** p < 0.001

OP456 RISK FACTORS OF EPSTEIN-BARR VIRUS REACTIVATION AFTER RENAL TRANSPLANTATION: RESULTS OF A LARGE, MULTI-CENTRE STUDY

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Background: Epstein-Barr virus (EBV) reactivations and primary infections are a very common and potentially lethal complication of renal transplantation. However, the risk factors of EBV reactivations are not well known and there exist no effective risk assessment models for the prediction of EBV reactivation to assist therapeutic decisions. The goal of this study is to identify potential risk factors, as well as describing transplant complications associated with EBV reactivation.
Methods: We have analysed a large, multi-centre cohort (N = 512), with an incidence of EBV reactivation of 18.4% during the first post-transplant year. The patients were characterized pre-transplant and two weeks post-transplant for a multi-level biomarker panel. The panel consisted of gene expression, leucocyte subsets, antibody reactivity profiles, urine metabolome, serum metabolites and clinical markers.
Results: Several novel potential risk factors were identified: Pre-transplant EBV shedding was associated with a quadruplicated incidence of post-transplant EBV reactivation. Male patients also suffered from significantly increased post-transplant EBV incidence. Pre-transplant alterations of the lipidic metabolism were found to be prognostic for EBV reactivation. In the early post-transplant period, the expression of the tolerogenic genes LAG3 and CD200 was significantly associated with EBV, as well as increased concentrations of alanine aminotransferase. Importantly, we also identified a significant association of post-transplant EBV with clinical complications, including acute rejection, reduced haemoglobin levels and transaminases.
Conclusions: We provide for the first time evidence on the significance of pre-transplant EBV viral load for the transplant course and describe novel risk factors for EBV reactivation. Our results highlight that EBV reactivation has potentially serious consequences for the patient even for relatively low viral loads.

OP457 BKV-SPECIFIC IFN-Γ ELISPOT ASSAY IN KIDNEY TRANSPLANTATION: A META-ANALYSIS AND SYSTEMATIC REVIEW

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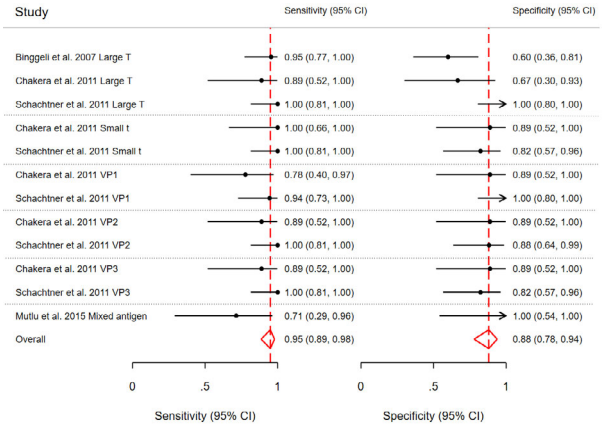
Background: BK virus (BKV) infection after kidney transplantation can cause BKV nephropathy (BKVAN) resulting in graft dysfunction and allograft loss. There is no biomarker to monitor BKV activity besides BK viral load. The value of the Enzyme-Linked Immunosorbent Spot (ELISPOT) assay as a tool to monitor the recipient's anti-BKV immune response after transplantation was investigated systematically.
Methods: Electronic databases were searched for studies of ELISPOT evaluating the immune response against BKV. BKV status was categorized as active BKV replication, and as inactive BKV replication. Random-effects model meta-analysis was performed to determine the diagnostic performance of the ELISPOT assay, which stratified patients into non-responders and responders.
Results: Nine studies were included. Non-responders had an increased risk to have active BKV replication (odds ratio of 71.9 (95%-CI 31.0–167.1). Pooled sensitivity was 0.95 (95%-CI 0.89–0.98) and specificity was 0.88 (95%-CI 0.78–0.94). The standardized mean difference of the number of IFN-γ producing cells between patients with active BKV replication compared with patients who had inactive BKV was −2.09 (95%-CI −2.50, −1.68).
Conclusions: IFN-γ ELISPOT non-responders have a 71.9 higher risk to have active BKV replication. The ELISPOT assay is a useful tool for BKV risk assessment and in combination with BKV load may support clinicians in guiding immunosuppressive therapy in patients with BKV replication.

Table 1 Summary of studies

Authors and year of publication	BK antigen used for ELISPOT assay	Patient with active BKV reactivation (*n*)	Patients with inactive BKV reactivation (*n*)	Definition of BKV reactivation
Binggeli et al. 2007	Large T, VP1	22	20	Viremia
Prosser et al. 2008	Large T	8	8	BKV-associate nephropathy
Chakera et al. 2011	Large T, small t, VP1, VP2, VP3	9	9	Urine decoy cell and viremia
Schachtner et al. 2011	Large T, small t, VP1, VP2, VP3	18	17	Viremia
Costa et al. 2014	Mixed antigen	12	-	Viruria or viremia
Schachtner et al. 2014	Large T, small t, VP1, VP2, VP3	12	12	Viruria or viremia
Mutlu et al. 2015	Mixed antigen	12	6	Viremia
Schachtner et al. 2015	Mixed antigen, large T, VP1	16	-	Viremia
Bae et al. 2020	Large T, small t, VP1, VP2, VP3	17	34	Viremia

Figure 1: Sensitivity and specificity of BKV-specific IFN-γ ELISPOT assay



OP458 IMPACT OF COVID-19 IN PATIENTS AWAITING LIVER TRANSPLANTATION

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Background: The SARS-CoV-2 pandemic has raised two main issues in patients awaiting liver transplantation (LT). Firstly, some care must have been delayed. Secondly, in case of COVID-19, patients could have experienced hepatic decompensation. This context motivated us to contact all our patients awaiting LT. We aimed to evaluate the impact of COVID-19 in these patients and the outcomes of the confirmed infection.
Methods: A questionnaire was sent to all patients on waiting list for LT between 15 April and 15 May 2020 in Hepatobiliary Center of Paul Brousse Hospital, France. Patients with positive PCR or compatible CT scan features were defined as "certain". Patients in contact with a confirmed COVID-19 person or with symptoms suggesting COVID-19 were defined as "suspects". In our center, all candidates for LT have PCR, CT scan and anti-SARS-CoV-2 serologies the day of their transplantation. The patients were followed up and data were actualized in February 2021.
Results: We included 91 patients awaiting LT. 45% were on list for cirrhosis, 35% for hepatocellular carcinoma (HCC) and 20% for other cause. 44% of patients were older than 60 years-old. 14 (15.3%) patients were suspect, and 3 (3.3%) patients were certain for COVID-19. Two certain patients were hospitalized in intensive care unit and one of them died after LT. No patient died before LT. Concerning patients experience, 71% of patients felt themselves more at risk compared to general population, 41% felt stressed, but also 82% felt informed on COVID-19 and 97% of patients respected strict lockdown rules. On February 2021, 43 (47.5%) patients were transplanted. Two (2.2%) of our patients were dropped out of waiting list because of HCC progression. Anti-SARS-CoV-2 serologies were available for 41 (45.1%) patients. Of them, 4 (4.4%) were positive.

Conclusions: COVID-19 has been uncommon in patients awaiting LT during the first period of the pandemic. We did not observe deterioration of liver functions or death related to COVID-19 before LT. This fact could be explained by the global respect of the lockdown rules. Since then, about half of the patients were transplanted and only 4% had a positive serology the day of LT.

FROM PRIMARY TO CHRONIC LUNG ALLOGRAFT DYSFUNCTION: THE DEVIL IS NOT AS BLACK AS HE IS PAINTED

OP459 HEMODYNAMIC EFFECTS OF INTEGRATING COMPLIANCE IN THE DESIGN OF AN ARTIFICIAL LUNG: ASSESSMENT WITH A HYBRID SIMULATOR

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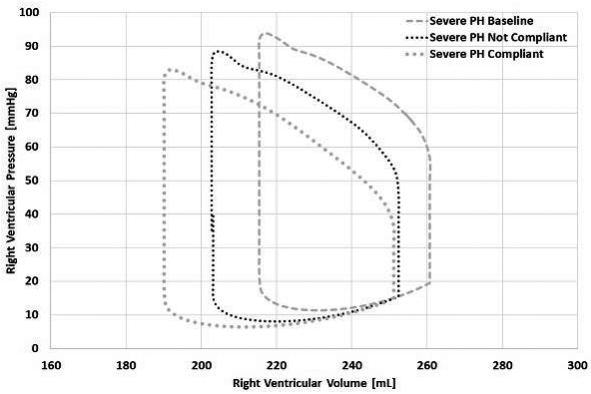
Background: Lung transplantation may be the destination therapy in lung failure, but limited donor organ availability creates the need for artificial lung (AL) technology. In this study we aim to assess the hemodynamic effects of an AL with fiber-bundle-integrated compliance (RAS-Q®) implanted between pulmonary artery (PA) and left atrium (LA).
Methods: A hybrid cardiovascular simulator was adapted to reproduce 4 pulmonary hypertension (PH) profiles: mild, moderate, severe and cardiogenic shock. A RAS-Q prototype was connected between the simulated PA and LA. For each profile, the hemodynamic effects of this prototype with and without integrated compliance were assessed in terms of pressures, flows and right ventricular (RV) volumes.
Results: Results are reported in the Table and Figure for severe PH. The introduction of RAS-Q with disabled compliance led to an increase of arterial blood pressure and cardiac output in all PH profiles as well as a decrease in central venous pressure, peak RV pressure, end-diastolic volume, and pressure-volume area. Additionally, an increase in stroke work and RV power was observed in the severe PH and cardiogenic shock profiles. Enabling the integrated compliance in this RAS-Q prototype amplified these hemodynamic and ventricular energetic improvements even further, which came into their own in a severe PH status.

Severe PH	Baseline	No compliance	Compliance
mABP (mmHg)	71	82	83
mPAP (mmHg)	74	65	56
mCVP (mmHg)	19	16	14
AL Flow (l/min)	0.0	1.9	3.4
Total CO (l/min)	3.8	5.0	5.1
Peak RV pressure (mmHg)	94	88	83
RV EDV (ml)	261	255	251
RV SW (ml × mmHg)	3043	3290	3513
RV PVA (ml × mmHg)	13 016	12 146	11 357

PH = pulmonary hypertension; mABP = mean Arterial Blood Pressure; mPAP = mean Pulmonary Arterial Pressure; mCVP = mean Central Venous Pressure; AL = artificial lung; CO = Cardiac Output; RV = right ventricular; EDV = end diastolic volume; SW = stroke volume; PVA = pressure volume area.



Conclusions: This innovative RAS-Q prototype, when tested in a PA-LA configuration results in improved organ perfusion, RV unloading, and RV recovery for different stages of PH. The integrated compliance elicits more pronounced improvements compared to an equivalent AL without compliance. Our results support applying this strategy in the severe PH status before cardiogenic shock emerges.

OP460 CYTOKINE FILTRATION REGENERATED PULMONARY FUNCTION IN ARDS DAMAGED LUNGS AND REDUCE PRIMARY GRAFT DYSFUNCTION

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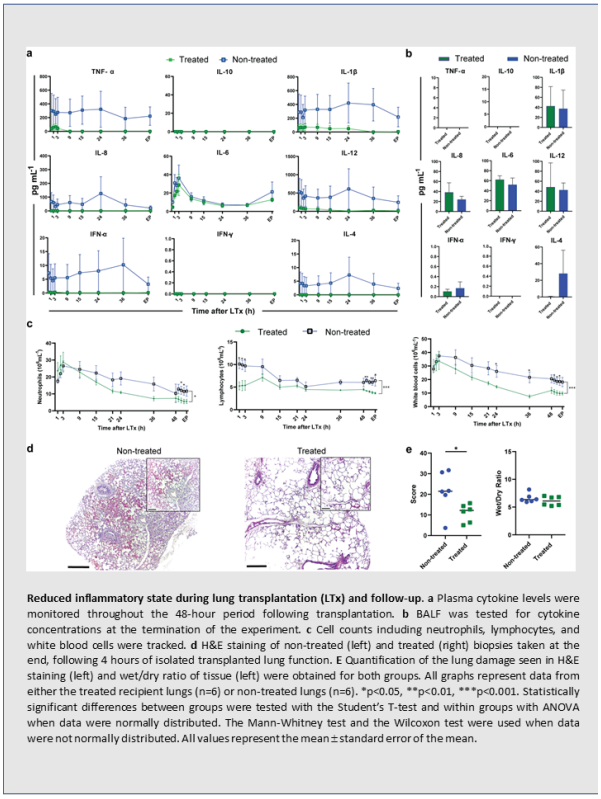
Background: Despite improvements, lung transplantation (LTx) remains hampered by both a scarcity of donor organs and by mortality following primary graft dysfunction (PGD). Since acute respiratory distress syndrome (ARDS) limits donor lungs utilization, we investigated cytokine filtration as a means of regenerating ARDS donor lungs.
Methods: In the present study, we induced mild to moderate ARDS using lipopolysaccharide in 12 donor pigs. Following lung harvest and 2 h of cold storage, lungs were treated with or without cytokine filtration during 4 h of *ex vivo* lung perfusion (EVLP). The left lung was thereafter transplanted and the recipients were treated with or without cytokine filtration post-transplantation during 12 h using extracorporeal hemoperfusion. After 48 h a right pulmektomi was done and the transplanted lung was evaluated regarding PGD. Measurements of cytokine levels (IL-1beta, IL-4, IL-6, IL-8, IL-10, IL-12, IFN-alfa, IFN-alfa and TNF-alfa) in plasma and bronchoalveolar lavage fluid (BALF), and measurements of leukocyte, neutrophils, and total white blood cell counts regularly throughout the study. Lung biopsies were taken in the donor, after EVLP and in the recipient.
Result: The treatment significantly decreased cytokine levels during EVLP and decreased levels of immune cells post-transplantation. Histology demonstrated fewer signs of lung injury across both treatment periods and the incidence of PGD was significantly reduced among treated animals.
Conclusion: Overall, cytokine filtration was able to regenerate lung function in ARDS damage lungs and reduce PGD in lung transplantation . We suggest this treatment will increase the availability or donor lungs and increase the tolerability of the donor lungs in the recipient.



Reduced inflammatory state during lung transplantation (LTx) and follow-up. **a** Plasma cytokine levels were monitored throughout the 48-hour period following transplantation. **b** BALF was tested for cytokine concentrations at the termination of the experiment. **c** Cell counts including neutrophils, lymphocytes, and white blood cells were tracked. **d** H&E staining of non-treated (left) and treated (right) biopsies taken at the end, following 4 hours of isolated transplanted lung function. **E** Quantification of the lung damage seen in H&E staining (left) and wet/dry ratio of tissue (left) were obtained for both groups. All graphs represent data from either the treated recipient lungs (n=6) or non-treated lungs (n=6). *p<0.05, **p<0.01, ***p<0.001. Statistically significant differences between groups were tested with the Student's T-test and within groups with ANOVA when data were normally distributed. The Mann-Whitney test and the Wilcoxon test were used when data were not normally distributed. All values represent the mean ± standard error of the mean.

OP461 PROPHYLACTIC DESENSITIZATION IN LUNG TRANSPLANT CANDIDATES WITH PRE-FORMED DONOR-SPECIFIC ANTIBODIES: 3-YEAR POST-TRANSPLANTATION OUTCOME.

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Background and aims: Pre-formed donor-specific antibodies (pf-DSA) are associated with worse outcome after lung transplantation (LTx) and might limit access to LTx. A virtual crossmatch (CXM)-based strategy for perioperative desensitization protocol has been used for immunized LTx candidates since 2012 at Foch hospital. We compared the outcome of desensitized LTx candidates with high pf-DSA mean fluorescence intensity (MFI) and those with low or no pf-DSA, not desensitized.
Methods: For all consecutive LTx recipients (January 2012-March 2018), freedom from CLAD and graft survival were assessed by Kaplan–Meier analysis and Cox proportional-hazards multivariate analysis.
Results: We compared outcomes for desensitized patients with high pf-DSA ($n = 39$) and those with no ($n = 216$) or low pf-DSAs ($n = 66$). The desensitization protocol decreased the level of immunodominant pf-DSA (class I/II) at 1, 3, and 6 month post-LTx ($P < 0.001$, $P < 0.01$, $P < 0.001$, respectively). Freedom from CLAD and graft survival at 3 years was similar in the desensitized group as a whole and other groups. Nevertheless, incidence of CLAD was higher with persistent high- than cleared high-level ($P = 0.044$) or no pf-DSAs ($P = 0.014$). Conversely, graft survival was better with cleared high pf-DSA than persistent high-, low-level, and no pf-DSAs ($P = 0.019$, $P = 0.025$, and $P = 0.044$, respectively). On multivariate analysis, graft survival was associated with cleared high pf-DSA (HR: 0.12 [95% CI 0.02–0.85] vs no DSAs, $P = 0.035$) and CLAD with persistent pf-DSA (HR: 3.04 [1.02–9.17] vs no pf-DSA, $P = 0.048$).
Conclusion: wThe desensitization protocol in LTx recipients with high pf-DSAs was associated with satisfactory outcome, with cleared high pf-DSAs after desensitization identified as an independent predictor of graft survival.

OP462 LUNG TRANSPLANT RECIPIENTS DEVELOPING EARLY DSA WITHIN THE FIRST MONTH EXHIBIT A HIGHER FREQUENCY OF NAÏVE AND A LOWER FREQUENCY OF MEMORY B CELLS

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Background: After lung transplantation (LTx), the development of early donor HLA-specific antibodies (eDSA) has been shown to be associated with antibody-mediated rejection (AMR) and poor graft survival. Since 2013, patients with eDSA within the first month after LTx are treated with IgA/IgM enriched intravenous immunoglobulins (IgGAM), combined with anti-CD20 antibody (Rituximab). We hypothesized that a higher proportion of naive IgD+CD27$^-$ B cells in relation to memory B cells (IgD-CD27$^+$) is associated with eDSA development.
Methods: In a pilot study of 58 LTx recipients, B cell subsets were by analyzed flow cytometry using CD19, CD20, IgD, CD24, CD27, CD38 antibodies for the time points pre, post (T0), 24 h (T24) and 3 weeks after LTx. The proportions of B cell subsets were compared between two groups: eDSA-positive ($n = 13, 22, 41\%$) and –negative ($n = 45, 77, 58\%$) patients.
Results: During the first 24 h post-transplant, patients without DSAs showed a significant increase in naïve B cells ($P < 0.0001$). The memory B cells showed a significant decrease, independently of DSA presence (all, $P < 0.0007$). In eDSA-positive patients, higher frequencies of IgD+CD27-CD24hi naïve and lower frequencies of IgD-CD27-CD24lo memory B cell subsets were observed constantly pre, T0, T24 and 3 weeks. A transient increase in IgD$^+$CD27$^+$ switch memory B cells was detected at T0 in both groups, returning to baseline levels already at T24.
Conclusions: Lung transplant recipients show remarkable dynamics of naïve, memory and switch memory B cells within the first 24 h. Based on preliminary data, a refined B cell monitoring with additional markers may be able to identify patients with a higher risk for eDSA development. In both groups we see a shift in the B cell population: increase in naïve B cells and decrease in memory B cells. The changes are more constant in the group with DSAs. The impact of the treatment regimen on these B cell subsets is currently investigated.

OP463 ALTERATION OF T LYMPHOCYTE SUBPOPULATIONS IN LUNG TRANSPLANTED PATIENT RECEIVING PROPHYLACTIC EXTRACORPOREAL PHOTOPHERESIS

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Background: Extracorporeal Photopheresis (ECP) is a common treatment option for lung transplanted patients suffering of chronic rejection but its use as a prophylactic treatment has been barely described so far. Therefore, a prospective, randomized, controlled trial of lung transplant recipients receiving prophylactic ECP treatment is being carried. As part of this trial, the effect of ECP on the frequency of lymphocyte subpopulations is being investigated.
Methods: Lung transplanted patients were randomized to receive or not receive 16 ECP treatments in the first 3 months after transplantation, additionally to their tacrolimus-based immunosuppressive regimen. Fresh whole blood samples were collected in both treatment groups and stained with validated, lyophilized antibody panels including markers for CD4$^+$ and CD8$^+$ population as well CD197 and CD45RA for analysis of naïve, effector, central memory and effector memory T cells, respectively. FACS analysis was performed pretransplant and three months after surgery, when the last ECP treatment was conducted. According to data distribution of each investigated cell population, statistical analysis is performed with paired *t*-test or Wilcoxon signed-rank test ($\alpha = 0.05$).
Results: In total 54 (27 in each group) patients receiving bilateral lung transplantation were analysed in this interim analysis. While in the control group the percentage of CD3$^+$ ($P = 0.035$) and CD8$^+$ naïve T cells ($P = 0.001$) were significantly increased at 3-month visit, no change is found in the ECP treated group ($P = 0.964$; $P = 0.369$ respectively). Frequency of CD4$^+$ and CD8$^+$ effector memory T cells were significantly reduced in the control group ($P < .001$; $P = 0.03$ respectively), whereas no alteration is found in the ECP-treated group ($P = 0.052$; $P = 0.13$ respectively). However, percentage of CD8$^+$ effector cells was significantly increased in the ECP-treated group ($P = 0.02$).
Conclusions: In this study, we reveal the first data on monitoring lymphocyte subpopulations in lung transplanted patients with and without prophylactic ECP treatments. Various alterations in distinct T lymphocyte subpopulations were found in both groups, in particular with regard to CD8+ T cell subsets.

OP464 PARTICLE FLOW RATE FROM THE AIRWAYS AS A MARKER FOR CHRONIC LUNG ALLOGRAFT DYSFUNCTION (CLAD)

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Background: Long-term survival after lung transplantation is significantly shorter compared to other solid organ transplantations. Chronic lung allograft dysfunction (CLAD) including bronchiolitis obliterans syndrome (BOS) remains the major barrier of survival. CLAD is diagnosed according to ISHLT's guidelines: 20% drop in FEV1 using spirometry for CLAD grade 1. Given the difficulties of confounders using spirometry, other methods for precise diagnostics are being explored. Exhaled breath particles measured as particle flow rate (PFR) from the airways have been explored as a potential method to diagnose lung injury in preclinical and clinical settings of acute respiratory distress syndrome (ARDS) and primary graft dysfunction (PGD). In fact, PFR has been shown to indicate early signs of lung injury in both ARDS and PGD settings (1, 2). In the present study we explored if PFR could be used as marker for BOS.
Methods: 48 lung transplant patients were included (28 BOS grade 0, 9 BOS grade 1, 6 BOS grade 2, 5 BOS grade 3). All patients were in stable condition without ongoing infections, and more than 2 years post

transplantation. PFR (particles per liter) was measured using a PExA 2.0 device (PExA, Gothenburg, Sweden) containing an optical particle counter (OPC) at the start of the study and then 1 year out, in total 2 time points (0 and 1 year). Particles in the diameter range of 0.41–4.55 μm were measured, then divided by OPC dependent on size in 8 different groups (1–8).
Results: At both the start of the study and one year out, patients with BOS grade 0 had significantly higher PFR than patients with BOS grade 2–3. During the study period only 5 patients progressed in their BOS grade. All 5 patients expressed lower PFR as they progressed in BOS grade while patients who remained in BOS grade did not. The particle distribution between the different BOS grade had similar pattern; however, significantly decreased PFR with severity in BOS grade.
Conclusions: Exhaled breath particles expressed as PFR could be used to distinguish severity in BOS grade, and could be used to follow the progression of BOS over time. PFR could possibly be used as a new diagnostic tool for BOS and to follow the development of lung function over time.
1.Stenlo M, et al. Am J Physiol Lung Cell Mol Physiol. 2020.
2.Broberg E, et al. Exp Clin Transplant. 2019;17(6):803-12.

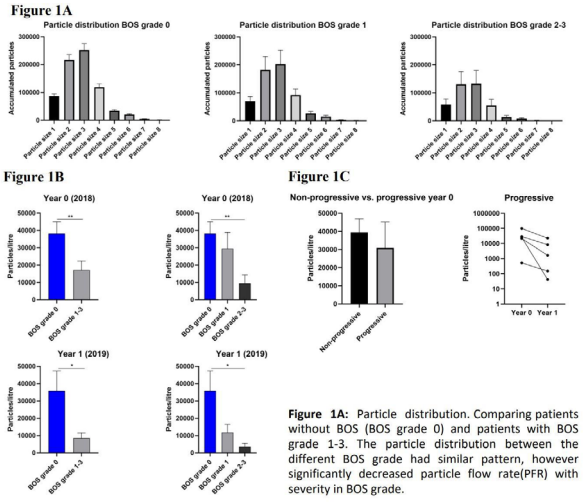

Figure 1A: Particle distribution. Comparing patients without BOS (BOS grade 0) and patients with BOS grade 1-3. The particle distribution between the different BOS grade had similar pattern, however significantly decreased particle flow rate(PFR) with severity in BOS grade.

Figure 1B: Exhaled breath particles expressed as particle flow rate (PFR) comparing patients with and without BOS at timepoint 0 (year 0; 2018) and after 1 year (year 1; 2019). At both the start of the study and one year out, patients with BOS grade 0 had significantly higher PFR than patients with BOS grade 2-3.

Figure 1C: Figure 1C (left) shows the difference in PFR at year 0 (2018) comparing patients with non-progressive BOS and patients with progressive BOS. The non-progressive group includes patients without BOS who did not develop BOS between the two timepoints and patients with any grade of BOS who do not progress in BOS grade between the two timepoints (2018 and 2019). Figure 1C (right) shows individual values for patients with a progressive BOS between the two timepoints. Interestingly all patients with a progressive BOS exhibit a decrease in PFR between the two timepoints. More studies in larger cohorts are needed to further explore if all patients with progressive BOS exhibit a decrease in PFR.

Significance was defined as: $p < 0.001$ (***), $p < 0.01$ (**), $p < 0.05$ (*), and $p > 0.05$ (not significant)

ENHANCED RECOVERY IN KIDNEY AND LIVER TRANSPLANTATION: MAKE IT FAST AND MAKE IT RIGHT

OP507 ENHANCED RECOVERY AFTER LIVER TRANSPLANTATION OUTSIDE A STRICT FAST TRACK PROTOCOL: A SINGLE CENTER FEASIBILITY STUDY

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Background: Liver transplantation has changed the natural history of irreversible end-stage liver failure. **E**nhanced **R**ecovery **A**fter **S**urgery (ERAS) is a multi-modal protocol implemented to optimize peri-operative management, improve patient recovery, reduce post-operative complications, and reduce hospital stay. However, complex multimodal protocols can often be difficult to implement leading to a significant drop outpatient rate. The aim of the study is to examine the feasibility and safety of a non-strict, simplified enhanced recovery protocol in cases of liver transplantation in highly selected liver transplantation recipients.
Methods: A small-scale pilot study was designed to assess the impact of hospitalization, compliance and safety of an ERAS protocol adapted to liver transplantation. An ERAS protocol group focused on immediate nasogastric tube removal, early feeding by postoperative day 2, mobilization and Foley catheter removal by postoperative day 3, central line removal by postoperative day 5 and abdominal drain removal by postoperative day 6, was compared with a control group of patients with similar characteristics treated by traditional protocols. All patients presented comparable demographic, anthropometric and epidemiological characteristics, their MELD score being ≤25. Nine patients (average MELD score 15.1) were included in the ERAS group and compared with 9 patients in the control group (average MELD score 15.3), treated with classic protocols. All patients were in priority due to either concomitant hepatocellular carcinoma or severe complications of portal hypertension.
Results: There was a 55.6% reduction in total hospitalization time: 10.8 (7–13) days for the enhanced protocol group versus 22.1 (17–26) days for the control group. Postoperative complications or hospital re-admission rates showed no difference. Specifically, none of the patients in the enhanced protocol group was readmitted nor developed complications after being discharged.
Conclusions: This small-scale preliminary study suggests that implementing a non-strict and simple enhanced recovery protocol can be feasible, effective, and safe for selected patients following liver transplantation. The authors have designed a larger-scale randomized study to confirm the results described above.

OP508 A NATIONAL SURVEY ON ENHANCED RECOVERY FOR RENAL TRANSPLANT RECIPIENTS: CURRENT PRACTICES AND TRENDS IN THE UNITED KINGDOM

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Background: Despite being established in many specialties, Enhanced Recovery after Surgery (ERAS) has not been widely adopted in renal transplantation. The aim of this survey was to understand current national practices and sentiment with regards to implementation of ERAS for renal transplant recipients in the UK.
Methods: A national web-based survey was designed and sent to consultant surgeons at all 23 UK adult renal transplant units. Completed questionnaires were collected between May and July 2020. The survey was designed to capture current perioperative practices in the period preceding the SARS-COV2 pandemic. Data was analysed according to individual responses and grouped according to transplant units where appropriate.
Results: All transplant units were represented. Three units had a formal ERAS pathway for all recipients. Of the remaining units, 65.9% were considering implementing an ERAS pathway within 1yr. Perceived barriers to implementation included "imbedded culture within transplant units" and "complex background of transplant recipients" (54.8% and 45.2% of respondents respectively). Only 13.1% had a formal prehabilitation programme. A fifth of respondents would not routinely insert drains intraoperatively. Over two thirds routinely used 2–3 concomitant pain control modalities perioperatively, and only 11.7% routinely discontinued PCA's on day 1. Most respondents routinely remove urinary catheters on day 5 (70%) and ureteric stents 4–6 weeks post-transplantation (81.7%). Median length of stay for deceased-donor kidney transplant recipients was lower in units with ERAS programmes (5–7 d vs. 8–10 d respectively). The main barriers for discharge were cited as "suboptimal fluid balance" and "requirement of rejection treatment". Components considered most important for ERAS included "early counselling and education" (86%), "goal directed fluid therapy" (73.7%), "early mobilisation" (98.2%) and "early postoperative patient-education" (86%).
Conclusion: Despite slow uptake of ERAS in kidney transplantation, appetite is increasing particularly in the post COVID era. The opinions of transplant specialists have been highlighted and may help with standardisation of a future ERAS protocol.

OP509 ENHANCED RECOVERY AFTER SURGERY (ERAS) FOR RENAL TRANSPLANT RECIPIENTS: THE EARLY NEWCASTLE EXPERIENCE

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Background: There is a drive towards patient-centred, integrated care in many modern healthcare systems. Existing pressures to reduce length of hospital stay (LOS) have been further compounded by the SARS COV-2 pandemic. Enhanced recovery after surgery (ERAS) pathways have consistently demonstrated reduced LOS and improved patient satisfaction but despite being established in many specialties, ERAS has not been widely adopted in renal transplantation. Our aim was to demonstrate the safety and feasibility of our recently developed ERAS pathway for recipients of renal transplants.
Methods: We designed a multimodal ERAS pathway and trialled it in adult living-donor transplant recipients over a 4-month period in 2020. The pathway included patient counselling and engagement; goal-directed fluid replacement; opioid sparing analgesia; targeted physiotherapy; proactive post-operative care and tailored early follow-up. Outcome measures for each of these elements were evaluated against pre-set quality indicators. A web-based questionnaire was used to capture patient feedback.
Results: Ten patients with a mean age of 44 years were included. There was a 30% reduction in median LOS to 7 days. All patients received pre-operative counselling. IV fluids were discontinued within 24 h in 70% of recipients. All received transversus abdominis plane (TAP) catheters with a 51% reduction in opioid use and a 70% reduction in postoperative nausea and vomiting score. Eighty percent of patients mobilised within the first 24 h postoperatively. All patients received a single surgical drain. The median time of surgical drain and urinary catheter removal was 2.5 and 3.5 days respectively. All patients reported feeling empowered during their recovery and well prepared to manage at home on discharge.
Conclusion: Enhanced recovery after surgery is safe to implement in renal transplantation. A multimodal approach has led to increased patient satisfaction and a shorter length of hospital stay. This successful programme is now being expanded to include recipients of all deceased donor renal transplants.

OP510 POSITIVE IMPACT OF ERAS PROGRAMME ON LIVING AND DECEASED DONOR RENAL TRANSPLANT RECIPIENTS DURING COVID PANDEMIC

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Background: Enhanced Recovery After Surgery (ERAS) programmes have been introduced in many surgical specialties to effectively reduce length of stay (LOS) while maintaining safe care. We implemented an ERAS programme in order to minimise the risk of nosocomial COVID-19 transmission through a shorter hospital stay.
Methods: A protocol was implemented after a literature review and finalised in MDT discussion and then distributed to wards with informative posters (Figure 1 ERAS bedside checklist). Patients on the renal transplant waiting list were provided with detailed information about the programme and received prehab and post-op exercise advice. The primary outcome was hospital LOS with secondary outcomes including opiate use, level of mobilisation, bowel function and patient reported outcomes. Compliance to the ERAS protocol was monitored and recorded prospectively. The ERAS patients ($n = 28$) were compared with a historical control group of 25 consecutive patients transplanted 12 months previously (pre-ERAS patients). Data were analysed in GraphPad Prism and groups compared with student t-test and Chi^2 test.
Results: Since December 2020, 28 recipients completed the ERAS recovery protocol. The baseline characteristics of this group were comparable with pre-ERAS patients. Median LOS was significantly reduced in the ERAS group (5 days) compared to the pre-ERAS group (8 days, $P = 0.01$). 54% of ERAS patients were discharged within 5 days compared with only 8% in the pre-ERAS group (X^2 12.59, $P < 0.001$). For those with stays longer than the target 5 days, 33% had graft issues e.g. need for biopsy but there were also potential preventable reasons including medication education and delayed physiotherapy input. ERAS had a positive impact on time to 1st bowel movement and was associated with reduced opiate use. 79.2% of recipients mobilised on day 1 post-op with either physiotherapy or nursing staff. Only one ERAS recipient was readmitted after discharge and only one patient required recatheterisation.
Conclusions: Introduction of an ERAS programme successfully reduced the median length of stay by 2.5 days and had a positive impact on patient care and minimal adverse events. It is hypothesised that appointment of a specialist ERAS nurse is likely to improve compliance and effectiveness and plans are in place to appoint.

ERAS bedside checklist

edinburgh transplant centre

Please note that this is a suggested plan and some patients may require a modified plan.

Plan		Check as complete
Pre-op	Check patient aware of enhanced recovery aims and anticipated progress (patient information booklet and physio advice sheet)	
	Based on confirmed theatre time, encourage diet until 6 hrs pre-op and clear carbohydrate drink 8 hrs and 2 hrs pre-op (check with anaesthetist)	
Post op day 0	Encourage oral intake as soon as able with aim to stop IVF early	
	Fluid balance as per team plan	
	Offer oral analgesia, laxatives and anti-emetics	
Day 1	Out of bed for meals with aim for 4hrs chair and circulatory exercises	
	Encourage normal diet as tolerated with access to independent snack trolley	
	Oxycodone MR by 0800 to allow PCA to come down 1000 Paracetamol QID Oxycodone IR as required (with laxatives)	
	walk supervised (aim for 20m)	
	walk supervised (aim for 40m)	
	Encouragement of deep breathing (described in physio sheet) Refer physio if on-going O2 requirements or high risk	
	Weight	
	Start self-medication discussion	
Day 2	Out of bed for meals with aim for 6 hours in chair	
	Encourage normal diet as tolerated with access to independent snack trolley	
	PCA down and regular oral analgesia	
	60m walk	
	60m walk	
	Encouragement of deep breathing	
	Weight	
	Self medication	
	Discharge discussion (clothes, family, medication, travel, follow-up)	
Day 3	Change into home clothes	
	Catheter out if no concerns about bladder function	
	6 hours in chair	
	60m walk	
	60m walk	
	60m walk	
	Weight	
	Routine physio review	
	Self medication	
Day 4	Aim for discharge with advice sheet, medication, information on phone numbers if concerns and anticipated follow-up calls	
	Weight	
	Complete self medication	
	Catheter out if anuria pre-op or high risk TWOC	
	Independent mobilisation +/- stair assessment	

All suggestions for improvement welcome to Rachel.thomas@nhslothian.scot.nhs.net

Edinburgh Transplant Centre Recipient checklist v5 19th November 2020

OP511 FACTORS ASSOCIATED WITH PROLONGED LENGTH OF STAY FOLLOWING RENAL TRANSPLANTATION: A NURSE LED AUDIT

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Introduction: The national average median length of stay (LOS) for adult recipients of renal transplantation is 8 days. Existing pressures to reduce LOS in the modern day NHS have been compounded by the recent SARS COV-2 pandemic. The aim of this project was to identify risk factors for delayed hospital stay in our current practice.
Method: We conducted a nurse-led, retrospective single-centre audit of living and deceased donor- adult renal transplant recipients over a 6-month period. Transplant data was collected from electronic medical records and nursing documentation. Length of stay was calculated and correlated with potential risk factors for prolonged stay.
Results: The study included 64 renal transplant recipients (40% living donor transplant recipients) with an average age of 52 years. The overall median LOS of was 12 days. (10 and 13 days for recipients of living and deceased donors respectively). Recipient weight on postoperative day 7 was found to be significantly associated with prolonged LOS if beyond 2 kg of admission weight (18 $\pm$ 13.7 d vs. 11 $\pm$ 4.8 d beyond and within 2 kg of dry weight respectively; $P = 0.01$) Other recipient factors significantly associated with prolonged stay included persistently raised blood pressure and the need for considerable social and physical support. Patients with LOS $\leq$9 days had

earlier catheter removal (postoperative day 5 ± 0.9 vs. 8 ± 5.8 when discharged on day 10 or later) earlier patient education (postoperative day 7 ± 1.3 vs. 13 ± 7 respectively) and lower average drain output (7 ± 27.5 ml vs. 71 ± 201.6 ml respectively) ($P < 0.05$).
Discussion: Our median LOS for renal transplantation was higher than the national average. Contributing risk factors included proximity to dry weight on day 7 and delayed catheter removal and patient education. We have now implemented a patient-centred Enhanced Recovery after Surgery (ERAS) programme, to address these contributing factors with the ultimate goal of reducing length of hospital stay and improving future patient outcomes.

OP512 PHYSICAL FUNCTION IMPAIRMENT AMONG KIDNEY TRANSPLANT RECIPIENTS AND PATIENTS ON DIALYSIS

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Background: Kidney transplantation (KT) improves physical function (PF) compared to dialysis. However, kidney transplant recipients (KTR) are increasingly elderly and have multiple comorbidities, potentially impacting their PF. We compare the prevalence of PF impairment (PFi) between patients on dialysis and KTR.
Methods: A cross-sectional sample of adults treated with renal replacement therapy (RRT: KT or dialysis) in Toronto, Canada completed the Patient Reported Outcome Measurement Information System (PROMIS) PF item bank (either short form [4 items] or computer adaptive test) and a sociodemographic questionnaire. PROMIS PF is scored on a T-score metric with a mean of 50 (US population mean) and a SD of 10. Severe PFi is defined as a PROMIS PF T-score <35. Association between RRT and PFi was assessed in multivariable regression models. Covariables included: age, sex, ethnicity, Charlson Comorbidity Index (CCI), hemoglobin (hb), and albumin.
Results: Of the 711 participants, 393 were KTR and 318 were on dialysis. The mean age (SD) was 57 (17), majority male (430 [60%]). Mean (SD) PF score for KTR vs dialysis was 48.2 (10) vs. 37.2 (9) ($P < 0.001$). Severe PFi was more frequent in patients on dialysis compared to KTR (43% vs. 11%, $P < 0.001$). 82% of patients on dialysis vs. 36% of KTR had a PF score <45. PF was correlated with age ($r = -0.42$), albumin ($r = 0.44$), CCI ($r = -0.29$) and hb ($r = 0.38$), $P < 0.001$ for all. In a multivariable adjusted linear regression model, KT was associated with higher PF score (B = 4.78, $P < 0.001$; 95% CI: 2.69–6.88). In this model, predictors of PF were age, sex, hb, and CCI. In a logistic regression, KT was associated with lower odds of severe PFi (OR: 0.52, $P = 0.034$; CI: 0.29–0.95).
Conclusions: PFi was less frequent in KTR compared to patients on dialysis, but a large proportion of KTR had T scores <45 indicating noticeable PFi compared to the US general population. In future research we will assess the impact of physical rehabilitation in these patients.

INDUCTION AND MORE

OP513 RABBIT ANTI-THYMOCYTE GLOBULIN AS INDUCTION THERAPY FOLLOWING DESENSITIZATION WITH IMLIFIDASE

Anna Runström[1], Annika Sundberg[1], Yvonne Stenberg[1], Angela Maldonado[1], Hakan Olsson[1], Lena Winstedt[1], Tomas Lorant[1,2], Christian Kjellman[1], Karl Markus Roupe[2]
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Background: Imlifidase (conditionally authorised in the EU for kidney transplant desensitization) is a cysteine protease which cleaves all subclasses of human and rabbit IgG to a $F(ab')_2$ fragment and a dimeric Fc fragment. Rabbit anti-thymocyte globulin (rATG) is the only depleting antibody therapy approved for induction in kidney transplantation. Antibody-based therapies such as rATG may be inactivated if given with imlifidase. The purpose of this study was to investigate the earliest time point to start rATG treatment while avoiding most of the cleavage activity of remaining imlifidase.
Methods: The cleavage pattern of rATG was investigated with sera from healthy subjects ($n = 11$) treated with 0.25 mg/kg imlifidase (EudraCT number: 2019-002770-31). Serum samples were incubated with a fixed, clinically relevant, concentration of 50 μg/mL rATG (commonly observed after a dose of 1.5 mg/kg), for 2 h at 37°C. Serum samples were collected pre-imlifidase through 14 days post-imlifidase and were analyzed using SDS-PAGE and Western blot, developed with a goat anti-rabbit IgG, $F(ab')_2$ specific antibody to evaluate the cleavage of rATG. Imlifidase concentration was analyzed using a validated electroluminescence immunoassay based on MSD technology.
Results: The imlifidase serum concentration in the subjects declined rapidly and at 96 h the mean concentration was 0.5 μg/ml, though with a large individual variation, <0.1–1.8 μg/ml (Figure 1). At this timepoint the level of imlifidase activity had decreased sufficiently to avoid complete cleavage of rATG in 8 of 11 subjects (Figure 2).
Conclusions: rATG may be started as early as 4 days post-imlifidase, taking into consideration that a portion of the first rATG administration may be cleaved in some patients. However, since the rATG dose is high and administration repeated for several days, this cleavage at the start of therapy is not anticipated to have a negative overall effect on the rATG treatment efficacy but will need to be confirmed with in vivo data.
Figure 1

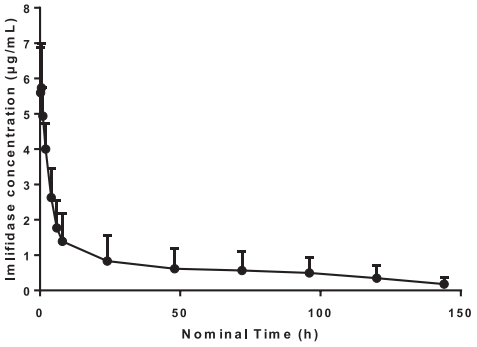

Figure 1. Mean imlifidase concentration vs. nominal time from dosing (N=15). Data BLQ are included in mean calculation as BLQ/2. SD indicated with bars.

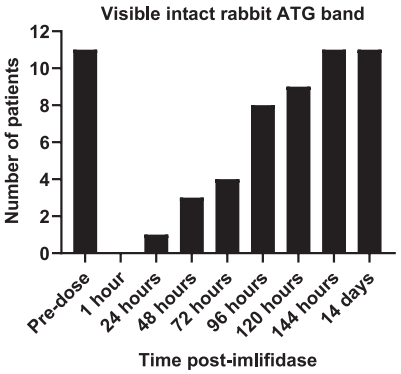

Figure 2. In vitro cleavage of rATG by imlifidase over time. Columns indicate number of subjects with visible intact rATG on Western blot post-imlifidase (N=11).

OP514 TACROLIMUS MONOTHERAPY IN IMMUNOLOGICALLY LOW-RISK KIDNEY TRANSPLANT RECIPIENTS: A RANDOMIZED-CONTROLLED TRIAL.

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Background: Malignancy and infection are major causes of death with a functioning kidney graft and therefore contribute significantly to overall graft loss. To diminish these complications, it is key to lower the immune suppression when possible. For this reason we have performed a randomized-controlled trial to evaluate the safety of tacrolimus monotherapy in immunologically low-risk kidney transplant recipients [NTR4672, www.trialregister.nl].

Methods: Inclusion criteria were HLA mismatches 3 or lower, peakPRA 4% or lower, and absence of an immunological disease. After a run-in period of 6 months after transplantation, recipients were randomized if the following criteria were met: eGFR >30 ml/min, proteinuria <50 mg/mmol, no BPAR after 3 months, and no lymphocyte depleting therapy. Recipients were randomized to either receive standard TAC/MMF or to taper and discontinue MMF at month 9 (TACmono). Advagraf target trough levels were 5–8 μg/l in both groups.
Results: Between March 2015 and October 2018, 121 recipients were included of which 79 could be randomized to either TACmono ($n = 38$) or TAC/MMF ($n = 41$). Mean recipient age was 59, 37% were ≥65 years of age and 59% received a living donor transplant. After randomization and at a median follow-up of 46 months, 3 TACmono and 4 TAC/MMF recipients experienced BPAR. One graft loss occurred in the TACmono group (month 35, chronic prostatitis and borderline rejection), and 2 in the TAC/MMF group (mixed Banff IIA/ antibody-mediated rejection due to non-adherence at month 28, and one Banff IIA vascular rejection at month 35). In each group four recipients have died. Kidney function did not differ with eGFR 57.6 (SEM 3.6) vs. 52.2 (SEM 2.5, P 0.22) ml/min in respectively TACmono versus TAC/MMF at last follow-up. Luminex screening did not detect any HLA-antibodies in both groups 15 months after transplantation. Tacrolimus trough levels were 6.5 and 6.3 μg/l in TACmono vs TAC/MMF at month 15. In addition, gastrointestinal symptoms were less troublesome and medication adherence was better in TACmono (data presented separately).
Conclusion: Tacrolimus monotherapy does not increase the risk of rejection or graft loss in immunologically low-risk kidney transplant recipients. Weaning to tacrolimus monotherapy from six months after transplantation is a safe strategy.

OP515 COMBINATION OF EXTENDED-RELEASE TACROLIMUS PLUS EVEROLIMUS ONCE-DAILY IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS: ER-TAC VS LCPT.

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Introduction: Combination of Everolimus (EVR) with Tacrolimus (Tac) permits reduced calcineurin inhibitors exposure and has been demonstrated safe and effective. Two different once-daily Tac formulations, with different pharmacokinetic profiles are now available: ER-Tac and LCPT. Aim of this study was to compare in kidney transplant recipients (KTx), the 2-year efficacy and safety of ER-Tac versus LCPT, both in combination with EVR, administered concomitantly once a day.
Methods: We conducted a prospective, observational study in eighty-one KTx randomized to once-daily maintenance immunosuppressive regimen based on ER-Tac + EVR + Steroids (ER-Tac + EVR, $n = 43$) or LCPT + EVR + Steroids (LCPT + EVR, $n = 38$). All patients received induction therapy with Thymoglobuline (total dose 200 mg).
Results: Median follow-up was 31 months (range 9–46). Here we present the intention-to-treat analysis at 24-month (80% of patients). There were no differences in patients as well as in graft survival. Moreover, we found no differences in renal function, acute rejection rate, CMV infection. According to the Concentration/Dose ratio of Tacrolimus, there was a significantly higher number of slow metabolizers 1-month after transplant in the LCPT+EVR group. Data are detailed below (Table).

2-year	ER-Tac+EVR	LCPT+EVR	*P*
Patients Survival (%)	95	94	0.852
Graft Survival death-censored (%)	85	90	0.874
Serum Creatinine (mg/dL)	1.79 ± 0.88	1.60 ± 0.58	0.339
Acute Rejection N, (%)	2 (4.7)	3 (7.9)	0.441
Cytomegalovirus viremia (%)	12 (28)	9 (24)	0.430
Drop-out N, (%)	10 (23)	12 (32)	0.277
EVEROLIMUS trough blood levels (ng/ml)	4.63 ± 0.97	4.62 ± 1.13	0.978
TACROLIMUS trough blood levels (ng/ml)	5.58 ± 1.22	5.45 ± 1.36	0.707
1-month Tacrolimus C/D [fast/intermediate/Slow] (%)	60/19/20	34/13/53	**0.012**

Conclusions: Our experience shows that the two extended-release Tac formulations, when administered with EVR once-daily, have comparable 24-month safety and efficacy profile. Further, the higher number of slow metabolizers in the LCPT group may be an advantage to reach Tac target exposure early after transplantation. In the long-term, it may result in higher graft function and graft survival, according to recent data reporting the association between fast Tac metabolizers and IF/TA progression.

OP516 OUTCOMES OF IL2-RA INDUCTION THERAPY IN STANDARD-RISK RENAL TRANSPLANT RECIPIENTS MAINTAINED ON TACROLIMUS - A META-ANALYSIS

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Background and Aims: Interleukin-2 (IL-2) antagonist has been used as an induction therapy in many centres in calcineurin inhibitor-sparing regimens. Tacrolimus has overwhelmingly replaced cyclosporine in the maintenance immunosuppressive protocols in many transplant centres. The aim of our study and meta-analysis is to explore the effect of IL-2 induction therapy on the rate of rejection and patient and graft survival in standard-risk renal transplant patients with tacrolimus-based maintenance immunotherapy.
Method: Inclusion criteria for our meta-analysis were all studies that compared IL-2 induction therapy with placebo or no induction therapy in standard-risk renal transplant recipients on tacrolimus-based maintenance immunosuppressive therapy. A random effects model was used for the meta-analysis. We divided the studies included in this meta-analysis into two groups: Group A (included studies that used same dose of tacrolimus in both arms of each study) and Group B (included studies that compared patients who received induction therapy and low dose tacrolimus versus those who received no induction therapy and high dose of tacrolimus). Standard-risk renal transplant was defined as HLA mismatch <5 and PRA < 50%.
Results: In group A, 11 studies were included ($n = 2886$). IL2-RA induction therapy was not associated with significant differences in comparison to no induction therapy in terms of acute rejection rates (Risk Ratio = 1.03, 95% Confidence Interval [CI] range: 0.84–1.26, I squared = 0%, $P = 0.79$), graft survival (Risk Ratio = 1.15, 95% CI range: 0.82–1.62), delayed graft function (Risk Ratio = 1.01, 95% CI range: 0.82–1.24), CMV infection (Risk Ratio = 1.37, 95% CI range: 0.53–3.51) or malignancy (Risk Ratio = 1.29, 95% CI range: 0.61–2.75). In group B, two studies were included ($n = 669$). There was no difference between both arms in terms of acute rejection rates (Risk Ratio = 0.62, with 95% CI range: 0.33–1.14) or graft survival (Risk Ratio = 1, 95% CI range: 0.57–1.74) or delayed graft function (Risk Ratio = 0.88, 95% CI range: 0.45–1.71).
Conclusion: IL2-RA induction therapy does not improve outcomes in patients maintained on tacrolimus-based immunotherapy in standard risk population.

OP517 IMPACT OF TYPE OF CALCINEURIN INHIBITOR ON OUTCOME IN EUROPEAN KIDNEY TRANSPLANT RECIPIENTS AGED ≥60 YEARS – A COLLABORATIVE TRANSPLANT STUDY REPORT

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Background and Aims: Patients aged ≥60 years represent the fastest growing fraction of kidney transplant (KT) waitlist patients and KT recipients. The standard immunosuppression, also among elderly KT recipients, consists of a calcineurin inhibitor (CNI), either tacrolimus (Tac) or cyclosporine (CsA), mycophenolic acid (MPA) and steroids. Whether the choice of CNI has an influence on outcome in this population is unknown.
Methods: 31 177 KTs from deceased donors performed during 2000–2019 at European centres and reported to the Collaborative Transplant Study were analysed using multivariable Cox and logistic regression analyses. All recipients were aged ≥60 years and received Tac or CsA on an intention-to-treat basis with MPA or azathioprine plus/minus steroids. Death-censored graft loss, patient mortality and secondary outcomes were analysed.
Results: Demographics are shown in Table 1. There was a continuous shift towards Tac-based therapy from 29.3% of cases in 2000/2001 to as high as 94.4% in 2018/2019 (Figure 1A). Risk of five-year death-censored graft loss and patient mortality did not differ significantly between the Tac- and CsA-group (hazard ratio = 0.98 and =0.95, $P = 0.56$ and =0.088, respectively; Figure 1B). Further subgroup analyses also revealed no significant differences for death-censored graft loss (Figure 1C). However, secondary outcomes at the end of year one differed significantly with a lower risk of rejection treatment (odds ratio OR = 0.77, $P < 0.001$) and hypercholesterolemia (OR = 0.64, $P < 0.001$) but a higher risk of de novo post-transplant diabetes in the Tac- versus CsA-group (OR = 1.92, $P < 0.001$). No difference was observed regarding hospitalization due to infection during year one (OR 0.97; $P = 0.61$).

Table 1. Demographics of study patients stratified by type of calcineurin inhibitor, n (%)

Characteristic	Unknown (%)	Type of CNI		P
		Cyclosporine n = 9,694	Tacrolimus n = 21,483	
Transplant year	–			<0.001
Median [IQR]		2006 [02–10]	2012 [08–15]	
Mean ± SD		2006.4±4.7	2011.4±4.8	
2000 – 2009		7,155 (74)	7,087 (33)	<0.001
2010 – 2019		2,539 (26)	14,396 (67)	
Retransplants	–	464 (5)	2,283 (11)	<0.001
Female recipients	–	3,351 (35)	7,643 (36)	0.08
Recipient age (years)	–			<0.001
Median [IQR]		65 [62–68]	66 [63–69]	
Mean ± SD		65.6±4.0	66.2±4.5	
60 – 64		4,102 (42)	8,486 (40)	<0.001
≥ 65		5,592 (58)	12,997 (60)	
Cold ischemia time (hours)	–			<0.001
Median [IQR]		15 [11–19]	15 [11–18]	
Mean ± SD		15.7±6.5	15.1±6.1	
PRA >0%	29.8	993 (12)	3,816 (28)	<0.001
Donor age (years)	–			<0.001
Median [IQR]		64 [52–70]	64 [54–71]	
Mean ± SD		60.0±14.0	61.2±13.4	
Cause of donor death	4.9			<0.001
Trauma		1,680 (19)	2,897 (14)	
Cerebrovascular		6,367 (71)	13,936 (68)	
Other		953 (11)	3,803 (18)	
Donation after cardiac death	2.4	322 (3)	3,643 (17)	<0.001
Donor history of hypertension	4.0	2,692 (29)	3,899 (19)	<0.001
HLA-A+B+DR mismatches	10.3			<0.001
Mean ± SD		3.29±1.55	3.48±1.43	
0 – 1		1,149 (12)	1,679 (9)	<0.001
2 – 4		5,928 (64)	12,491 (67)	
5 – 6		2,128 (23)	4,584 (24)	
Induction treatment	–	4,897 (51)	10,418 (48)	<0.001
Antimetabolite	–			<0.001
MPA		8,121 (84)	18,966 (88)	
Azathioprine		746 (8)	740 (3)	
None		827 (9)	1,777 (8)	
On steroids	–	9,302 (96)	18,512 (86)	<0.001

CNI, calcineurin inhibitor; PRA, panel-reactive antibodies; MPA, mycophenolic acid; IQR, interquartile range; SD, standard deviation

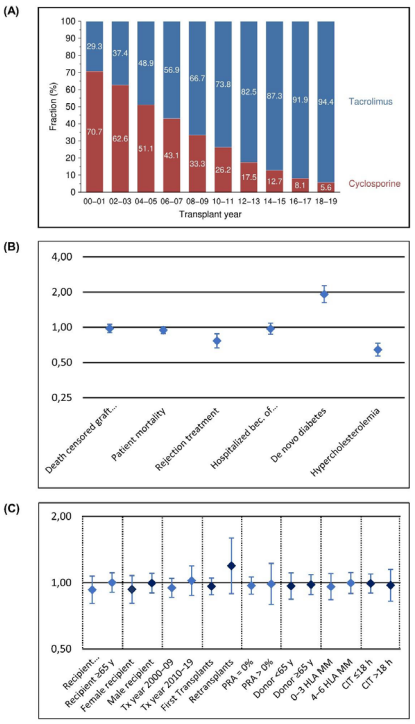

Figure 1
(A) Distribution of the type of calcineurin inhibitor of study patients stratified by transplant year. (B) Risk of tacrolimus versus cyclosporine for death-censored graft loss and patient mortality during the first five post-transplant years as well as side effects during the first post-transplant year. Hazard ratios (HR) or odd ratios (OR) with 95% confidence interval (CI) of multivariable Cox or logistic regressions are shown. (C) Subgroup analysis with hazard ratios and 95% CI of tacrolimus versus cyclosporine on 5-year death-censored graft loss.

Conclusions: Choice of CNI does not influence death-censored graft loss and mortality in recipients aged ≥60 years. Selection of CNI in this population should be influenced by the patient's individual susceptibility to the reported secondary outcomes.

INTRODUCING CELLS FOR IMMUNE REGULATION

OP519 MESENCHYMAL STROMAL CELLS COMBINED WITH EVEROLIMUS PROMOTE T REG EXPANSION BUT DO NOT SYNERGIZE IN A RAT LIVER TRANSPLANT REJECTION MODEL

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Background: Mesenchymal stromal cells (MSCs) have particular properties that can be of interest in organ transplantation, including expansion of regulatory T cells (Tregs), a key factor in graft tolerance induction. The immunosuppression to be associated with MSCs has not yet been defined. Additionally, the impact of the association of everolimus with MSCs on Treg expansion and on induction of liver graft tolerance has never been studied. The aim of this study was to evaluate the effects of MSCs combined, or not, with everolimus, on Treg expansion and in a model of liver transplantation (LT) rejection in the rat.
Methods: Firstly, Lewis rats received intravenous MSCs at D9 with/without subcutaneous everolimus from D0 to D14. Analysis of circulating Tregs was performed at D0, D14 and D28. Secondly, 48 h after LT with a Dark Agouti rat liver, 30 Lewis rats were randomized in 3 groups: everolimus (subcutaneous for 14 days), MSCs (intravenous injection at D2 and D9), or both everolimus and MSCs. Rejection of the liver graft was assessed by liver tests, histology and survival.
Results: Individually, MSC infusion and everolimus promoted Treg expansion in rats, and everolimus had no negative impact on Treg expansion when combined with MSCs. However, in the LT model, injections of MSCs 2 and 9 days following LT were not effective at preventing acute rejection, and the combination of MSCs with everolimus failed to show any synergistic effect when compared to everolimus alone.
Conclusion: Everolimus may be used in association with MSCs. However, in our model of LT in the rat, post-transplant MSC injections did not prevent acute rejection, and the association of MSCs with everolimus did not show any synergistic effect.

OP520 EFFICIENT EXPANSION OF HUMAN GRANZYME B–EXPRESSING B CELLS WITH POTENT REGULATORY PROPERTIES

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Background: Granzyme B (GZMB)-expressing B cells have been shown to be an important regulatory B cell subset in humans. However, it is unclear which subpopulations of B cells express GZMB under normal conditions and which protocols effectively induce ex vivo expansion of GZMB$^+$ B cells.
Methods: Fresh human PBMCs were isolated from healthy blood donors by Ficoll gradient centrifugation and phenotyped by flow cytometry. B cells and CD4$^+$CD25$^-$ effector T cells were negatively selected using magnetic beads. GZMB$^+$ B cells were expanded using a cytokine cocktail and cocultured with effector T cells. The phenotype and the mechanisms underlying the suppressive capacity of expanded GZMB+ B cells were studied.
Results: We found that in the peripheral blood of normal individuals, plasmablasts were the major B cell subpopulation that expressed GZMB. However, when using an in vitro plasmablast differentiation protocol, we obtained only

2% GZMB$^+$ B cells. Nevertheless, using an expansion mixture containing IL-21, anti-BCR, CpG oligodeoxynucleotide, CD40L, and IL-2, we were able to obtain more than 90% GZMB$^+$ B cells after 3 d culture. GZMB$^+$ B cells obtained through this protocol suppressed the proliferation of autologous and allogenic CD4$^+$CD25$^-$ effector T cells. The suppressive effect of GZMB$^+$ B cells was partially GZMB dependent and totally contact dependent but was not associated with an increase in effector T cell apoptosis or uptake of GZMB by effector T cells. Interestingly, we showed that GZMB produced by B cells promoted GZMB$^+$ B cell proliferation in ERK1/2-dependent manner, facilitating GZMB$^+$ B cell expansion. However, GZMB$^+$ B cells tended to undergo apoptosis after prolonged stimulation, which may be considered a negative feedback mechanism to limit their uncontrolled expansion. Finally, we found that expanded GZMB$^+$ B cells exhibited a regulatory phenotype and were enriched in CD307bhi, CD258hiCD72hi, and CD21loPD-1hi B cell subpopulations.
Conclusions: Our study shed new insight into biology of GZMB$^+$ B cells and provided an efficient method to expand GZMB$^+$ B cells for potential cell therapy in transplantation and autoimmune diseases.

OP521 GAMMA-DELTA T CELL THERAPY FOR THE TREATMENT OF POST-TRANSPLANT CMV INFECTION: PROOF OF CONCEPT

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Background: Human cytomegalovirus (CMV) infection in solid organ transplant recipients (SOTRs) is associated with increased risks of allograft loss, morbidity and mortality. Current gold standard treatment, based on the use of Valganclovir, fails to prevent late CMV reactivation or emergence of viral resistance in a significant percentage of SOTRs. Importantly, long-term CMV clearance relies on the establishment of an anti-CMV T-cell response. There is therefore a growing interest in developing anti-CMV cell therapy. Both $\alpha\beta$ and $\gamma\delta$ T cells are key effectors of the anti-CMV immune response. The goal of this study was to explore a potential $\gamma\delta$ T cells-based immunotherapy.
Methods: Healthy donors (both CMV-positive and CMV-negative) and kidney transplant recipients (KTRs) undergoing refractory CMV infection were enlisted in this preclinical study. $\gamma\delta$ T cells were sorted from peripheral blood, then amplified and activated *in vitro,* using a T cell receptor (TCR) agonist combined to different cytokines, notably IL-4 and IL-15. The reactivity of expanded $\gamma\delta$ T cells against CMV-infected target cells was then measured *in vitro*.
Results: $\gamma\delta$ T cells amplification from both CMV-positive and CMV-negative healthy donors, as well as KTRs, was reproducible and compatible with a human cell-immunotherapy. Amplified cells displayed an activated and differentiated phenotype, but low exhaustion, produced IFNγ in the presence of infected target fibroblasts, endothelial cells and macrophages, and were able to control viral dissemination *in vitro*. At the mechanistic level, anti-CMV reactivity was independent of the $\gamma\delta$TCR but involved the co-stimulatory receptor lymphocyte function-associated antigen 1 (LFA-1).
Conclusions: Altogether, these data provide a proof of concept for a future use of amplified $\gamma\delta$ T cells, in the prevention and curative treatment of CMV disease in SOTRs. These results pave the way for a future phase I clinical trial.

OP522 MESENCHYMAL STEM CELLS LOCAL THERAPY FOR INDUCTION OF IMMUNOSUPPRESSION IN LIVER TRANSPLANTATION: RESULTS OF PILOT STUDY.

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Aims: The aim of the study was to evaluate the efficiency of the adipose tissue mesenchymal stem cells (MSC) local therapy (LT) for induction of immunosuppressive therapy (IIT) in patients after liver transplantation (KT) in the early postoperative period.
Methods: This is a report of pilot, prospective, single center, open label, randomized study of the superiority MSC induction of immunosuppression over standard IIT in regard of immunological dysfunction development and liver transplant function improvement. Inclusion criteria: adult liver transplant recipients who received liver transplant from DBD. Exclusion criteria were living-donor LTx, recipient portal vein thrombosis. MSCs introduction was performed in 10 patients through the portal vein during the reperfusion in total dose of 20 million cells. Maintenance therapy includes calcineurin inhibitor, mycophenolic acid, steroids. The protocol liver transplant biopsies were performed on the 7th day.
Results: Results of our research showed that the frequency of graft dysfunction which were associated with rejection, was developed in 2 patients. The severity of ACR was mild (RAI 5). Median GFR at the beginning and end of protocol was 27 $\pm$ 6.2 ml/min. Median trough level of tacrolimus was 2.1 $\pm$ 1.5 ng/ml with range of 0–5.3 ng/ml. There were no severe adverse effects of MSC therapy. All patients were switched to 3 component IS composed of tacrolimus (5–8 ng/ml), MMF (1 g/day) and steroids (medrol 16 mg tapering after 28 POD). Patients with decreased GFR were managed by the minimizing of Tac and substitution of overall IS by prolonged steroids, increased MMF and addition of Everolimus.
Conclusions: Local infusion through the portal vein of allogeneic adipose tissue MSC for induction of immunosuppressive therapy in liver transplantation is effective and safely.

OP523 CREATION OF BIOENGINEERED VASCULARIZED SPLEEN MATRIX AS AN ENDOCRINE CELL SUPPORT

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Background: Diabetes is currently treated by insulin injection. However, its ideal cure, pancreas transplantation, is limited by donor shortage and side effects of a lifelong immunosuppressive treatment. Aiming to overcome these limits, we used tissue engineering techniques in order to create a decellularized spleen matrix (DSM), thereafter seeded with B-cells, to regenerate a functional, biocompatible and transplantable graft.
Methods: Rat spleen grafts were harvested on the celiac trunk and decellularized by detergents perfusion. DSM was characterized by DNA, collagen, elastin, GAGs and residual SDS quantification, as well as by classical histology and immunohistochemistry. PrestoBlue Cell Viability Assay evaluated cytotoxicity after 5 days static culture of MIN-6 cells, seeded on DSM patches. Biocompatibility was analyzed after subcutaneous implantation of DSM or native tissue; the infiltration of CD68 and CD3 cells was assessed by IHC at 14 & 30 days. Finally, whole DSM were recellularized with HUVECs and MIN-6 cells, then cultured in a perfusion bioreactor for 5 days. MIN-6 cells function was evaluated with Glucose-stimulated insulin secretion (GSIS) test.
Results: Spleens were successfully decellularized by detergents perfusion, becoming white while preserving their 3D architecture. The reduction of 99% of DNA amount and histology confirmed the complete cell removal and the preservation of the micro-architecture. IHC for collagens I & IV, fibronectin, laminin and ECM proteins assays showed the preservation of the main ECM components. The low amount of SDS residues (<1%) and the unchanged cell viability emphasized the non-toxicity of the DSM. Biocompatibility was confirmed by a lesser infiltration of CD68 cells in DSM than in native tissue. DSM cultured in a bioreactor allowed HUVECs engraftment to the vascular wall, and the formation of MIN-6 cells clusters into the DSM, while preserving their insulin release during a perfused GSIS.
Conclusion: Vascularized DSM can be obtained by perfusion-decellularization while retaining its macro- & microarchitecture. ECM components are also preserved, with a good biocompatibility and without any cytotoxicity. Moreover, DSM could be a potential vascularized scaffold for pancreatic regeneration.

OP524 CHARACTERIZATION OF MESENCHYMAL STEM CELL INDUCED REGULATORY B CELLS (MSC-INDUCED BREG)

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Background: Several studies described association between increase of regulatory B cells (Breg) and tolerance in kidney transplanted patients. However, a lack of unique defining Breg markers limits their clinical potential. Breg induction by mesenchymal stem cells (MSC) has been proposed to induce and expand Breg in vitro for downstream applications, that will constitute an optimal *in vitro* system to improve characterization and applicability of Breg.
Methods: Tonsil isolated resting B cells were cultured with MSC and T cell-like stimulating cocktail (aIgM, CD40 agonist, IL-2) in 96 w plates for 7 days. Cell surface markers and intracellular cytokines were assessed by flow cytometry, and cytokine production was quantified by ELISA. To test induced Breg immunomodulatory capacity, cells were cocultured with CFSE-labelled autologous T cells at different ratios. In parallel experiments, B cells were sorted based on IL-10 production to perform transcriptomic analysis by RNA sequencing (RNA-seq) and identify differentially expressed genes (DEG) by DESeq2.
Results: Compared to activated B cells, MSC induced Breg, showed an increase of transitional B cell populations, IL-10 secretion and expression, and no TNFα induction. Breg modulated T cell proliferation by 40% in 2 to 1 cell ratios (Table 1). In the RNA-seq analysis, 43 DEG were identified with fold changes over ±2 log2. Gene ontology analysis showed a significant enrichment of genes involved in immune regulation and extracellular matrix organization among others.
Conclusions: MSC induce Breg to express and secrete high levels of IL-10, no TNFα, and induce a shift to transitional B cell phenotype, highlighting a strong regulatory induction, further validated by modulation of T cell proliferation. RNA-seq of IL-10+ vs IL-10− B cells identified 43 differentially expressed genes related to several immune relevant processes.

Table 1 Summarized results data.

Results	MSC-induced Breg	Activated B cell
IL-10 Secretion (ELISA, pg/ml)	94	6
TNFα Secretion (ELISA, pg/ml)	2	11
Transitional B cell (Flow cytometry, % from total B cells)	15	2
Intracellular IL-10 (Flow cytometry, % from total B cells)	45	25
Intracellular TNFα (Flow cytometry, % from total B cells)	6	13
Modulation T cell proliferation (% CFSE-MFI modulation, 2:1 B cell-T cell ratios)	40	8

FOCUS GROUPS - CLINICAL CASES

CLINICAL CASES: ALLOIMMUNITY

OP129 THE OUTCOME OF PLASMA CELL-RICH ACUTE REJECTION IN KIDNEY TRANSPLANTATION, IS IT REALLY POOR?

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Introduction: The outcome of Plasma cell-rich acute rejection (PCAR) in kidney transplant is reported to be poor. However, PCAR which can be associated with any type of rejection, may not be considered as independent morphological prognostic feature. Different treatment modalities were prescribed with variable responses. We report here four cases of PCAR and describe their presentations, type of rejection, associated conditions and treatment outcome.
Methods: Out of 1920 kidney transplant recipients under follow-up in our center from 1996 to 2019, four patients were reported to have PCAR according to 2007 Banff classification. They were re-evaluated based on 2015 Banff classification. The treatment protocol was tailored according to the type of rejection and associated conditions.
Results: The four patients, aged 28, 44, 46 and 54 years, had live unrelated renal transplant done somewhere abroad with no data about donor HLA typing. Two of them were females. One had high PRA and she was positive for HBsAg. One patient received induction immunosuppression with basiliximab. They all received prednisolone, mycophenolate and cyclosporine as the maintenance immunosuppression and had immediate graft function. Rejection happened between 23 to 180 months post-transplant. Two patients had acute T-cell mediated Banff 1A rejections with features consistent with early membranous nephropathy. One had acute T-cell mediated rejection Banff 1B and the fourth had borderline T-cell mediated rejection with morphological changes suggestive of chronic active antibody mediated rejection (AMR). Plasma cells constituted 10 to 30% of the interstitial infiltration. All patients received solumedrol pulse. Both patients with features of membranous nephropathy received rituximab and one of them had additionally IVIG. The patient with AMR received plasma exchange and IVIG. However, she did not receive rituximab as she was positive for HBsAg. All patients responded well to treatment and the mean improvement in eGFR was 12.8%, 24.9%, 40.3% and 39.1% at 1-, 3-, 6- and 12-month post-treatment. Repeat kidney biopsy at 3 to 12 weeks post-treatment showed resolution of plasma cell infiltration in all patients.
Conclusion: Outcome of PCAR management was favorable among our patients irrespective of the type of rejection and associated conditions.

OP130 SUCCESSFUL SECONDARY TRANSPLANTATION AFTER PLASMAPHERESES FOR SUSPECTED ANTI-ENDOTHELIAL CELL ANTIBODIES

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Tissue-specific non-HLA antigens can play crucial roles in allograft immunity and have been shown to trigger humoral responses leading to rejection of HLA-matched kidney allografts. Interest in the role of endothelial-specific antigens has grown over the past years as it has been shown that antibodies reacting with endothelial cells (ECs) are associated with rejection. Such antibodies escape the detection in conventional crossmatch tests, as they do not react with lymphocytes. We present a case report of a 69 year old male patient, whose kidney allograft was hyperacutely rejected in spite of the absence of HLA-specific antibodies. Endothelial-specific antibodies were detected *in vitro* after transplantation in a locally developed endothelial cell-based assay and were considered to be responsible for rejection. Patient serum was reactive with primary renal ECs, demonstrated by antibody binding and complement-dependent-cytotoxicity. Antibodies from this patient did not react with lymphocytes, nor were HLA DSAs found. Two years later, the patient successfully received a second kidney transplant, after extensive immunological preparations with rituximab and therapeutical plasmaphereses before and after transplantation. We could demonstrate that therapeutic removal of antibodies against non-HLA ECs specific molecules can be monitored by our renal EC crossmatch test, resulting in successful transplantation.

OP131 HYPERACUTE HUMORAL NON-HLA ALLOGRAFT REJECTION AND PROTEIN S DEFICIENCY DISEASE, CASE REPORT AND REVIEW

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Introduction: Kidney transplantation continues to be the therapy of choice for patients with ESRD, improving quality of life and survival. Thrombophilic disorders predispose for thromboembolic and probably other occlusive vascular events that occur when additional risk factors play in concert. Immune responses to non-HLA antigens are recognized as part of the acute and chronic results of kidney transplantation, 22% develop non-HLA antibody after transplantation, with a poor prognosis in this case.
Aim: To describe a clinical case of a patient that present and hyper acute rejection and Protein S deficiency disease, and show the relationship of both disorders.
Results: 32-year-old female with undetermined CKD etiology in 2017 and SAH, on the waiting list for a deceased donor of blood group O since 2019, October 11, 2020 selected for kidney transplantation, a SARS-CoV-2 PCR test is performed and Chest CT as a protocol to rule out COVID-19, histocompatibility tests CDC (-), DDT (-), PRA class I 3%, PRA Class II 2% HLA equal 5/14, without ADES. Warm ischemia time 27 minutes, cold ischemia time 16:07 hours, thymoglobulin and methylprednisolone as induction. At second post-transplant day presented severe pain in graft, macroscopic hematuria, Doppler ultrasound showed acute thrombosis of the renal vein of the graft, and was admitted to surgery showing violaceous graft, renal vein thrombi, and allograft nephrectomy was performed. The Histopathology report was acute rejection suggestive of humoral component, positive C4d, and recent thrombosis of the renal artery and vein. The study protocol was started, with no evidence of ADES HLA, and finding Protein S deficiency.
Conclusion: Renal allograft recipients with thrombophilia are at risk of developing an acute rejection or other vascular event. No se pudieron cargar todos los resultadosThrombophilic disorders predispose patients for thromboembolic and probably other occlusive vascular events that occur when additional risk factors play in concert.

OP132 ALLOIMMUNE CELLULAR AND HUMORAL MONITORING IN A KIDNEY TRANSPLANT RECIPIENT THAT PRESENTS AN ACUTE LEUKEMIA TREATED WITH BLINATUMOMAB

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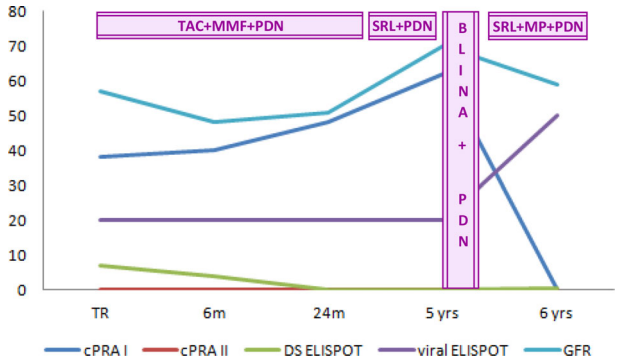
Few cases of B-Acute Lymphoblastic Leukemia (B-ALL) are reported in kidney transplant (KT) recipients. Chemotherapy strategies are limited due to rejection risk and nephrotoxicity. Alloimmune monitoring is mandatory. We present a case of a KT patient affected with B-ALL, describing the haematological treatment and alloimmune response appraisal.
A 55-year-old man received a living KT (5 HLA mismatches), with basiliximab induction and maintenance therapy of tacrolimus, mycophenolate and steroids.
The patient was diagnosed of B-ALL. Consolidation therapy was mercaptopurine, prednisone, vincristine and methotrexate. Antirejection therapy

included mycophenolate withdrawal and tacrolimus into rapamycin conversion. Peg-asparaginase and rapamycin were withdrawn due to hepatotoxicity. Treatment was maintained in prednisone monotherapy with toxicity resolution. Also, Blinatumomab treatment was stablished with an efficient B-cell depletion. HLA donor-specific (ds) antibodies were persistently negative and dsIFN-γ T-cell Elispot assay resulted negative, while viral antigens T-cell response was maintained. At this moment anti-rejection therapy was solely based on corticosteroids. Rapamycin was reintroduced and prednisone adjusted. 2yrs later, allograft function is stable (GFR 59mL/min).
Blinatumomab mediates the formation of a cytolytic synapse between T-cells and tumour-cells, releasing proteolytic enzymes to kill both proliferating and resting B-cells. Concerns in the use of this kind of molecule in SOT recipients may arise due to rejection risk secondary to T-cell activation. However, the specific activation against target antigens did not produce cross-reactivity against allogenic antigens. Strict monitoring of both humoral and cellular responses was performed to safely adapt the anti-rejection regimen during blinatumomab. A close immunomonitoring strategy at humoral but also at T-cell level translates an individualized improvement in graft and patient survival.



OP133 GRAFT-VERSUS-HOST-DISEASE AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION WITH SEVERE GASTROINTESTINAL AFFECTION TREATED WITH VEDOLIZUMAB

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Until recently, only few cases of graft versus host disease (GVHD) after pancreas transplantation have been reported, usually with fatal outcome. We present a case of 41-yo female patient who received a simultaneous pancreas-kidney transplant (SPKT). Immunosuppression included ATG induction, tacrolimus, mycophenolate mofetil, and prednisolone. Both allografts had immediate excellent function.
Four months after SPKT, she complained diarrhea, nausea, and an oral ulcer was detected. Microbiological analysis for viral, fungal and enteric pathogens were negative. Colonoscopy revealed petechial redness in ileum and circumferential purulent covering over the valvula, which were suggestive of GVHD. The histopathologic evaluation showed focal crypt cell atrophy and crypt cell apoptosis.
Initial GVHD-treatment included IV methylprednisolone combined with oral budesonide. After an initial positive response, symptoms gradually worsened. Second line treatment was initiated, consisting of ruxolitinib 10 mg TID and extracorporeal photopheresis (ECP). Due to severe pancytopenia, ECP and ruxolitinib were paused. The peripheral blood chimerism analysis was performed four times (Droplet Digital PCR Technology) showing only 1.3% donor chimerism.
Later on, sudden acute abdominal pain led to an emergency laparotomy. Bowel perforation was diagnosed, caused by necrotic ulcerations 30 cm along the small bowel, and treated with partial bowel resection. A third line treatment started with two vedolizumab 300 mg infusions and ECP continued. Afterwards, a relaparotomy was done due to occlusion, and an ileostomy was set in place. Tacrolimus concentration was kept high, but it oscillated due to excessive stoma excretion causing repeated episodes of dehydration. The ileostomy was closed nine months after initial laparotomy.
To our knowledge, this is the first solid organ transplant recipient treated successfully with vedolizumab for GVHD. Both allografts are functioning and the patient survived.

OP134 TRANSPLANTING A TRANSPLANTED KIDNEY- A SAFE STRATEGY IN TIMES OF ORGAN SHORTAGE?

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Background: Organ Shortage is a common worldwide problem. Due to the urgent need to raise the renal transplant rate, new options such as the transplantation of an already previously transplanted kidney when a deceased donor presents with a well-functioning renal allograft might be a possibility to expand the pool of donors. We provide our experience of the successful reuse of transplanted kidneys in the Eurotransplant region.
Methods: We searched in the Eurotransplant database from January 1, 1995 until December 31, 2015, to detect kidney donors who received a renal transplant previously. Donor and transplant data were analyzed with a follow-up until graft loss or the patient´s death.
Results: 68554 kidneys were allocated for transplantation in the given 20-year time period. Nine kidneys had already previously been transplanted and were offered again. Four of the nine kidneys were finally transplanted. The mean interval between first transplantation of the renal graft and retransplantation offer was 1689±1682 days (standard deviation (SD); range 55 to 5333 days).
At the time of the first transplantation, mean serum creatinine of the donors was 1.0 (range 0.6–1.3 mg/dl) with a mean eGFR of 87ml/min, ranged between 68 and 114ml/min/1.73m^2. At the time of the second transplantation, mean serum creatinine level of the donors was 1.4 mg/dl (range 0.8 – 1.5 mg/dl) with a mean eGFR of 55 ranged from 37 to 76 ml/min/1.73 m^2). Considering that the second donor had only one functioning kidney, graft function appeared well preserved. The mean graft survival in the first recipient was 50 months and in the second was 111 months (range 40 – 215 months).
Conclusion: Our report shows that a previously transplanted kidney may successfully be transplanted again, even if graft survival in the first recipient was up to 9 years. Such organs may be considered for older and younger recipients in carefully selected cases.

CLINICAL CASES: DONORS, ZEBRAS AND COVID: CHALLENGES IN INFECTION MANAGEMENT

OP135 LETERMOVIR TREATMENT FOR RESISTANT/ REFRACTORY CYTOMEGALOVIRUS INFECTION IN KIDNEY AND PANCREAS TRANSPLANTATION

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Background: Cytomegalovirus (CMV) infection remains a major challenge in transplantation. Ganciclovir changed the prognosis, but viral resistance has emerged as a new threat. New antiviral drugs, such as letermovir, was approved for CMV prophylaxis after hematopoietic stem cell transplantation. In solid organ transplantation showed variable effectiveness in the prophylaxis or treatment of CMV infection. Experience is limited, and letermovir for treatment in pancreas transplantation has not been yet studied.
Results: We report on letermovir treatment in one kidney and two kidney/pancreas transplant patients with refractory or ganciclovir-resistant CMV infection (UL54/ UL97 mutations confirmed in two patients) in Finland. In kidney/pancreas transplant patients, persistent leukopenia undermined both immunosuppressive and antiviral treatment, and favored life-threatening bacterial infections. Letermovir at 480 mg OD dose was started after ganciclovir treatment failure or because of severe leukopenia. Letermovir was well tolerated. All three patients achieved viral clearance after letermovir monotherapy lasting from 1.5 to 6 months, although in all cases mofetil mycophenolate was discontinued. One patient had an acute rejection because of under immunosuppression. Granulocyte-stimulating-factors were discontinued after switching to letermovir.
CMV recurred in all patients after letermovir was stopped in the context of other complications (acute rejection, intercurrent infections, pulmonary thromboembolism and cancer). Antiviral treatment was reinitiated in only

two patients. All patients have currently CMV-DNAemia under the detection threshold. Both patient and graft survival is 100%. Patients´ CMV-DNAemia and leukocytes count are shown in Figure 1.
Conclusions: Letermovir seems like an effective and safe option for difficult to treat CMV infections in kidney and pancreas transplant patients. After letermovir treatment, CMV reactivation is common and associated with intercurrent complications. Letermovir is a valuable option for the treatment of refractory CMV infection in patients with severe drug-induced leukopenia.

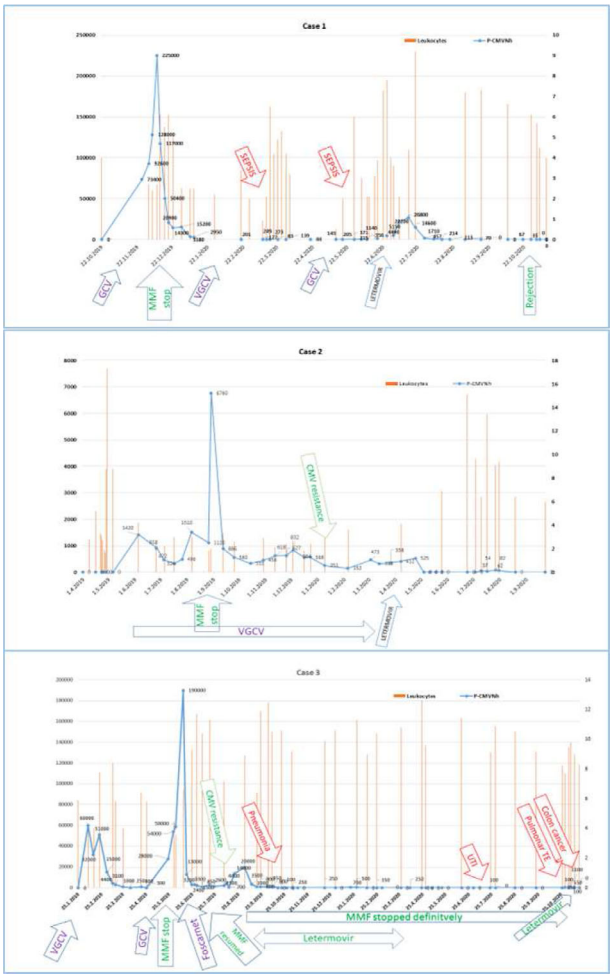

Figure 1. CMV-DNAemia and leukocytes count in the three patients. CMV treatment and main complications showed with arrows.

OP136 DISEASE COURSE AND TREATMENT OF SARS-COV-2 INFECTION IN AN ISOLATED INTESTINAL TRANSPLANT RECIPIENT

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Age and co-morbidity (including immunosuppression (IS)) are risk factors for severe coronavirus disease 2019 (COVID-19). Due to exposure to high-dose IS, intestinal transplant (ITx) recipients may be at high risk for severe disease course. COVID-19 and potential gastroenterological manifestations have not been reported after isolated ITx.
A 41-year-old ITx recipient was hospitalized because of dehydration during the second European COVID-19 wave. One year ago, she had undergone an intestinal re-transplantation for chronic allograft enteropathy, 14 years after a first ITx for chronic intestinal pseudo-obstruction. IS consisted of Tacrolimus, Azathioprine, and corticosteroids. On admission, COVID-19 PCR was negative. One week later, she tested positive on screening COVID-19 nasopharyngeal PCR swab. At that time, she was asymptomatic, had normal inflammatory markers and chest X-ray. Azathioprine was halted and Tacrolimus slightly raised. Prophylactic low-molecular weight heparin (LMWH) was administered, because of elevated D-dimers. One week after positive testing, she developed anosmia, mild dyspnea, and a mildly elevated inflammatory markers were present. Remdesivir was started and continued for 5 days. She presented a high stomal output 2 days in a row. An ileoscopy and biopsy showed no signs of infection or rejection. She was discharged after 4 weeks and remains in good health since then.
Despite presenting a mild form of COVID-19 infection, we preventively treated this ITx patient with LMWH and Remdesivir. Similar to common practice in other solid organ Tx, azathioprine was temporarily halted. A transient increase in stomal output was observed but without proven rejection or infection.
This is a first report of COVID-19 after isolated ITx. The disease was mild and the treatment similar to other organ transplant recipients. Registry data are needed to determine the real incidence and severity of COVD-19 after ITx and its potential gastrointestinal manifestations.

OP137 COVID-19 ASSOCIATED NEPHROPATHY IN A KIDNEY TRANSPLANT RECIPIENT AND HIGH RISK APOL1 VARIANT DONOR

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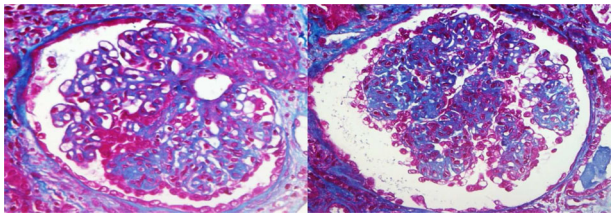
Introduction: Since the beginning of pandemic SARS-CoV-2 infection, several cases of collapsing glomerulopathy on native kidneys with acute kidney injury were reported, almost exclusively in patients of African ethnicity. However, data are lacking in kidney transplant patients.
Clinical presentation: A 74-year-old Caucasian woman received first kidney transplantation in 2018 for end-stage kidney disease related to Goodpasture disease. After transplantation, immunosuppressive treatment included tacrolimus and corticosteroids, and baseline creatinine was around 1.5 mg/dL without significant albuminuria. In January 2021, she was hospitalized because of nephrotic syndrome; creatinine increased to 4.8 mg/dL, albuminemia was 2.7 g/dL and urinary albumin/creatinine ratio was 12 g/g. Kidney biopsy showed collapsing glomerulopathy with tubular necrosis without any argument for acute rejection (Figure 1). She was tested negative for HIV, HBV, HCV, Parvovirus B19, CMV, EBV. No treatment potentially responsible for collapsing glomerulopathy had been administered. Nasal SARS-CoV-2 PCR came back positive, with positive blood IgG and IgM. APOL1 donor gene sequencing revealed a high risk *APOL1* variant (G1/G1). Patient was initially asymptomatic, but rapidly developed SARS-CoV-2 pneumonia needing oxygen (up to 3L/min) for a few days, with positive evolution. After kidney biopsy, corticosteroids were increased to 1mg/kg/day, but unfortunately patient became rapidly dialysis dependent without kidney function improvement.
Discussion: SARS-CoV-2 infection could have played the role of « second hit » in a genetic predisposed kidney transplant. Case reports of collapsing glomerulopathy caused by SARS-CoV-2 infection in native kidneys reported high prevalence of high risk *APOL1* variant. Here, we show that in kidney transplant patients, high risk *APOL1* donor variant could be the first hit of the disease (genetic predisposition for the disease). Secondarily, SARS-CoV-2 infection could trigger collapsing glomerulopathy as it has been described for HIV associated patients in native kidney. Thus, genotyping *APOL1* donor gene could help clinicians understand the origin and severity of COVID associated nephropathy in kidney transplant recipients.

Figure 1. Light microscopy showing collapsing glomerulopathy.



OP138 ORGAN DONOR WITH RT-PCR POSITIVE FOR SARS-CoV-2, IS IT ALWAYS NO?

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The COVID-19 pandemic is conditioning important changes in the field of organ donation. Although no case of donor-derived COVID-19 infection has been described, there is a theoretical possibility of infection transmission.
We present a 21-year-old organ donor with a history of cured COVID-19 (more than 14 days from the onset of symptoms and more than 72 hours asymptomatic), but with PCR for SARS-CoV-2 positive in which it was decided to continue with the donation process. The donor was admitted due to severe head trauma, presenting positive RT-PCR in nasopharyngeal exudate, as well as positive IgG serology for SARS-CoV-2, which is why it was decided not to isolate. He evolved to brain death persisting positive PCR result.
For the study of SARS-CoV-2 infection a real-time RT-PCR was performed that detects 3 different genes: E (envelope), RdRp (RNA polymerase-RNA-dependent) and gene N (nucleocapsid). As an urgent technique, a real-time RT-PCR detecting two targets (S and ORF1ab) was used. The serological study was carried out using a chemiluminescence microparticle immunoassay technique. The microbiological results performed on the donor are shown in Table 1. Heart transplantation was performed without notable incidences, with a favorable evolution and discharge from hospital of the patient, who did not present symptoms compatible with COVID-19. Moreover, RT-PCR for SARS-CoV-2 and serological controls were negative during admission.
We consider that the option of donation could be considered even with a positive RT-PCR for SARS-CoV-2, if certain circumstances exist in the donor: i) asymptomatic or oligosymptomatic COVID-19; ii) long-term asymptomatic period; iii) Elevated RT-PCR CT, particularly if the positivity is for certain genetic targets; iv) positivity for IgG antibodies. With these requirements, the benefit of transplantation in terms of survival and quality of life would prevail in decision-making.

Table 1. COVID-19 in the donor

	RT-PCR					IgG
Date	E (Ct)	RdRp (Ct)	N (Ct)	S (Ct)	ORF1ab (Ct)	SARS-CoV-2
Day 0	+ (35.7)	+ (37.6)	+ (35.2)			
Day +37	-	-	+ (34.7)			+
Day +44				+ (32.2)	+ (33.1)	
Day +44 diferido*	-	-	-			

Ct: Cycle threshold;

OP139 ORGAN DONATION IN KSA: COVID-19 PANDEMIC

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Background: March 2, 2020 marked the first positive case of COVID-19 in the Kingdom, and in order to prevent further spread of the disease, preventive measures were ordered by the government, this includes the position statements on organ transplantation and donation during COVID-19 pandemic released by the Saudi Center for Organ Transplantation (SCOT) which provides recommendations on transplantation.
Aims: Determine the impact of the COVID-19 pandemic on organ donation and transplantation in KSA. Application of special measures using PCR both donors and recipients.
Methods: Analysis of organ donation in KSA year 2020 and 2019
Results: Comparing the year 2020 and 2019 deceased donation, the total number of possible donors were 585 to 408 respectively, potential donors declared brain dead based on neurological criteria 411 to 286, families approached for donation 354 to 231 and consents for donation 126 to 74; actual donors 114 to 65 and utilized donors 113 to 63. In general, a decreased of 30 to 35% in possible to potential donors; 41% in consent for donation; 43% in actual donor; and 44% in utilized donors. In 2020, only 191 organs were transplanted compared in 2019's 343 a 44% decline in transplanted deceased organs. In living donation, out of 11 govt. transplant centers, 9 centers have stopped their activity from March 15 until September 2020. To date, all transplant centers have resumed their activity by following the protocol recommended by SCOT.
Conclusions: The COVID-19 pandemic has greatly affected the organ donation activities in the Kingdom, resulting in a huge loss in the number of donors. Position statements were made available for all the transplant centers, which includes a thorough investigation of all donors and recipients for transplant; and application of special measures in COVID-PCR testing. The following measures created, were to ensure the continuity of organ donation program while, prioritizing patient's safety and well-being.

OP140 BILATERAL PNEUMONIA IN A KIDNEY TRANSPLANT RECIPIENT THE COVID-19 ERA- SOMETIMES IT'S A ZEBRA

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Introduction: COVID-19 is an ongoing pandemic caused by SARS-CoV-2. Symptoms are highly variable, ranging from none to severe illness, with bilateral interstitial pneumonia being the hallmark of the disease.
Case presentation: A 72-year-old male patient presented at the outpatient clinic in September 2020 with complaints of dyspnea. He was afebrile, spO2 95% on ambient air. Past medical history included DD kidney transplantation in 2013. He was recently converted to everolimus from CnI because of PCC of the skin. Maintenance IS included everolimus, MMF and prednisone. His graft function was good, with eGFR of 74 ml/min. CRP was 90 mg/L. Everolimus trough level was 6ug/L. He was referred for SARS-CoV-2 testing which came negative, but the Rx revealed bilateral infiltrates, so he was hospitalized. IS was minimized and piperacillin with tazobactam initiated. Serology for SARS-CoV-2 came negative. CT of the thorax was performed, which revealed bilateral diffuse alveolar-interstitial infiltrates. Therapy was escalated to meropenem, vancomycin and fluconazole. Despite that, he reported worsening of dyspnea and was started on supplemental oxygen. Due to the discrepancy of the impressive radiological findings and clinical status (afebrile, minimal oxygen support, microbiology negative), the differential diagnosis of non-infectious pneumonitis was considered and everolimus was discontinued. Bronchoscopy and lung biopsy were performed. All BAL remained sterile and the PHD was concordant with medication caused pneumonitis. Upon discontinuation of everolimus, the clinical condition improved with complete regression of infiltrates. During 4 months of follow-up, he remains well.
Conclusion: Providing healthcare during the pandemic is challenging, especially for populations at high risk such as transplant recipients. There are reports of patients who test negative in the nasopharynx but are positive in BAL. Immunocompromised patients pose an additional challenge because they do not always seroconvert. Nevertheless, even during a pandemic and the predominance of one diagnosis, it is still as important as ever, to perform thorough diagnostic work-up. Everolimus-induced pneumonitis is a rare but serious adverse event which must be thought of in cases of bilateral pneumonia in patients receiving everolimus.

CLINICAL CASES: SURGICAL ISSUES IN KIDNEY TRANSPLANTATION

OP263 BENCH SURGERY AND KIDNEY AUTO-TRANSPLANTATION IN RESCUE OF GERM-CELL RESIDUAL MASS. 3D MODELS UTILITY IN SURGICAL PLANNING

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Introduction: Post-chemotherapy retroperitoneal lymph node dissection (RPLND) in the management of germ-cell testicular cancer is a challenging surgery, especially when vascular or organ invasion is present. Nephrectomy may be imperative in some cases.
En bloc removal of the mass, ex vivo excision of the tumor and kidney auto-transplantation (KA) is a technical option to preserve renal function.

Methods: A 26-year-old man with a history of mixed germ cell tumor undergone a left radical orchiectomy. After receiving 3 courses of chemotherapy (BEP), tumor markers normalized but an 85x75x100 mm retroperitoneal mass located in the left paraaortic area. 3D model reconstruction showed renal artery encased by the tumor in the upper pole of the mass. Posterior wall of the vein and renal pelvis and upper part of the ureter were intimately adhered to the tumor.
Left renal artery, vein and ureter were encroached by the tumor. After difficult removal of the tumor from the psoas and retro-aortic area, renal vessels were clamped and the ureter cut. "En bloc" removal of the kidney and the mass was performed. Kidney was flushed with Celsior® solution at backtable and removed from the tumor with meticulous dissection of the artery, the vein and the ureter.
Kidney was auto-transplanted to the right iliac vessels in a standard manner and successfully reperfused with a cold-ischemia time of 1 h 05 min. Postoperative course was uneventful and the patient was discharged home 8 days after surgery. Pathology report revealed immature teratoma and yolk sac tumor. Surgical margins were free of the tumor.
Conclusion: In selected cases of post-chemotherapy germ-cell residual masses with renal vascular involvement, en bloc excision and bench surgery with kidney perfusion and tumor removal allows renal salvage and KA. Nephron sparing surgery and renal function preservation is important in patients with germ-cell tumors due to their young age and the probable need of future nephrotoxic chemotherapy.

OP264 THE USE OF 3D AUGMENTED REALITY DURING ROBOT-ASSISTED LIVING DONOR NEPHRECTOMY (RALDN): A CASE REPORT TECHNICAL OVERVIEW

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Background: Robot-assisted approach for living donor nephrectomies (RALND) was proposed as alternative to laparoscopic technique. The aim of this case-video presentation is to describe the application of Augmented Reality (AR) technology of 3D renal model during RALDN for a safe hilum.
Methods: We present a female living donor of 29-year-old who donates left kidney to her partner of 39-year-old affected by end-stage renal. A virtual 3D reconstruction of the left kidney based on contrast enhanced CT scan was elaborated with D2PTM software. AR intraoperative dedicated workstation was used to match camera (Da Vinci Xi/X Endoscope with Camera, 8 mm, 30˚) video output with virtual 3D model. Processed image was then sent back real-time to surgeon console through multi-input TilePro™ system. DaVinci Xi® surgical system was equipped with Maryland bipolar forceps, monopolar curved scissors, proGrasp™ forceps and Intuitive Endowrist curved-tip stapler 30®. A Pfannensteil incision and GelPort® Laparoscopic System was applied. Additional two 8mm and 12mm robotic trocars and one 12mm AirSeal® trocar were placed. Vascular control was achieved with Stapler, Hem-o-lock® and metallic clips. Firefly™ Fluorescence with Indocyanine Green was used to verify adequate vascular supply of resected ureter. AR-3D video stream was then used for the exact dissection of renal hilum.
Results: Operative time was 270 min, console time was 178min and time from renal artery division to graft harvest was 3 min. Overall cold ischemia time was 140 min. Patient was discharged 4 days after surgery. No complications were reported, and graft transplantation was successful.
Conclusions: The use of AR during RALDN may improve the understanding of renal anatomy thus enhancing the safety of living donor.

OP265 AN ALTERNATIVE WAY OF LAPAROSCOPIC PERITONEAL FENESTRATION BY USING A SECOND LAPAROSCOPE AND TRANSILLUMINATION TO MANAGE POST-TRANSPLANT LYMPHOCELES

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Introduction: The Incidence of lymphocele after renal transplantation varies between 0.6% and 49%. Laparoscopic marsupialisation with intraoperative laparoscopic ultrasound identification of the lymphocele represents the standard method of treatment for symptomatic lymphoceles. Herein, we present an alternative method for the identification of the lymphocele with the use of a second laparoscope and transillumination.
Case presentation: We present the case of a 38-year-old deceased-donor renal recipient, who complained for frequent urination 1 month after renal transplantation. CT examination revealed a large fluid collection (15cm in diameter) between the lower pole of the renal graft and the urinary bladder. The cyst was drained under CT guidance and a fluid sample analysis confirmed the diagnosis of a lymphocele. Due to the fact that the drainage did not reduce, a surgical approach was decided.
Surgical technique description: Three trocars were used (one 12 mm optical trocar at infraumbilical region, one 5 mm at the right lumbar region and one 12 mm at the right iliac fossa). The patient was placed at Trendelenburg potion and tilted to the right. A bulge between the graft and the urinary bladder was apparent. Due to the lack of intraoperative ultrasound facility, the confirmation of its nature (lymphocele) was done with transillumination by using a second laparoscope adjoining lymphocele's wall and transferring the light source from the optical laparoscope to the second one with diffuse of the light into the cavity of lymphocele. After that, a 5 cm window was created guided by a Veress needle. Finally, marsupialisation of the edges of peritoneum and lymphocele's wall was performed.
Postoperative period and follow-up: The postoperative course of the patient was uneventful. CT examination 1 week and 1 month after the operation revealed no fluid collection.
Conclusion: Identification of a post-transplant lymphocele during the attempt of laparoscopic fenestration is greatly facilitated by using a second laparoscope and transillumination, especially in cases where intraoperative ultrasound guidance is not available.

OP266 BENCH THROMBOLYSIS AND "AUTO-TRANSPLANTATION" AS A RESCUE TREATMENT FOR VENOUS THROMBOSIS AFTER LIVING-DONOR KIDNEY TRANSPLANTATION

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Background: Allograft venous thrombosis is a severe complication after pediatric kidney transplantation (KT). Early diagnosis and prompt treatment are crucial in preserving the survival of the allograft. This work described an innovative strategy for the management of allograft venous thrombosis.
Case presentation: A four-year-old girl, weighting 13.5 kg, was diagnosed with bilateral congenital renal hypodysplasia, urogenital sinus and anorectal malformation. The patient was referred to our Department for pediatric living-donor KT. Her mother was eligible as donor, presenting a body weight ratio of 1:4.5. Thrombosis of the inferior vena cava (ICV) was also identified, without any predisposing factor for thrombophilia. KT was performed through extraperitoneal approach without complications. Venous anastomosis required a human vascular graft sutured to the ICV, and renal artery was anastomosed to the aorta. On post-operative day (POD) eight, abdominal pain, hematuria and tachycardia lead to diagnose an allograft venous thrombosis. An emergent laparotomy allowed the explantation of the allograft, followed by bench surgery. The allograft was irrigated with

thrombolytic agents and lactated Ringer's solution, then, after removing the vascular graft, re-implanted through vascular anastomosis with ICV and aorta. The recovery of perfusion and function was good with diuresis since POD four. At two-year follow-up, the child presented good allograft function.
Conclusions: Careful diagnostic work-up is recommended when dealing with pediatric KT. In case of allograft venous thrombosis, explantation of the allograft followed by bench surgery, consisting in irrigation with thrombolytics, and re-implantation, might be safe and feasible.

OP267 THE USE OF EX VIVO NORMOTHERMIC PERFUSION TO REDUCE COLD ISCHAEMIC TIME IN A CASE OF DUAL KIDNEY TRANSPLANT FROM A DONOR OF ADVANCED AGE

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Ex vivo normothermic perfusion (EVNP) is an emerging technology for the assessment and reconditioning of kidneys prior to implantation. The revised kidney allocation scheme in the UK (as of 2019) is offering donor grafts from the highest risk donor category (D4), where age is over 70 years, as dual transplants.
A kidney pair was offered from a 71yo D4 donor from circulatory death for a 66yo highly sensitised patient who previously had bilateral lung transplant and was struggling on haemodialysis due to difficulties with access. The kidneys arrived to the recipient unit with 9 hours of cold ischaemia.
Both kidneys were inspected and prepared for transplantation. Whilst the first kidney was implanted, the second kidney was placed on EVNP with a red blood cell-based perfusate for 90 minutes. The cold ischaemic time (CIT) for the first implanted kidney was 12h35mins. The second kidney was being perfused ex vivo prior to in situ reperfusion of the first. CIT was therefore, 11h5mins, plus an additional 1h15mins following EVNP (total 12h20mins). During EVNP the graft demonstrated moderate global perfusion, and good urine output and renal blood flow (EVNP assessment score = 2). The kidneys achieved primary function and the patient remains well with a serum creatinine of 85μmol/L and eGFR 61.7ml/min.
Grafts from donors from advanced age are particularly susceptible to ischaemic reperfusion injury and are prone to higher rates of delayed graft function. EVNP may offer a method of reducing cold ischaemic time for dual transplants in high-risk recipients who would most benefit.

OP268 FIBROMUSCULAR DYSPLASIA IN LIVING RENAL DONORS STILL A CHALLENGE TO KIDNEY TRANSPLANTATION: CASE REPORT AND REVIEW OF THE LITTERATURE

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Background: Fibromuscular dysplasia (FMD) represents a group of non-atherosclerotic and non-inflammatory arterial disease that most commonly involve the renal and extra-renal arteries. FMD is the second-most frequently encountered anatomic abnormality, with an incidence of 2%-6% in potential living renal donors, up to 4% with concurrent extra-renal involvement. Resorting successfully to allografts with arterial disease has become a necessity as result of shortage of organs available all over the world.
Case presentation: We evaluated 3 patients with FMD as potential living renal donors. In one case, donation was declined due to bilateral renal localization, with severe extra-renal involvement. In two cases, nephrectomy was performed on the side with FMD, and transplantation achieved by resecting the affected arterial segment. In one of the two cases, subsequent replacement with a cryopreserved iliac artery graft from a deceased donor were performed, while in the other, a direct anastomosis with the recipient vessels. No intraoperative nor post-operative complications were reported in both cases. The allograft function promptly resumed, with satisfying creatinine clearance, and adequate patency of the vascular anastomoses was detected by Doppler ultrasounds.
Conclusion: Literature lacks clear guidelines on the eligibility of potential living renal donors with asymptomatic FMD. Preliminary assessment of the FMD living donor should always rule out any extra-renal involvement. Whenever possible, resection and reconstruction of the affected arterial segment should be taken into consideration as this condition may progress after implantation. Both the donor and the recipient need to be on close and long-term follow-up.

CLINICAL CASES: PERSON-CENTRED APPROACH TOWARDS THE PERSON SUBJECTED TO ORGAN TRANSPLANTATION

OP421 KIDNEY TRANSPLANTATION IN THE TRANSGENDER PATIENT- A CHALLENGE FOR CARE

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Background: Kidney transplantation and gender affirmation treatments are becoming increasingly more prevalent due to advances in technology. Hormone therapy and gender-affirming surgery present distinct anatomic, hormonal, infectious, and psychosocial issues among transgender kidney transplant recipients. This study aims to report kidney transplant care in a transgender patient and highlight the outcome and the challenges to kidney transplants.
Methods: A single-center case comprising one transgender kidney transplant was analyzed.
Results: 20-year transgender patient identified as male-to-female. He received a kidney transplant from a deceased donor on 04.07.2017. The graft has done well during the observation period (serum creatinine of 146 umol/l; eGFR 53 ml/min). The patient encountered various complications: recurrent urinary tract infection, pufferoureteral anastomosis, ureteral stricture (needed surgical correction). After one year of transplantation, he started hormone therapy. During the hospitalizations, the patient needed urgent psychiatric intervention due to thoughts of suicide. He has adaptation disorders, depressive symptoms. She needed psychiatric medical support. Finally, in January 2020, he changed sex to female. She feels good, and she does not report any complaints
Conclusions: Kidney transplantation can be safely and effectively managed in transgender patients regarding postoperative complications like recurrent urinary tract infection and risk of drug interaction and mental health/lifestyle counseling.

OP422 FIRST PERSON CONSENT: CHALLENGES TO APPROACHING FOR DONATION

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A 69-year-old male dependent on Veno-Venous Extracorporeal membrane oxygenation due to influenza A and parenchymal fibrosis requested that organ donation be explored when discussing end of life care plans. On assessing suitability, a specialist requester (SR) attended the hospital to explore organ donation with the patient and his family. Whilst first person consent has occurred in previous referrals, this practice is highly unusual.
The patient, who was Glasgow Coma Scale 15, requested detailed information about the process to make an informed decision with the help of his family. He was registered as opt-in on the organ donor register.
Donation after Cardiac Death was explained to the patient and family who found several aspects of the process difficult to reconcile with the end of life, in particular the 5-minute timeframe of saying goodbye post asystole. The patient also found knowing that he was going to theatre when he was sedated for the final time hard to envisage.
It was an emotional conversation for all involved with unique challenges for the SR. This included who to address questions and answers to and how to refer to the patient; directly or as dad/husband. Advocating for the patient whilst both he and the family were in the room made exploring and probing of the relative's hesitancies inappropriate.
Ultimately the patient decided to withdraw his organ donor registration as he did not want to limit the time that his family could spend with him after his death. He noted that when he signed up to the organ donor register, he never imagined that he would have to make that decision again.
The case was taken to the London team's shared practice session for learning and comments. The main learning points were as follows; 1. Could a prolonged time post asystole have been discussed with renal transplant centres to accommodate the family post withdrawal. 2. Terminology and how thoroughly the process was explained to the patient, discussing whether this was in his best interests. 3. How to refer to the patient 4. Family placement in the room during the conversation.
There have been first person consents in situations where the patient did not wish to receive detailed information. It is important to share and discuss the terminology required in first person approaches to maximise opportunity and improve patient experience.

OP423 SUICIDE IN THE UK 2020 – ITS IMPACT ON ORGAN DONATION AND STAFF WELL-BEING

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Introduction: NHSBT received a substantial increase in referrals from suicide. Specialist Nurses-Organ Donation (SNOD) supporting these families and indeed critical care units are subsequently put under additional strain. Grief following suicide is recognised as varying hugely to non-suicide grief. SNODs identified that they required additional skills to enhance care when supporting these families. However, it was also identified that the impact of supporting such families in turn created health and well-being concerns for the SNODs themselves, particularly when the frequency of being exposed to these situations increased. The Education team were challenged to recognise and implement a comprehensive and rapidly implemented education package to meet the needs of the organisation.
Method: An extensive resource review was undertaken, this not only identified organisations and charities we could signpost families too but also sites, charities and organisations we could refer Healthcare Professionals (HCPs) too. This information was collated and placed upon the internal internet for rapid access to enable prompt and appropriate action for families and NHSBT employees.
Sourcing communication strategies proved more difficult, many of the sources immediately found were based upon suicide prevention and much less about strategies which HCP's can implement when supporting families following suicide.
It was recognised by the Education team that suicide methods and mechanisms had also evolved in recent years with little education around such changes for the SR and SNOD teams, the introduction of suicide resources on the dark web being such an example.
Outcome/Conclusion: The education package places emphasis on the differences in suicide grief and the communication skills and nuances required for HCP's. We provided Specialist Nurses the insight into the clinical impact suicide methodology can have on patients and the implications these give for end of life decisions.
Small group sessions were chosen for the delivery, with time and encouragement given to shared practice, optimising learning opportunity for all. Safeguards were implemented, to ensure any attendees who required further debrief opportunity had time and support including referral to psychological specialists.

OP424 COLLABORATIVE WORKING- KEY TO MAINTAINING NORMAL ORGAN DONATION AND TRANSPLANT SERVICE DURING COVID PANDEMIC IN NORTHERN IRELAND

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Introduction: National lockdown in March 2020 presented the healthcare sector with many challenges, Organ Donation and Transplant services was not exempt, it was unclear and uncertain as to how the service would be affected. Nationally transplant centres had to close or reduce services due to lack of Intensive Care Unit (ICU) capacity. Despite the restrictions Northern Ireland (NI) Organ Donation Team adapted to maintain service quality and at times to improve.
Why this was possible.
NI is a relatively small region 86 miles wide and 82 miles long, with a population of 1.8million.
There are 10 intensive care units within the region and each unit has an embedded Specialist Nurse Organ Donation (SNOD).
The advantage of working in a small area is that good working relationships are formed and maintained. The SNOD team in NI have good relationships with multidisciplinary teams who are essential to the smooth process of organ donation such as ICU staff, virology team, tissue typing staff and transport providers. The team maintained a visible presence on embedded units, providing reassurance and encouragement to staff to continue to refer potential donors.
Outcome: NI maintained a normal service and had an increase in donor numbers, 20 donors from March 2020 to June 2020, double the figure from the same time period in 2019.
The Belfast renal transplant team performed a record 101 transplants in 101 days.
The increased activity enabled myself as trainee SNOD to complete training required to enable me to practice independently thus providing additional support for the team.
Conclusions: Communication and collaboration with multidisciplinary teams ensured organ donation and transplant service were not adversely affected. Encouraging staff to refer potential donors early allowing timely planning.
Pride in achievements was encouraging and rewarding. This inspired team members to be resilient and positive in ensuring a continued service.

OP425 THE OPERATIVE ITALIAN NATIONAL TRANSPLANT CENTRE (CNTO): THE ROLE OF NURSES

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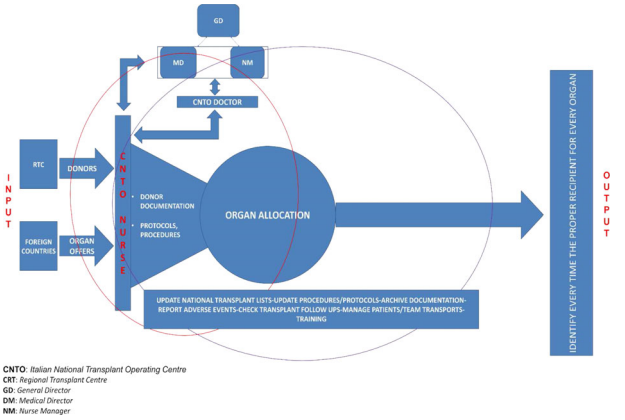
Background: From November 4th 2013, CNTO itself as sole interlocutor has been operating nationally, interfacing directly with the regional centers and ensuring the h/24 support necessary for the operational management of national programs. Centralizing management of organ allocations and also of waiting lists for national programs, certainly has following advantages:
1. -streamline the path allocation through standardization of processes;
2. -provide an unambiguous interpretation of the rules that currently govern the programs and therefore more effective to apply;
3. -a real-time control of donations, allocative flows and the outcome of processes.

Methods:



Results: Every day an average of 8 assessments of brain death are notified. These make possible about 22 organ offers a day to be allocated on national programs and about 4 are actually accepted by the transplant centers to be transplanted. Considering the fact that every donor must still be reported to the CNTO, the operational core is composed of 13 nurses of coordination and 6 doctors who rotate in case of clinical problems.
In addition, nurses cooperate with other countries in order to handle organ offers internationally. Thanks to the Italian Gate to Europe, every year almost 130 organ offers are managed between Italy and other countries and an average of 20 organs are accepted in order to be transplanted.
Every activity and process is promptly reported on written documents, which are constantly updated, shared and archived.
Conclusions: Nurses are a precious resource for the Italian Transplant Network and their fundamental role has now been recognized.
They work with other disciplines to obtain the goals fixed by the Italian National Transplant Center prioritizing and co-ordinating the organ donation activity in Italy and maintaining relations with foreign organizations.
Thanks to their everyday activities nurses continually establish and update procedures and documentation in order to appropriately tackle the needs of the transplantation network.
The nurses are professionals who collect and analyze results, following innovative paths and all available resources to achieve optimal results. The final goal of their activity was to identify the proper recipient every time for every organ, implementing the current procedures and rules.

OP426 IMPLEMENTING AND EMBEDDING CHANGES IN LEGISLATION FOR ORGAN AND TISSUE DONATION IN ENGLAND

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Background: To save and improve more lives, the Organ Donation (Deemed Consent) Act 2019 was implemented in May 2020. With certain groups excluded as a safeguard the Opt-out system assumes all adults are willing to be organ and tissue donors when they die, unless they have opted out or expressed a decision not to donate. National Health Service Blood and Transplant (NHSBT) were tasked to ensure everyone working in organ and tissue donation were trained and supported through this legislative change.
Methods: Three education modules were developed, tested and delivered to the Specialist Nurse (SN) workforce;
1. Outline the legislation principles
2. Practice the donor family conversation
3. Consolidate bringing theory and practice together.

The aim was to empower the SN's to confidently navigate a deemed conversation whilst supporting hospital staff and the donor family. The training was successfully completed amidst a global pandemic, forcing the redesign of the final modules to virtual platforms, whilst the workforce was deployed to support the wider NHS. We continuously improved by evaluating throughout.
Post implementation, to help support and embed the change in practice, semi-structured debriefs were facilitated with SNs of cases where Deemed Consent may apply. These debriefs allowed real-time assessment that training was understood and identify any gaps or unintended practice.
Results: Training evaluated well:

Module	Format	Score
1	Face to Face	8.7/10
2	Face to face	9.1/10
	Virtual	8.3/10
3	Virtual	8.6/10

The debriefs enhanced learning having a positive impact on mental health and wellbeing with SNs being able to discuss difficult cases. These continue within regional teams and shared practice.
Conclusion: Training was delivered on time despite the pandemic to all SNs fulfilling on call duties. Training evaluated well regardless of the mode of training. We continue to embed the change with the aim of saving and improving lives.

CLINICAL CASES: CHALLENGES IN PAEDIATRIC LIVER TRANSPLANTATION

OP465 NEW FRONTIER FOR BILIARY RECONSTRUCTION IN PEDIATRIC LIVER TRANSPLANTATION: BIODEGRADABLE STENTS

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Liver transplant is the only curative treatment for end-stage liver disease in children. Biliary complications (BC) remain the weakness of pediatric liver transplantation (PLT). The incidence of BC reported varies between 6% and 32%. Biliary reconstruction (BR) can be performed as duct-to-duct anastomosis (DDa) or Roux-en-Y hepaticojejunostomy (RY-H). In both cases, a stent can be placed. We describe our experience with Archimedes biodegradable stent (ABS) (Amg International GmbH, Winsen, Germany) for BR in PLT. ABS is already used in adult HPB and transplant surgery. It has an helical-channel that facilitates bile outflow. Degradation occurs by hydrolysis. Radiological monitoring is guaranteed by barium sulfate. The video attached shows the case of a 9months old baby (10kg weight) affected by glycogenosis type1 who underwent a living donor transplantation (SII-III). Although we selected the smallest ABS available (6Fr, 40mm length) we had to shorten the stent to fit it for a pediatric RY-H. Posterior wall of the anastomosis was performed with a continuous suture (PDS). So, the stent was completely inserted in the bile duct at the cut surface and then pulled into the jejunal loop. Anterior wall of the anastomosis was completed with interrupted stitches (PDS). Postoperative (PO) radiological evaluation showed a correct transanastomotic stent placement. On X PO day the ABS was completely degraded. At 4months no BC occurred. An ABS stent was used in 2further cases: a split liver (LLs) and a whole liver with DDa. ABS were placed using the same technique. After a mean FU of 16weeks, we didn't document neither anastomotic leakage nor stricture. No cholangitis occurred. Fluoroscopic monitoring showed a good stent placement. Degradation occurred in the expected time. In our experience, ABS combined the advantages of internal-external stents: low risk of accidental removal, low migration rate, excellent bile flow, optimal fluoroscopic visualization. Biodegradability prevented any permanent obstruction. In conclusion, although stents with a smaller diameter and length would be advisable for pediatric use, preliminary results showed that stent placement is technically feasible and safe both in DDa and RY-H. Even though ABS seems to be a promising device to prevent BC, further studies are needed to demonstrate our findings.

OP466 KAPOSI'S SARCOMA (KS) IN PEDIATRIC LIVER TRANSPLANTATION (LT) – 3 CLINICAL CASES

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KS is an immunosuppression-related tumor rare in children. We report 3 cases of KS after LT.
11-year-old boy submitted to LT due to familial intrahepatic cholestasis. Fever, dyspnea and cough presented 5 months later with enlarged lymph nodes, splenomegaly, anemia 9 g/dl and thrombocytopenia 55000/uL. Analytically elevated liver enzymes and positive EBV viral load (VL). On suspicion of post transplantation lymphoproliferative disease (PTLD) tacrolimus was discontinued and started methylprednisolone (methylPDN). Clinical deterioration with hepatosplenomegaly and pancytopenia. Hemophagocytic lymphohistiocytosis criteria were met and etoposide, cyclosporine, dexamethasone and ganciclovir were initiated. The lymph node biopsy diagnosed KS with a high HHV8 VL. Sirolimus was started with improvement. After 5 years, he has good graft function and no recurrence.
8-year-old boy submitted to LT at age 2 due to biliary cirrhosis. He presented graft dysfunction 2 years later with positive EBV VL, anemia 10 g/dl and thrombocytopenia 50000/uL, massive enlargement of cervical lymph nodes with cavum infiltration and splenomegaly. Tacrolimus was discontinued and started methylPDN. Bone marrow aspiration revealed hemophagocytosis and lymph node biopsy diagnosed KS, Castleman's disease and plasmablastic lymphoma related to HHV8 infection. Sirolimus and chemotherapy were started with good response. 5 years later, he remains free of the disease.
2 year old girl undergoing 2 LT at 8 months of age due to acute on chronic liver failure. After 6 months, she presented diarrhea and abdominal distension. She was critically ill with anemia 9 g/dl and thrombocytopenia 45000/uL. Liver enzymes were normal. CMV VL was detected and started ganciclovir. Clinical deterioration with enlarged lymph nodes, splenomegaly and severe thrombocytopenia. Tacrolimus was discontinued and started methylPDN. Axillary lymph node biopsy diagnosed KS and HHV8 infection. Sirolimus was associated, she maintains excellent condition.
KS presentation after LT may mimic PTLD. Elevated HHV8 VL is of added value but lymph node histology is of upmost importance. The replacement of tacrolimus to mTOR inhibitors has been proven beneficial. In the reported cases this strategy allowed good outcomes. In the absence of a response, chemotherapy should be added.

OP467 SPLENIC STEAL SYNDROME AS A CAUSE OF UNEXPLAINED REFRACTORY ASCITES AFTER PEDIATRIC LIVER TRANSPLANTATION

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Background: Splenic Steal Syndrome is a possible complication of liver transplantation. It is determined by a preferential shift of blood flow into the splenic or gastroduodenal arteries with consequent relative hypoperfusion of the hepatic artery and hyperperfusion of the portal vein.
Aim: To describe a case of Splenic Steal Syndrome after pediatric liver transplantation.
Case report: We describe the case of a 9-years-old male (20 Kg) affected by Caroli Syndrome who underwent a split liver transplantation due to severe complications of portal hypertension (i.e. massive splenomegaly, recurrent episodes of life threatening esophageal variceal bleeding, spontaneous bacterial peritonitis). Soon after transplantation he developed a massive ascites refractory to medical treatment. Blood tests showed a mild coagulopathy (INR 1.7) and a slight elevation of liver enzymes. Imaging studies, including a cavography with measurement of the suprahepatic-caval pressure gradient and a portography with wedged hepatic venous pressure measurement, demonstrated the presence of severe portal hypertension without vascular anatomic anomalies. Liver histology resulted inconclusive. A Doppler US of the liver revealed the presence of a high flow rate in the splenic artery (130 cm/sec), suggesting the presence of Splenic Steal Syndrome. Diagnosis was then confirmed with arteriography of the coeliac tripod. Proximal embolization of the splenic artery, performed without complications, allowed rapid resolution of the ascites and a significant reduction of the spleen volume.
Conclusions: Splenic Steal Syndrome should be considered in all children with previous severe portal hypertension who develop refractory ascites after liver transplantation. Proximal embolization of the splenic artery is safe and effective also in the pediatric population.

OP468 EX SITU LIVER SPLITTING DURING HYPOTHERMIC OXYGENATED MACHINE PERFUSION

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Dual hypothermic oxygenated perfusion (D-HOPE) is an emerging method to reduce ischemia-reperfusion injury (IRI) in whole liver transplantation (LT), but it has not been applied to split-liver procedure for transplantation (SLT). We report the first clinical case of ex situ SLT performed under D-HOPE, with further hyper-reduction of the left lateral segment to monosegment-2 (S2), in a liver from a 19-year-old cadaveric donor. The technique was adopted to minimize IRI due to donor hemodynamic instability and long cold ischemia times. During the procedure, D-HOPE maintained stable flows (portal: 200-300 mL/min; arterial: 50-80 mL/min) and pressures (portal: 6 mmHg; arterial: 25 mmHg). At the end of the liver splitting, the S2 monosegment was disconnected from D-HOPE and transplanted into a 3.7 Kg neonate with acute liver failure, after 11 hours of total ischemia time (TIT). On the other hand, the extended right graft (ERG) remained connected on D-HOPE in double perfusion. After 14 hours of TIT, the ERG was transplanted into a 9-year-old boy with biliary atresia. Both grafts showed early functional recovery and mild IRI on histology. After 14 months, the ERG recipient exhibits normal liver function. The S2 monosegment recipient developed portal vein thrombosis and was re-transplanted on day 14 post-operative. This case demonstrated that SLT is feasible with D-HOPE, without development of primary dysfunction and with mild IRI despite the long ischemic times. However, further experience is needed to define the potential benefits of D-HOPE in SLT.

OP469 LONG-TERM SURVIVAL AFTER CHORIOCARCINOMA TRANSMITTED BY LIVER GRAFT: A SUCCESSFUL REPORT IN PAEDIATRIC TRANSPLANTATION

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In last decades long-term outcomes for Liver Transplantation (LT) have improved. However, some rare complications as transmission of occult tumors have been reported with an estimated incidence of 0.02% to 0.2%.
An adolescent diagnosed with tyrosinemia type I was listed for LT because of a hepatocellular carcinoma (HCC). He received a whole liver from a female donor with a brain event as cause of death. The transplant was uneventful but the early post-transplant period was complicated by hepatic vein thrombosis.
Almost 8 months after LT, the patient presented a 6 cm poorly defined lesion on ultrasound (US) confirmed by computerized tomography (CT). Clinically he had mild weight loss and gynecomastia without abdominal pain. Alpha fetoprotein (AFP) presented normal values at this point. Thorax CT found lesions in the left lung parenchyma and PET SCAN characterized them as non-capturing nodular lesions. Bone scintigraphy was negative for metastatic disease.
Percutaneous liver biopsy revealed a carcinoma with abundant desmoplastic stroma. Immunosuppression withdrawal and palliative chemotherapy was initiated presuming an HCC relapse. AFP remained normal but human chorionic gonadotropin (HCG) has reached unexpected values over 1984 IU/L. Meanwhile, a request for more details about the other organ recipients from the same donor revealed that one kidney was grafted and the recipient passed away due to a disseminated tumour difficult to clearly diagnose, but assumed to be a choriocarcinoma.
Five months later, the patient underwent resection of V and VI. Histological examination confirmed metastatic choriocarcinoma.
At the time of writing, with 11-year follow-up, the patient has a sustained remission with no signs of relapse and no need for a re-transplant.
This case reports a diagnostic challenge in an adolescent with a particular unique background and a very rare transmitted new tumor. The authors aim is to highlight the risk of cancer-bearing organs reveled post-LT and to testimony the experience of the successful outcome after a choriocarcinoma transmitted by liver graft.

OP470 BILE CAST NEPHROPATHY CAUSING ACUTE KIDNEY INJURY AFTER LIVER TRANSPLANTATION AND PROGRESSION TO CHRONIC KIDNEY DISEASE

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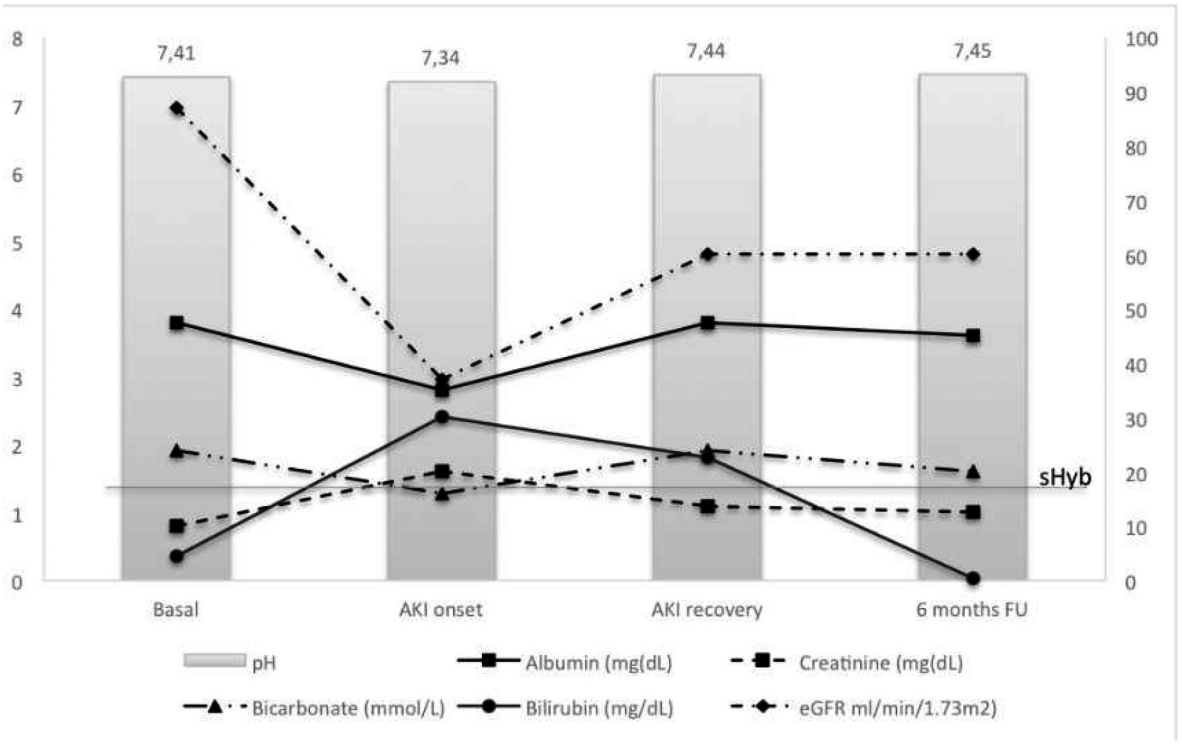
Bile cast nephropathy (BCN) is a renal complication associated with cholestasis, characterized by acute kidney injury (AKI) in patients with hyperbilirubinemia (HyB) and jaundice. Pathophysiological mechanisms are not completely understood but AKI seems to be caused by direct toxicity (epithelial cell damage) and tubular obstruction of bile casts on nephrons.
Here, we describe the case of an Italian female patient who underwent liver transplantation (LT) due to biliary atresia in 1990, at the age of 8. Post-transplant liver and renal function were normal under standard immunosuppression.
In 2015, the patient voluntarily suspended the immunosuppressive therapy, experiencing a biopsy proven severe acute liver rejection, associated with progressive jaundice, increasing of transaminases 24 times above the upper limits, peak total bilirubin of 30.1 mg/dL and reduced liver protein synthesis activity (serum albumin 28 g/L and INR 1.7).
She also developed AKI stage 2 (sCr from 0.8 to 1.6 mg/dl in 48 hours) and metabolic acidosis.
Urine examination demonstrated pH of 6, bilirubinuria (6 mg/dL), bilirubin crystals with numerous bilirubin casts and white blood cells (10/μL).

BCN was diagnosed on the basis of AKI with severe HyB, bilirubin casts in urine and hypoalbuminemia and metabolic acidosis as promoting factors (PF).
Treatment included restoration of immunosuppression and steroid pulses, correction of PF, with decreasing of bilirubin serum levels and improvement of renal function (sCr 1.11 mg/dL-60 ml/min/1.73m^2) (figure). Bilirubin crystals and casts disappeared at urine examination.
Despite recovery of renal filtration after AKI, the follow-up demonstrated a slight deterioration of renal function over years, with decreasing measured GFR of 39 ml/min/1.73m^2, notwithstanding good control of conditions associated with renal damage progression.
Early identification and treatment of BCN are crucial in order to obtain resolution of symptoms and improvement of prognosis, especially in patients with acute liver failure (ALF).
An important percentage of patients who experienced AKI do not return to normal renal function, underlying the role of AKI on the development of CKD, regardless of the cause of the injury.



WHAT REALLY MATTERS AFTER TRANSPLANT? BEYOND SURVIVAL: SECRETS OF SUCCESS

OP009 WATERLOW SCORE ON ADMISSION AND POST-SURGERY RISK OF PROLONGED LENGTH OF STAY, EMERGENCY READMISSION AND MORTALITY RISK

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Background: Waterlow scoring was introduced in the 1980s as a nursing tool to risk stratify for development of decubitus ulcers (pressure sores). It provides an objective cumulative risk score based on a combination of co-morbidities, mobilisation, nutritional factors and demographics. Recent interest has focussed on its value as a pre-op surrogate marker for surgical outcomes, with utility seen in a small cohort of simultaneous kidney-pancreas patients (n = 57), but no data exist for kidney transplantation.
Methods: In this single-centre observational study, data were extracted from hospital informatics systems for all kidney allograft recipients transplanted between January 1st 2007 and June 30th 2018 with linkage to national datasets. Waterlow scores were categorised as per national standards; 0-9 (low risk), 10-14 (at risk), 15-19 (high risk) and ≥20 (very high risk). Primary outcomes of interest were post-operative length of stay, emergency re-admission within 90-days and mortality.
Results: Data were available for 1,767 kidney transplant patients. Waterlow scores pre-operatively were; low risk (n = 650), at risk (n = 526), high risk (n = 134), very high risk (n = 40) and missing data (n = 417). Median length of stay in days (± interquartile range) varied with pre-op Waterlow scores; low risk (8±5), at risk (9±6), high risk (10±7) and very high risk (11±7) (p = 0.0242). No difference was observed in risk for emergency readmission within 90-days of surgery; low risk (36.3%), at risk (39.2%), high risk (36.6%) and very high risk (45.0%) (p = 0.5731). In unadjusted Kaplan-Meier analysis, patients with 'very high risk' Waterlow scores had increased risk for mortality (30.0%) versus high risk (9.0%), at risk (8.7%) and low risk (8.3%). However, while in a univariable Cox model 'very high risk' Waterlow score was associated with mortality (Hazard Ratio 3.43 [95% CI 1.83-6.42], p < 0.001), Waterlow scores were no longer found to be significant after adjustment with baseline variables including age, sex, ethnicity, waiting time, donor type and recipient diabetes.
Conclusions: Pre-operative Waterlow scoring is a simple nursing tool that serves as a surrogate marker identifying kidney transplant patients in need of greater post-operative support but is not independent of baseline demographics.

OP010 FRAILTY AND KIDNEY TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: Frailty is a multidimensional condition and is the result of the body's age-associated decline in physical, cognitive, physiological and immune reserves. The aim of this systematic review is to assess the quality of evidence of the included studies, determine the prevalence of frailty among kidney transplant candidates and evaluate the relationship between frailty and associated patient characteristics and outcomes after kidney transplantation.
Methods: A systematic search was performed for relevant literature on frailty and kidney transplantation. This was followed by a meta-analysis for patient characteristics and outcomes reported by a minimum of two studies.
Results: A total of 18 studies were included in the systematic review and 14 of those studies were suitable for meta-analysis. Overall pooled prevalence of frailty prior to transplantation was estimated at 17.1% (95% confidence interval (CI): 15.4 – 18.7). Frailty was significantly associated with the patient characteristics older age (mean difference (MD) 3.6, 95% CI: 1.4 – 5.9) and lower rate of pre-emptive transplantation (relative risk (RR) 0.60, 95% CI: 0.4 – 0.9). The outcomes longer duration of delayed graft function (DGF) (RR 1.80, 95% CI: 1.1 – 3.0) and length of stay (LOS) longer than 2 weeks (odds ratio 1.64, 95% CI: 1.2 – 2.3) were significantly associated with presence of frailty.
Conclusions: One in six kidney transplant recipients are frail prior to transplantation. The presence of frailty is associated with lower rates of pre-emptive transplantation, older recipient age, higher rates of DGF and longer LOS. Future research is required to explore the association of frailty with other adverse outcomes after kidney transplantation and the effects of intervention programs to improve the different frailty domains.

OP011 ASSESSING RISK FACTORS OF NON-ADHERENCE AND POST-TRANSPLANT OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS

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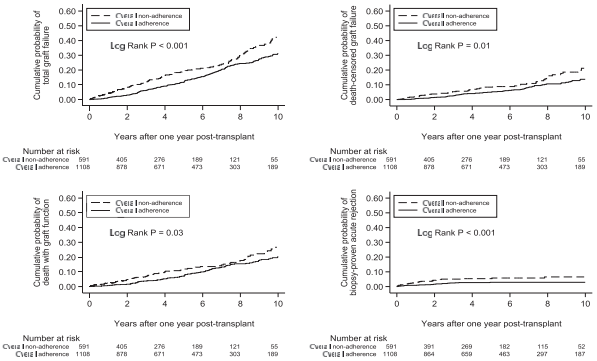
Background: Kidney transplant recipients' (KTR) adherence to prescribed regimens is vital for optimal recovery and long-term graft function. The aim of this study was to identify factors of KTR non-adherence and its impact on post-transplant outcomes.
Methods: A retrospective single-centre cohort study was conducted among KTR from January 1, 2003 to December 31, 2017. Non-adherence was defined as one or more of the following in the first year post-transplant: (1) any missed clinic visits, (2) >30% missed laboratory visits, and/or (3) >40% coefficient of variation of calcineurin inhibitor levels. Multivariable logistic and Cox proportional hazards models were fitted to identify adherence risk factors and outcomes, respectively.
Results: From a total of 2,714 patients, 1,803 (66.4%) were included in the analysis. The mean recipient age was 51.7 (±13.4) years, and 60.7% were male. Overall non-adherence was identified in 34.9% patients; 11.2% patients were non-adherent to clinic visits, 5.4% to lab tests, and 25.2% to medication. Recipient history of psychiatric disorders (OR 1.57 [95% CI: 1.22, 2.02]) or non-adherence (OR 1.82 [95% CI: 1.31, 2.54]) were independent risk factors for non-adherence. Private (vs. public) drug coverage reduced the risk for non-adherence (OR 0.62 [95% CI: 0.48, 0.80]). Any episode of non-adherence over the first-year after transplant was associated with total graft failure (HR 1.52 [95% CI: 1.20, 1.91]), death with graft function (HR 1.51 [95% CI: 1.11, 2.05]), and biopsy-proven acute rejection (HR 2.35 [95% CI: 1.38, 3.99]). A trend toward an increased risk of death-censored graft failure was observed (HR 1.39 [95% CI: 0.96, 2.01]).
Conclusions: KTR adherence is influenced by psychosocial and socioeconomic factors which impact post-transplant outcomes. Our results emphasize the need for interventions to improve patient adherence. Further investigation is required to determine if our results are generalizable to younger patient populations.



OP012 IMPACT OF THE COVID-19 PANDEMIC ON DAILY LIVES, EMOTIONS AND BEHAVIOURS OF KIDNEY TRANSPLANT RECIPIENTS

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Introduction: While the COVID-19 pandemic has a huge impact on all our lives, it is important to assess the specific impact on those belonging to

vulnerable groups in society. Kidney transplant recipients (KTRs) are one such group who are at extra risk of being infected with COVID-19 due to immune suppression. We investigated to what extent COVID-19 has had an impact on the daily lives, emotions and behaviours of KTRs.
Methods: We conducted a prospective observational study, whereby we interviewed 153 KTRs between the end of April and the end of May 2020. We recruited KTRs from the cohort who were transplanted between February 2019 and February 2020. We developed 7 qualitative questions relating the COVID-19 pandemic. For depression, anxiety, loneliness, social support and medication adherence, we used validated questionnaires. During the second wave (November 2020), we conducted a follow-up online questionnaire, whereby 79 of the 153 KTRs participated.
Results: The impact of COVID-19 on the lives of KTRs varied considerably. The qualitative results showed that the majority reported no impact on emotions, but for some participants the pandemic had a lot of impact. Symptoms of depression and anxiety did not change between the first and second time point. Almost half of the participants (49.7%) reported feeling lonely which decreased over time (33%) ($t = 3.879$; $p = .00$). Social support was high and this decreased over time ($t = -1.943$; $p = .06$). Level of medication non-adherence was 20.3%, which did not significantly differ between first and second wave or to the rate prior to COVID-19.
Conclusions: These results highlight that, at group level, there is no clinically relevant impact on emotional and social well-being or health behaviours. At the individual level, there could be a need for psychological support.

OP013 SOCIAL DISTRESS AND HEALTH-RELATED QUALITY OF LIFE IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Background and Aims: Health-Related Quality of Life (HRQOL) is an important patient-centred outcome for patients with chronic diseases. Social distress may add to physical burden and psychological distress and impair HRQOL. The objective of this study is to assess if social distress assessed by the Social Difficulty Inventory(SDI) is associated with HRQOL in Solid Organ Transplant (SOT) recipients.
Methods: Secondary analysis of a cross-sectional convenience sample of adult SOT (kidney, liver, kidney-pancreas) recipients who completed the SDI and PROMIS (Patient-Reported Outcomes Measurement Information System) Global-10 on electronic data capture on tablets. Global-10 yields a Global Physical Health (GPH) and a Global Mental Health (GMH) score. SDI score $\geq$10 was used to identify patients with social distress. Sociodemographic and clinical characteristics were collected from health records. Descriptive statistics, correlation analysis and multivariable-adjusted linear regression were used to analyse the data. To address missingness, multiple imputation by chained equations was used.
Results: Mean (standard deviation [SD]) age of the 220 participants was 53 (13) years, 63% was male, 70% White. The median (interquartile range [IQR]) SDI was 5(9), the mean(SD) GPH and GMH score was 48(9) and 49 (9) respectively. 30% of participants had social distress. Both GPH and GMH correlated moderately with SDI (rho = 0.66 and 0.64, respectively; $p < 0.001$). In multivariable-adjusted linear regression models (adjusting for sociodemographic, clinical factors and ethnicity to account for potential confounding), the association between the SDI and GPH and GMH remained strongly significant. Participants with vs without social distress had 11 (95% confidence interval [CI] 8-13) point lower GPH and 11 (8-14) point lower GMH score ($p < 0.001$ for both).
Conclusion: Social distress is associated with physical and mental HRQOL in SOT recipients.

OP014 RENAL TRANSPLANT OUTCOMES IN YOUNG ADULTS BEFORE AND AFTER THE INTRODUCTION OF A YOUNG ADULT SERVICE

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Background: Young adults are at higher risk of losing a kidney transplant compared to older adults. A young adult kidney service tailored to improve outcomes was initiated in 2011, further developed becoming a substantive service in 2016 in Newcastle. Transplant outcomes were reviewed aiming to assess any impact of the young adult service.
Methods: Retrospective review of electronic hospital records. Young adults aged up to and including 25 years at the time of transplantation were divided into two groups. These were young adults transplanted before and after 2011 which was the year of initiation of the young adult service. Rates of graft loss were explored before and after 2011. Graft loss after 2011 was further assessed for the time periods 2011 to 2016 and 2016 to 2021.
Results: Overall, there were 85 transplants in 78 recipients up to 2021, median age (range) 17 (3 to 25) years. In 58 young adults transplanted before 2011, the overall graft loss was 22 (38%) with 4 (7%) lost between 2011 and 2016 and 3 (5%) lost between 2016 and 2021.
In 26 young adults transplanted after 2011, the overall graft loss was 6 (23%) with 3 (11%) between 2011 and 2016 and 3 (11%) between 2016 and 2021. Of these one graft loss was deemed potentially avoidable by expert opinion.
Conclusions: In Newcastle, the rate of graft loss has reduced since 2011. The reasons are likely to be mutli-factorial but are coincidental with the introduction of a young adult service in 2011. There was no change in graft survival before and after the young adult service became a permanent post in 2016. Some graft failure was unavoidable due to disease recurrence and co-morbidities. Young adults may benefit from intensive support with a dedicated kidney care coordinator to address their complex needs and potentially prolong the lifespan of their renal transplants possibly by reducing the development of transplant rejection. Work is ongoing to determine the most effective strategies.

OP015 SUPPORTING TEENAGE AND YOUNG ADULT TRANSPLANT RECIPIENTS DURING COVID-19 PANDEMIC USING A SOCIAL MEDIA PATIENT GROUP

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Background: Teenage and young adult transplant patients have become increasingly isolated due to the UK Government policy of shielding during the COVID-19 pandemic over the last 12 months. This has almost totally halted social interaction with peers, friends and family causing increasing anxiety and stress.
Methods: We have developed a regular young adult clinic resulting in a young adult community of 143 kidney failure, dialysis and transplant teenagers and young adults over the last 5 years. We opted to maintain face to face clinic appointments for this age group (16-30) during the pandemic to facilitate regular input whilst observing social distancing. In addition, we introduced a series of regular group social media sessions to maintain peer support, reduce anxiety and actively engage and reassure our community of young adult transplant recipients and ESKD/CKD patients during the COVID-19 pandemic (n = 103).
Results: This included monthly medical update and Q and A sessions about risk of COVID-19; risk minimisation strategies and information on vaccination. Four specific psychology sessions on handling anxiety and stress; 65- 1:1 Zoom support sessions with the youth worker; a range of 15 entertainment sessions from celebrity comedians; chef; magician and regular quizzes (see table).

Type of Interaction Since March 01/03/20	Total number of young patient (16-30yrs) participations	Median	Range	Number of sessions
Interactive live with Psychologist	87	29	22-35	4
Interactive live with Consultant	105	27	20-33	6
Interactive session with Professional Comedians	73	25	22-27	3
Interactive session with Professional Chef	15			1
Interactive session with Magician	13			1
Interactive quiz sessions ran by youth worker	154	13	9-20	10
Interactive 1-1 sessions with youth worker	33			65

Conclusions: Establishment of a dedicated young adult clinic fostering peer support enables successful engagement of young adult patients in

group social media sessions providing support through crisis situations such as the current COVID-19 pandemic. This provides ongoing engagement and support reducing the potential for anxiety, stress and potential adverse outcomes.

OP016 SHORT- AND LONG-TERM PREGNANCY OUTCOMES AFTER ORTHOTOPIC LIVER TRANSPLANTATION IN THE NETHERLANDS

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Background: Survival after orthotopic liver transplantation (OLT) has significantly improved over the past decades. Many transplanted women reach fertile age and become pregnant. Post-transplant pregnancy potentially puts the mother, transplanted organ and child at risk. Data about outcomes of pregnancy after OLT is limited.
Methods: We performed a retrospective multicenter cohort study to evaluate short- and long-term outcomes of pregnancy after OLT in the Netherlands. Descriptive statistics and generalized estimating equation analysis were used. Administrative censoring at 20-year follow-up was performed.
Results: 60 women with 89 pregnancies >20 weeks were included. Besides, eight early miscarriages (<12 weeks) were reported. In the majority of pregnancies (86%), a calcineurin inhibitor-based immunosuppressive regimen was used. In 22% of pregnancies, hypertension occurred, leading in 13% to preeclampsia (Table 1). Graft failure occurred in one pregnancy and in two pregnancies biopsy-proven chronic rejection without graft failure. Live birth rate was 93%. 33% of the infants was born <37 weeks and 25% with birth weight <2500 grams. Ten mothers (17%) died during follow-up, at median 8 (IQR = 4-12) years after delivery. Two of them died within one year after delivery, due to recurrence of original disease and a massive pulmonary embolism. Long-term follow-up (median 7 (IQR = 4-11) years) only showed significant changes over time for ALT and AST levels, and creatinin (slight increase resp. decrease) ($p < 0.000$, Figure 1). Creatinin levels 3 months before and one year after delivery did not differ ($p = 0.548$). Pre-pregnancy creatinin >90 umol/L significantly increased the risk for preeclampsia ($p = 0.015$).
Conclusion: In conclusion, in pregnancies after OLT, we report a high live birth rate but a substantial proportion (17%) of mothers not seeing their child reach adulthood. Pregnancies seem safe for the transplant. In line with literature, pregnancy complications were common.

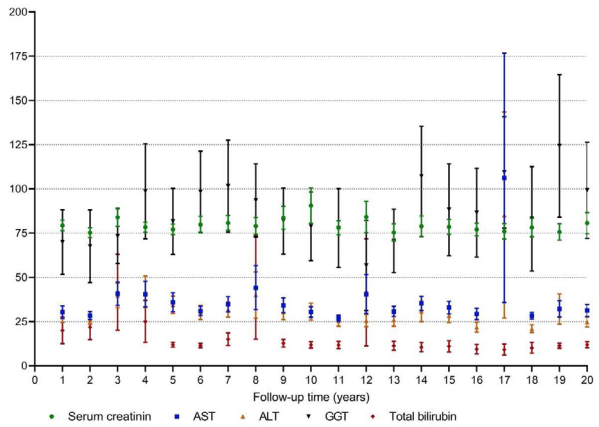

Figure 1. Long-term yearly follow-up after pregnancy in OLT patients
Long-term follow-up of serum creatinin (umol/L), AST (U/L), ALT (U/L), GGT (U/L) and bilirubin (umol/L) levels from 1 year after delivery of the first child born after OLT till 20 years after delivery. Creatinin, AST and ALT significantly changed over time, p<0.000. Bilirubin and GGT did not change, p=0.169, p=0.266, resp. The number of patients varies per follow-up moment between 44 and 9. *Abbreviation: OLT: orthotopic liver transplantation.*

Table 1. Short-term pregnancy outcomes

Maternal outcomes		
Hypertension (n=60)		13 (22%)
	Preeclampsia (n=63)	8 (13%)
	HELLP syndrome (n=60)	1 (2%)
	Eclampsia (n=61)	0 (0%)
Gestational diabetes (n=62)		3 (5%)
Infection (n=61)		3 (5%)
Thrombosis (n=62)		0 (0%)
Bleeding (n=61)		0 (0%)
Graft failure during pregnancy (n=77)		1 (1%)
Biopsy proven rejection (n=72)		2 (3%)
Neonatal outcomes		
Gender (female) (n=79)		42 (53%)
Gestational age (weeks) (n=64)	Gestational age	38 [36-39]
	Preterm birth	21 (33%)
	Very preterm birth	6 (9%)
Birth weight (grams) (n=61)	Birth weight	2870 [2475-3177]
	Low birth weight	15 (25%)
	Very low birth weight	5 (8%)
APGAR score	1 minute (n=50)	9 [7.8-9]
	5 minutes (n=53)	10 [9-10]
	10 minutes (n=17)	10 [9-10]
Congenital malformation (n=59)		0 (0%)
Congenital infection (n=59)		1 (2%)
Neonatal death (n=75)		2 (3%)
Stillbirth (n=75)		3 (4%)

Short-term pregnancy outcomes during pregnancy and up to seven days after delivery. Data given as median [IQR] or n (%) where appropriate. Stillbirth pregnancies excluded. All complications were scored if the diagnosis was mentioned in the patient record. Definitions: Hypertension: pre-existent or pregnancy induced hypertension, neonatal death: death <7 days after birth, preterm birth: <37 weeks of gestation, very preterm birth: 28-32 weeks of gestation, low birth weight: <2500 grams, very low birth weight: <1500 grams. *Abbreviations: APGAR: Appearance- Pulse - Grimace - Activity – Respiration, HELLP: Hemolysis Elevated Liver enzymes and Low Platelets.*

OP017 FATIGUE AMONG HEART RECIPIENTS- A BARRIER TO SELF-EFFICACY?

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Background: Recovery after heart transplantation is challenging and many heart recipients struggle with various transplant-related symptoms, side-effects of immunosuppressive medications and mental challenges. Fatigue has been reported to be one of the most common and distressing symptoms after heart transplantation and might therefore constitute a barrier to self-efficacy, which acts as a moderator of self-management. Therefore, the aim was to explore the prevalence of fatigue and its relationship to self-efficacy among heart recipients one to five years after transplantation.
Method: This study is part of a cross-sectional, Swedish, multi-centre study 1-5 years post-heart transplantation called Self-Management after Thoracic Transplantation, including 79 heart recipients. Three different self-assessment instruments were employed; The Multidimensional Fatigue Inventory-19, Self-efficacy for managing chronic disease 6-Item Scale and The Post-operative Recovery Profile.
Results: The reported levels of fatigue for the whole group were moderate in all dimensions of the Multidimensional Fatigue Inventory-19, with highest ratings in the General Fatigue sub-scale. Those most fatigued were younger than 50 years, had pre-transplant treatment with Mechanical Circulatory Support, were not recovered and had not returned to work. Heart recipients reporting a high level of fatigue in the General Fatigue sub-dimension had a significantly lower level of self-efficacy ($p \leq .001$) than those reporting a low level of fatigue. Self-efficacy was associated with the sub-dimensions Mental Fatigue ($\rho = -.649$) and Reduced Motivation ($\rho = -.617$), which explained 40.1% of the variance when controlled for age and gender.
Conclusions: Fatigue is not a widespread problem after heart transplantation as evidenced by the moderate levels. However, for those suffering from severe fatigue, it is a troublesome symptom affecting their ability to return to work and the recovery process. The association between fatigue and self-efficacy suggests that fatigue might act as a barrier to self-management. Efforts should be made to identify those troubled by fatigue, in order to provide sufficient self-management support and targeted person-centered health promotion after heart transplantation.

OP018 SYMPTOM OCCURRENCE AND DISTRESS AFTER HEART TRANSPLANTATION - A NATIONWIDE CROSS-SECTIONAL COHORT STUDY

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Background: The rationale was to focus on the illness experience after heart transplantation by means of the relationships between symptom distress, psychological well-being and relevant sociodemographic variables rather than on the side-effects of the immunosuppressive medication. There is an expectation that the heart recipients should manage a multitude changes in everyday life. However, the unfamiliar health and life situation of being a heart recipient has been described as a source of uncertainty and a possible source of distress. It has also been argued that an extensive symptom burden, might reduce performance, that constitutes a barrier to self-efficacy and subsequently self-management.
Aim: To explore self-reported symptom occurrence and distress after heart transplantation and its relationship with self-reported psychological well-being, and sociodemographic factors.
Methods: A multicentre, cross-sectional cohort study involving two questionnaires that were handed out during 2014 - 2017 at the heart recipients' yearly follow-up, one to five years post-transplant at three Swedish university hospitals.
Results: Symptoms occurred differently depending on type and duration of follow-up among the 79 heart recipients, 54 men and 25 women, with a mean age 53 years. The most common symptoms, trembling hands, and decreased libido were also the most distressing. Heart recipients most burdened by symptoms were younger than 50 years, not working, had poor psychological well-being and living alone. Fatigue explained more than 60 % of the variation in transplant specific wellbeing and those who experienced fatigue were over 1.43 times more likely to report poor psychological well-being than those who did not report fatigue.
Conclusion: The most common symptoms are also the most distressing and heart recipients most burdened by symptoms are young, unable to work and with psychological distress. Fatigue is a strong predictor for low transplant specific wellbeing.

OP019 RECOVERY AND SELF-EFFICACY AFTER HEART TRANSPLANTATION- IMPORTANT ASPECTS OF SELF-MANAGEMENT

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Background: Recovery after heart transplantation is challenging and many heart recipients struggle with various transplant-related symptoms, side-effects of immunosuppressive medications and mental challenges. Self-efficacy refers to a person´s confidence in carrying out treatment-related activities and constitutes the foundation of self-management. Thus, the focus of long time follow-up after transplantation. Symptoms, setbacks and complications potentially decreases self-efficacy if adequate support is lacking. Therefore, the aim was to explore self-efficacy in relation to the self-reported level of recovery and psychological well-being, among adult heart recipients, 1-5 years after transplantation.
Methods: This study is part of a cross-sectional, Swedish, multi-centre study 1-5 years post heart transplantation called Self-Management after Thoracic Transplantation, including 79 heart recipients. Three different self-assessment instruments were employed; Self-efficacy for managing chronic disease 6-Item Scale, The Postoperative Recovery Profile and the Psychological General Well-being instrument.
Results: The reported level of self-efficacy was high (median 8.3, maximum score 10). Significantly higher self-efficacy was seen among those who had returned to work ($p = .003$); those without pre-transplant mechanical circulatory support ($p = .033$) and those reasonably recovered was ($p = .047$). In total, 65.5 % ($n = 52$) reported being reasonably recovered, while 18.8 % ($n = 12$) were not recovered. The median total Psychological General Well-being score was 108 (p_{25} 24, p_{75} 117), suggesting overall good psychological well-being in the whole group of heart recipients.
Conclusion: The heart transplant recipients in our study had an overall high level of self-efficacy. However, the groups with low reported level of recovery; treatment with pre-transplant mechanical circulatory support or those who had not returned to work reported lower levels of self-efficacy. Gaining more knowledge regarding what heart recipients struggle with together with understanding about experiences after transplantation gives healthcare professionals guiding in how to adjust efforts to match the actual needs of the heart recipients.

OP020 THE MEANING OF SURVIVING THREE YEARS AFTER A HEART TRANSPLANT - A TRANSITION FROM UNCERTAINTY TO ACCEPTANCE THROUGH ADAPTATION

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Background: Of all medical interventions, heart transplantation (Htx) is without doubt the one that implies the greatest contrast of emotions, including deep pain, frustration and fear of death together with intense happiness and joy of life. Previous qualitative research on HTRs has taken the form of once-off interviews. There is thus a need for a prospective, qualitative design to grasp the presumed transition, where the rationale was to longitudinally follow-up previous interviews performed with HTRs at their one-year examination, in order to deepen the understanding of the meaning of surviving HTx.
Aim: To explore the meaning of surviving three years after a heart transplant compared to one year and to identify what constitutes the change process.
Methods: Prospective, qualitative design. The phenomenological–hermeneutic method developed by Lindseth and Norberg was used. This multicentre study was carried out at the two hospitals in Sweden where heart transplants are performed. A total of 13 heart recipients who survived three years after a heart transplant were invited to participate in this three-year follow-up study and 12 accepted, 3 women and 9 men with a mean age of 51.25 years.
Results: The *naïve* understanding revealed that the heart recipients strongly accepted their life situation and that time had enabled this acceptance of limitations through adaptation. The thematic structural analyses cover six themes illustrating the meaning of acceptance and adaptation, i.e., *accepting life as it is*, *adapting to post-transplant limitations*, *adapting to a changed body*, *social adaptation*, *showing gratitude* and *trusting oneself and others*.
Conclusion: Achieving acceptance and a solid sense of self-efficacy after heart transplantation is a time-consuming process that involves courage to face and accept the reality and adapt in every life dimension.

OP021 FATIGUE, SELF-EFFICACY AND RECOVERY 1-5 YEARS AFTER LUNG TRANSPLANTATION

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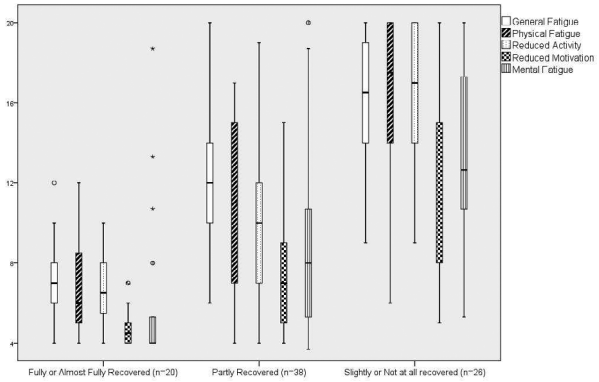
Background: The knowledge is scarce regarding how recovery and wellbeing and after lung transplantation (LuTx) is affected by various symptoms. Thus, little is known about what kind of self-management support the lung transplant recipients require. Since fatigue is a symptom that might severely impair wellbeing the primary research question was what is the prevalence of fatigue 1-5 years after lung transplantation and which parts of transplant specific and psychological well-being are related to fatigue?
Aim: To explore associations between fatigue and its influencing factors as perceived social and psychological well-being, self-efficacy and recovery.
Methods: Cross-sectional, multicenter cohort study from the Swedish SMATT-project (Self-Management after Thoracic Transplantation). Lung receptions ($n = 117$) due for an annual follow-up 1-5 years after transplantation were screened with four instruments; The Multidimensional Fatigue Inventory (MFI-20), Self-Efficacy for Managing Chronic Disease scale, Postoperative Recovery Profile questionnaire (PRP) and the Organ Transplant Symptom and Well-being Instrument (OTSWI).
Results: In a total 56% reported high general fatigue (≥ 12) regardless of follow-up. There was no relationship between lung function (FEV_1) and any of the five dimensions of fatigue. There was a weak relationship between mental fatigue and the grade of Bronchiolitis obliterans syndrome (r_s-.202*). There was a strong relationship between all dimensions of fatigue and both mental and social wellbeing. A high level of fatigue was related to impaired self-efficacy. Regardless of follow-up time, those reporting to be fully or almost fully recovered were significantly less fatigued in all dimensions of fatigue (figure 1).
Conclusion: Fatigue should be a preferred target of interventions in clinical praxis due to its association to self-efficacy and recovery. An impaired self-management might be a consequence of this association.

Figure 1. Median fatigue scores between patients´ reports on recovery. Subscales of the Multidimensional Fatigue Inventory range 4-20 where a score >12 indicates severe fatigue. Kruskal Wallis test significant ($p < 0.001$) across the three different groups in all dimensions. Mann- Whitney U test significant ($p < 0.001$) between all dimensions.



OP022 ADAPTATION AFTER LUNG TRANSPLANTATION UP TO THREE YEARS AFTER TRANSPLANTATION

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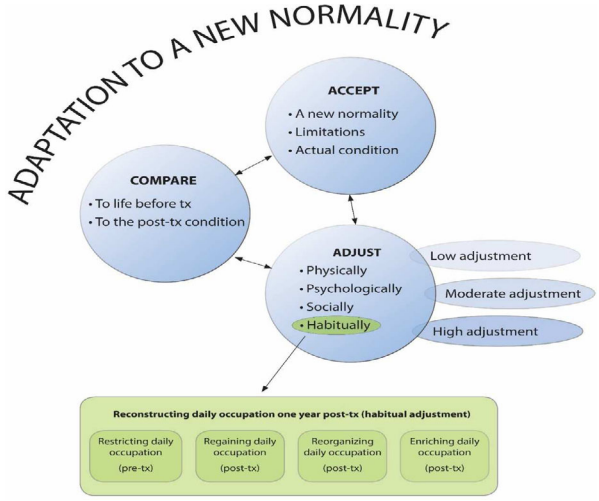
Background: Previous research reveals that it is possible for lung recipients (LuRs) to experience health one-year post-transplant, despite not being fully recovered. However, an in-depth long-term perspective on how LuRs' health transition evolves over time is lacking.
Aim: The aim of this study was to further develop a grounded theory of health transition by exploring the process of change 1-3 years after lung transplantation (LuTx).
Methods: The Grounded Theory Method was used prospectively to analyze the narratives of 14 adult LuRs, 10 men and 4 women with a mean age of 56 years who were included at their one-year follow-up and re-interviewed two years later.
Results: This novel study contributes an in-depth understanding of the adaptation process after LuTx. The greatest concern in the three years after LuTx was *Adaptation to a new normality,* which was achieved by three main strategies; Compare, Accept and Adjust (figure 1). Adaptation to a new normality involved understanding that one's previous life no longer exists and that a new way of living requires adaptation. Successful adaptation resulted in the experience of health and well-being, whereas too many symptoms and restrictions in everyday life led to difficulties and a profound sense of illness.
Conclusion: Lung recipients can experience health despite symptoms and complications by adapting to a new normality. This individual process begins post-tx and continues throughout life.



A WHISTLE STOP TOUR OF METABOLIC COMPLICATIONS AFTER TRANSPLANT

OP039 IMPACT OF INHIBITION OF PCSK-9 AMONG RENAL TRANSPLANT RECIPIENTS WITH HIGH CARDIOVASCULAR RISK

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Background: Monoclonal antibodies inhibiting proprotein convertase subtilisin/Kexin type A(PCSK-9) have emerged as one of the new cholesterol-lowering agents. It is not evaluated among renal transplant recipients despite its favorable safety profile. We aimed to evaluate the safety and efficacy of evolocumab in reducing lipids and cardiovascular events among risky renal transplant recipients.
Methods: 195 kidney transplant recipients- with high cardiovascular risk (>20)-were enrolled in this randomized controlled study during the period between 6.2017 and 6.2018. Patients who received statin and evolocumab (140mg/ 2 weeks, group1, n = 97) while those who were maintained on statin alone comprised group 2(n = 98). They were followed up for 24 months.
Preliminary Results: The 2 groups were comparable regarding their demographics ($p > 0.05$). Before enrollment in the study, post-transplant complications were comparable apart from a higher prevalence of NODAT in group 2($p = 0.033$). Smokers were significantly more prevalent in group 1. Basal graft function was significantly higher in group 1 despite equivalent regimen of immunosuppression in both groups($p > 0.05$). Clinically the 2 groups were comparable concerning cardiovascular events and both graft and patient outcomes ($p > 0.05$). Basal cholesterol was significantly higher in group 1(5.5 vs. 4.7, $p < 0.001$) which dropped significantly after 3 months (vs.12 months in group2) and thereafter ($p = 0.031$). We observed that triglycerides in the two groups were comparable ($p > 0.05$) till the end of the study.
Conclusions: Evolocumab is a promising add on lipid-lowering agent. In high-risk renal transplant, earlier reduction of cholesterol was observed in the add-on evolocumab group but without significant positive cardiovascular impact.

OP040 IMPACT OF FULL CORRECTION OF POST-TRANSPLANT ANEMIA ON CARDIOVASCULAR SYSTEM IN RENAL TRANSPLANT RECIPIENTS RECEIVING ESA: PROSPECTIVE RCT

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Background: Several studies have shown that PTA might be associated with increased mortality and decreased graft survival and de-novo congestive heart failure, so we aimed from this prospective randomized controlled study to assess the impact of full correction of post-transplant anemia on the cardiovascular system of renal transplant recipients receiving erythropoietin stimulating agents.
Methods: We recruited 247 kidney recipients with stable graft function in this RCT with 2 groups according to their target hemoglobin (11-12 g/dl, group 1, n = 183) and (13:15 g/dl, group 2, n = 64). After correction of deficiencies, the target hemoglobin was achieved using ESA. All patients were followed up clinically and by serum creatinine and eGFR monthly for 12 months.
Results: Diabetic nephropathy was the main cause of ESKD in group 1 ($p = 0.005$). The studied groups were comparable regarding pre-transplant co-morbidities. Most patients received thymoglobulin as induction then cyclosporine based maintenance immunosuppression. We did not find any significant difference between the two groups concerning post-transplant diabetes, BK viremia or malignancies and even cardiovascular events (TIA, stroke, ACS), uncontrolled hypertension, heart failure or arrhythmias ($p > 0.05$). Group 1 showed higher mean blood pressure ($p = 0.003$), lower LV internal dimensions, higher LVH, LV mass, IVSD and LV mass index after one year of the study ($p < 0.05$). Group 2 did not show any significant change in the same parameters ($p > 0.05$). Moreover, IVSD, mean ejection fraction and FS were comparable in both groups ($p > 0.05$). Graft outcome

was comparable between both groups (p = 0.125), meanwhile, mortality cases were significantly higher among group 1 (16 cases, 8.7%) (p = 0.005).
Conclusions: Full correction of PTA is associated with stabilized cardiac dimensions indices without any significant cardiovascular comorbidities.

OP041 IS ERYTHROCYTOSIS MORE FREQUENT AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION?: A SINGLE-CENTER EXPERIENCE

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Background: Post-transplant erythrocytosis (PTE) is reported on 8 to 22% of kidney transplant recipients. Multiple mechanisms have been proposed to explain its occurrence, including erythropoietin overproduction, renin–angiotensin system activation, increased endogenous androgens production, and recently described increased insulin-like growth factor 1 levels. This study aims to evaluate the prevalence of PTE on a cohort of simultaneous pancreas-kidney (SPK) and single kidney transplant patients and find predictive factors for PTE development.
Methods: We developed a single-center retrospective cohort study with 65 SPK transplant patients and paired (same donor) single kidney transplant patients. PTE was defined as a hematocrit superior to 51% for more than six months in the absence of thrombocytosis, leukocytosis, or a known cause of erythrocytosis.
Results: Erythrocytosis was present on 23.1 % patients and was more frequent on SPK transplant patients (p < 0.001). Mean time for PTE development was 11.2 ± 13.3 months. The erythrocytosis group had a shorter previous dialysis time (p = 0.024), was more frequently on peritoneal dialysis before transplantation (p = 0.022) and needed more often blood transfusions on the early post-transplant period (p = 0.016). Post-transplant use of erythropoietin-stimulating agents was not different between groups. In the multivariate model, SPK transplant was the only predictor for PTE development (OR 7.7, 95% CI (1.9-34.5)). Of the 30 patients with PTE, 4 needed phlebotomies and in 4 patients a renin-angiotensin-aldosterone inhibitor was initiated. *De novo* hypertension was more frequent on PTE group (p = 0.002) but there was no difference in terms of stroke and pancreas or kidney thrombosis.
Conclusions: PTE is more common after SPK transplantation than after single kidney transplantation. *De novo* hypertension after transplantation was more frequent on the PTE group but kidney and pancreas thrombosis rates were similar.

OP042 COMPARING SURVIVAL OUTCOMES FOR KIDNEY TRANSPLANT RECIPIENTS WITH PRE-EXISTING DIABETES VERSUS THOSE WHO DEVELOP POST-TRANSPLANTATION DIABETES

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Background: Kidney transplant recipients with known diabetes have inferior survival to non-diabetic recipients. However, there are conflicting data concerning survival outcomes for kidney transplant recipients who develop post-transplantation diabetes (PTDM). The aim of this study was to explore clinical outcomes for kidney transplant recipients with pre-transplant versus PTDM in a contemporary kidney transplant recipient cohort.
Methods: This is a retrospective observational study of adults with kidney failure receiving a kidney transplant between 2007-2018 at a single centre with follow-up to 31st December 2020. Data were extracted from hospital electronic patient records, with clinical outcomes linked to national administration datasets including Hospital Episode Statistics. PTDM was diagnosed in accordance with international consensus guidelines. Unadjusted and adjusted survival outcomes were assessed with Kaplan-Meier curves and Cox regression models respectively, with PTDM handled as a time-varying covariate.
Results: Data were analysed for 1,757 kidney transplant recipients, of whom 11.8% (n = 207) had pre-transplant diabetes and 13.8% (n = 243) developed PTDM with median time to onset of PTDM 108 days (IQR 46 to 549 days). Median follow-up for the cohort was 1,839 days (interquartile range 928-2985 days). After adjustment with varying selection models, PTDM was associated with lower mortality and pre-diabetes was associated with higher mortality (see Table). However, if analyses are restricted to those with at least 5-year follow-up, then PTDM has no association with mortality but pre-transplant diabetes remains associated with higher mortality.
Conclusions: In the contemporary era, pre-transplant diabetes remains associated with increased risk for mortality after kidney transplantation but PTDM effects are time dependent. Development of PTDM should be encouraged as a mandated registry return to allow better long-term analyses of impact on survival outcomes.

Model analysed		Hazard Ratio	95% CI	Hazard Ratio	95% CI
		Full cohort (n=1,757)		Cohort with ≥5-year follow up (n=1,586)	
Unadjusted	PTDM	0.942	0.702-1.264	1.117	0.768-1.624
	Pre-transplant diabetes	**1.870**	**1.433-2.441**	**2.303**	**1.607-3.301**
Model 1	PTDM	**0.719**	**0.535-0.966**	0.824	0.566-1.200
	Pre-transplant diabetes	**1.417**	**1.085-1.850**	**1.731**	**1.208-2.482**
Model 2	PTDM	**0.718**	**0.534-0.964**	0.821	0.563-1.197
	Pre-transplant diabetes	**1.415**	**1.078-1.858**	**1.809**	**1.253-2.611**
Model 3	PTDM	**0.712**	**0.512-0.990**	0.823	0.553-1.225
	Pre-transplant diabetes	**1.509**	**1.113-2.046**	**2.003**	**1.360-2.948**

Model[1] Adjusted for age
Model[2] Adjusted for age, sex and ethnicity
Model[3] Fully adjusted model (age, sex, ethnicity, waitlist time, requiring dialysis at transplant, index of multiple deprivation, repeat transplant, history of myocardial infarct, history of stroke, history of peripheral vascular disease, history of cancer).

OP043 OUTCOMES OF SODIUM–GLUCOSE COTRANSPORTER 2 INHIBITORS AND GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS IN KIDNEY TRANSPLANT RECIPIENTS WITH DIABETES

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The impact of the new glucose lowering therapies like sodium–glucose cotransporter 2 inhibitors (SGLT2i) and Glucagon-like peptide-1 receptor agonists (GLP-1 RA) in managing patients with type II diabetes mellitus (T2DM) is very impressive for reducing the burden of cardiovascular and renal complications and improving the outcomes. Kidney transplant recipients (KTRs) with pre-transplant or post-transplant diabetes mellites have higher risks for cardiovascular and renal morbidities and mortalities. The use of these drugs was limited by the postulated higher incidence of side effects. Few case series and small prospective trials in KTRs were published in the literature. We retrospectively assessed the safety and short-term outcome of these drugs in our diabetic KTRs.
Patients and Methods: We assessed 97 KTRs with T2DM who received SGLT2I (Canagliflozin) for at least 3 months and compared them to a matched group of 97 KTRs with T2DM on standard of care (SOC) therapy with follow-up for one year. All patients were at least 3 months post-transplant with stable renal function at the time of inclusion and minimum estimated glomerular filtration rate (eGFR) of at least 30 ml/min/1.73m^2. We performed subgroup analysis of 41 KTRs on GLP-1 RA, 15 of them were also on SGLT2i.
Results: The groups were matching regarding age, gender, donor, immunosuppression, post-transplant duration, type of diabetes and BMI. There was significant improvement in HbA1c in both groups but more with SGLT2i (p < 0.0001) and reduction of BMI (p = 0.0106).
SGLT2i group had significantly increasing levels of eGFR towards the end of the year (p = 0.0356) specially at eGFR ranges of 45-59 and >90 ml/min/1.73 m^2. There was also significant reduction of proteinuria in SGLT2i group at all ranges (p < 0.0001) with no recorded side effects. By doing a subgroup analysis we found that patients on SGLT2i and GLP-1 RA have parallel and significant increase in eGFR compared to SOC group and the increase was more pronounced in the group on both SGLT2i and GLP-1 RA. The improvement of proteinuria was significantly better in patients on SGLT2i compared to patients on either GLP-1 RA or SOC. However, the maximum improvement was noticed in patient on both SGLT2i and GLP-1 RA.
Conclusion: Use of SGLT2i and GLP-1 RA in KTRs was associated with better outcome with no increase in side effects.

OP044 HLA ALLELES CW12 AND DQ4 IN KIDNEY TRANSPLANT RECIPIENTS ARE INDEPENDENT RISK FACTORS FOR THE DEVELOPMENT OF POST-TRANSPLANTATION DIABETES

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Background: The association between specific HLA alleles and risk for post-transplantation diabetes (PTDM) is not clear. The aim of this study was to explore the link between routinely collected recipient HLA alleles and the risk of PTDM development, after adjustment for known PTDM risk factors, in a large single-center cohort.
Methods: We undertook a retrospective cohort analysis of all consecutive kidney-alone transplants performed at a single centre in the United Kingdom between 1st January 2007 and 30th June 2018. Recipients of multiple organs and those with pre-existing diabetes were excluded. Diagnosis of PTDM was aligned with International Consensus recommendations and developed in 231 kidney transplant recipients. All cases were typed by DNA analysis using Lifecodes SSO kits (supplied by Imucor) and reported at the resolution required for the national allocation scheme. HLA alleles were accordingly assigned as serological equivalents.
Results: After exclusions, data were retrospectively analyzed for 1,560 non-diabetic kidney transplant recipients at a single centre between 2007 and 2018, with median follow-up 33 months (interquartile range 8-73). Data relating to HLA alleles were recorded in 1,501 cases, with a total of 99 alleles considered in the analysis, and this formed the final study cohort. In total, 231 patients developed PTDM, giving Kaplan-Meier estimated rates of 12.7%, 19.1% and 27.4% at 1, 5 and 10 years respectively. The presence of Cw12, B52, B38, B58, DQ4, A80, and DR13, and the absence of DQ3 and DR04, were associated with significant increases in PTDM risk. In a multivariable Cox regression model, adjusting for other clinical risk factors for PTDM, the presence of Cw12 (Hazard Ratio 1.57 [95% CI 1.08-2.27], $p = 0.017$) and DQ4 (Hazard Ratio 1.78 [95% CI 1.07-2.96], $p = 0.026$) were found to be independent risk factors for PTDM. There was also evidence that the presence of B58 increases PTDM risk within the subgroup of recipients of White ethnicity (Hazard Ratio 5.01 [95% CI 2.20-11.42], $p < 0.001$).
Conclusion: Our data show an association between particular HLA alleles and PTDM risk. However, association is not causality and this work requires replication and further investigation to understand underlying biological mechanisms.

OP045 SEMAGLUTIDE IS A SAFE AND EFFECTIVE TREATMENT IN PATIENTS AFTER LIVER TRANSPLANTATION WITH POST-TRANSPLANT DIABETES MELLITUS

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Background and Aim: Post-Transplant Diabetes Mellitus (PTDM) is a frequent consequence of solid organ transplantation with an incidence of over 30%. Treatment options for management of PTDM are limited with regards to the availability of strong clinical evidence. Glucagon-like peptide 1 receptor agonists (GLP-1RA) are a relatively new class of injectable drugs used in the treatment of T2DM. GLP-1RAs mimic endogenous GLP-1, stimulating insulin release from the pancreas, suppressing glucagon secretion, slowing gastric emptying and increasing satiety. These agents lack hepatic metabolism and hence have limited drug–drug interactions. Our aim was to evaluate the safety and efficacy of semaglutide in the treatment of PTDM in patients following orthotopic liver transplantation (OLTx).
Methods: Patients following OLTx, >18 years, BMI >30 kg/m^2, with recorded PTDM, and without a history of bariatric surgery and any contraindications for the use of GLP-1RA, were treated with semaglutide once weekly. Weight, blood pressure, metabolic parameters (including HbA1c and lipid profile), liver enzymes and immunosuppressant levels were measured.
Results: In 10 OLTx patients (mean ± SEM, age 54 ± 5 years), 6 months treatment with semaglutide resulted in a significant decrease in weight (111 ± 3 to 101 ± 2 kg, $p < 0.05$) and HbA1c (61 ± 5 to 48 ± 4 mmol/mmol, $p < 0.05$). Blood pressure, liver enzymes, and lipids improved, but not significantly. There were no differences in AUC of tacrolimus concentrations. One patient suffered from nausea the day following injection, this could be ameliorated by reducing the dosage.
Conclusions: Semaglutide is safe and effective in the treatment of PTDM in obese patients following OLTx. These findings need to be confirmed in larger studies.

OP046 DETERMINATS OF THE APPERANANCE OF POST-TRANSPLANT DIABETES MELLITUS AFTER KINDEY TRASNAPLANTION

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Background: The appearance of diabetes mellitus after kidney transplantation (Post-Transplant Diabetes Mellitus- PTDM) is a common disorder of it, which enhances not only the cardiovascular risk but also the risk for kidney graft loss. The incidence of PTDM is about 5-50%. The aim of this study is to examine the potential risk factors which determine the appearance of PTDM.
Methods: We studied retrospectively 284 patients of our center, who have been subjected to kidney transplantation during the last 10 years. Kidney recipients with diabetes mellitus prior to transplantation or those with follow-up less than 6 months were rejected from the study. We examine overall 263 recipients with mean age 52 ± 26 years. Their immunosuppressive treatment included CNI inhibitors (tacrolimus or cyclosporine), MPA and steroids. The mean time of monitoring was 63 ± 18 months. The diagnosis of PTDM was based on the criteria of the American Diabetes Association (ADA 2018).
Results: Out of a total of 263 kidney transplant recipients, PTDM was developed in 30 (11%), over a period of 13 ± 8 months after transplantation. Given that immunosuppressive therapy was identical in the vast majority, statistical analysis did not correlate the incidence of diabetes with treatment. However, there was a correlation, for the occurrence of PTDM, between the presence of hypomagnesaemia (Mg <1.55mg/dl) and uric acid ≥6.9 ± 0.75 mg/dl with respect to lower values ($p < 0.05$ respectively). No statistically significant association was found between the recipient's primary kidney disease and β-blocker intake and the occurrence of PTDM. Finally, there was a negative correlation between the age of the recipient and the time of onset of PTDM, with the elderly developing hyperglycemia faster than younger recipients.
Conclusions: Hypomagnesaemia and hyperuricemia increase the risk of developing PTDM in the aforementioned patients. Given the association between hypomagnesaemia and the development of diabetes mellitus after kidney transplantation, it is necessary to have prospective studies with a larger number of patients to determine if there is a causal relationship and to examine whether magnesium supplementation contributes to its prevention.

OP047 AMPUTATION AND ULCERATION IN TYPE-1 DIABETIC PATIENTS UNDERGOING SIMULTANEOUS KIDNEY-PANCREAS TRANSPLANTATION: A SYSTEMATIC REVIEW

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Background: Simultaneous pancreas and kidney transplantation (SPK) in Type-1 diabetic patients with renal insufficiency improves both long-term survival and quality of life. However, the effect of transplantation on vasculopathy remains unknown. Complication(s) arising from peripheral vascular disease, particularly amputation and ulceration, significantly impact quality of life. The aim of this systematic review was to identify the rate of amputation and ulceration in Type-1 diabetic patients following SPK and to determine whether this differed when compared with patients undergoing kidney transplantation alone (KTA).
Methods: Data were obtained from MEDLINE, EMBASE AND PUBMED databases; 371 patients underwent SPK and 218 KTA.
Results: KTA patients were older (50.7±7.4 vs 43.0±7.7; $p < 0.001$), had higher pre-transplant HbA1c (7.14±1.73 vs 7.9±1.1; $p = 0.004$) and had higher prevalence of ischaemic heart disease (28.8% vs 25.0%; $p = 0.002$). However, SPK transplant patients had a longer duration of Type 1 diabetes (28.8±5.8 vs 23.7±5.8 years; $p = 0.007$). There was no difference in the number of smokers, or prevalence of peripheral vascular disease between groups. There was no difference in the rate of amputation (SPK 9.4% *vs*

KTA 11.0%; p = 0.539) or ulceration (SPK 14.3% *vs* KTA 13.8%; p = 0.919) between patients undergoing SPK or KTA for Type-1 diabetes.
Conclusion: These data demonstrate that pancreatic transplantation appears not to affect the progression of vasculopathy in Type-1 diabetes.

OP048 EVEROLIMUS, GLUCOSE METABOLISM, AND ANTI-VISCERAL OBESITY EFFECT IN KIDNEY TRANSPLANT CANDIDATES

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Background: Glucose intolerance and weight gain early after transplant are risk factors for non-immunologic post-transplant renal insufficiency. Mammalian target of rapamycin inhibition everolimus is known to cause hyperglycemia but may prevent on the post-transplant weight gain after liver transplantation. We examine the impact of everolimus on post-transplant glucose metabolism and body composition in kidney transplant candidates.
Method: This is a retrospective single-center observational study of kidney transplant recipients who received transplantation 2008 to 2017 (n = 162 cases) and were followed during at least 1-year period. We ulticen (1) Everolimus group (EVR: introduced 3-months after transplantation), mPSL, MMF and reduced tacrolimus (TAC) (n = 82) (2) No everolimus group (mPSL, MMF and normal tacrolimus) (n = 80. These patients were transplanted before EVR was approved in Japan). In this analysis, 75g-OGTT, change of body weight and visceral fat area (CT-scan) at pre-transplant, 3/12 months after transplant were compared between two groups.
Results: There were no significant differences about gender, age, pre-transplant dialysis, primary disease, glucose/lipid metabolism and visceral fat area between the 2 groups. Twelve months after transplantation, visceral fat obesity was significantly increased in No-everolimus group (p = 0.003). Evaluated-GFR was slightly lower in No-everolimus group. There were no differences of Insulinogenic index (IGI) by 75g OGTT on 3-months after transplantation between the 2 groups (0.99 vs 0.86 p = 0.356), but in 12-months after transplantation, everolimus group was significantly lower than No-everolimus group (0.7 vs 1.1 p = 0.016). Proteinuria and hyperlipidemia were not significant in both groups.
Conclusion: Everolimus suppresses the excessive insulin secretion and may prevent insulin resistance and visceral obesity. It may also contribute to protect kidney graft function.

OP049 OUTCOMES OF LIVER TRANSPLANTS FOR NASH FROM A LARGE SINGLE INSTITUTIONAL COHORT

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Background and Aims: Non-alcoholic steatohepatitis (NASH) is the fastest growing indication for liver transplant (LT) and is deemed to be the foremost indication in near future. However, the outcomes following transplantation for NASH are poorly understood.
Methods: This is a retrospective analysis of adult LT with histological diagnosis of NASH, carried out between 2004 – 2019. Patient and graft survival were assessed.
Results: There were 151 out of 3462 of liver transplants performed for NASH – related cirrhosis during that period in our Institution. The median follow-up term was 35 (0-165) months. Recipients characteristics were as the following: median age of 63 years (30-82), BMI 31.7 kg/m2 (16-48), UKELD 53 (51-64), metabolic comorbidities in 105 (71%) patients, 11 (7.4 %) underwent coronary intervention, 3 (2%) had bariatric surgery pre-transplantation, 16 (9.5%) patients had PVT and 50 patients (33%) had HCC in explant. The median ICU and hospital stay were 3 and 15 days respectively. 41patients (27%) had renal support in ICU, 11 (7 %) patients had laparotomy for complications. Patients received DBD (98), DCD (47), Living donor (1) and Domino (3). Median CIT 480 (120-960) mins. 1, 5 and 10 year patient survival was 96.6 %, 92.9 % and 82.1 % respectively. 1, 5 and 10 year graft was 95.9%, 90.4% and 79.3% respectively. Three out of 11 patients' death (27.3%) were caused by systemic comorbidities more than 4 years post-LT. On the contrary, most of the mortality related to liver diseases was observed earlier than 3 years after LT. Only 6 (4%) patients had recurrence of NASH in the graft. Median recipient weights were 86 kg (46-157) 6 months post-LT, which decreased significantly from weight 92 kg (46- 142) before LT.
Conclusions: Patient and graft survivals at 10 years showed constant decline after 5 years, The incidence of the recurrence of NASH was significantly lower than what has been reported in previous publications. Further analysis needs to be carried out to identify factors relevant to patient and graft outcome.

OP050 VARIATIONS IN TM6SF2 RS58542926, PCSK9 RS505151 AND PCSK7 RS2277287 WITH THE RISK OF HEPATIC STEATOSIS AFTER LIVER TRANSPLANTATION

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Background and Aims: Genetic abnormalities might have important role in pathogenesis of hepatic steatosis after liver transplantation. We aimed to investigate association between genetic variations in transmembrane 6 superfamily member 2 (*TM6SF2)* rs58542926, proprotein convertase subtilisin/kexin type 9 (*PCSK9)* rs505151 and proprotein convertase subtilisin/kexin type 7 (*PCSK7)* rs2277287 with hepatic steatosis in liver transplant recipients.
Methods: Adult (>18 years) liver transplant recipients who referred for their routine post-transplant follow-up between June 2018 and September 2018 were included in the study. Hepatic steatosis in transplant recipients was assessed by controlled attenuation parameter (CAP). Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used to study *TM6SF2* rs58542926, *PCSK7* rs2277287 and *PCSK9* rs505151 genotypes.
Results: 107 liver transplant recipients were included. There was no association between different genotypes of *PCSK9* rs505151 and *PCSK7* rs2277287 with hepatic steatosis in liver transplant recipients (p > 0.05). The presence of TT genotype of *TM6SF2* rs58542926 was associated with hepatic steatosis measured by CAP after liver transplantation (OR: 1.057; 95 % CI: 0.978-1.146; p-value = 0.045). In patients with high grade hepatic steatosis (grade 2 and 3 steatosis), AG+GG genotypes of PCSK9 rs505151 were more prevalent than AA genotype (OR: 8.667; 95 % CI: 1.841-40.879; p-value = 0.004) compared to patients with low grade steatosis (grade 1). In multivariate regression model, AG+GG genotypes of *PCSK9* rs505151 was associated with high grade steatosis in liver transplant recipients (OR: 5.747; 95% CI: 1.086-30.303; p-value = 0.040) (Table).
Conclusions: Genetic variations in *TM6SF2* rs58542926 and *PCSK9* rs505151 might be associated with hepatic steatosis in liver transplant recipients.

Univariate				Multivariate analysis		
	High grade Steatosis	Low grade Steatosis	p-value	OR	95 % CI	p-value
BMI (kg/m^2)	30.81 ± 5.11	25.99 ± 5.38	0.008	1.055	0.855-1.301	0.620
WC (cm)	109.74 ± 11.74	99.29 ± 9.95	0.006	1.062	0.953-1.183	0.276
PTDM	57.9 %	64.7 %	0.676			
Post-transplant HLP	47.4 %	47.1 %	0.985			
TM6SF2 genotype						
CT+TT vs CC	75 %	76.5 %	0.917			
PCSK9 Genotype						
AG+GG vs AA	65 %	17.6 %	0.004	5.747	1.086-30.303	0.040
PCSK7 Genotype						
CT+TT vs CC	65 %	88.2 %	0.101			

OP051 IMPACT OF ELECTIVE LIGATION OF A PATENT ARTERIOVENOUS FISTULA IN KIDNEY TRANSPLANT RECIPIENTS ON BLOOD PRESSURE AND SERUM LEVELS OF CARDIAC BIOMARKERS

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Aims and Background: The management of a functioning arterio-venous fistula (AVF) in kidney transplant recipients (KTRs) is debated.
Methods: From 2017 to 2019, KTRs prospectively underwent a 24-hour ambulatory blood pressure (BP) monitoring (ABPM) at baseline (T0) and at 12 months *post*-AVF ligation (T12). Changes were assessed by a paired Student t-test or Wilcoxon sign rank test, as well as by McNemar test. Serum levels of the cardiac biomarkers ST2 and NT-proBNP were compared at T0, T6 and T12 using a general linear mixed model.
Results: Our cohort included 36 KTRs, with 12 women. Mean age was 52.4 $\pm$ 16.0 years. The AVF ligation occurred 16.8 [14.4; 24.6] months *post*-transplantation. Body mass index slightly increased over time (from 26.3 $\pm$ 4.8 kg/m^2 at T0 to 26.8 $\pm$ 5.3 kg/m^2 at T12, p = 0.043). The 24-hour diastolic BP (DBP) increased from T0 (79.0 $\pm$ 8.9 mmHg) to T12 (83.3 $\pm$ 8.3 mmHg, p = 0.0009). A similar pattern was observed for both daytime (from 81.7 $\pm$ 9.2 to 85.2 $\pm$ 8.4 mmHg, p = 0.0054) and nighttime (from 71.1 $\pm$ 10 to 78.3 $\pm$ 9.9 mmHg, p < 0.0001) DBP, as well as in both genders. The nighttime DBP load significantly increased over time (from 15% [8; 47] to 43 % [20; 77], p = 0.032), with a decreased proportion of dippers at T12 (p = 0.033). No significant change was observed for 24-hour systolic BP and heart rate. The antihypertensive treatment remained stable over the 12-month period. The serum levels of NT-proBNP significantly dropped from T0 (368 pg/ml [192; 554]) to T6 (231 pg/ml [118; 424]) and then remained stable until T12 (192 pg/ml [149; 344]) (p = 0.0004). The serum levels of ST2 (26.7 $\pm$ 13.5 ng/ml at baseline) did not change over time *post*-AVF ligation (p = 0.98).
Conclusion: The elective ligation of a functioning AVF in KTRs causes a significant rise of 24-hour DBP above the criterion of hypertension, with an increased nighttime DBP load. A concomitant diminution of serum levels of NT-proBNP is observed, with no change of ST2 biomarker of cardiac ulticentre.

OP052 POSITIVE IMPACT OF KIDNEY TRANSPLANTATION ON OLFACTORY ABILITY: RESULTS OF A CROSS-SECTIONAL CASE-CONTROL STUDY

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Background: Several studies have suggested that chronic kidney disease (CKD) may be associated with olfactory impairment. However, to date, the impact of renal replacement therapies has been only partly defined.
Methods: We tested the olfactory function of 235 participants [50 kidney transplant recipients (KT), 49 hemodialyzed patients (HD), 30 peritoneal dialysis patients (PD), 51 patients with CKD on conservative treatment (ND-CKD) and 55 healthy subjects (HS)] by the "Sniffin 'Sticks" test, including the sub-tests for the determination of odor threshold (T), odor discrimination (D), odor identification (I). The Sino-nasal Outcome Test-22 (SNOT22), Montreal Cognitive Assessment (MoCA) test and olfactory function Visual Analogue Scale (ofVAS) were also performed.
Results: The mean TDI score was significantly lower (and consistent with hyposmia), in HD, PD and ND-CKD compared to HS and KT (ANOVA p < 0.001). Similar results were observed in I and D tests. A similar condition was also found for T score, but only in PD and ND-CKD patients. Multiple comparisons among groups demonstrated no significant differences between KT and HS. After adjustments for confounding factors, a significant linear association was found between urea (β -0.03, p < 0.003) and eGFR (β 0.08, p < 0.001). No significant association was observed between the TDI score and the ofVAS score (p = 0.293).
Conclusions: Olfactory impairment affects a large number of CKD patients in both conservative and dialysis treatment. Kidney transplantation may reverse this condition with a significant positive impact on the quality of life and social behaviours/relationships.

LATEST NEWS IN ALLOIMMUNITY

OP053 IMPACT OF FCGR3A POLYMORPHISMS ON AMR OUTCOME AND IVIG RESPONSE IN KIDNEY TRANSPLANT RECIPIENTS

Alice Koenig[1,2], Virginie Mathias[3], Emmanuel Morelon[2], Beatrice Charreau[4], Maud Rabeyrin[2], Veronique Fremeaux Bacchi[5], Dany Anglicheau[6], Nicolas Pallet[5], Valérie Dubois[3], Olivier Thaunat[1,2]
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Background: Antibody-mediated rejection (AMR) is a major cause of late allograft failure. AMR outcome and response to treatment is however highly heterogeneous at the individual level, making difficult to assess the risk of graft loss and to determine the appropriate therapeutic strategy.
The binding of donor-specific antibodies (DSA) on graft endothelial cells is responsible for the recruitment of innate immune cells (in particular NK cells) via their surface Fc receptors, leading to damage of graft vasculature through antibody-dependent cell-mediated cytotoxicity (ADCC). NKs express a unique receptor: FcγR3A (CD16), for which a SNP (Fcγ RIIIa*559A > C, rs396991) that modulates FcγR3A binding capacity to IgG has been described.
This translational study aimed at determining whether recipient's FcγR3A polymorphism could be used to predict AMR outcome and response to IVIg in kidney transplant recipients.
Methods and Results: Among the renal transplant recipients followed in our center that had a graft biopsy between 2004 and 2015, 101 presented an AMR. The 15.9 % of patients that were homozygous for the "high-binding" FcγR3A allele ("FcR3A high binders") had an inferior allograft survival as compared with patients with a "low-binding" FcγR3A (p = 0.03).
An in vitro model of ADCC, in which purified human NKs were co-cultured with endothelial cells coated with DSA, confirmed that NKs of FcR3A high binders displayed stronger activation and promoted more endothelial damages. This model was also used to demonstrate that FcR3A high binders responded better, including at lower concentration, to IVIg treatment. This latter finding was confirmed in an independent clinical cohort.
Conclusions: Our work demonstrates that FcγR3A polymorphisms impact AMR outcome and suggests that this biomarker could be a useful tool for precision medicine, helping physicians to stratify the risk of graft loss at diagnosis of AMR and to guide IVIg therapy.

OP054 THE FCGR3A-158 V/V-GENOTYPE IS ASSOCIATED WITH DECREASED SURVIVAL OF RENAL ALLOGRAFTS WITH CHRONIC-ACTIVE ANTIBODY-MEDIATED REJECTION

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Background: An important factor compromising long-term allograft survival in kidney transplantation (KT) is chronic- active antibody-mediated rejection (c-aABMR). Immune cells expressing Fc-receptors (FCGRs) interact with IgG-antibodies bound to endothelial cells and genetic variation in *FCGRs* may affect susceptibility for antibody-mediated rejection. Natural killer (NK) cells express CD16 (*FCGR3A*) and could mediate renal endothelial cell damage in cases of c-aABMR. The V/V-genotype of the *FCGR3A* 158 F/V polymorphism is associated with increased CD16-expression and cytotoxicity by NK cells. This study evaluated whether this genotype is associated with the diagnosis of c-aABMR and renal allograft loss.
Methods: Cases of c-aABMR (N = 133) and control KT recipients without c-aABMR (N = 116) were genotyped for *FCGR3A* 158 F/V. In addition, CD16 expression by NK cells and CD16-dependent NK-cell function were evaluated. Follow-up of cases of c-aABMR was until 1st of January 2020 and graft loss/failure was defined as the need for dialysis or a retransplantation. The dates of diagnosis of c-aABMR and graft failure were used to calculate graft survival upon diagnosis.
Results: The distribution of the *FGCR3A* 158 F/V-genotypes was not different for c-aABMR cases compared to control KT recipients (p = 0.65). The V-allele was associated with increased median fluorescence intensity (MFI) of CD16 by NK cells (MFI 3.5x10^4 versus 1.3x10^4 for V/V and F/F-genotype, p < 0.001). Increased expression of CD16 correlated with increased CD16-dependent degranulation of NK cells (R = 0.4; p = 0.02). Moreover, the V/V-genotype was significantly associated with a higher glomerulitis score and an independent risk factor (HR 1.98; p = 0.04) for decreased allograft survival. Death-censored graft survival in c-aABMR cases at 3 years

follow-up was 33% for the *FCGR3A* 158 V/V-genotype versus 62% for the F/F-genotype.
Conclusions: The *FCGR3A* V/V-genotype increases CD16-mediated NK cell cytotoxicity and is associated with a higher glomerulitis score and decreased graft survival in cases with c-aABMR.

OP055 PREFORMED T-CELL ALLOIMMUNITY AND HLA EPLET MISMATCH TO GUIDE IMMUNOSUPPRESSION MINIMIZATION WITH TACROLIMUS MONOTHERAPY IN KIDNEY TRANSPLANTATION

Maria Meneghini[1], Elena Crespo[2], Frederike Bemelman[3], Martina Koch[4], Ondrej Viklicky[5], Magali Giral[6], Bernhard Banas[7], Juan Carlos Ruiz[8], Petra Reinke[9], Josep M Grinyó[1], Oriol Bestard[2]
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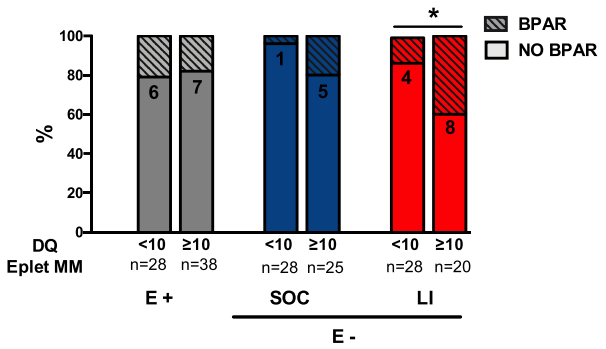
Background: Personalizing and minimizing immunosuppression is a major objective in kidney transplantation (KT). Transplant recipients are heterogenous regarding their humoral and cellular immunological memory and their primary alloimmune susceptibility, thus accurate immune-monitoring is warranted.
Methods: We performed a prospective, European, ulticentre, biomarker-guided trial in low immunological-risk first KT recipients. Pre-transplant donor-specific T cells were assessed by a standardized IFN-γ ELISPOT assay, and we investigate whether in Elispot negative patients(E-), de novo low immunosuppression (LI) with tacrolimus monotherapy would be non-inferior regarding 6-month BPAR rates than tacrolimus-based standard-of-care (SOC). Due to low recruitment rates, the trial was prematurely terminated: 101 E- patients were randomized to either LI (n = 53) or SOC (n = 48), and E+ (n = 66) received SOC. All patients received anti-IL2 induction therapy.

	E-/SOC	E-/LI	E+	E-/LI vs E-/SOC	E+ vs E-/LI	E+ vs E-/SOC
6-mo PP (n=133)	**n=43**	**n=35**	**n=55**	**p values**		
BPAR (excluding BL)+	1 (2)	4 (13)	12 (22)	0.158*	0.394	**0.006**
BPAR	3 (7)	8 (23)	12 (22)	0.056	0.908	0.051
12-mo PP (n=131)	**n=41**	**n=35**	**n=55**			
BPAR	3 (7)	9 (26)	13 (24)	0.055	0.823	0.051
BPAR ITT (n=167)	**n=53**	**n=48**	**n=66**	**p values**		
6-mo BPAR	5 (9.5)	11 (23)	12 (18)	0.064	0.534	0.175
12-mo BPAR	6 (11.3)	12 (25)	13 (20)	0.073	0.499	0.213
3/12-mo sc-BPAR	**n=35**	**n=38**	**n=33**	**p values**		
Sc-BPAR	1 (2.9)	10 (26.3)	6 (18.2)	**0.005**	0.413	**0.038**
Sc-BL	4 (11.4)	4 (10.5)	2 (6.1)	0.902	0.500	0.435
De novo DSA	**n=47**	**n=43**	**n=59**	**p values**		
Total dnDSA	1 (2)	3 (7)	7 (12)	0.345	0.513	0.074
Class I dnDSA	1 (2)	3 (7)	2 (3.4)	0.345	0.648	1.000
Class II dnDSA	0	1 (2)	7 (12)	0.478	0.134	**0.017**

Data are mean±SD, or n (%).
+Patients having received rescue therapy due to borderline BPAR prior to 6 months (n=4, in the E-/LI and n=2 in the E-/SOC), were excluded of this per protocol analysis.
*Statistical comparison of the primary end point of the CELLIMIN trial.
All BPAR analyses include Banff borderline (BL) lesions but the primary study end point.

Abbreviations: E+: donor-specific ELISPOT positive; E-/SOC: donor-specific ELISPOT negative/standard of care Immunosuppression; E-/LI: donor-specific ELISPOT negative/Low Immunosuppression; BPAR: biopsy proven acute rejection; BL: Banff borderline lesions



Results: At *intend-to-treat* analysis, although 6-month BPAR rates were not different between E-/LI and E-/SOC (4/35[13%] vs 1/43[2%], p = 0.15), at 12-months E-/LI showed higher incidence of BPAR than E-/SOC (12/48 [25%] vs 6/53[11.3%], p = 0.073, respectively). Notably, E+/SOC showed similarly high BPAR rates than E-/LI, being higher than E-/SOC at 6 and 12 months (12/66[18%] and 13/66[20%] respectively). These differences were stronger in *per-protocol* analyses.
Post-hoc analysis revealed that poor class-II eplet matching, especially at DQ locus, discriminated E- patients, especially E-/LI, at higher risk of BPAR (4/28[14%] low-risk vs 8/20[40%] high-risk, p = 0.043). Eplet mismatch also predicted anti-class-I and anti-DQ *de novo* DSA.
Global adverse events were similar, but E-/LI developed significantly lower viral infections, both CMV and BKV infections.
Conclusions: Pre-transplant T-cell alloreactivity and HLA eplet mismatch assessment may refine current baseline immune-risk stratification and guide immunosuppression decision-making in kidney transplantation.

OP056 HLA EPITOPE MISMATCHES IN KIDNEY TRANSPLANT RECIPIENTS WITH HISTOLOGICAL ANTIBODY-MEDIATED REJECTION WITH AND WITHOUT HLA DONOR-SPECIFIC ANTIBODIES

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Epitope mismatch analysis has been proposed as a better strategy to prevent de novo HLA donor-specific antibodies (HLA-DSA) compared with classical HLA antigen matching based on a refined evaluation of donor-recipient matching.
One-hundred eighteen patients with histological ABMR (n = 52), normal (n = 19) or IFTA (n = 47) biopsies (Banff'2015 classification) were included. We evaluated pre- and post-KT serum samples for HLA antibodies and calculated HLA antigen mismatch (AM). HLAMatchmaker software (V3.1 July-20) was used to define potential HLA epitope mismatches (EM) between donors and recipients.
HLA-DSA were more frequent in ABMR before (46% vs. normal 11% and IFTA 21%, p = 0.006) and after KT (73% vs. normal 16% and IFTA 17%, p < 0.001). Similar HLA-AM and EM were found in all groups until we dissected the ABMR group in those 38 who had HLA-DSA at biopsy (ABMR-DSA$^+$) and 14 who did not (ABMR-DSA$^-$). ABMR-DSA$^+$ presented higher class II EM (8 vs. 4.5 in ABMR-DSA$^-$, p = 0.046) and DRB-EM (5 vs. 0.5, p = 0.044, Figure 1). In the other hand, 34 patients developed *de novo* HLA-DSA (dnDSA) (79% ABMR, 3% normal, 18% IFTA, p < 0.001). The amount of class II EM (p = 0.031) but not class II AM (p = 0.26) was associated with dnDSA class II. The number of DRB-EM associated with DRB-dnDSA (p = 0.024), but the number of DRB-AM did not (p = 0.27). The rate of DQB-EM showed a weak association with DQB-dnDSA (p = 0.077), but DQB-AM did not (p = 0.21). A cut-off of 11 DRB-EM predicted DRB-dnDSA detection (p = 0.051), but for DQB-EM showed no relation with DQB-dnDSA (p = 0.16).
Patients with ABMR-DSA$^-$ showed lower amount of class II and DRB AbVer EM compared with ABMR-DSA$^+$, contradicting the hypothesis that HLA-DSA undetected with current techniques are mostly responsible for this type of damage. EM but not AM predicted class II dnDSA and DRB dnDSA post-KT. HLA EM assessment is a valuable tool for better DSA and ABMR-DSA$^+$ prediction in KT patients.

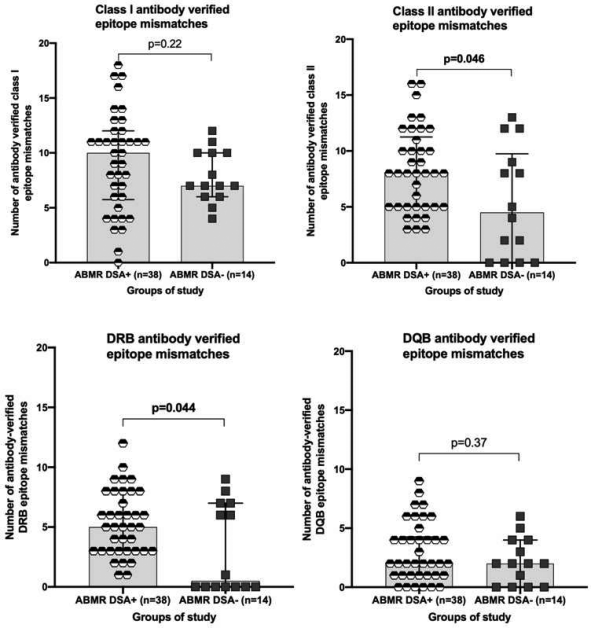

Figure 1. Number of antibody-verified class I, class II, DRB and DQB epitope mismatches in ABMR with HLA-DSA (black and white hexagons) and ABMR without HLA-DSA (black squares) cases. All plots show median and interquartile range (IQR).

OP057 UNSUPERVISED MACHINE LEARNING IDENTIFIES FAST AND SLOW MODULATION OF DSA DYNAMICS FOLLOWING HLA- INCOMPATIBLE TRANSPLANTATION – 5 YEAR OUTCOMES

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Background and Aims: The outcomes following HLA-incompatible (HLAi) kidney transplantation are poor compared to compatible kidney transplantation. Such a risk is variable though, and in some cases, patient clinical circumstance results in no choice but HLAi, especially when lower risk scenarios could be identified. The aim of this work is to determine if early antibody dynamic patterns are informative of mid-term clinical outcome- 5-year graft failure over and above of other predictive factors.

Methods: 88 cases that underwent HLAi and had high frequency monitoring of DSA in the first month post-transplantation with five year follow-up were included. The cases were classified by unsupervised machine learning clustering experiments into distinct groups. Difference in characteristics of cases in these groups and association with 5-year graft outcome were analysed using multivariable logistic regression.
Results: Cases were classified into five distinct groups (Figure 1a). In terms of acute rejection, a trend appeared with fast modulation cases (group 1) demonstrating a rate of 87% through to the sustained group which demonstrated the lowest rates at 19%. This can almost be viewed in complete contrast to the graft failure which saw rates of 4-7% with modulation (groups-1&2) and rates of 25-31% in the sustained group (groups-3&4). Kaplan-Meir analysis suggested sustained group was significant associated with higher 5-year graft failures (Figure 1b). Multivariable analysis suggested a pre-treatment DSA level (↑), male gender and absence of early acute rejection (first 30days) were strongly associative of a sustained DSA response (ROC-AUC = 0.86, PR-AUC = 0.84). The multivariable model for association with GF with: Age (↓), sustained DSA response and post-transplant plasmapheresis all significant indicators (ROC-AUC = 0.85, PR-AUC = 0.60).
Conclusions: Unsupervised machine learning identified patterns of post-transplant DSA behaviour which were associated with 5-year outcome. In particular, the modulation group had excellent 5 year outcomes despite higher rates of early rejection episodes. This work may also help in future tailoring of treatment, so that lower risk HLAi patients are not subjected to over-immunosuppression, and vice-versa even if had early acute rejection episodes.

OP058 MYELOID-DERIVED SUPPRESSOR CELLS IN KIDNEY TRANSPLANT RECIPIENTS AND THE EFFECT OF MAINTENANCE IMMUNOTHERAPY

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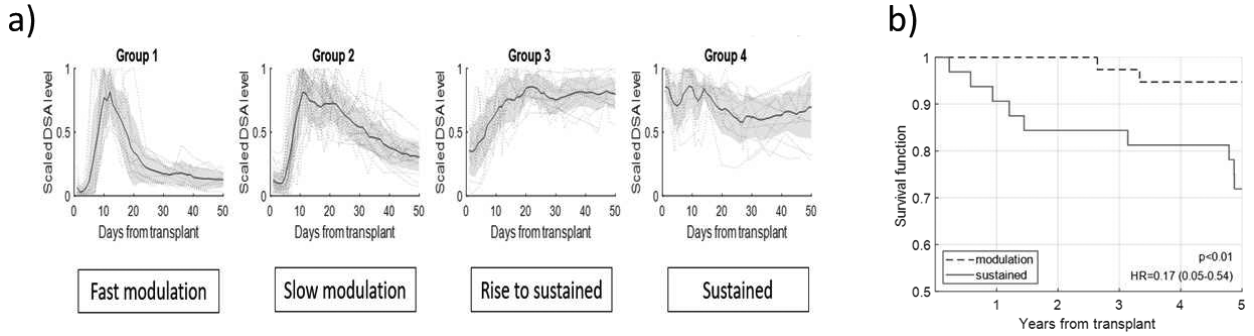
Background: Myeloid-derived suppressor cells (MDSC) represent a heterogeneous group of myeloid regulatory cells that were originally described in cancer. Several studies in animal models point to MDSC as important players in the induction of allograft tolerance due to their immune modulatory function. Most of the published studies have been performed in animal models, and the data addressing MDSCs in human organ transplantation are scarce.
Methods: We evaluated the phenotype and function of different MDSCs subsets in 38 kidney transplant recipients (KTRs) at different time points.
Results: Our data indicate that monocytic MDSCs (Mo-MDSC) increase in KTR at 6 and 12 months post-transplantation. On the contrary, the percentages of polymorphonuclear MDSC (PMN-MDSC) and early-stage MDSC (e-MDSC) are not significantly increased. We evaluated the immunosuppressive activity of Mo-MDSC in KTR and confirmed their ability to increase regulatory T cells (Treg) in vitro. Interestingly, when we compared the ability of Mo-MDSC to suppress T cell proliferation, we observed that tacrolimus, but



not rapamycin-treated KTR, was able to inhibit CD4+ T cell proliferation in vitro.
Conclusions: These results that, although mTOR inhibitors are widely regarded as supportive of regulatory responses, rapamycin may impair Mo-MDSC function, and suggests that the choice of immunosuppressive therapy may determine the tolerogenic pathway and participating immune cells that promote organ transplant acceptance in KTR.

OP059 CLINICAL VALUE OF THE USE OF COMPLETE HIGH-RESOLUTION HLA TYPING FOR THE DEFINITION OF DNDSA AFTER KIDNEY TRANSPLANTATION

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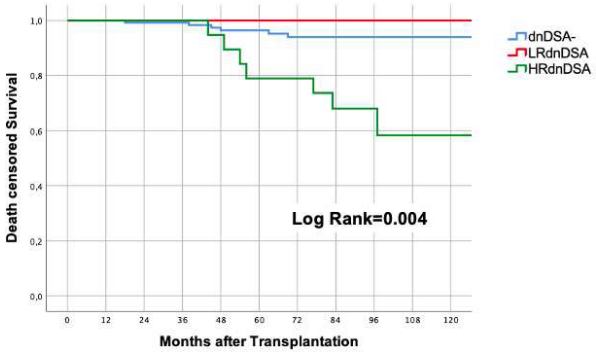
Background: NGS technology for HLA typing is a recent innovation in the field of kidney transplantation (KT). While it is known that high-resolution (HR) typing improves the accuracy of assessing donor-recipient compatibility and characterization of pre-transplant anti-HLA antibodies with donor-specificity, it is still unknown the utility of using HR typing for definition of *de novo* donor-specific antibodies (dnDSA) after kidney transplantation.
Methods: In 156 consecutives donor/recipient KT pairs without pre-transplant DSA, available DNA samples were re-evaluated for HR HLA typing using NGS technology at 6 HLA loci (A/B/C/DRB1/DQB1+A1/DPB1). De novo anti-HLA antibodies were assessed using solid-phase assays, and dnDSA were classified either by 1) as per current clinical practice according to Low-resolution (LR) typing at 3 loci (A/B/DRB1) and estimating donor C and DQ typing with public available frequency tables, or 2) according to complete 6 loci HR typing. The impact on graft outcomes was compared between groups. Mean follow-up was 83 $\pm$ 31 months.
Preliminary Results: Using LR HLA typing, 30/156 (19%) patients developed dnDSA, 7 (23%) class I, 20(67%) class II and 3(10%) class I & II. Out of these, 26 (87%) were confirmed to be dnDSA by HR typing (HRdnDSA), whereas 4 not (LRdnDSA).
Three patients developed anti-DP dnDSA not predicted by LR typing but none of them developed ABMR neither graft loss. In 9 patients, we found that the donor allele against which the antibody was directed, was not represented in the single antigen bead platform used.
HRdnDSA patients were at higher risk of ABMR as compared to dnDSA- and LRdnDSA (log Rank < 0.001; dnDSA- vs HRdnDSA $p < 0.001$, LRdnDSA p = NS) and had lower 3 and 5 years eGFR, higher proteinuria, as well as higher risk of death-censored graft loss (log Rank = 0.004; dnDSA- vs HRdnDSA p = 0.001, LRdnDSA p = NS)
Conclusions: The implementation of HR HLA typing improves the characterization of "biologically true" anti-donor specificities of de novo anti-HLA antibodies and discriminates patients with poorer graft outcomes.



OP060 DONOR-SPECIFIC ELISPOT ASSAY FOR PREDICTING ACUTE REJECTION IN KIDNEY TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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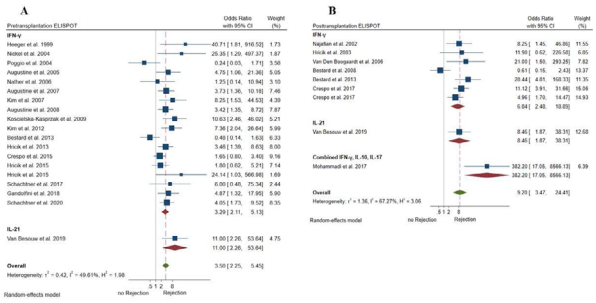
Background: Acute rejection remains an important problem in kidney transplantation. The enzyme-linked immunosorbent spot (ELISPOT) assay has been investigated extensively and has shown promising results as a predictor of allograft rejection by evaluating donor-reactive, cytokine-producing T lymphocytes. The objective of this study was to systematically review and analyze the predictive value of the donor-specific ELISPOT assay to identify recipients at risk for acute rejection.
Methods: Electronic databases were searched for studies reporting donor-specific ELISPOT and kidney transplantation outcomes. The odds ratio (OR) for acute rejection was calculated, along with the standardized mean difference (SMD) of cytokine-producing cells between recipients with and without acute rejection. Pooled estimates were calculated using random-effect models. The positive ELISPOT cutoff frequencies were extracted as reported differently in each study.
Results: From the 665 articles found, 32 studies were included in the meta-analysis. IFN-γ was the most investigated cytokine (30 out of 32 studies). Patients with positive pre-transplantation donor-reactive IFN-γ ELISPOT had an OR of 3.3 for acute rejection (95%-CI 2.1-5.1), and an OR of 6.8 (95%-CI 2.5-18.9) for post-transplantation ELISPOT. Recipients with rejection had significantly higher frequencies of pre- and post-transplantation cytokine-producing cells (SMD 0.47, 95%-CI 0.07-0.87 and SMD 3.68, 95%-CI 1.04-6.32, respectively). A positive ELISPOT result was associated with a lower estimated glomerular filtration rate compared with a negative ELISPOT (SMD -0.59, 95%-CI -0.83 to -0.34).
Conclusions: Patients with high frequencies of donor-reactive IFN-γ ELISPOT were at higher risk for acute rejection. The donor-specific IFN-γ ELISPOT assay can serve as an immune-monitoring tool in kidney transplantation.
Figure 1: Forest plot of OR for acute rejection in patients with positive pre-transplantation ELISPOT assay (A) and post-transplantation ELISPOT assay (B).



OP061 HLA AND NON-HLA ANTIBODIES IN KIDNEY TRANSPLANT RECIPIENTS WITH A HISTOLOGICAL PICTURE OF ANTIBODY-MEDIATED REJECTION

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Antibody-mediated rejection (ABMR) has been classically linked to the detection of HLA donor-specific antibodies (HLA-DSA) in kidney transplant (KT) recipients. However, the participation of non-HLA antibodies contributing to ABMR is not well defined.
We evaluated pre- and post-KT serum samples for HLA and non-HLA antibodies (against angiotensin-II type 1 receptor (AT_1R), endothelin-1 type A receptor (ETAR), MICA and crossmatches with primary aortic endothelial cells (EC-XM)) in 118 patients with histological ABMR (n = 52), normal

(n = 19) or IFTA (n = 47) diagnosis in their biopsies scored according to Banff'2015 classification.
Graft survival was worse in ABMR patients (p = 0.001). Pre-KT HLA-DSA (p = 0.006) and AT_1R-antibodies (AT_1R-Ab) (p = 0.003) were more frequent in ABMR cases, without differences in other non-HLA antibodies. Detection of pre-KT AT_1R-Ab correlated with persistent preformed HLA-DSA (52%) and *de novo* HLA-DSA detection (44%), but not with preformed HLA-DSA which cleared after KT (17%) or no HLA-DSA (4%, p < 0.001). Fourteen patients with histological ABMR (26.9%) had no detectable HLA-DSA post-KT and only three presented with non-HLA antibodies (21%). All ABMR patients with pre-KT AT_1R-Ab developed ABMR with HLA-DSA (ABMR-DSA$^+$, 56% with preformed and 44% with de novo HLA-DSA), whereas no histological ABMR without detectable HLA-DSA showed pre-KT AT_1R-Ab (p = 0.029). Both pre-KT HLA-DSA and AT_1R-Ab were independent predictors of post-KT ABMR-DSA$^+$ in a multivariate analysis (DSA: OR: 3.65 [1.30-10.23], p = 0.014; AT_1R-Ab: OR: 5.78 [1.92-17.35], p = 0.002).
HLA-DSA is prevalent before and after KT in cases with ABMR. Pre-KT AT_1R-Ab strongly associates with ABMR-DSA$^+$ cases, but not pre-KT antibodies against MICA, ETAR or EC-XM$^+$. None of these non-HLA antibodies associates significantly with ABMR-DSA$^-$ cases. Pre-KT AT_1R-Ab seem to act synergistically with HLA-DSA to produce ABMR-DSA$^+$ or facilitate *de novo* appearance of HLA-DSA.

OP062 DEVELOPMENT OF DE NOVO DONOR-SPECIFIC HLA ANTIBODIES AND ABMR IN RENAL TRANSPLANT PATIENTS DEPENDS ON CYP3A5 GENOTYPE

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Background: The single-nucleotide polymorphism CYP3A5 rs776746 is related to the reduced metabolizing activity of CYP3A5 enzyme. Individuals carrying at least one copy of the wild-type allele, defined as CYP3A5 expressers, exhibit higher tacrolimus clearance and lower trough concentrations than homozygous nonexpressers which might affect long-term allograft function.
Methods: 411 kidney transplant patients on tacrolimus-based immunosuppression were assessed retrospectively for the CYP3A5 genotype, de novo HLA antibody and donor-specific antibody (DSA) formation and clinical outcome up to 5 years post-transplant. CYP3A5 genotype was determined by pyrosequencing.
Results: We found that 70 (17%) of the 411 patients were CYP3A5 expressers. CYP3A5 expressers showed more frequently de novo anti-HLA antibodies and DSAs than for nonexpressers (de novo anti-HLAs 24 (34%) vs. 84 (25%), p = 0.05; de novo DSAs 13 (19%) vs. 34 (10%), p = 0.02). De novo anti-HLA antibody- und DSAs-free survival rates were lower for expressers than for nonexpressers (p = 0.03; p = 0.026). CYP3A5 genotype had no impact on allograft failure. But CYP3A5 expressers exhibited a significantly higher frequency of antibody-mediated rejection and lower rates of antibody-mediated rejection-free survival compared to nonexpressers.
Conclusions: CYP3A5 expresser status was an independent risk factor for the development of de novo DSAs (relative risk 2.51, p = 0.006). Early identification of CYP3A5 expressers enabling genotype-based dose adjustment of tacrolimus immediately after renal transplantation may be a useful strategy for reducing the risk of de novo DSA production and improving long-term allograft survival.

OP063 EVOLUTION OF HUMORAL LESIONS ON CONTROL BIOPSY STRATIFIES THE RISK FOR RENAL GRAFT LOSS AFTER ANTIBODY-MEDIATED REJECTION TREATMENT

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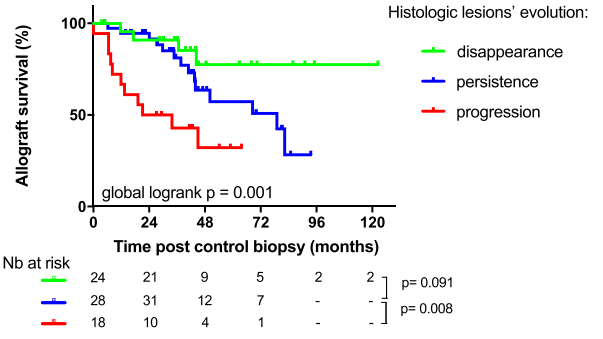
Background: Plasma exchanges, high dose IVIg and optimization of maintenance immunosuppression can slow down the evolution of antibody-mediated rejection (AMR) but with high inter-individual variability.
Identification of a reliable predictive tool of the response to AMR treatment is mandatory to improve personalization of the follow-up and guide the use of second line therapies.
Methods: Interrogation of the electronic databases of 2 French University retrospectively identified 81 renal transplant recipients diagnosed with AMR with limited chronic lesions (cg ≤ 1) at diagnosis, and for whom a control biopsy had been performed within 6 months after initiation of therapy. Clinical, biological and histological parameters were analysed at baseline and after treatment.
Results: The evolution of humoral lesions on control biopsy (disappearance vs persistence vs progression, defined as increase of g+ptc scores >2 or progression of cg lesions ≥ 1 point) correlated with the risk for allograft loss (Logrank test, p = 0.001, Figure 1).
Patients with disappearance of humoral lesions had around 80% graft survival at 10 years. Hazard ratio for graft loss in multivariate analysis was 3.91 (p = 0.04), and 5.15 (p = 0.02) for patients with persistence and progression of lesions respectively.
The main limitation of this approach is that it requires an invasive biopsy procedure. A post hoc analysis was performed to determine if non-invasive parameters could predict the histological evolution of patients. Neither characteristics at diagnostic nor the parameters used to follow the humoral alloimmune response (evolution of DSA MFI) or renal graft function (eGFR loss, proteinuria) showed interesting predictive value for histological evolution after AMR therapy.
Conclusions: A control biopsy performed within 6 months after the initiation of therapy is the best tool to predict long-term outcome after AMR treatment.
Figure 1



OP064 CHALLENGING EARLY CHRONIC-ACTIVE ANTIBODY-MEDIATED REJECTION AFTER SUCCESSFUL DESENSITIZATION FOR CDC-CROSSMATCH-POSITIVE KIDNEY TRANSPLANTATION

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Background: Eligibility criteria for the Dutch HLA-incompatible (HLAi) desensitization program are a complement-dependent cytotoxicity (CDC) positive crossmatch with a living kidney donor and either two years participation in the Eurotransplant Acceptable Mismatch program or one year participation in the national kidney-exchange program.
Methods: Desensitization consisted of 5 plasma exchange cycles (1.5 x plasma volume) with IVIG 0.1 g/kg, and daily tacrolimus, mycophenolate mofetil and prednisone. If the CDC remained positive after one week, another 5 cycles of plasmapheresis were performed. After CDC seroconversion, transplantation was scheduled with rATG. Alemtuzumab was used for combined HLAi and ABO-incompatibility (AB0i).
Results: Between 2013 and 2019, 14 desensitization procedures were performed (7 men, 7 women, median age 37 years). In 2 patients CDC remained positive after two weeks desensitization due to persistently high DQ6 levels (MFI 11.000 resp. 19.000). Four of 12 recipients were both HLAi and ABOi. One-year kidney function was 41 ml/min (range 32-78). Acute ABMR occurred in 9 out of 12 recipients (75%). caABMR developed in 8

out of these 9 recipients and occurred early (median 13 months, range 7-53). The IL-6 receptor blocker tocilizumab (8 mg/kg monthly) was initiated in 6 caABMR recipients with rejection refractory to methylprednisolone and IVIG. Tocilizumab stabilized rapid function decline: Median eGFR loss was 26% in 6 months before tocilizumab, and 5% in 6 months after initiation. While proteinuria had increased by 89% in 6 months before, it decreased by 42% 6 months after initiation. Class II DSA were more persistent than class I, remained detectable in Luminex SAB testing after desensitization, rebounded during AMR and mostly remained detectable at lower levels over time. One recipient died of myocardial infarction 43 months post-transplant. One recipient (not treated with tociliuzmab) lost her graft due to ongoing caABMR 5 years post-transplant. With a median follow-up of 44 months, uncensored graft survival is 83%.
Conclusion: (ca)ABMR is frequent after successful desensitisation for CDC-positive kidney transplant combinations. Tocilizumab is a promising agent to treat early caABMR: a decrease in eGFR loss and proteinuria was obtained in the majority of treated recipients.

OP065 TEMRA CD8 T CELLS FROM KIDNEY TRANSPLANT RECIPIENTS EXHIBIT ENHANCED PURINERGIC P2X4 RECEPTOR-DEPENDENT PROINFLAMMATORY AND MIGRATORY RESPONSES

Gaelle Tilly[1,2], Tra-My Doan-Ngoc[1,2], Orianne Bonizec[1,2], Christophe Masset[1,2], Richard Danger[1,2], Pierrick Guérif[1], Sarah Bruneau[1,2], Alexandre Glémain[1,2], Jean Harb[1,2], Magali Giral[1,2], Claire Pecqueur[3], Sophie Brouard[1,2], Nicolas Degauque[1,2]
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Background: Whereas the role of effector memory and TEMRA CD8 in allotransplantation has been clearly evidenced and particularly the direct correlation between intragraft infiltrating CD8 and rejection, the mechanisms regulating the migration of CD8 T cells to nonlymphoid tissue during inflammation have not been fully elucidated, and the migratory properties of effector memory (EM) re-expressing CD45RA (namely, TEMRA) CD8 are still unclear.
Methods: Adhesion of EM and TEMRA CD8 from Kidney Transplant Recipient (KTx) and Healthy Volunteers (HV) to primary endothelial cell line, their transmigration, and time-lapse microscopy were used and the underlying mechanism was investigated using blocking antibodies and small inhibitory molecules. Activation (CD25, CD69; calcium flux) and cytotoxic function (CD107a) of EM and TEMRA CD8 were measured in response to chemokine CXCL12 stimulation and the role of purinergic receptor (P2XR1,4 and 7) were assessed.
Results: Using static and dynamic models, we showed that, after transplantation, the migratory fitness of TEMRA CD8 are enhanced compared to effector memory (EM) CD8, with enhanced adhesion to activated endothelium, a stronger ability to transmigrate across a monolayer of activated endothelial cells in response to CXCL12 and stronger patrolling behavior. In contrast, the migratory properties of TEMRA and EM CD8 from HV were very similar. Whereas the blockade of the interaction between functional PSGL1 and P-selectin prevent the adhesion and transmigration of TEMRA and EM CD8 from KTx, only TEMRA CD8 were susceptible to LFA-1 blockade. We found that the chemokine CXCL12 directly triggers a stimulatory signal involving an increase in cytosolic Ca2+ and a Panx1-dependent release of extracellular ATP, leading to autocrine stimulation of the purinergic receptor P2X4. Finally, we found that TEMRA CD8 from KTx exhibit a greater functional response as compared to EM CD8 upon CXCL12 stimulation
Conclusions: Our findings suggest that therapeutic strategies such as LFA-1 blockade or impairing functional PGSL-1 could prevent TEMRA CD8 migration and activation and be directedly beneficial to patients with allotransplantation.

OP066 GRANZYME B POSITIVE B CELLS ENRICH REGULATORY T CELL COMPARTMENT AND INDUCE INHIBITION OF EFFECTOR CD4+ CD25- T CELL RESPONSE

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Background: Granzyme B (GZMB)+ B cells have been shown to be increased in blood from transplanted patients who tolerate their graft without immunosuppressive treatment. We reported that GZMB+ B cells are able to prevent effector CD4+CD25-T cell proliferation in vitro. But until now, nothing is known on their direct effect on CD4+CD25-T cells.
Methods: We showed that GZMB+ B cells can be expanded in vitro from sorted B cells stimulated with a cocktail of IL-2, IL-21, anti-human IgG IgA IgM F(ab)'2, CpG oligodeoxynucleotides and CD40L, while keeping their suppressive properties. We analyzed by SingleCell RNAseq the effect of expanded GZMB+ B cells and resting B cells on CD3/CD28 stimulated CD4+ CD25- T cells from healthy donors.
Results: All B cell subsets (naïve, memory B cells and plasmablasts) proliferate in response to the prestimulation, associated with upregulation of BCR, phagocytosis and B cell activation pathways. Cell annotation distinguished two major populations of T cells: T helper 1 and regulatory T cells (Tregs) with an enrichment in Tregs when cocultured with expanded GZMB+ B cells. Differentially expressed genes (DEG) in T cells were associated with an inhibition of effector T cell activity and induction of antiviral type 1 IFN response. The major effect of GZMB+ B cells on CD4+CD25-T cells is a drastic decrease of *GZMB* expression whereas resting B cells have no effect.
Among the genes that are differentially expressed on T cells and based on the literature, we identified ligands present on B cells that may be responsible for that differential expression. Among them, *LTA/LTB* and *CD45* linked to apoptosis and TCR activation appear as potential modulators of effector T cell response. *CXCL10* decrease in GZMB+ B cells is also linked to DEG associated to cytoplasm reorganization in T cells.
Conclusions: These results, open new ways to characterize the interaction between GZMB+ B cells and one of their primary targets and potential modulation of their activity.

OUTCOME IMPROVEMENTS IN LIVER TRANSPLANT: GOING THE EXTRA MILE

OP095 ASSOCIATION OF PROCUREMENT TIME WITH SHORT- AND LONG-TERM OUTCOMES AFTER LIVER TRANSPLANTATION

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Background: Brain death may impair organ function through cytokine storm and increased inflammatory activation, but how the time from brain death to organ procurement affects liver transplant outcomes has not been studied. In other solid organ transplants, longer procurement times have been associated with noninferior or better outcomes. Our aim was to assess the association of time from brain death to organ procurement with liver allograft outcomes in two nationwide cohorts.
Methods: Donation after brain death (DBD) liver transplantations in Finland from June 2004 to December 2017 were followed until death, retransplantation, or October 2020. All DBD liver transplants in the US between January 2008 and August 2018 were included from the Scientific Registry of Transplant Recipients. The association of procurement time with graft survival and short-term complications (available for the Finnish cohort) were analysed in multivariable models.
Results: Altogether 644 and 58,025 orthotopic liver transplantations were included from Finland and the US, respectively. Median delay from brain death to cold perfusion was 10.5 hours in Finland and 34.6 hours in the US. 131 and 11,398 patients died, and 42 and 1,509 were retransplanted during follow-up in Finland and US, respectively.
In the US cohort, longer delay associated non-linearly with better graft survival (Figure) in multivariable models adjusted with Donor Risk Index (DRI) and recipient factors (age, MELD and indication for transplantation). In the Finnish cohort, procurement time was not significantly associated with graft survival,

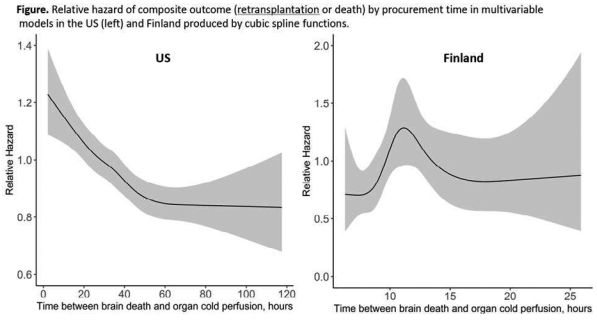

Figure. Relative hazard of composite outcome (retransplantation or death) by procurement time in multivariable models in the US (left) and Finland produced by cubic spline functions.

biliary strictures, acute kidney injury or acute rejection episodes. However, longer procurement time was associated with better liver allograft early function measured using Model of Early Allograft Function (MEAF)-score (p = 0.003).
Conclusions: Longer time from brain death to organ procurement may be associated with better short-term and long-term outcomes after liver transplantation.

OP096 HEPATITIS B OCCULT INFECTION IN DECEASED LIVER DONORS: LONG-TERM POST-TRANSPLANT CLINICAL EVALUATION

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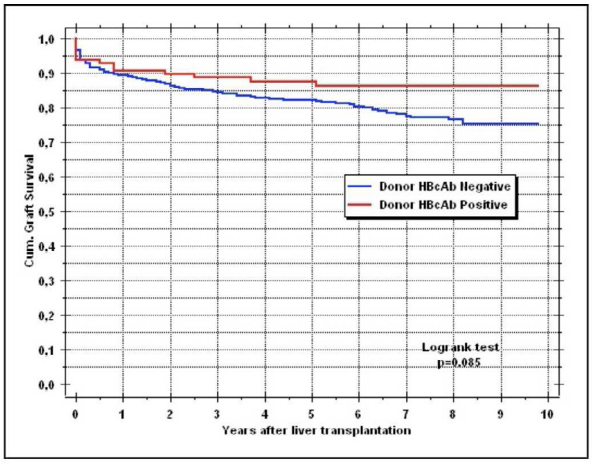
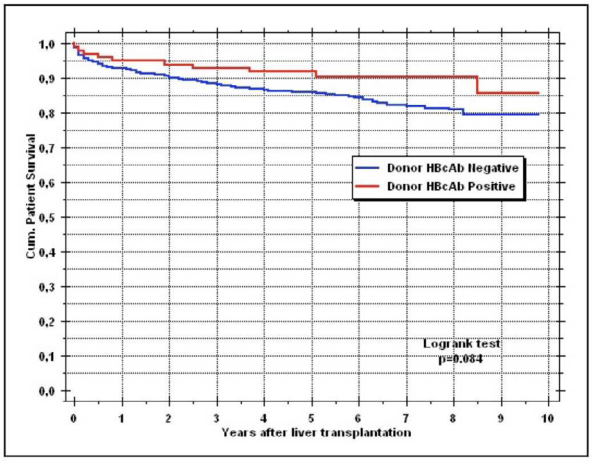
Background: Occult hepatitis B infection (OBI) is defined as detectable HBV-DNA in liver of HBsAg-negative individuals, with or without detectable serum HBV-DNA. We investigated the prevalence of OBI in deceased liver donors and the long-term clinical outcome of the recipients.
Methods: From 12/10 to 2/17, in liver biopsies of 97 deceased donors HBcAb-positive/HBsAg-negative suitable for transplantation, a nested-PCR for diagnosis of OBI according to Taormina criteria (positivity for at least 2 out of 4 HBV targets S, Core, Pol e X of HBV genome) and a droplet digital PCR to search covalently closed circular-DNA (cccDNA) were employed. Combined long-term prophylaxis with nucleos(t)ide analogues and high doses of intravenous anti-HBs immunoglobulins was employed in HBsAg-positive recipients, while HBsAg-negative recipients of an anti-HBc-positive graft received lamivudine and low doses of intra-venous anti-HBs immunoglobulins.





Results: OBI prevalence on liver biopsy was 52.6% (51/97) while cccDNA was positive in 27.8% (27/97) of cases and only in OBI-positive grafts; in 7 donors (7.2%) HBV-DNA was detectable at extremely low level. Median [IQR] donor's age was 68.3 [57.3-75.2] years, with a Donor Risk Index of 1.94 [1.61-2.1]. Recipient's underlying liver disease was: HBV = 58%, HCV = 13%, alcohol = 15%, other = 14%; 19 patients (20%) were completely negative for HBV serology. Median [IQR] recipient age was 56.4 [50.7-61.5] years. 1-, 3- and 5-years graft and patient survival was 89.7%, 87.6%, 86.6%, and 93.8%, 91.8%, 90.7% respectively; it was similar to 1-, 3- and 5-years graft and patient survival of recipients of an HBcAb negative graft in the same period (Graft: 89.4%, 84.4%, 82.1%, p = 0.085; Patient: 92.7%, 88.1%, 86.0%, p = 0.084). None of the recipients experienced HBV-recurrence; only one HBV-naïve recipient (1.1%), transplanted with an OBI-positive/cccDNA-negative graft, developed an HBV-de novo infection 7.6 years after transplantation, treated with the switch from lamivudine to entecavir.
Conclusions: The use of HBcAb-positive grafts in liver transplantation was safe. Using HBcAb/OBI-positive grafts, post-transplant HBV-de novo infection is rare under anti-HBV combined prophylaxis and didn't negatively affect graft and patient survival.

OP097 PROPOSAL AND VALIDATION OF A LIVER GRAFT DISCARD SCORE FOR LIVER TRANSPLANTATION: A MULTICENTRE ITALIAN STUDY

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Background: In recent years, several studies have mainly focused on assessing the risk of organ dysfunction after liver transplantation(LT), while scanty data exist on pre-procurement selection of liver grafts. The study aimed at identifying and externally validating a score for prediction of the risk of liver function-related graft discard before transplantation. The secondary aim was to test the score in terms of its diagnostic ability to identify biopsy-related features and risk of 3-month graft loss.
Methods: 4,207 deceased donors evaluated for liver donation from Jan 2004 to Dec 2018 were retrospectively analyzed. This group was divided into a Training Set of 3,156 candidates(75.0%) and a Validation Set of 1,051 candidates(25.0%) using a causal number generator randomization.
Results: 1,565 (37.2%) grafts were discarded, while 2,642 (62.8%) grafts were considered suitable for LT. Reasons for discard were liver-related in 1,254/1,565 (80.1%) cases. Using the beta-coefficients obtained in the multivariable logistic regression model, the following score was obtained: Donor Rejected Organ Pre-transplant (DROP) Score = -2.68+ (2.14 if Regional Share)+ (0.03*age)+ (0.04*weight)- (0.03*height)+ (0.29 if diabetes mellitus (DM2))+ (1.65 if anti-HCV-positive)+ (0.27 if HBV-core)- (0.69 if hypotension) + (0.09*sCr)+ (0.38*log10AST)+ (0.34*log10ALT)+ (0.06*total bilirubin). The DROP Score AUC for prediction of liver-related graft discard was 0.83-0.82(p < 0.001), and (0.68-0.71; p < 0.001) for prediction of graft macrovesicular steatosis ≥30% in the 1,795 cases in which a biopsy was performed. Based on 3-month post-transplant graft survival rates, patients with DROP >90th centile had worse survivals vs. the 25th centile (82.8 vs. 91.3%; log-rank p = 0.024).
Conclusions: DROP might be a useful tool for prediction of liver function-related graft discard. The score seems to also predict some histological variables and the early post-transplant graft survival rates. Further studies are strongly favored.

OP098 EXTENDED CRITERIA DONORS IN LIVER TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: During the last three decades, the use of Extended Criteria Donors (ECD) has been progressively increased related to the scarcity of organ availability. ECD criteria are well reported in the literature, adopted by centres, and recommended by international societies. However, ECD use varies across transplant centres, and it is based on different definitions. The present study aimed to compare 1-year graft survival in standard and ECD.
Methods: A search of PubMed, Scopus and Cochrane Library performed. Articles published from the time of inception to February 2020 were included. The primary outcome was 1-graft survival (GS). The pooled effect was calculated using either the fixed effects or the random-effects model.
Results: One hundred forty-one full-text articles were assessed for eligibility, and 34 studies were included in the meta-analysis (335569 overall donors) (Table 1). The meta-analysis included 28 studies for the 1-year graft survival analysis, involving 7,979 cases in the ECD group and 208,061 cases in the control group. ECD donors had a reduced 1-year graft survival compared to standard donors, with a hazard ratio (HR) of 1.50 (95% CI: 1.34-1.68). In the subgroup analysis 1-year graft survival was reduced in the DCD (HR 1.63, CI95% 1.32-2.02), age group (HR 1.76, CI95% 1.26-2.34) and multiple criteria (HR 1.56, CI95% 1.23-1.98). The meta-regression analysis showed a significant correlation between the HR of the studies and the year of publication (coef. -0.0177 CI -0.0325 to -0.0029, p = 0.0193).
Conclusion: ECD donors have a worse 1-year graft survival than the standard donors independently from the used criteria and with a significant association to the year of publication. The present results show a wide grade of variability in the ECD definition and high heterogeneity in graft loss probability within the same criteria. Therefore, a prospective study should define a new model based on Liver donor functional assessment through new biomarkers and technologies.

OP099 DONATION AFTER CIRCULATORY DEATH LIVERS CAN BE SAFELY USED FOR TRANSPLANTATION IN PATIENTS WITH PRE-EXISTING PORTAL VEIN THROMBOSIS

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Introduction: Donation after circulatory death (DCD) livers are generally considered of lower quality than livers donated after brain death (DBD). Many centers avoid the use of DCD livers in high-risk recipients, such as patients with pre-existing portal vein thrombosis (PVT). However, there are little data on the results of DCD liver transplantation in recipients with PVT. We aimed to compare outcome after DCD liver transplantation in recipients with PVT (DCD/PVT+), with DBD liver transplantation in recipients with PVT (DBD/PVT+), and DCD liver transplantation in recipients without PVT (DCD/PVT-).
Methods: We performed a retrospective cohort study in two European centers with large experience in DCD liver transplantation. Between 2000 and 2019, a total of 312 DCD liver transplantations were performed (excluding partial or machine perfused livers): 41 in PVT+ patients and 271 in PVT- patients. In the same time period, 95 DBD liver transplantations were performed in PVT+ recipients. PVT was defined as a thrombus in the portal vein at time of transplantation, graded according to Yerdel. The primary endpoint was graft survival, and groups were compared by the Kaplan-Meier method and log-rank test.
Results: There were no significant differences in baseline recipient characteristics between the three groups. Median (IQR) cold ischemia time was shorter for the DCD/PVT+ group (405 [328-450] min), compared to the DBD/PVT+ group (511 [421-497] min), but not different from the DCD/PVT- group (356 [301-456] min). DCD/PVT+ one-, three- and five-year graft survival did not differ from DBD/PVT+ graft survival (Table and Figure). Moreover, DCD/PVT+ graft survival was lower compared to the DCD/PVT- group. Comparison of the three groups revealed no significant differences in the incidence of post-transplant cholangiopathy, biliary anastomotic strictures or hepatic artery thrombosis (Table).

Authors	Years	Source of data	Criteria	Patient numbers		Donor Age			PNF n (%)				Biliary complications leading to re-LTx n (%)			Re-transplant n (%)		
				ECD	Control	ECD	Control	p	ECD	Control	p	def.	ECD	Control	p	ECD	Control group	p
Wall et al.	1990	centre level	Age	23	161	54.3(50.2-65.2) *"	23.9(0.6-49.5) *"	0.001	none	1 (0.62%)	-	A	-	-	-	1(4.3%)	6(3.7%)	NS
Agnes et al.	1996	centre level	multiple	15	60	-	-	-	-	-	-	A	-	-	-	-	-	-
Hoofnagle et al.	1996	multicenter	Age	193	579	-	-	-	5 (33%)	7 (32%)	-	A	none	1(5%)	-	15(7.8%)	22 (3.8%)	0.5
Washburn et al.	1996	centre level	Age	29	194	63.7±2.9 *+	30.7±13.1 *+	<0.0001	2 (6.7%)	7 (3.6%)	0.4	A	-	-	-	3(10.3%)	13(6.7%)	-
Ghobrial et al.	2001	centre level	HCV	59	419	-	-	-	-	-	-	A	-	-	-	-	-	-
Velidedeoglu et al.	2002	centre level	HCV	13	103	36.5±2.4 &	36.9±1.6 &	nr	none	3(2.9%)	-	A	-	-	-	none	6(5.8%)	-
Saab* et al.	2003	centre level	HBcAb	74	42	-	-	-	-	-	-	A	-	-	-	-	-	-
Saab* et al.	2003	centre level	HCV	27	212	-	-	-	-	-	-	A	-	-	-	-	-	-
Nardo et al.	2004	multicenter	Age	30	60	82.3±3.1 &	27.6 ±7.94 &	<0.001	none	2 (3.3%)	NS	B	none	1 (3.3%)	-	1 (3.3%)	6 (10%)	NS
Neipp et al.	2004	centre level	Age	67	1141	49±11 *+	36±20 *+	<0.001	8 (12%)	-	-	A	1 (1.5 %)	-	-	10 (14.9%)	-	-
Peter et al.	2004	national database	DCD	144	26856	35.3±16.5 &	36.7±17.3 &	0.31	17(11.8%)	1719(6.4%)	008	B	-	-		20(13.9%)	2229(8.3%)	0.04
Grazi et al.	2005	centre level	Age	236	623	-	-	-	-	-	-	A	-	-	-	-	-	-
Renz et al.	2005	centre level	multiple	49	116	-	-	-	-	-	-	A	-	-	-	6 (2.9%)	6(7%)	-
Merion et al.	2006	national database	DCD	472	23598	-	-	0.0002	-	-	-	A	-	-	-	-	-	-
Mateo et al.	2006	national database	DCD	367	33111	35.3±16.7 &	36.8±18.8 &	0.14	-	-	-	A	-	-	-	-	-	-
Tector et al.	2006	centre level	multiple	388	183	41.8 * 43(6-81) $"	36.8 * 38(9-59) $"	<0.01	4 (1.0 %)	1 (0.5%)	-	A	-	.-	-	-	-	-
Schemmer et al.	2007	centre level	multiple	94	71	-	-	-	5 (7%)	9 (9,6%)	0.6	B	-	-	-	10 (11%)	13 (13.9%)	0.2
McCormack et al.	2007	centre level	STEATOSI	20	40	55(26-67) $"	44(13-71) $"	0.007	1(5%)	none	0.721	B	-	-		-	-	
De Vera et al.	2009	centre level	DCD	141	282	37.1±15.9 &	39.1±16.1 &	0.23	17 (12%)	6 (2%)	<0.001	B	-	2(0.7%)	<0.01	26 (18%)	16 (7%)	0.001
Jay et al.	2011	national database	DCD	1095	41853	36.4±15.4 *+	40.2±17.6 *+	<0.001	-	-	-	A	-	-		14.70%	6.80%	<0.001
Fondevila et al.	2012	centre level	DCD	34	538	47(27-56) $"	-	-	-	-	-	A	3(8%)			-	-	-
Harring et al.	2012	national database	DCD	2351	85148	34.37(0.31) *£	36.97(0.065) *£	<0.001	-	-	-	A	-			-	-	-
Callaghan et al.	2013	multicenter	DCD	352	2220	42 (16) &	46 (15) &	<0.01	-	-	-	A	4(1.1%)	4(0.2%)	0.04	-	-	-
Hoyer et al.	2014	centre level	ardiac arre	77	807	45(3-75) $"	53(3-88) $"	<0.001	7(9,1%)	63(7,8%)	0.69	B	-	-		-	-	-
Stepanova et al.	2016	national database	hcv	1930	31738	42.0±11.8 &	39.6±16.4 &	<0.0001	-	-	-	A	-	-		-	-	-
Dondossola et al.	2017	centre level	CIT	22	35	55(18-80) $"	64(17-84) $"	0.69	none	1 (3%)	NS	B	1 (4.5%)	none	-	2 (9%)	4(11%)	0.58
Halazun et al.	2017	centre level	multiple	960	770	-	-	-	11(1,1%)	5(0,6%)	0.193	A	-	-	-	76(7,9%)	29(3,7%)	0.002
Halazun et al.	2018	national database	Age	3073	68044	-	-	-	-	-	-	A	-	-	-	258(8,4%)	3334(4,9%)	0.002
Lozanovski et al.	2018	centre level	multiple	353	112	62.7±16.6 *+	48.3±12.9 *+	0.001	10(2,7%)	5(4%)	0.53	B	-	-	-	-	-	-
Nesher et al.	2018	centre level	Age	45	265	74.3±2.7 *+	46.2±15.0 *+	<0.01	2 (4.4%)	25 (9.4%)	NS	A	-	-	-	3 (6.7%)	20 (7.5%)	NS
Mihaylov et al.	2019	centre level	multiple	32	124	46(12-62) $"	-	-	-	-	-	A	none	-	-	1(3%)	2(2%)	0.82
Wong et al.	2019	centre level	HBcAb	548	416	47.5(14-77) &	35(2-84) &	<0.001	none	none	-		-	-	-	-	-	-
Pagano et al.	2020	centre level	multiple	146	99	62.0(49.2-72) $"	42.0(23.5-54) $"	<0.001	-	-	-	A	-	-	-	-	-	-
van Reeven et al.	2020	multicenter	DCD	21	63	38.0(19.5-45) $"	42.0(25-53) $"	0.11	-	-	-	A	1(4.8%)	1(1.6%)	-	1 (4.8%)	5 (7.9%)	>0.99

*= mean; $= median; &= not specified; += standard deviation; £= standard error; "= range
A= no definition of PNF; B= non recoverable liver failure within 2 weeks leading to retransplantation or causing death

Table 1. List of articles included with the related charachteristics

Conclusion: DCD liver transplantation in patients with pre-existing PVT results in reduced graft survival, compared to patients without PVT. However, in patients with PVT, there are no major differences between DCD or DBD liver transplantation. These findings suggest that DCD liver grafts can be safely used on recipients with PVT.

Variable	DCD/PVT+ (n= 41)	DBD/PVT+ (n=95)	DCD/PVT- (n=271)	P-value DCD/PVT+ vs DBD/PVT+	P-value DCD/PVT+ vs DCD/PVT-
Postoperative results					
Graft survival*					
1 year	30 (73%)	80 (84%)	234 (86%)	0.15	0.03
3 year	26 (63%)	75 (79%)	216 (80%)	0.06	0.02
5 year	26 (63%)	66 (69%)	206 (76%)	0.32	0.06
Post-transplant cholangiopathy*	5 (13%)	16 (17%)	65 (24%)	0.51	0.10
Biliary anastomotic strictures*	12 (30%)	26 (27%)	77 (28%)	0.78	0.88
Hepatic artery thrombosis*	2 (5%)	2 (2%)	10 (4%)	0.58	0.66

* Categorical data are shown in percentages

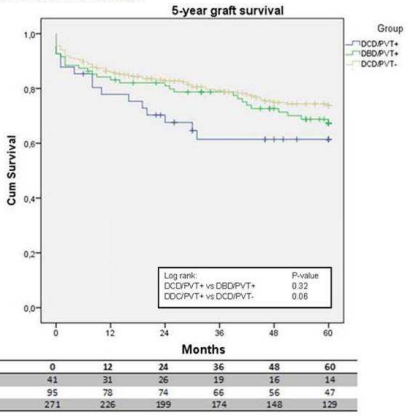

Figure 1: Five year graft survival analysis after liver transplantation

Table 1 Postoperative results

OP100 RISK FACTORS ASSOCIATED WITH HISTOLOGICAL INJURY TO THE DEEP PERIBILIARY GLANDS AND PERIBILIARY VASCULAR PLEXUS PRIOR TO LIVER TRANSPLANTATION

Willemijn van der Plas[1], *Otto B. van Leeuwen*[1], *Isabel Brüggenwirth*[1], *Yvonne de Vries*[2], *Marius van den Heuvel*[3], *Anette S.H. Gouw*[3], *Vincent E. de Meijer*[1], *Robert J. Porte*[1]

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Introduction: Post-transplant cholangiopathy strongly inhibits widespread use of donation after circulatory death livers. Several donor and preservation-related risk factors have been associated with the development of non-anastomotic biliary strictures (NAS) after liver transplantation. In addition, histological injury to the deep peribiliary glands (PBG) and peribiliary vascular plexus (PVP) has been associated with NAS. This study was designed to investigate the association between donor and preservation-related risk factors and injury to the PBG and PVP, which is currently unknown.
Methods: Bile duct biopsies were collected from human donor livers after static cold storage and prior to transplantation. Histological injury to the deep PBG and PVP was assessed using a previously established grading system. Logistic regression analysis was used to analyze the impact of donor and preservation-related risk factors on histological bile duct injury.
Results: Of the total cohort of 84 livers, deep PGB injury could be assessed in 74 biopsies, where PVP injury could be assessed in all. Injury to >50% of deep PBGs was observed in 14 biopsies (19%), whereas 26 biopsies (31%) had >50% PVP injury. After multivariable analysis, cold ischemia time was associated with an increased risk of >50% deep PBG injury (odds ratio [OR] 2.01, 95% CI 1.22-3.29, p = 0.01]), whereas donor age was associated with an increased risk of PVP injury (OR 1.05, 95%CI 1.01-1.08, p = 0.02).
Conclusion: Donor age and cold ischemia time were associated with the severity of pre-transplant histological injury to the PVP and deep PBG, respectively.

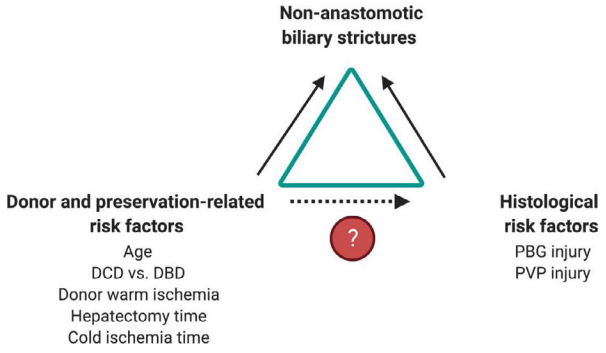

Figure 1. Theoretical relation between non-anastomotic biliary strictures, donor and preservation-related risk factors, and histological risk factors. The relation between donor and preservation-related risk factors and injury to the PBG and PVP is currently unknown.

OP101 INDICATIONS AND WAITING LIST PRIORITY FOR DECEASED DONOR LIVER TRANSPLANTATION IN HIV/HCV CO-INFECTED PATIENTS IN JAPAN

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Background: In Japan, where HIV/HCV coinfection via blood products has become a social problem, there is an urgent need to provide a stable supply of liver transplantation (LT) as a treatment option for liver failure.
Methods: Since 2009, the Ministry of Health, Labor and Welfare's Scientific Research Group (Kanematsu project, Eguchi project) has been working on this theme and has been proposing priorities for waiting list for deceased donor (DD) LT in HIV/HCV co-infected patients in Japan from a medical and scientific point of view.
Results: Co-infected patients, especially those infected with blood products due to hemophilia, had a faster progression of fibrosis than HCV mono-infected patients, and once the portal hypertension occurs, the prognosis is poor. As a result, we proposed the priority score in those patients for DDLT waiting list in 2013 and to establish a scoring system corresponding to MELD (Model for End-stage liver disease) of DDLT waiting list in 2019. We investigated MELD score at the time of registration under the existing brain death registration standard in Japan to examine the prognosis of co-infected patients and found out that median MELD scores were 16 points for an emergency level of 6 (CP-C, which corresponds to a CP-B of co-infected patients) and 27 points for an emergency level of 8 (CP-C with MELD score of 25 points and more, which corresponds to a CP-C of co-infected patients), respectively. Since an increase of MELD score by one point takes about 100 days (about 3 months) due to a difference in the survival period on the waiting list between patients with an emergency level of 6 and 8 on the regular transplant waiting list, we drafted the plan to add 2 points to the MELD score even for co-infected patients every six months after the registration. This means HIV/HCV co-infected patients with CP-B and those with CP-C register with MELD points of 16 and 27 respectively, and subsequently, 2 points are added to their respective MELD scores every six months. As described above, the mean MELD score of patients who underwent DDLT is 27 points in Japan today, and the system allows patients with serious HIV/HCV co-infection to wait for LT on a timely manner.
Conclusions: This paper introduces the history and current status of priority of waiting list for DDLT in HIV/HCV coinfected patients in Japan.

OP102 RECENT TRENDS AND INTENTION-TO-TREAT SURVIVAL OF LIVER TRANSPLANTATION FOR NONALCOHOLIC STEATOHEPATITIS: AN ITALIAN LIVER TRANSPLANT REGISTRY STUDY

Chiara Di Renzo[1], Alessandro Vitale[1], Silvia Trapani[2], Patrizia Burra[3], Alessandra Bertacco[1], Renato Romagnoli[4], Silvia Martini[4], Paolo De Simone[5], Paola Carrai[5], Matteo Cescon[6], Maria Cristina Morelli[6], Luciano De Carlis[7], Luca Belli[7], Salvatore Gruttadauria[8], Riccardo Volpes[8], Michele Colledan[9], Stefano Fagiuoli[9], Giorgio Rossi[10], Maria Francesca Donato[10], Fabrizio DI Benedetto[11], Nicola De Maria[11], Amedeo Carraro[12], Antonio Colecchia[12], Andrea Ricci[2], Massimo Cardillo[2], Umberto Cillo[1]

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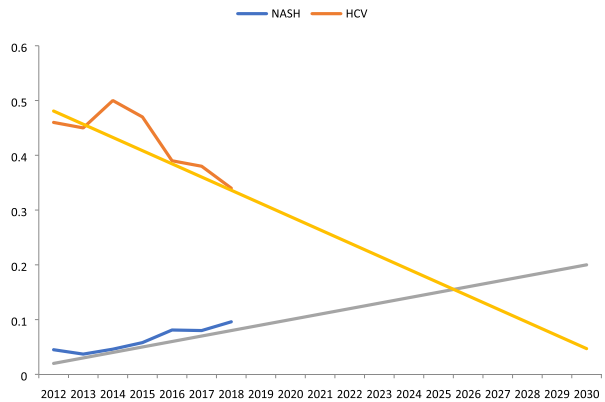
Background and Aims: A recent ELTR study showed that the proportion of liver transplants for nonalcoholic steatohepatitis (NASH) in Europe has increased from 2002 through 2016, with comparable post-transplant outcomes with regard to other disease indications. There are few data on recent trends in waiting list dynamics and on intention-to-treat transplant survival of NASH patients.
Method: We analysed data from adult patients listed for primary LT for chronic end-stage liver disease 2012-2018 using the Italian Liver Transplant Registry database. We evaluated annual trends of waiting list inscriptions according to main liver diseases. We also forecasted future epidemiological Italian scenarios and evaluated patients characteristics and intention-to-treat survival outcomes in NASH versus non-NASH populations.
Study supported by AISF, SITO, CNT.
Results: Among 8,567 adults listed for first LT in Italy in the study period, 550 (6.4%) had NASH. The proportion of NASH patients significantly increased from 4.5% in 2012, to 9.6% in 2018 ($p < 0.001$); conversely, the proportion of hepatitis C patients significantly decreased from 46.0% to 33.6% ($p < 0.001$). In Italy NASH patients should overcome non-NASH ones in about six years.
NASH patients were older than the others (60 vs. 55 years, $p < 0.05$), and with more often associated hepatocellular carcinoma (56% vs. 45%, $p < 0.05$). The 1-, 3- and 5-year intention-to-treat survival rates were 81%, 70% and 65% in the no-NASH group vs. 74%, 64% and 56% in the NASH group, $p = 0.002$. NASH itself was a significant risk factor for death (hazard ratio 1.36; 95% CI 1.22 - 1.52) also at multivariable Cox survival analysis.
Conclusion: The proportion of NASH patients listed for LT in Italy significantly increased from 2012 to 2018. This preliminary analysis suggests a significant negative impact of NASH aetiology on intention-to-treat transplant survival.
Figure 1 Future trends of LT for NASH and HCV in Italy using linear regression models.



Variables	Univariate ITT survival HR (95%CI), p value	Multivariate ITT survival
Age*	1.02 (1.01-1.02),<0.0001	1.02 (1.02-1.03),<0.0001
Male sex	0.93 (0.84-1.02),0.1369	-
Body Mass Index > 25*	0.92 (0.84-1.00),0.05	-
NASH*	1.32 (1.10-1.55),0.002	1.22 (1.02-1.44),0.03
Blood group B-AB	0.96 (0.85-1.07),0.45	-
HCC*	0.82 (0.75-0.89),0.0001	0.96 (0.86-1.06),0.41
Meld sodium*	1.04 (1.03-1.04),0.0001	1.04 (1.03-1.05),<0.0001
Centre volume > 50 patients/year	0.93 (0.85-1.01),0.09	0.97 (0.88-1.06),0.47

Table 1 Univariable and Multivariable intention-to-treat survival Cox analyses.

OP103 OUTCOMES OF DONORS WITH BMI ≥ 30 FOR LIVING DONOR LIVER TRANSPLANTATION

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Background and Aim: Donor BMI above 30 is generally considered contraindication for donor hepatectomy. We present the outcomes of donors with BMI ≥ 30 following donor hepatectomy.
Methods: All potential donors between 2005-2015 and perioperative data were collected retrospectively. Steatosis was assessed based on liver-spleen Hounsfield unit difference and absolute liver intensity values. We compared BMI ≥ 30 (n = 32) and BMI < 30 (n = 64) donor outcomes. Complications were graded by Clavien-Dindo classification. Univariable analysis was performed.
Results: All donors underwent open right donor hepatectomy. There was no difference between BMI ≥ 30 and <30 groups in terms of age, duration of surgery, length of stay, post-operative day 7 liver function tests. BMI ≥ 30 group had slightly higher rates of major (class 3) complications compared to BMI < 30 group [3 (9.3%) vs. 5 (7.8%) p = 1.0], which was insignificant (table 1). There were no class 4 or 5 complications.
Conclusion: Donors with BMI ≥ 30 have similar outcomes and complication rates compared to BMI < 30 donors. BMI ≥ 30 is not an absolute contraindication to donate right liver provided that there is no significant steatosis and remnant liver is satisfactory. Larger cohort would improve the power of these findings.

	BMI ≥ 30 (n = 32)	BMI < 30 (n = 64)	p-Value
Age (mean, SD)	35.5 (9.6)	35.3 (8.4)	0.91
Major complication (%)	3 (9.3%)	5 (7.8%)	1.0
LOS (mean, SD)	9.6 (5.1)	10.2 (5.5)	0.58
D7 Bilirubin (mean, SD)	2.0 (1.9)	2.09 (2.7)	0.86
D7 INR (mean, SD)	1.1 (0.1)	1.17 (0.1)	0.24
OP time (mean, SD) (min)	441.5 (83.8)	448.1 (100.4)	0.74
Graft weight (mean, SD)(g)	941.3 (157.5)	930.4 (147.9)	0.72
aGRWR (mean, SD)	1.1 (0.2)	1.2 (0.2)	0.5
RLV (%)(mean, SD)	33.2 (3.4)	34.9 (3.5)	0.19

OP104 PERFORMANCE OF ARTIFICIAL INTELLIGENCE IN PREDICTING SURVIVAL FOLLOWING LIVER TRANSPLANTATION: STUDY USING DATA FROM THE KOREAN TRANSPLANT REGISTRY

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Background: Although the Model for End-stage Liver Disease (MELD) score is commonly used to prioritize patients awaiting liver transplantation, previous studies have indicated that MELD score may fail to predict well for the postoperative patients. Similarly, other scores (D-MELD score, balance of risk score) that have been developed to predict transplant outcome have not gained widespread use. These scores are typically derived from linear statistical models. The aim of this study was to compare the performance traditional statistical models with machine learning approaches in predicting survival following liver transplantation using multi-center data.
Methods: Data came from 785 deceased donor liver transplant recipients enrolled in the Korean Organ Transplant Registry (KOTRY, 2014~2019). Five machine learning methods and 4 traditional statistical models were compared for the prediction of survival.
Results: Of the machine learning methods, random forest (RF) yielded the highest area under the receiver operating characteristic curve (AUC-ROC) values (1 month = 0.94, 3 month = 0.97, 12 month = 0.92) for predicting survival. The AUC-ROC values of Cox regression analysis were 0.80, 0.89 and 0.84 for 1month, 3month and 12 month post-transplant survival, respectively. However, the AUC-ROC values of the MELD, D-MELD and BAR score were all below 0.70.
Conclusions: Machine learning algorithms such as random forest was superior than conventional cox regression and previously reported survival scores in predicting 1 month, 3month 12 month survival following liver transplantation. Therefore, artificial intelligence may have significant potential in providing assistance with clinical decision-making during liver transplantation including matching donors and recipients.

OP105 UPDATE ON WAITLIST MORTALITY OF YOUNG PATIENTS WITH BILIARY ATRESIA - RESULTS FROM THE EUROTRANSPLANT DATABASE

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Background: Mortality on the waitlist for liver transplantation (LT) negatively affects the prognosis of young patients with biliary atresia (BA). Decreasing the time on waitlist by changing allocation rules or by living donor LT (LDLT) could decrease pre-transplant mortality. From 2014 onwards, BA patients aged <2 years have become more prioritized for organ allocation by Eurotransplant (ET). We evaluated the recent developments in waitlist mortality of young BA patients.
Methods: We performed a retrospective cohort study including all patients aged <2 years at listing for LT in the ET database, between 2001 and 2018. Competing risks analyses were performed to evaluate the outcomes 'deceased on waiting list', 'transplanted (LDLT or LT with deceased donor graft)' and 'still on waiting list' before and after (country-dependent) implementation of the new allocation rule (Period A and B, 2001 ~2014 and ~2014-2018, resp.).
Results: We included 877 BA patients in Period A and 165 BA patients in Period B. The waitlist mortality decreased from 6.7% in Period A to 1.8% in Period B (p = 0.02; Figure). However, the median time to LT with a deceased donor graft had not decreased in Period B, compared to Period A (A: 3.2 vs. B: 3.0 months; p = 0.98). Interestingly, the proportion of LDLT to total LT increased from 55% to 77% of BA patients between Period A and B (p = 0.001; Figure). The proportional increase in LDLT strongly decreased the median waitlist duration of all transplanted patients from 1.5 months in Period A to 0.8 month in Period B, respectively (p = 0.001).
Conclusions: Waitlist mortality in young BA patients has decreased by more than 70% over the last years. The decrease can be attributed to a higher proportion of patients undergoing LDLT, rather than to increased prioritization of deceased donor organ allocation. Absence of LDLT possibilities and declining availability of suitable post-mortem grafts remain a challenge to guarantee timely transplantation of young BA patients.

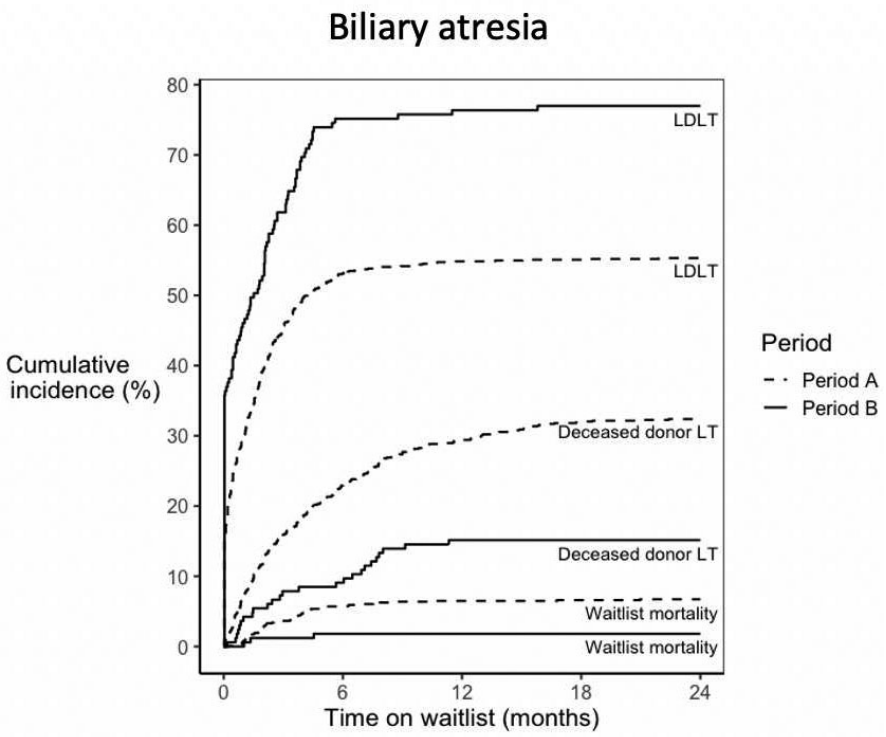

Figure 1 Cumulative incidence curves of biliary atresia patients listed for liver transplantation (LT) before the age of 2 years in Period A (2001-2014; dashed lines) and Period B (2014-2018; solid lines). LDLT; living donor liver transplantation.

OP106 LIVER TRANSPLANTATION (LT) IN HIGH-MELD (≥30) PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE (ACLF): SINGLE-CENTER EXPERIENCE WITH 90 CASES

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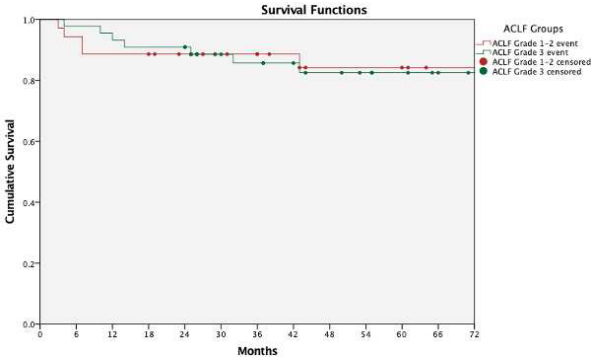
Background: LT in patients with high MELD score is usually correlated to poor outcomes. Particular disappointing are data reported in Germany, with national 1-year survival rates of only 53% recently described in patients with MELD score ≥30. A particular cohort of recipients in this setting are those presenting with ACLF, where the presence of organ failure seems to have an incisive impact on outcome. Aim of the study was to analyze the outcomes of LT (i.e. futility and survival) of a cohort of high-risk recipients with Lab-MELD score ≥30 and ACLF.
Methods: Single-center retrospective analysis of adult deceased donor LT (DDLT) in recipients with chronic liver disease with Lab-MELD score ≥30 and ACLF, transplanted from January 2007 to December 2019. Primary end-points were analysis of futility (i.e. in-hospital or 90-days mortality/re-transplantation), long-term survival of nonfutile patients and overall postoperative morbidity. A separate analysis of patients with ACLF grade 3 was also conducted.
Results: During the study period, a total of 550 adult DDLT were performed: 93 recipients (16.9%) had Lab-MELD score ≥30 at the moment of LT, and 90 (16.4%) presented with ACLF. Recipients in the ACLF cohort were distributed as follow: 8 (8.9%) patients with ACLF grade 1, 32 (35.6%) with ACLF grade 2, and 50 (55.6%) with ACLF grade 3. Overall futility rate in ACLF patients was 12.2% (n = 11), and survival rates at 1, 3 and 5 years for nonfutile patients were 91.1%, 89.9%, and 83.2% respectively. Survival curves for ACLF grade 1-2 and grade 3 are reported in the graphic below. Remarkable good results were achieved also in the ACLF grade 3 cohort, with futile outcome only in 12% (n = 6) of cases, and survival rates at 1, 3 and 5 years of 93.2%, 85.7%, and 82.5% respectively.
Conclusion: Our results seem to be in countertendency with those reported in recent german studies on high-MELD patients, but substantially in line with series reported from other european countries, especially in the contest of ACLF. These results confirmed that LT represents a valid therapeutic option also in high-risk recipients with ACLF, provided an accurate selection of candidates according to the ethical principle of utility and efficiency of LT in times of organ paucity.



OP107 EVOLUTION OF INDICATION IN LIVER TRANSPLANTATION IN ITALY: THE CNT REGISTRY STUDY; ECALITA STUDY. ON BEHALF OF ECALITA STUDY GROUP

Tommaso Maria Manzia[1], Silvia Trapani[2], Andrea Ricci[2], Ilaria Lenci[1], Tullia De Feo[3], Martina Milana[1], Alessandra Nardi[4], Giuseppe Tisone[1], Massimo Cardillo[2], Mario Angelico[5]
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Background: Given the changes in liver transplant indications observed in recent years in different parts of the world, this study aims to analyze any changes in indications to adult liver transplantation in Italy in the last 15 years.
Methods: Data on indications for liver transplantation in Italy were collected prospectively from the transplant information system and analyzed retrospectively to explore the evolution of the indications and etiology in the liver transplant list between January 2004 and December 2018.
Results: During the study period, 23,221 adult patients were listed for liver transplantation. The percentage of entries on the list for liver cirrhosis decreased from 74.6% (2004) to 41.8% (2018) while those for hepatocarcinoma increased [20.1% (2004) to 53.5% (2018)]. The HCV-related cirrhosis decreased from 47.1% (2004) to 19.7% (2018) while alcohol and HBV increased from 18.9% and 19.7% to 29.6% and 25.6%. These same etiologies, in the presence of hepatocarcinoma, remained unchanged between 2012 and 2018 [HCV: 57.2% vs 53.7%; HBV: 28.1% vs 27.2%; alcohol: 3% vs 6.4%] while non-alcoholic steato-hepatitis (NASH) increased from 4.4% to 10%.
Conclusions: Indications for transplantation in Italy are changing rapidly. The hepatocarcinoma was the leading reason for listing in the last years (2016-2018). Interestingly, In HCV patients, hepatocarcinoma has exceeded cirrhosis as a primary indication of transplantation, while alcohol in recent years has been the leading cause of cirrhosis in patients on the national waiting list.

OP108 IMPACT EXTENDED LIVING DONOR CRITERIA FOCUSING ON DONOR SAFETY IN LIVING DONOR LIVER TRANSPLANTATION

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Background: Donor safety has been the primary concern during living donor liver transplantation (LDLT) and therefore most centers keep the strict selection criteria for donor safety. Recently, conventional donor selection criteria have been modified to expand the donor pool in LDLT. Herein, we describe out center's experience for extended living donor criteria focusing on remnant liver volume (RLV) and graft steatosis.
Methods: We retrospectively reviewed the outcomes of 452 living donor right hepatectomy (LDRH) including 115 extended criteria donors who performed at our institution from January 2010 to June 2020. Extended Donor was defined with criteria as follows; 1) old donor (age >40 years) with RLV of <35%, 2) young donor (age ≤40 years) with RLV <29% and minimal fatty change (<15%), 3) young donor with mild hepatosteatosis (15%-30%) and RLV of < 35%. The outcomes in extended living donors were compared with those in living donors under conventional criteria.
Results: Posthepatectomy liver failure (PHLF) occurred in 48 donors (10.6%) and most cases were grade A except one case. PHLF and major complications were not more frequent in extended donor group. In multivariate only, the event for major complications was associated with PHLF but neither extended criteria nor RLV ratio was related to PHLF.
Conclusions: LDRH under our extended criteria could be performed to expand donor pools without adverse effects on donor safety and could be performed safely in donors with RLV ratio <30% under our strict criteria when no other donors are available.

ADDRESSING RISK FACTORS IN KIDNEY TRANSPLANTATION

OP109 HLA-DQ DISPARITIES AND KIDNEY TRANSPLANT OUTCOME

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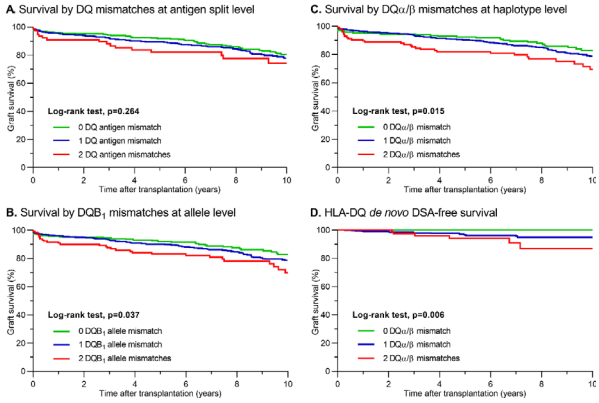
Background: It is becoming clear that de novo donor-specific antibodies (dnDSA) against HLA-DQ are the most prevalent and the leading cause of antibody-mediated rejection and poor allograft outcome after kidney transplantation. A well-known problem with the most HLA matching approaches is that they don't include systematic genotyping of DQ locus. Herein we evaluate the role of DQ matching at antigen, allele and haplotype levels to minimize the generation of DQ-dnDSA and improve graft outcome in kidney transplantation.

Methods: All adult patients who underwent kidney transplantation between 2004 - 2013 at a single center were included in this study (N = 926). Each transplant pair was retrospectively genotyped at 2nd field HLA level for DQA_1 and DQB_1.
Results: The mean follow-up time of this kidney transplant cohort was 7.62 ± 3.78 years. 152 patients (16.4%) experienced graft failure during this period. DQ dnDSA occurred in 23 of 889 patients with antibody follow-up data within the first ten years. The 10-year survival rates were not statistically different between the groups with 0, 1 and 2 DQ antigen MM (80.4%, 77.7% and 74.3% respectively, p = 0.27) (Figure 1). In contrast, the different degrees of allele mismatches for the DQB_1 locus provided better risk stratification of the patients (82.8% with 0 MM, 78.6% with 1 MM and 70.0% with 2 MM, p = 0.04). Next, we calculated the mismatches in the DQα/β pairs by considering DQA_1 at the 1st and DQB_1 at the 2nd field HLA genotyping level. The Kaplan-Meier curves showed that primarily the degree of mismatches for DQα/β haplotypes associated with the risk of graft failure after kidney transplantation (83.0% with 0 MM, 78.7% with 1 MM and 69.4% with 2 MM, p = 0.02). Finally, the patients with both matched DQα/β haplotypes had 100% DQ dnDSA-free survival compared to the decreased DQ dnDSA-free survival in patients with one (95.1%) or both (87.1%) mismatched DQα/β haplotypes (p = 0.006).
Conclusions: By comparing the HLA-DQ mismatches at antigen, allele and haplotype levels, we found that DQα/β haplotype mismatch analysis provides the best risk stratification of the kidney transplant patients. These findings indicate that adding DQα/β haplotype matching to the current antigen A, B, or DR matching algorithm will decrease de novo formation and improve graft survival after kidney transplantation.

Figure 1. Kaplan-Meier estimates of 10-year kidney graft outcome according to the different levels of HLA-DQ mismatches.



OP110 KIDNEY RECIPIENTS CHARACTERISTICS QUESTIONED THE DISCRIMINATIVE CAPACITIES OF KIDNEY DONOR RISK INDEX: AN EXTERNAL VALIDATION FROM A FRENCH COHORT

Anne-Hélène Querard[1,2], Etienne Dantan[2], Florent Leborgne[2,3], Magali Giral[4,5], Angelina Dion[2], Yohann Foucher[2,6]
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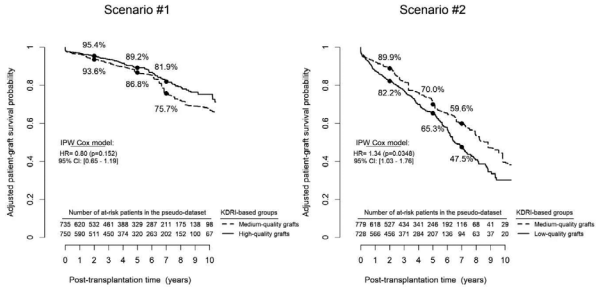
Background: While elderly patients, with more frequent comorbidities, were more likely to receive grafts from older donors, the Kidney Donor Risk Index (KDRI) predictive capacities may be related to the recipients' characteristics. We proposed a validation of the KDRI considering the recipients' covariates related to the organ allocation policies.
Methods: From 4114 kidney recipients of the French DIVAT cohort, we estimated the KDRI adjusted discriminative capacities using the standardized and weighted time-dependent ROC curve. We studied the causal effect of KDRI-based transplantations on the adjusted patient and graft (PG) survival. We proposed two counterfactual worlds where recipients of high-quality graft would have received medium-quality grafts (Scenario #1), and recipients of low-quality grafts would have received medium-quality grafts (Scenario #2).
Results: The unadjusted AUCs of the ROC curves ranged from 65% [95% CI 62%-68%] for a prognostic of PG failure up to 1-year post-transplantation to 68% [95%CI 65%-70%] for a prognostic up to 7-years. After adjustment on recipients features, the intrinsic KDRI discriminative capacities were lower with covariate-adjusted AUC varying from 55% [95%CI 51%–60%] for a prognostic up to 1 year post-transplantation to 56% [95%CI 52%–59%] up to 7 years. Furthermore, as showed on Figure 1, we estimated low differences in PG survival, suggesting that the KDRI-based graft quality has no relevant impact.
Conclusions: We demonstrated that the KDRI discriminative capacities were mainly explained by the recipient characteristics. This questions the interest of the KDRI as an indicator to evaluate the intrinsic quality of a graft from a deceased donor. We reported close counterfactual post-transplantation outcomes of the recipients regardless of the quality of the graft they received. This suggests that the KDRI-based graft quality has no relevant impact on patient-graft survival in France and may be in favor of an donor pool expansion.
Figure 1



OP111 DONOR FACTORS -FOR KIDNEYS ACCEPTED FOR TRANSPLANTATION- MARGINALLY IMPACT TRANSPLANT OUTCOMES. CONCLUSIONS FROM NATIONWIDE PAIRED OUTCOME ANALYSES

Alexander Schaapherder[1], Maria Kaisar[2,3,4], Lisa Mumford[2], Matthew Robb[2], Rachel Johnson[2], Michele de Kok[1], Frederike Bemelman[5], Jacqueline van de Wetering[6], Arjan Van Zuilen[7], Maarten Christiaans[8], Marije Baas[9], Azam Nurmohamed[5], Stefan Berger[10], Aiko De Vries[1], Edward Sharples[11], Rutger Ploeg[11], Jan Lindeman[1]
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Background: There is an increased reliance on donor characteristics-based algorithms in the decision process whether or not to accept a donor kidney graft for transplantation. While this may improve outcomes, it is consistently concluded that the performance characteristics of the algorithms are moderate at max, and consequently that a strong focus on decision algorithms may result in unjustified decisions to reject a donor graft and consequently increasing waiting lists and time on the waiting list. The objective of this study was to evaluate the impact of donor factors on kidney transplantation outcomes for kidney.
Methods: An instrumental variable analysis based on national registry data for all donor pairs transplanted in the Netherlands (1990-2018, 2187 pairs), and the UK (2000-2018, 10,175 pairs). The primary study focus was on early graft loss (EGL, i.e. all death-censored graft losses occurring within 90-days of transplantation) as this represents the most unambiguous short-term outcome measure.
Results: Overall EGL rates for the Dutch and UK cohorts were 7.9% and 6.6%, and the incidences of congruent EGL 1,2 and 1.1% respectively, these incidences were 2.3 and 2.9-fold higher than the anticipated arithmetical (stochastic) incidences. Although these data confirm an impact of donor-factors on incident EGL, the large majority of EGLs (>80%) were non-concordant. An impact of donor factors was further explored by comparing outcomes for functional grafts for which the contralateral graft was lost due to EGL with symmetrically functional grafts. Survival analysis showed similar recipient survival, but marginally impaired graft survival (Exp(B) 1.160 (95% CI: 1.002-1.343), p < 0.046) for grafts in the asymmetrical outcome group. One- and 5-years eGFRs were respectively slightly impaired (OR: 1.017 (1.010-1.025), p < 0.0001) and equal (1.000 (0.994-1.007)).A summary of the results of the research
Conclusions: This analysis implies that donor factors of grafts accepted for transplantation minimally impact transplant outcome. A strong focus on

donor characteristics or donor risk indices of grafts deemed acceptable for transplantation may result in an unjustified discard of viable organs and prolonged stay on the waiting list.

OP112 IMPACT OF ASIAN AND BLACK DONOR AND RECIPIENT ETHNICITY ON THE OUTCOMES AFTER DECEASED DONOR KIDNEY TRANSPLANTATION IN THE UNITED KINGDOM

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Background: Patients of Asian and black ethnicity face disadvantage on the renal transplant waiting list in the United Kingdom, because of lack of HLA and blood group matched donors from an overwhelmingly white deceased donor pool. This study evaluates outcomes of renal allografts arising from Asian and black donors.
Methods: The UK Transplant Registry was analysed for adult deceased donor kidney only transplants performed during January 2001-December 2015. Cox regression analysis was performed to identify and adjust for factors influencing 5-year graft outcome, and to study donor-recipient ethnicity interactions.
Results: Asian and black ethnicity patients constituted 12.4% and 6.7% of all deceased donor recipients over the study period but comprised only 1.6% and 1.2% of all deceased donors, respectively. The HLA match was better where donor and recipient ethnicities were matched. Across all recipients, and unsurprisingly given the predominantly white recipient pool, HLA matching was superior for grafts from white donors than from Asian and black donors ($p < 0.0001$). Unadjusted survival analysis demonstrated significantly inferior long-term allograft outcomes associated with Asian and black donors, compared to white donors (7-year graft survival 71.9%, 74.0% and 80.5%; log-rank $p = 0.0007$, respectively). On Cox regression analysis, Asian donor and black recipient ethnicities were associated with poorer outcomes than white counterparts ($p \leq 0.02$), and when looking at ethnicity matching, compared with the white donor–white recipient baseline group and adjusting for other donor and recipient factors, 5-year graft outcomes were significantly poorer for black donor-black recipient [HR 1.92 (1.11-3.32), $p = 0.02$], Asian donor-white recipient [HR 1.56 (1.09-2.24), $p = 0.02$] and white donor-black recipient [HR 1.22 (1.05-1.42), $p = 0.01$] combinations in decreasing order of worse unadjusted 5-year graft survival.
Conclusions: Increased deceased donation among ethnic minority communities would benefit the entire recipient pool by increasing the numbers of available organs and may specifically benefit the Asian and black recipients by increasing the numbers of blood group and HLA-compatible grafts for allocation but may not improve allograft outcomes.

OP113 PREDICTING NUCLEAR RENOGRAPHY BASED SPLIT RENAL FUNCTION IN LIVING DONOR TRANSPLANTATION WITH CT BASED MEASURED SPLIT RENAL VOLUMES

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Background and Aims: Nuclear renography (NR) is performed to determine the split renal function (SRF), when multi-detector computerized tomography (MDCT) reveals significant difference of size between the kidneys, when there are giant cysts or one of the kidneys has atypical morphology at the living donor. In this study, we compared the correlation of craniocaudal length (CCL) and the Split Kidney Volume (SKV) measurements which was derived from MDCT to the results of SRF measured by NR.
Methods: We performed 749 kidney transplants in between January 2013 and March 2020 at our center. 44 kidney donors (31 female, 13 male) had required NR to evaluate SRF. 19 cases were referred because of having more than one cm difference at CCL. 7 cases had giant cysts and 18 cases had atypical morphology. All images were analyzed retrospectively by three radiologist who were blinded to previous studies. SKV for separate kidneys was calculated by dividing individual kidney volume by total kidney volume. Independent *t* test was performed to find differences between variables. The correlation between the variables was analyzed by Spearman correlation coefficient. We also calculated the difference of volume reflecting 5% difference in SRF of two kidneys.
Results: There were statistically significant differences in height and body surface area between female and male donors and there were no differences in total volume, eGFR, other demographic data and anthropometric measurements. There was a high positive correlation between SKV and SRF (r 0.779, $p < 0.001$), moderate positive correlation between difference in SKV and difference in SRF (r 0.546, $p < 0.001$) and a negligible correlation between difference in CCL and difference in SRF (r 0.290, $p = 0.81$). The positive correlation between SKV and SRF (r 0.776, $p < 0.001$) was significantly more at the group of donors who have size mismatch of more than one cm at CCL measurement between the native kidneys. ROC analysis revealed that 4.7% difference in volume reflects 5% difference of GFR between the function of two kidneys (AUC: 0.703, p:0.038).
Conclusions: Difference in kidney volume is more valuable than difference in CCL of kidney when correlated to SRF in NR. SKV is the recommended measurement for referring to NR, especially for those cases with more than one cm difference at CCL measurement.

OP114 EPITOPE DISTRIBUTION AND FEASIBILITY OF PIRCHE-II T-CELL MATCHING FOR RENAL TRANSPLANTATION IN CANADA

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Background: HLA epitopes are cardinal allogeneic targets on HLA proteins and offer an innovative strategy for donor/recipient matching to reduce graft rejection. We have previously demonstrated the feasibility of within-centre matching using antibody-verified epitopes (via HLAMatchmaker). Here, we model organ allocation using T-cell epitope-matching via PIRCHE-II scores in Canada.
Method: PIRCHE-II (v3.3.36) scores were pre-calculated for 300,150 possible recipient/donor pairs, using NGS HLA data for 1,150 patients and 261 deceased donors. PIRCHE-II score was calculated using 5 principal genes (HLA-A, B, C, DRB1, DQB1). Simulation models implemented in R (3.5.3) incorporated ABO identity, waitlist rank and optimal score for matching and employed Canadian provincial waitlist sizes (88 – 2032 patients) and donor rates (16 – 762 donors/yr.) for a 1 year simulation without burn-in period. Scenario analyses, considering three previously published thresholds (up to 9, up to 35 and up to 90) and 9 Canadian provincial programs of varying size (wait list <100 – >2000) were also conducted.
Results: Active donor/recipient matching markedly improves the cumulative probability of achieving optimal PIRCHE-II scores compared with the Canadian base case (Fig.1). In the matched model, the average median PIRCHE-II score was 29 over 10 repeated simulations and 95% of donor/recipient pairs had a score of 49 or less, compared with an average median score of 79.25 for the base case simulation with a 95%-cumulative probability score of 170. Scenario analyses showed an improvement of median match score with increasing wait list size for the intermediate stratum (scores 9-35). However, the probability of matching was independent of wait list size for the lower (score up to 9) and higher (score 35-90) strata. Whilst using PIRCHE-II scores for all 5LOCI did not demonstrate significant improvement in probability of matching for these thresholds, this result is similar to the probability of matching using HLAMM at all loci.
Conclusion: Modeling shows that active donor/recipient matching substantially reduces the PIRCHE-II score for renal transplant in Canada. The magnitude of improvement is directly related to the size of the wait list for intermediate matching, suggesting that regional or national organ sharing may enhance success.

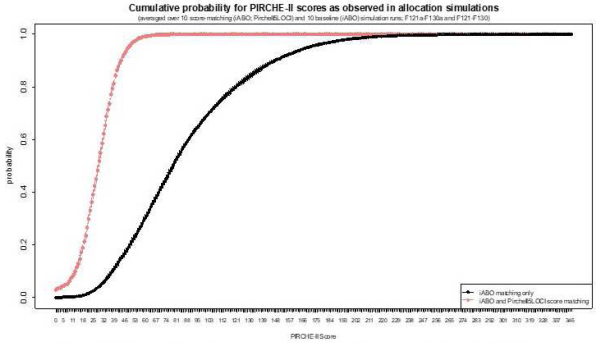

Fig 1. Cumulative probability curves for simulations incorporating identical blood group matching (iABO) only (black) and iABO+PIRCHE-II 5-loci score-matching (red) using recipient and donor numbers observed in Canada (wait list size 2,032; 1,424 kidneys from 762 donors over the course of one year; numbers for 2019). Error bars represent standard deviation derived over 10 repeated simulation runs.

OP115 ITALIAN NATIONAL KIDNEY ALLOCATION ALGORHITM (INKAA): APPLICATION AND FIRST RESULTS

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Background and Aims: In 2017 the National Transplant Center promoted the development of a single national allocation algorithm for kidney transplantation in order to find the right balance between the parameters of equity (AB0, Dialysis seniority, Patient age) and those of beneficence (PRA, HLA match, delta age). The algorithm was approved on 31/10/2018 and adopted by all regions by summer 2019.
The purpose of the work was to verify the first results of applying the algorithm, in terms of selecting transplant patients for the aforementioned parameters.
Methods: Transplants performed in the following periods were compared:
- 01/07 / 2017-31 / 12/2017 (pre-INKAA period)
- 01/07 / 2019-31 / 12/2019 (INKAA period)

All the variables used by the algorithm were analyzed in terms of mean and median for continuous variables and in terms of percentage distribution for categorical variables.
Results: A total of 1570 transplants (760 pre-INKA and 810 INKAA) were analyzed. On the INKA sample, all the variables changed in line with the algorithm's operating logic: increase in dialysis and list seniority (respectively from 4.4 to 4.8 years, from 2.1 to 2.4 years), decrease in patient age (51 to 49.2 years), increase in HLA mismatches (3.2 to 3.7 mm), increase in PRA (10.5 to 13.1), increase in transplants isogroup (from 94.7 to 97.2%).
Conclusions: Despite some regional customizations, the adoption of the INKA algorithm was found to be effective in modifying the selection of transplant recipients, improving the equity of the allocation. Prospectively, it will be important to harmonize customizations and evaluate the outcome of transplant patients and the effects on the beneficial effect of the transplant.

OP116 THE IMPACT OF COLD ISCHAEMIA TIME ON OUTCOMES OF LIVING DONOR KIDNEY TRANSPLANTATION IN THE UK LIVING KIDNEY SHARING SCHEME

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Background: Living donor KTx (LDKT) provides the best treatment option for patients with end-stage kidney disease (ESKD). Even ESKD patients who have an incompatible living donor still have an opportunity to be transplanted through Kidney Exchange Programmes (KEP). The UK Living Kidney Sharing Scheme (UKLKSS) is the largest KEP in Europe with excellent outcomes in recipients who may otherwise not have been transplanted. In KEPs where kidneys travel rather than donors, such as the UKLKSS, cold ischaemia times (CIT) can be prolonged. This study examines results of KEP versus non-KEP LDKT and studies the effect of prolonged CIT within the KEP (which is UKLKSS unless otherwise stated).
Methods: All adult UK LDKT between 2007 and 2018 were analysed. We acquired NHSBT data, including patient characteristics and transplant outcomes from all adult kidney transplant centres. We compared results of KEP versus non-KEP LDKT and studied the effect of CIT within the KEP specifically.
Results: A total of 9956 LDKT were included, of which 1396 (14%) were KEP. CIT in KEP was significantly longer than in non-KEP LDKT (median 339 versus 182 min, $p < 0.001$). KEP had a higher incidence of delayed graft function (DGF) (6.97% versus 4.08%, $p < 0.0001$), and lower graft function at 1-year (eGFR 57.9 versus 55.3, $p = 0.04$) and at 5-years (eGFR 55.6 versus 53.1, $p = 0.01$) compared to the non-KEP group. A lower unadjusted 1-year graft survival (96% versus 98%, $p < 0.01$) was found but when risk-adjusted, there was no difference. There was no difference in 5-year graft survival.
Within the KEP-cohort, a CIT longer than 339 minutes (median) was associated with a higher incidence of DGF (9.26% versus 4.80%, $p = 0.02$), and lower graft function at 1-year (eGFR 54.6 versus 55.9, $p = 0.03$) and 5-years (eGFR 50.0 versus 55.0, $p = 0.02$) compared to shorter CIT. Risk factor analyses showed that different risk factors were involved in graft loss in the non-KEP and KEP group.
Conclusions: CIT was significantly longer in KEP versus non-KEP LDKT. KEP had a higher incidence of DGF and lower graft function. However, 5-year graft survival was similar in KEP versus non-KEP LDKT. Within KEP, a longer CIT impacts on DGF and graft function. However, graft survival is still excellent. These data in combination with the risk-factor analysis can be used to update algorithms to further optimise KEP outcomes.

OP117 CLOSING THE GAP: EXAMINING WAIT LIST OUTCOMES FOR THE MOST HIGHLY SENSITIZED CANDIDATES IN THE USA ACROSS REGIONS

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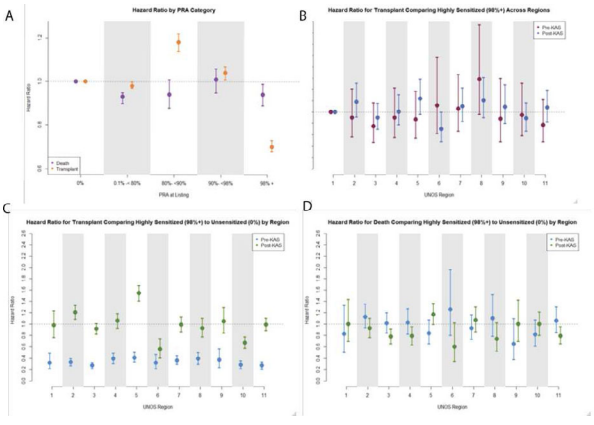
Background: Improving equity in deceased donor transplantation for sensitized candidates has been a goal and success of the new US kidney allocation system (KAS). Despite benefit for most sensitized candidates, inequities remain for the most highly sensitized candidates. In this analysis, we examined the impact of geographic region on waiting list outcomes for highly sensitized candidates in the post-KAS era.
Methods: Adult, kidney waiting-list candidates between Pre-KAS: January 1, 2010 – Dec 3, 2014 & Post-KAS: Dec 4, 2014 – Sept 1, 2018 were analyzed by era, geographic region (1-11), waitlist outcomes (mortality and transplant), and peak cPRA (within 3mo of listing). Cox Proportional Hazards model with competing risks for death on waitlist and transplant, with time-varying covariates for era were used. Cause-specific hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated, comparing the risk of death and transplant for the most highly sensitised (cPRA>98%) relative to unsensitized (cPRA 0%) patients in each era and between regions.
Results: 326,302 candidates were eligible, of whom 8746 had a cPRA ≥98%. The number of deceased donor transplants amongst all sensitized candidates increased in all regions post-KAS. However, the post-KAS transplant benefit was reduced in the >98% cPRA category (Fig 1A). The likelihood of transplant and death for the >98% cohort is comparable across regions, with more similar HRs post-KAS (Fig 1B). Compared to unsensitized (0%), >98%+ candidates had a lower risk of transplant in the Pre-KAS Era [HR 0.32, 95%CI (0.22, 0.49)], which improved post-KAS across regions [HR 0.98, 95% CI (0.77, 1.24)] Fig 1C. The risk of death demonstrated a similar improvement post-KAS but equity differed between regions [pre-KAS HR 0.83, 95%CI (0.51-1.34), post-KAS HR 1.0, 95% CI (0.7, 1.44)] Fig 1D.
Conclusions: The new KAS has improved transplant opportunities and reduced the risk of death for sensitized candidates, yet differences remain across regions. For most highly sensitized candidates (within the top category >99.8%), the likelihood of transplant remains low.



OP118 THE REMUZZI SCORE IS A SAFE DECISION-MAKING TOOL AND UTILIZES MORE KIDNEYS FOR TRANSPLANT COMPARED TO DONOR EGFR

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Background: Discard rates of procured marginal kidneys are still high, especially when they are not considered adequate for single kidney transplantation. Considering such kidneys for dual transplantation is an alternative. The aim of our analysis was to compare the outcomes after single and dual kidney transplantation in regard to their utilization according to either the Remuzzi score or donor eGFR.
Methods: A retrospective single-center analysis of consecutive kidney allografts which were transplanted after a zero biopsy for Remuzzi scoring was taken. Uni- and multivariate logistic and Cox regression analyses were performed.
Results: Overall, 193 kidneys were transplanted; 132/193 (68.4%) ECD DBD, 22/192 (11.4%) DCD and 45/193 (23.3%) had acute kidney injury. Single organs were transplanted in 155 recipients, 38 kidneys were transplanted as duals. If the stratification for single or dual transplants would have been made according to donor eGFR, 50 allografts would have been discarded. The most important independent factors for the decision single/dual were donor diabetes (Wald 12.2, OR 6.9, 95%CI 2.3-20.8, $p < 0.001$) and Remuzzi score (Wald 19.4, OR 3.4, 95%CI 1.9-5.9, $p < 0.001$). Dual kidney donors were significantly older (70.1 $\pm$ 9.1 vs 56.5 $\pm$ 14.4 years, $p < 0.001$) and had higher kidney donor profile indices (93.7 $\pm$ 6.2% vs 72.1 $\pm$ 24.3%, $p < 0.001$). Recipients of single kidneys were significantly younger (59 $\pm$ 10.4 vs 64.4 $\pm$ 7.6 years, $p = 0.003$). Delayed graft function was comparable between single and dual recipients; 71/155 (45.8%) single vs 9/19 (47.4%) dual; $p = 0.8$. Recipient eGFR was significantly better in dual transplants; 47.5 $\pm$ 31.1 vs 34.5 $\pm$ 20.7, $p = 0.002$. The decision single or dual transplant had no impact on graft survival (Wald 0.9, HR 0.31, 95%CI 0.0-47.1, $p = 0.4$). No difference in patient survival was demonstrated either. However, all dual transplant recipients died with functioning graft. The most important independent factors influencing patient survival were donor eGFR (Wald 6.51, HR 1.02, 95%CI 1.004-1.032, $p = 0.01$) and donor BMI (Wald 5.02, HR 0.82, 95%CI 0.69-0.98, $p = 0.03$).
Conclusions: It is safe to utilize more kidneys by performing dual transplants. The Remuzzi score is a useful addition to take a decision. Recipients of dual transplants need meticulous re-assessment before transplantation.

OP119 LONG-TERM EVOLUTION OF KIDNEY GRAFT DONATION PROCEDURES IN UNCONTROLLED DONORS AFTER CARDIAC DEATH IN THE COMMUNITY OF MADRID

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Objective: the uncontrolled donors after cardia death (uDCD) has been decreasing in recent years. One of the possible reasons is the lower efficiency of the organs generated by this type of donation. The objective is compare the survival rates of the organ receptor.
Method: The Madrid Registry of Renal Patients (RЄMЭЯ) collects the evolution of kidney transplants since its creation in 2008. Kaplan–Meier for data analysis.
Results: 6598 transplants were analyzed, 5129 Brain Death Donors (DBD), 844 of uDCD, 357 controlled donors after cardiac death (cDCD) and 357 of living donor (LD). The 20-year survival curve shows that LD renal injectors have more survival than the other types of donation, which takes place in the first 5 years, although with a similar decline to the rest of the antibodies in the upper ones. Survival at 10 years is similar inDBDversus uDCD.Cdcd has a survival rate similar to uDCD in the first year but subsequently declines more rapidly.
Conclusions: The immediate survival of the uDCD recipients is somewhat lower at the beginning than the recipients of DBD, but at 10 years there is a concordance in them. The trends of both types of donation are almost parallel until the end of the study period.

OP120 MODIFIED FRAILITY INDEX (MFI-11): A SIMPLE TOOL TO ACCESS FRAILTY IN OLDER KIDNEY TRANSPLANT WAITING LIST POPULATION

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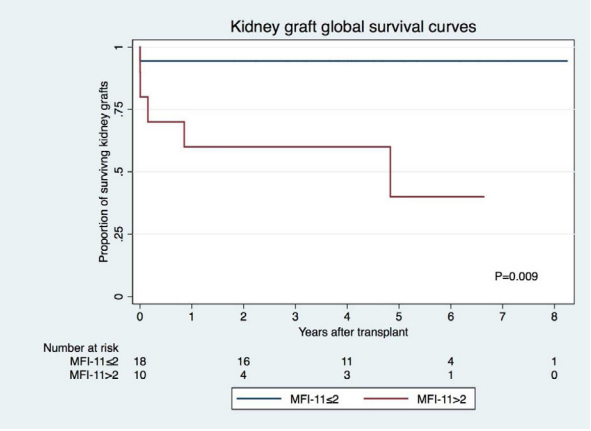
Background: The selection of older kidney transplant (KT) candidates is challenging, since there are insufficient predictive tools that identify candidates who would benefit most from transplant, considering the scarcity of available organs.
Modified Frailty Index (mFI-11) is a deficit accumulation measure of frailty (score 0-11) that was derived from the Canadian Study of Health and Aging Frailty Index and from the American College of Surgeons' National Surgery Quality and Improvement Project.
Even though this score is not validated in KT population, it´s a simple and non-subjective tool to access frailty and is well validated in older and surgical populations.
The aim of this study was to evaluate associations between MFI-11 and the outcomes of wait-listed older candidates for KT.
Methods: We retrospectively analyzed candidates with ≥65 years old that were approved for KT at our center between 2012-2014. The follow-up is until September 2020. We access mFI-11 at all the patients at time of the entry on waiting list. This index was correlated with the outcomes: death or definitive contraindication (DC) while on the waiting-list and KT outcomes.
Results: Sixty-six candidates were included, mainly men (65.2%), with a mean age of 67.4 years old (min-max: 65-73).
In the period of follow-up, 39% (26) of the candidates died or had a DC for transplant. These patients had more frailty with higher mFI-11 (2.88 $\pm$ 1.53 vs 2.05 $\pm$ 1.40 p value = 0.030). Patients that were transplanted (59%) had lower mFI-11 (2.05 $\pm$ 1.41 vs 2.85 $\pm$ 1.51 p value = 0.033).
Patients with MFI-11 index >2 had higher probability of death or DC (hazard ratio (HR): 7.727; 95% Confidence Interval (CI) 2.797-21.344; p value <0.001) and less probability of KT (HR: 0.450; 95% CI 0.223-0.909; p value 0.026) when adjusted to age, sex, calculated panel-reactive antibody, and time between dialysis initiation and KT waiting list.
Analyzing the subpopulation that was transplanted (28 patients) there is also a significant association between MFI-11 index >2 and lower global renal graft survival in 5 years (MFI-11 index >2: 40% vs ≤2: 94%; log-rank p value 0.009).
Conclusions: MFI-11 could be a useful tool to evaluate older candidates to kidney transplant. A higher score, in these population, was associated with a worse outcome, both while on the waiting-list and after KT.



OP121 COMPARING OUTCOMES IN RIGHT VERSUS LEFT KIDNEY TRANSPLANTATION; A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Transplantation of right kidneys can pose technical challenges due to the short right renal vein. Whether this results in inferior outcomes remains controversial.
Method: We used Healthcare Database Advanced Search (HDAS) to identify studies comparing outcomes of right versus left kidneys. Two authors independently reviewed each study. Statistical analyses were performed using random effects models and results expressed as HR or relative risk (RR) with 95% confidence intervals. Subgroup analyses were performed in kidneys from deceased donors (DD) and living donors (LD).
Results: 35 studies (257,429 participants) were identified. Both deceased and living donor right kidneys were at increased risk of delayed graft function (DGF; RR = 1.10[1.07-1.12] $p < 0.00001$; Figure 1). In absolute terms, for each 100 kidney pairs of deceased donor kidneys transplanted there are 2.72 (1.67-3.78, $p < 0.00001$) excess episodes of DGF in right kidneys.

Graft thrombosis rate was also significantly higher in right kidneys, in both DD and LD settings (RR = 1.55[1.41-1.69] p < 0.00001). Compared to DD left kidneys, DD right kidneys were at significantly higher risk of graft failure due to technical causes (RR = 1.54[1.25-1.90], p < 0.0001). The two largest DD studies (179,124 participants) found right kidneys to have significantly poorer graft survival; time-varying analyses demonstrated this was caused by early graft losses within the first year post-transplant. When graft survival was meta-analysed there was significant heterogeneity in deceased donors (I^2 = 70%, p < 0.001) and no evidence that laterality impacts of long-term graft survival in living donors (1.07[0.90, 1.28], p = 0.42).
Conclusion: Right kidneys are at increased risk of early complications in both DD and LD settings, although the absolute effects are small. Improved vascular reconstruction techniques for the right renal vein, which avoid detrimental impacts on ischaemia times, are essential.

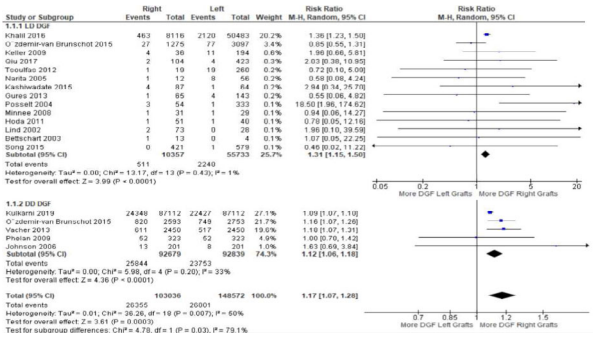

Figure 1 relative risk of DGF

OP122 ARE UNSPECIFIED KIDNEY DONORS TREATED DIFFERENTLY TO SPECIFIED KIDNEY DONORS? VIEWS OF UK TRANSPLANT PROFESSIONALS

Mira Zuchowski[1], Hannah Maple[2], Heather Draper[3], Peter Gogalniceanu[2], Sam Norton[1], Joseph Chilcot[1], Alexis Clarke[4], Lynsey Williams[4], Timothy Auburn[4], Nizam Mamode[2]
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Background: Unspecified kidney donation has made significant contributions to the UK living donor programme. Some transplant professionals approach these donors with caution, mainly due to beliefs that wishing to donate is a manifestation of an underlying psychopathology. One of the aims of this study was to explore the attitudes of the UK professional transplant community towards Unspecified Kidney Donors (UKDs) in comparison to Specified Kidney Donors (SKDs).
Methods: As part of the Barriers and Outcomes in Unspecified Donation (BOUnD) study, we conducted a qualitative study, interviewing 60 transplant professionals. Semi-structured interviews were subjected to inductive thematic analysis. This rigorous and data-driven method involved coding 500 pages of transcripts and grouping codes into themes and sub-themes.
Results: The majority of participants reported that the main difference in the treatment of the two groups was the rigorous psychological workup for UKDs, which is not compulsory for SKDs. Many staff members emphasized the importance of this mandatory psychological assessment for UKDs to fully understand their motivations and to ensure that it was not pathological. In regard to SKDs, some staff highlighted the complex family dynamics associated with this type of donation including guilt, family obligation, or reciprocity.
Discussion: This study provides in-depth data exploring the views of UK transplant professionals towards UKDs and SKDs. The key findings were that the same screening standards were not applied to SKDs, and that the motivations of UKDs were more strongly interrogated. This study provides valuable guidance for improving the overall UKD programme, including managing staff stereotypes in support of a more positive appraisal of motivations for both UKDs and SKDs, and possibly extending the psychological assessment to SKDs to avoid situations where personal relationships may inappropriately play a role in the donation decision.

COVID-19 AND ELSE: OVERCOMING THE PANDEMIC

OP181 CXCR3+ CIRCULATORY FOLLICULAR HELPER T LYMPHOCYTES COULD HELP IN COVID-19 RESOLUTION IN KIDNEY TRANSPLANT RECIPIENTS

Patricia Suàrez Fernández[1], Daniel Arroyo-Sánchez[2], María Lasa-Lázaro[2], Alberto Utrero-Rico[1], Cecilia González-Cuadrado[1], Esther Mancebo[2], María José Castro-Panete[2], Esther González[3], Hernando Trujillo[3], Amado Andrés[3], Estela Paz-Artal[1,2], Rocio Laguna Goya[1,2]
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Background: Kidney transplant recipients (KTR) are at increased risk of severe-COVID-19 due to pre-existing comorbidities. Circulatory T follicular helper cells (cTFH), specialized in assisting B cell differentiation towards antibody-producing-plasma cells, have been shown to protect against HIV, Influenza and HBV through secretion of neutralizing antibodies. cTFH are divided in cTFH1, 2 and 17 based on their expression of CXCR3 and CCR6 and cytokine pattern. We aimed to study if cTFH, or any of its subtypes, could protect against SARS-CoV-2 infection in KTR
Methods: We studied 2 cohorts: 29 KTR infected by SARS-CoV-2, and 25 healthy controls (HC). PBMCs were collected at their arrival to the hospital and every 3-4 days during hospitalization. All patients presented bilateral pneumonia. cTFH were identified as $CD4^+CXCR5^+$ and cTFH1, 2 and 17 subtypes as $CXCR3^+CCR6^-$, $CXCR3^-CCR6^-$ and $CXCR3^-CCR6^+$ respectively. Activated cells were those co-expressing $ICOS^+PD1^{hi}$ and exhausted cells were $ICOS^-PD1^{hi}$
Results: At day 5-6 of hospitalization activated cTFH numbers were elevated in comparison with day 1 (0.5 cells/ul vs 4.9 cells/ul, p = 0.005) as well as activated cTFH1 numbers (p = 0.003), cTFH2 (p = 0.02) and cTFH17 (p = 0.004). Frequencies of cTFH, as well as cTFH1 and cTFH2, also tended to increase after hospitalization (p = 0.06, p = 0.08 and p = 0.09, respectively) but not cTFH17 (p = 0.38). Additionally, KTR with high percentages of cTFH1 (above the median) at days 5 to 10 had a shorter hospital stay than KTR below the median (9 vs 17 days, p = 0.01). The proportion of activated cells inside each subtype differed: cTFH1 cells were more activated than cTFH2 and cTFH17 at day 1 (p = 0.04, both), at week 1 (p = 0.004 and p = 0.007), at week 2 (p = 0.0003 and p < 0.0001) and week 3 (p = 0.008 and p = 0.001) of hospitalization. Subsequently, exhaustion was higher in cTFH1 than cTFH2 and cTFH17 (p = 0.008 and p = 0.04) at week 3.
Conclusions: cTFH1 could promote COVID-19 resolution by mechanisms still under study.

OP182 INCREASING DIAGNOSTIC ACCURACY IN RENAL TRANSPLANT PATIENT WITH ACUTE COVID-19 AND GRAFT FAILURE BY T CELL ANALYSIS IN PERIPHERAL BLOOD AND BIOPSY

Ulrik Stervbo[1], Jan Zapka[1], Bodo Hoelzer[2], Julia Kurek[1], Moritz Anft[1], Jochen Hecht[3], Adrian-Atila-Nicolas Doevelaar[2], Timm H. Westhoff[2], Nina Babel[1]
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Background: Several lines of evidence suggest that the novel coronavirus SARS-CoV-2 can infect the human kidney and induce acute renal or renal transplant (RTx) injury. Due to the focal occurrence within the RTx, the histology can miss the infected area providing thereby false negative results. Here, we present an application of two modern diagnostic technologies in a case of a living-related RTx patient hospitalized due to COVID-19 induced pneumonia followed by acute transplant failure.
Methods: SARS-CoV-2- and donor-reactive T cells were evaluated in peripheral blood after stimulation with SARS-CoV-2 peptides and lysates of donor PBMCs. In parallel, kidney infiltrating T cells were evaluated in a biopsy by multiparametric flow cytometry after stimulation with SARS-CoV-2 peptides. In addition, T-cell receptor (TCR) sequences of the SARS-CoV-2 and allograft-specific T cells in peripheral blood were extracted by means of next generation sequencing. These were compared to the TCRs of the graft infiltrating T cells to identify the clonal specificity of these T cells.

Results: A large degree of CD3+ T cell infiltration was found in the biopsy, however, acute rejection was ruled out by pathological findings. Furthermore, in situ hybridization showed no SARS-CoV-2 indicating no renal SARS-CoV-2 infection. Flow cytometric analyses showed that in contrast to the substantial level of SARS-CoV-2 specific T cells in the peripheral blood, none were observed in the biopsy. In addition, there were no measurable levels of allograft-reactive T cells either in the peripheral blood or in the biopsy.
Conclusions: The applied technologies ruled out transplant rejection and SARS-CoV-2-related graft function deterioration suggesting unspecific T cell infiltration due to bystander activation. Analyzing SARS-CoV-2-reactive and donor-reactive T cells in peripheral blood and in kidney transplant biopsy can improve diagnostic accuracy enabling differential diagnosis and personalized therapy.

OP183 DETECTION OF PRE-EXISTING SARS-COV-2-REACTIVE T CELLS IN UNEXPOSED RENAL TRANSPLANT PATIENTS

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Background: Recent data demonstrate potentially protective pre-existing SARS-CoV-2-reactive T cells in samples of healthy blood donors collected before SARS-CoV-2 pandemic. Whether pre-existing immunity is also detectable in immunosuppressed patients is not known so far.
Methods: 57 patients were included in this case-control study. We compared the frequencies of SARS-CoV-2-reactive T cells in samples of 20 renal transplant patients (RTx) to 20 age/gender matched non-immunosuppressed/immune competent patients collected before SARS-CoV-2 pandemic onset. 17 COVID-19 patients were used as positive control. T-cell reactivity against Spike-, Nucleocapsid-, and Membrane- SARS-CoV-2 proteins were analyzed by multi-parameter flow cytometry. Antibodies were analyzed by neutralization assay.
Results: Pre-existing SARS-CoV-2-reactive T cells were detected in majority of unexposed patients. In RTx, 13/20 showed CD4+ T cells reactive against at least one SARS-CoV-2 protein. CD8+ T cells reactive against at least one SARS-CoV-2 protein were demonstrated in 12/20 of RTx patients. The frequencies and Th1 cytokine expression pattern of pre-formed SARS-CoV-2 reactive T cells did not differ between RTx and non-immunosuppressed individuals.
Conclusions: This shows that the magnitude and functionality of pre-existing SARS-CoV-2 reactive T-cell immunity in transplant patients is non-inferior compared to the immune competent cohort. Although several pro-inflammatory cytokines were produced by the detected T cells, further studies are required to prove their antiviral protection.

OP184 COVID-19 SEVERITY INFLUENCES ANTI-SARS-COV2 ANTIBODIES TITER IN KIDNEY TRANSPLANT RECIPIENTS

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Background and Aims: Immunosuppression (IS) decreases the ability to develop seroconversion to infectious diseases. We evaluated rate of seroconversion and factors influencing antibody (Ab) levels against SARS-CoV-2 in kidney transplant recipients (KTR).
Methods: KTR with confirmed COVID-19 through December 31, 2020 were included. Disease was classified as severe (including critical) and non-severe (including asymptomatic, mild, and moderate). SARS-CoV-2 IgG Ab targeting the S1 subunit of the spike protein (anti-S1; Euroimmun) and the nucleocapsid protein (anti-N; Abbot) were measured on sera collected ≥20 days after symptom onset (ASO). KTR negative for both assays were considered seronegative. Seropositive KTR were categorized as having IgG titer below or above the 50th percentile (50thPc) median titer.
Results: Sera was available for 34 (66.7%) KTR: median 31.5 [IQR 24.8-53.5] days ASO; median age 55.5 [IQR 48.8-65.3] years; 20 men [58.8%]; median eGFR 57.5 [IQR 43.8-79.3] mL/min/1.73m^2; 16 [47.1%] with severe disease); median time from transplant 96 [IQR 21-196] months; most on triple immunosuppression; mycophenolate withdrawn in 67.6%. Seronegative patients accounted for 11.8% of KTR and all had non-severe disease. Seropositive patients accounted for 88.2% of KTR and included all 5 KTR in the first-year post-transplant. Severe disease was associated with positivity for anti-N (OR 9.6, 95% CI 1.02 – 89.2, $p < 0.05$) and with a titer above the 50thPc of anti-N (titer > 4.6; OR 6.0, 95% CI 1.3 – 28.7, $p < 0.05$) and anti-S1 (titer > 6.7; OR 16.0, 95% CI 2.7– 95.8, $p < 0.005$) Ab. No association was found between seropositivity or titer above or below the 50thPc and variables such as age, gender, eGFR, baseline IS, mycophenolate withdrawal and time from transplant.
Conclusions: In this study, most KTR developed Ab against SARS-CoV-2. Moreover, KTR with severe disease had higher Ab levels against the S1 and N protein. Presence and titer of Anti-S1 Ab, which likely correlate to neutralizing Ab, suggest that many KTR may be protected from reinfection – albeit for an uncertain period time.

OP185 OUTCOMES OF KIDNEY TRANSPLANTATION AT THE EPICENTRE OF THE COVID-19 PANDEMIC: THE EXPERIENCE OF THE OSPEDALE MAGGIORE POLICLINICO

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Background: The SARS-CoV2 pandemic has resulted in a sharp reduction of the number of kidney transplant (KT) performed worldwide. Beyond the obvious health care crisis, there is also a concern of significant complications arising from COVID-19 infection. We herein report the experience of a KT unit operating at the epicentre of the pandemic.
Methods: Single-centre observational study comparing the outcomes of patients transplanted during the pandemic (SARS-KT; 71#) with those remaining on the transplant waiting list (WL) during the same period (SARS-WL; 142#) or transplanted in 2019 (KT; 75#) at the Ospedale Maggiore Policlinico (Milan). Data refer to the latest follow-up available. Donor and recipient screening included: real-time reverse transcriptase PCR based molecular assay on nasal swab and BAL, serologic test, CRP, and chest high-resolution CT scan.
Results: Baseline characteristics of the groups were similar. Patient survival was 99% in SARS-KT, 96% in KT, and 97% in SARS-WL (P = ns) whereas transplant survival was 97% in SARS-KT and 96% in KT (P = ns). There were 3 episodes of COVID-19 infection in SARS-KT (4%; 2 asymptomatic and 1 with moderate respiratory symptoms), 6 in KT (8%; 5 asymptomatic and 1 fatal), and 3 in SARS-WL (2%; all fatal). Infections were acquired during hospital stay or ambulatory dialysis. Due to reduced theatre slots and ICU beds available, we observed longer median cold ischemia time and higher DGF rates during the pandemic than before (42% vs 27%; $p < 0.05$); rejection rates were 6% vs 4%, respectively (P = ns). Median tacrolimus C0, MMF and steroid daily doses in SARS2-KT and KT were not significantly different at any time point of the study, reflecting the fact that we did not change our immunosuppressive strategy.
Conclusions: Our data seem to reassure centres willing to continue their KT programme as no clinically relevant differences were observed among patients transplanted before or during the pandemic. The perceived higher risk of SARS-CoV-2 death observed among patients on the WL further supports this point of view as long as strict and rigorous infection control strategies are embraced. A national multicentre study with larger population and longer follow-up is warranted to confirm these findings and help clinicians offer adequate counselling.

OP186 IMPACT OF SARS-COV-2 INFECTION IN WAITING LIST FOR LIVER TRANSPLANTATION

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Background and Aims: Infections in cirrhotic patients are associated with an increased risk of liver-related complications (LRC) and mortality. Limited data regarding the prevalence of Coronavirus disease (COVID-19) in cirrhotic patients' awaiting liver transplantation (LT) are available. The aim of this study was to evaluate the prevalence of SARS-CoV2 in a cohort of cirrhotic patients and its impact on LRC rate and on LT.
Methods: We retrospectively included 187 waitlist patients for LT from 24-January-2020 (2020-cohort) and 123 patients from 24-January-2019 (2019-cohort). All 2020-cohort patients were screened for COVID-19 symptoms with a survey. COVID-19 infection was defined by a positive PCR assay for SARS-CoV-2 on nasopharyngeal swab or the positivity for specific antibodies or typical lung lesions on CT scan. We also assessed the indirect impact of SARS-CoV2 infection on LRC and LT rate, estimated by competitive risk survival analyses in 2020-cohort vs. 2019-cohort (Fine and Gray method).
Results: In 2020-cohort, 72.7% (n = 136) of patients were male with mean age of 55.5 ± 12, 47.2% (n = 85) patients have alcohol and/or NASH related cirrhosis, with a median MELD score of 14.1 ± 7.4. 45.5% (n = 71), 38.5% (n = 60) and 14.8% (n = 23) of patients were A, B and C for Child-Pugh-score, respectively. 172 patients responded to survey and 22% (n = 38) had symptoms. 20/38 patients were tested for SARS-CoV2 and 4 patients were positive. 3/4 patients with COVID-19 disease needed hospitalization and 1 intensive care support. No death was reported and 1 patient was LT. The 2020-cohort and 2019-cohort were comparable for sex (p = 0.6), age (p = 0.7), comorbidities (p = 0.2) and Child-Pugh-score (p = 0.2). The cumulative incidence of LRC was not significantly higher in the 2020-cohort vs. 2019-cohort (SHR 0.65, 95% CI 0.36-1.15, p = 0.138). The cumulative incidence of LT was significantly lower in the 2020-cohort than in the 2019-cohort (SHR0.21, 95% CI 0.13-0.33, p < 0.001).
Conclusions: Our study reported a low prevalence rate of SARS-CoV2 infection in a cohort of cirrhotic patients waiting for LT. No SARS-CoV2 infection direct or indirect impact on mortality and LRC rate was reported. However, a significant shortage of LT was found in 2020 cohort.

OP187 LIVER TRANSPLANTATION IN PATIENTS WITH LIVER CIRRHOSIS RECOVERED FROM COVID-19 INFECTION

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Background and Aims: Coronavirus disease 2019 (COVID-19) has resulted in significant morbidities and mortalities in nearly all parts of the world. There are major concerns about management, timing and safety of liver transplantation in patients recovered from COVID-19. We aimed to study clinical course and outcomes of patients with liver cirrhosis who recovered from COVID-19 and underwent liver transplantation from deceased donors
Methods: A retrospective assay was conducted on liver transplant recipients who underwent liver transplantation between April, 1, 2020 and January, 30, 2021. We evaluated all liver transplant recipients from deceased donors and from living related donors during this period of time in the COVID-19 pandemic.
Results: There were 13 patients who had been recovered from COVID-19 documented by RT-PCR for SARS-Cov-2. Mean duration from COVID-19 to transplant surgery was 53.53 ± 29.49 days. Mortality was occurred in 3 patients, 2 of them had been hospitalized and received medications for COVID-19 before transplantation. Mean duration of survival was 222.10 ± 21.72 in patients without lung involvement during COVID-19 compared to 49 ± 30.21 days in patients with lung involvement during COVID-19 (p = 0.023). Five patients had positive RT-PCR results for SARS-Cov-2 after liver transplantation.
Conclusion: This is the largest series of patients with liver cirrhosis who underwent liver transplantation after recovery of COVID-19. Liver transplantation from deceased donors can be considered in patients recovered from COVID-19 especially in those with deterioration of clinical status.

	Age	sex	Underlying disease	MELD	Lung involvement	Time from COVID-19 to transplant	Mortality After transplant	Survival
Patient 1	53	M	PSC	25	No	45	no	240
Patient 2	45	M	NASH	40	Yes	32	yes	12
Patient 3	29	F	PBC+ Liver abscess	30	No	90	No	110
Patient 4	50	F	PSC	23	No	86	No	130
Patient 5	20	M	Budd-Chiari Syndrome	33	Yes	62	No	118
Patient 6	41	M	AIH	20	No	20	No	49
Patient 7	54	F	NASH	19	No	56	yes	16
Patient 8	6	F	HCC	13	No	91	No	58
Patient 9	50	M	NASH	31	No	34	No	86
Patient 10	45	F	AIH	21	Mild	15	Yes	12
Patient 11	42	M	PSC	24	No	22	No	148
Patient 12	39	M	Budd-Chiari Syndrome	23	Mild	45	No	28
Patient 13	45	M	AIH	19	No	98	No	28

OP188 SARS-COV-2 INFECTION IN KIDNEY TRANSPLANT RECIPIENTS: ONE YEAR LATER. WHAT HAVE WE LEARNT?

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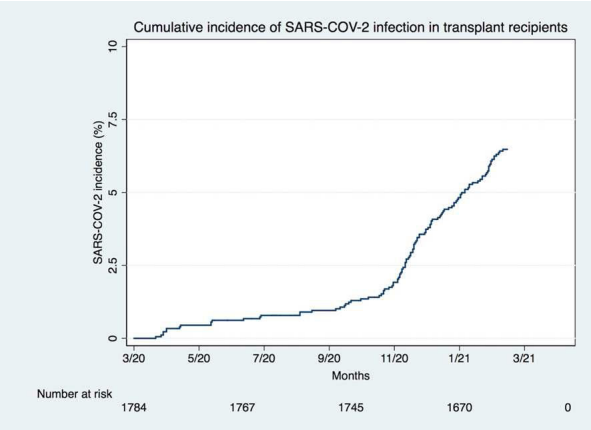
Background and Aims: Kidney transplant recipients are highly susceptible to infections, namely to viral infections as COVID-19, a form of coronavirus identified in December 2019 that quickly became a worldwide pandemic. We aim to study, one year later, the impact of this infection in our transplant recipients.
Methods: We retrospectively reviewed all kidney transplant patients, from our program, with a laboratory-confirmed COVID-19 infection from March 1st to February 4th of 2020. Transplant characteristics, comorbidities, symptoms, hospital admission, oxygen need, escalation of care, acute kidney injury, renal replacement therapy and, ultimately, death were registered.
Results: A hundred and fourteen out of the 1784 patients from our program got a positive test for SARS-CoV2. Cumulative incidence is shown in Graph 1. Most of the patients (61%) were male, with a mean age of 52.9 ± 13.8 years old. Age-standardized incidence of COVID-19 in our transplant population was of 6,5% (95% CI: 5,4-7,8%), similar to the general Portuguese population, SMR 0.869 (95% CI: 0.717-1.044). However, the crude incidence of death age and sext-standardized was of 8,4% (95% CI: 3.6-16.6%), representing a SMR of 4,5 (95% CI: 1,9-8,8) comparatively with the general population. Out of the 114 patients, 7 patients got COVID-19 secondary to nosocomial transmission, and 28 patients of the remaining (26%) needed hospital admission. Immunosuppression regimen was changed in all patients of the inpatient group and in 59% of the whole population. The median time of hospital stay was 14 (IQR 7-31) days. Fever and respiratory symptoms were more frequent in the inpatient group. Oxygen therapy was performed in 73% of the patients and 42% needed invasive mechanical ventilation. More than half (61%) of the patients developed acute kidney injury, with 20% of them needing renal replacement therapy. No risk factors for adverse outcomes were identified.
Conclusions: COVID-19 incidence in kidney transplant recipients, although comparable to the general population, seems to be associated with a higher mortality rate. Inpatient recipients, not surprisingly, had the poorest outcomes.



1 – Cumulative incidence of COVID-19 infection in our kidney transplant recipients

OP189 LIVER TRANSPLANT RECIPIENTS WITH SARS-COV-2 INFECTION: RESULTS FROM AN ITALIAN MULTICENTER COHORT

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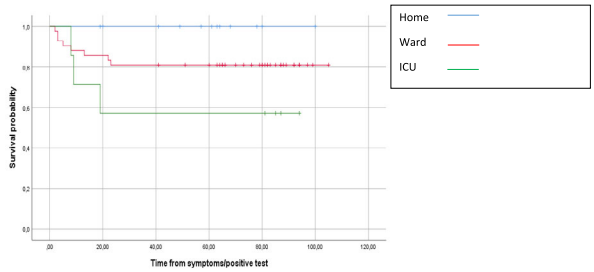
Background: Liver transplant (LT) recipients are potentially vulnerable to SARS-CoV-2 infection, with immunosuppression, aging and cardiovascular co-morbidities likely being risk factors for symptomatic disease and its severe complications. Aim of this study was to evaluate the impact of COVID-19 on LT recipients.
Methods: Data from adults LT with laboratory-confirmed SARS-CoV-2 infection were collected from 6 LT centers of Northern Italy.
Results: Between March 1st and April 30 2020, 61 LT recipients and confirmed SARS-CoV-2 infection were included (median age 64 years, 73% men). At diagnosis, 46 (75%) of patients presented fever, 22 (36%) dyspnea, 29 (47%) dry cough. 49 (81%) patients required hospitalization. Respiratory support was required in 67% of patients: 20 (33%) required O2-supply, 16 (26%) non-invasive ventilation and only 4 (7%) mechanical ventilation. The most frequent prescribed treatments are reported in the table. The immunosuppression regimen (IS) was modified in only 30% of patients. The most common changes were reduction/stopping of CNI drugs (11.5%) and withdrawal of anti-metabolites (11%), or mTOR inhibitors (8%). Twelve patients died after a median of 8.5 days (2-23) from COVID-19 diagnosis, with a 30-day-mortality rate of 20%. Only one patient died for bacterial sepsis, the remaining 11 patients for respiratory failure. In the univariate analysis, factors associated with 30-days mortality were male sex (0.001), age >60 years (0.02), LT performed >5 years before the diagnosis (age of transplant?) (0.12), active smoking (0.05), presence of two or more comorbidities (0.025), heparin treatment (0.093) and tacrolimus-based IS regimen (0.086). In the cox-regression analysis, tacrolimus-based regimen and heparin treatment had a positive independent effect on survival (HR 0.2, CI 0.1-0.7 and 0.3, CI 0.1-0.9, respectively).



Conclusions: The risk of 30-days mortality is LT recipients is 20%. Use of heparin and tacrolimus regimen were associated with a better survival.

OP190 COVID-19 MANAGEMENT IN PATIENTS AFTER HEART TRANSPLANTATION

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Objective: to estimate the frequency and outcomes of COVID-19 in patients after heart transplantation (HTx).
Materials and Methods: Between January 2010 and February 2021 it was performed 156 HTx. All patients were treated with immunosuppression: Tacrolimus, Mycophenolic acid/Everolimus, steroids plus induction (Basilix-imab / Thymoglobulin). We analyzed retrospectively results of 116 patients whose follow-up period was more than 1 month, and they were included in the dispensary observation group.
Results: From February 2020 to February 2021 44% (n = 51; 47 ± 11 years-old, n = 36 - male) of heart transplanted patients were diagnosed with COVID-19: pneumonia was developed in 90% (n = 46) of them; swabs were positive in 71% (n = 36) cases. Six of them faced COVID-19 reinfection in more than 1 month after the first recovery. From the 1st day of the onset of clinical symptoms, mycophenolic acid / everolimus were temporarily discontinued (<14 days). Outpatient treatment included the appointment of antiviral therapy (Oseltamivir), mucoactive agents, levofloxacin and anticoagulants. Steroids were prescribed in 24 cases. Eleven patients with moderate course of COVID-19 admitted to the hospital underwent oxygen inhalation through nasal cannulas. In 2 weeks after the onset of fever 3 recipients with pneumonia (COVID-19 plus bacterial) developed heart transplant dysfunction that was successfully treated by pulse steroid therapy and resumption of Mycophenolic acid in high doses. Four patients are still in the hospital with a positive dynamic on their management, others recovered. One recipient with an interstitial pneumonitis had been diagnosed with COVID-19 (48% of lung involvement), later developed IgG to SARS-CoV-2 and died from a bacterial pneumonia with sepsis. In 6 months after the recovery from COVID-19 Epstein-Barr virus, antibody tests were positive in 66% recipients, no Cytomegalovirus was found.
Conclusion: The possibility of remote consultation of recipients after HTx leads to the timely diagnosis of COVID-19. Starting treatment from the 1st day of the onset of the disease allows you to manage successfully this infectious process. In addition to standard management (antibacterial and antiviral therapy, mucoactive agents, anticoagulants), temporal reduction of immunosuppression is a key to manage COVID-19.

OP191 COVID-19 IN DECEASED RENAL TRANSPLANT RECIPIENTS

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Background: The new coronavirus disease 2019 (COVID-19) became a worldwide pandemic that affects millions of people. Due to a long-term immunosuppression, there is a common belief that kidney transplant (KT) recipients have a high risk of infection and worse outcomes. Data regarding manifestations and outcomes of these patients when infected with SARS-COV2 is still scarce.
Methods: We retrospectively analyzed patients of our kidney transplant unit that had COVID-19, between March 2020 and February 2021. Data related to kidney disease, kidney transplant, symptoms of COVID-19, the immunosuppressive therapy, and the outcomes, were assessed for this study.
Results: Fifteen patients (7.5%) of 201 active patients of our unit were infected with SARSCOV2.
These were mainly man (66.7%), with mean age of 54.26 ± 12.01 years old. Most of the patients had many years of transplant (KT) with a mean of 10.53 ± 4.71 years. Four patients (26.7%) did not have any symptoms. Of

the 73.3% of patients with symptoms, the majority had minor symptoms (60%). The most common symptom reported was fever followed by cough.
Six of the patients (40%) were hospitalized because of COVID-19. Four (26.6%) of these had severe respiratory insufficiency requiring high dose of corticosteroids (CS) and non-invasive ventilation in two cases and intensive care treatment with mechanical ventilation the other two. All the patients were hospitalized for more than 14 days. These patients suffer from complications such as pulmonary thromboembolism, bacteriemia and encephalitis. Two patients died (one of them was 34 years old).
In all hospitalized patients, the antimetabolite drug was discontinued, and the CS dose was increased. In ambulatory patients, the antimetabolite drug dose was reduced or stopped.
We did not identify any risk factor for higher severity of the disease.
Conclusion: The presentation of COVID-19 and its incidence was not different from the general population (national incidence of 8%). Since most patients had minor or no symptoms, we believe that our transplant patients did not behave differently. When they had severe manifestations, both hospitalization time and recovery time increase significantly.

OP192 EPIDEMIOLOGY AND CLINICAL RELEVANCE OF ACUTE KIDNEY INJURY IN COVID-19 KIDNEY TRANSPLANT RECIPIENTS

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Background: The impact of COVID-19 on kidney transplant recipients (KTRs) is still under investigation. Acute Kidney Injury (AKI) is known to be associated with a decreased graft function and patient survival. Causes: systemic inflammation, direct viral infection, nephrotoxic drugs, sepsis. We evaluated prevalence, stage, causes of AKI and mortality in COVID-19 KTRs in our Hospital compared with general COVID-19 hospitalized patients.
Methods: In March-June 2020, we evaluated in 25 COVID- KTRs demographic and transplant characteristics, comorbidities, immunosuppressive therapies (IT). Patients were screened for type of symptoms, management of IT, complications and outcomes. AKI was graded according to KDIGO guidelines, its prevalence in KTRs was compared to the whole hospitalized COVID-19 patients.
Results: During the first wave of pandemic, 945 COVID19 patients were admitted to hospital with AKI prevalence of 37% (stage1 18%, st2 12%, st3 7%). 25 KTRs had a positive molecular diagnosis for SARS-CoV-2: median age was 58 years and 80% were males, 100% had hypertension and 30% had diabetes. Clinical symptoms: fever (95%), cough (47%), dyspnea (30%). Regarding IT, 100% of patients were taking CNI, 64% antimetabolite agents and 76% steroids. Of note, 76% KTRs was hospitalized and 32% were admitted to Intensive Care Unit. All KTRs stopped MMF and increased steroid, concomitantly decreasing CNI trough levels. AKI occurred in 60% of KTRs: stage1 24%, st2 12%, st3 24%; development favored by low basal GFR: 16% required hemodialysis and the most frequent cause of AKI was sepsis. Overall mortality in KTRs was 37%: of note 88% of those patients developed AKI. 1 of KTRs (6%) developed acute rejection (ABMR, DSA negative+TCMR), 30% KTRs decreased significantly their graft function.
Conclusions: AKI prevalence was significantly higher in KTRs than in non-transplanted COVID-19 patients and associated with an increased risk of mortality, of note, mortality rate in KTRs was significantly higher than that observed in the non-transplanted patients. COVID-19 lead to a difficult management of IT, in particular for elevated CNI levels due to associated therapies. COVID-19-associated AKI in KTRs may lead to an increased risk of rejection and premature loss of graft function.

OP193 INFLUENZA VACCINATION IN SOLID ORGAN TRANSPLANT RECIPIENTS: A NATIONWIDE POPULATION-BASED COHORT STUDY

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Background: Influenza is a main vaccine preventable disease among solid organ transplant (SOT) recipients. We evaluated influenza vaccination coverage and vaccine effectiveness in a nationwide cohort of SOT recipients.
Methods: Nationwide register-based cohort study including all SOT recipients living in Denmark during nine consecutive influenza seasons (2007–2016, from December 1st–April 1st in each season). The vaccination status for SOT recipients at each season was registered. We calculated SOT recipients' season-specific risk of hospitalization for influenza, all-cause pneumonia, ICU-admission, and all-cause mortality during the same influenza season. Crude and adjusted Hazard Ratios (HR) with 95% confidence intervals (CI) were estimated using Cox proportional hazards regression models.
Results: 5745 adult SOT recipients (≥18 years) contributed with 11,381person-years of follow-up (PYFU), 52% were never vaccinated before an influenza season. Patients who were vaccinated prior to the beginning of at least one season (n = 2790) were older (median age 53.5 vs. 46.8years, $p < 0.001$) and had more often underlying comorbidities compared to non-vaccinated SOT recipients. Influenza vaccination was significantly associated with a reduced risk of all-cause pneumonia admission (adjusted HR 0.83, 95% CI 0.69-0.99; $p = 0.035$) and all-cause mortality (adjusted HR 0.60; 95% CI 0.47–0.77; $p < 0.001$); but not for ICU-admission (adjusted HR 0.84, 95%CI 0.67-1.06; $p = 0.14$).
Conclusions: The uptake of influenza vaccination in SOT recipients was low. Influenza vaccination was significantly associated with a reduced risk of hospitalization due to pneumonia and all-cause mortality during the same season. Efforts to increase influenza vaccine uptake in SOT recipients are warranted.

OP194 KIDNEY TRANSPLANT PATIENTS ARE ABLE TO GENERATE AND MOUNT VARICELLA ZOSTER-REACTIVE T CELL AND HUMORAL IMMUNITY FOLLOWING VARICELLA ZOSTER VACCINATION

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Background: Reactivation of the latent varicella zoster virus (VZV) can lead to serious complications including shingles and encephalitis with the risk of a fatal outcome in immunocompromised patients. To improve VZV protection, vaccination is recommended for individuals with impaired immunity such as immunosuppressed transplant patients. This study aimed to characterize long-term humoral and cellular immunity following VZV vaccination in kidney transplant recipients (KTx).
Method: In a cross-sectional study, 39 immunosuppressed KTx were vaccinated with Shingrix®. To evaluate long-term humoral responses, VZV specific IgG titers were analyzed one year after the second VZV vaccination. In 23% of patients, pre-vaccination titers were also available. VZV-reactive T cell immunity was characterized by flow cytometry. To elaborate T cell assays for clinical utility, VZV-reactive T cells were compered in blood and peripheral blood mononuclear cells (PBMC) after VZV vaccine stimulation.
Results: VZV-specific IgG titers were detected in all vaccinated patients. In patients with available pre-vaccination titer, we observed a 2.1 ± 1.5 fold titer increase, indicating humoral responsiveness. Both protocols used for the detection of VZV specific T cells allowed the characterization of CD4 and CD8 T cell responses. In 70 % and 65% of the vaccinated KTx, we

observed a CD4+ VZV-specific T cell response in the PBMC and whole blood assay, respectively. Interestingly, CD8+ VZV-reactive T cells were observed in 43% and 57% of PBMC- and whole blood assay, respectively. Neither the amounts of VZV-reactive CD4+ nor CD8+ T cells correlated with the amount of VZV IgG titers.
Conclusion: Despite the immune suppression, the majority of KTx patients develop measurable humoral and T cells response after VZV vaccination. Whether the detected CD8+ T cells result from previous convalescent VZV infection or from vaccine cross-presentation should be addressed in future studies

IRI MECHANISM WITH AN EYE ON TREATMENT

OP195 CORRELATION BETWEEN COLD ISCHEMIA TIME AND THROMBOCYTOPENIA AFTER LIVER TRANSPLANTATION

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Background: Thrombocytopenia is one of the most frequent haematological disorders of end-stage liver disease and can also occur in the early post-transplant period. It can be due to the increased consumption of platelets, as in inflammation. During the transplant, the graft ischemia/reperfusion can cause injuries of the liver tissue, with the development of local inflammatory processes. The aim of our work is to find a relationship between the cold ischemic time(CIT)of the graft and the degree of thrombocytopenia in the early post-transplant period.
Methods: All patients undergoing liver transplant performed in our Center from November 2006 to July 2020 were enrolled. Perfusion machine was considered an exclusion factor. Only grafts from brain-dead(DBD)donors were included. CIT and the nadir platelet(PLT)count recorded in the early post-transplant period were analyzed. In addition, the following recipient parameters were considered: age, gender, body mass index (BMI),model for end-stage liver disease(MELD)score, indication for transplant, pre-transplant haemoglobin(Hb)concentration, pre-transplant platelet count, presence of ascites at transplant, red blood cell transfusion, PLT transfusion, fresh frozen plasma transfusion. Categorical variables were compared with the chi-square test, the continuous variables were analyzed with Student's T test. A regression analysis was performed to find a correlation between the length of CIT and the degree of thrombocytopenia.
Results: We enrolled 359 liver recipients, with a 71.6% male patients, a median age of 58,a median BMI of 25.5 and a median MELD of 22.Ascites was found in 56.8% of cases. The median pre-transplant values of PLT and Hb were 71x10^9/l and 10.4 g/dl, respectively. The median CIT was 480 minutes while the median nadir of post-transplant PLT was 28 x10^9/l. The regression analysis of the two former parameters showed a statistically significant correlation($p = 0.016$),with an inverse proportion.
Conclusions: Our data, in addition to underlining the need for minimize the duration of graft ischemia, prove that the length of CIT can predict an increased risk of thrombocytopenia. Post-transplant assessment is also based on PLT count, but our results demonstrate a crucial importance of CIT in the evaluation of the liver recipient

OP196 DANGER SIGNALS IN ORGAN PRESERVATION SOLUTION AFTER COLD ISCHEMIA IN LIVER TRANSPLANTATION: ACTIVATION OF MACROPHAGES AND ENDOTHELIAL CELLS

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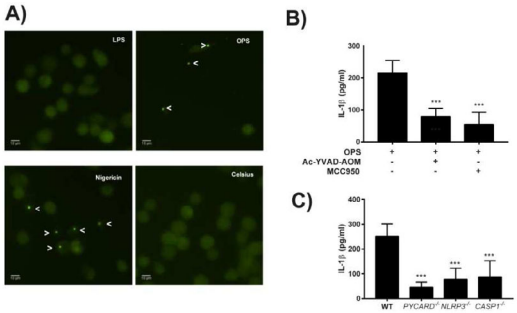
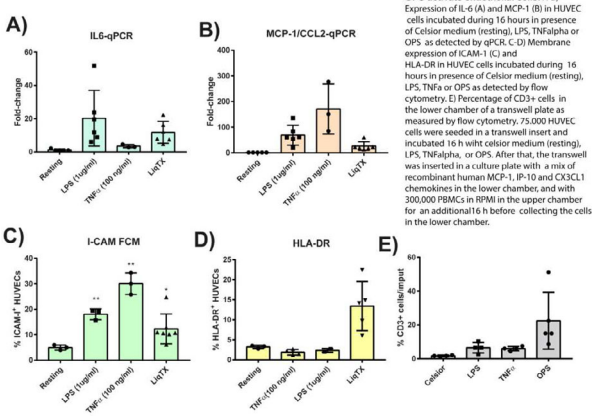
Background: The innate immune system can sense and respond to danger signals (DAMPs). DAMPs are body's own molecules that appear extracellularly after tissue damage, and are able to activate the inflammasome in macrophages and other cells. The inflammasome is a multiprotein complex formed by a sensor (NLRP3), which recruits ASC, which recruits pro-casp1. Casp1 processes IL-1beta which acts on the tissue, causing an inflammatory environment, which can influence the rejection. Likewise, endothelial cells (EC) lining of graft vessels play several roles in allograft rejection. The aim of this work was to detect DAMPs into the organ preservation solution (OPS) after cold ischemia and to study its ability to activate macrophages and EC.
Methods: DAMPs in the OPS after ischemia were quantified. THP1 cells activation was carried out by the detection of IL1β release or the formation of the inflammasome by IF. HUVEC cells activation was analyzed by the expression of IL6 and MCP1, or the expression of membrane ICAM-1 or HLA-DR. Transwell experiments were performed to study the ability of the OPS to attract lymphocytes through HUVEC cells.
Results: OPS activated the release of IL1β in THP1 cells, which was reduced after NLRP3 inhibition or in THP1 KO for NLRP3, ASC or Casp1. Likewise, THP1 cells assembled the inflammatory complex forming specks. Correlation between THP1 activation and the concentration of uric acid, IL-18, fibronectin or soluble ASC specks in the OPS was found. Regarding EC, OPS activated the expression of MCP1 and IL6 in HUVEC cells, similar to LPS or TNFα. Likewise, OPS increased the membrane expression of ICAM-1 and HLA-DR, which favored lymphocyte translocation toward a chemokine gradient.
Conclusions: The analysis and quantification of DAMPs in the post-ischemic OPS could predict the progression of the transplants. Moreover, inhibitors directed against inflammosome pathway could be developed to ameliorate the damage produced by ischemia in donated organs.



OPS activate NLRP3 inflammasome in the monocyte/macrophage THP-1 cell line. A) ASC specks as detected by immunofluorescence. B) Release of IL-1β by LPS primed THP-1 cells after incubation with OPS during 16 hours in the presence of 100 μM of the caspase-1 inhibitor Ac-YVAD-AOM or 25 μM of the NLRP3 inhibitor MCC950. C) Release of IL-1β by LPS primed wild-type (WT), NLRP3−/−, PYCARD−/− and CASP1−/− THP-1 cells after incubation with OPS during 6 hours.



OPS activate endothelial cells. A-B) Expression of IL-6 (A) and MCP-1 (B) in HUVEC cells incubated during 16 hours in presence of Celsior medium (resting), LPS, TNFalpha or OPS as detected by qPCR. C-D) Membrane expression of ICAM-1 (C) and HLA-DR in HUVEC cells incubated during 16 hours in presence of Celsior medium (resting), LPS, TNFα or OPS as detected by flow cytometry. E) Percentage of CD3+ cells in the lower chamber of a transwell plate as measured by flow cytometry. 75.000 HUVEC cells were seeded in a transwell insert and incubated 16 h wiht celsior medium (resting), LPS, TNFalpha, or OPS. After that, the transwell was inserted in a culture plate with a mix of recombinant human MCP-1, IP-10 and CX3CL1 chemokines in the lower chamber, and with 300,000 PBMCs in RPMI in the upper chamber for an additional16 h before collecting the cells in the lower chamber.

OP197 ROLE OF ACETYLCHOLINE IN LIVER GRAFTS FROM BRAIN DEAD DONORS WITH HEALTHY AND MARGINAL LIVERS WITH SIMPLE STEATOSIS OR NON-ALCOHOLIC STEATOHEPATITIS

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Background & Aims: Currently, 80% of grafts are obtained from brain death (BD) donors, which may also show hepatic steatosis, being both risk factors in liver transplantation (LT). Furthermore, a large number of cadaveric donor livers are discarded because of excess steatosis, exacerbating the critical shortage of donor livers. We examined how acetylcholine (ACh) pre-treatment affects non-steatotic and steatotic livers from BD undergoing LT in two preclinical models (simple moderate steatosis and non-alcoholic steatohepatitis, NASH).
Methods: Genetically induced obesity (for simple steatosis) and deficient-choline diet (for NASH) were used. Steatotic and non-steatotic grafts from BD donors were cold stored for 6 h and then transplanted. The treatment with ACh and its action mechanisms were characterized.

Results: The induction of BD reduced ACh (the primary neurotransmitter released by the vagus nerve) in liver graft, whereas ACh administration increased antioxidants and reduced lipid peroxidation, nitrotyrosines and neutrophil accumulation, altogether protecting against damage evidenced by a reduction in the biochemical parameters of hepatic damage and necrotic areas and increasing survival rate. Of scientific and clinical interest, ACh treatment protected liver grafts independently of the type of the liver. ACh treatment in BD donors did not induce changes in NO synthesis but increased PKC activity. In line with this, the concomitant administration of ACh and a PKC inhibitor abolished the benefits induced by ACh.
Conclusions: Our findings propose that the cholinergic anti-inflammatory pathway through treatment with ACh after BD is a feasible and protective strategy to reduce the adverse effects of BD to ultimately improve liver graft quality and reduce the waiting-list for transplant.

OP198 PERSISTENT BILIARY HYPOXIA AND LACK OF REGENERATION ARE KEY MECHANISMS IN THE PATHOGENESIS OF NON-ANASTOMOTIC STRICTURES AFTER LIVER TRANSPLANTATION

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Background: Non-anastomotic biliary strictures (NAS) are a major cause of morbidity after liver transplantation. Although ischemic injury of peribiliary glands (PBGs) and peribiliary vascular plexus (PVP) during transplantation has been associated with the later development of NAS, the exact underlying mechanisms remain unclear. We hypothesized that livers with NAS suffer from ongoing biliary hypoxia and lack of regeneration from PBG stem/progenitor cells. To test this hypothesis, we performed a histomorphologic analysis of livers requiring retransplantation for NAS, hepatic artery thrombosis (HAT), or non-biliary causes of graft failure (controls).
Methods: Forty-two patients, requiring retransplantation for either NAS (n = 18), HAT (n = 13) or non-biliary graft failure (controls; n = 11), were included in this study. Histomorphologic analysis of perihilar bile ducts was performed to assess differences in markers of cell proliferation and differentiation in PBGs, microvascular density, and hypoxia. In addition, isolated human biliary tree stem cells (hBTSCs) were used to examine exo-metabolomics during *in vitro* differentiation toward cholangiocytes.
Results: Bile ducts of livers with NAS or HAT had significantly reduced indices of PBG mass, cellular proliferation (PCNA) and differentiation (mucus production, secretin receptor expression, primary cilia), reduced microvascular density, and increased PBG apoptosis and hypoxia marker expression (HIF-1α), compared to controls. Metabolomics of hBTSCs during *in vitro* differentiation toward cholangiocytes revealed a switch from a glycolytic to oxidative metabolism, indicating the need for oxygen.
Conclusions: NAS are characterized by a microscopic phenotype of chronic biliary hypoxia due to loss of microvasculature, resulting in reduced proliferation and differentiation of PBG stem/progenitor cells into cholangiocytes. These findings suggest that persistent biliary hypoxia is a key mechanism underlying the development of NAS after liver transplantation.

OP199 ANG-3777 TREATMENT ATTENUATES ISCHEMIA-REPERFUSION-INDUCED RENAL INJURY IN RAT AND DOG MODELS

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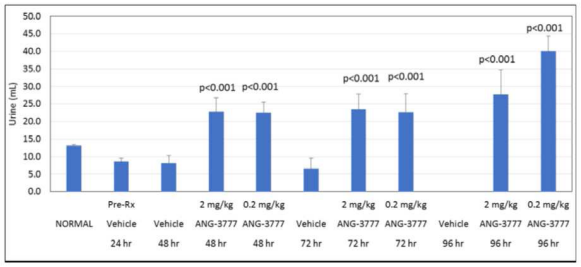
Aim: The effect of ANG-3777, a small-molecule mimetic of hepatocyte growth factor, was evaluated on reducing ischemia-reperfusion-induced renal injury and mortality in rats and dogs subjected to normothermic renal ischemia and reperfusion (nRIR).
Method: In study 1, Sprague Dawley (SD) rats were subjected to 60-min renal ischemia and 24-hr reperfusion. ANG-3777 (2 mg/kg, intravenous [IV]; N = 26) or vehicle (N = 26) was given pre-ischemia and 18 hrs post-reperfusion. At the onset of reperfusion, the contralateral (right) kidney was excised. Blood urea nitrogen (BUN) and creatinine (Cr) levels were assessed at 24 hrs pre-sacrifice. In study 2, SD rats were subjected to 60-min renal ischemia and 96-hr reperfusion and were dosed 24-hr post-onset of reperfusion then once daily (QD) x 96 hrs with ANG-3777 IV (0.2, N = 48; or 2 mg/kg, N = 15) or vehicle (N = 70). Blood and urine were collected daily. In study 3, beagle dogs were subjected to 120-min renal ischemia and 7d reperfusion. For immediate treatment, dogs were dosed QD with ANG-3777 IV (10 mg/kg; N = 4) or vehicle (N = 4), and reperfusion was started. For delayed treatment, dogs were dosed QD with ANG-3777 IV (10 mg/kg; N = 5) 1d post-ischemia-reperfusion. Dogs were dosed QD through Day 4. Renal function was assessed daily for 8d.
Results: Following immediate ANG-3777 treatment, reduction in BUN was statistically significant ($p < 0.05$) in male rats, whereas reduction in Cr was statistically significant ($p < 0.05$) in male and female rats. For dogs initiating ANG-3777 24-hr post-ischemic injury, treatment significantly reduced BUN and Cr ($p < 0.005$) vs vehicle at all times and for both doses with exception of BUN at 48 hrs post-reperfusion for the 0.2 mg/kg group. ANG-3777 (2 and 0.2 mg/kg) significantly increased urine output vs vehicle at 48, 72, and 96 hr post-reperfusion ($p < 0.001$; Fig 1). Survival was significantly greater ($p = 0.035$) at Day 4 for 0.2 mg/kg ANG-3777 (10 of 15; 67%) vs vehicle (24 of 70; 34%). In the dog model, immediate and delayed treatments with ANG-3777 reduced BUN and Cr ($p < 0.0001$) vs vehicle.
Conclusions: ANG-3777 attenuated renal dysfunction, increased urine output, and improved survival in animals subjected to nRIR. ANG-3777 was efficacious, both when administered at onset of ischemic injury and when initiated 1d post-ischemic injury.

Figure 1 Effect of Delayed Treatment with ANG-3777 on Urine Output in Rats Subjected to Renal Ischemia and 96-Hour Reperfusion



hr=hour; Rx=treatment; SEM=standard error of the mean.
Note: Data were collected from surviving rats. The data are presented as mean ± SEM. Normal rats are untreated rats that were not subjected to renal ischemia.

OP200 INFLUENCE OF THE ANESTHETIC METHOD ON THE OUTCOME OF A RODENT MODEL OF INTESTINAL ISCHEMIA-REPERFUSION INJURY

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Introduction: Knowledge on intestinal ischemia reperfusion injury (IRI) has significantly increased due to the development of preclinical models. However, the anesthetic method can have an important impact on the outcomes,

measured in these models, including survival. Surprisingly, this has been rarely studied. Gas-anesthesia with Isoflurane (Iso) is more easily administered than intraperitoneal injection of Ketamin-Xylazine (K+X) but may have distinct hemodynamic and/or anti-inflammatory effects. Using a rat model of IRI, we evaluated the effect of 3 anesthetic methods.
Materials and Methods: IRI was provoked by clamping the superior mesenteric artery in male Sprague-Dawley rats for 60min. Three different anesthetic methods were studied (n = 6/group; 60min. reperfusion): i/ K+X; ii/ K+X+O_2; iii/ Iso+O_2. 1/ Blood pressure; 2/ serum endotoxin as marker for intestinal permeability (ELISA); 2/ Vascular permeability: endothelial glycocalyx markers (syndecan-1 and heparan sulfate (ELISA)); 3/ Inflammatory cytokines: IL-6 (ELISA), IL-1β (qPCR); and 4/ 7-day survival were determined (n = 10/group).
Results: K+X and K+X+O_2 led to progressive hypotension post-reperfusion whereas blood pressure normalized rapidly with Iso+O_2. Iso+O_2 improved intestinal/vascular permeability, and systemic inflammation. Survival improved by addition of 100% O_2 (K+X+O_2) and even further with Iso+O_2. (See table).
Conclusion: K+X anesthesia provokes an ongoing low-flow ischemia during reperfusion, in our rat model of intestinal IRI, which negatively affects the outcomes. O_2-supplementation and particularly O_2 + Isoflurane led to improved survival, intestinal and vascular permeability, and inflammation. As demonstrated with this study, the potential effect of anesthesia on the measured outcome parameters needs to be considered in the choice of anesthetic method and in the interpretation of data.

Outcome *median (range)*	A K+X + 21% O_2	B K+X + 100% O_2	C Iso + 100% O_2	p-values *(A vs. B) / (A vs. C)*
Endotoxin *(U/mL)*	0.07 (0.06 – 0.15)	0.02 (0.01 – 0.03)	0.01 (0.01 – 0.01)	0.0012 / 0.0002
Syndecan-1 *(ng/mL)*	125 (91 – 170)	95 (79 – 109)	78 (63 – 103)	0.0183 / 0.0011
Heparan Sulfate *(ng/mL)*	243 (104 – 394)	68 (12 – 137)	81 (12 – 168)	0.2745 / 0.5064
IL-6 *(pg/mL)*	1703 (471 – 2445)	889 (440 – 2003)	150 (61 – 202)	0.3376 / 0.0002
IL-1β *(fold change)*	5.3 (3.2 – 12.6)	8.2 (3.2 – 12.6)	2.3 (0.5 – 6.1)	0.7381 / 0.0511
7-day survival	0%	70%	90%	<0.0001

OP201 CLINICALLY APPLICABLE INTRALUMINAL PRESERVATION OF HUMAN SMALL BOWEL DOES NOT REDUCE HISTOLOGICAL DAMAGE COMPARED TO STANDARD VASCULAR FLUSH

Guido Trentadue[1,2], Mathias Clarysse[3], Anne Marye de Jong[1,2], Jasper van Praagh[1,2], Emilio Canovai[3], Jan Willem Haveman[1,2], Gursah Kats-Ugurlu[1,2], Jacques Pirenne[3], Henri Leuvenink[1,2], Klaas Nico Faber[1,2], Laurens Ceulemans[3], Gerard Dijkstra[1,2]
[1]University Medical Center Groningen, Groningen, Netherlands; [2]University of Groningen, Groningen, Netherlands; [3]University Hospitals Leuven, Leuven, Belgium

Background and Aims: Luminal preservation (LP) of the small intestine with polyethylene glycol (PEG) has shown benefits on graft viability in preclinical studies. This study examined the applicability and effects of LP with a PEG-based bowel preparation fluid compared to vascular flush (VF) with University of Wisconsin (UW) or Institut Georges Lopez-1 (IGL-1) solution.
Methods: Responsible committees of transplant institutes in the Netherlands and Belgium approved this study. Donors who fulfilled the standard transplant criteria (age extended to ≤70) were randomised into VF only or additional LP (see table). Ice-cold PEG (6.4% w/v) was administered through a nasoduodenal tube during procurement. Jejunum and ileum were sampled at procurement (t = 0) and after 7, 14 hours of cold storage (CS). Primary outcome was the histological Chiu/Park score, statistical analyses used were Kruskal-Wallis and Dunn's multiple comparison tests.
Results: Twenty-five donors with similar demographic variables were included. Procurement duration was not influenced by LP. On average, 1.5 (± 0.5) litres of PEG were used for LP, which reached the terminal ileum in all cases but one. Histological analyses showed that the intestine can withstand up to 14 hours of CS without severe morphological changes regardless of use of LP. The histopathological scores of all groups were similar at all studied time points. However, a proportional decrease in the severity of the lesions of 67% and 40% was found in the IGL-1 LP group after 7 and 14 h CS, respectively, resulting in less areas of necrosis.

	Control		Treatment	
Groups	UW	IGL-1	UW+PEG	IGL-1+PEG
N	7	6	6	6
Procedure	VF		VF + LP	
Age (median, IQR)	32 (30–40)	52 (40–64)	56 (43–65)	51 (30–67)
Duration LP (minutes, median, IQR)			52 (16–82)	90 (79–100)
Chiu/Park at t = 7 (median, min–max)	3 (2–4)	3 (2–6)	3 (3–5)	3 (1–6)

Conclusions: This study shows that LP with a PEG-based solution applied during procurement is feasible but not superior to standard VF. Further studies on epithelial integrity and function with different LP fluids together with reperfusion studies are needed to establish the role of luminal preservation in intestinal transplantation.

OP202 CALCIUM CARBONATE NANOPARTICLES IN AN EX VIVO RAT INTESTINAL PERFUSION MODEL: PREVENTION OF ISCHEMIC INJURY IN COLON AND SMALL INTESTINE

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Introduction: Intestinal ischemia is a pathological condition consequent to various clinical situations and it plays a crucial role in the intestinal transplantation. Recently, the calcium-sensing receptor (CaSR) has been suggested to play an important role in the homeostasis during the ischemia, and in particular in the cascade of ischemia/reperfusion injury.
Methods: In this study, Calcium Carbonate Nanoparticles (CaCO3 Sky-Spring Nanomaterials, Inc, Houston), were used as an innovative tool to lead to activation of the intestinal CaSR.
We used an ex-vivo intestinal perfusion model to perfuse the rat intestine with different CaCO3 concentration in different conditions, in order to evaluate the effect of CaCO3 in the intestinal ischemia.
Results: The small intestine (Proximal, Middle and Distal segments) and Distal Colon, when exposed to 100% N2, developed ischemic damage in comparison to intestine perfused with Normal HEPES. In the same ischemic environment, the presence of of 1, 2.5 and 5 mM of NanoCaCO3 prevented the ischemic damage.
Conclusion: Nanoparticles can mitigate ischemic damage in the distal colon. These results suggest that the use of nanoparticles may be a potential method of reducing ischemic and inflammatory injury during intestinal harvesting/transport perfusion and in inflammatory bowel diseases

OP203 L-ARGININE PREVENTS ISCHEMIC INJURY IN EXPLANTED RAT INTESTINAL REGIONS IN AN EX VIVO PERFUSION MODEL

Michele Finotti[1], Maria Barahona[2], Chiara DI Renzo[1], David Mulligan[2], Jonh Geibel[2], Francesco D'amico[1,2]
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Background: The small intestine is one of the most sensitive organs to ischemia. We hypothesize that perfusion with L-Arginine of explanted intestinal segments from rats can reduce the ischemic injury.
Methods: 45 small intestinal segments were harvested from male rats and connected to an ex vivo intestinal perfusion device providing independent intraluminal and extraluminal perfusion. Ischemic damage was induced by perfusing the extraluminal side with Ringer-HEPES buffer saturated with 100% N_2. Segments were then perfused intraluminally with and without l-arginine. We conducted a set of experiments with intraluminal perfusion with both l-arginine and L-NAME, an inhibitor of the nitric oxide – arginine pathway. Control segments were perfused extraluminally under non-ischemic conditions and intraluminally with and without l-arginine. In all experiments, the fluorescence signal of FITC-inulin was periodically measured in order to calculate average fluid secretion, which directly corresponds to the extent of ischemic injury.
Results: In both ischemic and control non-ischemic conditions, intestinal segments perfused with l-arginine had significantly decreased secretion over time in comparison to intestinal segments perfused without l-arginine ($p < 0.0001$). Perfusion with L-NAME abrogated the protective effect of l-arginine.
Conclusion: Intraluminal perfusion with l-arginine reduced ischemic damage to harvested intestine exposed to a ischemic environment and under physiological conditions.

OP204 ATTENUATION OF INTESTINAL ISCHEMIA-REPERFUSION INJURY IN A RODENT MODEL BY INTRAVENOUS ADMINISTRATION OF POLYETHYLENE GLYCOL

Mathias Clarysse[1,2,3], Alison Accarie[4], Arnau Panisello-Roselló[5], Ricard Farré[4], Tim Vanuytsel[3,4,6], Laurens Ceulemans[3,7,8], Jacques Pirenne[2,3]
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Introduction: Polyethylene glycol (PEG) is safely used in various clinical settings and are included in certain organ preservation solutions. They are known as non-toxic, water-soluble polymers. Protective effect of intravenous (IV) administration of high-molecular weight PEG (35kDa) has been shown for liver and heart ischemia-reperfusion injury (IRI). This was mainly due to anti-inflammatory, anti-apoptotic, immunosuppressive, and membrane stabilising effects. In a rodent model of intestinal IRI, we studied the potential effect of IV PEG administration.
Materials and Methods: To provoke intestinal IRI, the superior mesenteric artery was clamped for 45min. in male Sprague-Dawley rats. Three different groups were investigated (n = 6/group; 60' reperfusion): i/ Control: NaCl; ii/ PEG 50mg/kg; and iii/ PEG 100mg/kg. PEG (IIBB Barcelona, Spain) or NaCl were administered IV in single dose, 10min. before ischemia. 1/ Serum endotoxin as marker for intestinal permeability (ELISA); 2/ Vascular permeability: endothelial glycocalyx markers (syndecan-1 and heparan sulfate (ELISA)); 3/ Inflammatory cytokines: IL-6 (ELISA), IL-1β and TNF-α (qPCR); 4/ Anti-inflammatory cytokine: IL-10 (qPCR); and 5/ 7-day survival were determined (n = 10/group).
Results: Highest-dose PEG IV administered as pretreatment, statistically improved intestinal and vascular permeability, and inflammatory profile. A trend for better survival was seen with increasing dosage of PEG. (See table).
Conclusion: IV preconditioning with high-dose, high-molecular weight PEG attenuates the damage provoked by intestinal IRI. The easy availability of PEG opens the road for further investigations in intestinal IRI, organ preservation and transplantation.

Outcome *median (range)*	A Control	B PEG 50mg/kg	C PEG 100mg/kg	p-values *(A-B) / (A-C)*
Endotoxin *(U/mL)*	0.06 (0.02 – 0.27)	0.06 (0.03 – 0.12)	0.03 (0.02 – 0.04)	0.9999 / 0.1175
Syndecan-1 *(ng/mL)*	120 (86 – 168)	116 (79 – 160)	91 (79 – 119)	0.8541 / 0.0734
Heparan Sulfate *(ng/mL)*	193 (98 – 281)	192 (12 – 319)	12 (12 – 95)	0.9999 / 0.0088
IL-6 *(pg/mL)*	612 (259 – 1287)	496 (236 – 1172)	228 (146 – 357)	0.9074 / 0.0231
IL-1β *(fold change)*	1.1 (0.6 – 1.4)	0.5 (0.3 – 0.8)	0.5 (0.2 – 0.9)	0.0048 / 0.005
TNF-α *(fold change)*	1.1 (0.7 – 1.5)	0.8 (0.5 – 1.0)	0.8 (0.5 – 1.0)	0.8655 / 0.9223
IL-10 *(fold change)*	1.4 (0.2 – 2.7)	0.8 (0.4 – 1.3)	0.5 (0.1 – 0.7)	0.0829 / 0.0217
Survival	40%	70%	80%	0.19 / 0.075

OP205 IN VIVO PHOSPHORYLATION OF C-MET BY ANG-3777, A HEPATOCYTE GROWTH FACTOR MIMETIC

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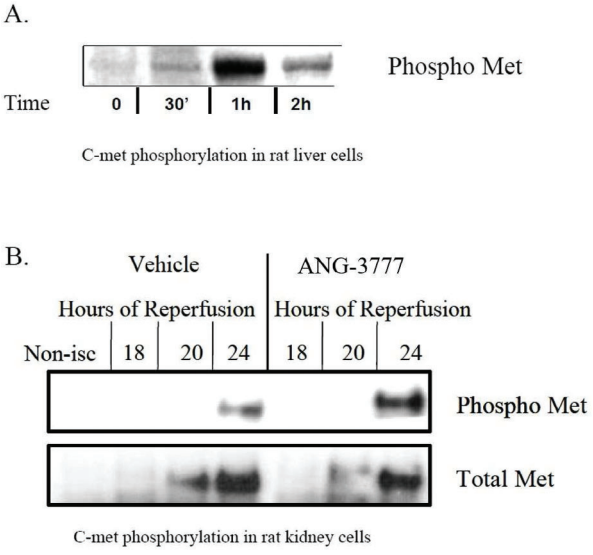
Background: The biological effects of hepatocyte growth factor/scatter factor (HGF) and its mimetics are mediated by a signal cascade initiated by binding of HGF to its tyrosine kinase receptor, c-Met, which is constitutively expressed at low levels on the epithelial cells of most tissues and unregulated in the setting of injury Interaction of HGF and c-Met causes activation of cellular pathways that results in cellular proliferation. We examined the ability of ANG-3777 to phosphorylate c-Met *in vivo* in rat hepatocytes, and rat kidney in a model of renal ischemia and reperfusion
Methods: For the hepatocyte study, adult male Sprague-Dawley (SD) rats were treated with 40 mg/kg ANG-3777 or vehicle via intraperitoneal injection. Animals were sacrificed at 0-minute, 30-minute, 1-hour, and 2-hour time points and perfused with phosphate-buffered saline for 5 minutes. The liver samples were collected, normalized by weight, and homogenized. The sample aliquots were diluted with radioimmunoprecipitation assay buffer and analyzed by Western blot using rabbit phosphorylated-c-Met antibody. For the model of renal ischemia and reperfusion, adult male SD rats were subjected to 60-minute normothermic unilateral ischemia followed by 24-hour reperfusion; ANG-3777 (2 mg/kg, intravenously) or vehicle was administered at the onset of reperfusion and again at 18 hours of reperfusion. Animals were sacrificed at 18, 20, or 24 hours of reperfusion, and total c-Met and phosphorylated c-Met in kidney extracts were assessed by Western blot analysis.
Results: For *in vivo* liver cells, ANG-3777 phosphorylated c-Met with peak intensity at 1-hour post-injection (Figure 1A). Ischemia-reperfusion injury provoked a time-dependent increase in kidney total c-Met. In rat kidney cell, 60 minutes of ischemia followed by 24 hr reperfusion provoked a time-dependent increase in kidney total c-Met in both vehicle and ANG-3777-treated rats. Treatment with ANG-3777 (2 mg/kg, i.v.) resulted in a robust increase in phosphorylated c-Met levels (Figure 1B).
Conclusion: ANG-3777 induces phosphorylation of c-Met in normal rat liver in a time-dependent manner, and in a rat renal ischemia reperfusion model, ANG-3777 induced a robust increase in phosphorylated c-Met at 24 hours post-reperfusion.

Figure 1.



OP206 OXYGENATED VERSUS NON-OXYGENATED FLUSH OUT AND STORAGE OF DCD PORCINE LIVERS

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Background: During donor procurement and subsequent static cold storage (SCS), hepatic adenosine triphosphate (ATP) levels are progressively depleted. Loss of ATP during ischemia contributes to ischemia-reperfusion injury (IRI). This study sought to investigate a simple and cheap approach to prevent ATP depletion and subsequent IRI using a porcine liver reperfusion model.
Methods: After 30 min warm ischemia, porcine livers were flushed via the portal vein with cold (○4C) non-oxygenated University of Wisconsin (UW) solution (n = 6, control) or with oxygenated UW (n = 6, OxyFlush). Livers were then subjected to 4 hr SCS in non-oxygenated (control) or oxygenated (OxyFlush) UW, followed by 4 hr normothermic reperfusion using autologous whole blood. ATP levels were compared and hepatobiliary function and injury were assessed.
Results: At the end of SCS, ATP levels were higher in the OxyFlush group compared to the control group (median 0.26 vs. -0.68 μmol/g protein, p = 0.045). After reperfusion, ATP levels were similar in both groups. All livers produced bile and metabolized lactate, and there were no differences between the groups. Grafts in the OxyFlush group had lower blood glucose levels after reperfusion compared to controls (p = 0.04). Biliary pH, glucose and bicarbonate were not different between the groups. Alanine aminotransferase and lactate dehydrogenase levels in the SCS solution and during

reperfusion were also similar. There were no differences in bile duct and parenchymal histological injury between the groups.
Conclusions: Oxygenated flush out and storage of DCD porcine livers prevents ATP depletion during ischemia, but this does not seem sufficient to mitigate IRI.

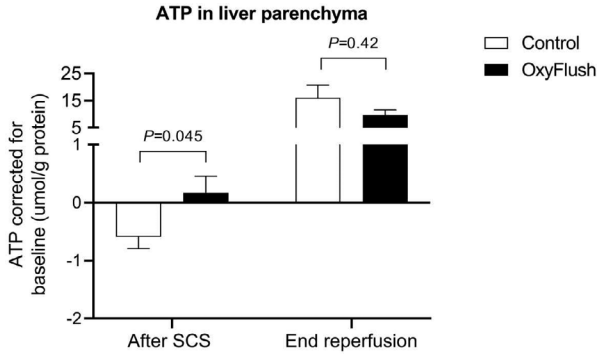

Figure 1. ATP levels at the end of static cold storage and reperfusion.

OP207 THE IRRADIATION-INDUCED RENAL ISCHEMIC PRECONDITIONING IS BLUNTED BY THE ORAL ADMINISTRATION OF THE ANTI-ANGIOGENIC AGENT, SUNITINIB

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Background: Whole-body irradiation induces renal ischemic preconditioning (RIP) in mice, possibly via neoangiogenesis. Here, we test whether Sunitinib-mediated inhibition of angiogenesis prevents the irradiation-associated RIP.
Methods: After kidney-centred irradiation (8.56 Gy), the right kidneys were removed and harvested, and the left kidneys underwent ischemia (30min) / reperfusion (48h) (I/R) at Day 14. Three groups were compared (n = 8/group): 1/irradiation; 2/irradiation and gavage with Sunitinib (40 mg/kg) from D2 to D13; 3/control group without irradiation or gavage. Renal sections from the 3 groups post-I/R were stained by Periodic Acid Schiff (PAS). I/R-associated acute tubular necrosis was blindly evaluated by a renal pathologist using the histological Jablonski score. The expression of inflammatory markers CD11b and F4/80 was comparatively quantified by immunostaining. The expression of vascular markers CD31 and VEGF in non-ischemic kidneys were quantified by real-time qPCR.
Results: One-way analysis of variance followed by Tukey's test showed that, following I/R, serum levels of urea (BUN) and creatinine (SCr) were significantly lower in pre-irradiated mice compared to controls (BUN: 106.1 ± 33.6 vs. 352.2 ± 54.3mg/dl; SCr: 0.3 ± 0.13 vs. 1 ± 0.2mg/dl), as well as in pre-irradiated mice compared to the irradiated mice fed with Sunitinib (BUN: 106.1 ± 33.6 vs. 408.4 ± 54.9mg/dl; SCr: 0.3 ± 0.12 vs. 1.5 ± 0.3mg/dl). No difference was observed between the Sunitinib group and the control group. Jablonski's severity score was lower in pre-irradiated mice compared to control group and Sunitinib group ($p < 0.01$). The renal infiltration by CD11b- (560 ± 32 vs. 308 ± 21/mm²) and F4-80 positive cells (430 ± 35 vs. 312 ± 19/mm²) was significantly reduced in the irradiated group compared to controls. At mRNA levels, the renal expression of VEGF and CD31 was increased in the irradiated group but not in the Sunitinib group ($p < 0.01$).
Conclusions: Renal irradiation before I/R is associated with preserved renal function and attenuated inflammation post-I/R. Sunitinib administration prevents the irradiation-induced RIP.

OP208 ILOPROST INFUSION ACCELERATES THE RECOVERY OF RENAL FUNCTION IN PATIENTS EXPERIENCING IRI-RELATED DELAYED GRAFT FUNCTION AFTER KIDNEY TRANSPLANT

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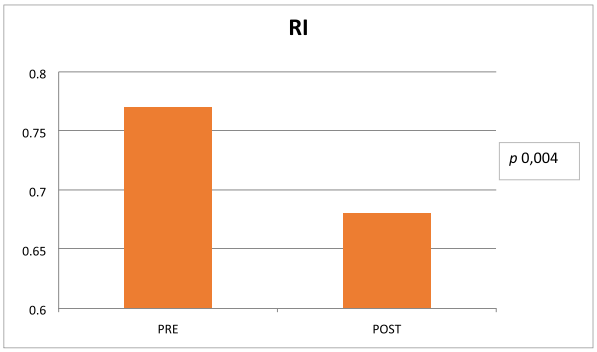
Background: Iloprost is a synthetic analogue of prostacyclin, which closely mimics its whole range of physiological effects. It shows vasodilating, antiplatelet, cytoprotective and immunomodulating properties and it is therefore suited for treatment of micro and macrocirculatory diseases and pulmonary hypertension. Pre-clinical studies have shown that Iloprost can ameliorate renal ischemia-reperfusion injury (IRI) and has the potential to serve as a therapeutic agent to protect the kidney against IRI. Renal ischemia–reperfusion injury is almost unavoidable in kidney transplantation and contributes significantly to delayed graft function (DGF), which significantly affects long-term graft survival. Currently, there are no pharmacological treatments available for prevention or amelioration of ischemia reperfusion -induced renal injury.
Methods: This is a retrospective monocentric study on 13 kidney transplant recipients whose clinical course was characterized by DGF. They were treated with intravenous Iloprost, in addition to standard immunosuppressive therapies. We measured serum creatinine concentrations, diuresis and resistive index (RI) using renal doppler sonography, prior and after the beginning of Iloprost infusion.
Results: The mean duration of Iloprost therapy was 7 days. Mean creatinine pre was 9.24 ± 1.79 mg/dl vs 3.58 ± 1.52 mg/dl post; mean diuresis pre was 485 ± 498 ml vs 1546 ± 420 ml post; mean RI pre was 0.77 ± 0.08 vs 0.68 ± 0.06 post. 23% of donors was ECD. Iloprost has shown a statistically significant reduction of renal resistive index and a statistically significant increase of diuresis.
Conclusions: An established treatment to reduce IRI related DGF after kidney transplantation does not exist. Our data suggest that a well-timed Iloprost infusion could improve IRI related DGF and functional recovery after kidney transplantation. More studied are needed to confirm our data.

Table 1. Mean resistive index (RI) prior and after the beginning of iloprost infusion.
p 0.004. SD pre-iloprost infusion 0.08. SD post-iloprost infusion 0.06.



POT POURI OF CARDIOTHORACIC TRANSPLANTATION: FOLLOW YOUR OWN STAR

OP235 ANASTOMOSIS TIME IS AN INDEPENDENT RISK FACTOR FOR PRIMARY GRAFT DYSFUNCTION AFTER LUNG TRANSPLANTATION: A RETROSPECTIVE COHORT STUDY

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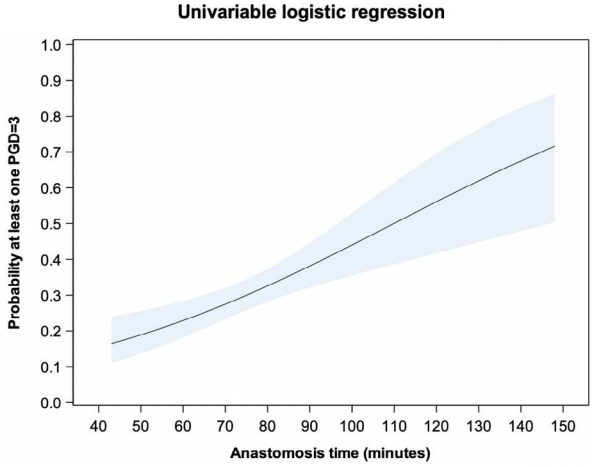
Background: Primary graft dysfunction (PGD), mainly resulting from the deleterious cascade following ischemia and reperfusion injury, remains a major obstacle after lung transplantation (LTx). The incidence of PGD is associated with increased early morbidity and mortality. In liver and kidney transplantation, it has been shown that prolonged anastomosis time (AT) is an independent risk factor for impaired short-term outcome. We aim to investigate if AT during LTx is an independent risk factor for development of PGD grade 3 (PGD3), the most severe form of PGD.
Methods: Data on all primary sequential single-lung transplantations (SSLTx) from our single-center cohort between 2008 and 2016 were retrospectively collected. Univariable and multivariable logistic regression analysis was performed to study the association of AT with any PGD3 within the first 72 hours post-transplant.
Results: Out of 484 first SSLTx, 451 (93%) had available data on AT and PGD. PGD3 occurred in 138 (30.5%) patients. AT was independently associated with development of PGD3 in univariable (odds ratio (OR) per minute 1.025, 95%CI (1.012-1.037), p = 0.0001) and multivariable (OR per minute 1.019, 95%CI (1.003-1.034), p = 0.016) logistic regression analysis. There was no evidence that the relation between AT and PGD3 differed between recipients from donation after brain death versus donation after circulatory death donor lungs.
Conclusions: This study identified for the first time AT as independent risk factor for development of PGD3 post-SSLTx. We suggest that the implantation time should be kept short and the lung cool to decrease PGD-related morbidity and mortality post-SSLTx.



OP236 FEASIBILITY OF SURVEILLANCE AFTER LUNG TRANSPLANTATION USING MULTIVOLUME MRI INSTEAD OF IONIZING RADIATION TECHNIQUES IN CYSTIC FIBROSIS PATIENTS

Alessandro Palleschi[1,2], Francesca Pennati[3], Caterina Salito[3], Irene Borzani[4], Andrea Gramegna[5,6], Valeria Musso[1,2], Letizia Corinna Morlacchi[6], Margherita Cattaneo[1,2], Rosaria Carrinola[2], Gianpaolo Carrafiello[7], Mario Nosotti[2,5], Andrea Aliverti[3]

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Background: Lung transplantation (LT) is a consolidated therapy for end-stage cystic fibrosis (CF) patients. Post-LT surveillance requires several computed tomography (CT) scans, entailing a high radiological hazard for such young immunosuppressed patients. The acquisition of a conventional proton magnetic resonance (^{1}H-MRI) at different lung volumes has been recently used to study ventilation impairment. We aimed to investigate the use of multivolume ^{1}H-MRI to identify signs of lung structural damages in CF patients after LT, and to compare regional variations on ^{1}H-MRI with classical markers of acute lung allograft dysfunction.
Methods: CF patients, of both sexes and all ages, undergoing LT at our centre in Milan were enrolled. Re-LT and single LT were excluded. As per our surveillance protocol, multivolume CT scan and pulmonary function tests are performed 3, 6 and 12 months after LT. In addition, a conventional ^{1}H-MRI of the lung was obtained. Four classes of ventilation defects were considered (consolidation, air trapping, low ventilation, healthy). To process CT and MR images, we developed an algorithm describing ventilation distribution in the follow-up of LT patients.
Results: From August 2018 to September 2019, 35 patients underwent LT. Twelve recipients had an indication other than CF and one underwent re-LT, and they were therefore excluded. We enrolled 22 subjects; due to early graft failure (1 case) and logistical issues (4 cases), only 17 patients completed the 1-year protocol. Our results show that expiratory-inspiratory difference in MRI signal-intensity correlated to both CT-density ($r = 0.52$, $p < 0.0001$) and FVC percent predicted (%pred)($r = 0.42$, $p = 0.03$). Linear correlation between MRI and CT functional maps including all categories of ventilation defects is $r = 0.79$ ($p < 0.0001$). MRI percent volumes of low ventilation correlated to FEV1 %pred ($r = -0.41$, $p = 0.01$) and to FVC % pred ($r = -0.63$, $p < 0.001$).
Conclusions: Our study confirms the feasibility of a novel radiation-free imaging technique for young CF patients' surveillance after LT, providing new functional imaging biomarkers for early detection of acute lung allograft dysfunction. This approach may increase the quality of diagnostic examination by improving survival and quality of life of CF patients undergoing LT.

OP237 CHRONIC KIDNEY DISEASE: A FREQUENT COMPLICATION IN PATIENTS WITH LUNG TRANSPLANT

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Background: Chronic kidney disease (CKD) is a growing complication after a lung transplantation (LTx). The older age and higher comorbidity of recipients, immunosuppressive (IS) toxicity and longer survival have increased the progression of CKD. There's no enough information about risk factors or specific preventive management of CKD.
Methods: Retrospective, single-center study including all patients with LTx follow-up by Nephrology among 2007 and 2020. Demographic, comorbidity and intercurrent events, renal function impairment, proteinuria and IS were analyzed since LTx. We use composite renal event (MARE) defined as need of renal replacement therapy (RRT), death or double serum creatinine.
Results: 69 LTx receptors (79.4% double LTx) were followed in specific outpatient Nephrology clinic. 52.2% male, mean age at LTx 48.3 years (SD 16.6). Etiology of lung disease: cystic fibrosis (30.4%), obstructive lung

disease or emphysema (33.3 %), interstitial disease (30.4%). Infection was the most frequent event (89.7%) and 49.3% presented neoplasic illness.
Mean time from LTx untill 1st nephrologist evaluation was 6,6 years (2 months – 19.9 years) and presented arterial hypertension (81.2%), diabetes mellitus (52.2%), dyslipidemia (50.7%), 60.3% former smokers and 26.1% had suffer from a previous CV event. At 1st evaluation, mean eGFR was 30.9 ml/min (SD 15.3) with a CKD distribution: 39.4% CKD 3; 45.5% CKD 4; 12.1% CKD 5 (<15) (table 1).
Clinical study and biopsy define CKD etiologies: CNI toxicity (68.1%) thrombotic microangiopathy (11.6%), tubular (10.1%), vascular (7.3%) and glomerulopathies (2.9%).
88.4% patients reached MARE at the end of the study. 24 patients required RRT (mean time since LTx 9.2 years) and thereafter 10 received a kidney transplantation (KTx). At the end of follow-up 15 patients died (14 were in RRT), 5 continues on HD and 5 with a functional KTx and 44 patients are still without RRT.

Conclusions:

- CKD is an increasing complication of LTx and its progression is associated with higher mortality.
- Although CNI toxicity is leading cause, early nephrologist evaluation may identify other causes and develop renoprotective measures, which may reduce CKD progression and improve prognosis.
- Many patients would need RRT and are eligible for KTx, although RRT increases mortality risk.

		1 month post lung Tx	3 month	1 year	2 year	4th year	6th year	8th year	10th year
	n	69	69	65	65	57	46	28	23
Dialysis	serum cr (mg/dl)	0,8 (0,2)	1,4(0,6)	1,6(0,5)	2,2(1,6)	2,0(0,6)	2,3(1,2)	2,0(0,5)	2,1 (0,5)
	GFR (ml/min)	98,9 (22,3)	58,0 (26,2)	46,6(20,6)	37,7(17,6)	34,5 (11,4)	34,2 (18,6)	34,6 (12,8)	31,7 (12,8)
	UACR (g/g)	0,02 (0,06)	0,05(0,1)	0,06(0,2)	0,1 (0,3)	0,2(0,4)	0,3 (0,5)	0,3(0,5)	
Not Dialysis	serum cr (mg/dl)	0,9 (0,3)	1,1 (0,5)	1,5(0,5)	1,6(0,5)	1,7(0,6)	1,7 (0,6)	1,8 (0,6)	1,7(0,5)
	GFR (ml/min)	95,2 (17,0)	70,1 (23,5)	51,9 (17,9)	47,6(18,4)	44,3 (19,2)	46,2 (21,4)	45,3(23,8)	46,3(21,2)
	UACR (g/g)	0,09 (0,129	0,03 (0,05)	0,04(0,09)	0,04(0,08)	0,06(0,1)	0,2 (0,2)	0,2 (0,4)	
Total	serum cr (mg/dl)	0,8 (0,2)	1,2(,5)	1,5(0,5)	1,8 (1,0)	1,8(0,6)	1,9(0,9)	1,8(0,6)	1,8(0,5)
	GFR (ml/min)	96,6(19,0)	65,8(25,0)	49,8(19,0)	46,9(18,6)	40,6(17,3)	41,7 (21,0)	41,5(21,0)	41,2 (19,7)
	UACR (g/g)	0,04 (0,1)	0,04 (0,07)	0,05(0,1)	0,08(0,2)	0,1(0,2)	0,2(0,3)	0,2(0,4)	

OP238 COMPARATIVE ANALYSIS OF SURVIVAL OF PATIENTS WITH CONGENITAL HEART DISEASE TRANSPLANTED FROM HEART OR HEART-LUNG

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Background: Congenital heart disease (CHD) has a high infant mortality rate in its severe forms. Thanks to advances in surgical treatment and subsequent management of CHD patients, a high percentage of children with CHD now reach adulthood. This has led to a progressive increase in the number of these patients with advanced heart failure who eventually require heart transplantation (HTx) or combined heart-lung transplantation (HLTx).
Methods: This is a retrospective analysis of all HTx and HLTx in our hospital. ReHTx and other combined transplants are excluded. The HTx are divided into 2 groups (CHD or non-CHD) according to the recipient and their baseline characteristics and survival are analysed comparatively. Similarly, HLTx are subdivided and analysed. Comparative analysis between HTx and HLTx is not performed.
Results: A total of 930 HTx (including reHTx and combined) were performed between 1987 and 2020, 872 (93.8%) were first HTx and 42 (4.5%) were HLTx (all bipulmonary).
In the HTx group (table 1), 18 recipients (2.1%) have CHD and 854 (97.9%) do not. CHD recipients are younger (34.6 years vs. 51.9), have a lower BMI and almost none have cardiovascular risk factors (CVRF). Only 1 (6.7%) CHD was transplanted urgently (vs. 30.1). Median survival (figure 1a) was significantly longer in the CHD group (18.8 vs. 10.7 years, p = 0.027). This could be due to the fact that CHD patients are younger and have fewer comorbidities.
In the HLTx group (table 1), 18 recipients (42.8%) have CHD and 24 (57.2%) do not. In this group, CHD patients are also younger (32.1 vs. 38.6 years), predominantly female (66 vs. 33%) and have a lower BMI. In both groups, there are few patients with CVRF and none of the patients were transplanted while previously on circulatory support. Mean survival (figure 1b) shows a significant trend, being higher in the CHD group (7.4 vs. 4.7 years, p = 0.162).
Conclusions: Patients with congenital heart disease increasingly represent a greater percentage of patients who require HTx or HLTx. In both modalities, CHD patients have a longer survival than non-CHD, which may be due to the fact that these patients are generally younger and without major comorbidities.

Table 1. Baseline characteristics

	HEART TRANSPLANT (n=872)			HEART-LUNG TRANSPLANT (n=42)		
	Non-CHD (n=854)	CHD (n=18)	p	Non-CHD (n=24)	CHD (n=18)	p
Recipient						
Age, years	51.96±11.9	34.67±17.5	0.001	39.58±9.9	32.1±10.1	0.022
Male, n (%)	702 (82.2)	13 (72.2)	0.276	16 (66.7)	6 (33.3)	0.032
Body Mass Index, kg/m2	28.85±4.1	20.89±3.4	<0.001	24.9±5.02	20.4±2.97	0.001
Hypertension, n (%)	288 (33.7)	0 (0)	0.00	2 (8.33)	1 (5.6)	0.738
Diabetes, n (%)	84 (9.8)	0 (0)	0.161	0	0	
Dyslipidaemia, n (%)	351 (41.1)	1 (5.6)	0.002	2 (8.33)	0	0.191
Smoker last year, n (%)	220 (25.8)	1 (5.6)	0.051	2 (8.33)	1 (5.6)	0.729
Creatinine, mg/dL	1.14±0.41	1.20±0.40	0.547	0.93±0.23	0.95±0.18	0.817
NYHA IV, n (%)	236 (27.6)	4 (22.2)	0.611	3 (12.5)	9 (50)	0.008
Previous cardiac surgery, n (%)	166 (19.4)	11 (61.1)	<0.001	2 (8.3)	7 (38.9)	0.017
IV inotropes, n (%)	278 (32.5)	2 (11.1)	0.053	5 (20.8)	1 (5.6)	0.146
Circulatory assistance, n (%)	141 (16.5)	1 (5.6)	0.212	0	0	
Donor						
Age, years	36.47±13.5	31.39±14.01	0.115	28.3±10.8	34.2±13.5	0.137
Male, n (%)	540 (63.2)	9 (50)	0.484	13 (54.2)	3 (16.7)	0.013
BMI, kg/m2	25.15±3.6	24.3±4.9	0.329	24.07±4.1	21.9±3.2	0.070
Donor-recipient interaction						
Donor female/Recipient male, n (%)	228 (26.7)	6 (33.3)	0.536	6 (25)	6 (33.3)	0.554
Predicted Heart Mass Ratio	1.01±0.19	1.09±0.19	0.075	1.02±0.21	1.02±0.18	0.994
Surgical procedure						
Urgent code, n (%)	257 (30.1)	1 (6.7)	0.024	3 (12.5)	2 (11.1)	0.891
Cold ischemia duration, min	148.8±56.8	149.8±76.4	0.958	184.4±83.08	190.3±75.1	0.815

CHD: Congenital Heart Disease; NYHA: New York Heart Association
Continuous variables are presented as mean ± standard deviation

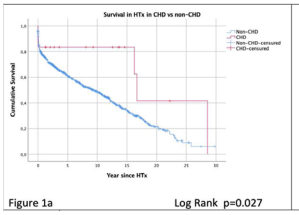

Figure 1a Log Rank p=0.027

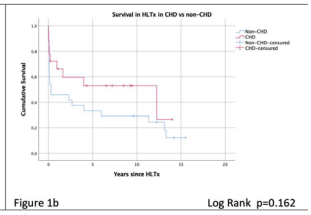

Figure 1b Log Rank p=0.162

OP239 CURRENT STATUS AND DEVELOPMENT OF CARDIOPULMONARY TRANSPLANTATION IN SPAIN

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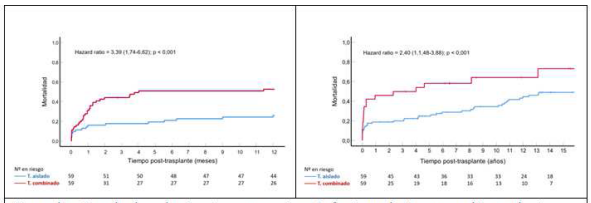
Background: Combined heart-lung transplantation (HLTx) prolongs the life of patients with coincident severe cardiac and pulmonary heart disease.

HLTx has been carried out in Spain for more than 30 years. The objective of the study was to evaluate the Spanish experience by analyzing the global results of HLTx and depending on the etiologies that indicate it.
Methods: A retrospective study on 1751 consecutive transplants (HLTx: 78, HT: 1673) performed in Spain from January 1990 to December 2020 in the two centers accredited for HLTx. Overall survival was compared, adjusted for clinical profile and etiological subgroups. Seven subgroups were considered: 1) Cardiomyopathy with pulmonary hypertension (CM + PH). 2) Eisenmenger syndrome. 3) Congenital heart disease. 4) Idiopathic pulmonary arterial hypertension (IPAH). 5) Cystic fibrosis. 6) Chronic obstructive pulmonary disease (COPD) / Emphysema. 7) Diffuse interstitial lung disease (ILD).
Results: There were differences between HLTx and HT in unadjusted ($p < 0.001$), adjusted ($p < 0.001$), and with a similar clinical profile ($p = 0.04$) survival. Early mortality was 44% and that of the rest of the follow-up was 31%. There were differences in the median survival between the subgroups. Thus, MC + PH (18 days), ILD (29 days), and congenital (114 days) were low; intermediate in Eisenmenger syndrome (600 days); and more prolonged in IPAH (1654 days), COPD / Emphysema (1918 days) and cystic fibrosis (2448 days).
Conclusion: HLTx is a procedure with low activity in Spain and with high mortality. The etiological analysis of the causes that indicate it is of utmost interest to make the most of the organs and improve survival.

Table: Multivariate analysis for mortality in the first year post-transplantation

Variable	HR	IC 95%	Significación estadística
Cardiopulmonary Transplant	3.16	2.19-4.55	<0.001
Female receptor	0.78	0.54-1.15	0.21
Predicted Heart Mass (receptor)	1.00	0.99-1.00	0.21
Bilirubin > 2 mg/dL	1.28	1.00-1.63	0.05
Glomerular filtration (mL/min/1,73 m^2)	0.99	0.99-1.00	0.003
Previous infection	1.23	0.88-1.72	0.22
Mechanic ventilation	1.37	1.01-1.85	0.04
Previous sternotomy	1.68	1.37-2.07	<0.001
Donor age (years)	1.01	1.00-1.02	0.03
Female donor	0.99	0.78-1.26	0.93
Predicted Heart Mass (donor)	1.00	0.99-1.00	0.44
Urgent Code	1.30	1.01-1.67	0.04
Ischemia time (minutes)	1.00	1.00-1.00	0.68
Variable (adjusted by "inverse probability weighting").			
Cardiopulmonary Transplant	2.26	2.00-2.56	<0.001
Inverse probability weighting	1.01	1.01-1.01	<0.001

Figure: Cumulative mortality curves (Kaplan Meier) for heart-lung transplantation vs. Isolated heart transplantation for propensity score-matched populations.



Hazard ratio calculated using Cox regression. Left: Cumulative mortality to the 1st year. Right: Cumulative mortality at follow-up.
Red: Cardiopulmonary transplant
Blue: Heart transplant

OP240 IS HEART TRANSPLANTATION A VALUABLE OPTION IN PATIENTS WITH SYSTEMIC RARE DISEASES?

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Background: Current guidelines affirm that systemic diseases with a predominant heart involvement may be listed for heart transplantation (HTx); however, they have been historically considered as potential contraindications to HTx. Aim of the study was to assess the cardiovascular, non-cardiovascular outcome and quality of life (QoL) of HTx patients with systemic diseases.
Methods: We have reviewed all the cases of HTx in rare diseases performed in our Cardiothoracic Department from 1985 to Feb 2021. QoL was assessed by SF-36 questionnaire.
Results: Since 1985, out of the 680 HTx performed at our Centre, 25 patients had a systemic rare disease as cause of advanced heart failure (HF) needing of HTx (Table 1). Considering the HF phenotypes, the most predominant was the dilatative, followed by infiltrative cardiomyopathy, hypertrophic, and restrictive phenotypes.
Mean age was 45 ± 15 years old, mostly males (76%); 3 patients were in urgent list. The peripheral muscular involvement was present in 11 cases; however, almost all patients retained the capacity of walking. Donors mean age was 37 ± 11 and 16 (64%) were male. Eleven (44%) were considered non-standard donors (ischemic time >4 hours in 5 (20%), cardiac arrest or LVEF <50% or coronary artery disease in 3 (12%), previous drug abuse in 2 (8%).
Considering the cardiovascular outcome, the survival was 100% at 30-days, 96% and 90% at 1 and 5 years after HTx (median follow-up of 69 (range 7-318) months (Fig.1). Rejection >2 grade was in 6 (24%), while cardiac allograft vasculopathy in 4 (16%). Related the non-cardiovascular outcome, there was a vision and muscular worsening in 6 (24%) and 9 (36%) cases, while 3 (12%) developed severe psychosis. Lastly, the SF-36 questionnaire showed lower scores for the items related to Physical Component Summary, while similar scores compared to the general population for the Mental Component Summary (Fig.1).
Conclusions: Patients with systemic disease showed a satisfied general survival and their cardiovascular outcome is similar to other HTx patients. The ocular and muscular worsening related to the systemic disease could be very frequent, conditioning the QoL. The relapse of the systemic disease is a rare event, although possible. These preliminary encouraging results need to be validated in larger population and in longer follow-up.

Pathology	Age	M/F	Systemic involve	Ocular involve	Muscular involve	Other	Emergency	NHYA	MCS
AL Amyloidosis	46	M	Kidney	-	-	Lymphnodes	-	3	-
AL Amyloidosis	54	M	-	-	-	Dupuytren sdr	-	2	-
AL Amyloidosis	65	F	-	-	-	-	-	3	-
SSA Amyloidosis	65	M	-	-	-	-	-	3	-
AL Amyloidosis	50	F	-	-	-	Macroglossia	-	2	+
AL Amyloidosis	60	F	-	-	-	-	-	3	-
SSA Amyloidosis	66	M	-	-	-	-	-	3	-
AL Amyloidosis	46	M	Kidney	-	-	-	+	3	-
AL Amyloidosis	59	M	-	-	-	-	-	3	-
Anderson-Fabry disease	56	M	Kidney, Brain	-	-	-	-	3	+
Becker Dystrophy	18	M	-	-	+	-	-	3	-
Becker Dystrophy	47	M	-	-	+	-	-	3	-
Becker Dystrophy	42	M	-	-	+	-	-	3	-
Becker Dystrophy	38	M	-	-	+	-	-	4	-
Becker Dystrophy	57	M	-	-	+	-	-	3	-
Kearns-Sayre syndrome	16	M	Brain, Kidney	+	+	-	+	4	-
Emery-Dreifuss dystrophy	28	M	-	-	+	-	-	2	-
Danon disease	29	M	-	-	+	-	-	4	-
Danon disease	40	F	-	+	+	-	-	3	-
Danon disease	34	M	-	-	+	-	-	3	-
Danon disease	52	F	-	-	+	-	-	4	-
Sarcoidosis	41	M	Lungs	-	-	-	-	2	-
Sarcoidosis	56	M	-	-	-	-	-	2	-
Loeffler sdr	34	M	-	-	-	-	+	4	+

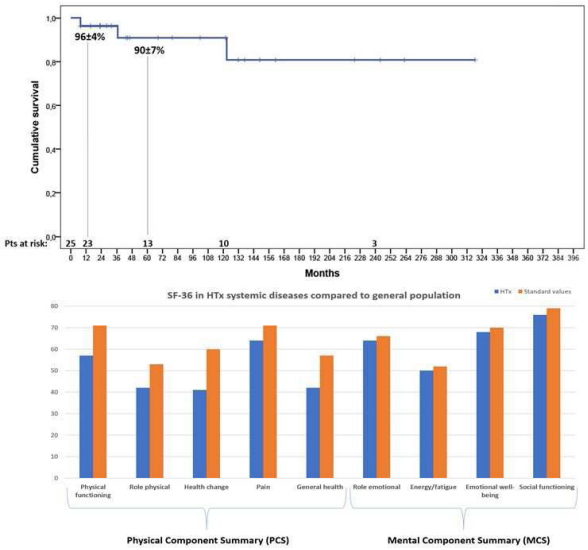

Figure 1

OP241 SINGLE-CENTER ASSESSMENT OF CARDIAC TRANSPLANTATION RESULTS COMPARING URGENT VERSUS ELECTIVE REGIMEN

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Introduction: Organs' shortage for heart transplantation and recipients' conditions led to an increasing request to the National urgency program since 2006. Moreover, from 2020, three levels of allocation have been created: elective, Level I (national priority access) and Level II (regional macro-area) urgency. The aim of this study is to analyze the characteristic of donors and recipients in our center and the results for different levels of urgency.
Methods: Of 684 cardiac transplantation since 1991, 306 were performed from 2006 until August 2020. Of them 54 (17.6%) in urgency (UG). Patients on ECMO 24, 8 in IABP and 13 on inotropes, 4 arrhythmic storms and 5 complicated LVAD. From January 2020, 5 from 16 were on Urgency (31.5%).
Results: The donors of urgent patients were younger than the elective ones (EG) (8.9 vs 42.4 years (p 0.06). Donor's gender (68% males) and cause of brain death (brain trauma 44.4%, and cerebral hemorrhage 35.2%) were similar. In the UG population, recipients were predominantly male (68.5 % vs 77.4 % EG p 0.17) and significantly younger than in the EG (46.4 vs 52.2 years, p 0.001). Mean ischemic time was longer in UG (211 minutes vs 191 minutes, p 0.01). Severe Early Graft Failure (EGF) requiring ECMO occurred in 27 (8.8%) patients, (8% EG vs 12.9% in UG, p 0.2). In hospital mortality was 8.8% in the whole group (11.1% UG vs 8.3% EG p 0.46). Episodes and grade of rejection did not diverge between groups. Mean follow-up time for UG was shorter (53.6 vs 75.6 months (p 0.007). Overall survival at 5 and 10 years was 88.1% and 72.8% vs 79.7% and 62% in EG vs UG group (p 0.13).
Conclusions: This retrospective analysis with the different allocation systems shows little differences in terms of mortality and complications. Although the clinical characteristics of the emergency/urgent transplant recipients are more thoughtful, they do not significantly impact on the results, denoting the importance of donor quality in this population.

OP242 WAITLIST OUTCOMES AFTER THE IMPLEMENTATION OF A NEW ALLOCATION SYSTEM FOR URGENT HEART TRANSPLANTATION IN ITALY

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Background: Donor availability strongly limits accessibility to heart transplantation (HT), affecting mortality rate of sicker patients in waiting lists. Heart allocation algorithms aim to prioritise patients at higher risk for death or deterioration. Because of a steady increase in the number of patients included in the national urgency (NU) program during the last 5 years, including a growing number of exemptions that topped to 46% of the total requested in 2019. Hypothesizing that the algorithm, developed in the late 90's, was not effective in capturing the current features of most of severe heart failure patients listed, we developed a new algorithm (NA) redefining the criteria to access urgency programs, introducing two urgency tiers, as opposed to the single tier of the previous system. Herein, we compared waiting list outcomes of urgent patients listed under NA, with those listed according to the old algorithm (OA) during a same span of time, one year before.
Methods: Data from all waitlisted patients, including urgency requests are prospectively collected in a mandatory national registry. Herein we compare the period March-December 2019 (OA) with March-December 2020 (NA) in terms of waitlist outcomes, number of exemptions and rate of urgency requests.
Results: During the OA period, 87 patients were listed on NU, and 12 (14%) died or deteriorated. Exemption was asked for 40 (46%) patients. During the NA period, 101 patients were listed in the two tiers, with only 9 (9%) exemptions ($p < 0.01$); 12(12%) died or deteriorated ($p = 0.8$). Rate of urgent HT during OA and NA over the total of HT was similar (70 (38%) vs. 40%; $p = 0.7$). ECMO was a major indication for urgency during both period, but was less frequently used during the NA period (20(20%) vs. 25 (29%); $p = 0.15$)
Conclusions: The NA allowed to significantly reduce the requests for exemptions, while keeping stable the rate of urgency requests and waitlist survival. A prolonged observation time is needed to confirm the initial reduction in ECMO use and the impact on post-transplant survival of the NA.

OP243 LIFE OF AN HEART FAILURE AND HEART TRANSPLANT CENTER IN THE COVID ERA: NEVER GIVE IN TO FEAR, USE TELEMEDICINE

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Background: Italy faced COVID-19 as first country outside China: there was a urgent need of finding spaces for these patients (pts), reducing visits and continuing to take care of heart failure (HF), heart transplanted (HT) or LVAD pts. We used telemedicine (TM) as a strategy, even if its role in this very sick cohort is largely unknown.
Methods: During the first and the second virus wave (03-05 and 11/2020), we made a phone triage about COVID symptoms to all pts a few days before the scheduled visit, and decided to make either a phone (PV) or an in presence (IV) visit, selecting for IV those listed for HT, with LVAD, recently HT or scheduled for a biopsy or a RHC. In PV, we assessed symptoms, drugs, and programmed a subsequent IV. COVID-19 swabs were performed 48 hrs before RHC or biopsy. The endpoints were the combined incidence (survival rates) at 6 months of: MACE (HF hospitalization, CV death and need for anticipated IV) in HF/VAD group and MACE, rejection and any cause-hospitalization in HT group.
Results: Among 592 pts (59±16 y, 250 HT, 318 HF, 23 LVAD), 52% had a PV and a subsequent IV was scheduled after 3±2 months. Pts on PV were healthier: in HF-VAD group they were less frequently listed, with severe MR, post-capillary PH (pC-PH), LVAD (2/21), had higher LVEF; in HT group they received less frequently HT in the last year, and had fewer cellular (>1B) or pAMR rejection ($p < 0.05$ all). The PV group had a lower incidence of the endpoints in both HF/VAD and HT cohorts (94.7 ± 1.8% vs 81.1 ± 3.2%; 95.7 ± 1.8% vs 81.1 ± 3.8%, $p < 0.01$). Overall, the predictors of the endpoints at multivariate analysis were pC-PH and PV (HR: 7.7 and 12.0, $p < 0.01$) and a recent >1B/pAMR rejection (HR: 7.6, $p < 0.01$) in the HF/VAD and HT group respectively. Overall, we had no cases of COVID-19 in IV; 20 pts got infected at home in a context of 5% prevalence in our region and

up to 40% of hospital beds dedicated to COVID in the peak pandemic phases.
Conclusions: Our retrospective study, reporting an organization set up in a emergency situation and replicated thereafter, shows that TM can be safely used to manage HF, VAD and HT patients, selecting for IV only those listed, with pC-PH, LVAD or a recent cellular rejection or pAMR. These data support the efforts in the use of TM and of devices able to monitor changes in hemodynamics in these patients in the current pandemic times and may be even subsequently.

OP244 MYOCARDIAL SCAR BURDEN CORRELATES WITH CHANGES IN LEFT VENTRICULAR DIASTOLIC FUNCTION AND NT-PROBNP SERUM LEVELS IN HEART TRANSPLANT RECIPIENTS

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Purpose: While myocardial scar burden represents an established prognostic marker in heart failure, its predictive value after heart transplantation (HTX) remains poorly defined. We sought to investigate clinical correlates and prognostic impact of myocardial scar burden in patients after HTX.
Methods: In a prospective single-center study we enrolled 112 consecutive HTX recipients transplanted between 2010 and 2018. At 1-year after HTX all patients underwent cardiac echo and cardiac magnetic resonance imaging (cMRI). Cardiac echo was repeated again at 2 years after HTX. Patients with a history of primary graft dysfunction, CAV or rejection >1R were excluded. Allograft myocardial fibrosis was quantified with late gadolinium enhancement (LGE).
Results: Extent of myocardial fibrosis was above mean value (2.5%) in 54 patients (48%; Group A) and below mean in 58 patients (52%; Group B). The two groups did not differ in age (56 $\pm$ 8 years in Group A vs. 54 $\pm$ 11 years in Group B, p = 0.10), gender (male: 87% vs. 73%, p = 0.25), creatinine (92 $\pm$ 19 μmol/L vs. 92 $\pm$ 22 μmol/L, p = 0.96), troponin (0.01 $\pm$ 0.02 μg/L vs. 0.01 $\pm$ 0.04 μg/L, p = 0.64), tacrolimus trough levels (7.1 $\pm$ 1.8 μg/L vs. 7.3 $\pm$ 1.6 μg/L, p = 0.54), hypertension (48% vs. 63%, p = 0.11) or diabetes (33% vs. 24%, p = 0.11). The two groups also had similar rates of pre-transplant LVAD support (11% in Group A vs. 17% in Group B, p = 0.33) and comparable allograft ischemic time (185 $\pm$ 76 min vs. 199 $\pm$ 69 min, p = 0.30). On echocardiography we found no differences in LVEF (66.4 $\pm$ 8.4% in Group A vs. 66.1 $\pm$ 6.8% in Group B, p = 0.79), TAPSE (1.57 $\pm$ 0.34 cm vs. 1.58 $\pm$ 0.38 cm, p = 0.80) or E/e' (10.6 $\pm$ 3.9 vs. 11.2 $\pm$ 4.1, p = 0.42). However, we found significantly higher NT-proBNP levels in Group A than in Group B (median: 693 pg/mL (IQR 210-716) vs. 366 pg/mL (IQR 160-514), p = 0.04). At 1 year after cMRI E/e' increased in Group A, but not in Group B (+2.8 $\pm$ 4.9 vs. 0.1 $\pm$ 4.9, p = 0.004); the same was observed when analyzing changes in NT-proBNP (+93.4 $\pm$ 455.9 pg/mL in Group A vs. -12.1 $\pm$ 158.2 pg/mL in Group B, p = 0.03).
Conclusion: In HTX recipients myocardial scar burden appears to correlate with NT-proBNP serum levels. High myocardial scar burden at 1 year post-HTX may be associated with subsequent increases in left ventricular filling pressures and could thus serve as a predictor of adverse remodeling of the transplanted allograft.

OP245 DECREASED CIRCULATING CD34+ CELL COUNT IS ASSOCIATED WITH CORONARY ALLOGRAFT VASCULOPATHY IN HEART TRANSPLANT RECIPIENTS

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Background and Aims: The underlying mechanisms of coronary allograft vasculopathy (CAV) after heart transplantation (HTX) remain incompletely understood. Since $CD34^+$ cells represent one of the central determinants of coronary vascular homeostasis we investigated the potential association between CAV and circulating $CD34^+$ cell count in HTX recipients.
Methods: In a single-center pilot study we included 23 adult heart transplant recipients without history of multi-organ transplantation or oncologic therapy. All patients underwent coronary CT angiography (CTA)and the presence of CAV was defined in accordance with the ISHLT criteria. At the time of CTA, we collected blood samples and measured circulating $CD34^+$ cell count using Beckman-Coulter Navios EX flow cytometry with standard antibodies according to ISAGE protocol.
Results: CAV was present in 8 patients (35%; Group A) and absent in 15 patients (65%; Group B). The two groups did not differ in age (60 $\pm$ 8 years in Group A vs. 57 $\pm$ 15 years in Group B, p = 0.60), gender (male: 100% vs. 83% in Group B, p = 0.32), underlying disease etiology (ischemic: 65% vs. 35%, p = 0.22), presence of hypertension (87% vs. 63%, p = 0.22), diabetes (38% vs. 44%, p = 0.22) or renal insufficiency (38% vs. 31%, p = 0.51). Furthermore, donor age (46 $\pm$ 8 years in Group A vs. 41 $\pm$ 12 years in Group B, p = 0.29), allograft ischemic time (201 $\pm$ 61 min vs. 187 $\pm$ 54 min, p = 0.42), tacrolimus trough levels (6.7 $\pm$ 1.2 μg/L vs. 6.4 $\pm$ 1.4 μg/L, p = 0.77), and NT-proBNP serum levels (512 $\pm$ 261 pg/mL vs. 453 $\pm$ 349 pg/mL, p = 0.97) were comparable. Although total leukocyte count was similar in both groups (6.7 $\pm$ 3.2x10^9/L in Group A vs. 6.4 $\pm$ 1.9x10^9/L in Group B, p = 0.60), we found significantly lower $CD34^+$ cell count in Group A compared to Group B (1.12 $\pm$ 0.23x10^6/L vs. 2.07 $\pm$ 0.81x10^6/L, p = 0.01). When stratifying patients according to $CD34^+$ cell count, patients with cell count below the median displayed increased incidence of CAV compared to patients with cell count above the median (58% vs. 10%, p = 0.02).
Conclusion: In heart transplant recipients decreased circulating $CD34^+$ cell count appears to be associated with CAV. Further clinical trials are warranted to better define the underlying mechanisms and investigate the potential of $CD34^+$ cells in the prevention and treatment of CAV in this patient cohort.

OP246 MONITORING LYMPHOCYTE SUBPOPULATIONS IN PERIPHERAL BLOOD IN HEART TRANSPLANT RECIPIENTS. A NEW TOOL TO DETECT CAV?

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Background: Heart transplantation (HT) is the treatment of choice for a selected group of patients with advanced heart failure. Cardiac allograft vasculopathy (CAV) is one of the main limiting long-term survival causes. Although non-immunological factors are involved, previous studies suggested that T lymphocytes play a main role.
Our objective was to evaluate correlation between the values of peripheral lymphocyte subpopulations and CAV in HT recipients.
Methods: Between January 2014 and October 2019, 79 consecutive HT recipients were included. CAV was evaluated by coronary angiography or coronary CT at one month, one, two and five years, and graded according ISHLT recommendations. $CD4^+$ effector T cells ($CD4^+CD25^+CD127^+$) and regulatory T cells (Tregs)($CD4^+CD25^+CD127^-$) lymphocyte subpopulations were analyzed in peripheral blood by flow cytometry at the time of coronary study and thereafter once a year. The significance of differences was evaluated using *t*-test. Significance level was established at $p < 0.05$.
Results: Baseline characteristics are summarized in Table 1. Basiliximab was used as an induction therapy in 96% of patients. Immunosuppression therapy included tacrolimus (97.5%), mycophenolate mofetil (88.6%) and prednisone (100%). Median follow-up period was 48.5 months. 28 patients developed CAV (CAV1 33.3%, CAV2 1.5%, CAV3 4.2%).
We found that at the second and third years after HT, patients with CAV had a greater number of Treg lymphocytes compared to those who did not present CAV, and these differences were significant ($p < 0.01$). No significant differences were observed between circulating $CD4^+$ T cells and presence of CAV.
Conclusions: In our study, HT recipients that developed CAV had significantly higher peripheral Treg lymphocytes absolute values than HT recipients without CAV. Monitoring lymphocytes subpopulations in peripheral blood may be useful to detect CAV development in HT recipients. More studies are needed.

Age, in years	51.2 ± 1.6
Male	57 (72.2%)
Reason for heart transplantation	
Ischemic cardiomyopathy	23 (29.1%)
Idiopathic dilated cardiomyopathy	22 (27.9%)
Congenital heart disease	12 (15.2%)
Other	22 (27.9%)
Immunosuppressive therapy	
Tacrolimus	77 (97.5%)
Mycophenolate mofetil	70 (88.6%)
Prednisone	79 (100%)
Everolimus	5 (6.3%)
Cyclosporine	2 (2.5%)
Azathioprine	1 (1.3%)
Transplant vasculopathy	28 (38.9%)
Mild (CAV 1)	24 (33.3%)
Moderate (CAV 2)	1 (1.5%)
Severe (CAV 3)	3 (4.2%)
Diabetes	26 (32.9%)
Statin therapy	74 (93.7%)
Creatinine, mg/dl	1.5 ± 0.1

Values are expressed as means ± SD, or number

Table 1 Baseline characteristics

OP247 RISK FACTORS AND OUTCOMES OF ACUTE KIDNEY INJURY AFTER HEART TRANSPLANT

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Background: Acute kidney injury (AKI) is a severe complication in the peri-operative phase of heart transplant (HTx) and is defined as an increase in serum creatinine from baseline values, with or without reduction in urine output. This study aims to investigate risk factors for peri-operative AKI and its outcomes.
Methods: This study is a retrospective analysis of all 220 HTx recipients at our Centre between January 1st, 2008 and June 30th, 2018. We excluded multiorgan transplants, re-HTx and patients needing pre-HTx dialysis. Study endpoint of AKI was defined by KDIGO criteria. Demographic, clinical and hemodynamical data have been collected from clinical charts and institutional database. Mortality was recorded at discharge and at 1-year follow-up.
Results: Study population consisted of 190 patients, mainly male (141, 74.2%) with a mean age of 52.5 ± 11.2 years. 28 patients were on mechanical circulatory support (MCS) at the time of HTx (1.6% LVAD, 7.9% ECMO, 5.2% IABP). At 12 hours from Htx 35 patients (19%) had a mean arterial pressure (MAP) <70 mmHg. AKI occurred in 124 patients (65.3%) and 34 patients (18%) needed dialysis. PGD needing MCS occurred in 27 patients (14.2%) and 18 patients (9.5%) required ECMO implantation. In-hospital and 1-year mortality were 11% and 15.3%. We identified three risk factors for AKI (table 1): recipient age >60 years (p = 0.0118), eGFR <45 ml/min (p = 0.0403) and a MAP <70 mmHg 12 hours after Htx (p = 0.0149). At multivariate analysis only MAP <70 mmHg at 12 hours emerged as an independent risk factor (OR 2.8, CI 1.1–7.9). Patients with AKI had a higher in-hospital mortality (16.9% vs 0%, p < 0.001). Among patients discharged alive, there was no difference in 1-year mortality.
Conclusions: AKI is a common complication after HTx and is associated with significantly higher rate of in-hospital mortality. AKI is related to recipients' characteristics and post-HTx hemodynamics. In particular, hypotension in the first 12 hours in ICU emerged as an independent risk factor.

TOT n= 190	AKI n=124	no AKI n=66	p	OR multivariate analysis	p multivariate analysis
Age > 60 years	n= 42 (33.8%)	n= 11 (16.7%)	**p= 0.0118**		p=0.06
eGFR < 45 ml/min	n= 37 (30.3%)	n= 11 (16.7%)	**p= 0.0403**		p= 0.19
eGFR ml/min	60 ± 24	67 ± 24	p= 0.06		
Diabetes	n= 30 (25%)	n= 11 (20%)	p=0.5		
MAP < 50 mmHg during CPB	n= 6 (0.4%)	n= 2 (0.3%)	p= 0.72		
MAP < 70 mmHg after 12h in ICU	n= 29 (24.2%)	n= 6 (9.4%)	**p= 0.0149**	2.8 CI 1.1 – 7.9	**p= 0.03**
MAP mmHg after 12h in ICU	76 ± 13	81 ± 8	**p= 0.007**		
MCS pre Htx	n= 20 (16.1%)	n= 8 (12.1%)	p= 0.458		
Male sex	n= 91 (73.4%)	n= 50 (75.8%)	p= 0.722		
Induction	n= 97 (79%)	n= 58 (88%)	p=0.14		

OP248 THE RISK OF SKIN CANCER DOES NOT CORRELATE WITH VITAMIN D SERUM LEVELS IN HEART TRANSPLANT RECIPIENTS

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Background: There are inconsistent data on the association between vitamin D (VitD) serum levels and risk for skin cancer in general population. Since heart transplant recipients routinely receive VitD supplements, we investigated a potential association between VitD serum levels and the incidence of skin cancer in this patient cohort.
Methods: We analyzed baseline and follow-up clinical, biochemical and malignancy-related data of all heart transplant recipients at our center between 2004 and 2015. All patients received induction therapy with basiliximab and steroids and TAC/MMF/steroids maintenance immunosuppression therapy, and received vitamin D supplementation with cholecalciferol (7000 IE/week) and alphacalcidiol (0.25 mcg qd) for osteoporosis prevention. At 1-year after heart transplantation, vitamin D (25-hydroxy vitamin D) serum levels were measured using chemiluminescence method with commercially available kit.
Results: During follow-up (mean: 6.9 ± 3.5 years) we found skin cancer in 20/164 patients (12%, Group A) and 144 had no skin malignancy (88%, Group B).In Group A mean time to diagnosis of skin cancer was 5.5 ± 3.3 years. The groups did not differ in gender (male: 95% in Group A vs. 78% in Group B, p = 0.08), presence of hypertension (78% vs. 59%, p = 0.10), renal dysfunction (32% vs. 24%, p = 0.52), or diabetes (31% vs. 25%, p = 0.57). The duration of steroid therapy (36.2 ± 39.8 months vs. 34.7 ± 28.9 months, p = 0.83) mean tacrolimus trough levels (7.1 ± 2.3 ng/mL vs. 7.3 ± 1.8 ng/mL, p = 0.31) and mean dose of mycophenolate mofetil (2275 ± 499 mg vs. 2428 ± 503 mg, p = 0.32) were also comparable between the two groups. Patients in Group A were significantly older at the time transplantation (61.2 ± 6.9 years vs. 52.8 ± 12.3 years in Group B, p = 0.003). Vitamin D serum levels did not differ between the two groups (70.6 ± 23.7 nmol/L vs. 61.9 ± 30.0 nmol/L, p = 0.23). When stratified by cancer type, patients with squamous cell carcinoma (N = 5), basaliomas (N = 11) and multiple tumors (N = 4) had comparable vitamin D serum levels (80.8 ± 29.9 nmol/L vs. 69.6 ± 22.8 nmol/L vs. 72.4 ± 26.2 nmol//L, p = 0.30 for inter-group differences).
Conclusion: In heart transplant recipients the risk of skin malignancies does not to appear to be associated with vitamin D serum levels.

ORGAN PERFUSION, A PLATFORM TO PRESERVE, PREDICT, AND PROTECT

OP249 MAGNETIC RESONANCE IMAGING TO ASSESS RENAL FLOW DISTRIBUTION DURING EX VIVO NORMOTHERMIC MACHINE PERFUSION

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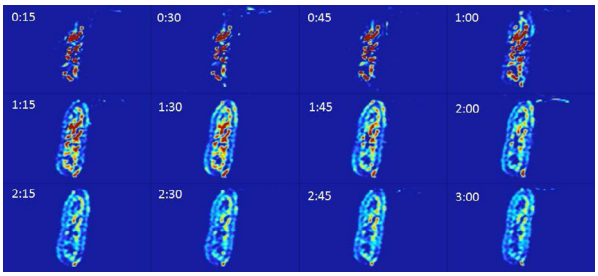
Background: With increased use of renal grafts from suboptimal donors, objective pre-transplant organ quality assessment has become more important. Novel technologies could play a pivotal role in making pre-transplant

donor kidney evaluation more objective. Ex vivo normothermic machine perfusion (NMP) is a potentially promising method for evaluating kidney viability prior to transplantation, but we need a better understanding of how physiological conditions within the organ evolve over time during NMP, and how these differ from in vivo physiology. This study utilized magnetic resonance imaging (MRI) to determine how regional flow distribution develops during NMP and indicates an appropriate window for on-pump viability assessment.
Methods: Nine viable porcine kidneys were subjected to our MRI compatible setup for ex vivo NMP. Longitudinally for 180 minutes, arterial spin labeling (ASL) sequences were performed. This technique is used to quantify perfusion without the use of an exogenous contrast agent. Through an overlay of an anatomically detailed image with the ASL perfusion map, regions of interest were drawn in the renal cortex and medulla. For each time point, we calculated the ratio of the average cortical and medullar signal intensity on the perfusion map (CM ratio). Absolute perfusate flow values for the whole kidney were externally measured with a flow sensor.
Results: All kidneys showed a gradual increase of CM ratio over time, with CM ratios of 1.6 after 15 minutes, 1.9 after 30 minutes, 4.8 after 1 hour, 6.2 after 2 hours and 4.9 after 3 hours. During the first 30 minutes of NMP perfusion was mainly medullar, while after approximately 2 hours a more physiological state was achieved in which renal flow distribution reached a predominantly cortical perfusion. Externally measured whole-kidney flow rates stabilized earlier after 60-90 minutes. In vivo CM ratios in healthy human volunteers are approximately between 5 and 7.



Conclusion: From the start of NMP onwards, flow distribution gradually shifted from mainly medullar to predominantly cortical. After approximately 2 hours, CM ratios approach human in vivo perfusion conditions. Since most functional units of the kidney are located in the cortex, ex vivo viability assessment should most likely be performed at time points past 2 hours from the start of NMP.

OP251 DONATION AFTER CIRCULATORY DEATH (DCD) STRATEGY IN ITALY: THE BARRIER OF A PROLONGED NO-TOUCH PERIOD CAN BE OVERCOME

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Background: DCD programs in Italy suffered from self-exclusion due to 20-min no-touch period for death diagnosis. Recent factors have facilitated both controlled (c) and uncontrolled (u) DCD donation: 1) national end-of-life care recommendations; 2) diffusion of advanced emergency care and availability of ECMO Teams for normothermic Regional Perfusion (nRP); 3) widespread use of Machine Perfusion. This study analyzes 3-year DCD conversion rate and graft outcome in Italy.
Methods: Data on DCD donors (ds) and transplant (Tx) outcomes have been prospectively collected in the national Dataset (Informative Transplant System) since 2017.
Results: In 3 years 124 cDCD and 130 uDCD potential ds were referred (only consented cDCD were referred, 23 uDCD ds were excluded for family refusal) leading to 93 (75%) and 47 (46%) utilized ds respectively. Length of ICU stay was longer in cDCD than in DBD (8 vs 3 days). WIT was longer than 60 min in only 21% of cDCD utilized ds. 37% of cDCD potential ds were older than 60 years; among them 28 (61%) became utilized ds. 315 Txs (3.3% of the total deceased donor Txs) were performed: 19 Lung, 190 Kidney, 106 Liver. 1-year graft survival was better in cDCD than uDCD for Kidney (91% vs 74%, $p < 0.05$) and Liver (94% vs 79%, $p < 0.05$). cDCD graft survival rates were similar to DBD for Kidney (95%) and for Liver (86%).
Conclusions: The Italian experience proves that DCD organs can be successfully transplanted despite 20 min no-touch period. Tx results from cDCD were similar to those from DBD while uDCD led to less utilized ds and worse Tx outcome. Since prehospital and emergency care is improving, higher uDCD potentiality and graft quality may be expected in the future. If both cDCD and uDCD options are included in diagnostic-therapeutical pathways and critical care personnel are aware that organ donation is their social and professional responsibility, a substantial increase in DCD donors with limited warm ischemic insult will be an achievable target.

OP252 NORMOTHERMIC LIQUID VENTILATION ATTENUATES INFLAMMATION FROM ISCHEMIA-REPERFUSION INJURY IN AN EX VIVO RAT MODEL

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Background: Ischemia-reperfusion injury (IRI) leading to allograft dysfunction is a major concern with marginal donor lungs, often resulting in a discarded organ prior to use. Alveolar macrophages and damage associated molecular patterns contribute strongly to inflammation during reperfusion. Here we share normothermic liquid ventilation as a novel lung reconditioning method for IRI to decreases the inflammatory milieu in ischemic organs prior to transplant.
Methods: We compared liquid ventilation (LV) followed by ex vivo lung perfusion (EVLP) (LV Group) to EVLP alone (EVLP Group) in an ischemia-reperfusion rat lung model with and *without* macrophage depletion (MD) to assess for inflammation mediated changes between the two organ perfusion methods. Non-ischemic EVLP controls were also performed. Data were collected for dynamic compliance (C_{dyn}), pulmonary vascular resistance (PVR), wet-to-dry ratio, acid-base disturbance, glucose consumption, oxygenation capacity, apoptosis, cell surface adhesion protein expression, and alveolar inflammatory markers.
Results: The LV Group *without* MD showed a significant decreased Interleukin-1a and Makrophagen-Chemoattraktorprotein-1 production compared to positive controls and all other experimental groups, respectively. This group also demonstrated a significantly lower expression of the macrophage activation marker F4/80, which correlates with the cytokine findings. The LV Group *without* MD also showed significantly lower percentage of apoptotic cells and trended toward lower total cell counts in the bronchoalveolar lavage samples. The LV group *without* MD displayed improved maintenance of a physiologic pH. Among the experimental groups, the LV Group *without* MD had the lowest wet-to-dry ratio, lowest PVR, and high C_{dyn}, although these did not reach statistical significance.
Conclusions: Liquid ventilation is a viable ex-vivo reconditioning method that can attenuate inflammatory mediators and improve lung physiologic parameters in ischemia-reperfusion injury independent of macrophage depletion. These methods could be applied to reconditioning marginal lungs prior to transplantation.

OP253 NORMOTHERMIC MACHINE PERFUSION FACILITATES DELIVERY OF RNA INTERFERENCE THERAPEUTICS IN DONOR KIDNEYS

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Background & Aims: Normothermic machine perfusion (NMP) of donor kidneys prior to transplantation provides a platform for direct delivery of novel therapeutics to optimize organ quality. This includes RNA interference (RNAi) therapeutics e.g. antisense oligonucleotides (ASO) that block detrimental microRNAs. The intracellular kinetics of RNAi therapeutics are crucial for their pharmacological effect, however, they remain poorly understood. NMP provides an ideal platform to investigate this further.
Methods: During NMP, human kidneys ($n = 12$) were treated for 6hours with a fluorescently labelled ASO designed to block microRNA-24-3p activity. Biopsies were taken at 0, 2, 4, and 6hours. Kidney sections were stained with antibodies against early endosomes (Rab5), late endosomes (Rab7), RNA-induced silencing complexes (GW182) and lysosomes (LAMP2). Confocal microscopy images were obtained and co-localisation

quantified using Hugyens™ software following batch deconvolution. The global impact of ASO therapy on the transcriptome was also assessed using RNA sequencing.
Results: Following 2hours of NMP, ASO was primarily found in proximal tubular epithelial cells. Co-localisation studies revealed ASO uptake via endocytosis and endosomal sorting occurring during NMP. This was followed by cytoplasmic escape and co-localisation of ASO with GW182 proteins. This pattern of co-localisation was not seen in scrambled sequence or cold perfusion controls. RNAseq analysis revealed a protective decrease in inflammatory pathways and upregulation of microRNA-24-3p targets.
Conclusions: This is the first study to demonstrate NMP facilitates gymnotic ASO delivery directly into the RNA-induced silencing complex, whereby, it blocks microRNA-mediated mRNA silencing and increases bioavailability of protective targets. This study highlights the capacity of NMP to re-programme gene expression in donor kidneys using RNAi therapeutics.

OP254 TREATING CIRCULATORY DEATH DONOR KIDNEYS WITH ANTI-FIBROTIC DRUGS USING EX VIVO PRECISION CUT KIDNEY SLICES

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Suboptimal kidneys such as circulatory death donor (DCD) kidneys are increasingly used to enlarge the donor pool. Unfortunately, these kidneys undergo ischemia/reperfusion injury (IRI), frequently leading to renal fibrosis and failure. Transforming growth factor beta 1 (TGF-β) and matrix metalloproteases have been identified as central mediators of fibrosis, and inhibition of these targets could attenuate fibrosis in DCD kidneys. We therefore studied whether galunisertib (GALU), doxycycline, taurine, and febuxostat alleviated fibrosis in precision-cut kidney slices (PCKS).
PCKS were prepared from porcine kidneys exposed to 30 min of warm ischemia followed by 3h of oxygenated hypothermic machine perfusion. PCKS were incubated for 48h at 37 °C with either GALU (10 μM), doxycycline (113 μM), taurine (80 mM), or febuxostat (16 μM). ATP levels were measured to assess viability and real-time polymerase chain reaction was used to investigate expression of fibrosis-related genes. To further elucidate the antifibrotic effects of GALU, we cultured PCKS with TGF-β to promote fibrosis.
ATP levels remained stable for all groups, showing that PCKS were viable for up to 48h. We first screened the effects of the compounds in the absence of TGF-β. Significant effects were only observed for GALU, which lowered the expression of α-SMA, and FN2. We then investigated the effects of GALU in fibrotic PCKS that were cultured with TGF-β. TGF-β promoted fibrosis in PCKS as shown by a significantly increased expression of TGF-β, FN1, PAI-1, HSP47, and COL1A2 after 48h of incubation. GALU, however, clearly attenuated the expression of all tested fibrosis-related genes (FIG 1).
We convincingly demonstrated that GALU exhibited strong antifibrotic effects in PCKS. GALU therefore appears to be a promising drug for further research in a preclinical model, and may ultimately be implemented during machine perfusion in a clinical setting as treatment to prevent or to attenuate fibrosis in DCD kidneys.

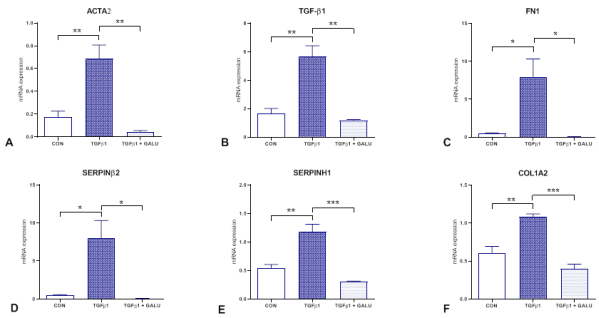

Figure 1. Expression of fibrosis-related genes in kidney cortex tissue after 48h incubation with TGF-β1 or TGF-β1 and galunisertib. **A**. Actin alpha 2, smooth muscle (ACTA2). **B**. Transforming growth factor beta receptor 1 (TGF-β1). **C**. Fibronectin 1 (FN1). **D**. Serpin family B member 2 (Serpinβ2). **E**. Serpin Family H Member 1 (SERPINH1). and **F**. Collagen, type I, alpha 2 (COL1A2). Significant differences were analysed using ANOVA (*p<0.05; **P<0.01, ***<0.001). Data are presented as mean±SD

OP255 COMPLEMENT IS ACTIVATED DURING NORMOTHERMIC MACHINE PERFUSION OF PORCINE AND DISCARDED HUMAN KIDNEYS

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Background: The increasing gap between demand and supply of kidneys for transplantation has led to increasing use of marginal donor kidneys. However, transplantation of marginal donor kidneys is associated with inferior outcome. Normothermic machine perfusion (NMP) provides the opportunity to assess donor kidneys and could be used to recondition and improve the quality of marginal donor kidneys. The impact of NMP on inflammation is largely unknown. We hypothesized that NMP activates the innate immune response, represented by the complement system, which leads to a pro-inflammatory cytokine response and affects renal function.
Methods: Both porcine (n = 20) and discarded human (n = 10) kidneys were perfused at 37 degrees Celsius for 4-6 hours with a blood-based perfusion solution in a pulsatile flow driven machine perfusion system. Perfusate samples were taken every hour to assess complement activation, pro-inflammatory cytokines and renal function.
Results: NMP of porcine kidneys lead to significant increase of complement activation products C3a and C5b-9 in perfusate and both were positively correlated with IL-6, IL-8 and TNF-alpha levels. Porcine kidneys with high C5b-9 perfusate levels had a significant lower creatinine clearance after 4 hours of NMP. High complement perfusate levels, reflected by C3d/C3 ratio, were also seen during NMP of discarded human kidneys. In addition, kidneys retrieved from brain-dead donors had significantly higher complement C3d/C3 perfusate levels during NMP than kidneys retrieved after circulatory death.
Conclusions: The complement system gets activated during NMP of porcine and human-discarded kidneys. Complement activation is positively correlated with the release of cytokines, leading to reduced kidney function. Therefore, inhibition of complement during NMP should be evaluated as a strategy to improve renal graft quality prior to transplantation.

OP256 NORMOTHERMIC REGIONAL PERFUSION VERSUS RAPID RECOVERY IN CONTROLLED DONATION AFTER CIRCULATORY DEATH KIDNEY TRANSPLANTATION

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Background: In Donation after the Circulatory Determination of Death (DCDD) the effects of warm ischemia during the cessation of circulation makes kidneys grafts more likely to experience primary nonfunction (PNF), delayed graft function (DGF) and early dysfunction. As Normothermic Regional Perfusion (NRP) allows the in situ perfusion of organs with oxygenated blood, we aimed evaluating the impact of NRP on the short-term outcomes of kidney transplants versus the standard rapid recovery (RR) technique
Methods: Multicenter retrospective study comparing cDCDD kidneys obtained with NRP versus RR from 2012 to 2018 in Spain. NRP and RR groups were compared by the Chi-square test for qualitative variables and the Mann-Whitney U test for quantitative.
Logistic regression models, adjusting with variables which differed in NRP and RR groups, were used to analyze DGF and PNF and Kaplan-Meier curves and Cox models to assess graft survival.
We undertook an analysis of sensibility using the propensity score with a 1:1 matching without replacement (PSM) through which obtained two cohorts with similar characteristics.
Results: 2,302 cDCDD adult kidney transplants were performed using NRP or RR with remarkable difference between groups (Figure 1).Through matching by propensity score we obtained two similar cohorts of 350 patients each.
After the matching, the RR technique was associated with higher risk of DGF ($p < 0.001$) and 1-year graft loss ($p = 0.034$) (Table 1).
Conclusions: Due to the differences observed between groups, a propensity score matching was used to build comparable groups by confounding factors that might affect upon outcome variables. We observed that NRP was associated with improved outcomes of kidneys from cDCDD donors, in terms of DGF and 1-year graft survival.

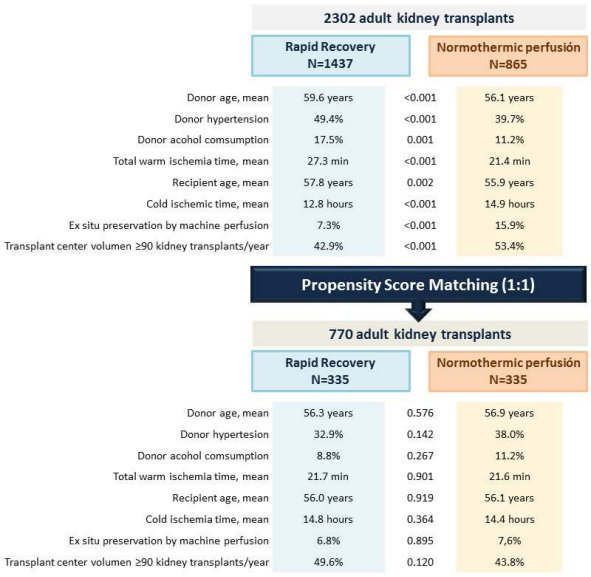

Figure 1. Characteristics of transplants performed by recovery technic and cohorts built through PSM.

Table 1 Effects of RR versus NRP on short-term outcomes

	ADJUSTED			PSM			
RR vs NRP	p	OR	[CI95%]	ATT (%)	p	OR	[CI95%]
Primary nonfunction	0.426	1.26	[0.71-2.22]	(6.6 vs. 4.7)	0.261	1.44	[0.73-2.91]
Delayed graft function	<0.001	2.1	[1.60-2.78]	(45.4 vs. 29.7)	<0.001	1.97	[1.43-2.72]
		HR					HR
1-year graft loss	0.051	1.49	[1.00-2.28]	(9.9 vs. 5.8)	0.034	1.77	[1.01-3.17]

OP257 IMMUNE CELL PROFILING AND ASSESSMENT OF INFLAMMATORY CYTOKINE LEVELS IN THE PERFUSATE DURING NORMOTHERMIC MACHINE PERFUSION OF HUMAN LIVER ALLOGRAFTS

Margot Fodor[1,2], Susanne Ebner[3], Giorgi Otarashvili[1,2], Rupert Oberhuber[1,2], Benno Cardini[1,2], Julia Hofmann[1,2,3], Annemarie Weissenbacher[1,2], Thomas Resch[1,2], Jakob Troppmair[3], Dietmar Öfner[1], Stefan Schneeberger[1,2], Theresa Hautz[1,2,3]
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Background: Liver transplantation remains the only effective therapy for end-stage liver disease. Normothermic machine perfusion (NMP) allows to maintain the liver *ex vivo* in a complete functional state at 37°C under physiological conditions. The aim of this study was to assess for immune cell migration and cytokine quantification in the perfusate during NMP of liver allografts.
Methods: Twenty-six liver allografts were subjected to NMP. Perfusate samples were collected at 1, 4, 6, 12, and 24 hours (h) or at the end of NMP. Immune cell profiling in serial perfusate samples was performed with flow cytometry, while cytokine levels were measured using the Luminex technology.
Results: For CD3+ T cells highest perfusate levels were observed early (1h) after NMP start, which decreased over time ($p = .007$). While the proportion of CD8+ cytotoxic T cells decreased over perfusion time, a remarkable increase of CD4+T-helper cells was observed. The proportion of CD20+ B cells ($p < .001$) and monocytes increased significantly ($p < .001$), while granulocytes remained constant over time. FoxP3+ regulatory T cells, CD4+CD27+CD28- and CD8+CD27+CD28- regulatory T cells increased significantly during NMP ($p < .001$, $p = .024$, $p = .014$ respectively). Hepatocytes were rarely detected in the perfusate, indicating structural integrity of the liver cell architecture. The proportion of Kupffer cells gradually diminished within 6 hours and augmented significantly until perfusion end ($p < .001$). A similar tendency could be detected for dendritic cells. The percentage of natural killer cells remained constant over NMP period. Pro-inflammatory cytokines IL-1b ($p = .047$), MIP-1a, SDF-1a, IL-27, IL-2, IP-10, IL-7, IL-8, Eotaxin, IL-17a, IFNg, GM-CSF, TNFa, MIP-1b, MCP-1, IL-9, GROa, IL-1a and IL-18 and anti-inflammatory cytokines IL-4 and IL-13 ($p < .001$) levels constantly increased over time, while IL-10 levels drastically dropped after 4 hours until perfusion end ($p < .001$).
Conclusions: Liver-specific immune cell migration out of the allograft and subsequent filtration during NMP may serve as a novel tool for immunmodulation of an organ prior to transplantation.

OP258 EXPLORING THE RELEASE OF EXTRACELLULAR VESICLES IN PERFUSATE AND BILE AS AN ADDITIONAL TOOL TO UNRAVEL MECHANISMS OF FUNCTION OF LIVER NMP

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Background: Although liver Normothermic Machine Perfusion (NMP) reduces hepatic (but not cholangiocytes) ischemic injury, its mechanism of action is not understood. Extracellular Vesicles (EVs) are paracrine mediators released by all cells in physiological and pathological processes. EVs carry a cargo of mRNA and microRNA (miRNA) selected in response to stressors, reflecting the functional state of parental cells. We hypothesized that during NMP parenchymal cells (hepatocytes, sinusoidal cells, leukocytes) and cholangiocytes release EVs in perfusate and bile, respectively, that their RNA cargo changes in response to Warm Ischemia (WI) and that its sequencing unravels NMP mechanisms of action.
Methods: Porcine livers exposed to 60min WI (WI60, $n = 5$) or not (no-WI, $n = 5$) underwent 6h NMP. Perfusate and bile were sampled at 1, 3, and 6h for EVs and RNA isolation. RNAseq identified EVs-associated genes, their levels of expression were compared between groups to identify Differentially Expressed Genes (DEG) in WI60. Gene function was investigated with gene ontology enrichment analysis to gain insights on liver cells biology during NMP.
Results: Small EVs are released in perfusate and bile during NMP regardless of WI. In WI60, less EVs were released but their RNA content was higher than in no-WI in both perfusate ($p < .0001$) and bile ($p = .008$). In

WI60, 19 DEG were identified in perfusate EVs (adj.p < .001). Tissue regeneration processes were enriched in perfusate EVs of both groups (adj.p < .001). In WI60, aerobic metabolic pathways were also enriched and 5 antiproliferative miRNAs downregulated (adj.p < .001). In WI60, 91 DEG were identified in bile EVs (adj.p < .001). Regenerative processes were enriched in biliary EVs of no-WI, whereas in WI60 anaerobic metabolic pathways and 19 antiproliferative miRNAs were upregulated (adj.p < .001; Tab.1).
Conclusions: 6h NMP promotes proliferative pathways in parenchymal cells. In contrast, cholangiocytes exposed to WI fail to recover aerobic metabolism during NMP and have impaired regenerative potential

Table 1 Overview of significantly enriched ontology and miRNAs in perfusate and biliary EVs according to experimental group.

	Perfusate EVs		Biliary EVs	
	no-WI	WI60	no-WI	WI60
Tissue regeneration	↑	↑	↑	↓
Aerobic metabolism		↑		
Anaerobic metabolism				↑
Antiproliferative miRNAs		↓		↑↑

OP259 METABOLIC AND IMMUNOLOGICAL ALTERATIONS IN NORMOTHERMIC MACHINE PERFUSION OF THE LIVER AS COMPARED TO STATIC COLD STORAGE

Maria Letizia Lo Faro[1], Adam M. Thorne[2], Honglei Huang[1], Maria Kaisar[1], Simon Davis[3], Fungai Dengu[1], Sadr Shaheed[1], John Mulvey[1], Roman Fischer[3], David Nasralla[4], Alberto Santos Delgado[3], Benedikt Kessler[3], Henri Leuvenink[2], Peter Friend[1], Rutger Ploeg[1]
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Background: Liver preservation by normothermic machine perfusion (NMP) involves perfusion of the graft with oxygenated blood and nutrients. A recent randomized NMP Liver trial by the Consortium for Organ Preservation in Europe (COPE), has shown that NMP is associated with a 50% reduction in graft injury and increased organ utilisation when compared to conventional static cold storage (SCS). The aim of the present study is to provide insight into the mechanisms involved in NMP liver preservation by proteomics analysis.
Methods: Biopsies from DBD livers preserved using SCS or NMP were collected as part of the COPE Liver trial. Biopsy time-points were the end of preservation (LT2, N = 107) and 1 hour after reperfusion in the recipient (LT3, N = 106). Proteins were extracted, digested and analysed by quantitative label-free proteomics (LFQ LC-MS/MS, timsTOF Pro). Protein levels were compared between NMP and SCS for the two time points (LT2 and LT3) (T test with permutation-based FDR). Statistical enrichment gene ontology (GO) and pathway analysis (Reactome) were conducted using PANTHER (Mann–Whitney rank-sum test).
Results: At the end of preservation, significant differences were demonstrated in the expression of 181 proteins ($p < 0.05$, FDR 1%) between NMP and SCS. GO enrichment and pathway analysis found fatty acid metabolism, humoral immune response and complement activation significantly downregulated in NMP at the end of perfusion, while protein translation, autophagy and mitochondrial ATP production were significantly upregulated ($p < 0.05$, FDR < 0.05). These biological alterations persisted post-reperfusion, with additional upregulation of proteins related to mitochondrial organisation in NMP.
Conclusions: These findings represent the first large set of proteomics data from the COPE NMP Liver trial. They suggest that fatty acid metabolism is downregulated during NMP in favour of oxidative phosphorylation and mitochondrial ATP production. Additionally, NMP liver biopsies show a decreased humoral immune response and complement activation as well as upregulation of protein translation and stress response pathways. These molecular features provide an insight into which immunological and metabolic pathways are impacted by NMP to potentially contribute to its beneficial effects in liver transplantation.

OP261 MICROVASCULAR OBSTRUCTIONS IN PORTAL BILE DUCT CAPILLARIES AND HEPATIC SINUSOIDS DURING NORMOTHERMIC MACHINE PERFUSION OF MARGINAL HUMAN LIVERS

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Background: Normothermic machine perfusion (NMP) is increasingly used for storage, reconditioning and viability testing of livers. Despite previous hopes, NMP has been shown to have no effect on ischaemic cholangiopathy in grafts from donors after circulatory death (DCD). It has recently been demonstrated that red blood cell (RBC) aggregates cause microvascular obstruction during renal NMP.
Methods: We analysed core biopsies taken during NMP of seven human livers which had been declined for transplant due to steatosis (2 DCD, 5 donation following brainstem death; mean age 48yrs; mean cold ischaemic time 15hrs 27mins). All livers received normothermic pressure-guided perfusion. Perfusate was free of platelets and clotting factors.
Results: Figure 1 shows representative images from the seven livers. There were no RBC occlusions before NMP in any liver, however, every liver had accumulated RBC occlusions by one hour. This was true even for livers with cold ischaemic time less than 10 hours. MSB staining demonstrates that these occlusions are 'fibrin-rich' as they stain for both RBC (yellow) and fibrin(ogen) in red. These occlusions obstruct sinusoids, often around areas with a heavy burden of steatosis (Figure 1i). Critically, in the two DCD livers, RBC aggregates obstructed the portal tract capillaries which supply the cholangiocyte lined bile ducts (Figure 1ii).
Conclusions: RBC aggregates, similar to those seen in the kidney, form during liver NMP in sinusoids and in the portal tract capillaries which supply ischaemia-sensitive bile ducts. Future research should investigate the use of agents to improve the microcirculation.

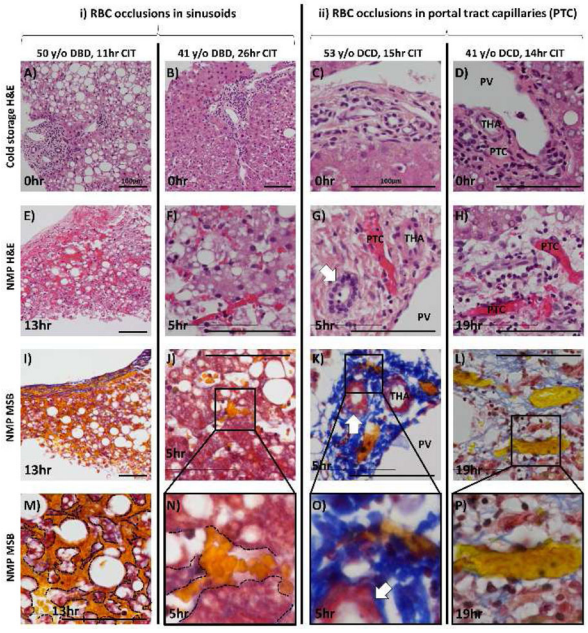

Figure 1 Fibrin(ogen)-rich red blood cell (RBC) aggregates causing microvascular occlusions during NMP. White arrows – bile ducts, Dashed lines - hepatic sinusoids, MSB - Martius Scarlet Blue, PV – portal vein, THA – terminal hepatic arteriole.

OP262 RE-WRITING THE DEFINITION OF HIGH-RISK AND FUTILE DCD LIVER TRANSPLANTATION WITH NRP

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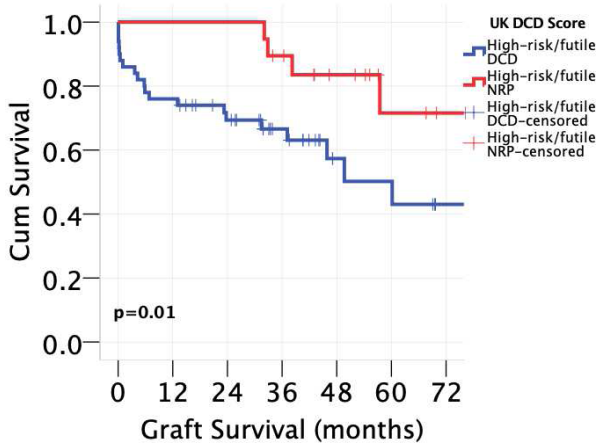
Background: UK Donors after circulatory death (DCD) risk score is widely utilised to identify low-risk, high-risk and futile liver transplants. Normothermic regional perfusion (NRP) has shown excellent survival outcomes compared with standard DCD grafts. We thought to investigate if the high-risk and futile transplants as defined by the UK DCD risk score should be reconsidered in the era of novel perfusion technologies.
Methods: Data on all DCD liver transplant recipients were retrospectively collected in a UK liver transplant centre (2005-2018). The primary outcomes were graft and patient survival compared according to the mode of retrieval (standard DCD retrieval vs NRP retrieval). The secondary outcome was the incidence of ischemic cholangiopathy (IC) in both groups. Statistical analysis using Kaplan Meier survival curves and log-rank test was performed.
Results: 22 NRP and 101 DCD liver transplants were undertaken in the study time period. In the standard DCD group had 51 were low-risk (50.5%) and 50 high-risk/futile transplants (49.5%), while NRP had 3 low-risk (13.6%) and 19 high-risk/futile transplants (86.4%). Donors and recipients characteristics were comparable between groups. IC was not observed in the NRP group, but developed in 25 patient in the standard DCD group (24.7%). Graft survival for the high-risk or futile transplants was significantly lower at 1 and 5 years post-transplant with standard DCD compared with NRP, log-rank test p = 0.01 (Figure 1).
Conclusions: The majority of livers transplanted in the NRP group were categorised as high-risk or futile but had better graft survival outcomes compared to standard DCD. The definitions of the UK DCD risk score need to be reconsidered with the use of novel perfusion technologies.



CLINICAL ASPECTS OF KIDNEY REJECTION

OP283 INCIDENCE AND PREDICTORS OF FAILED KIDNEY ALLOGRAFT INTOLERANCE SYNDROME

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Background: Up to 40% of patients with failed kidney allograft develop immunologic intolerance syndrome (IS). Is it characterized by chronic inflammation and confers high morbidity. Most require transplantectomy, but this procedure is associated with various complications. It could be beneficial to predict which patients with failed allograft would benefit from early transplantectomy. This syndrome is poorly understood and there are scarce data about it in the literature. Therefore, our aim was to evaluate the incidence and predictive factors of IS in our kidney transplant unit.
Methods: Cohort observational retrospective study. We included all kidney transplant patients from our center that had a failed allograft at least 6 months after transplantation, from 2008 to 2018. All patients were followed until 1st January 2021. Clinical and analytical data were collected. Descriptive, univariate and multivariate analysis were performed with *SPSS Statistics*.
Results: A total of 160 patients had a failed allograft in the study period. IS incidence was 39.4% (n = 63). The median time from graft failure to IS development was 7.1 months(4.2-13.0). Patients who developed IS, compared with those who didn't, had more frequently a graft from a deceased donor(95.0% vs 67.9%; p = 0.005, OR 3.4, 95%CI 1.2-9.8), acute antibody-mediated rejection episodes(36.2% vs 19.6%; p = 0.024, OR 2.3, 95%CI 1.1-4.9) and shorter graft survival (9.4 vs 11.2 years; p = 0.042). These factors were predictive of IS in a multivariable analysis. ROC curve analysis showed that this predictive model had a fairly accuracy for IS(AUC = 0.72). Patient and donor age, immunologic profile and type of immunosuppression were not associated with IS.
Conclusion: IS was frequent in failed allograft patients in our unit and its incidence was comparable to other series. Type of donor, antibody-mediated rejection episodes and graft survival can reasonably predict IS. Larger and prospective studies are needed to validate these results.

OP284 LONG-TERM APHERESIS IN THE MANAGEMENT OF PATIENTS WITH RECURRENT FOCAL SEGMENTAL GLOMERULOSCLEROSIS AFTER KIDNEY TRANSPLANTATION: A CASE SERIES

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Background: Focal segmental glomerulosclerosis (FSGS) can recur after kidney transplantation and is usually treated with apheresis. Following initial treatment, a subset of patients achieves an apheresis-dependent response. These patients are treated chronically to remain in remission, but little is known about their clinical outcomes.
Methods: We analyzed a multi-center, international, retrospective case series to determine the clinical course of patients with post-transplant FSGS treated with long-term apheresis (>6 months).
Results: A total of 27 patients with recurrent FSGS were included from 11 transplant centers in Europe, the USA and Brazil. Median (IQR) time of follow-up was 4.1 (3.0-6.3) years, median time on apheresis was 23 (12-48) months. Long-term apheresis was performed by plasmapheresis (74%), immunoadsorption (11%) or both (15%). Nine patients received continued apheresis at maximum follow-up with a median frequency of twice a month (median time on apheresis 47 (36-54) months), while 10 patients were successfully weaned off apheresis. In four patients, apheresis was terminated due to rising levels of proteinuria (n = 3) or infection (n = 1). Four patients never achieved remission despite long-term treatment. Rituximab was commonly used (78%), although timing and number of doses (1-8) varied widely. Viral and/or bacterial infections were observed in 89% of patients. During follow-up, four grafts were lost due to recurrent FSGS.
Conclusion: Our case series shows that long-term apheresis can be effective in a subset of patients with post-transplant FSGS, being well tolerated and achieving continued partial remission for multiple years.

OP285 TRANSPLANTECTOMY VERSUS NON-TRANSPLANTECTOMY AFTER FAILED KIDNEY TRANSPLANT. A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: There is limited evidence regarding the impact of allograft nephrectomy (AN) on the long-term outcome of subsequent kidney re-transplantation compared to no prior allograft nephrectomy. The aim of the present study was to conduct systematic review and meta-analysis. Primary outcomes were 5-year graft and patient survival
Methods: Cochrane library, scholar Google, Pubmed, Medline and Embase were systematically searched.
Results: Sixteen studies were included, with a total of 2256 patients. All included studies were retrospective and comparative. There was no significant difference in 5- year graft survival (GS) [Hazard Ratio (HR) = 1.11, 95% Confidence Intervals (CI): 0.89, 1.38, p = 0.37, I^2 = 10%) or in 5-year patient survival (PS) (HR = 0.70, 95%CI: 0.45, 1.10, p = 0.12, I^2 = 0%]. Patients in the AN cohort were significantly younger than patients in the

non-allograft nephrectomy(NAN) cohort by one year. Prior allograft nephrectomy was associated with a significantly higher risk of delayed graft function (DGF), acute rejection, primary nonfunction (PNF), percent of panel reactive antibodies (% PRA), and allograft loss of the subsequent transplant
Conclusions: Although, DGF, % PRA, acute rejection and primary nonfunction rates were significantly higher in the AN cohort; allograft nephrectomy prior to re-transplantation had no significant association with five-year graft and patient survival.

OP286 ASSOCIATION BETWEEN DECEASED DONOR ACUTE KIDNEY INJURY ASSESSED BY BASELINE SERUM CREATININE BACK-ESTIMATION AND GRAFT SURVIVAL

Rémi Lenain[1], Camille Prouteau[1], Aghilès Hamroun[1], Yohann Foucher[2,3], Magali Giral[4], Aurélie Deshayes[5], Mehdi Maanaoui[1,6], Marc Hazzan[1]
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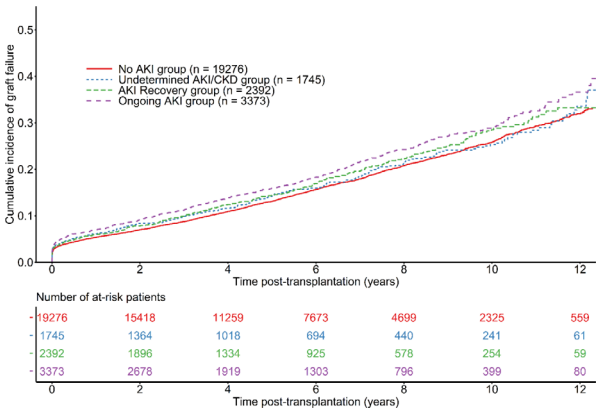
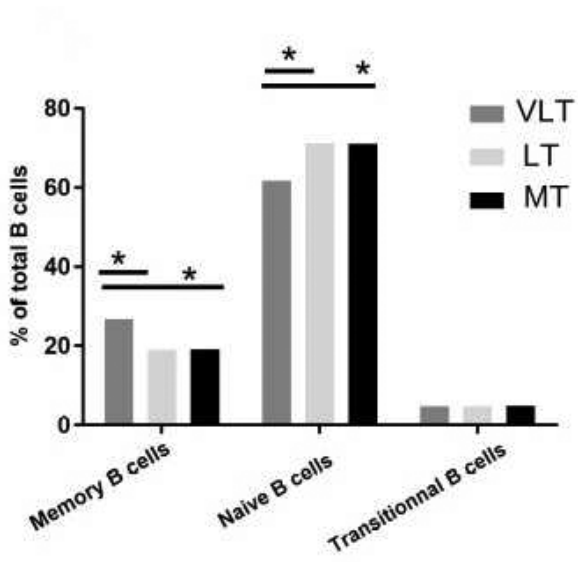
Background: While deceased-donor acute kidney injury (AKI) frequently leads to kidney discard, its impact on long-term graft survival in kidney transplant recipients remains unclear. We sought to investigate the association between deceased-donor AKI and death-censored graft survival.
Methods: We examined 26,786 patients who received single kidney transplantation from deceased donors in France from 2006 to 2017. Because donor baseline SCr is generally unavailable, we back-estimated a MDRD-derived baseline value assuming a glomerular filtration rate at 75 mL/min/1.73 m^2. The following refined classification system for donor AKI was implemented: no AKI (n = 19,276), undetermined AKI/chronic kidney disease (CKD; n = 1745), recovery from AKI (n = 2392), and ongoing AKI (n = 3373).
Results: We observed 4458 kidney graft losses during a median follow-up of 5.7 years. Compared to no-AKI, ongoing AKI was associated with an increased risk of graft failure (HR = 1.24; 1.13–1.35). The HRs for graft failure in the undetermined AKI/CKD (HR = 1.22; 1.07–1.38) and recovery from AKI (HR = 1.18; 1.06–1.31) groups were similar. This deleterious effect was no longer evident when relying either on the admission or the lowest SCr value throughout the procurement procedure as baseline.
Conclusions: Deceased-donor ongoing AKI, undetermined AKI/CKD, and recovery from AKI according to back-estimated baseline SCr are associated with lower long-term graft survival.



OP287 CLINICAL AND IMMUNOLOGICAL FOLLOW-UP OF VERY LONG-TERM KIDNEY TRANSPLANT RECIPIENTS TREATED WITH CALCINEURIN INHIBITORS

Amaury Dujardin[1,2], Melanie Chesneau[2], Florian Dubois[2], Richard Danger[2], Linh Bui[3], Clarisse Kerleau[1], Pierrick Guérif[1], Sophie Brouard[1,2], Jacques Dantal[1,2]
[1]University Hospital of Nantes, Nantes, France; [2]INSERM UMR1064, Nantes, France; [3]Hospital of Béthune, Béthune, France

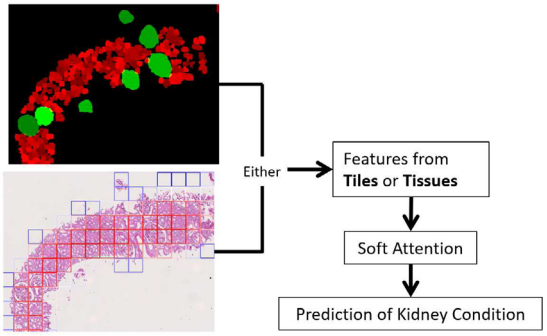
Background: Operationally tolerant kidney transplant recipients harbor an immunological signature, associated with low rejection risk, focused on B lymphocytes. We investigate whether patients with long-term transplantation and still on immunosuppressive therapy would present such a signature of low immunological rejection risk, compared to more recently transplanted patients.
Methods: A total of 114 kidney transplant recipients were enrolled. Thirty-eight recipients with more than 25 years of graft survival, with a stable graft function under calcineurin inhibitors, were matched with two different groups of transplanted patients (10-15 and 5-7 years after transplantation). Three phenotypes associated with low immunological rejection risk (Tfh, B and regulatory T cells), initially found in operationally tolerant kidney transplant recipients, and the composite score of tolerance (cSoT, combining 6 transcriptomic markers, age at transplantation and age at sampling) were analyzed.
Results: We found that very long-term patients are characterized by a lower percentage of total B cells ($p = 0.0017$), a higher proportion of CD24HiCD38Lo memory B cells ($p = 0.0247$), fewer CD24LoCD38Lo naive B cells ($p = 0.0130$), and a lower proportion of PD1HiCCR7Lo Tfh lymphocytes ($p = 0.0017$) than more recently transplanted patients.
Conclusion: This phenotype is associated with a positive cSoT score in patients transplanted for more than 25 years. This study suggests a dual phenotype in very long-term kidney transplanted patients with an immunological profile associated with low rejection risk.
Figure. B cell phenotype: B cells subsets distribution depending on the post-transplantation delay (* for $p < 0.05$).



OP288 DEEP-LEARNING BASED PREDICTION OF CLINICAL ENDPOINTS IN RENAL PRE-IMPLANTATION BIOPSIES USING SLIDE-LEVEL LABELS

Ka Ho Tam[1], Maria Fernanda Soares[2], Edward Sharples[3], Maria Kaisar[4,5], Rutger Ploeg[4,5], Jens Rittscher[1]
[1]University of Oxford, Engineering Science, Oxford, United Kingdom; [2]Oxford University Hospitals NHS Foundation Trust, Department of Cellular Pathology, John Radcliffe Hospital, Oxford, United Kingdom; [3]Oxford University Hospitals NHS Foundation Trust, Nuffield Department of Surgical Sciences, Churchill Hospital, Oxford, United Kingdom; [4]University of Oxford, Oxford Transplant Centre, Nuffield Department of Surgical Sciences, Oxford, United Kingdom; [5] NHS Blood and Transplant Filton and Oxford, Research and Development, Oxford, United Kingdom

Background: Although most transplant centres accept higher-risk kidneys, clinical uncertainty remains, and many usable kidneys are still discarded. Deep learning-based histological analysis can assist clinical decision-making by providing valuable information on a kidney's condition. However, training convolutional neural networks (CNN) can be expensive as they often require massive number of expert annotations. Our workflow extracts feature from preimplantation biopsies and aim to classify clinical endpoints and visual changes based on only slide-level expert input. We analysed biopsies stained with Periodic Acid-Schiff (PAS) and Sirius Red (SR) and evaluated whether prediction of Delayed Graft Function (DGF) was possible.
Methods: Biopsies from 354 deceased donor kidneys from the QUOD UK biobank was used to develop a feature extraction pipeline. A combination of handcrafted and deep features was extracted. An attention model was trained to classify each slide using Multi-Instance Learning (MIL) with 5-fold cross-validation. We assessed how well the models could predict the presence of DGF, as well as detect visual changes such as Acute Tubular Injury (ATI). Results were characterised using Receiver Operating Characteristic Area-Under-the-Curve (AUC).
Results: Our framework was able to predict DGF with SR (AUC: 0.693) and PAS (AUC: 0.585). This indicates subclinical pro-fibrotic alterations could be detected in the former. As for classification of visual changes in PAS slides, we notice AUC was higher when features were extracted from tissues rather than rectangular tiles.
Conclusions: In this study, we present an easily scalable and novel approach for predicting DGF and visual changes from preimplantation renal biopsies. In addition to assisting clinical decision-making by assessing potential post-transplantation complications, our workflow can be used to study the relative importance of different histological features in constructing whole organ tissue atlases.



Stain	Prediction	n (Donors/Slides)	Dataset	Tissue Feature - AUC	Tile Feature - AUC
PAS	TA (Tubular Atrophy)	95 /117	QUOD + Reperfusion	**0.854**	0.840
PAS	ATI (Acute Tubular Injury)	89 / 95	QUOD	**0.722**	0.670
PAS	DGF (Delayed Graft Function)	283 / 321	QUOD	0.585	0.550
SR	DGF (Delayed Graft Function)	143 / 143	QUOD	0.672	**0.693**

OP289 MOLECULAR AND CELLULAR MECHANISMS OF LIPOCALIN-2 MEDIATED RENOPROTECTION IN KIDNEY TRANSPLANTATION

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Background: Lipocalin-2 (Lcn2) is distinctly upregulated in kidney transplants and serves as an early marker of AKI, DGF and acute rejection. Using a mouse model of kidney transplantation we recently demonstrated a renoprotective role of recombinant Lcn2:Siderophore:Fe (rLcn2). However, the molecular and cellular events underlying the renoprotective effects of rLcn2 in kidney allografts are not yet understood. Elucidating these events forms the primary focus of this study.
Methods: Kidneys were transplanted from Balb/c to C57Bl/6 mice (± rLcn2, 250mg/kg). A detailed immunophenotyping of the adaptive and innate immune cells, isolated from the graft, spleen, lymph nodes and blood was performed by flow cytometry at POD 3 and 7. Graft function was assessed by serum creatinine and urea levels. For in vitro analyses of intracellular signaling, oxidative stress and cell death, murine primary PTEC were isolated and subjected to hypoxia (0.5% O_2, w/o FCS, 24h) and reoxygenation (30min, 6h, 12h, 24h), ±rLcn2 (1μg/ml).
Results: rLcn2 significantly lowered $CD8^+$ T cells in the allograft, lymph nodes and blood at POD 7, whereas their number remained unaffected in spleen. Nevertheless, the number of $CD4^+$ T Lymphocytes was reduced only in lymph nodes. NKG2D+CD8+T cells and CD27+CD11b+NKp46+NK cells were the most prominent subpopulations of the cytotoxic lymphocytes whose frequencies were significantly reduced in graft, spleen, and blood with the treatment of rLcn2. Besides, a significantly reduced infiltration of monocytes/macrophages was also observed at POD-7 with the said treatment. Importantly, the degranulation capacity and IFNγ production of intragraft and splenic CD4+ and CD8+ T cells were impaired in the treated animals. Moreover, rLcn2 lowered hypoxia and reoxygenation induced cytotoxicity of the primary RTECs, associated with reduced caspase-3 cleavage and activation of Erk and AKt signaling.
Conclusions: rLcn2 treatments differentially affects the relative frequencies and activation status of various immune cells and additionally depicts cytoprotective effects on murine primary RTECs during H/R, possibly via activation of Erk and Akt signaling.

OP290 REVISITING THE CHANGES IN THE BANFF CLASSIFICATION FOR ANTIBODY-MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

Jasper Callemeyn[1], Heleen Ameye[2], Evelyne Lerut[3], Aleksandar Senev[1], Maarten Coemans[1], Elisabet Van Loon[1], Ben Sprangers[4], Vicky Van Sandt[5], Maud Rabeyrin[6], Valérie Dubois[7], Olivier Thaunat[8], Dirk Kuypers[1], Marie-Paule Emonds[5], Maarten Naesens[1]
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Background: The Banff classification for antibody-mediated rejection (ABMR) has undergone important changes, mainly by inclusion of C4d-negative ABMR in Banff'13 and elimination of suspicious ABMR (sABMR) with the use of C4d as surrogate for HLA-DSA in Banff'17. We aimed to evaluate the numerical and prognostic repercussions of these changes.
Methods: In a single-centre cohort study of 949 single kidney transplantations between 2004 and 2013, all 3662 post-transplant biopsies were classified according to Banff'01, Banff'13 and Banff'17 based on histological scoring by a single pathologist. The predictive performance for death-censored allograft failure for each classification was evaluated by the concordance index.
Results: Overall, the number of ABMR and sABMR cases increased from Banff'01 to Banff'13 (**Figure**). In Banff'17, 248/292 sABMR biopsies were reclassified to No ABMR, and 44/292 to ABMR. However, reclassified sABMR biopsies had worse and better outcome than No ABMR and ABMR, which was mainly driven by the presence of microvascular inflammation and absence of HLA-DSA, respectively. Consequently, the discriminative performance for allograft failure was lowest in Banff'17, and highest in Banff'13. Introduction of an intermediate "DSA negative MVI" category increased the predictive performance, as well as the inclusion of a separate "DSA positive suspicious" category.
Conclusions: The clinical and histological heterogeneity of ABMR is inadequately represented in a binary classification system. This study provides a framework to evaluate updates of the Banff classification and assess the impact of proposed changes on the number of cases and risk stratification. Two alternative classifications introducing an intermediate category are explored.

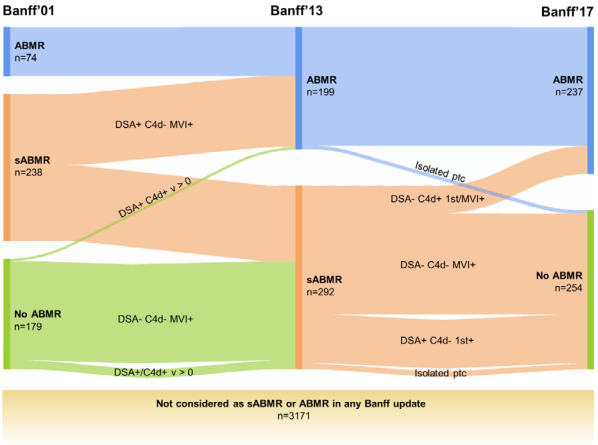

Figure All post-transplant biopsies were classified according to Banff'01, Banff'13 and Banff'17. Of these, 3171 biopsies were not considered as sABMR or ABMR in any classification. The evolution of diagnostic categorization of the other 491 biopsies across different Banff versions is depicted.

OP291 INTERSTITIAL FIBROSIS IN PREIMPLANTATION KIDNEY BIOPSIES OF EXTENDED CRITERIA DONORS PREDICTS LONG-TERM GRAFT SURVIVAL

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Background and Aims: The shortage of organs led to adoption of renal graft from extended-criteria donors (ECD) aiming at expanding the donors' pool. Currently, pre-implantation histological evaluation plays a major role in dual or single graft allocation, but its prognostic value in clinical practice is still matter for debate.
Methods: We evaluated 96 consecutive kidney transplant recipients (KTRs) from ECD who underwent pre-implantation graft biopsy from 2000 to 2009. During the follow-up period, we collected data regarding histological score, immunological data, demographic characteristic and subsequent complication and comorbidities including malignancies, recurrent infections, cardiovascular events, diabetes, and hypertension development. KTRs who developed biopsy-proven acute rejection were excluded from our analysis.
Results: Forty-six KTRs (54%) were allocated to receive dual transplant, while 39 KTRs received single transplant. During a follow-up of 13.0 years (IQR 7.7-18.3) graft loss occurred in 17 patients (19%) and 16 patients died. The multivariate Cox regression analysis demonstrated that dual-graft death-censored survival was influenced only by malignancy occurrence. When considering only single-graft KTRs, the univariate analysis highlights the predictive role pre-implantation biopsy interstitial fibrosis (IF); in the multivariate analysis, IF was confirmed as an independent predictor of death-censored graft survival together with recipient age at transplantation time (respectively HR 5.98 CI 95% 1.05-33.98, $p = 0.04$ and HR 1.16 CI 95% 1.01-1.32, $p = 0.03$).
Conclusions: This is the first study reporting IF score as a predictor of renal graft loss in the long-term follow-up, regardless of the total histological score. A new model, interstitial fibrosis-weighted may be developed to reach an optimal accuracy in organ allocation.

OP292 THREE-MONTH GRAFT FUNCTION OF KIDNEYS RETRIEVED 4.5 HOURS AFTER CIRCULATORY DEATH

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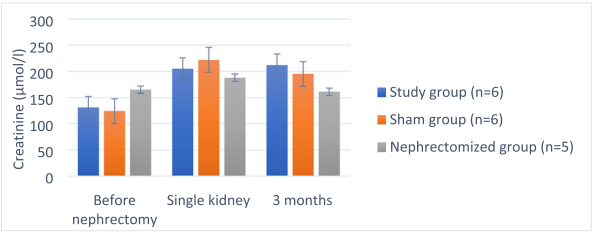
Background: Increasing the donor pool by using cardiac death donor kidneys (DCD) for transplantation could solve organ shortage globally. DCD kidneys are not the current choice of clinicians due to warm ischemia time (WIT) associated with delayed graft function (DGF).
We present data from pigs surviving three months after being transplanted with a reconditioned kidney from an uncontrolled DCD with 4.5 hours WIT.
Methodology: Two hours after circulatory death, ice slush was added in the pig abdomen. Organs were procured after a total of 4.5 hours of ischemia. The study group kidneys ($n = 6$) were injected on back-table with antithrombolytic agents (Lys-Plasminogen, Anti-thrombin-III and alteplase) through the renal artery. Thereafter, kidneys were machine-perfused for three hours with an albumin-rich cell free solution at a temperature of 15 °C and pressure of 20 mmHg. Washed erythrocytes were added to the solution and the perfusion continued for another 3 hours at 32°C and 30 mmHg. Following reconditioning, kidneys were transplanted to pigs using a novel auto-transplant technique with a single functioning autologous kidney. These pigs were observed for 3 months. Sham-operated pigs ($n = 6$) underwent the same surgical procedure and trauma as the study group pigs, but without the kidney reconditioning protocol, were used as a control group. These pigs were observed for 3 months as well. Nephrectomized controls ($n = 5$) had one kidney removed and survived for 3 months with only one remaining native kidney.
Results: At the end of the 3 months 4/6 pigs in the study and 4/6 in the sham control group survived. All the pigs in the nephrectomized group survived. Serum creatinine was not significantly different between the groups. Renal histology revealed a well-maintained kidney morphology and architecture, with no signs of rejection.
Conclusion: Our findings suggested that even after 4.5 hours of WIT in a uDCD kidney, transplantation can be successful, long-term.



OP293 ENDOTHELIAL TO MYOFIBROBLAST TRANSITION (ENMT) AND CAPILLARY VEGF LOSS ENHANCES THE DEVELOPMENT OF INTERSTITIAL FIBROSIS AND GLOMERULOSCLEROSIS

Binnaz Handan Ozdemir[1], Eda Akcay[1], Alev Ok Atilgan[1], Mehmet Haberal[2]
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Background: Although the rate of microvascular destruction (MVD) is similar in recipients with ABMR, some develop higher IF and GS during follow-up. We aimed to understand why some patients compared to others show higher IF and GS rates, although they have similar MVD due to ABMR.
Methods: To determine the mean number of glomerular capillaries (GCs) and peritubular capillaries (PTCs), biopsies of 102 ABMR cases stained with CD31, HLA-DR, and VEGF. Capillary expression of α-SMA, F-actin and VEGF was studied to show the development of EnMT.
Results: The mean capillary numbers were 43.4 ± 11.8 and 30.3 ± 8.7 for GCs and PTCs, respectively. The number of PTCs correlated significantly with PTC inflammation (r -0.56, $p < 0.001$), PTC-VEGF expression ($r = 0.41$, $p < 0.001$), EnMT ($r = -0.45$, $p < 0.001$), proteinuria ($r = -0.34$, $p = 0.001$), the development of IF ($r = -0.56$, $p < 0.001$), and graft loss ($r = -0.57$, $p < 0.001$). The glomerular capillary loss was also significantly associated with GC inflammation ($r = -0.64$, $p < 0.001$), GC-VEGF expression ($r = 0.89$, $p < 0.001$), EnMT ($r = -0.61$, $p < 0.001$), proteinuria ($r = -0.89$, $p < 0.001$), the development of GS ($r = -0.70$, $p < 0.001$), and graft loss ($r = -0.44$, $p < .001$). The incidence of proteinuria, IF and GS development, and graft loss increased with decreasing PTC and GC VEGF expression and increasing EnMT ratio ($p < .001$). Although the mean number of PTCs and GCs in some cases was higher than the cutoff point, it was observed that patients with high EnMT and low capillary VEGF expression showed a higher incidence of IF and GS development and, as a result, increased graft loss.
Conclusion: Monitoring PTC and GC numbers with the presence or absence of EnMT and capillary VEGF expression may become a valuable predictive marker for graft loss. The preservation of capillary endothelium by higher capillary VEGF and lower EnMT can play an essential role in preserving graft survival. Thus the usage of angiogenic factors may become a new approach in the treatment of renal transplantation.

OP294 AGGRAVATION OF FIBRIN DEPOSITION AND MICROTHROMBUS FORMATION WITHIN THE GRAFT DURING KIDNEY TRANSPLANTATION

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Background: In kidney transplantation, microthrombi and fibrin deposition may lead to local perfusion disorders and subsequently poor initial graft function. Microthrombi are often considered to be donor-derived. However, the incidence, time of development, potential difference between living donor kidneys (LDK) and deceased donor kidneys(DDK), and use of intra-operative heparinization during transplantation, remains unclear.
Methods: Two open-needle biopsies, taken at preimplantation and after reperfusion, were obtained from 17 LDK and 28 DDK transplanted between 2005 and 2008. Eight LDK-recipients received unfractionated heparin prior to reperfusion. Paraffin-embedded sections were immunohistochemically stained with an anti-fibrinogen antibody. Fibrin deposition intensity in peritubular capillaries(PTC) and glomeruli was categorized as negative, weak, moderate or strong and the number of microthrombi/mm2 was quantified.
Results: Reperfusion biopsies showed more fibrin deposition (20% to 100% moderate/strong, $p < 0.001$) and more microthrombi/mm2 (0.97 ± 1.12 vs. 0.28 ± 0.53, $p < 0.01$) than preimplantation biopsies. In addition, more microthrombi/mm2 (0.38 ± 0.61 vs. 0.09 ± 0.22, $p = 0.02$) and stronger fibrin intensity in glomeruli (28% vs. 0%, $p < 0.01$) and PTC (14% vs. 0%, $p = 0.02$) were observed in preimplantation DDK than LDK biopsies. After reperfusion, microthrombi/mm2 were comparable ($p = 0.23$) for LDK (0.09 ± 0.22 to 1.19 ± 1.38, $p = 0.02$) and DDK (0.38 ± 0.61 to 0.90 ± 1.11, $p = 0.07$). Heparinized LDK biopsies showed fewer microthrombi/mm2 in reperfusion biopsies than non-heparinized (0.13 ± 0.24 vs. 1.19 ± 1.38, $p < 0.01$).
Conclusions: Upon reperfusion, there is an aggravation of microthrombus formation and fibrin deposition within the graft in both LDK and DDK. The prominent increase of microthrombi in LDK indicates that they are not merely donor-derived.

Figure 3 Number of microthrombi/mm^2

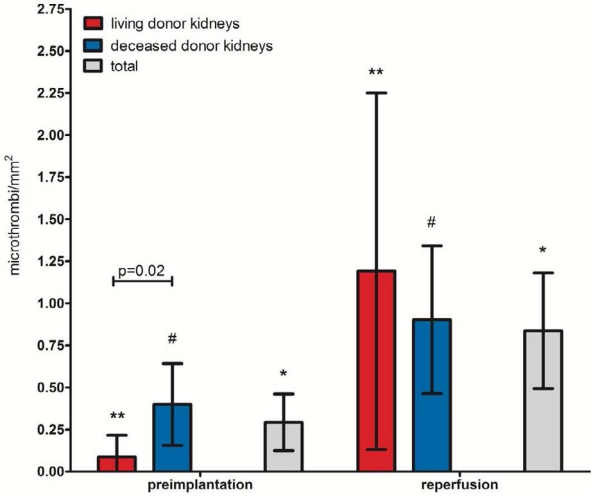

Figure. Number of microthrombi/mm2. Data are shown as mean with 95% confidence interval. microthrombi/mm2, microthrombi per square millimeter; *$p < 0.01$; ** $p = 0.02$; # $p = 0.07$

OP295 HYPERLEPTINAEMIA AND LOW VALUES OF INTERLEUKIN 10 AS RISK FACTORS FOR GRAFT REJECTION IN PROTOCOL BIOPSY AFTER KIDNEY TRANSPLANTATION

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Faculty of Medicine Comenius University, Transplant Center, University Hospital Martin and Jessenius, Martin, Slovakia

Background: White adipose tissue secretes a number of peptide hormones, including leptin, adiponectin, and several cytokines. The aim of this paper was to determine the role of selected adipocytokines (leptin and adiponectin) and interleukins (IL-10 and IL-6) on the development of graft rejection in protocol biopsy after kidney transplantation.
Methods: In a prospective analysis ($n = 104$), we monitored the values of leptin, adiponectin, IL-6, and IL-10 prior to the transplantation and in the 3rd, 6th, and 12th months after the transplantation. The protocol biopsy of the graft was performed in the 3rd month after the transplantation. The group was divided into the following according to the biopsy result: negative result, IFTA 1, TCMR/borderline, and ABMR/DSA positive.
Results: After adjusting for the differences in the baseline recipient and donor characteristics, we identified the hyperleptinaemia baseline ($HR = 2.0444$, $p = 0.0341$) and month 3 ($HR = 49.8043$, $p < 0.0001$) as independent risk factors for rejection in the protocol biopsy. The hyperleptinaemia baseline ($HR = 7.4979$, $p = 0.0071$) and month 3 ($HR = 9.7432$, $p = 0.0057$) are independent risk factors for ABMR and de novo DSA positivity. A low value of IL-10 month 3 is a risk factor for rejection in the protocol biopsy ($HR = 3.0746$, $p = 0.0388$).
Conclusions: Higher leptin levels might play a role in rejection and de novo DSA production. We also confirmed the influence of low values of IL-10 on the development of rejection. We assume that values of adipocytokines in context of other risk factors can predict the immunological risk of patients after kidney transplantation.

OP296 POST-TRANSPLANTATION EARLY BLOOD TRANSFUSION AND KIDNEY ALLOGRAFT OUTCOMES: A SINGLE-CENTER OBSERVATIONAL STUDY

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Background: Although blood transfusions are a reputed cause of allo-sensitization, very few studies have assessed the impact of early blood transfusions on post-transplant outcomes, especially the risk of rejection or donor-specific antibodies (DSA) emergence.
Methods: Every kidney recipient transplanted from the 01/01/2007 to the 31/12/2018, with at least one month of follow-up, were included in an observational monocentric study. Baseline characteristics were compared between recipients who benefited or not from a blood transfusion before M1 post-transplantation. Cox proportional hazards regression models were built with the following outcomes of interests: the emergence of de novo DSA (Luminex, One Lambda), the risk of biopsy-proven acute rejection (BPAR) and graft survival.
Results: 1424 patients were included, with a median follow-up of 4.52 years IQR[2.41-7.56]. 258 recipients had at least one blood transfusion, with a median number of two blood transfusions IQR[1-3]. Significant differences at baseline between transfused and non-transfused recipients were the following: donor age (56.00 yo [46.00-65.00] vs 52.00 yo [41.00-62.00], $p = 0.001$), recipient age (56.25 yo [45.26-62.80] vs 51.89 yo [39.19-60.47], $p < 0.001$), recipient sex (women: 51.16% vs 33.36%, $p < 0.001$), HLA class I and class II sensitization (23.64% vs 16.04%, $p = 0.008$ and 27.52% vs 17.41%, $p = 0.001$), cold ischemia time (18.27 hours [14.08-23.42] vs 15.83 hours [11.68-20.67], $p < 0.001$), induction therapy (thymoglobulin: 61.24% vs 59.61%, $p = 0.008$) and M1-serum creatinine (2.1 mg/dl [15.00-27.50] vs 1.7 mg/dl [13.00-21.85], $p < 0.001$). In multivariate analyses, blood transfusion was neither associated with the risk the emergence of de novo DSA (1.35 [0.86-2.11], $p = 0.19$), the risk of BPAR ($HR = 1.33$ [0.94-1.89], $p = 0.11$), nor the risk graft loss ($HR = 1.04$ [0.73-1.50], $p = 0.82$).
Conclusions: Blood transfusion was not associated with the risks of de novo DSA, graft loss and rejection in our cohort.

DE NOVO CANCER IN TRANSPLANT PATIENTS: KNOWLEDGE IS POWER

OP309 MALIGNANCIES BEFORE AND AFTER HEART TRANSPLANTATION – A SINGLE-CENTRE LONG-TERM OUTCOME STUDY

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Background: Heart transplantation (HTx) has become the standard treatment for patients with end-stage heart disease. The aim of this study was to report cancer incidence and survival after HTx at Sahlgrenska University Hospital in Sweden.
Methods: The study is a single centre retrospective study of 664 patients, who underwent heart transplantation between 1985-2017. Data were retrieved from the Cancer Registry and the Cause of Death registry, both of which are obligatory national registries managed by the National Board of Health and Welfare.
Results: In total, 279 malignancies were diagnosed in 90 patients. The median follow-up time was 6.9 years (IQR 2.4-13.1). No patient was lost to follow-up. The excess risk of cancer following organ transplantation was 6.1-fold and 2.9-fold when excluding nonmelanoma skin cancer. The three most common malignancies were; nonmelanoma skin cancer, non-Hodgins lymphoma and lung cancer. Risk factors for malignancy (excluding skin cancer) in a multivariable model were: smoking (no (reference): HR 1.0; stopped >6 months: HR 1.7 (95CI 0.96-3.02, $p < 0.070$); stopped <6 months: (HR 3.46 (95CI 1.69-7.07, $p < 0.001$), hypertension (HR 2.16 (95CI 1.10-4.26), $p < 0.026$), and ischemic time (<3 hours (reference): HR 1.0; 3-4 hours: HR 1.93 (95CI 1.09-3.40, $p = 0.024$); >4 hours (HR 1.92 (95CI 0.87-4.24, $p = 0.11$). Risk factors for skin cancer in a multivariable model were: age per 10 years (HR 2.90 (95CI 1.85-4.55, $p < 0.001$), CMV+ donor (HR 0.47 (95CI 0.24-0.90, $p = 0.024$), and the use of proliferation inhibitor Azathioprin (versus MMF) (HR 2.53 (95CI 1.20-5.36, $p < 0.015$).
Conclusions: Nineteen percent of patients had experienced a malignancy after nearly 7 years of median follow-up after HTx. We have shown an overall risk of cancer to be over 6-fold higher than among the general population, and almost 3-fold higher when non-melanoma skin cancer was excluded, after heart transplantation.

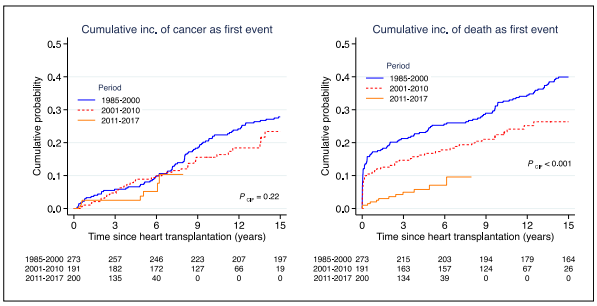

Figure 1 Cumulative incidence of competing risks cancer and death, and related to time-era after heart transplantation.

OP310 CANCER TRANSMISSIONS AND NON-TRANSMISSIONS FROM SOLID ORGAN TRANSPLANTATION: AN AUSTRALIAN COHORT STUDY

James Hedley[1], Patrick Kelly[1], Imogen Thomson[1], Karen Waller[1], Nicole De La Mata[1], Brenda Rosales[1], Kate Wyburn[1,2], Angela Webster[1,3]
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Background: Large-scale studies of cancer transmission from donors to recipients are sparse. We sought to identify any cases of cancer transmission or non-transmission from transplantation in a cohort of NSW donors and recipients.
Methods: We included all NSW solid organ transplants from deceased donors 2000-2012 and from living donors 2004-2012 in a cohort study using linked data from the NSW Biovigilance Public Health Register (SAFEBOD). Linked data from the Central Cancer Registry (CCR) was available to 2013, providing a minimum one-year follow-up. Donor-recipient pairs (transplants) were classified as having likely, possible, or excluded transmission using categorisation defined by international guidelines. Non-transmissions were recipients with transmission excluded, but where the donor had a cancer history in the CCR or a transmission to another recipient. All other transplants were non-events.
Results: In our cohort 2,502 recipients underwent 2,544 transplant procedures, 1,828 (72%) deceased donor and 716 (28%) living. We found 4 (<1%) transmissions from deceased donors (2 likely, 2 possible), and 1 (<1%) possible transmission from a living donor. Four transmissions were from donors with a kidney cancer found during retrieval, while one was from a donor with a family reported cancer of unknown site that could not be verified in the CCR. The 4 deceased donors involved in transmissions donated to 10 recipients with 4 transmissions and 6 non-transmissions. Overall, 61 (2%) non-transmissions occurred (55 with donor cancer history, 6 from donors who transmitted to another recipient).
Conclusions: Cancer transmission from transplantation is rare. Among recipients whose donor had a cancer history, non-transmission is much more likely than transmission.

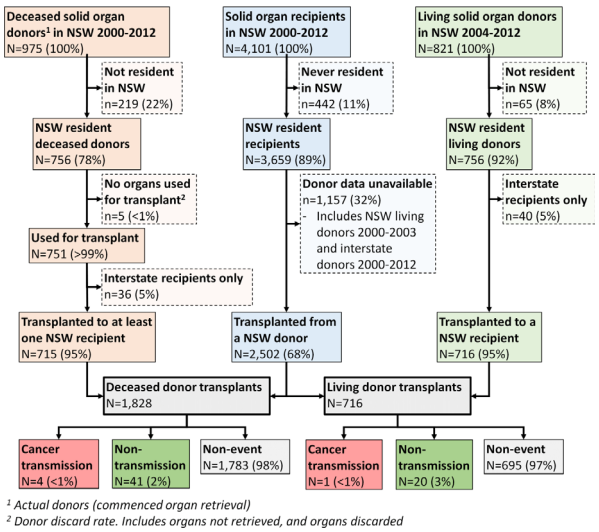

Figure 1 Flowchart of donors and recipients included in the study cohort

OP311 SURVIVAL WITH TABELECLEUCEL IN PATIENTS WITH EPSTEIN-BARR VIRUS-DRIVEN POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE AFTER SOLID ORGAN TRANSPLANT

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[1]Memorial Sloan Kettering Cancer Center, New York, NY, United States; [2]Atara Biotherapeutics, South San Francisco, CA, United States

Background: Tabelecleucel is an investigational, off-the-shelf, allogeneic Epstein–Barr virus (EBV)-specific T-cell immunotherapy being studied in patients (pts) with serious EBV-driven diseases, including post-transplant lymphoproliferative disease (EBV+ PTLD). Pts with EBV+ PTLD after solid organ transplant (SOT) who relapsed with rituximab and did not respond to or did not receive additional chemotherapy (CT) had a median overall survival (OS) of <3 months (Zimmermann EHA 2019), demonstrating a substantial unmet need in relapsed/refractory (R/R) EBV+ PTLD after SOT. We have previously shown that pts with EBV+ PTLD after SOT who responded (complete response [CR] or partial response [PR]) to tabelecleucel have clinical benefit, including 100% 2-year survival rates (Prockop ASH 2019 and JCI 2019). Here, we report aggregate OS in patients with EBV+ PTLD after SOT with CR or PR with tabelecleucel treatment.
Methods: Treatment response and OS were assessed in three studies (NCT00002663, NCT01498484 and NCT02822495). All pts received

tabelecleucel at ≈2 x 106 cells/kg on Days 1, 8 and 15 in a 35-day treatment cycle. Pts received a median (range) of 2 (1–9) cycles.
Results: Twenty-six SOT recipients with EBV+ PTLD R/R to rituximab (SOT1 n = 7) or rituximab+CT (SOT2 n = 19) were treated. The objective response rate (PR+CR) was 65% (17/26) overall, 86% (6/7) in SOT1, and 58% (11/19) in SOT2. Similar survival rates were observed across pts with best overall response (BOR) of CR or PR, including in the SOT1 and SOT2 subgroups (Table 1, Figure 1). Treatment was well tolerated with no confirmed evidence for graft vs host disease, cytokine release syndrome or neurotoxicity in relation to tabelecleucel in these very sick, treatment refractory, and immunocompromised pts.
Conclusions: These data show that not only pts with complete responses, but also pts with partial responses to tabelecleucel, may obtain longer-term clinical benefit, demonstrating a favorable risk–benefit profile in this high-risk population for whom there are no approved alternative therapies.

Figure 1

Kaplan-Meier Plot of OS By Response per Investigator

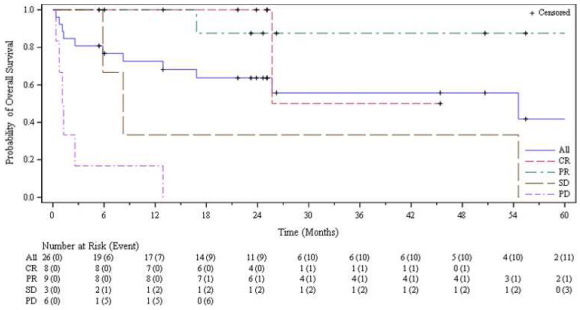

Table 1. OS by BOR

	All SOT EBV+ PTLD (n=26)		SOT1 (n=7)		SOT2 (n=19)	
BOR	**CR (n=8)**	**PR (n=9)**	**CR (n=4)**	**PR (n=2)**	**CR (n=4)**	**PR (n=7)**
1-year OS rate	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**
2-year OS rate (95% CI)	**100%**	**87.5%** (38.7,98.1)	**100%**	**100%**	**100%**	**83.3%** (27.3,97.5)
Median follow-up (min,max) months	**24.5** (6.0,45.4)	**26.2** (5.4,115.0)	**22.8** (12.9,25.7)	**38.4** (26.2,50.7)	**25.1** (6.0,45.4)	**24.6** (5.4,115.0)

CI=confidence interval

OP312 DONOR-TRANSMITTED CANCERS: THE SPANISH EXPERIENCE

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Background: Donor-transmitted cancers (DTC) are infrequent complications in organ transplantation, but have devastating effects. While the occurrence of DTC must be minimized, the unnecessary loss of organs from donors with a history of malignancy must be avoided and requires a careful risk-benefit analysis based on the best available evidence that is however scarce. The Spanish experience on DTC has been reviewed to contribute to better define risks of malignancy transmission.
Methods: We compiled information on all deceased donors with a history of malignancy identified either before or after transplantation during 2013-2018. Donor malignancies were classified according to the risk of transmission proposed by the Council of Europe.
Results: Of 10,076 utilized deceased organ donors, 283 (3%) had a past or present history of malignancy known before transplant, with 669 recipients transplanted. 11 malignancies met high-risk criteria. No case of DTC was reported after a median follow-up of 24 (IQR:19-25) months. In addition, 64 deceased donors were diagnosed of a malignancy after at least one organ had been transplanted, with 126 recipients involved. Despite 23 of these malignancies were considered of high or unacceptable risk of transmission, no DTC was reported after a median follow-up period of 26 (IQR: 22-37) months after transplantation. Finally, 10 donors transmitted an occult malignancy to 16 recipients, consisting of lung cancer (n = 9), extrahepatic cholangiocarcinoma (n = 1), undifferentiated cancer (n = 1), duodenal adenocarcinoma (n = 2), renal cell carcinoma (n = 2), and prostate cancer (n = 1). After a median follow-up time of 30 (IQR: 17-52) months, the evolution of recipients with DTC was fatal in 9 of the 16 recipients affected. In total, 357 utilized deceased organ donors were known to have a malignancy either before or after transplantation (3.5%). Of 820 recipients at risk, 16 (2%) developed a DTC, which corresponds to 6 cases *per* 10,000 solid organ transplants (Table 1).
Conclusion: Current standards guiding professionals in making decisions on the transplantation of organs from donors with a history of malignancy seem appropriate, avoiding the unnecessary loss of organs for transplantation. DTC usually occurs as a result of the transmission of malignancies unknown in the donor.

Table 1: Outcomes of recipients of organs from donors with malignancies identified before or after transplantation

MALIGNANCY (location in the donor)	DONORS WITH MALIGNANCY	RECIPIENTS AT RISK	RECIPIENTS WITH CONFIRMED MALIGNANCY TRANSMSSION*	GRAFT LOSS RELATED TO DONOR MALIGNANCY	DEATH RELATED TO DONOR MALIGNANCY
ADENOCARCINOMA OMENTUM	1	2	0	1	0
BREAST	9	28	0	0	0
CNS	104	279	0	0	0
COLORECTAL CANCER	18	33	0	0	0
CHOLANGIOCARCINOMA	1	3	1	0	0
DUODENAL	1	2	2	0	2
ESOPHAGEAL	1	4	0	0	0
GALLBLADDER ADENOCARCINOMA	1	3	0	1	0
GASTRIC	3	9	0	0	0
GIST	6	17	0	0	0
HEMATOPOIETIC	16	28	0	0	0
LIVER	3	5	0	0	0
LUNG	10	26	9	10	7
NEUROENDOCRINE	2	6	0	0	0
OROPHARYINGEAL (HEAD & NECK)	14	25	0	0	0
OVARIAN	3	9	0	0	0
PROSTATE CANCER	41	91	1	0	0
RENAL CELL	71	116	2	2	0
SUPRA-RENAL	6	18	0	0	0
TESTICULAR	2	5	0	0	0
THYROID	4	13	0	0	0
UROTHELIAL	17	38	0	0	0
UTERUS	8	21	0	0	0
UTERINE CERVIX	7	19	0	0	0
OTHER	7	19	0	0	0
UNDIFFERENCIATED	1	1	1	1	0
TOTAL	357	820	16	15**	9

*Donor-origin of malignancy in the recipient classified as either possible, probable, or definite/certain according to the algorithm of the Disease Transmission Advisory Committee.
**Includes 5 prophylactic transplantectomies.

OP313 SERIOUS ADVERSE EVENTS (SAE) AND SERIOUS ADVERSE REACTIONS (SAR) REPORTING IN GERMANY FROM 2016-2020: ANALYSIS OF DONOR-TRANSMITTED MALIGNANCY

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Background: Analysis of aggregate SAE and SAR cases can help to identify risks of transmitting donor disease to transplant recipients. The German organ procurement organization (Deutsche Stiftung Organspende – DSO) is the delegated body assigned by the German competent authority (Federal Ministry of Health) responsible for managing and monitoring the reporting of SAE and SAR.

Methods: All incoming SAE and SAR reported to the DSO from January 1st 2016 to December 31st 2020 related to a potential malignant disease were analyzed. All diagnoses were verified by histopathological examination. A donor-transmitted malignancy was defined as a malignancy present within the organ at the time of transplantation. It was further categorized as proven or probable according to the definition of EUSTITE and SoHO V&S.
Results: A total of 118 reports were analyzed. In 31 reports, the final histopathological examination showed a benign tumor (31/118, 26%). Of the remaining 87 reports showing a malignant tumor either in the donor (45 cases) or at least one of the recipients (42 cases), 13 reports were classified as proven/probable malignancy transmission from donor to recipient. These 13 cases involved 19 recipients resulting in 7 attributable deaths (37% of all transmissions). The mean time until the diagnosis was made in the 19 recipients was 6,2 months (0-36 months). The reports with proven/probable malignancy transmission included two renal cell carcinomas, two lung carcinomas, two urothelial carcinomas, two lymphomas, two melanomas, one carcinoma of unknown primary, one angiosarcoma and one pleural mesothelioma. In summary, in the 5 years from 2016 to 2020, 0,2 % of the 6359 utilized donors (13/6359, 0,2%) transmitted a proven/probable malignancy to 0.13 % of all recipients (19/14.467, 0.13%).
Conclusions: With careful donor screening, transmission of a malignancy to a recipient is a rare event, but when it occurs, tumor transmission can lead to significant morbidity and mortality. Reporting of SAE and SAR can identify possible risks in organ donation and solid organ transplantation and help to improve donor characterization and to increase awareness of transmission events.

OP314 HETEROGENEOUS INFLUENCE OF DIFFERENT FORMS OF POST-TRANSPLANT DE NOVO CANCER ON SURVIVAL OF KIDNEY GRAFTS – A COLLABORATIVE TRANSPLANT STUDY REPORT

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Background: We analysed the influence of different post-transplant *de novo* neoplasm diagnoses on kidney graft survival.
Methods: 17,907 adult recipients of first deceased donor kidney transplants transplanted during 1990–2019 that developed a *de novo* neoplasm post-transplant were matched 1:1 with a transplant recipient on recipient sex and age, transplant centre, and transplant year. The risk of graft loss from the time of cancer diagnosis was analysed in Cox regression. For a fair comparison, the graft survival time of the statistical sibling without neoplasm was reduced by the corresponding time between cancer diagnosis and transplantation.

Table 1. Results of 23 Cox regression analyses for graft survival 5 year after diagnosis of cancer. 1:1 matched controls without cancer served as reference.

Diagnosis	N	HR	Lower CI	Upper CI	P
Overall	2*17,947	1.92	1.81	2.03	<0.001
Brain	2*185	5.02	2.94	8.58	<0.001
Haematopoietic or lymphoid tissues	2*1,913	3.65	3.11	4.29	<0.001
Mesenchymal	2*492	2.28	1.80	2.90	<0.001
Lip, oral cavity or pharynx	2*442	2.01	1.40	2.89	<0.001
Digestive organs	2*1,548	5.50	4.56	6.62	<0.001
Middle ear, respiratory or intrathoracic organs	2*1,207	7.10	5.78	8.73	<0.001
Melanoma skin	2*397	1.89	1.29	2.78	0.001
Non-melanoma skin	2*6,995	0.56	0.50	0.64	<0.001
SQCC	2*3242	0.58	0.48	0.70	<0.001
BCC	2*2639	0.48	0.39	0.60	<0.001
Retroperitoneum, peritoneum or omentum	2*24	3.67	1.12	12.01	0.032
Breast	2*610	2.33	1.60	3.39	<0.001
Female	2*596	2.36	1.61	3.44	<0.001
Male	2*14	1.17	0.07	18.91	0.91
Female genital organs	2*472	3.40	2.25	5.15	<0.001
Male genital organs	2*947	0.83	0.64	1.07	0.15
Urinary tract	2*1,696	2.60	2.15	3.14	<0.001
Eye or ocular adnexa	2*25	0.58	0.14	2.44	0.46
Endocrine glands	2*191	1.26	0.68	2.33	0.47
Metastases	2*16	31.84	3.84	264.4	0.001
In situ	2*599	0.70	0.43	1.13	0.14
Benign	2*193	0.70	0.34	1.42	0.32

Results: As shown in Table 1, the majority of neoplasms were associated with an increased risk of graft loss, mainly due to a higher mortality. Patients with neoplasms of the respiratory or thoracic tract showed a very high risk of graft loss with a high hazard ratio (HR) of 7.10, followed by patients with neoplasms of the digestive tract with a HR of 5.50 or brain neoplasms with a HR of 5.02 ($p < 0.001$ in all cases). As expected, 16 patients who were diagnosed with a metastasising neoplasm had an extremely high HR for graft loss of 31.84 ($p = 0.001$). Importantly, non-melanoma skin cancer as the most frequent diagnosis did not increase the risk of graft loss; in contrast, these patients showed a strongly decreased HR for graft loss of 0.56, most probably due to a suppressed immune system ($p < 0.001$). *De novo* neoplasms of male genital organs, eye or ocular adnexa, endocrine glands and in situ or benign neoplasms did not influence graft outcome significantly.
Conclusion: Patients with non-melanoma skin cancer as the most frequent cancer in kidney transplant recipients perform well after the diagnosis of the neoplasm. The risk of graft loss is at least twice as high in cancers with the next highest frequencies, such as neoplasms in haematopoietic or lymphoid tissue, urinary tract or digestive organs, indicating that *de novo* malignancies represent a field with room for substantial improvement regarding transplant outcomes.

OP315 POST-TRANSPLANT MALIGNANCIES AFTER PANCREAS TRANSPLANTATION: INCIDENCE AND IMPLICATIONS ON LONG-TERM OUTCOME FROM A SINGLE-CENTER PERSPECTIVE

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Background: The advancement of immunosuppressive regimens paved the way for widespread implementation of solid organ transplantation as treatment of choice for end-stage organ failure by significantly improving patient and graft survival. However, long-term immunosuppressive therapy is associated with a high risk of malignancy. Pancreas transplant recipients require particularly high doses of immunosuppression. The main objective of this study is to evaluate the incidence and effect of post-transplant malignancies (PTMs) after pancreas transplantation.
Methods: 484 consecutive first pancreas transplants at the Medical University of Innsbruck performed between 1985 and 2015 were evaluated for this study. 348 patients were included in the final analysis. Chi-square tests and rank-sum tests were applied as appropriate. Kaplan-Meier-Plots, log-rank test and cox proportional hazard regression adjusted for donor and recipient factors were used to analyse patient and graft survival.
Results: 71 out of 348 patients (20.4%) developed a PTM. Median time to diagnosis was 130 months. Thirty-six patients (50.7%) developed skin cancers (four patients with melanoma, 32 patients with non-melanoma skin cancers). Solid organ malignancy occurred in 25 (35.2%), hematologic malignancy in 10 patients (14.1%). Affected patients were more likely to have received a graft from a male donor (81.7% vs. 62.5%, $p = 0.002$). No differences in induction therapy were seen. Both groups demonstrated comparable patient and graft survival. In comparison to patients with skin cancer, pancreas transplant recipients with solid organ and hematologic malignancies had a 3- and 6-fold increased hazard of death, respectively [aHR 3.04 (IQR 1.17-7.91); $p = 0.023$; aHR 6.07 (IQR 1.87-19.71); $p = 0.003$]. When compared to patients without malignancies hazards of death were similar to those with solid and hematologic cancers. Patients with skin malignancies had a significantly decreased risk of death (aHR 0.37 [IQR 0.18-0.76], $p = 0.007$).
Conclusions: Malignancies after pancreas transplantation are common. Development of a post-transplant malignancy per se is not associated with decreased patient or graft survival. Differences, however, exist between different types of malignancies.

OP316 T AND B CELL ABUNDANCE ARE STRONGLY REDUCED IN THE IMMUNE MICROENVIRONMENT OF POST-TRANSPLANT MALIGNANCIES

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Background: Immunosuppressive medication is mandatory in the majority of solid organ transplant recipients to reduce the risk of allograft rejection. An increased risk to develop cancer is a negative side effect of long-term immunosuppression. However, the impact of immunosuppression on the tumor immune microenvironment (TME) is poorly understood. We aimed to elucidate differences in the TME of post-transplant malignancies and non-immunosuppressed cancer patients.
Methods: 117 primary tumor samples from 80 organ recipients (kidney, heart, lung and liver) were included. Immunohistochemistry of whole section slides used for digital image analysis. We assessed abundance and localization of T cells (CD3, CD8) and B cells (CD20) in the TME of 14 different cancer types. These data used to calculate the Immune-score and to quantify tertiary lymphoid structures in the TME. Results were compared to a matched cohort of cancer samples from non-immunosuppressed control patients. Expression of human-leucocyte-antigene-I (HLA-I) and programmed cell death ligand 1 (PD-L1) was analyzed in tissue microarrays.
Results: The increased risk of cancer in solid organ transplant recipients was reflected by a remarkably reduced immune infiltrate in the center of the analyzed tumors (CT) and the invasive margins (IM). T cell abundance was significantly decreased in CT of skin (814 vs. 1440 $CD3^+$ cells/mm^2, $p < 0.01$) and non-skin tumors (479 vs. 781 $CD3^+$ cells/mm^2, $p < 0.01$) when compared to non-immunosuppressed controls. These differences were more pronounced in the IM than in the CT and higher when assessing the abundance of $CD8^+$ T cells. The Immune-score integrating results from CT and IM was also decreased in transplant recipients. Finally, B cell abundance and density of tertiary lymphoid structures were lower in cancer samples of transplant recipients. Strikingly, HLA-I expression was more common in transplant recipients whereas PD-L1 expression was higher in controls.
Conclusions: Our study supports the hypothesis of reduced anti-tumor immune response as important mechanism underlying increased risk of cancer in solid-organ recipients. Optimized immunosuppressive protocols may reduce cancer incidence and cancer therapies need to consider the distinct immune microenvironment of post-transplant malignancies.

OP317 IMPACT OF CANCER ON THE RISK OF DEATH AMONG ITALIAN KIDNEY TRANSPLANT RECIPIENTS WITH A FUNCTIONING GRAFT: ITALIAN TRANSPLANT & CANCER COHORT STUDY

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Background: Kidney transplant (KT) recipients are at increased cancer risk, but the influence of cancer on survival has been rarely evaluated. This study assessed the impact of cancer on the risk of death in KT recipients with a functioning graft, as compared to corresponding recipients without cancer.
Methods: A nested case-control study was conducted based on a cohort of 13,245 individuals who underwent KT in 17 Italian centers from 1997 to 2017. Cases were subjects diagnosed with any cancer after KT. For each case, two controls - matched for gender, age, and year at KT - were randomly selected from cohort members free of cancer at the time of diagnosis of the index case. Hazard ratios (HRs) for death within 5-years after cancer diagnosis and 95% confidence intervals (CIs) were estimated using Cox models.
Results: Overall, 292 (20.5%) deaths with a functioning graft within 5-years after cancer diagnosis were recorded among 1425 cases identified in the cohort. When compared to matched controls (where 238 out of 2850 controls deaths were observed, i.e. 8.4%), KT recipients with cancer had a 3-fold increased risk of death with a functioning graft (HR = 3.31, 95% CI: 2.70-4.06) within 5-years. This pattern was consistent for a broad range of cancer types, including non-Hodgkin lymphoma (NHL) (HR = 33.09, 95% CI: 7.96-137.62), lung (HR = 20.51, 95% CI: 8.21-51.26), breast (HR = 8.80, 95% CI: 2.54-30.57), colon-rectum (HR = 3.51, 95% CI: 1.49-8.26), and kidney (HR = 2.38, 95% CI: 1.05-5.40). The survival gap was observed throughout the entire follow-up period, though the effect was more marked within 1 year from cancer diagnosis. No difference in risks emerged for prostate, head and neck, and Kaposi's sarcoma.
Conclusions: These results call for close post-transplant surveillance to detect cancers at earlier stages when treatments are more effective to improve survival outcomes. For the Italian Transplant & Cancer Cohort Study.

OP318 MANAGEMENT OF THE KIDNEY TRANSPLANT PATIENT WITH CANCER": REPORT FROM A CONSENSUS CONFERENCE

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Background: Cancer is the second most common cause of mortality and morbidity in kidney transplant recipients (KTRs). Immunosuppression can influence the efficacy of cancer treatment and modification of the immunosuppressive regimen may restore anti-neoplastic immune responses improving oncologic prognosis. However, patients are usually reluctant to modify their immunosuppression, fearing rejection and potential graft loss. Due to the lack of extensive and recognized data supporting how to manage immunosuppressive therapy in KTRs, in the context of immunotherapy, chemotherapy, radiotherapy and loco-regional treatments, a Consensus Conference was organised under the auspices of the European Society of Organ Transplantation and the Italian Society of Organ Transplantation, involving a multidisciplinary group of experts in the field across Europe.
Methods: The overall process included the formulation of 12 specific questions (Figure 1), literature review and summary for experts for each question, a two days conference celebration and the collection of experts'

Figure 1 All the 12 Conference Questions divided in the three Conference Sessions.

Questions	Session
Does maintaining as opposed to withdrawing or reducing calcineurin inhibitors in kidney transplant recipients with non-metastatic, non-skin cancer undergoing chemotherapy worsen patient or graft survival?	"Immunosuppressive Therapy and Immunotherapy"
Does maintaining as opposed to withdrawing calcineurin inhibitors in kidney transplant recipients with PTLD, undergoing first-line chemotherapy worsen patient or graft survival?	
Does the switch from calcineurin inhibitors to mTOR-inhibitors improve patient or graft survival of kidney transplant recipients with metastatic non-skin cancer undergoing chemotherapy?	
Should immunosuppression be stopped or modified before oncological surgery in the kidney transplant recipient?	
Does the use of checkpoint inhibitors in kidney transplant recipients with metastatic skin and non-skin cancer have a negative impact on patient or graft survival?	"Systemic Therapy"
Can anti-angiogenic drugs be safely used in kidney transplant recipients with cancer?	
Can hormone therapy be safely used in kidney transplant recipients with cancer?	
Can platinum salts be safely used in kidney transplant recipients with cancer?	
Does withdrawing antimetabolites and/or CNI inhibitors and/or mTOR-inhibitors as opposed to continuing maintenance immunosuppression improve patient survival in kidney transplant recipients with cancer undergoing radiotherapy?	"Integrated Therapy"
Should a kidney transplant patient with cancer avoid standard radiotherapy technique (EBRT, BT, SBRT, protons), dose and volume in order to preserve the transplanted kidney?	
In case of cancer of the transplanted kidney, is focal treatment (thermoablation, radiofrequency, brachytherapy, electrochemotherapy, cryoablation, stereobody radiotherapy, protons) indicated as the standard treatment as opposed to graft nephrectomy?	
In case of focal treatment, is percutaneous approach (thermoablation, radiofrequency, brachytherapy, electrochemotherapy, cryoablation) indicated as the standard treatment as opposed to external beam radiotherapy (stereobody radiotherapy, protons)?	

agreements. The conference was articulated in three sessions: "Immunosuppressive therapy and immunotherapy", "Systemic therapy", "Integrated therapy"; the final experts' agreement was collected with a 2-rounds televoting procedure and defined according to the majority criterion.
Results: Twenty-six European experts in the field attended the conference and expressed their vote. A total of 14 statements were finally elaborated and voted. *Strong agreement* was found for 10/14 (71.4%) statements, *moderate agreement* for 2/14 (14.2%), *moderate disagreement* for 1/14 (7.1%) and *uncertainty* for the last one 1/14 (7.1%).
Conclusions: The statements represent very solid and important reference points to guide transplant physicians in their everyday practice and clearly indicate the key aspects that need to be addressed in the clinical research in this setting.

OP319 RETROSPECTIVE STUDY OF NEOPLASM TRANSMISSION FROM ORGAN DONOR TO RECIPIENT

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Introduction: The growing need of organs has been accompanied by increase in donor's age acceptance. However, older donors imply a higher associated morbidity and hence, the presence of neoplasm that can be transmitted to recipient. There is few reported incidental neoplasm transmissions from organ donors to recipients, depending on the type of tumor and the moment of diagnosis.
Objectives and Methodology: The main aim of our study is to describe the population of organ donors with neoplasm with the following characteristics: type and histological grade of donor's neoplasm, analyze the possible neoplasm transmission from organ donor to recipient and check the possible impact in patient's survival. To do so, our study was based in recipients from Hospital Clinic who received and organ from a donor diagnosed with a neoplasm. Data from donors and their respective recipients were collected since June 2007 with a follow-up done the 1st of January 2020 and statistically analyzed.
Results: Donors had a normal gender distribution between male 55.3% (26/47) and female 44.7% (21/47) (p = N.S). According to donor's distribution in relation to the moment at which their neoplasm was diagnosed, 9/47 (19.1%) were "Known and cured" neoplasm in the past (>10 years), 9/47 (19.1%) were classified as "Known and active" neoplasm and 29/47 (61.8%) as Incidental finding. Demographic characteristics of recipients: 78.5% were male (51/65) and 21.5% female (14/65). Their status (alive/dead) at the end of follow-up: 42/65 were alive (64.6%), 15/65 were dead (23.1%), none related with donor's neoplasia and 8 recipients were lost (12.3%). 14/65 recipients developed a "de novo" neoplasia (21.5%), 43/65 (66.2%) did not develop a neoplasia and 8/65 patients were lost (12'3%).
Conclusions: A total of 14 recipients out of 65 developed a "de novo" neoplasm but none of these neoplasms were histological related with donor's neoplasm so there was not any case of neoplasm transmission from donor to recipient. However, what we have seen is that a 13/14 (92.8%) of the cases of "de novo" neoplasm, happened in recipients whose donors had an active (not cured) neoplasm at the moment of organ procurement. This could be a coincidence fact but not necessarily a risk factor for development of "de novo" neoplasia in the recipient.

OP320 POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE IN KIDNEY TRANSPLANT RECIPIENTS: A SINGLE-CENTER STUDY

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Background: Post-transplant lymphoproliferative disease (PTLD) comprises a serious complication following renal transplantation. The aim of the study was to examine the incidence and clinical outcome of PTLD in kidney transplant recipients followed in our transplant center.
Methods: We retrospectively reviewed the data of all adult kidney transplant recipients diagnosed with PTLD in our center over a three-decade period (1987 - 2020).
Results: A total of 35 cases out of 2394 kidney transplants were identified, corresponding to a cumulative incidence of 1.46% for the study period. The median age at transplantation was 39 years (IQR25-52). PTLD occurred in a median time of 11 years (IQR7-19) from renal transplantation. Two patients (5.7%) presented with early PTLD, within a year after transplantation, one of whom had received T-cell depleting agent OKT3 as induction therapy. Twenty-one patients (60%) developed PTLD in 10 or more years post-transplant. The EBV serologic status was available in 15 renal transplant recipients. Three patients were EBV-negative, all of whom presented with late PTLD. According to WHO classification, there were 30 monomorphic PTLD (85.7%), most of which DLBCL, and 5 classical Hodgkin lymphomas (14.3%). At a median follow-up time from diagnosis of 24 months (IQR12-72), 22 patients (62.9%) achieved clinical remission, while 12 patients (37.1%) died of a PTLD-related cause. The estimated median survival time was 10 years. Immunosuppressive therapy, except for a low dose of corticosteroids, was discontinued in all patients during chemotherapy. The patients who achieved complete remission received a combination of mTOR inhibitors with low-dose corticosteroids. Renal graft function was preserved in 72.7% of the responders. The remainders reached ESRD at a median time of 3 years (IQR0.9-6) from diagnosis. One patient exhibited biopsy-proven antibody-mediated rejection.
Conclusion: Kidney transplant recipients develop predominantly late PTLD, probably as a result of cumulative immunosuppression. Most patients achieve clinical remission, preserving their renal allograft function.

OP321 DISTINCT IMPACT OF POST-TRANSPLANT MALIGNANCIES AND MORTALITY IN DIFFERENT IMMUNOSUPPRESSIVE THERAPY PROTOCOLS BASED-PERIODS IN A LONG-TERM FOLLOW-UP

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Background: Post-transplant malignancies(PTM) and mortality in long-term FU across the different immunosuppressive (IS) therapy protocols used in past and recent Eras of Transplant remains unknown. Our aim lies in to evaluate the coincidence factors associated with PTM and patient survival in kidney transplant patients from different periods.
Methods: Kidney transplants recipients(KTRs,2003-2015) were enrolled. Different Eras of Transplant (2003-2006;2007-2009;2010-2012, 2013-2015) were evaluated due to different IS protocols implemented in this long-term analysis. Ethics Committee approved the study.
Results: 1505 KTRs (60.5% male; mean age 55.63+/-14.16(20-87)yrs; 17% diabetics); mean FU:62.78+/-158.01Mo. 169 out of 1505 (11.2%) developed any kind of neoplasia, being in the multivariant analysis (binary logistic regression) older(p = 0.000;Exp(B)1.039;univariant:62.8+/-11.1yrs vs 54.7+/-14.3yrs p = 0.000), rejection (p = 0.002;Exp(B)0.493), less patient survival (p = 0.000 Exp(B)2.445), and less with CNI+mTORi (p = 0.023 Exp(B) 0.448); PTM was also related with the Era of Transplant (p = 0.000;Exp(B) 0.772). To understand the impact of the different Eras of the transplant, we made a multinomial regression analysis: rejection(p = 0.048), PTM (p = 0.000), and the CNI+mTORi(p = 0.000) the main factors, and we found greater mortality(p = 0.002). As the PTM, with lower survival in the long-term FU analyzed by Kaplan-Meyer curve (73.4% vs 88.7%,Log-rank 0.001), and Eras of Transplant (p = 0.000) were associated to the patient survival, we performed a multivariant binary logistic regression and the rejection rate(p = 0.000; Exp(B)6.310), and the IS protocol based on CNI+mTORi(p = 0.007;Exp(B)0.444) were the coincidence factors associated with patient survival, PTM and the Era of Transplant.
Conclusions: In the long-term FU, the rejection and the use of CNI+mTORi were the coincidence factors associated to PTM and patient survival considering the different Eras of Transplant.

OP322 PREVALENCE AND CLINICAL SIGNIFICANCE OF PANCREATIC CYSTIC LESIONS IN IMMUNOSUPPRESSED PATIENTS WITH SOLID ORGAN TRANSPLANTATION

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Background: Solid organ transplant recipients have an increased risk of cancer due to immunosuppressive therapy. Pancreatic cystic lesions (PCLs)

are increasingly being detected, some with malignant potential. We aimed to determine the prevalence of these lesions and describe their clinical course in these patients.
Methods: We identified the presence of pancreatic cystic lesions in a retrospective cohort of 804 consecutive solid organ transplant recipients from 2009 to 2019 and compared lesion characteristics at initial and follow-up imaging, when available. We also compared these features with an immunocompetent control group encompassing patients under surveillance for greater than 12 months and were matched for age and sex.
Results: There were 15 patients in the study group and 60 patients in the control group. Among the solid organ transplant recipients with PCLs, there were 7 and 8 patients undergoing liver and kidney transplantation, respectively. Lesion prevalence was 1.86% (15/805). Median diameter of the largest lesion was 20 mm (range: 0.2–60 mm) and most lesions were benign (9/15, simple cyst or pseudocyst). During follow-up imaging, the cysts size remained stable in 79.7%, increased in 6.6%, and decreased in 13.7%. Among patients diagnosed with IPMN (6/15), worrisome features were noted in one patient at the time of cyst diagnosis. However, due to multiple comorbidities, the patient received only conservative management. There were no significantly different features including the rate of size increase or the development of worrisome features between the study and control group ($p < 0.05$).
Conclusions: Pancreatic cystic lesions are somewhat common in solid organ transplant recipients. In lesions without high-risk features, the development of features worrisome for cancer is rare. These lesions can be managed conservatively, and their presence should not affect transplant eligibility.

STRATEGIES TO IMPROVE QUALITY AND DURATION OF LIFE AFTER KIDNEY AND LIVER TRANSPLANTATION

OP331 MAXIMIZE THE USE OF ARTIFICIAL INTELLIGENCE IN ORGAN DONATION AND TRANSPLANTATION MANAGEMENT TO IMPROVE EFFICACY AND SAFETY

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Background: The power of AI has been proved, especially in the COVID-19 pandemic. This study aims at building an AI solution to help enhance the efficiency and quality in organ donation and transplantation (OD & OT).
Methods: We create an intelligence platform for procedures monitoring, tracking, data reporting & statistical analysis, education & information dissemination, professional network building and scientific research to meet the business needs from all sides.
Results: The platform has been developed jointly with OPOs from 2016. At present, it covers 4 OPOs in 4 provinces and 354 medical staffs from 134 hospitals. Since the platform was launched, the number of potential donors reported has increased by 115%, and the utilization rate of organs has been increased from lower than 70% to 74%. Meanwhile, personal time consumption time and risks of exposed to COVID-19 were reduced while the number of organ donation has been remained. AI technologies have been applied to reduce the burden of manual input and to better improve the efficiency of the workflow, including:
1. GPS technology enables the collection of location of donation coordinators, cars, and organ transportation box so as to assign and track the current progress in real time through the platform.
2. Speech recognition technology is used to obtain the donor diagnosis and treatment information by speech processing.
3. OCR technology is used to read and input the patient's laboratory test reports when data are not shared electronically among hospitals.
4. Visualization technology is used to dynamically present the results of organ traceability and allocation.
5. Donors are monitored remotely by real-time recording system using 5G network.
6. Legal and ethical approval procedures are processed in a paper-free & electronic manner.
7. Media communication tools were embedded into the platform where patient & organ assessment data can be shared safely.
8. E-Training tools & BLOG modules have been embedded into the platform to remain the professional knowledge network and patient educations.
Conclusions: The use of AI technologies to improve efficacy and safety during the OD & OT procedures has been demonstrated by the positive results shown in the study. Our next study will be also focused on estimating the cost-efficiency of using such technologies for OD & OT.

OP332 OUTPATIENT URETERIC STENT REMOVAL FROM KIDNEY TRANSPLANT RECIPIENTS USING ISIRIS IS FEASIBLE, SAFE AND COST-EFFECTIVE

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Background: Ureteric stents are routinely implanted intra-operatively during kidney transplantation to reduce major urological complications. In the UK, stent removal is usually performed by flexible cystoscopy in the operating theatre under local anaesthesia as a day procedure. In our centre, we made use of a disposable flexible cystoscope with an integrated grasper system (Isiris™ by Coloplast) to move the stent removal service to the outpatient department.
Methods: The Isiris™ cystoscope was used to remove ureteric stents from kidney transplant recipients under local anaesthesia between May 2017 and March 2020, in two different settings at our UK-based transplant centre (operating theatres and in outpatients' department). For both settings, data on mortality, timing, intra- and post-procedural complications, biochemistry, microbiology, and cost were compared.
Results: From May 2017 until August 2018, 227 ureteric stents were removed from 221 kidney transplant recipients in theatre. Whereas, between August 2018 and March 2020, 313 ureteric stents were removed from 308 transplant recipients in the new outpatient-based stent clinic. In the outpatient setting, we observed shorter removal intervals and lower re-admission rates, including unplanned admissions from clinic and emergency admissions. Biochemical and microbiology related outcomes were similar between the two settings. Moreover, cost analysis revealed overall savings and the transplant recipients were satisfied with the service provided.
Conclusions: Our data demonstrate that the Isiris™ cystoscope can be used safely for ureteric stent removal in transplant recipients and an outpatient ureteric stent removal service is feasible, cost-effective and safe in experienced hands.

OP333 MULTILINEAR EGFR PROGRESSION PATTERN IS ASSOCIATED WITH GRAFT FAILURE IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Patients with CKD and after kidney transplantation are assumed to have a linear progression pattern of kidney function loss, but a large proportion of patients with CKD were found to have a nonlinear eGFR progression. In this study, we defined the eGFR patterns after kidney transplantation and differentiated between mono-linear and multilinear patterns.
Methods: We calculated eGFR using all creatinine values available from one-year post-transplantation to the end of follow-up. For pattern analysis, we used a piecewise linear model. We divided the patients into 5 predefined groups according to eGFR pattern (Fig.1). Patients with mono-linear eGFR were divided into *stable–pattern* and *decreasing pattern*. Patients with bilinear progression pattern were divided into patients with a *decreasing pattern* (second slope steeper than the first slope) and *stabilizing pattern* (second slope more moderate than the first slope). The fifth group included patients with a *trilinear pattern*
Results: 998 patients were included in the study. After a median follow-up of 5.2 years, 297(30.1%) patients had a multi-linear pattern. Patients with a multi-linear pattern had an increased risk for graft failure (OR 6.45, 95% CI 4.53-9.75, $p < 0.001$), had a significantly longer follow-up time, were younger, were less likely to be diabetic, had longer cold ischemia times, had a higher prevalence of acute rejection, were less likely to be treated with tacrolimus and had lower initial eGFR.Patients with a multi-linear pattern had an increased risk for graft failure (OR 6.45, 95% CI 4.53-9.75, $p < 0.001$). Among the 144 patients who lost their graft, the decreasing bilinear pattern was the most observed (66 events, 45.8%).
Conclusions: Determining the timing of the eGFR decline (the break point) can help determine the precipitating events predating the decline and be a valuable tool in evaluating mechanisms of graft loss.

OP334 PERSPECTIVES OF AUTOLOGOUS BLOOD TRANSFUSION AS A TOOL FOR PREVENTING IMMUNIZATION DURING NATIVE KIDNEY NEPHRECTOMY IN WAITING LIST CANDIDATES

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Background: Native kidney nephrectomy (NKN) is necessary in up to 40% patients with autosomal polycystic kidney disease before kidney transplantation (KT). It was observed that NKN significantly increases time to KT. The need of blood transfusion and the consecutive immunization are regarded as the most plausible explanations of this finding. We hypothesized that the use of autologous blood transfusion (ABT) can be helpful approach to mitigate this problem. However, ABT is usually not proposed to haemodialysis (HD) patients due to secondary anemia and high comorbidity. The aim of our study is to identify perils and prospectively follow outcomes of ABT in HD patients undergoing NKN.
Method: Here we present our experience with 3 (2F/1M) consecutive maintenance HD patients with ADPKD referred to NKN in our center. We evaluated pre- and post-donation haemoglobin, ESA dose, blood volume collected, complications collection and time between nephrectomy and KT.
Results: In all 3 cases, blood collection was uneventful. During 2 collections 450 ml of blood was collected (2 units of RBC concentrate and one unit of plasma).

	Patient 1	Patient 2	Patient 3
Age and sex	66, F	48, F	38, M
BMI (kg/m^2)	26	23	31
Time on HD (days)	554	88	65
Predonation hemoglobin (g/dl)	11.4	12.9	13.3
Postdonation hemoglobin (g/dl)	11.4	12.3	11.8
Time between collections (days)	7	8	10
ESA (epoetin β) dose U/week	6000	6000	6000
Time between nephrectomy and KT (days)	N/A	221	177
PRA before KT (%)	N/A	0	0
Intraoperative blood loss (ml)	100	500	200

In all 3 cases collected blood was transfused after the surgery. No adverse reactions to ABT were observed. One patient was subsequently disqualified from KT, but 2 others underwent successful KT after 221 and 177 days after nephrectomy. In both cases, kidney function was excellent after 6 months of observation.
Conclusions: Autologous blood collection is possible and safe in HD patients. ABT should be regarded as the procedure of choice when qualifying potential waiting list candidates to elective surgeries.

OP335 QUALITY OF LIFE AFTER LIVER TRANSPLANTATION, A CROSS-SECTIONAL SINGLE CENTRE STUDY

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Background and Aims: Orthotopic liver transplantation (OLT) remains the only curative treatment for end-stage liver disease, selected cases of hepatocellular carcinoma and acute liver failure. Outcome has greatly improved, and nowadays patient 1-year survival is almost 100%. However patient morbidity remains significant and knowledge of its impact on patients Quality of life (QoL) is still limited. Therefore, in this single-center study, we aimed to determine the quality of life before and after liver transplantation using RAND-36.
Methods: Data were collected using the local transplantation registry and medical records of adult patients undergoing OLT between the years 2016-2019 at Karolinska University Hospital. RAND-36 is routinely collected from patients on the waiting list and 1-year post-transplantation and prospectively registered. RAND-36 scores from the waiting list were compared with RAND-36 scores 1 year after OLT using Mann-Whitney U test. Subgroup analysis for complications according to Clavien-Dindo, gender and indication was performed.
Results: Of the 384 patients having undergone OLT between 2016-2019, QoL data were available on 103 patients before OLT and 42 patients at their 1-year follow-up. Patient characteristics are described in table 1. Patients showed a significantly higher mean RAND-36 score in 6 out of 8 domains 1 year after OLT compared to on the waiting list, see figure 1. Subgroup analysis showed no significant difference in terms of gender, indication or complications.
Conclusions: Self-reported QoL was significantly higher in responders 1-year post-OLT compared with pre-transplant. Surgical complications, gender or indication were not associated with decreased QoL. Although there is an improvement regarding QoL post-OLT, liver transplanted patients still report inferior QoL than an aged matched group of the general population.

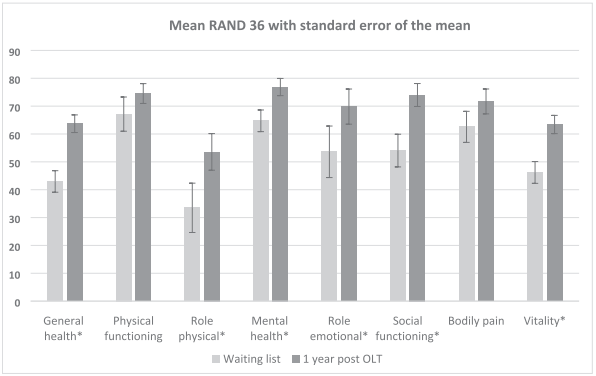

Figure 1 Patient reported mean RAND-36 on the waiting list compared to 1-year post-OLT. *p < 0.05

Table 1 Describing patient characteristics

	Total OLT (2016-2019) N = 384	Responders on Waiting list N = 103	Responders 1 year post-OLT N = 42
Age mean years (SD)	53 (+/- 13)	55 (+/- 12)	55 (+/- 11)
Gender Male/female	265/119	68/35	25/17
Indication Malignant/Other	111/273	38/65	17/25
Complications Mild ≤3a/ Severe ≥3b	132/216	-	12/30

OP336 QUALITY OF LIFE AND FATIGUE IN DE NOVO LIVER TRANSPLANT RECIPIENTS; 24-MONTH RESULTS FROM A MULTI-CENTER OPEN LABEL, RANDOMIZED CONTROLLED STUDY

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Background: We investigated the impact of the combination of sirolimus (SRL) and low-dose tacrolimus (TAC) compared to normal-dose TAC on the quality of life (QoL) and the severity of fatigue.

Methods: In this multicenter RCT, patients were randomized in a 1:1 ratio to 1) once daily normal-dose TAC, trough levels 5–10 μg/L (control group) or 2) once daily combination therapy of SRL and low-dose TAC, trough levels 3–5 μg/L for both SRL and TAC (interventional group). This trial was initially designed to investigate whether the therapy results in superior renal function and comparable rates of rejection, graft and patient survival 36 months after transplantation.
QoL was the secondary endpoint as measured with the EQ-5D-5L questionnaire and the severity of fatigue questionnaire using the Fatigue Severity Score (FSS). The EQ-5D-5L scores on the dimensions were translated to the values given by the general public to the health states. Next, the patient's self-rated QoL scores were given by the EQ-VAS.
Results: In total, 196 patients were included and baseline characteristics were comparable for both groups. At baseline, 89 (92.7%) FSS and EQ-5D-5L questionnaires in both groups were returned. At year 2, 70% of the patients in both groups returned FSS and EQ-5D-5L questionnaires.
During the follow-up, for both arms, the societal values of the EQ-5D-5L health states were a little below those of the general Dutch population. This also applied to the patient's self-rated QoL scores as expressed with the EQ-VAS. Notably, patients included in the control group reported significantly higher fatigue scores and the average score approached clinical levels.
Conclusions: Patients treated with SRL and low-dose TAC experienced significantly less fatigue compared to normal-dose TAC. The QoL of all transplanted patients approached that of the general Dutch population, suggesting little to no residual symptoms.

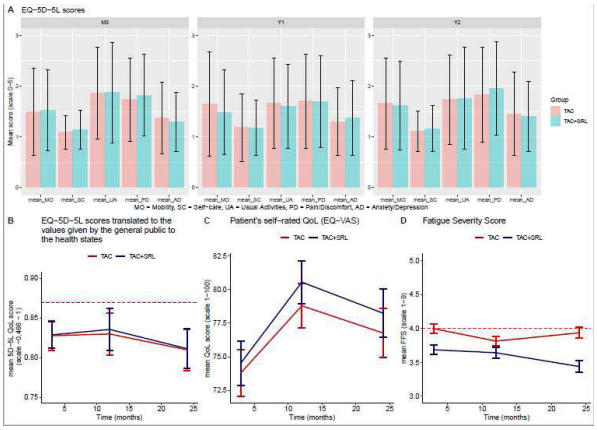

Figure 1 EQ-5D-5L scores and Fatigue Severity Scores
(A) EQ-5D-5L scores (mean ± SD) at 3 months, 1 and 2 year after LT. (B) EQ-5D-5L score translated to the values given by the general public to the health states(mean ± 95%CI). Dashed red line refers to the general Dutch population. (C) Patient's self-rated QoL scores given by the EQ-VAS (mean ± 95%CI). (D) Fatigue Severity Score (mean ± 95%CI). Dashed red line refers to "fatigue".

OP337 COMPARING RENAL FUNCTION IN LT RECIPIENTS WITH LOW-DOSE TACROLIMUS AND SIROLIMUS VERSUS NORMAL-DOSE TACROLIMUS, A MULTICENTER RCT; 24-MONTH RESULTS

Midas Mulder[1,2], Sarwa Darwish Murad[2,3], Koert de Jong[4], Aad A.P. van den Berg[5], Bart van Hoek[6], Ian Alwayn[7], Nicole Erler[8], Wojciech Polak[2,9], Brenda de Winter[1], Caroline den Hoed[2,3], Herold Metselaar[2,3]
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Background: The hypothesis of this study was that a combination of sirolimus (SRL) and low-dose tacrolimus (TAC) compared to normal-dose TAC will result in superior renal function with comparable rates of rejection, graft and patient survival.
Methods: In this multicenter RCT, patients were randomized between 80-100 days after liver transplantation (LT) in a 1:1 ratio to 1) normal-dose TAC with target trough levels 5–10 μg/L (control group) or 2) combination therapy of SRL and low-dose TAC with target trough levels 3–5 μg/L for both SRL and TAC (interventional group). The primary endpoint was chronic kidney disease (CKD) defined as eGFR ≤60 mL/min/1.73m^2 at 36 months after Tx. Secondary endpoints included: treated biopsy-proven acute rejection (tBPAR), retransplantation (re-Tx), mean eGFR, incidence of de *novo* diabetes mellitus (NODAT), incidence of and time to *de novo* or recurrent malignancy and safety.
Results: In total, 196 patients were included and baseline characteristics were comparable for both groups.
At 24 months, the primary endpoint was reached in 30.3% and 31% of the patients in the control and interventional group. The intention-to-treat analysis showed no difference at 24 months in the eGFR for the control and interventional group: 69.4 *versus (vs)* 72.8 ml/min/1.73m^2. These results persisted in the per protocol analysis.
No differences were found in the control and interventional group for tBPAR (2% *vs* 5.1%), NODAT (5.1% *vs* 5.1%), re-Tx (1% *vs* 3.1%) and malignancy (3.1% *vs* 7.1%). In total, 42.3% (83/196) of the patients developed serious adverse events (SAEs, n = 178). SAEs most frequently reported: fever (22.5%), infections (18.5%) and cholangitis (14.6%).
Conclusions: Low-dose SRL combined with TAC is a safe strategy to minimize TAC exposure in LT recipients. However, this combination does ultimately not provide a better renal function at 24 months compared to normal-dose TAC.

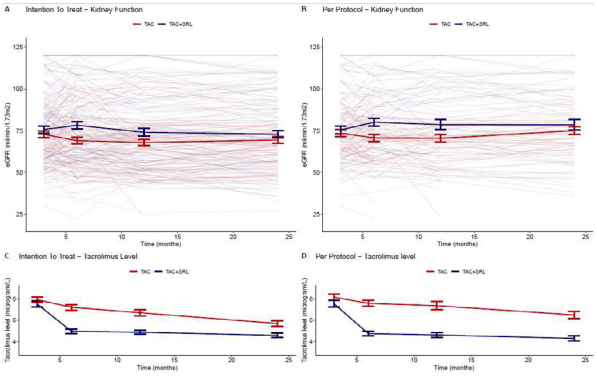

Figure 1 Kidney function (eGFR with CKD-EPI formula) and tacrolimus levels in the ITT and PP population
(A) Mean and individual eGFR (CKD-EPI formula) with 95%-CI of the ITT population. (B) Mean and individual eGFR (CKD-EPI formula) with 95%-CI of the PP population. (C) Mean tacrolimus level (μg/L) with 95%-CI of the ITT population. (D) Mean tacrolimus level (μg/L) with 95%-CI of the PP population.

OP338 CLIF-C ACLF SCORE DOES NOT PREDICT SURVIVAL AFTER LIVER TRANSPLANTATION IN PATIENTS WITH ACUTE ON CHRONIC LIVER FAILURE

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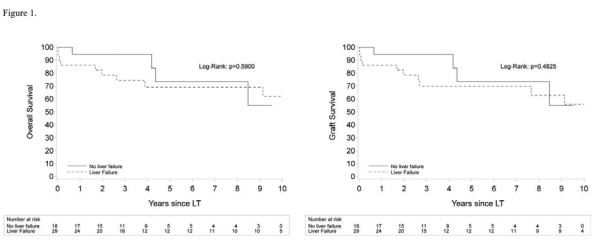
Introduction: Recent studies have shown favourable outcomes in liver transplantation (LT) for acute on chronic liver failure (ACLF), even in the most severely ill patients. However, there is still some debate on optimal patient selection. The chronic liver failure consortium (CLIF-C) ACLF score is shown to predict survival, and hence potential benefit (or futility) of intensive care (IC) admission. However, limited data exist on whether it also predicts survival after LT. Therefore, we evaluated the relation of the CLIF-C ACLF score at day 1 of IC admission and specific organ failures (liver, coagulation, cerebral, kidney, circulatory and respiratory failure, determined based on the CLIF-C organ failure score) on survival after LT for ACLF.
Methods: Data on all LT performed between 2007 and 2019 in our tertiary care centre were retrospectively analysed. Patients with hepatocellular carcinoma and re-LT were excluded. ACLF was graded using the European

Association for the Study of the Liver – Chronic Liver Failure (EASL-CLIF) criteria. Endpoints were early allograft dysfunction (EAD), reflected by Model for Early Allograft Function score (MEAF), and overall patient- and graft survival.
Results: Out of a total of 446 LT patients, 47 ACLF patients were transplanted after or during their IC stay. One year patient survival was similar in patients with or without ACLF (90% [95% CI 77-76%] vs. 92% [89-94%]). We did not observe a correlation between CLIF-C ACLF score (mean 56 [SD 7.9]) at IC admission and MEAF (Spearman rho -0.04, p = 0.79), patient- and graft survival (odds ratio 1 [0.94-1.1] and 1 [0.93-1.1], respectively). There was no relation between CLIF-C ACLF score and Model for End-stage Liver disease (MELD) score (rho 0.22, p = 0.15). When comparing specific organ failures, only patients with liver failure (serum bilirubin >12 mg/dL), were more prone to EAD (median MEAF 5.3 [IQR 2.6-7.7]) than patients without liver failure (3.2 [4.3-6.8], p = 0.04), whereas patient- and graft survival were similar (Figure 1).
Conclusion: Whilst CLIF-C ACLF score is shown to predict survival in ACLF patients, our findings suggest that it does not predict post-transplant survival. Therefore, as patient survival was excellent, even in patients with high CLIF-C ACLF scores, IC should not be withheld and LT should be considered for these patients.



OP339 LIVER TRANSPLANTATION IN PATIENTS WITH ACUTE ON CHRONIC LIVER FAILURE: A SINGLE CENTRE EXPERIENCE

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Background: Donor organ shortage and high waiting list mortality have compelled transplant clinicians to restrict indications for listing in order to avoid futile transplantation. In this context, the role of liver transplantation (LT) as a potentially life-saving treatment for acute on chronic liver failure (ACLF), characterized by extra-hepatic organ failure and a high short-term mortality, remains under debate. Therefore, we compared post-LT survival in patients with and without ACLF.
Methods: Data on all LT performed between 2007 and 2019 in our tertiary care university centre were retrospectively analysed. Patients with hepatocellular carcinoma and re-transplantations were excluded. Patients with ACLF admitted to intensive care (IC) were identified using the European Association for the Study of the Liver – Chronic Liver Failure (EASL-CLIF) criteria. ACLF was graded on day 1 of IC admission as 1, 2 or 3 depending on the number of organ failures, determined based on the CLIF-consortium organ failure score. Cumulative patient survival post-LT was compared between patients with or without ACLF and between different ACLF grades.
Results: A total of 446 patients were included, 47 of which had ACLF (ACLF grade 1: n = 11, grade 2: n = 10; grade 3: n = 26). Recipient and donor characteristics did not differ between groups, except for model of end-stage liver disease (MELD) score (median 27 [IQR 21-32] in patients with ACLF vs. 16[11-26] without ACLF, p < 0.001) and days on the waiting list (21[7-120] vs. 87[18-239], p = 0.007). 30-day mortality was 6% in the ACLF group versus 3% in patients without ACLF (p = 0.15); all deceased ACLF patients had ACLF-3 (12%, [p = 0.24]). One year patient survival was similar in patients with ACLF compared to patients without ACLF (89% [95% CI 76-95%] vs. 92% [89-95%]) (Figure 1A). In the ACLF group, 1-year patient survival with ACLF-3 (85% [64-94%]) did not differ from patients with ACLF-1+2 (95% [71-99%]) (Figure 1B).
Conclusion: Our results show excellent survival rates after LT for ACLF, comparable to LT for other indications and regardless of ACLF grade. This suggests that LT for ACLF, even ACLF grade 3, should not be considered futile. However, as selection bias in this retrospective analysis is inevitable, prospective validation in larger cohorts is needed.

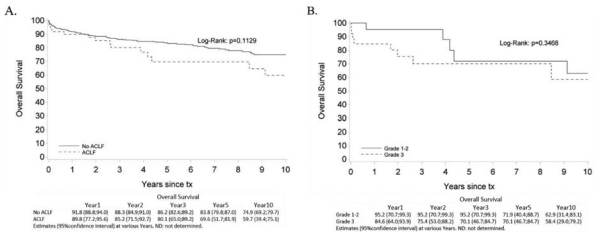

Figure 1.

OP340 VARIOUS SELECTION CRITERIA FOR PRETRANSPLANT MYOSTEATOSIS AND THEIR VALUE IN THE ASSESSMENT OF SHORT- AND LONG-TERM OUTCOMES FOLLOWING OLT

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Background: Myosteatosis and alterations of body composition (BC) affect clinical outcomes in orthotopic liver transplantation (OLT). There are various definitions in terms of selection criteria and clinical cutoffs for computed-tomography based BC and myosteatosis without clear international consensus. Here we aimed to comparatively investigate various selection criteria for pre-transplant myosteatosis and their value in the assessment of short- and long-term outcomes following deceased donor OLT.
Methods: We retrospectively analyzed the data of 264 consecutive recipients who underwent deceased donor OLT between May 2010 and December 2017. Body composition and myosteatosis were evaluated by preoperative computer-tomography based segmentation. Patients were stratified based on sex-specific muscle-radiation-attenuation of the whole

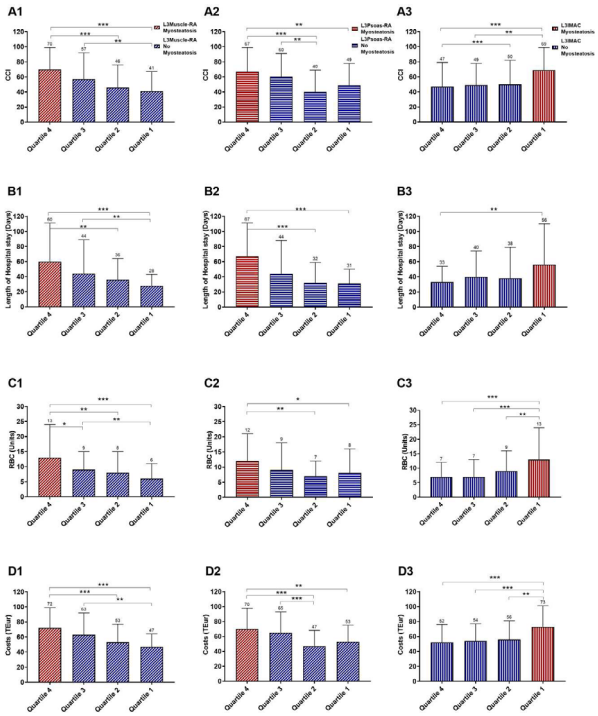

Figure 1: Quartile-based analysis of transfusion requirements, length of hospital stay, postoperative complications, and costs

muscle area (L3Muslce-RA), psoas-radiation-attenuation (L3Psoas-RA) and intramuscular adipose tissue content (IMAC) values.
Results: L3Muslce-RA, L3Psoas-RA and IMAC performed well without major differences and identified patients at risk for inferior outcomes in the group analysis, Quartile-based analyses (Figure 1), receiver operating characteristic curve and correlation analyses showed a superior association of L3Muslce-RA with perioperative outcomes when compared to L3Psoas-RA and L3IMAC. Long-term outcome did not show any major differences between the used selection criteria.
Conclusion: This study confirms the prognostic role of myosteatosis in OLT with especially strong value in the early perioperative phase with the use of L3Muscle-RA, L3Psoas-RA, L3IMAC. L3Muscle-RA showed slightly superior performance in predicting clinical outcomes in deceased donor OLT.
Abbreviations used: L3Muscle-RA: lumbar 3 muscle radiation attenuation, L3Psoas-RA: lumbar 3 Psoas radiation attenuation, L3IMAC: lumbar 3 intramuscular adipose tissue content

OP341 ULTRA-LONG-TERM OUTCOME AND ITS DETERMINANTS AFTER LIVER TRANSPLANTATION IN ADULTS

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Background: Information is limited about patient survival more than 10 years after orthotopic liver transplantation (OLT), the life expectancy of long-term survivors, and factors determining this. It is unclear whether long-term outcome has improved over the years.
Methods: Single-center observational cohort study including consecutive adult OLT recipients between 1979-2020. Patient data were retrieved from the institutional database, and donor information was obtained from Eurotransplant. Kaplan-Meier survival analyses with log-rank testing were performed to determine patient survival and differences between groups. Loss of life years was determined by comparing the survival of patients with that of age-, sex, and period-matched population controls obtained from Statistics Netherlands. Cox proportional hazard regression analyses were performed to identify patient and donor factors associated with survival.
Results: A total of 972 consecutive adult OLT recipients (53% male) were included with a median age of 50.4 years (IQR 38.3-58.1). One-year survival increased stepwise per decade from 65% between 1979-1989 to 95% between 2009-2019 (p = <0.01). The 831 recipients (85%) who survived the first year had 10-, 20- and 30-year survival rates of 77, 56, and 37%, respectively. In contrast to the one-year survival, there was no improvement in long-term survival. Median life expectancy of the one-year survivors was 22.9 years (95% CI: 20.1-25.7), which was eight years shorter compared to population controls (Table 1). Age at OLT (HR = 1.03 [per year of age], 95% CI: 1.01- 1.05, p = 0.01) and malignancy in the explanted liver (HR = 2.37, 95% CI: 1.47-3.83, p = <0.01) were independently associated with decreased survival (figure 1, table 1). Underlying liver disease, type of immunosuppression, and donor factors were not associated with outcome. The most common cause of death in patients transplanted because of malignancy was recurrent cancer (26%).
Conclusions: Ultra-long-term outcome in one-year survivors after OLT is excellent. Age at OLT and absence of malignancy were independently associated with good outcome. Further analysis should determine whether the median loss of eight life years in patients can be improved, and why short-term survival improvements did not translate into improved long-term survival.

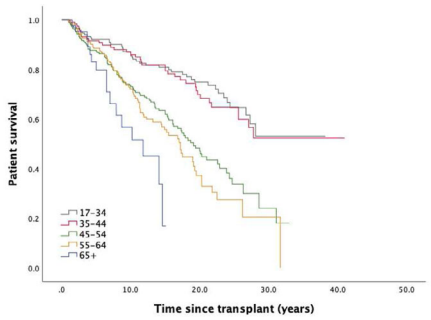

Figure 1. Kaplan Meier survival estimates by age at OLT for patients transplanted between 1979 and 2020.

Table 1. Independent factors associated with life expectancy and years of life lost

Factor	Life expectancy OLT recipients (yrs)*	Population controls	Life years lost	Patients	Deaths
All recipients	22.9 (20.1-25.7)	30.9	8.0	831	284
Age categories					
17-34	>38.2**	53.1	<14.9**	175	43
35-44	>41.0**	39.5	<-1.5***	126	36
45-54	19.1 (16.7-21.5)	30.6	11.5	253	102
55-64	17.2 (15.0-19.4)	22.9	5.7	233	87
≥65	11.8 (6.8-16.8)	17.5	5.7	44	16
Malignancy					
Yes	15.0 (9.5-20.5)	24.4	9.4	108	45
No	24.3 (21.6-27.0)	32.0	7.7	723	239

* Median (95% CI)
** The median has not been reached yet.
*** The median life expectancy in recipients was higher than that of controls in this subgroup

OP342 THERAPEUTIC ANTICOAGULATION IN PREVENTION OF RECURRENT PORTAL VEIN THROMBOSIS AFTER LIVER TRANSPLANTATION: UTILITY OR FUTILITY?

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Background: Portal vein thrombosis (PVT) is no longer a contraindication for liver transplantation (LT). While therapeutic anticoagulation (TAC) is recommended during the waiting period, there is no evidence regarding its utility in prevention of PVT recurrence after LT. The aim of our study was to evaluate the association of TAC post-LT in prevention of PVT recurrence.
Methods: All adult LT performed in 2 high volume centers between 2003 and 2018, were retrospectively analyzed. Only patients with a PVT classified as Yerdel grade I or II and with a porto-portal anastomosis performed during the procedure (after complete thrombectomy or not) were included. PVT recurrence within 1 year as well as morbidity were compared between patients receiving TAC (TAC group) or not (noTAC group). Patient and graft survival were analyzed using Kaplan-Meier curves and compared with log-rank test.
Results: During the study period, out of 2612 LT performed, 235 (9%) patients with a PVT were included. The Yerdel classification was grade I in 147 (62.6%) patients and grade II in 88 (37.4%) patients. 113 (48.1%) patients received TAC while 122 (51.9%) patients did not. Within the first year after LT, a PVT recurrence was observed in 8 (3.4%) patients without difference between TAC and noTAC group (6 (5.1%) vs 2 (1.7%), p = 0.28). The Incidence of severe complications (Clavien-Dindo ≥3) was significantly higher in the TAC group vs. noTAC group (54 (47.8%) vs. 32 (26.2%), p < 0.01), as well as the hospitalization duration (21 vs. 17.5 days, p < 0.01). A severe complication due to TAC (i.e., requiring a temporary or definitive withdraw of TAC) was observed in 13 (11.5%) patients. The graft (logrank: p = 0.05) and patient (logrank: p = 0.2) survival were similar between the 2 groups. In univariate analysis, only the recipient age was associated with PVT recurrence (OR = 0.94, p = 0.03).
Conclusion: Therapeutic anticoagulation seems not necessary in the prevention of grade I/II PVT recurrence and is associated with higher morbidity and longer hospital stay.

OP343 A PHOTOGRAPH OF PATIENTS APPROACHING LIVER TRANSPLANTATION: ASSESSMENT OF THE PSYCHOLOGICAL OUTCOME PREDICTORS

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Background and Aims: patients with end-stage liver disease face psychological distress during the different phases of the Liver Transplantation (LT). Aims of the present study were to evaluate psychological and psychosomatic variables both at the time of evaluation for screening for LT (T0) and at insertion in the waiting list (T1).

Methods: the study had a cross-sectional design. 50 patients were recruited (68% males, mean age of 57 ± 7 years, 62% married/cohabitant, 44% 30% with a lower school degree).
Participants underwent the following assessments: The Structured Clinical Interview for Dsm-5 Disorders, the structured interview according to the Diagnostic Criteria for Psychosomatic Research (DCPR), Kellner's Symptom Questionnaire (SQ), Questionnaire on the State of Health (SF-12), Coping Orientation to Problem Experienced – brief version (Brief-COPE-BC), The Gratitude Questionnaire-Six Item Form (GQ-6) and the Interpersonal Support Evaluation List (ISEL). Wilcoxon test is utilized to assess tendencies.
Results: a DSM 5 diagnosis was detected in 10 patients (14% alcohol use disorder, 3% adjustment disorder). A DCPR syndrome was present in 22 subjects (30% demoralization, 12% alexithymia, 2% irritable mood).
Enrolled subjects at T0 showed anxiety, depression and somatic symptoms. In comparison with control group, experimental one displayed lower score in PCS and MCS of SF-12 ($p = 0.000$, $p = 0.000$, respectively), BC positive refraining, instrumental support, humor, behavioral disengagement, emotional support, self-blame ($p < 0.05$) and in ISEL and PTG Scale ($p = 0.000$). Experimental group reported higher scores in the scale of SQ in anxiety, depression, somatic symptom and BC substance use ($p < 0.05$).
Twenty-five patients were admitted in the waitlist (T1). From T0 to T1, there was an increase of DSM-5 and DCPR diagnosis. At T1 in comparison with T0, we registered higher scores in SQ Hostility subscale ($p = 0.084$) and BC Self distraction ($p = 0.079$).
Conclusions: patients in screening for LT report several psychopathological vulnerabilities that tend to worsen from T0 to T1. These might have negative prognostic impact on the transplant outcome. Clinical support and multidisciplinary view might be powerful tool to support patients during the steps of transplant process.

OP344 AN ECONOMIC EVALUATION OF THE COST OF COMPLICATIONS FOLLOWING LIVER TRANSPLANTATION IN THE UK NATIONAL HEALTH SYSTEM

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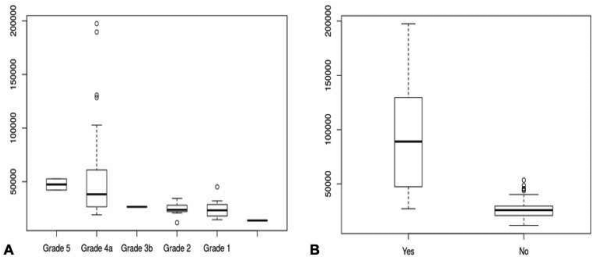
Background: In an effort to decrease the mortality of patients waiting for a liver transplant (LT), more marginal donor organs are increasingly being used but at the price of increased complications following LT. Furthermore, several patient related factors are associated with postoperative complications. However, evidence on the relation of different grades of severity and type of complications on hospital costs are lacking. The purpose of this study was to evaluate the effect of grade and type of complications on the actual costs of liver transplantation in the UK NHS system.
Methods: An economic evaluation of the association of actual hospital costs with post-LT complications was performed, based on a prospectively collected dataset from a cohort of patients recruited from March 2016 to July 2017. Demographics, complication grade according to Clavien-Dindo (CD) classification, Comprehensive Complication Index (CCI), survival outcomes and costs were collected. Complications and costs were reported up to 90 days postoperatively.
Results: A total of 60 patients were analysed. The median age of the participants was 54 (IQR 47-60) years and 43 (28%) were female. The overall complication rate of any severity was 60%. The major complication (CD Grade ≥3a) rate was 50%. The mean overall cost at 90 days was £42,128 (SD 38,407). Costs significantly increased with each of the Clavien-Dindo grades. A CCI > 60 was associated with significantly higher cost when compared to CCI < 60 (median cost £89,013 (IQR £47,396 to £100,000) vs. £25,828 (IQR £20,973 to £29,645), $p < 0.001$. The most frequent complications associated with higher costs were wound complications, bleeding, renal, pulmonary and infections ranging from 43k to 63k GBP.
Conclusions: These findings suggest that minimising post-LT complications is not only clinically relevant for patients with liver disease undergoing liver transplant but represents also a significant financial benefit for healthcare organisations.
Figure. Association of the actual hospital costs with post-LT Clavien-Dindo Complications Grades (A) and high (>60) vs. low (<60) CCI® groups (B).



PANCREAS AND ISLETS TRANSPLANTATION AT 360°

OP387 THE EFFECT OF DONOR DIABETES-ASSOCIATED GENOTYPES ON OUTCOMES AFTER PANCREAS TRANSPLANTATION

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Background: Identifying predictors of long-term pancreas transplant outcomes is crucial for optimising organ selection and improving patient survival. The effects of donor associated diabetes risk on pancreas graft outcomes are unknown. The aim of this study was to investigate whether donor HLA-DR3, HLA-DR4 and HLA-DR3/DR4 heterozygosity, which are strongly associated with autoimmune diabetes, are associated with poorer pancreas transplant outcomes.
Methods: This was a single centre retrospective study of 919 pancreas transplants (721 simultaneous pancreas-kidney [SPK], 130 pancreas transplant alone [PTA] and 68 pancreas after kidney [PAK]) performed at the Oxford Transplant Centre between 2003 and 2019. Data were requested from NHSBT and Oxford Transplant Immunology. For each operation type (i.e. SPK, PTA and PAK), death-censored Kaplan-Meier and Cox regression analyses were performed to assess the impact of the diabetes-associated HLA types on graft and patient survival.
Results: Donor HLA-DR3 and donor HLA-DR3/DR4 heterozygosity showed no association with graft and patient survival in our analyses. In contrast, the presence of donor HLA-DR4 was associated with reduced PTA transplant survival ($p = 0.010$). Furthermore, in a multivariate analysis, with operation type included as a covariate, donor HLA-DR4 was confirmed as a negative predictor of pancreas graft survival ($p = 0.039$; hazard ratio [HR], 1.379; 95% confidence interval [CI], 1.017-1.870). Donor HLA-DR4 had no effect on patient survival and, in SPK recipients, it had no effect on kidney graft survival.
Conclusions: For the first time, this study has demonstrated that the presence of diabetes-risk HLA-DR4 in donors correlates with reduced pancreas transplant survival, particularly for PTA recipients.

OP388 PANCREAS TRANSPLANTATION FROM DONORS DECLARED DEATH BY CIRCULATORY CRITERIA: INITIAL EXPERIENCE IN SPAIN

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Coruña. A Coruña, Nephrology, A Coruña, Spain; [8]Complexo Hospitalario Universitario de A Coruña. A Coruña, Surgery, A Coruña, Spain; [9]La Fe University Hospital. Valencia, Hepato-Pancreatico-Biliary Surgery and Transplant Unit, Valencia, Spain; [10]Hospital Universitario Reina Sofía. Córdoba, Surgery, Córdoba, Spain; [11]Hospital Universitario de Canarias. Tenerife, Nephrology, Tenerife, Spain; [12]Hospital Universitario de Canarias. Tenerife, Surgery, Tenerife, Spain; [13]Hospital Clinic. Barcelona, Renal Transplant Unit, Barcelona, Spain; [14]Hospital Clinic. Barcelona, Coordination Department, Barcelona, Spain

Background: In the face of the shortage of organs for transplantation, the transplant community is increasingly considering controlled donation after the determination of death by circulatory criteria (cDCDD). There is a scarcity of studies concerning the use of Normothermic Regional Perfusion (NRP), an in situ preservation strategy well established in Spain.
Aim: To report on the Spanish experience on the outcomes obtained from cDCDD donors.
Methods: Data from the Spanish National Transplant Organization database and from transplant centers were retrospectively analyzed (2015-2020).
Results: During the study period, 471 pancreas transplants were performed, including 20 combined kidney-pancreas transplants from cDCDD donors. Of these, NRP was used in 18 procedures, all with ante-mortem cannulation, and rapid recovery (RR) in 2 cases.
The median donor age was 33 years, 65% were male. The median total warm ischemia time (WIT) and the functional WIT were 19 (13.2-23.7) min. and 10 (7-15.5) min., respectively. Postmortem NRP was run for a 113.5 (91.5-134.5) min. The median pancreas cold ischemia was 412.5 (330-636.7) min. The pancreatic graft function was optimal in all cases except for three (NRP cases), for which the cause was primary nonfunction in two (one of them requiring transplantectomy of pancreatic and kidney grafts) and cardiogenic and septic shock secondary to pancreatic fistula for a fatal case. Seven patients presented with delayed kidney graft function, with five cases requiring dialysis. Pancreas related surgical complications were present in 70% cases, haemorrhage being the most common. After a median follow-up of 13.6 (5.6-36.4) months, 5-year pancreas graft survival was 85% for the whole series, kidney graft survival was 90% for and patient survival was 94.7%.
Conclusion: To date, this is the largest series describing the use of post-mortem NRP in cDCDD pancreas transplantation, displaying competitive results in terms of graft/patient survival.

OP389 METABOLIC OUTCOMES OF PANCREAS TRANSPLANT ALONE FROM DONATION AFTER CIRCULATORY DEATH DONORS - THE UK REGISTRY ANALYSIS

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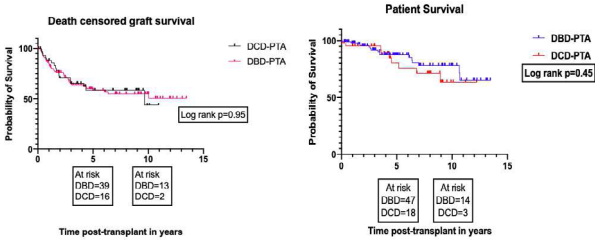
Background: Extrapolating data from early DCD (donation after circulatory death) kidney transplantation, pancreas transplants from DCD grafts were feared to have worse metabolic outcomes. Hence, we aimed to address the question of solitary pancreas transplant from DCD donors– are our concerns justified?
Methods: A UK registry analysis (retrospective) of 185 PTA (pancreas transplant alone) performed from January 2005 to December 2018 was conducted. All early graft losses (<3 months) were excluded in this analysis to allow focus on the metabolic outcomes. The primary aim was to compare the metabolic outcomes between DBD (donation after brainstem death) & DCD grafts (HbA_1C, weight gain & incidence of secondary diabetic complications); secondary outcomes of interest were to compare rejection rates (including the need for steroids), patient & graft survival between the two groups. Functioning graft is defined as remaining insulin independent. Secondary diabetic complications are defined as any of the following events: myocardial infarction, cerebrovascular accident, limb amputations.
Results: After excluding early graft losses (n = 23, DBD = 16 & DCD = 7); data from 162 PTA (DBD = 114 & DCD = 48) were analyzed to compare the metabolic outcomes. Normothermic regional perfusion was not used in DCD group. The average functional warm ischemia time (time from systolic BP < 50mmHg to commencement of perfusion) for DCD group was 17 ± 5.1 mins. Transplant characteristics and outcomes as shown in table-1. Body mass index of the donor was less in DCD cohort (DBD = 23.40 vs. DCD = 22.25, p = 0.006). Both the DBD & DCD recipients had similar rates of depleting antibody induction (alemtuzumab or anti-thymocyte globulin) and de novo steroid usage (Table-1). The steroid-free maintenance rates were equivalent in both the groups (DBD = 75% vs. DCD = 73%, p = 0.79). There were no significant differences in the HbA_1C, weight gain, rejection rate, & incidence of secondary diabetic complications post-transplant between DBD & DCD recipients (Table-1). The 1-, 5-, &10-years patient and graft survival were similar in both the groups (Figure-1).
Conclusions: This is the first & the biggest study worldwide reporting equivalent metabolic outcomes and survival (patient/graft) after PTA from DCD grafts to that of DBD grafts with more than 10-years follow-up.

Table-1

Transplant characteristics and Outcomes	DBD	DCD	P value
Donor age in years-Median	33	29	0.11
Donor BMI in kg/sq.m- Median	23.40	22.25	0.006
Donor abdomen girth in cm-Median	84	81.5	0.14
Recipient age in years- Median	41	43	0.63
Recipient BMI in kg/sq.m- Median	24.65	24.40	0.62
Recipient HbA_1C at registration in mmol/mol-Median	76	75	0.52
Recipient insulin use at registration in IU/Day-Median	40	40	0.80
% of sensitized recipient (CRF>5%)	36	29	0.39
% of highly sensitized recipient (CRF>85%)	8.7	10.4	0.73
Cold ischemia time (mins)-Median	688	720	0.19
0 DR mismatch (%)	24.5	14.5	0.15
1 DR mismatch (%)	51	48	0.72
2 DR mismatches (%)	24.5	37.5	0.09
Bladder drainage (%)	33.3	35.4	0.79
Depleting antibody induction (%)	81	87.5	0.31
Non-depleting antibody induction(%)	19	12.5	0.31
De-novo steroid usage (%)	18	17	0.87
IFCC HbA_1C at 3-months-Median, in mmol/mol (Functioning grafts)	36	32	0.08
IFCC HbA_1C at 1-year-Median, in mmol/mol (Functioning grafts)	34	36	0.25
IFCC HbA_1C at 3-years-Median, in mmol/mol (Functioning grafts)	35	33	0.39
IFCC HbA_1C at 5-years-Median, in mmol/mol (Functioning grafts)	36	35	0.49
% Weight gain at 3-months (Functioning grafts)	-4.5	-1.4	0.20
% Weight gain at 1-year (Functioning grafts)	-1.8	-1.6	0.60
% Weight gain at 3-years (Functioning grafts)	0.2	-1.1	0.41
% Weight gain at 5-years (Functioning grafts)	1.5	1.5	0.95
Rejection rate at 3-months (%)	10	12.5	0.63
Rejection rate at 1-year (%)	19	10	0.15
Rejection rate at 3-years (%)	12	10	0.71
Rejection rate at 5-years (%)	10	10	1.00
Secondary diabetic complications at 3-months(%)	0.8	2	0.51
Secondary diabetic complications at 1-year(%)	-	-	-
Secondary diabetic complications at 3-years(%)	-	-	-
Secondary diabetic complications at 5-years(%)	-	-	-



OP390 HUMAN AMNIOTIC EPITHELIAL CELLS PROTECT PANCREATIC ISLETS AGAINST PRO-INFLAMMATORY CYTOKINES

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Background: Inflammation is a primary contributor to early graft loss and poor islet engraftment. Human amniotic epithelial cells (hAEC) possess regenerative, immunomodulatory and anti-inflammatory properties. In particular, these cells express HLA-G and HLA-E, involved in immunomodulation and immune tolerance. Here, we hypothesized that hAECs could protect islets from cellular damage induced by pro-inflammatory cytokines and we assessed the cytokine-induced expression of HLA-G and HLA-E in hAECs.
Methods: Rat islets were cultured with or without hAECs for 24 hours, followed by 48-hour exposure to IFN-γ, TNF-α and IL-1β. Controls included mono or cocultures without cytokines. For all conditions, glucose stimulated insulin secretion (GSIS), apoptosis by detection of histone-associated DNA

fragments, and Th1/Th2 cytokines secreted in the culture media were evaluated by ELISA. Gene expression modifications were assessed by qPCR. hAEC surface marker expression (CD105, CD90, CD326, HLA-E, HLA-G, SSEA-4) was assessed by flow cytometry after culture in control culture medium or in medium containing various concentrations of human recombinant IFN-γ for 24–48H.
Results: Exposure to a pro-inflammatory cocktail significantly increased the secretion of the anti-inflammatory cytokines IL6, IL10 and G-CSF by hAECs at both 24H and 48H. IL6, IL8 and IL10 gene expression was significantly upregulated, as well as HLA-G and HLA-E. This correlated with an upregulation of STAT1, STAT3 and NF-κB1gene expression levels. RI co-cultured with hAECs maintained a normal insulin secretion after cytokine exposure compared to RI cultured alone, and a significantly lower apoptosis rate.
Conclusions: In conclusion, hAECs increase their anti-inflammatory and immunomodulatory potentials when exposed to inflammation in vitro, and protect pancreatic islets against pro-inflammatory cytokines in a coculture set-up.

OP391 OUTCOMES OF SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTS FROM DONATION AFTER CIRCULATORY DEATH DONORS IN THE UK: A NATIONAL REGISTRY ANALYSIS

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Background: The UK is a world leader in the use of pancreases from donation after circulatory death (DCD) donors. However, there is a perception that pancreases from DCD donors are sub-optimal when compared to similar grafts from donation after brain death (DBD) donors. We compared outcomes of pancreases transplanted from controlled DCD donors to those from DBD donors in the largest reported study to date.
Methods: Data were obtained from the UK Transplant Registry on deceased donor adult SPK transplants between 2005 – 2018. Kaplan-Meier estimates were used to compare pancreas, kidney, and patient survivals between those receiving organs from DCD or DBD donors, and multivariable analyses were used to identify factors associated with pancreas graft loss.
Results: 2,228 SPK transplants were implanted (1825 DBD; 403 DCD donors). Kidneys from DCD donors had equivalent graft survivals to those from DBD donors (p = 0.99), and there were no differences in longer-term renal allograft function, or in 5-year patient survivals when stratifying by donor type. On univariate analysis, there were no significant differences in 5-year death-censored pancreas graft survival between the two donor types (Figure 1. 79.5% vs 80.4%; p = 0.86). Multivariable analysis showed no significant differences in 5-year pancreas graft loss between transplants from DCD (n = 343) and DBD (n = 1492) donors (hazard ratio 1.28, 95% CI 0.95-1.73; p = 0.10). A Cox proportional hazards regression model for pancreas graft loss from DCD donors showed that increasing donor age or pancreas cold ischaemic time (CIT) were not associated with worse outcomes (Table 1).
Conclusions: This large national study supports the increased utilisation of organs from DCD donors in SPK transplantation within the UK and globally. Data on the effect of donor age and CIT on DCD donor graft outcomes suggest that a re-examination of donor age criteria and the national pancreas offering schemes are warranted.

Table 1

Risk factor	Level	N	Hazard ratio (95% CI)	p
Donor age, years	N/A	352	1.02 (0.99 - 1.04)	0.08
Recipient age, years	N/A	352	0.95 (0.92 - 0.97)	<0.01
Pancreas cold ischaemic time, hours	<8	40	1.0	-
	8-9.9	112	0.53 (0.22 - 1.23)	0.14
	10-11.9	110	0.92 (0.42 - 2.01)	0.83
	12+	117	0.82 (0.38 - 1.78)	0.61

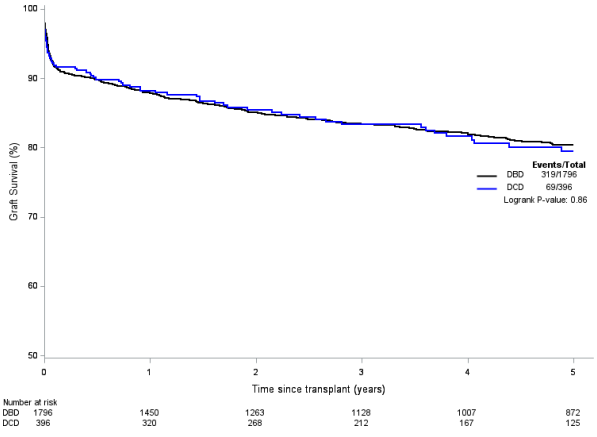

Figure 1

OP392 DEVELOPMENT OF EX VIVO NORMOTHERMIC PERFUSION AS AN INNOVATIVE METHOD TO ASSESS PANCREASES AFTER PRESERVATION

Ann Etohan Ogbemudia[1,2], Fungai Dengu[1], Gabriella Hakim[2], Faysal El-Gilani[1], John Mulvey[2], Thomas Prudhomme[3], Maria Letizia Lo Faro[2], Kaithlyn Rozenberg[2], Joshua Oliver[4], James Hunter[1,2], Paul Johnson[2], Rutger Ploeg[1,2], Peter Friend[1,2], Julien Branchereau[2,5]
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Background: Static cold storage (SCS) is the standard method for pancreas preservation but does not facilitate objective organ assessment prior to transplantation.
Normothermic machine perfusion (NMP) has been used to test other solid organs' function and viability in transplantation settings. Our aim was to develop a NMP protocol specific for pancreases and then investigate its potential as an organ assessment strategy.
Methods: 15 porcine pancreases were procured in conditions replicating donation after circulatory death with warm ischaemia time of 25 minutes. After 3 hours of static cold storage (SCS), the pancreases were divided into 4 experimental groups (figure 1)
1) 2 pancreases in the feasibility group, which after backbench preparation were placed directly on NMP in order to develop the NMP protocol
2) 5 pancreases in the HMP Institut Georges Lopez (IGL2) group
3) 4 pancreases in the HMP University of Wisconsin MPS (UW) group
The IGL2 and UW groups above received HMP supplemented with 21% oxygen.
4) 4 pancreases in the control (SCS) group were stored at 4 degrees in UW as is the standard practice in the United Kingdom.
The latter three experimental groups (IGL2, UW and SCS) received their intervention for 6 hours prior to assessment on NMP for 1 hour.

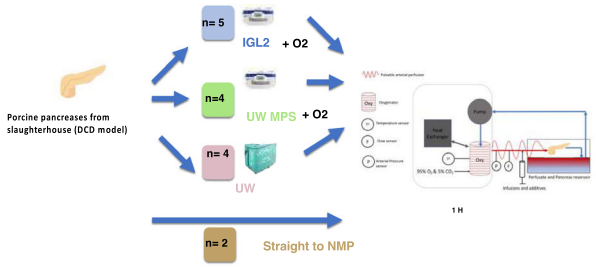

Figure 1 Study schema showing the experimental groups

The NMP protocol used autologous, leucodepleted blood delivered at a mean arterial pressure of 40mmHg with a temperature of 37°C. At timed intervals during HMP and NMP, perfusate and tissue samples were collected for analysis and perfusion parameters were recorded.
Results: During hypothermic preservation, lactate and LDH was noted to be highest in the SCS group. During NMP assessment the SCS group displayed a worse resistance, poorer flows and worse macroscopic appearances compared to both HMP groups.

Tissue wet to dry ratio technique was used as a surrogate for oedema assessment and the highest weight gain observed in the SCS compared to both the HMP groups.
Conclusions: Our work although with small numbers suggest NMP of whole pancreases is feasible after cold preservation and is potentially useful as an assessment strategy. Furthermore, it appears to demonstrate that oxygenated HMP may be beneficial for pancreas preservation compared to SCS.

OP393 THE EUROPEAN P-PASS AND US PDRI SCORES ARE ASSOCIATED WITH INCREASED RISK OF PANCREAS GRAFT REJECTION

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Background: The European Preprocurement Pancreas Allocation Suitability (P-PASS) and the US Pancreas Donor Risk Index (PDRI) scores were designed to assist the decision of accepting pancreas organs for transplantation, with P-PASS and PDRI scores of <17 and ≤1.57 deemed 'ideal' respectively. The aim of this study was to determine whether these scores could predict outcomes in pancreas transplantation.
Methods: The P-PASS and PDRI scores were retrospectively calculated from a prospectively maintained database for consecutive pancreas transplant recipients in a single centre. Outcomes measured were rate of acute rejection and graft survival.
Results: Of a total of 159 pancreas transplants performed (SPK n = 108, PAK n = 33, PTA n = 18) over a 13-year period (Dec 2004-Nov 2017), full data were available for 129 to calculate the P-PASS and PDRI scores. Median P-PASS and PDRI scores were 17 (10–24) and 1.53 (0.67-3.12) respectively. There was good correlation between P-PASS and PDRI scores ($r^2 = 0.539$, $p < 0.0001$).
Thirty patients (30%) experienced at least one episode of biopsy-proven acute rejection, excluding those with borderline changes. Of these, 12 (21%) and 27 (37%) were in 'P-PASS < 17' and 'P-PASS≥17' groups respectively (p = 0.05), and 12 (18%) and 27 (44%) were in 'PDRI≤1.57' and 'PDRI > 1.57' groups respectively (p = 0.002). There was a positive correlation between rejection and donor age (p = 0.005).
One-year graft survival was 95% and 80% for 'P-PASS < 17' and 'P-PASS≥17' groups respectively (log rank p-value of 0.132), and 95% and 81% for 'PDRI≤1.57' and 'PDRI > 1.57' groups respectively (log rank p-value of 0.141).
Conclusion: This study showed that high P-PASS and PDRI scores were associated with significantly increased episodes of pancreas graft rejection, however, P-PASS and PDRI scores were unable to predict actual graft survival. An analysis of a larger cohort across different pancreas transplant centres is probably required in order to confirm or refute these findings.

OP394 IMPROVED PANCREATIC GRAFTS SURVIVAL WITH OPERATING PROTOCOL AMENDMENTS

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Background: Perfectly shaped protocol is the best way to improve solid organ transplantation results.Since January 2016 the pancreas transplant team of our institution has upgraded the standard operating procedure of pancreas transplantation.
Methods: On retrieval, duodenum is stapled after thorough flushing with 5% cold glucose. Back-table preparation is completed with extremely thorough closure of lymphatic and blood vessels and rinsing the pancreas graft with 20% cold albumin solution. Very short donor portal vein is anastomosed to recipient vena cava (VCI). We believe graft outflow is aided by negative VCI pressure acting as prophylaxis of graft thrombosis. To prevent stenosis or kinking, VCI is cut diamond-shaped for anastomosis. Improved blood flow is confirmed with radiological imaging. Enteric drainage is performed side to side to a proximal part of jejunum. Abdominal incision is closed in layers using "small bites technique". Postoperatively TAC, MMF, GKS treatment is administered. Antibiotic and antifungal prophylaxis was shortened to perioperative dosing only.

Results:

Recipient		2008-2015 (n = 33)	2016-2021 (n = 38)
Time of hospital stay	Average	25,61	20,29
Graftectomy during 3 months after transplantation		7 (21.2%)	2 (5.3%)
Loss of function during first year		10 (30.3%)	3 (7.9%)
One-year mortality		3	0

Every aspect of the results was improved. Over 3-fold reduction in early graftectomies and 5-fold improvement of functional graft survival was seen. No recipient death was recorded since protocol amendment.
Conclusions: New surgical and postoperative protocol for pancreas transplantation resulted in rapid reduction in early complications. With restrictive selection of donors and meticulous cardiological screening of the recipient, one year pancreas survival was 92.1% with 100% recipients survival.

OP395 POST-TRANSPLANT INFLAMMATION IS LOCALISED TO THE PANCREAS GRAFT AND ASSOCIATED WITH EARLY GRAFT THROMBOSIS

Kristina Rydenfelt[1,2], Gisle Kjøsen[2,3], Rune Horneland[4], Judith Krey Ludviksen[5,6], Trond Geir Jenssen[2,7], Pål-Dag Line[2,4], Tor Inge Tønnessen[1,2], Tom Eirik Mollnes[5,6,8], Håkon Haugaa[1,9], Søren Pischke[1,2,8]
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Background: Ischemia-reperfusion injury after pancreas transplantation can lead to thrombosis and pancreatitis. The early postoperative immune response of human pancreas grafts has not been clarified. In this clinical study, we investigated local pancreas graft inflammation in the first week after transplantation using microdialysis. Our aim was to describe the local inflammatory pattern in cases with early graft thrombosis compared to uneventful cases.
Methods: In 67 pancreas transplantations, microdialysis catheters were attached adjacent to the pancreas graft. Microdialysate was collected at two time-points daily during the first postoperative week and analysed for six cytokines and the complement activation product C5a using enzyme-linked immunoassays.
Results: Post-transplant, 32 patients had an uneventful course, 17 experienced various degree of graft vascular thrombosis diagnosed by protocol computed tomography or Doppler ultrasound and 18 had other complications. IL-10 and C5a were not detectable. IL-1ra, IL-6, IL-8, IP-10 and MIP-1β showed high levels immediately after surgery that decreased during the two first postoperative days. IL-6 and IL-8 were significantly higher in patients with a graft thrombosis compared to uneventful patients during the first postoperative week (p = 0.003 and p = 0.027, respectively).
Conclusions: Pancreas grafts experienced postoperative inflammation, which resolved during the first two postoperative days in uneventful cases. Patients with early pancreas graft thrombosis had significantly higher levels of IL-6 and IL-8 measured close to the organ, during the first postoperative week, as a sign of local thromboinflammation.

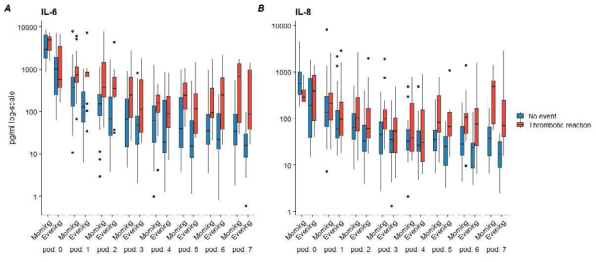

Figure 1 IL-6 (A) and IL-8 (B) measured at the pancreas graft, postoperative day (pod) 0 (operation day) to 7, were significantly higher in patients

with a thrombotic reaction (N = 17) compared to those with no events (N = 32). Median, interquartile range (IQR) and quartiles -/+ 1.5* IQR. Mixed model analysis.

OP396 COMPARISON OF DRB1 AND DQB1 ALLELE FREQUENCIES AND PRE-TRANSPLANT ANTI-HLA ANTIBODIES IN PATIENTS WAITING FOR PANCREAS VS. KIDNEY TRANSPLANT

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Background: The Major Histocompatibility Complex(MHC) plays an important role in the immune response and in transplant rejection. HLA DR3-DQ2 and DR4-DQ8 are both strongly associated with susceptibility to develop type 1 diabetes. Presence of donor-specific pre-transplant anti-HLA antibodies correlates with organ rejection.
The aim of this study is to investigate the frequency distribution of HLA alleles and its correlation with pre-transplant anti-HLA Ab level in patients waiting for pancreas transplantation with end-stage pancreas failure.
Methods: The study sample included 1003 patients waiting for pancreas, kidney/pancreas and kidney transplantation, stratified in: 72 Pancreas Transplant Alone (PTA), 211 Simultaneous Pancreas-Kidney (SPK) transplant, 20 Pancreas After Kidney (PAK) transplant, 750 Kidney Transplant Alone(KTA). HLA-A, B, C, DR and DQ typing was performed by molecular technology. Anti-HLA Ab were analyzed by xMAP technology (Luminex).
Results: PTA, SPK and PAK patients were combined due to their similar HLA frequencies, and the group was compared with the HLA "Allele Frequency Net Database" (AFND). The frequencies of HLA-DRB1*03, DRB1*04,DQB1*02 were significantly higher than in the general population, whereas the frequencies of HLA-DR11and DR15 were lower. On the contrary, no difference was observed between KTA patients and general population. PTA, SPK PAK and KTA patients showed the same (about 30%) pre-transplant anti-HLA Ab percentage.
Conclusions: Our results confirm the significantly higher frequencies of HLA DR3, DR4 antigens in PTA, SPK and PAK patients. In addition, we observe that other alleles may have a protective role (in particular, DRB1*11, DRB1*15, and DQB1*06, Table 1). However, the percentage of pre-transplant patients with anti-HLA antibodies in the combined PTA-SPK-PAK sample compared to KTA appears to be independent of the allele frequency distribution.

HLA	PTA+SPK+PAK (%)	*AFND (%)	**F.E Test	KTA (%)
DRB1*03	173 (33,4)	(10)		123 (9.6)
DRB1*04	120 (23)	(8)		111 (8.6)
DRB1*11	50 (9.6)	(23,8)		326 (25.4)
DRB1*15	13 (2.5)	(7.5)	*p<0,01*	85 (6.6)
Tot. Alleles	**517**			**1281**
DQB1*02	43	(21)		176 (19)
DQB1*06	6	(16)		134 (14,6)
n° Tot. Alleles	***144***			***918***
***Ab Anti-HLA	PTA (%)	SPK (%)	PAK (%)	KTA (%)
Positive Class I	15 (20,8)	45 (21,3)	5 (25)	171 (23,3)
Positive Class II	16 (22,2)	39 (18,5)	4 (20)	173 (23)
Positive Class I and II	8 (11,1)	19 (9)	3 (15)	95 (12,7)
Tot. Pos.	***23 (31,9)***	***65 (30,8)***	***6 (30)***	***253 (33,7)***
Negative Class I	57 (79,2)	166 (78,7)	15 (75)	575 (76,7)
Negative CLASS II	56 (77,9)	172 (81,5)	16 (80)	577 (76,9)
Tot. Neg.	***49 (68,01)***	***146 (69,2)***	***14 (70)***	***497 (66,3)***
n° Tot. Patients	*72*	*211*	*20*	*750*

*Table 1. *Frequencies of the general population from AFND **Fisher's Exact Test; ***Anti-HLA Antibody Screening*

OP397 TEN YEARS OF SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATIONS - SINGLE CENTRE NATIONWIDE EXPERIENCE

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Background: Type 1 diabetes (DM1) incidence in Finland is among highest in the world (37/100 000/year). Simultaneous pancreas-kidney transplantation (SPK) is an option for patients with DM1 and kidney failure. SPK programme started at the Helsinki University Hospital (HUH) in March 2010. Here we describe our 10-year experience.
Methods: This retrospective study includes all consecutive SPK transplantations during March 2010 to March 2020 at HUH, the only transplantation centre in Finland. All recipients had DM1 with kidney failure. Clinical data were collected from national transplantation registry. Immunosuppression combined tacrolimus, mycophenolate and steroids with anti-human-T-lymphocyte immunoglobulin induction. Portocaval anastomosis and enteric drainage were used. Thromboprophylaxis with low molecular weight heparin started preoperatively and continued for 1 month post-transplantation.
Results: A total of 166 SPKs were performed (Table 1). Finland had the highest rate of pancreas transplants globally in 2019 (7.06 per million population (PMP)).
Seven patients (4.1%) died with a functioning graft during median 43 months follow-up. One year overall survival was 98%. Five pancreatic grafts were removed during the first year after transplantation due to intra-abdominal infection (Figure 1). One graft lost function 3 years post-transplantation, 10 patients need oral diabetic medication and 3 patients occasionally use insulin. Graft function at one year was good, mean HbA1c was 36 (SD 5.57) and creatinine 107 (SD 34.69). All kidney grafts functioned at the end of follow-up.
Complications required re-laparotomy in 39 (23%) patients, mostly due to pancreas graft related problem (N = 28). Only one patient had partial venous thrombosis in the pancreatic graft, which resolved with tinzaparin treatment. No grafts were lost to vascular problems.
Conclusions: Modern era SPK is a safe and effective treatment of DM1 with kidney failure. Highly functional donor hospitals and logistics combined with high incidence of DM1 has led to world's highest rate of SPK PMP in Finland.

Table 1 Patient and donor characteristics and intraoperative factors.

All patients, n=166	n (%) or median (range)
Recipient characteristics	
Age, years	43 (19-60)
Female, n	56 (33.7%)
Body mass index	24.0 (17.9-31.1)
Duration of diabetes, years	34 (10-54)
Duration of dialysis, months	12 (0-78)
Donor characteristics	
Age, years	41 (5-62)
Female, n	81 (48.8)
Body mass index	23.6 (14.3-30.1)
Return of spontaneous circulation, min	0 (0-45)
Length of hospital stay, days	16 (7-100)
Pancreas cold ischemia time, min	479 (130-743)
Kidney cold ischemia time, min	596 (271-843)
HLA-mismatch	
A and B	3 (0-4)
DR	2 (0-2)

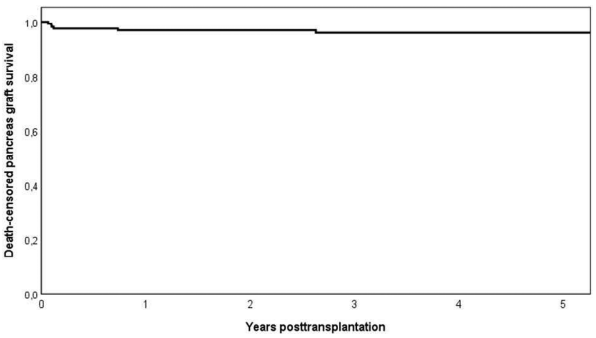

Figure 1 Death-censored pancreas graft survival (n = 166).

OP398 PANCREAS GRAFT SALVAGE AFTER DUODENAL LEAK - FOLEY OR FOLLY? OUTCOMES FROM OVER 1000 PANCREAS TRANSPLANTS

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Introduction: Duodenal leaks (DLs) are a rare yet devastating complication of solid organ pancreas transplantation, that can be life-threatening and typically result in graft loss[1]. Several interventions have been proposed to salvage grafts following DLs, but whether they are effective in this respect remains unclear. In this study, we have reviewed the characteristics, management and outcomes of DLs following pancreas transplantation in a high volume single centre with over 1000 pancreas transplants.
Methods: We conducted a retrospective review of case notes of patients in our centre identified from prospectively maintained transplant databases between 2004-2021. Identified patients were cross-referenced with Pathology reports of graft explants at our institution and audit data from the UK national transplant database. We report on timing, site of the leak, management strategy, salvage attempts and graft and patient outcomes.
Results: We identified 20 suspected DLs in 1040 pancreas transplants. Six cases were subsequently excluded with a confirmed alternative diagnosis. The characteristics of DLs are described in Table 1. Salvage was attempted in nine (64%) cases, with two successes using a foley catheter placed into the duodenum, and creating a controlled fistula. Overall, 12 (86%) grafts were lost after a DL and one patient died (7%) following an attempted salvage.
Summary: DLs have been uncommon in our series of pancreas transplants, and typically attributable to donor duodenum staple-line leaks. DLs were diagnosed clinically via detection of bile in surgical drains and confirmed by CT imaging. Salvage of pancreatic grafts by creating an enteric exocrine drainage using a foley catheter has not been really successful. Early pancreatectomy was associated with 100% patient survival, with a median of 1902 days post-DL survival to date. Alternative strategies including exclusion of the DL segment and its exocrine drainage and will need to be explored.

Table 1	Duodenal Leaks		
Transplant Type		%	n
	SPK	79%	10
	PTA	14%	2
	PAK	7%	1
Time to Duodenal Leak		**Days**	
	Median	**15**	
	IQR	15	
Duodenal Leak Diagnosis		%	n
	Bile in Drain	57%	8
	CT Imaging	29%	4
	Surgical Exploration	14%	2
Site of Duodenal Leak		%	n
	Donor Duodenum Staple Line	86%	12
	Anastamosis	14%	2
Attempted Salvage		**%**	**n**
	Yes	64%	9
	No	36%	5
Salvage strategy		**%**	**n**
	Direct closure	7%	1
	Floy Catheter insertion*	50%	7
	T-Tube insertion	7%	1
Successful salvage		**14%**	**2**

*both successfully salvaged grafts are still functioning at 2463 & 2597 days post Transplant

OP399 FIRST POSTOPERATIVE DAY PLASMA AMYLASE CAN BE USED TO DETECT PATIENTS AT RISK OF COMPLICATIONS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

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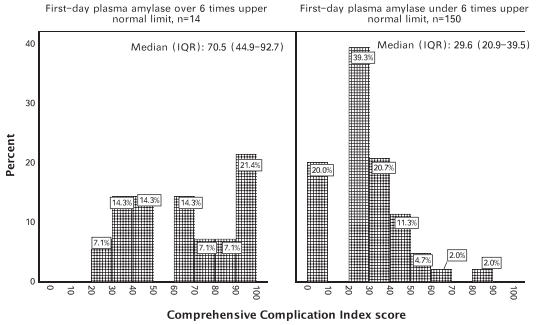
Background and Aims: Simultaneous pancreas-kidney transplantation (SPK) is associated with significant postoperative complications, but knowledge on early warning signs and surrogate-markers for these are scarce. We aimed to analyze the complication-predictive value of different laboratory tests, especially amylase, in SPK.
Methods: Medical records of 164 patients who underwent SPK at our center between January 2010 and February 2020 were analyzed. Levels of first three day plasma amylase, drain fluid amylase, C-reactive protein, c-peptide, plasma trypsinogen and white blood cell count were assessed for their performance predicting cumulative postoperative complications (assessed using Comprehensive Complication Index, CCI) within 90 days from transplantation by using ROC-analyses. A CCI-score of 47.7/100, which equals the morbidity of two relaparotomies, was chosen for distinguishing between high and low postoperative morbidity.
Results: First day plasma amylase had the best value in predicting complications based on its high AUC-values of 0.71 and 0.83 in predicting a CCI-score over 47.7 and pancreas graft related relaparotomies, respectively. An optimal cutoff of 6 times the upper normal limit was chosen for first day plasma amylase based on Youden-index. The ability of this cutoff to distribute between complications and high morbidity are expressed in Table 1 and Figure 1. Negative predictive values and positive predictive values of this cutoff were 0.81 and 0.71 for any relaparotomy, and 0.91 and 0.71 for CCI-score >47.7, respectively.
Conclusions: We suggest that a cutoff value of 6 times the upper normal limit for plasma amylase during the first postoperative day could be used to better characterize the patients with high and low risk of severe postoperative complications, during the first 90 postoperative days. We also suggest that plasma amylase could be used as a helpful surrogate-marker for postoperative complications in future clinical trials.

Table 1. Morbidity and complications of 164 simultaneous pancreas-kidney transplantations in view of first day plasma amylase (cutoff: 6 times the upper normal limit for plasma amylase)

	Plasma amylase over 6 times the upper normal limit (n=14)	*Plasma amylase under 6 times the upper normal limit (n=150)*	*p-value*
CCI-score over 47.7 (n=23)*	10 (71.4%)	13 (8.7%)	*<0.001*
Relaparotomy, any (n=39)	10 (71.4%)	29 (19.3%)	*<0.001*
Pancreas graft-related relaparotomy, bleedings excluded (n=13)	8 (57.1%)	5 (3.3%)	*<0.001*
Pancreas graft-related relaparotomy, all (n=28)	8 (57.1%)	20 (13.3%)	*<0.001*
Pancreas graft loss (n=4)	3 (21.4%)	1 (0.7%)	*<0.001*
Kidney graft-related complications (n=38)	6 (42.9%)	31 (20.7%)	*0.057*

*Value of 47.7 is equal to two relaparotomies or equivalent postoperative morbidity
Abbreviations: CCI – Comprehensive Complication Index.

Figure 1. Comprehensive Complication Index score of 164 SPKs divided by first postoperative day plasma amylase value of 6 times the upper normal limit.



OP400 ISLETS LOADED IN HYDROGEL DERIVED FROM HUMAN AMNIOTIC MEMBRANE REVERSE DIABETES IN IMMUNODEFICIENT MICE

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Background: Neovascularized devices and biopolymer scaffolds are getting a great deal of attention for their potential to improve islet transplantations. Human amniotic membrane (HAM) is considered as an inexpensive and natural source to produce ECM-based hydrogels with immunomodulatory, anti-inflammatory and antifibrotic properties. We developed a hydrogel (Amniogel) derived from HAM and evaluate its potential to support islet function in vitro and in vivo.
Methods: The Amniogels were generated from HAM and accessed for porosity, for ECM content and fibre integrity. The protein content in Amniogel and native HAM lysates were measured. To assess Amniogel impact on islet viability and function, isolated rat islets were incorporated into the Amniogel. The cell viability was evaluated by FDA/PI staining. Islet function was assessed during glucose stimulated insulin secretion (GSIS) tests. Then, in vivo engraftment and function was evaluated by transplanting 250 rat islets (IEQ) loaded into the Amniogel or rat tail Collagen or islets alone into the epididymal fat of diabetic Nod-Rag mice. Blood glucose levels were monitored daily and intraperitoneal glucose tolerance tests were carried out.
Results: The ECM concentration in the Amniogel affected the pore size. Insulin expression and viability of islets incorporated into Amniogel was significantly higher than the islets loaded in commercial collagen or that of control islets. Significant enhancement of GSIS was observed from islets embedded in Amniogel as compared to the two controls. In vivo experiments showed that transplantation of 250 IEQ embedded in Amniogel lead to enhanced engraftment, vascularization, viability and better glycaemic control compared to control mice transplanted with islets into commercial collagen or with islets alone.
Conclusions: Incorporation of pancreatic islet into amnion-derived Amniogel enhances islet engraftment and is a valuable approach to improve islet transplantation outcomes.

GENETIC AND IMMUNE FACTORS REGULATING ALLOREACTIVITY

OP401 BLOCKADE OF THE IL-21 PATHWAY: A NEW PERSPECTIVE FOR THE TREATMENT OF T AND B CELL-MEDIATED ALLOGENEIC RESPONSES AFTER TRANSPLANTATION

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Background and Aims: IL-21 is a T cell growth factor for and secreted by Th17 and T follicular helper (Tfh)-cells. This cytokine regulates CD8+ T cell expansion and their effector functions, and is crucial for T cell-dependent B cell differentiation into antibody-producing plasma cells. However, little is known about IL-21 mediated T and B cell responses after transplantation.
Methods: First, we explored the actions of IL-21 in alloreactive T cell proliferation and cytotoxicity in mixed lymphocyte reactions. Second, we tested the role of IL-21 producing Tfh cells in the regulation of B cells in an alloantigen-driven setting. Third, the effect of an αIL-21R blocking antibody in rejection was studied in a humanized skin transplantation model in mice reconstituted with human T and B cells.
Results: Alloactivated T and B cells highly express IL-21R. In the presence of IL-21, a marked increased proliferative response of alloactivated T cells was found. Also, the expanded CD8+ T cells had significant cytolytic functions, while blockade an αIL-21R antagonist inhibited the proliferation of alloactivated T cells. Next, we determined the role of IL-21 in T cell dependent B cell responses. Donor antigen stimulation of the co-cultured Tfh–B cell initiated expression of the activation markers ICOS and PD-1 on Tfh cells with a shift toward a mixed Tfh2 and Tfh17 phenotype. The alloantigen activated B cells underwent class switch recombination and differentiated toward IgM- and IgG-producing cells. Anti-IL-21R antagonists inhibited B cell differentiation. Finally, in mice treated with the αIL-21R antagonist reduced signs of alloreactivity were measured including significantly less CD4+ and CD8+ T and B cell infiltration and less expression of inflammatory markers Keratin 17 and Ki67.
Conclusions: These findings suggest that 1) IL-21 is crucial for both T cell and B cell-dependent allogeneic immune responses, and 2) treatment with IL-21R antagonists may ameliorate these anti-donor responses.

OP402 PROLIFERATION OF CO-STIMULATION BLOCKADE RESISTANT-T CELLS REQUIRED EARLY IFNA PATHWAY ACTIVATION

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Background: Belatacept was developed to replace calcineurin inhibitors in kidney transplantation. Its use has been shown to be associated with better kidney transplant function, reduced cardiovascular risk, reduced occurrence of anti-donor antibodies and increased standard graft survival. However, it is associated with a higher risk of cellular rejection. The aim of this work is to study the mechanisms of activation and proliferation of Belatacept resistant lymphocytes (LTs) to determine new pathways of control.
Methods: We performed a transcriptomic analysis of the CD4+CD57+PD1- memory LT that were identified as being associated with a higher incidence of graft rejection, after an allogeneic stimulation (MLR) with activated dendritic cells (aDC) in the presence or not of Belatacept. The population of interest was identified by VPD450 staining before MLR
Results: T lymphocytes from 6 donors were analyzed after 6 hours of contact with aDC. After analysis, the lymphocyte populations (CD4+CD57+PD1-) (CD4+CD57+PD1+) and (CD4+CD57-) had different transcriptional profiles with or without Belatacept. In the CD4+CD57+PD1- population, the IFNα/β-dependent activation pathway was positively overrepresented as compared to the control population (CD4+CD57-). This pathway was associated with an increase in IRF7 transcripts. IRF7 was associated with IFNα/β and IL6regulation. The inhibition of both cytokines in association with belatacept inhibits CD4+CD57+PD1- T cell proliferation in MLR.
Conclusions: We have identified that IRF7 is rapidly upregulated in Belatacept resistant CD4+CD57+PD1- LT. The inhibition of type I IFN or IL-6 by using blocking antibodies in association with belatacept reduce the proliferation of belatacept resistant LT and open up new therapeutic avenues for organ transplantation.

OP403 DETERMINING THE T CELL RECEPTOR REPERTOIRE IN DIRECT PEPTIDE-MHC ALLORECOGNITION BY CD8+ T CELLS

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Background: We have recently identified over 40 H-2K^b-peptide epitopes that are directly recognised by CD8$^+$ T cells from allogeneic B10.BR (H-2^k) or BALB/c (H-2^d) mice. Some "super-epitopes" are strongly recognised by T cells from both strains. As few as 5 of these K^b-peptide epitopes combined into a tetramer panel were able to bind almost 40% of alloreactive T cells from primed mice (https://www.biorxiv.org/content/10.1101/2020.11.09.359968v2). Here, we aimed to characterise the T cell receptor (TCR) repertoire responding to these epitopes.
Methods: B10.BR or BALB/c mice were primed with a K^b-bearing skin graft, and boosted by inoculation with AAV-K^b. Single-cell index sorting was followed by multiplex nested PCR and Sanger sequencing of PCR products. The TCR sequences from dextramer-positive and PD-1$^-$ bystander populations were compared. Results for K^b-SNYLFTKL are described in detail.
Results: 5-7 dominant clonotypes each representing between 4.2 and 26.7% of TCRs were found among the dextramer-positive cells from both B10.BR and BALB/c mice, while no clonal expansion was detected in the PD-1$^-$ cells from either strain. Among the dominant clonotypes, 85.8% of B10.BR clones and 60.1% of BALB/c clones used the TRBV13-2 segment, and strong pairing preferences were observed, with B10.BR cells using mainly TRAV14-1 or TRAV16D/DV11 in combination with TRBV13-2, while BALB/c cells principally used TRAV12D-2 or TRAV16D/DV11 in conjunction with TRBV13-2. Despite the pairing of TRAV16D/DV11 – TRBV13-2 being utilised by both B10.BR and BALB/c, only one CDR3b sequence was common to clones from the two strains. Similar clonal expansion was observed among T cells recognising K^b-RTYTYEKL and K^b-VGPRYTNL.
Conclusions: A limited number of dominant clonotypes are present within the T cell populations recognising K^b-SNYLFTKL, K^b-RTYTYEKL and K^b-VGPRYTNL. Biophysical and structural studies of these and additional receptor-ligand pairs will enhance our understanding of the basis for alloreactivity.

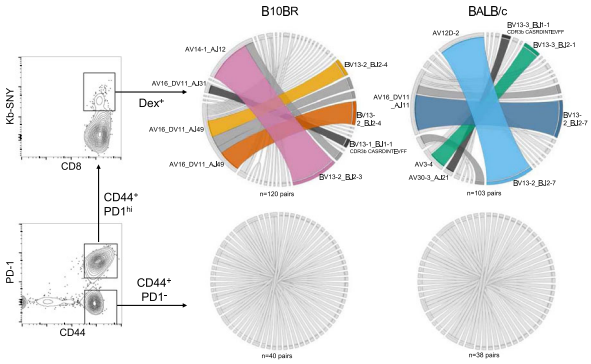

Figure 1. Dominant clonotypes were discovered within the activated ($CD44^+PD1^{hi}$) $K^{b\text{-}SNYLFTKL}$ Dex^+ $CD8^+$ T cell populations from both B10.BR and BALB/c mice, indicated in shading. Clones with a common CDR3b region are shown in black shading. By comparison, no clonal expansion was present in the $PD1^-$ cells.

OP404 INCREASED FREQUENCY OF T CELL-MEDIATED REJECTION ASSOCIATED WITH ANTIBODY-MEDIATED REJECTION IN HLA-DSA NEGATIVE TRANSPLANT RECIPIENTS

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Background: Banff 2017 categorized the previously "suspicious" Antibody-Mediated Rejection (ABMR) without circulating HLA Donor-Specific Antibodies (DSA) in Kidney Transplant (Ktx) biopsies. Recent series describe absent HLA DSA (DSANeg-ABMR) up to 60% of ABMR histologies.
Methods: To evaluate presentation and outcomes of biopsy-proven ABMRs (bpABMR) in patients with and without HLA-DSA Abs in solid-organ transplant (SOT) recipients.
Single-center descriptive study of SOT patients (27 KTx, 2 multiorgan) with ABMR under contemporary BANFF criteria between Feb 2014–Feb 2020 compared by HLA-DSA status.
Results: From 29 total bpABMR, 58.6% were DSANeg-ABMR. In this group, 58% were males, mean age of 41.8 ± 12.6 vs 51.8 ± 13.3 ($p = 0.04$). 4 of the former had preTx Class II DSAs that vanished post-KTx and 2 developed them after the index biopsy. Conversely, in 2 KTxs in the HLA DSA-Positive ABMR, the DSAs were performed. From the DSANeg-ABMR group, 47.1 % were first kidney allografts. 76.5% DSANeg-ABMR patients vs 41.7% ($p = 0.06$) had received antibody-induction. Notably, 41.2% of DSANeg-ABMR vs 8.3% had a description of associated acute TCMR ("Mixed Rejection") ($p = 0.06$).
There were no differences in creatinine (Cr) in the 1st month post-transplant (1.95 ± 0.69 vs 1.8 ± 1.14 mg/dl) neither pre-biopsy Cr and proteinuria between groups.
ABMR appeared earlier in DSANeg-ABMR (median 258 vs 2414 days, ($p = 0.03$)). Survival analysis showed no significant differences between groups after the diagnosis of ABMR and 50% of allografts were lost at the second year post-biopsy follow-up.
Conclusions: In our series, 58.6% of SOTs with ABMR had no circulating anti-HLA DSAs and as all ABMRs were diagnosed as *per indication* biopsy, this outcomes appeared earlier during follow-up than in those with mensurable HLA-DSAs. The DSANeg-ABMR group showed a clear trend to present as a Mixed Rejection. Both groups entail a poor prognosis with a 50% renal survival after two years.

OP405 DO NOT BLAME THE INNOCENT: ΓΔT CELLS ARE NOT INVOLVED IN DONOR-SPECIFIC ANTIBODY GENERATION AFTER SOLID ORGAN TRANSPLANTATION

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Background: The generation of donor-specific antibodies (DSA), the leading cause of graft failure in transplantation, requires that alloreactive B cells receive help from T follicular helper (Tfh) cells. According to the molecular composition of their TCR, 2 different types of T cells (Tc) are distinguished: α/β or γ/δ.
While the importance of α/βTc in the generation of DSA is well established, the implication of γ/δTc is unknown. Data from the literature suggest that γ/δTc could directly help B cells in a Tfh-like manner or contribute indirectly by priming follicular helper α/βTc.
This translational study aimed at determining whether and how γ/δTc were involved in DSA generation.
Methods and Results: After transplantation with a Balb/c (H-2d) heart, wild-type C57BL/6 (H-2b) mice (with normal α/βTc and γ/δTc) and TCR δKO (deficient in γδTc) develop a similar DSA response, in terms of kinetics, intensity, and of intrinsic qualities of DSA (avidity and isotype). On the contrary, CD3εKO (devoid of both α/βTc and γ/δTc) and TCR αKO (deficient in α/β Tc only) recipient mice do not develop any DSA, despite having a functional B cell compartment.
In vitro experiments were performed on human cells and confirmed that activated γ/δ Tc cannot acquire simultaneously CXCR5 and CD40L, 2 key functional molecules for T follicular helper cells. Furthermore, γ/δ Tc neither make B cells proliferate nor synergise with α/β Tc in proliferation assays.
The lack of role of γ/δ Tc in DSA generation was further validated in a cohort of 331 kidney transplant recipients for whom both DSA screening and γ/δTc quantification among PBMCs were available in their follow-up. The patients' alloimmune humoral response was strictly the same whether they had low or high circulating γ/δTc count at two years post-transplantation.
Conclusions: Our results demonstrate that γ/δTc are not involved in the generation of DSA, which remains the exclusive prerogative of α/β Tfh.

OP406 IMMUNOLOGICAL BEHAVIOR OF EARLY GRAFT INFILTRATING CELLS UNTIL 3 DAYS AFTER MURINE SKIN TRANSPLANTATION

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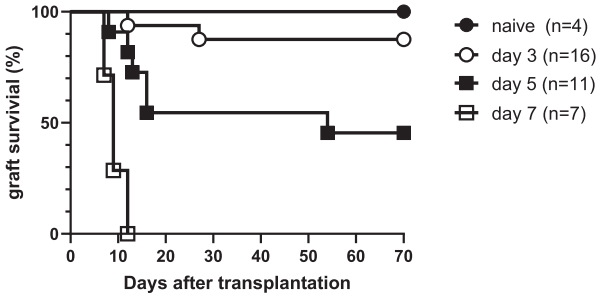
Background: The apparent roles of early graft infiltrating cells (GICs) remain unclear. Previous study revealed that early GICs are potentially correlated with tolerance induction (Goto R, Am J Transplant 2013). Herein, we attempted to precisely identify the role of early GICs by using immunodeficient mice.
Methods: Full thickness tail skin grafts from C57BL/6 (B6) mice were transplanted onto Balb/c mice. Skin grafts harvested during early post-transplant periods were re-transplanted to Balb/c $Rag2^{-/-}$ IL-$2R\gamma^{-/-}$ (BRG) mice.
Results: B6 skin grafts were rejected at median survival time (MST) 13 days in Balb/c mice. To identify the exact role of GICs, the transplanted B6 skin grafts on day 3, 5 and 7 post-transplantation were removed from Balb/c recipient mice and re-transplanted into BRG mice respectively. All day 7 skin grafts were immediately rejected in BRG mice (n = 7, MST 9 days,

open squares in Figure). Half of day 5 grafts has been accepted in BRG mice long-term (n = 11, MST 14.5 days, filled squares in Figure). Of note, 14 of 16 skin grafts harvested on day 3 (87.5%) were achieved a long-term acceptance (>70 days) in BRG mice (open circles in Figure). Sufficient numbers of CD3+ lymphocyte (>5%) derived from GICs of all skin graft were observed in peripheral blood of BRG mice. All reconstituted lymphocytes were derived from Balb/c mice suggesting that recipient lymphocytes had already infiltrated into the skin graft until day 3 post-transplantation. Of note, almost Balb/c derived GICs until day 3 post-transplantation, did not respond B6 allografts. When CD4+CD25+ Treg population of reconstituted lymphocytes from day 3 GICs, was depleted by PC61 antibody, day 3 skin graft acceptance was maintained in BRG mice (n = 3). In addition, when 10^5 of naïve Balb/c splenocytes were adoptively transferred into BRG mice which transplanted with naïve B6 skin grafts or those harvested on day 3, both grafts were rejected at similar timing (n = 3, MST 30.5 days, n = 3, MST 27 days, respectively) suggesting that day 3 GIC did not have a role of preserving allograft.

Conclusion: Isolation and adoptively transferred of GICs into immunodeficient mice clarified that early GICs until day 3 had capability of neither responding nor preserving allo-graft tissue.



OP407 GENOME-WIDE MISMATCH AND DELETION ANALYSIS IN KIDNEY TRANSPLANTATION

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Background: Acute rejection is a risk factor for the later allograft dysfunction and long-term graft loss after kidney transplantation. The first genome-wide association studies have not identified strong candidate genes for complication risks whereas matching of non-HLA genes may be promising. We determined the association of genome-level matching with acute rejection and survival in single-center study cohort.

Methods: Altogether 1026 pairs of deceased donors and first kidney transplant recipients transplanted in 2007–2017 were genotyped. The association between the sum of non-synonymous mismatches in transmembrane and secreted proteins and acute rejection was estimated with logistic regression. Additionally, we analyzed 40 deletion-tagging alleles in patient-only data with risk genotype defined by homozygosity for the deletion-tagging allele, and analyzed the association of deletion homozygosity with outcomes. We also performed a deletion matching analysis between donor-recipient pairs.

Results: The sum of mismatches in transmembrane and secretory proteins did not associate with acute rejection. In deletion analysis in patient-only data, we found an association between acute allograft rejection and rs7542235 genotype GG, tagging a homozygous deletion at the complement factor H (CFH) and CFH-related proteins loci on chr 1. The homozygous deletion among the recipients was significantly associated with a higher risk for rejection than the non-homozygous deletion genotypes (adjusted HR, 2.93; 95% CI, 1.44–5.97; $p = 2.9 \times 10^{-3}$, same for the deletion matching analysis). No replication for the previously reported effect of LIMS1 deletion was found.

Conclusions: The present study suggests that gene deletions are important novel histocompatibility loci in kidney transplantation. The relative importance of different gene deletions varies between populations as we found evidence for the CFH-related gene deletion but could not replicate the previously reported LIMS1 deletion.

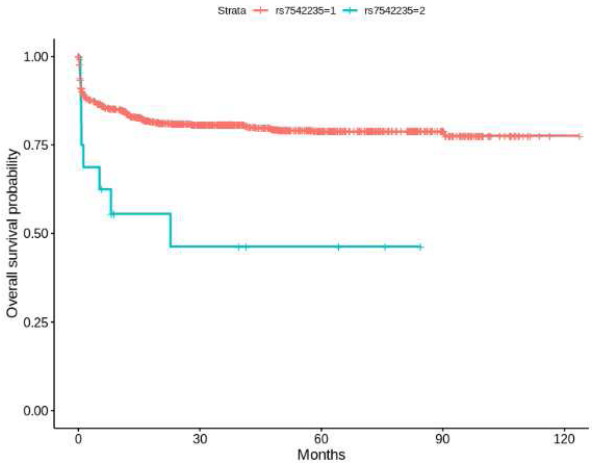

Figure 1. Unadjusted kaplan-meier

OP408 DONOR-RECIPIENT GENETIC MISMATCH IS ASSOCIATED WITH LIVER ALLOGRAFT REJECTION

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Background: Donor-recipient human leukocyte antigen (HLA) gene mismatch is implicated in graft rejection in kidney transplantation. For liver transplantation (LT), however, HLA matching is not routinely performed as the association with rejection remains controversial. Genetic mismatch of non-HLA haplotypes was recently associated with increased risk of kidney graft loss for the first time. Therefore, we sought to investigate the association of donor-recipient HLA- and non-HLA genetic mismatch on the incidence of graft rejection in LT.

Methods: Single-center study including adult and pediatric LT between 1993-2018. The primary outcome was biopsy-proven grade 2/3 graft rejection (Banff criteria) <1year post-LT. Genotyping of donor-recipient pairs was performed using Infinium Global Screening Array (Illumina, USA). Non-HLA genotypes were imputed with 1000 Genome Project Phase 3 European reference panel and classic HLA genotypes were imputed. To assess the burden of donor-recipient genetic incompatibility, we calculated sum scores for single nucleotide polymorphism (SNP) mismatch based on 10.550 non-HLA functional variants, with a mismatch score of 0, 1 or 2 for each variant (Figure 1A). Outcomes were assessed using a multivariable Cox proportional hazards model.

Results: During a median follow-up time of 10 years, 83 out of 680 (12%) recipients experienced 1-year grade 2/3 graft rejection. Median non-HLA mismatch score for all patients was 3366 (range 1335-4783). The non-HLA mismatch burden was associated with increased incidence of 1-year graft rejection (HR 1.001; 95%CI 1.000-1.001; p = 0.045), whereas HLA-mismatch was not (Table 1). Recipients with a mismatch burden >3360 were at increased risk of rejection (Figure 1B).

Conclusion: Genetic donor-recipient non-HLA incompatibility, but not HLA-mismatch, was associated with clinically relevant liver graft rejection. This could imply a patient-tailored approach based on non-HLA mismatch burden to optimize immunosuppressive regimen.

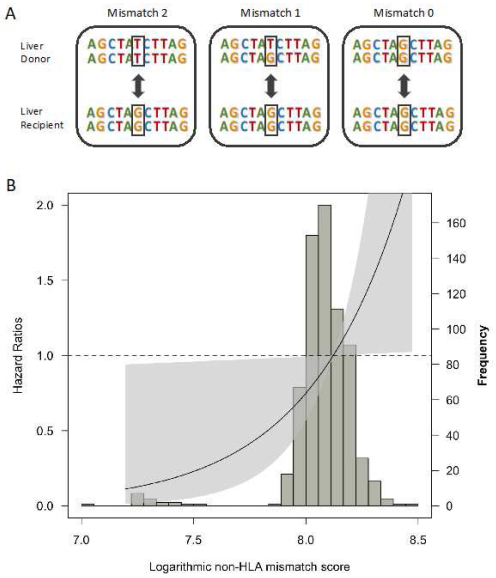

Figure 1. A. Generation of non-HLA mismatch score. A non-HLA variant mismatch is defined as an allele in the donor that was not present in the recipient. **B. Association of standardized log non-HLA variants mismatch score with one-year rejection based on restricted cubic spline regression.** The black line in the graph represents the hazard ratio of non-HLA variant mismatch score on one-year rejection. 95% confidence interval is shown in the gray area. After reverse log transfer, the non-HLA mismatch score, at the cut-off from which the amount of non-HLA mismatch becomes a risk factor, is identified as 3360 for one-year rejection.

Table 1. Multivariable regression analyses for 1-year grade 2/3 rejection

	1-year grade 2/3 rejection					
	Univariable			Multivariable		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Recipient age, years	0.999	0.989-1.009	0.831			
Recipient sex, male	0.879	0.570-1.355	0.559			
Recipient BMI	0.976	0.935-1.018	0.263			
Donor age, years	0.996	0.984-1.008	0.519			
Donor sex, male	0.769	0.499-1.184	0.233			
Donor BMI	1.000	0.948-1.055	0.998			
Donor cause of death (circulatory system indicator)						
External	0.917	0.560-1.502	0.732			
Other	1.714	0.686-4.281	0.249			
Cold ischemia time, minutes	1.001	1.000-1.002	0.088	0.999	0.998-1.001	0.458
Warm ischemia time, minutes	0.988	0.989-1.012	0.741			
Donor type (DBD indicator)						
DCD	0.621	0.286-1.349	0.229			
Living	0.934	0.229-3.805	0.924			
Blood loss per kg	0.999	0.996-1.001	0.237			
Operation time, minutes	0.999	0.997-1.001	0.197			
CMV primo infection	1.211	0.558-2.627	0.628			
HLA total eplet mismatch	1.069	0.943-1.211	0.297			
Non-HLA mismatch score	1.001	1.000-1.001	0.015	1.001	1.000-1.001	0.045
Time since transplantation	1.069	1.035-1.104	<0.001	1.072	1.031-1.113	<0.001

OP409 SOLVENT ACCESSIBLE AMINO ACID MISMATCHES CALCULATED BY HLA-EMMA AS INDEPENDENT RISK FACTOR FOR DEATH-CENSORED GRAFT FAILURE IN RENAL TRANSPLANTATION

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Background: Despite the decline of acute rejection rates in the last twenty years, long-term results after kidney transplantation have not improved accordingly. Refinement in HLA matching could result in improved graft outcomes. Polymorphic amino acids on mismatched donor HLA can lead to the induction of de novo donor-specific antibodies, resulting in inferior graft survival. HLA-EMMA is a recently developed software program that compares the amino acid sequences of donor and recipient HLA, and identifies the polymorphic solvent accessible amino acid mismatches (saAA MM) that may trigger a humoral allo-immune response. This is the first study that investigates the effect of amino acid mismatch on graft outcome in a large cohort of renal transplant recipients.
Methods: We conducted a retrospective cohort study of deceased-donor kidney transplant recipients transplanted through the Eurotransplant Kidney Allocation System from 1996 to 2019 to evaluate the effect of saAA MM on transplant outcome. Allele level HLA-A, -B, -C, DRB1 and DQB1 typing data were imputed from serologic HLA-A, -B, -DR and -DQ types using Haplostats. saAA MM were identified by using HLA-EMMA. Uni- and multivariate Cox proportional hazard models were fitted in a cohort of 34,401 unsensitized (panel reactive antibody 0%) first kidney transplant recipients with at least 1 HLA allele mismatch to assess the risk of death-censored graft failure (DCGF) by an increasing number of saAA MM. Multivariate models were corrected for donor and recipient age, donor sex, cold ischemia time, transplantation year, waiting time and cause of end-stage renal disease.
Results: Multivariate Cox proportional hazard models demonstrated HLA class I, HLA-DRB1 and -DQB1 saAA MM to be significantly associated with DCGF (Table 1).

Table 1 Multivariate hazard ratios for death-censored graft survival

saAA MM	HR	95% CI	p value
HLA class I	1.008	1.005, 1.012	<0.001
HLA-DRB1	1.009	1.003, 1.015	0.002
HLA-DQB1	1.006	1.002, 1.011	0.011

CI, confidence interval; HR, hazard ratio; saAA MM, solvent accessible amino acid mismatches.
Conclusions: Solvent accessible amino acid mismatches for HLA class I, HLA-DRB1 and DQB1 assigned by HLA-EMMA are significantly associated with DCGF. Further studies should validate these results in a cohort with high-resolution HLA typing and rejection data.

OP410 LIVING DONOR KIDNEY TRANSPLANTATION IN PATIENTS WITH DONOR-SPECIFIC HLA ANTIBODIES AFTER DESENSITIZATION WITH IMMUNOADSORPTION

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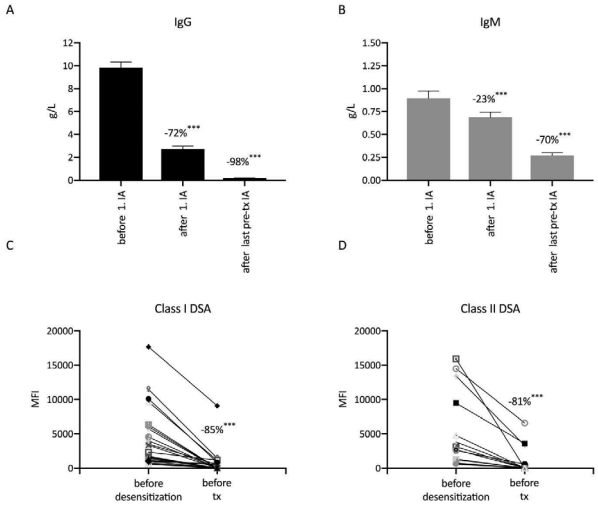
Background: Due to the current organ shortage, living donor kidney transplantation is increasingly performed across HLA (human leukocyte antigen) barriers. There is still uncertainty about the risk of antibody-mediated rejection (AMR) episodes. The present study evaluated the results of living donor kidney transplantations performed after desensitization in patients with donor-specific HLA antibodies compared to standard-risk recipients.
Methods: Thirty-eight desensitized living donor kidney transplant recipients were included in the study. Nineteen patients had a positive CDC crossmatch result with their donor and 36 patients had Luminex-detected donor-specific HLA antibodies (DSA). The patients were successfully desensitized with a median of 8 immunoadsorption treatments; 12 patients received

additional plasma exchange. After desensitization but before transplantation, the patients received the anti-CD20 antibody rituximab (N = 36) in combination with thymoglobulin (N = 20) or anti-IL2 receptor antibody (N = 18). The results of the 38 desensitized patients were retrospectively compared to 76 1:2-matched standard-risk recipients.
Results: Desensitized patients showed patient and graft survival rates similar to standard-risk recipients. There was a trend towards reduced death-censored graft survival in desensitized patients (p = 0.053) which, however, disappeared when the 34 patients who were transplanted after introduction of sensitive Luminex testing were analyzed (p = 0.43). Median 1-year serum creatinine was with 1.36 mg/dL similar to 1.38 mg/dL in standard-risk patients (p = 0.88). Thirty-six patients had pre-transplant HLA class I and/or II DSA that were reduced by 85% and 81%, respectively, during pre-transplant desensitization (p < 0.001 for both). On day 360 after transplantation, 18 of 36 (50%) patients had lost their DSA whereas 2 (6 %) patients with persistent and de novo DSA experienced AMR-related graft loss during further course.
Conclusions: Our desensitization protocol for pre-sensitized living donor kidney transplant recipients resulted in good graft outcomes with side effects and rejection rates like that of standard-risk recipients. Adequate patient selection prior to transplantation is critical to minimize rejection episodes and subsequent graft loss.



OP411 ANTI-THYMOCYTE GLOBULIN MEDIATED B-CELL ACTIVATION

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Background: Anti-thymocyte/anti-T-lymphocyte globulins (ATG) have been regularly used for decades as induction therapy across all organs. ATG provides profound T-cell depletion and thereby lowers the risk of acute rejections. Besides those desirable effects on T cells, recent experimental findings demonstrated that ATG induction also affects B cells and triggers B-cell mediated secretion of interleukin 1 and 6 (IL-6). Hence, ATG might provide a pro-inflammatory stimulus, pre-activate B cells and thereby accelerate the humoral allo-immune response.
Methods: Murine splenic B cells were purified using magnetic-activated cell sorting (>95% CD19+ B220+ purity). Unseparated murine splenocytes and sorted B cells were cultivated in presence or absence of anti-thymocyte globulin (Thymoglobulin, 2μg per 5mio splenocytes/well) without any further stimulus in a serum-free cell culture model for 24 or 72 hours. Surface expression of B-cell activation markers and intracellular IL-6 synthesis (in B cells) were assessed using flow cytometry.
Results: B cells within unseparated splenocytes cultivated with ATG demonstrated significantly higher expression of the activation markers CD86 and MHC-II (MFI of CD86 on B cells after 24h in-vitro in unseparated splenocytes; ATG: mean = 874, 95%-CI = 1026 – 722 vs. untreated: mean = 528, 95%-CI = 623–434; p = 0.0007). In contrast, when ATG was added to a highly purified murine B-cell culture for 24 or 72 hours, surface expression was not increased compared to B cells cultured without ATG. Additionally, B cells in unseparated splenocytes as well as in the purified B-cell culture showed significantly increased intracellular IL-6 levels in presence of ATG compared to the corresponding populations without ATG.

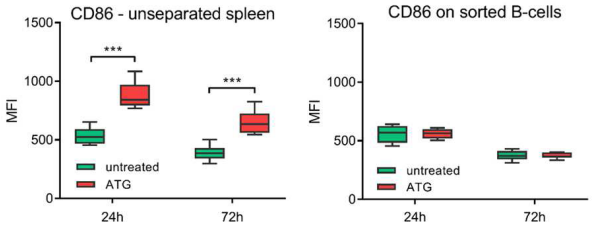

Figure 1 CD86 on unseparated splenocytes and sorted B cells
Surface expression of CD86 is depicted as mean fluorescence intensity (MFI) on unseparated splenocytes and sorted B cells upon 24h or 72h of culture in presence or absence of ATG
Conclusion: ATG directly triggers IL-6 secretion and indirectly causes upregulation of CD86 and MHC-II surface expression in B cells. Thereby ATG might stimulate the B cell-mediated allo-immune response.

OP412 MESENCHYMAL STROMAL CELL DERIVED MEMBRANE PARTICLES ARE INTERNALIZED BY MACROPHAGES AND ENDOTHELIAL CELLS AND EXHIBIT IMMUNOMODULATORY EFFECTS

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Background: Mesenchymal stromal cells (MSC) are studied as a potential therapy for immune modulation and regeneration in organ transplantation. However, MSC are large and become trapped in the lungs after intravenous infusion, where they have a short survival time, and working with living cells limits the possibilities for modifications to the therapeutic product.
Methods: To steer MSC therapy beyond the lungs and improve their mechanism of action, we generated nm-sized particles from MSC membranes (membrane particles, MP), which we demonstrated earlier to interact with various cell types and exhibit immunomodulatory and repair properties. Here we investigated the mode of interaction of MP with macrophages and human umbilical vein endothelial cells (HUVEC) under control and inflammatory conditions.
Results: We found that macrophages and HUVEC take up MP in a dose, time, and temperature-dependent manner. Specific inhibitors for endocytotic pathways revealed that MP internalization depended on heparan sulfate proteoglycan-, dynamin-, and clathrin-mediated endocytosis but did not involve caveolin-mediated endocytosis. MP uptake also involved the actin cytoskeleton and phosphoinositide 3-kinase, which are implicated in macropinocytosis and phagocytosis. Anti-inflammatory M2 macrophages took up more MP than pro-inflammatory M1 macrophages. Moreover, MP induced a mixed anti- and pro-inflammatory gene expression profile in macrophages by increasing IL10 and TGFβ mRNA, but also TNFα and IL1β. In HUVEC challenged with inflammatory stimuli, MP reduced HLA and co-stimulatory molecules expression, and elevated VE-cadherin protein expression, which is involved in endothelial cell barrier function.
Conclusions: Our findings on the mechanisms of uptake of MP under different conditions help the development of target-cell specific MP therapy to modulate immune and endothelial cell responses in transplant organs.

OP413 DELINEATING THE IMMUNOGENICITY OF GRAFT COMPONENTS IN COMPOSITE TISSUE ALLOTRANSPLANTATION

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Background: High frequencies of acute rejections remain an unsolved problem in Vascular Composite Tissue Allotransplantation (VCA). Here, we delineated components of VCA for their contribution to graft immunogenicity.

Methods: Early immune responses following skin and orthotopic hind limb (HL) Tx in allogeneic mouse models dissected the role of antigen presenting cells (APC). Grafts of zDC-DTR (diphtheria toxin receptor) transgenic and C57BL/6 wild type (WT) mice, pretreated with DT (DC depletion) or clodronate liposomes (CL; APC depletion), respectively, were transplanted into DBA2 recipients. Grafts from untreated WT mice served as controls. Immunophenotyping was performed by flow cytometry in blood, spleen and lymph nodes (LN) of recipients. Intragraft gene expression of cytokines was analyzed by qPCR, serum cytokine levels by Luminex assays. Rejections were assessed serially (POD 1,3,5) based on the BANFF criteria (grading 0-4).
Results: Both, WT hindlimb and skin grafts showed increased signs of acute rejection by POD 5 (grade 3) compared to DC-depleted groups (grade 2). DC counts ($CD11c^+$, $CD11c^+MHCII^+/CD40^+$) were markedly increased in recipients of skin WT grafts compared to HL WT grafts (blood, spleen, LN, POD6, $p < 0.0001$). Depletion of donor DC or APC significantly reduced DC counts in skin graft recipients ($p < 0.05$ vs. WT), but did not impact DC numbers following HL Tx. Recipients of HL grafts showed significantly higher cDC1 subset counts ($CD11b^-B220^-CD11c^+CD8^+$; blood, spleen, LN, $p < 0.05$ vs. skin Tx); cDC2 subset counts ($CD11b^+CD11c^{high}MHCII^{high}$) were significantly increased in recipients of skin grafts ($p < 0.01$). $CD4^+IL17A^+$ T cells were augmented significantly following skin Tx ($p < 0.0001$ vs. HL) while IL-6, TNF-alpha, IL-17, and TNF-beta protein levels were elevated in WT recipients of HL grafts ($p < 0.05$ vs. skin Tx).
Conclusions: Early immune responses differed significantly between recipients of skin and HL grafts. DC and Th17 immune responses may provide specific therapeutic targets in VCA transplantation.

OP414 LOCAL IMMUNOSUPPRESSION IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION: PAVING THE WAY FOR A SAFER ALTERNATIVE

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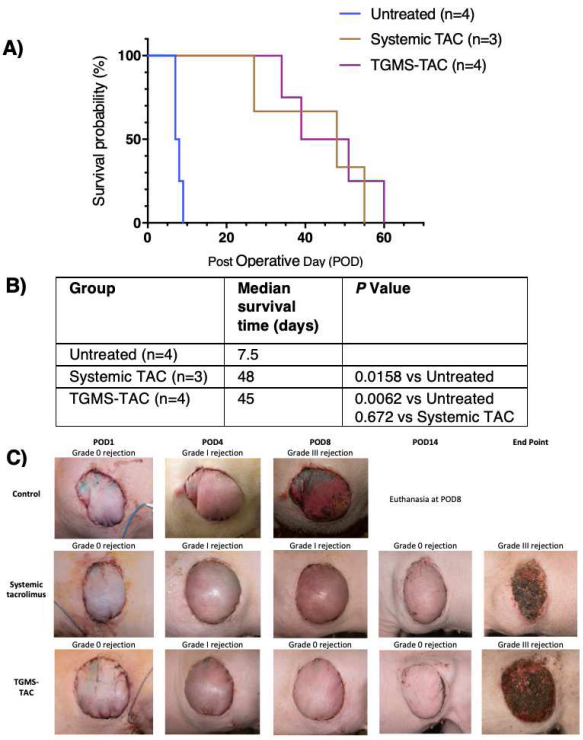
Background: Despite offering incomparable reconstructive results, Vascularized composite allotransplantation (VCA) is not yet the gold standard treatment for severe tissue loss, due to the side effects associated with the systemic immunosuppression required to avoid graft loss. Taking advantage that VCA allows local administration of immunosuppression, we aim to prolong graft survival by means of a tacrolimus-loaded drug delivery system (DDS), resulting in minimal off target toxicity.
Methods: An osteomyocutaneous flap allotransplantation was performed in SLA mismatched outbred pigs. Postoperatively, pigs were treated with a single injection of Triglycerol-monostearate Tacrolimus (TGMS-TAC) used as DDS, or with systemic tacrolimus; and compared with an untreated group (Control). Pigs were followed up until grade III rejection or post-operative day (POD) 90. Skin and blood samples were collected at defined time points to evaluate off-target toxicity, drug concentration levels and the immune response.
Results: A single dose of the DDS increased the median survival time (MST) to 45 days, compared to the untreated group (MST of 7.5 days). Similar results were observed with systemic tacrolimus treatment (Fig.1). Tissue levels of tacrolimus were significantly higher in the graft vs. contralateral side in the TGMS-TAC group, while in the systemic treatment group there was no difference. Prolonged graft survival seems to be a cumulative effect of higher tissue levels. No differences in off target toxicity were observed in the three groups. Confocal microscopy evaluation of the skin showed an increase in T cell and neutrophil infiltration in the control group, whereas increased vascularity and endothelial cell activation was more predominant in the treatment groups.
Conclusions: A one-time injection of a tacrolimus-loaded DDS is able to prolong graft survival in an outbred SLA-mismatched porcine model of VCA, leading to better drug distribution in the tissue as compared with systemic tacrolimus administration, without variations in off target toxicity. Additionally, variations in molecular and cellular infiltration in the rejected tissues suggest differences in the mechanism of rejection. A better understanding of how these influence the host's immune response could lead to tailored treatments in VCA.



Group	Median survival time (days)	*P* Value
Untreated (n=4)	7.5	
Systemic TAC (n=3)	48	0.0158 vs Untreated
TGMS-TAC (n=4)	45	0.0062 vs Untreated 0.672 vs Systemic TAC

Figure 1. A single injection of TGMS-TAC maintains graft survival. **A)** Kaplan-Meier survival curve of the groups, p value calculated by Mantel-Cox test. **B)** Macroscopic graft evaluation in the different groups.

BIOMOLECULAR TOOLS TO PREDICT, MONITOR AND INTERPRET: ELEMENTARY, MY DEAR WATSON

OP439 SOLUBLE UROKINASE RECEPTOR AND MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Soluble urokinase plasminogen activator receptor (suPAR) is an immunological risk factor for kidney disease and a prognostic marker for cardiovascular events.
Methods: We measured serum suPAR levels in a total of 1,023 kidney transplant recipients either before (cohort 1, n = 474) or at year 1 after transplantation (cohort 2, n = 549). The association of suPAR levels and all-cause and cardiovascular mortality was evaluated by multivariable Cox regression analysis.
Results: The highest suPAR tertile compared to the two lower tertiles had a significantly higher risk of all-cause mortality in both cohorts separately (cohort 1: hazard ratio (HR) 1.92, 95% confidence interval (CI) 1.20–3.08, p = 0.007; cohort 2: HR = 2.78, 95% CI 1.51–5.13, p = 0.001) and combined (n = 1,023, combined HR = 2.14, 95% CI 1.48–3.08, $p < 0.001$). The association remained significant in the subgroup of patients with normal kidney function (cohort 2: HR = 5.40, 95% CI 1.42–20.5, p = 0.013). The increased mortality risk in patients with high suPAR levels was attributable mainly to an increased rate of cardiovascular death (n = 1,023, HR = 4.24, 95% CI 1.81–9.96, $p < 0.001$).
Conclusions: A high suPAR level prior to and at 1 year after kidney transplantation was associated with an increased risk of patient death independent of kidney function, predominantly from cardiovascular cause.

OP440 COMPARATIVE TRANSCRIPTOME ANALYSIS REVEALS A POTENTIAL ROLE OF C1QB IN CHRONIC ANTIBODY-MEDIATED REJECTION OF KIDNEY ALLOGRAFTS

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Background: Background: Chronic antibody-mediated rejection (CAMR) is a multifactorial pathological condition that can affect more that 40-50% of transplanted organs. Its clinical evolution is often silent and this can delay its diagnosis. Although there have been many advances in understanding the biological mechanisms underlying its onset, there are no non-invasive biomarkers that can identify patients at risk of developing this complication at early stage.
Methods: By a microarray methodology (Agilent technology), we analyzed the transcriptomic profile of peripheral blood mononuclear cells (PBMCs) isolated from 10 patients with CAMR diagnosed according to the current BANFF criteria (randomly selected from a large cohort of patients) and 10 patients with normal-functioning graft (controls). For the bioinformatics analysis, we used both the ANOVA and the Kruskal-Wallis tests adjusted for multiple tests. Subsequently, a Weighted Gene Correlation Network Analysis (WGCNA) was employed to select those biologically associated in co-expressed networks.
Results: 935 genes were differentiated expressed between the two groups, demonstrating the great impact of this pèathological condition on circulating immune-inflammatory cells but, after WGCNA co-expression analysis, a group of genes (enclosed in a single co-expression module, 13 genes) appeared highly discriminating (p.value). This module included: Interferon-induced transmembrane proteins (IFITM) 2, 3, 4. Furthermore, the most discriminative gene between CAMR and controls was C1QB (Complement component 1, q subcomponent, B chain, $p < 000.1$), a key element of the classical complement path.
Conclusion: Our study confirmed the role of the interferon pathway and revealed a systemic activation of the complement system in CAMR. Finally, it suggested that C1QB could represent, if validated in a large cohort of patients, an efficient molecular diagnostic biomarker for this complication.

OP441 VALIDATION OF FLAVIN MONONUCLEOTIDE TO MONITOR QUALITY OF DONOR KIDNEYS DURING HYPOTHERMIC (OXYGENATED) MACHINE PERFUSION IN KIDNEY TRANSPLANTATION

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Background: Hypothermic machine perfusion (HMP) may allow for organ assessment prior to transplantation, helping the clinical decision whether to accept or decline an organ. Flavin MonoNucleotide (FMN), part of mitochondrial NADH:ubiquinone oxidoreductase enzyme (complex I), can dissociate from this complex after ischaemia-induced mitochondrial injury. Recent reports imply that FMN in perfusate can be used as a biomarker of organ quality during oxygenated HMP ($HMPO_2$) of livers and kidneys. The aim of this study was to validate the use of FMN as a biomarker for clinical outcomes in HMP preserved and subsequently transplanted kidneys.
Methods: Multiple perfusate samples (n = 367) were obtained from the COPE-COMPARE trial, a paired RCT comparing $HMPO_2$ vs. HMP in kidneys from donation after circulatory death (DCD) donors. FMN levels in perfusates were assessed by fluorescence spectroscopy (ex. 450nm; em 500-600nm). Fluorescence intensity (FI) was correlated with short- and long-term functional outcomes. FI findings were validated by targeted liquid chromatography mass spectroscopy (LC-MS).
Results: In both $HMPO_2$ and HMP groups, FI during machine perfusion increased over time ($HMPO_2$ $p = 0.0001$; HMP $p = 0.0004$). The observed increase was similar for both groups ($p = 0.829$). No correlation was found between FI and post-transplant outcomes, including day 5 or 7 serum creatinine ($p = 0.0756$ and $p = 0.1359$, respectively), immediate graft function ($p = 0.1279$), creatinine clearance and biopsy-proven rejection at one year ($p = 0.1330$ and $p = 0.6419$, respectively). In the light of these negative findings, we performed LC-MS based validation experiments to (dis)prove presence of FMN. Our validation experiments detected FMN in one perfusate sample, whilst the majority (n = 37, 97.4%) remained negative for FMN.
Conclusions: We conclude that the fluorescence spectrum of HMP kidney perfusates suggested to reflect FMN does not correlate with clinical outcomes in kidney transplantation. Moreover, we were unable to confirm presence of FMN in the majority of the perfusate samples. These data challenge previous reports to use direct FI and estimation of perfusate FMN levels and suggest that, in context of hypothermic kidney perfusion, FMN cannot be used as a biomarker to predict kidney graft function after transplantation.

OP442 MONITORING OF MOLECULAR PROFILING OF REGULATORY T CELL BIOMARKERS BY USING NON-INVASIVE STRATEGIES TO PREDICT OUTCOME IN RENAL TRANSPLANTATION

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Background: Acute T-cell mediated rejection (aTCMR) is still an issue in kidney transplantation for it is associated with chronic rejection, graft loss, and overall worse outcomes. For these reasons, a standard non-invasive molecular tool to detect is desirable to offer a simpler monitoring of kidney transplant recipients (KTRs). The purpose of our study was to examine in peripheral blood, before and after transplantation, the expression patterns of Treg-related genes, FOXP3 and the two CTLA-4 isoforms (full-length and soluble), to predict aTCMR onset, *de novo* donor-specific antibodies (DSA) development and renal dysfunction.
Methods: We profiled by using a qRT-PCR method the circulating mRNA levels of these biomarkers in peripheral blood of 89 KTRs within the first post-transplant year (baseline, at day 15, 60, 365 and when possible at aTCMR) and compared the results with 24 healthy controls.
Results: The three mRNA levels drastically reduced 15 days after transplantation and gradually recovered at one year in comparison with baseline, with very low levels by the time of aTCMR for FOXP3 (RQ = 0.445, IQR = 0.086-1.264, p = 0.040). Healthy controls exhibited higher FOXP3 levels than patients at baseline (median RQ: 2.132, IQR = 1.664-2.895 vs. aTCMR-free pts RQ:1.630, IQR = 1.072-2.367, p = 0.005). Noteworthy, solCTLA-4 displayed a dual profile: on the one hand, at multivariate analysis solCTLA-4 transcripts at 15 days were associated with an increased risk of aTCMR over time (HR = 3.905, 95%CI: 0.958-15.916, p = 0.050), and graft dysfunction at one year (AOR = 3.683, 95%CI = 1.165-12.079, p = 0.027); on the other hand, pre-transplant levels showed a protective association with *de novo* (DSAs) development (HR = 0.189, 95%CI = 0.078-0.459, $p < 0.001$).
Conclusions: mRNA levels of Treg-associated genes, mainly for solCTLA-4 in peripheral blood might help shape immunosuppression, tailor monitoring and achieve better long-term outcomes of kidney transplantation in the wake of "precision medicine".

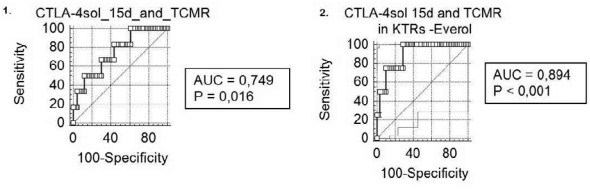

Figure - Receiver-operating characteristic (ROC) curve analyses for the expression of the CTLA-4sol at day 15. Prediction of aTCMR episodes within the first year in: 1) whole cohort of patients (stable transplantation n=67, acute cellular rejection episodes n=8) and 2) in patients receiving only mycophenolic acid (n=63).

1) AUC=0.749, p=0.016 95%CI=0.634-0.843. Younden's index threshold showed for solCTLA-4 log values >-0.05 a prediction of acute rejection with sensitivity of 83.3% and specificity of 56.7%. 2) AUC=0.894, 95%CI=0.791-0.953, p<0.001. solCTLA-4 15 days, Younden's criterion for values >0.13 a prediction of acute rejection with sensitivity of 100.0% and specificity of 71.2%

OP443 URINARY EXTRACELLULAR VESICLES AND VESICULAR CELL-FREE DNA AS POTENTIAL BIOMARKERS FOR KIDNEY ALLOGRAFT INJURY

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Background and Aims: Individualized strategies for early detection of kidney allograft injury are gaining increasing interest as current assessment methodology, based on invasive biopsy procedures, is not sustainable and compatible with repetitive monitoring. Urinary extracellular vesicles (uEVs) are stable carriers of pathophysiological signals from the transplanted kidney and could therefore serve as novel non-invasive biomarker (BM) for allograft injury. Among uEV-bound molecules, donor-derived DNA (dd-DNA) remains unexplored, whereas few studies investigated cell-free DNA (cfDNA) in urine. Our aim was to isolate uEVs, extract and analyse their DNA cargo, including ddDNA, and evaluate their potential use as BM for kidney allograft injury, compared with urinary cfDNA.
Methods: We collected kidney biopsy, whole blood, and second morning spot urine samples from 40 kidney allograft recipients. We isolated uEVs from 20 mL of urine using size-exclusion chromatography, which we have shown to efficiently separate uEVs from contaminants. Size and concentration of uEVs were determined using Nanoparticle Tracking Analysis (NTA). uEV-bound (EV-DNA) and urine cfDNA were isolated using QIAamp DNA Micro Kit and Zymo *Quick*-DNA Urine Kit, respectively, quantified by Qubit and analysed by digital PCR to evaluate donor-specific SNPs for % ddDNA and RPPH1/RPP30 to determine DNA fragmentation. To identify donor-specific SNPs, DNA isolated from blood and kidney biopsy using the E.Z.N.A. SQ Blood DNA Kit II and QIAamp DNA Micro Kit, respectively, was genotyped by digital PCR for 6 SNPs.
Results: The average mean size and concentration of uEVs were 170 nm and 7.5 x 10^8 particles per mL of urine, respectively. We obtained higer yield of cfDNA (206 ng) compared to EV-DNA (77 ng). Despite broad range (2-99%), the dd-DNA ratio in cfDNA and EV-DNA in each patient was comparable. The RPPH1/RPP30 ratio was higher for EV-DNA than cfDNA.
Conclusions: We have successfully characterized uEVs and their DNA content. EV-DNA and cfDNA displayed similar % dd-DNA, but results suggested greater stability of EV-DNA. As such, it should be further investigated as BM for monitoring kidney allograft injury.

OP444 NUCLEAR FACTOR OF ACTIVATED T CELLS AS POTENTIAL PHARMACODYNAMIC BIOMARKER FOR THE RISK OF ACUTE AND SUBCLINICAL REJECTION IN LIVER RECIPIENTS

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Background: NFAT-regulated gene expression (NFAT-RGE) has been proposed as a pharmacodynamic biomarker for Tac and CsA. Our aim was to evaluate the role of NFAT-RGE in modulating intralymphocytary IL-2 and IFN-γ expression and its clinical utility as an early non-invasive predictive biomarker for the risk of acute rejection (AR) and infection in adult LT recipients.
Methods: 56 LT recipients treated with Tac or CsA [with and without mycophenolate mofetil] were included: 30 free of rejection or infection, 11 rejectors (TCMAR), 5 with subclinical rejection (SCR) and 10 with cytomegalovirus (CMV) infection. Within the first 3 months after transplantation, NFAT-RGE of IL-2, IFN-γ and GM-CSF and intralymphocytary synthesis of IL-2 and IFN-γ were evaluated by real-time PCR and flow cytometry, respectively. For each patient receiving a CNi, the trough and 1.5-h concentrations after CNi administration were analysed within the 1st week, on the 15th day, and at 1, 2 and 3 months post-transplantation.
Results: A significant increase in NFAT-RGE was observed in patients who experienced TCMAR [75% (42%-100%)] or SCR [41% (18%-78%)] compared with patients without rejection or infection [14% (2%-23%)]. Positive correlations between the %NFAT-RGE-IFN and both the %CD8CD69IFN-γ and %CD4CD69IFN-γ and between the %NFAT-RGE-IL2 and the % CD8CD69IL2 were observed. NFAT-RGE was significantly lower in CMV^+ patients than in non-infected patients. No statistically significant differences between patients without rejection, patients with rejection and patients who had CMV infections were observed with regard to drug exposure. Finally, an inverse correlation between Tac or CsA concentration and inhibition of NFAT-RGE was observed.
Conclusions: The results of the present study suggest that NFAT-RGE is a potential biomarker for the risk of TCMAR and SCR and may provide guidance for CNi therapy after liver transplantation. The combination of sequential pre- and post-transplantation monitoring of intralymphocytary IL-2 and IFN-γ levels with NFAT-RGE may be considered to improve patient risk stratification, mainly pre-transplantation and at the 1st and 3rd months post-transplantation and provide physicians with broad information for early personalized treatment adjustment and better prevention of rejection.

OP445 CONNECTION OF BANK1, TOLERANCE, REGULATORY B CELLS, AND APOPTOSIS: PERSPECTIVES OF A REDUCTIONIST INVESTIGATION

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Operationally tolerant patients (TOL), who present a good and stable kidney graft function years after withdrawal of immunosuppression, display peripheral immune alterations that we want to elucidate. BANK1 (B-cell scaffold with ankyrin repeats 1) transcript is upregulated in blood of TOL, in comparison to patients with chronic rejection. TOL display also higher level of regulatory B cells (Bregs) expressing granzyme B ($GZMB^+$) that have the capability to prevent effector T cells proliferation. However, BANK1 was found to be decreased in these $GZMB^+$ Bregs.
We used a reductionist approach to investigate 7 different, public and own, transcriptomic studies and mined the literature and public data to understand link between BANK1, tolerance and Bregs.
We found that BANK1 is decreased in all subtypes of Bregs, including $IL10^+$ and $CD24^{hi}CD38^{hi}$ transitional, GZMB+ Bregs compared to B cells, as well as in differentiated B cells, like CD40-activated B cells, in leukemia and plasma cells. Biological concepts were extracted from BANK1 literature and allowed to infer indirect association between BANK1 and Bregs and immune tolerance, via STAT1, FcγRIIB, TNFAIP3, TRAF6, and TLR7 molecules. Based on interaction networks and expression data, we proposed a role of BANK1 in B cells of tolerant patients that involved BCR, IP3R and PLCG2, and a link with the apoptosis pathways.
Finally, we put in perspective our own experiments on apoptosis in total B cells and Bregs, with public data to suggest two different roles for BANK1 in these two cells: in TOL B cells, an increase of BANK1 complex seems to increase apoptotic PLCG2/IP3R/Ca2+ pathway leading to apoptosis, B homeostasis and tolerance, while in the $GZMB^+$ Bregs, BANK1 decrease does not trigger an apoptosis decrease as expected, but the increase of apoptotic TNF/Fas and intrinsic pathways activity, leading to a differentiated cell profile, hallmark of regulation.

OP446 IMPACT OF STEATOSIS AND COLD ISCHEMIA TIME ON MITOCHONDRIAL RESPIRATION IN HUMAN LIVER ALLOGRAFTS

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Background: In parallel with obesity and metabolic syndrome, the prevalence of non-alcoholic fatty liver disease is rapidly growing, influencing liver transplantation in two ways: (1) by increasing the indications of transplantation, and (2) by raising the proportion of steatotic donor livers obtained. Such grafts are prone to preservation injury and graft dysfunction. The role of mitochondria in the pathogenesis of liver steatosis is well described, but information on fatty acid oxidation (FAO) in liver after static cold storage (SCS) is scarce. Herein we evaluate the mitochondrial function using high-resolution respirometry (HRR) and investigate the impact of cold ischemia and steatosis on cell respiration prior to and after transplantation.

Methods: 34 patients (64.7 % male) were enrolled in a prospective clinical trial. Liver wedge biopsy samples were taken during SCS and upon reperfusion. Steatosis was graded by histology. Mitochondrial FAO was analysed using HRR (O2k, Oroboros Instruments) in tissue homogenates by the addition of 0.5 mM octanoylcarnitine in the presence of 0.1 mM malate and 5 mM ADP, while the NADH-linked respiration was assessed with pyruvate (5 mM), malate (2 mM) and glutamate (10 mM).
Results: The donor body mass index (BMI) was 25.34 ± 3.94 kg/m^2 (mean ± SD). 18 grafts presented without steatosis (52.9 %), the rest with mild or moderate steatosis, with a positive correlation between donor BMI, body mass excess (BME) and donor liver steatosis. We observed a significantly higher FAO in grafts with mild steatosis than in non-steatotic samples or in moderate steatosis. The cold ischemia time was 8.4 ± 2.01 hours. Importantly, an inverse correlation between cold ischemia time and the combined FAO and NADH-linked oxidative phosphorylation was detected upon reperfusion.
Conclusions: The pattern of mitochondrial respiration is significantly altered in liver allografts even with mild steatosis during cold ischemia, with possible effects on the graft quality upon transplantation. SCS and reperfusion selectively impair the FAO- and NADH-linked oxidative phosphorylation.

OP447 APPLICATION OF THIN-FILM SOLID-PHASE MICROEXTRACTION TO BILE ANALYSIS - BILE FINGERPRINT AS A PROGNOSTIC MARKER DURING LIVER TRANSPLANTATION

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Background: Recently, normothermic ex vivo liver perfusion (NEVLP) has been implemented in liver transplantation as an alternative to static cold storage (SCS). This method enables the maintenance of the liver's regular metabolic activity and the extension of the graft time's storage while maintaining its good quality. This study assessed the metabolomic profile of bile produced by the liver during the peri-transplant period under both conditions and looked for metabolites correlating with organ changes depending on degree of ischemia.
Methods: The study was performed on bile samples obtained from two types of porcine model donors: heart beating donor (HBD) and donor after cardiac death (DCD). Samples were collected during SCS and NEVLP at specific time points: before organ harvest, during perfusion (for NEVLP), reperfusion, and the first few days after transplantation. The DCD group was divided due to organ ischemia: 30' for SCS and 30', 60', 90' for NEVLP. Sample preparation was performed using thin-film solid-phase microextraction (TF-SPME). Extracts were analyzed using the LC-HRMS platform.
Results: Metabolomic profiling revealed a clear separation of bile samples according to the time points they were collected. For the 30'DCD group, higher concentration of Taurohyocholic acid ($p < 0.001$) and lower concentration of Glycocholic acid ($p < 0.001$) were found in the case of NEVLP compared to SCS during reperfusion. The compounds correlated with organ ischemia during perfusion were indicated, e.g. Kynurenic acid ($r = 0.61$), Acetylglutamic acid ($r = 0.65$), Tauroursodeoxycholic acid ($r = 0.72$), while during reperfusion LysoPE(18:2) ($r = 0.67$), PE(36:4) ($r = 0.67$), 7-dehydrodesmosterol ($r = -0.67$), and Cholestane-3,7,12,25-tetrol-3-glucuronide ($r = -0.72$).
Conclusions: The proposed strategy can be effectively used for bile profiling to search biomarkers of metabolic processes occurring in the transplanted organ.

OP448 VIABILITY ASSESSMENT USING THE "SIX GENE SIGNATURE" DURING LIVER PERFUSION

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Background: Dual hypothermic oxygenated perfusion (D-HOPE) can be used to recondition liver grafts prior to transplantation. Objective biochemical, haemodynamic and biliary parameters have proven successful in identifying livers for transplantation during clinical normothermic perfusion. We aimed to identify parameters associated with outcomes during HOPE and develop an objective assessment tool.
Methods: We analysed perfusion characteristics, biochemical and molecular signatures from livers (n = 16) undergoing D-HOPE perfusion. Mesoscale multiplex plates (MESO QuickPlex™ SQ120 multiplex analyser) were used to quantify tissue and vascular injury as well as inflammatory status at different time points. Receiver Operator Characteristics (ROC) curve analysis was performed to establish the optimum values for each molecule during the molecular analysis.
Results: 10 livers were transplanted (mild injury) and 6 livers (severe injury) were not transplanted on the basis of an integrated subjective assessment of donor and recipient factors. There were no significant differences between the two groups based on vascular flows, lactate clearance, bile duct flow, and oxygen consumption. ROC curve analysis revealed significant differences in various molecular patterns between the two groups. An algorithm integrating a specific combination of 6 molecules could discern between mild and severe injury with 100% sensitivity and specificity. Some of these molecules are associated with specific damage pathways during ischaemic injury.
Conclusions: A specific pattern of injury-associated biomarkers has been identified that can differentiate between severe and mild injury. This suggests both objective scoring of livers using molecular analysis during hypothermic injury is achievable and has identified potential targets for therapeutic intervention.

OP449 ADVANTAGES OF PLASMATIC CXCL10 AS A PROGNOSTIC & DIAGNOSTIC BIOMARKER FOR THE RISK OF REJECTION AND SUBCLINICAL REJECTION IN KIDNEY TRANSPLANTATION

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Background: CXCL-10 is a promising biomarker of kidney graft outcome. This study aimed to evaluate the potential of plasmatic CXCL-10 (pCXCL-10) as a pre- and post-transplantation prognostic and diagnostic biomarker of T cell-mediated rejection (TCMR), antibody-mediated rejection (ABMR) and subclinical rejection (SCR) risk in adult kidney recipients considering BKV and CMV infections as possible clinical confounder factors.
Methods: One hundred adult kidney recipients treated with tacrolimus, mycophenolate mofetil and methylprednisolone (90%) and tacrolimus, everolimus and methylprednisolone (10%) were recruited from four European centers. Pharmacokinetic parameters (trough concentration and AUC0-12h) and pCXCL-10 levels were evaluated before and at 1 week and 1, 2, 3 and 6 months after transplantation.
Results: Twenty-eight patients experienced rejection (TCMR:14; ABMR:14); 8 SCR; 13 and 16 were diagnosed with BKV infection and CMV infection, respectively. Pre-transplantation pCXCL-10 concentrations were significantly increased ($p < 0.05$) in TCMR and ABMR compared with nonrejectors (TCMR-cutoff: 156.89pg/mL PPV:90% NPV:95%; ABMR-cutoff:140.4pg/mL PPV:82.3% NPV:97.7%). Post-transplantation, pCXCL-10 concentrations were significantly increased ($p < 0.05$) in TCMR, ABMR and SCR compared with nonrejectors (TCMR-cutoff:177.7pg/mL PPV:80% NPV:100%; ABMR-cutoff:184.7pg/mL PPV:84% NPV:97.7%; SCR-cutoff:131pg/mL PPV:88% NPV:89%). All CMV+ patients showed pCXCL-10 levels above the cutoff values established for rejection whereas the 80% of BKV+ patients showed pCXCL-10 concentration values <100pg/mL before and at the time of the infection.
Conclusions: pCXCL-10 concentration could improve pre-transplantation patient stratification and immunosuppressive treatment selection according to rejection risk; and after kidney transplantation could be a potential early prognostic biomarker for rejection. Clinical confounding factor in BKV+ and particularly in CMV+ patients may occur and must be discarded.

OP450 MONITORING KIDNEY GRAFT INJURY BY MEASURING DONOR-DERIVED CELL FREE DNA (DD-CFDNA)

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Background: Routine follow-up of kidney transplant recipients (KTxR) is usually carried out by monitoring serum creatinine, proteinuria, immunosuppressive blood levels, polyomavirus viremia, and donor-specific antibodies (DSA). Despite this, the allograft can be suffering a significant T cell- or antibody-mediated damage that may only be detected by performing an invasive procedure such as a kidney biopsy. It would be of the outmost interest to have a non-invasive test to know the status of the allograft. Recent technological advances allow to detect the presence of donor derived cell free DNA (dd-cfDNA) circulating in the recipient's blood. Some studies have related the percentage of dd-cfDNA to alloimmune graft damage.
Methods: The percentage of dd-cfDNA (%dd-cfDNA) was measured by the CE IVD approved AlloSeq test (CareDx) in 10 KTxR on 10/Dec/2021. Briefly, plasma was collected in Streck BCT tubes. cfDNA was extracted using the QiAamp Circulating Nucleic Acid Kit. 202 SNP regions were amplified and sequenced in a MiSeq next generation sequencing (Illumina). The fraction of donor-specific sequences was calculated by a specifically developed CareDx Software. The relationship between the %dd-cfDNA and the clinical situation of the recipients was explored. dd-cfDNA of 3 patients was analyzed twice.
Results: Median %dd-cfDNA was 0.51% (IQR 0.34%, 0.98%). 6 KTxR with stable GFR and without DSA had %dd-cfDNA between 0.22 and 0.51%. The patient with the highest %dd-cfDNA (1.4%) was suffering and antibody-mediated rejection. The only other value above 1% (1.1%) came into a patient recovering from acute tubular necrosis of a donor after cardiac death on day 33 post-transplantation. A %dd-cfDNA of 0.94% related to a KTxR at 19 days after DBD transplant, whereas a patient with stable renal function but with de novo DSA had a %dd-cfDNA of 0.81%, suggesting the presence of subclinical antibody-mediated damage. %dd-cfDNA did not related to estimated GFR ($r = -0.201$, $p = 0.578$). Samples repeated twice gave exactly the same values.
Conclusions: AlloSeq test allows measuring %dd-cfDNA in a simple, non-invasive and reproducible way. %dd-cfDNA relates to underlying allograft damage that cannot be detectable by current monitoring methods such as serum creatinine.

OP451 HUMAN CD81 EXTRACELLULAR VESICLES ARE RELEASED DURING NORMOTHERMIC MACHINE PERFUSION

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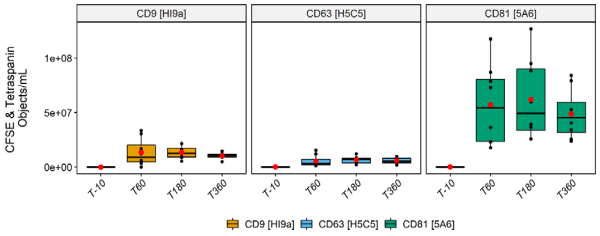
Background: Extracellular Vesicles (EVs) represent stable, tissue specific nano-sized particles that reflect the conditional state of their tissue of origin. Here, the dynamic release and phenotype of kidney EVs were characterized and quantified during Normothermic Machine Perfusion (NMP) of donor kidneys to examine whether EVs could function as a potential biomarker for assessing kidney quality before transplantation.
Materials & Methods: Eight discarded kidneys (~13 ± 5 hours of cold ischemia, age 68 ± 7 (mean ± standard deviation), all male) were perfused in a closed system at 37 ^{0}C for 6 hours. Perfusates were taken before and at 1, 3 and 6 hours and examined with Nanoparticle Tracking Analysis (NTA) and Imaging Flow Cytometry (IFCM). For IFCM, perfusates were stained with the tetraspanin EV markers CD9, CD63 or CD81, or a mix of the three markers in combination with CFSE to identify, quantify and characterize EVs.
Results
Analysis of perfusates with NTA revealed that the majority of nanoparticles present in the perfusates are <300 nm. Using IFCM, we selectively studied these small (<300 nm) nanoparticles. For CFSE and the mix of tetraspanin double-positive single small EVs (ssEVs), we observed a ~700 / 740 / 560 fold increase compared to ssEV levels before perfusion at 1, 3 and 6 hours of NMP, respectively. Especially after 1 hour of NMP, double-positive ssEV levels were found to be positively correlated with donor age whilst negative correlations were found for cold ischemia time. Furthermore, tetraspanin CD81 was found to represent the majority (~70%) of the excreted double-positive ssEVs (CD9: ~15% / CD63 <10%) (Figure).
Conclusion: ssEVs are excreted during NMP with highest excretion levels during the first hour of perfusion. Tetraspanin CD81 is predominantly present on these ssEVs. The characterization of the excreted ssEVs as well as their correlation with clinical parameters provide a starting point to study their role as potential biomarkers of kidney quality.



OP452 TRANSFORMING GROWTH FACTOR-B1 EXPRESSION IN RENAL TRANSPLANT URETER TISSUE AND POST-TRANSPLANT URETERAL STRICTURE

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Background: Post-transplant ureteral strictures can complicate the function of a renal allograft. Better risk stratification for this fibrotic complication is required. A significant upregulation of pro-fibrotic Transforming Growth Factor beta-1 (TGF-β1) expression is detected in renal allografts following ischemic injury and ischemic-reperfusion injury and predicts progressive kidney interstitial fibrosis. Therefore, the aim of this study was to evaluate whether enhanced TGF-β1 production in intra-transplant ureter tissue correlated with post-transplant ureteral stricture.
Methods: This retrospective case-control study (N = 28) analysed TGF-β1 protein and gene expression in ureter biopsies taken at the end of cold ischemia time (T1) and after reperfusion (T2) using both ELISA and qPCR. Controls were matched to cases on possible risk factors for ureteral strictures including donor type, diabetes of the receiver, and gender, age, and body mass index of both donor and receiver.
Results: Intra-transplant TGF-β1 protein and gene expression in ureter tissue showed no significant correlation with post-transplantation ureteral stricture. Variation in TGF-β1 concentrations between all study objects was observed. Significant correlations between TGF-β1 expression and several donor characteristics were found. Firstly, deceased donor and prolonged cold ischemia time was positively correlated with absolute TGF-β1 protein concentrations at T1 and in change over time (T2-T1). Additionally, male gender of the donor was correlated with increased absolute T1 protein levels.
Conclusions: Intra-transplant TGF-β1 expression in ureter tissue was not correlated with post-transplantation ureteral stricture. Moreover, significant correlations of donor type, cold ischemia time and gender with TGF-β1 expression were found. These correlations are described in literature on TGF-β1 expression in renal interstitial biopsies as well. Potentially, non-invasive ureter biopsies can replace invasive kidney biopsies for risk stratification for post-transplantation renal fibrosis. Future studies are required to determine whether intra-transplant TGF-β1 in the ureter is correlated with renal fibrosis.

BUGS IN TRANSPLANTATION: NEWS AND PERSPECTIVES

OP479 CIRCULATORY FOLLICULAR HELPER T LYMPHOCYTES PROTECT AGAINST CMV INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: CMV-infection in kidney transplant patients (KTR) increases rejection risk. T follicular helper cells (TFH) may contribute to protection through promoting neutralizing antibodies (Nabs) and/or secretion of IL-21, which has been shown to strengthen NK and CD8$^+$ cytolytic activity. TFH

cells have been identified circulating in peripheral blood (cTFH). We aimed to study if cTFH could protect against CMV in KTR post-transplantation (Tx).
Methods: PBMCs were collected pre- and early post-Tx from 90 CMV seropositive KTR not receiving antithymocyte globulin or antiviral prophylaxis, followed-up for one year. cTFH were identified as $CD4^+CXCR5^+$ and activated cTFH as $CD4^+CXCR5^+CCR7^{lo}PD1^{hi}$ by flow cytometry. CMV infection was defined as DNAemia >1000 UI/ml of blood and CMV-disease was considered when infection and symptomatology coexisted. Nabs titers were determined by microneutralization assays. CMV-specific $CD8^+$ T cell were identified by a modified version of the QuantiFERON-CMV test.
Results: KTR with CMV infection had significantly lower cTFH and activated cTFH pre-tx and early post-tx ($p = 0.01$, $p = 0.008$, $p = 0.01$ and $p = 0.02$). Pre-tx and 14 days post-tx activated cTFH were also lower within infected KTR who developed CMV disease ($p = 0.02$, $p = 0.01$). KTR with superior cTFH pre-Tx, 7 and 14 days post-tx counts suffered the CMV infection later ($p = 0.02$, $p = 0.01$ and $p = 0.006$). Pre- and 14 days post-tx activated cTFH were an independent protective factor for CMV infection (HR 0.41, $p = 0.01$; and 0.52, $p = 0.02$, respectively). KTR with low cTFH 7 days post-tx (<11.9%) had lower CMV infection-free survival than KTR with high cTFH (28.2% vs 67.6%, $p = 0.002$). cTFH were associated with positivity for CMV-specific Nabs ($p = 0.008$). In addition, IL-21 increased interferon-γ secretion by CMV-specific $CD8^+$ T cells in healthy controls ($p = 0.007$).
Conclusions: TFH may protect against CMV infection in KTR. Monitoring cTFH pre- and early post-tx could improve CMV risk stratification.

OP480 ANTIVIRAL TREATMENT PATTERNS FOR CYTOMEGALOVIRUS PREVENTION AMONG ADULT KIDNEY TRANSPLANT RECIPIENTS: A USRDS-MEDICARE LINKED DATABASE STUDY

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Background: Cytomegalovirus (CMV) is a common pathogen among kidney transplant recipients (KTRs). Although guidelines recommend the use of prophylaxis or pre-emptive antiviral (AV) therapy depending on the risk level, limited data exist on the recent national level treatment patterns of CMV antiviral agents (AV) among KTRs. We examined the real-world CMV-AV utilization patterns among adults KTRs in the United States (US) overall and by CMV serostatus of donor (D) and recipients (R).
Methods: We utilized a retrospective cohort design using the US Renal Data System registry-linked Medicare data from January 1, 2011, through December 31, 2017. The study cohort included adults undergoing their first KT during the study period with continuous medical coverage for at least 6-month pre- and 12-month post-KT and pharmacy benefits coverage for at least 12-month post- KT. CMV-AV prophylaxis was defined as ≥1 fill of either (val)acyclovir or (val)ganciclovir (VGC) within 28 days post-KT. Descriptive statistics were reported by CMV prophylaxis status by CMV risk strata (low: D-/R-; medium: R+; and high: D+/R-).
Results: The study cohort comprised of 23,445 KTRs of which 11%, 74% and 15% were at low, medium and high risk of CMV, respectively. The mean age (standard deviation, SD) of KTRs was 53.8 (13.9) years. The majority of KTRs were males (59%), Whites (59%) and African Americans (33%); and received anti-thymocyte globulin (54%), mycophenolate (96%), tacrolimus (95%), and steroids (96%). CMV-AV prophylaxis was used by 35%, 83%, and 85% of low-, intermediate- and high-risk KTRs, respectively. Valganciclovir was utilized in 98% of KTRs treated with CMV AV-prophylaxis. From 2011 to 2016, an increase in the use of VGC 900 mg in high-risk and a relatively stable trend of VGC 450 mg dose were noted in intermediate-risk KTRs. The mean duration of CMV prophylaxis was 102 (SD:70.4) days. Proportions of KTRs with duration of CMV prophylaxis ≥100 and ≥200 days were 50% and 11% of high-risk, and 25% and 5% of intermediate-risk KTRs, respectively.
Conclusions: Valganciclovir was commonly utilized as CMV-AV prophylaxis. The majority of KTRs had shorter than the guideline-recommended duration of 100 or 200 days of CMV-AV prophylaxis, especially among high-risk KTRs, which may lead to suboptimal efficacy for CMV prevention.

OP481 DONOR CYTOMEGALOVIRUS SEROPOSITIVITY CLUSTERS WITH RISK FACTORS FOR DELAYED GRAFT FUNCTION IN RENAL TRANSPLANTATION, BUT DOES NOT DIRECTLY CONTRIBUTE

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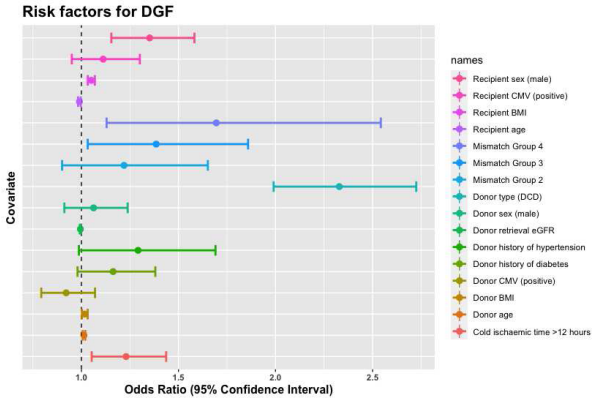
Background: Cytomegalovirus (CMV) is a major cause of morbidity and mortality amongst renal transplant recipients. Post-transplantation infection and serostatus have been shown to be associated with long-term patient and graft outcomes. CMV has also been shown to be transcriptionally active at the time of transplantation, and can be detected in implant biopsies. Animal model data suggest a) CMV reactivation may be partially driven by ischaemia-reperfusion injury; and b) results in impaired injury repair and greater proinflammatory cytokine production. However, the effect of donor and recipient CMV serostatus on acute injury at the time of transplantation is not known. We sought to test the hypothesis that CMV-associated injury would manifest as higher delayed graft function (DGF) rates in CMV donor positive/ recipient positive transplants.
Methods: National data concerning DGF, recipient and donor CMV serostatus, and relevant covariates were requested from the UK NHSBT registry. Multivariate regression and a paired analysis considering CMV+ kidneys donated to recipients discordant for CMV serostatus were used to delineate the effect of CMV serostatus. This was augmented with local data to examine any potential effect of CMV serostatus on functional definitions of DGF.
Results: The national cohort consisted of 4130 deceased-donor renal transplants performed between 01/01/2015 and 31/12/2017. 156 were excluding due to incomplete data, primary nonfunction, or recipient death or graft loss within the first seven days leaving 3974 for analysis. There was no relationship between CMV serostatus and DGF. A number of covariates known to contribute to DGF, including donor age and terminal donor eGFR did associate with donor CMV positivity and were demonstrated to predict DGF in this cohort. The paired analysis, and sensitivity analyses using complete cases only and restricting DGF to >1 day did not change this conclusion. Analysis of local data did not identify any relationship between dialysis or creatinine-based definitions of DGF and CMV serostatus.
Conclusions: Whilst donor/ recipient CMV serostatus may impact long-term graft survival, in both a large national registry study and with highly granular centre-specific data we found no evidence that it impacts peri-transplant injury manifesting as DGF.



OP482 PREVENTION OF CYTOMEGALOVIRUS INFECTION BY EVEROLIMUS IN SEROPOSITIVE KIDNEY TRANSPLANT RECIPIENTS

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Background and Aims: In this multicenter trial EVERCMV, we tested if everolimus (EVR) could decrease the incidence of cytomegalovirus (CMV) DNAemia and CMV curative treatment in seropositive kidney transplant recipients.
Methods: We randomized 186 CMV seropositive kidney transplant recipients to receive EVR (n = 95) or mycophenolic acid (MPA, n = 91) in association with basiliximab, cyclosporin, and steroids. No universal prophylaxis was administered. The composite primary endpoint was CMV DNAemia, CMV treatment, graft loss, death, and discontinuation of the study at 6 months post-transplantation.
Results: 48.3% and 80.5% of patients in the EVR and MPA groups reached the primary endpoint, respectively ($p < 0.0001$). Patients receiving EVR showed a lower incidence of CMV DNAemia (39.2% *vs.* 77.8%, $p < 0.0001$), however, EVR was stopped in 35.6% of them. 21.4% of patients with ongoing EVR treatment experienced CMV DNAemia (HR = 0.14, CI95% 0.08-0.24, $p < 0.0001$). Only 7.4% of them required a CMV treatment because CMV viral loads were low, when compared to 36.4% in those with EVR discontinuation and 46% in the MPA group (HR = 0.08, CI95% 0.03-0.2, $p < 0.0001$). The incidence of rejection, adverse events and graft loss was similar in the EVR and MPA groups.
Conclusions: In the absence of universal prophylaxis, EVR was associated with a reduced incidence of CMV DNAemia. Among them, a minority required a treatment. EVR could be considered as a new strategy to prevent CMV in seropositive recipients as long as it is tolerated and maintained.

OP483 VALGANCICLOVIR PROPHYLAXIS VERSUS PREEMPTIVE THERAPY FOR PREVENTION OF CYTOMEGALOVIRUS IN RENAL TRANSPLANT RECIPIENTS: A RANDOMIZED CONTROLLED TRIAL

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Background: Both valganciclovir preemptive therapy and universal prophylaxis significantly reduce CMV disease rates in renal transplant recipients. Still, preemptive therapy approach is often questioned for prevention of CMV indirect effects.
Methods: In a randomized, open-label, single-center trial, we enrolled renal transplant recipients (recipient [R] or donor [D] CMV seropositive). Before transplantation, patients were randomly allocated (1:1) to valganciclovir prophylaxis (900 mg daily for 3 months in R+, and 6 months in D+/R-, respectively) or to preemptive valganciclovir therapy (900 mg twice daily until 2 consecutive negative test a week apart) for significant CMV DNAemia (≥1000 IU/mL by quantitative PCR in whole blood) assessed weekly for 16 weeks and monthly up to 12 months. The primary endpoint was biopsy-proven acute rejection at 12 months. Analysis was by intention-to-treat.
Results: Between June, 2013 and May, 2018, 140 patients were assigned to valganciclovir prophylaxis (n = 70) or to preemptive therapy (n = 70). The 12-month incidence of CMV disease was not different (4% vs. 4%, $p = 0.974$) while CMV DNAemia was higher in the preemptive group (44% vs. 75%, $p < 0.001$) including CMV DNAemia with high viral load (≥2000 IU/mL, 21% vs. 49%, $p < 0.001$). Preemptive therapy was required in 38/70 (54%) patient with the necessity of additional course for recurrent CMV DNAemia in majority (29/38, 76%; 2.6 ± 1.4 courses per patient). The incidence of acute rejection was 9/70 (13%) in prophylaxis and 16/70 (23%) in preemptive therapy ($p = 0.112$). Subclinical rejections at 3-month protocol biopsy were higher with preemptive therapy (13% vs. 29%, $p = 0.027$) if borderline changes were included. In contrast, among patients without preformed donor-specific anti-HLA antibodies (DSA) before transplantation more patients with prophylaxis developed de-novo DSA (18% vs. 5%, $p = 0.029$). There was no difference in other infections (including polyomavirus BK), patient and graft survival.
Conclusion: Compared with preemptive therapy, valganciclovir prophylaxis does not decrease the incidence of acute rejection in spite of significant reduction of CMV DNAemia in renal transplant recipients. Preemptive therapy effectively prevents CMV disease, however, repeated courses are commonly needed.

OP484 INFECTION PATTERN IN EVEROLIMUS VERSUS MYCOPHENOLATE-BASED REGIMENS IN KIDNEY TRANSPLANT RECIPIENTS: 24-MONTH RESULTS FROM THE TRANSFORM STUDY

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Background: Infections remain a major cause of morbidity and mortality in kidney transplantation recipients (KTxRs). Many factors influence the infection rates in KTxRs. We evaluated the effect of everolimus+reduced-dose calcineurin inhibitor (EVR+rCNI) versus mycophenolic acid+standard-dose CNI (MPA+sCNI) on infections in KTxRs from the TRANSFORM (NCT01950819) study.
Methods: In this 24-month, multicentre, open-label study, low-to-moderate risk KTxRs were randomized to EVR+rCNI (N = 1022) or MPA+sCNI (N = 1015) with induction and steroids. Incidence of bacterial, fungal and viral (cytomegalovirus [CMV] and BK virus [BKV]) infections were evaluated in various subgroups including induction type, age, diabetes (baseline and new-onset diabetes mellitus [NODM]), body mass index (BMI), patients with delayed graft function (DGF), and by donor type.
Results: Overall, the rate of infections and infestations and viral infections was low; the rate of fungal infections was higher with EVR+rCNI than MPA+sCNI in all subgroups; and the rate of bacterial infections was comparable between treatment arms. Incidence of CMV events was significantly lower among patients in the EVR+rCNI versus MPA+sCNI arm, irrespective of the presence or absence of diabetes at baseline ($p < 0.001$) or NODM ($p \leq 0.001$), and BMI ($p < 0.01$), and was independent of CMV prophylactic treatment status. The incidence of CMV syndrome events was numerically lower in patients with BMI ≥30 kg/m^2 versus BMI <30 kg/m^2 and in those without DGF versus with DGF in both treatment arms. BKV infection was less in EVR+rCNI versus MPA+sCNI arm regardless of the presence or absence of diabetes at baseline or NODM, and in subgroups of induction type, DGF and donor type. With increasing age, a gradual increase in the incidence of infections was observed (Table).
Conclusion: The rate of infections such as CMV and BKV was lower with the EVR+rCNI versus MPA+sCNI arm among KTxR subgroups including diabetic and obese patients.

Table: Infection rate in different subgroups

		n (%)	Any infections and infestations	Bacterial	Fungal	Viral	CMV prophylaxis; n/M (%)		Clinical signs of CMV infection assessed		CMV syndrome		Histological signs for CMV		Any BKV infection
							Yes	No	Yes	No	Yes	No	Yes	No	
Induction type	Basiliximab	EVR+rCNI N=844	**582 (69.0)**	326 (38.6)	67 (7.9)	**175 (20.7)**	**37/413 (9.0)**	**34/431 (7.9)**	47 (5.6)	190 (22.5)	16 (1.9)	105 (12.4)	2 (0.2)	73 (8.6)	85 (10.1)
		MPA+sCNI N=841	**638 (75.9)**	333 (39.6)	42 (5.0)	**296 (35.2)**	**74/400 (18.5)**	**116/441 (26.3)**	114 (13.6)	213 (25.3)	50 (5.9)	162 (19.3)	8 (1.0)	110 (13.1)	119 (14.1)
	rATG	EVR+rCNI N=169	115 (68.0)	58 (34.3)	12 (7.1)	**33 (19.5)**	**7/116 (6.0)**	**10/53 (18.9)**	6 (3.6)	38 (22.5)	2 (1.2)	13 (7.7)	-	4 (2.4)	18 (10.7)
		MPA+sCNI N=171	130 (76.0)	78 (45.6)	12 (7.0)	**61 (35.7)**	**18/120 (15.0)**	**17/51 (33.3)**	18 (10.5)	50 (29.2)	9 (5.3)	28 (16.4)	-	21 (12.3)	35 (20.5)
Age	<45 years	EVR+rCNI N=379	**247 (65.2)**	112 (29.6)	25 (6.6)	**67 (17.7)**	**20/212 (9.4)**	**10/167 (6.0)**	25 (6.6)	69 (18.2)	10 (2.6)	37 (9.8)	-	23 (6.1)	21 (5.5)
		MPA+sCNI N=380	**275 (72.4)**	129 (33.9)	16 (4.2)	**119 (31.3)**	**28/189 (14.8)**	**36/191 (18.8)**	42 (11.1)	92 (24.2)	19 (5.0)	58 (15.3)	-	38 (10.0)	31 (8.2)
	≥45 to ≤65 years	EVR+rCNI N=509	**362 (71.1)**	211 (41.5)	45 (8.8)	**118 (23.2)**	**20/254 (7.9)**	**22/255 (8.6)**	21 (4.1)	128 (25.1)	7 (1.4)	65 (12.8)	2 (0.4)	44 (8.6)	62 (12.2)
		MPA+sCNI N=492	**380 (77.2)**	202 (41.1)	31 (6.3)	**190 (38.6)**	**55/265 (20.8)**	**63/227 (27.8)**	66 (13.4)	138 (28.0)	23 (4.7)	110 (22.4)	4 (0.8)	75 (15.2)	98 (19.9)
	>65 years	EVR+rCNI N=126	89 (70.6)	61 (48.4)	10 (7.9)	**23 (18.3)**	**4/64 (6.3)**	**12/62 (19.4)**	7 (5.6)	31 (24.6)	1 (0.8)	16 (12.7)	0	10 (7.9)	20 (15.9)
		MPA+sCNI N=140	113 (80.7)	80 (57.1)	7 (5.0)	**48 (34.3)**	**9/66 (13.6)**	**34/74 (45.9)**	24 (17.1)	33 (23.6)	17 (12.1)	22 (15.7)	4 (2.9)	18 (12.9)	25 (17.9)
Diabetes at baseline	Yes	EVR+rCNI N=278	189 (68.0)	121 (43.5)	21 (7.6)	**53 (19.1)**	**13/148 (8.8)**	**14/130 (10.8)**	16 (5.8)	69 (24.8)	5 (1.8)	35 (12.6)	1 (0.4)	24 (8.6)	35 (12.6)
		MPA+sCNI N=269	203 (75.5)	111 (41.3)	20 (7.4)	**85 (31.6)**	**21/154 (13.6)**	**35/115 (30.4)**	29 (10.8)	67 (24.9)	13 (4.8)	45 (16.7)	2 (0.7)	37 (13.8)	48 (17.8)
	No	EVR+rCNI N=736	**509 (69.2)**	263 (35.7)	59 (8.0)	**155 (21.1)**	**31/382 (8.1)**	**30/354 (8.5)**	37 (5.0)	159 (21.6)	13 (1.8)	83 (11.3)	1 (0.1)	53 (7.2)	68 (9.2)
		MPA+sCNI N=743	**565 (76.0)**	300 (40.4)	34 (4.6)	**272 (36.6)**	**71/366 (19.4)**	**98/377 (26.0)**	103 (13.9)	196 (26.4)	46 (6.2)	145 (19.5)	6 (0.8)	94 (12.7)	106 (14.3)
NODM	Yes	EVR+rCNI N=144	**106 (73.6)**	57 (39.6)	16 (11.1)	**28 (19.4)**	**6/73 (8.2)**	**6/71 (8.5)**	5 (3.5)	31 (21.5)	2 (1.4)	19 (13.2)	0	10 (6.9)	8 (5.6)
		MPA+sCNI N=138	**113 (81.9)**	60 (43.5)	11 (8.0)	**53 (38.4)**	**8/64 (12.5)**	**23/74 (31.1)**	19 (13.8)	33 (23.9)	9 (6.5)	24 (17.4)	2 (1.4)	16 (11.6)	29 (21.0)
	No	EVR+rCNI N=870	**592 (68.0)**	327 (37.6)	64 (7.4)	**180 (20.7)**	**38/457 (8.3)**	**38/413 (9.2)**	48 (5.5)	197 (22.6)	16 (1.8)	99 (11.4)	2 (0.2)	67 (7.7)	95 (10.9)
		MPA+sCNI N=874	**655 (74.9)**	351 (40.2)	43 (4.9)	**304 (34.8)**	**84/456 (18.4)**	**110/418 (26.3)**	113 (12.9)	230 (26.3)	50 (5.7)	166 (19.0)	6 (0.7)	115 (13.2)	125 (14.3)
BMI	<30kg/m²	EVR+rCNI N=841	**578 (68.7)**	304 (36.1)	64 (7.6)	**174 (20.7)**	**35/438 (8.0)**	**33/403 (8.2)**	47 (5.6)	180 (21.4)	15 (1.8)	99 (11.8)	2 (0.2)	62 (7.4)	88 (10.5)
		MPA+sCNI N=843	**646 (76.6)**	333 (39.5)	42 (5.0)	**307 (36.4)**	**72/428 (16.8)**	**116/415 (28.0)**	115 (13.6)	208 (24.7)	54 (6.4)	152 (18.0)	8 (0.9)	101 (12.0)	131 (15.5)
	≥30 kg/m²	EVR+rCNI N=173	120 (69.4)	80 (46.2)	16 (9.2)	**34 (19.7)**	**9/92 (9.8)**	**11/81 (13.6)**	6 (3.5)	48 (27.7)	3 (1.7)	19 (11.0)	-	15 (8.7)	15 (8.7)
		MPA+sCNI N=169	122 (72.2)	78 (46.2)	12 (7.1)	**50 (29.6)**	**20/92 (21.7)**	**17/77 (22.1)**	17 (10.1)	55 (32.5)	5 (3.0)	38 (22.5)	-	30 17.8)	23 (13.6)
DGF	Yes	EVR+rCNI N=107	**71 (66.4)**	48 (44.9)	10 (9.3)	23 (21.5)	**8/57 (14.0)**	**6/50 (12.0)**	7 (6.5)	26 (24.3)	3 (2.8)	15 (14.0)	1 (0.9)	12 (11.2)	11 (10.3)
		MPA+sCNI N=100	**84 (84.0)**	52 (52.0)	5 (5.0)	32 (32.0)	**14/49 (28.6)**	**16/51 (31.4)**	19 (19.0)	27 (27.0)	9 (9.0)	26 (26.0)	0	28 (28.0)	16 (16.0)
	No	EVR+rCNI N=907	**627 (69.1)**	336 (37.0)	70 (7.7)	**185 (20.4)**	**36/473 (7.6)**	**38/434 (8.8)**	46 (5.1)	202 (22.3)	15 (1.7)	103 (11.4)	1 (0.1)	65 (7.2)	92 (10.1)
		MPA+sCNI N=912	**684 (75.0)**	359 (39.4)	49 (5.4)	**325 (35.6)**	**78/471 (16.6)**	**117/441 (26.5)**	113 (12.4)	236 (25.9)	50 (5.5)	164 (18.0)	8 (0.9)	103 (11.3)	138 (15.1)
Donor type	LD	EVR+rCNI N=506	336 (66.4)	--	--	--	**19/287 (6.6)**	**8/219 (3.7)**	25 (4.9)	81 (16.0)	6 (1.2)	50 (9.9)	0	28 (5.5)	46 (9.1)
		MPA+sCNI N=505	365 (72.3)	--	--	--	**36/277 (13.0)**	**50/228 (21.9)**	60 (11.9)	104 (20.6)	23 (4.6)	83 (16.4)	2 (0.4)	51 (10.1)	72 (14.3)
	SCD	EVR+rCNI N=352	**249 (70.7)**	--	--	--	**20/182 (11.0)**	**19/170 (11.2)**	20 (5.7)	107 (30.4)	8 (2.3)	52 (14.8)	0	37 (10.5)	41 (11.6)
		MPA+sCNI N=345	**268 (77.7)**	--	--	--	**42/178 (23.6)**	**40/167 (24.0)**	39 (11.3)	111 (32.2)	19 (5.5)	71 (20.6)	2 (0.6)	51 (14.8)	50 (14.5)
	ECD	EVR+rCNI N=151	**109 (72.2)**	--	--	--	**5/60 (8.3)**	**16/91 (17.6)**	8 (5.3)	38 (25.2)	4 (2.6)	15 (9.9)	2 (1.3)	11 (7.3)	15 (9.9)
		MPA+sCNI N=159	**132 (83.0)**	--	--	--	**14/63 (22.2)**	**42/96 (43.8)**	33 (20.8)	45 (28.3)	17 (10.7)	36 (22.6)	4 (2.5)	28 (17.6)	30 (18.9)

-,not applicable; --, not available
Statistically significant differences between groups have been bolded
BKV, BKvirus; BMI, body mass index; CMV, cytomegalovirus; CNI, calcineurin inhibitors; DGF, delayed graft function; ECD, extended criteria donor; EVR, everolimus; LD, living donor; MPA, mycophenolic acid; NODM, new-onset diabetes mellitus; rCNI, reduced CNI; SCD, standard criteria donor; sCNI, standard CNI.

OP485 OUTCOME OF EBV NEGATIVE RECIPIENTS OF EBV POSITIVE DONOR ORGAN TRANSPLANT IN A SINGLE CENTRE

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Background: Epstein-Barr virus (EBV) is associated with post-transplant lymphoproliferative disease (PTLD), a life-threatening complication of solid organ transplantation. The risk of developing PTLD is greater in EBV-negative (EBV-) recipients who receive an organ from EBV-positive (EBV+) donors.
Methods: The aim of this prospective observational study was to follow-up EBV- recipients who received kidney or kidney pancreas transplants from EBV+ donors, assess the incidence of EBV viraemia, whether the patients seroconverted and complications including rejection and development of PTLD. Patients who received either a kidney or simultaneous kidney-pancreas transplant at Guy's Hospital from 2016 to 2020 were included. EBV levels were checked at regular intervals as per the Trust protocol.
Results: A total of 22 EBV- patients received transplants from EBV+ donors. Of these, 77.3% (17/22 patients) developed EBV viraemia, within a median time of three months (range: 1-11 months) post-transplantation. Four patients (23.6%) developed symptomatic EBV viraemia, with symptoms including diarrhoea, neutropenia and palpable lymph nodes. The viraemia in the thirteen other patients was detected due to routine surveillance of EBV levels. Immunosuppression was reduced in 70.6% (12/17) patients after development of EBV viraemia. The outcomes of patients who developed EBV viraemia compared to those who did not, is summarised in Table 1. Median follow-up of all patients was 41 months (range: 8-59 months). In total, there was only one case of PTLD. This patient is now 41 months post-transplantation and alive, with no transplant rejection.
Conclusions: In our cohort of EBV –ve recipients of EBV +ve organ, the outcomes for patients who developed viremia was similar to those who did not. This could be due to regular monitoring and early detection of EBV viremia with adjustment of immunosuppression. Larger study population and longer follow-up is needed to assess the appropriate monitoring period and interval for EBV viremia.

Table 1. Outcomes of patients with EBV viraemia compared to non-EBV viraemia patients.

	Rejection (% total)	PTLD (% total)	Dead (% total)	Functioning kidney (% total)	Seroconversion (% total)
EBV viraemia (n = 17)	3 (17.6)	1 (5.8)	0 (0)	16 (94.1)	16 (94.1)
No EBV viraemia (n = 5)	1 (20)	0 (0)	0 (0)	5 (100)	1 (20)

OP486 TACROLIMUS METABOLISM RATE AND BK INFECTION IN RENAL TRANSPLANT PATIENTS

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Background: The tacrolimus blood concentration to daily dose ratio (C/D ratio) has been identified as a simple stratification tool to describe a patient's tacrolimus metabolism rate. A previous publication by Thölking et al. 2014 found that fast metabolisers (C/D ratio <1.05) were significantly more likely to have BK viraemia compared to slow metabolisers (C/D ≥1.05) in a Caucasian cohort. This study analyses the impact of tacrolimus metabolism rate on BK infection in an ethnically diverse renal transplant cohort.
Methods: We retrospectively reviewed 303 renal transplants from 2016-2018. C/D ratios were calculated at month 1 post-transplant and participants were stratified into binary groups fast (<1.05) and slow (≥1.05) metaboliser status. BK PCR was performed monthly for the first 6 months post-transplant and then 3 monthly till 12 months post-transplant. Any positive BK PCR was recorded as a BK infection.
Results: Of 297 renal transplant patients, 192 (65%) and 105 (35%) of patients were classified as fast and slow metabolisers, with a median C/D of 0.85. The prevalence of BK viraemia at 12 months was 21%. Univariate logistic regression found that fast metabolisers were significantly less associated with BK viraemia in the first 12 months of transplantation (OR 0.5, $p = 0.017$).

Table 1 Participant numbers by ethnicity

		Fast metaboliser	Slow metaboliser
Ethnicity	White	82 (50%)	83 (50%)
	Asian	25 (76%)	8 (24%)
	Other	10 (62.5%)	6 (37.5%)
	Black	73 (91%)	7 (9%)

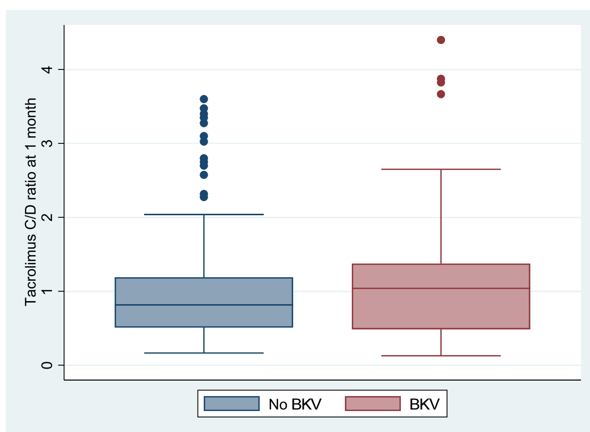

Figure 1 Boxplots of the relationship between BK viraemia and Tacrolimus C/D ratio 1 month after renal transplantation

Conclusions: This study with univariate analysis and an ethnically diverse cohort of renal transplant patients does not support previous findings of a positive association between fast metabolism and BK infection and in fact shows the opposite trend.

OP487 RELATIONSHIP BETWEEN CARBAPENEM-RESISTANT ENTEROBACTERALES CARRIAGE AND GUT MICROBIOME AFTER LIVER TRANSPLANTATION: A PROSPECTIVE COHORT STUDY

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Background: Liver transplant (LT) recipients are at high risk for acquiring and dying from carbapenem-resistant Enterobacterales (CRE) infection. Study aims are: to compare gut microbiome (GM) structure of LT recipients with and without CRE carriage; to investigate association between GM and development of CRE infection in colonized patients.
Materials: Single-center prospective longitudinal study on patients undergoing LT from January to December 2019. All patients were screened for CRE rectal carriage at the time of transplant and weekly after LT until hospital discharge. Fecal samples for GM analysis were obtained at LT, then weekly up to 1 month after LT. In CRE carriers, feces were collected up to 1 year after LT. After microbial DNA extraction from stools, the 16S rDNA V3-V4 region was sequenced on Illumina MiSeq. Raw sequences were processed using QIIME 2.
Results: Study cohort consisted of 97 LT recipients: 68 (70.1%) male, median age 58 (47-64) years. All-cause 180-day mortality was 6.2%. Overall, 466 fecal samples were obtained from 91 patients. Five patients were found to be CRE carriers at transplant and 9 after LT within a median of 31 (19-62) days. There was a significant separation between the GM of CRE carriers and non-carriers ($p \leq 0.001$). CRE carriers were characterized over time by a trend towards reduced alpha diversity ($p = 0.1$) and an increase in pathobionts (*i.e.*, *Klebsiella*, *Enterococcus*) ($p \leq 0.05$). In contrast, the GM of non-carriers showed higher proportions of health-associated microorganisms, e.g. *Blautia*, *Dorea*, *Lactobacillus* and *Ruminococcaceae* (Figure 1). Five out of 14 carriers developed CRE infection within 31 (3-46.5) days after LT. The GM of CRE-infected patients showed over-abundance of *Klebsiella*, *Enterococcus* and *Staphylococcus*, while beneficial taxa discriminated for uninfected patients (Figure 2).
Conclusions: GM of LT recipients with CRE carriage is distinct from that of non-carriers and exhibits different temporal dynamics, with less diversity, reduced proportions of health-associated taxa and increased amounts of pathobionts. This dysbiosis is even more pronounced in those who develop CRE infection.

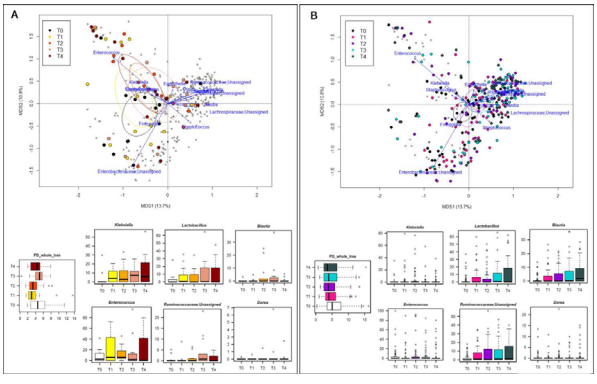

Figure 1. GM dynamics in CRE carrier vs. non-carrier patients undergoing LT.

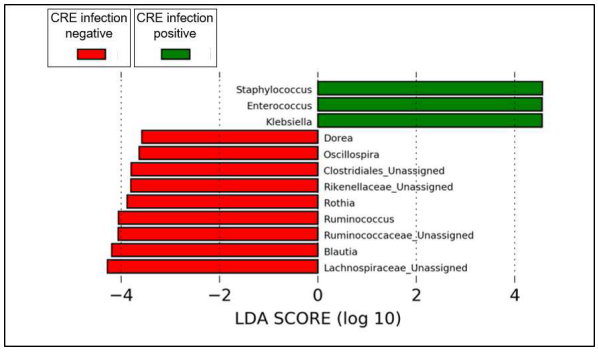

Figure 2. Gut microbial signatures of CRE infection in LT recipients with CRE carriage.

OP488 ASSOCIATION BETWEEN ACUTE GRAFT PYELONEPHRITIS AND KIDNEY GRAFT LOSS: A SINGLE-CENTER OBSERVATIONAL STUDY

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Background: Urinary tract infections and acute graft pyelonephritis (AGPN) are the most frequent type of infections occurring after kidney transplantation. To date, the association between AGPN and graft loss remains elusive. Several large-scaled cohorts did not reveal any impact of AGPN on the risk of graft loss, even if subgroups at risk were suggested (early AGPN or recurrent UTI). The objective was to assess the association between AGPN and the risk of graft loss.
Methods: The study was observational and monocentric. It included any adult recipients of a kidney transplant from 01/01/2007 to 31/12/2017. AGPN was defined according to 2019 international guidelines. Cox proportional hazards regression models were built using AGPN as a time-dependent covariate. Outcomes of interests were: graft and patient survivals, the evolution of eGFR, and the risk of rejection.
Results: 1480 recipients were included. Median time of follow-up was 5.04 years IQR[3.01-8.02]. 158 recipients presented at least one AGPN with a median time of 135 days IQR[31-470], for a total of 297 AGPN. AGPN was significantly associated with the risk of graft loss (HR = 1.66 IC95[1.05-2.64], $p < 0.03$), but not with death (HR = 0.89 IC95[0.49-1.62], $p = 0.71$) or biopsy-proven acute rejection (HR = 1.19 IC95[0.68-2.11], $p = 0.54$). Using a linear mixed model, longitudinal changes of eGFR were compared between recipients suffering or not from at least one AGPN. A median number of 22 (IQR[17-31]) serum creatinine values were available per recipient, resulting in 35877 available values of eGFR. The occurrence of a 1st AGPN was significantly associated with a persistent decrease of eGFR (fixed effect on intercept: -2.29 ml/min/1.73m² [-3.23; -1.35], $p < 0.01$), but not with a decrease of eGFR slope (fixed effect: -0.20 ml/min/1.73m² per year [-0.53; 0.13], $p = 0.23$).
Conclusions: AGPN is a frequent event after transplantation. It was associated with the risk of graft loss and the decrease of eGFR in our cohort.

OP489 BACTERIAL AND FUNGAL BLOODSTREAM INFECTIONS IN SOLID ORGAN TRANSPLANT RECIPIENTS: RESULT FROM A DANISH COHORT WITH NATIONWIDE FOLLOW-UP

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Background: Bloodstream infections (BSI) are prevalent and severe infections after solid organ transplantation (SOT). We aimed to investigate the incidence and risk factors for bacterial and fungal BSI in the first five years post-transplantation.
Methods: The study comprised 1322 SOT (kidney, liver, lung, and heart) recipients consecutively transplanted from 2010-2017 at Rigshospitalet, Denmark with a total of 5616 years of follow-up. Clinical characteristics and microbiology were obtained from the Centre of Excellence for Personalized Medicine of Infectious Complications in Immune Deficiency (PERSIMUNE) data repository with nationwide follow-up. Incidence rate and cumulative incidence were investigated in the different SOT groups. Risk factors associated with BSI were assed in the combined group in a time-updated multivariable Cox regression.
Results: A total of 523 BSI were observed in 142, 71, 45, and 3 kidney-, liver-, lung-, and heart transplant recipients, respectively. The incidence rate of first BSI was 1.29 (CI: 1.11-1.49) per 100 patients per month in the first year post-transplantation. The cumulative incidence of BSI differed in the SOT groups (Figure 1) and was significantly lower in heart transplant recipients compared to all other SOT groups (Heart: 4.4% (CI: 0.0-9.7) vs. Kidney: 24.6% (CI:20.9-28.2), Liver: 24.7% (CI:19.4-29.9), and Lung: 19.6% (CI:14.5-24.8), $p < 0.001$). Age above 55 years (HR: 1.71 (CI: 1.2-2.4), $p = 0.002$), higher Charlson comorbidity index score (HR: 1.25 (CI: 1.1-1.4), $p < 0.001$), current CMV infection (HR: 4.5 (CI: 2.6-7.9), $p < 0.001$), and current leucopenia (HR: 13.3 (CI: 3.7-47.9), $p < 0.001$) were all associated with an increased risk of BSI.
Conclusion: The incidence of BSI was high and differed according to the type of transplanted organ. Risk of BSI was higher in older recipients and in recipients with CMV infection, leucopenia, or comorbidity. Thus, increased attention towards BSI in recipients with these characteristics is warranted.

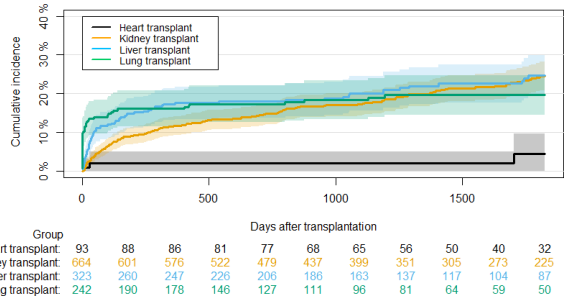

Figure 1 Cumulative incidence of first BSI in the first 5 years post-transplantation

OP490 ENTEROCOCCAL INFECTIONS IN THE FIRST YEAR AFTER LIVER TRANSPLANTATION

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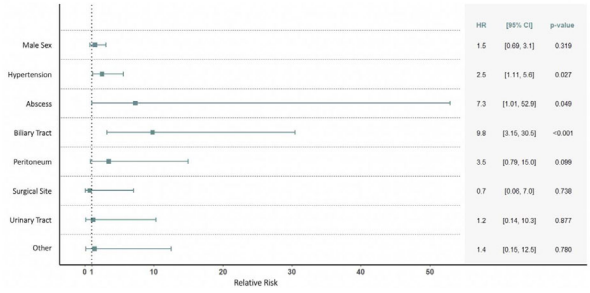
Background: Enterococcal bloodstream infections (BSI) post-liver transplantation (post-LTx) causes considerable morbidity and may be difficult to treat. We aimed to investigate the incidence of enterococcal infections and to determine risk factors associated with enterococcal BSI within the first year post-LTx.
Methods: We prospectively included 321 adult liver transplant recipients transplanted from 2011 to 2019 at Rigshospitalet. Recipient- and culture-related variables were collected from patient records, ScandiaTransplant, and the nationwide Danish Microbiology Database (MiBa). BSIs were considered as secondary culture if isolated within 14 days of a previous focal infection. Cumulative incidence of enterococcal cultures was investigated in a competing risk model, and risk factors associated with BSI were investigated in time-updated Cox models.
Results: The cumulative incidence of a first enterococcal culture was 39% (95%CI [33-44]) within the first year post-LTx. *Enterococcus faecium* was the most common species (77%), and vancomycin resistant enterococci were isolated from 8% of recipients. Enterococcal cultures were frequently isolated from the biliary tract (12%, CI [8-15]), while 11% (CI [7-14]) of recipients had an enterococcal BSI (Table 1). Risk factors associated with enterococcal BSI were previous enterococcal cultures from the biliary tract (HR: 9.8; CI [3.15-30.5]; $p < 0.001$) and abscesses (HR: 7.3; CI [1.01-52.9]; $p = 0.049$) and hypertension (HR: 2.5; CI [1.11-5.6]; $p = 0.032$). Enterococcal cultures from other sites were not significantly associated with BSI (Figure 1). In total, 14% and 2% of BSIs occurred secondary to biliary tract infection or abscess, respectively.
Conclusion: Enterococcal infections are highly prevalent during the first year post-LTx, and LTx recipients with enterococci in cultures from the biliary tract or an abscess had increased risk of enterococcal BSI. These findings may have implications for choice of empiric antibiotics early post-LTx.

Characteristics of enterococcal cultures

		E. faecium	*E. faecalis*	Other *spp.*	Total	Cumulative incidence (%)	Confidence interval (95%)
Enterococcal events, n (%)		241 (77)	58 (18)	16 (5)	315	38	33-44
Site of enterococcal culture, n (%)	Biliary Tract	57 (75)	16 (21)	3 (4)	76	12	8-15
	Urinary Tract	32 (68)	12 (26)	3 (6)	47	10	7-14
	Peritoneum	39 (89)	4 (9)	1 (2)	44	10	7-14
	Surgical Site	19 (73)	4 (15)	3 (12)	24	6	4-9
	Abscess	7 (70)	3 (30)	0 (0)	7	3	1-5
	Other sites	49 (78)	9 (14)	5 (8)	59	15	11-19
	BSI	38 (78)	10 (20)	1 (2)	40	11	7-14

Time updated Cox proportional hazard models



OP491 SUPERFICIAL SURGICAL SITE INFECTION AT HAND-PORT SITE AFTER HAND ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY FOR LIVING DONOR KIDNEY TRANSPLANTATION

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Background and Aims: Recent analysis showed the preventive effect of antibiotics on superficial surgical site infection after hand assisted laparoscopic donor nephrectomy (HALDN) for living donor kidney transplantation. However, the factors which may affect the superficial surgical site infection at hand-port site have not been investigated.
Methods: Between January 2008 and December 2018, consecutive 951 living kidney donors (LKDs) undergone HALDN were included in this study. In 92 LKDs, superficial surgical site infection at hand-port site was identified. To investigate the factors which may affect superficial surgical site infection at hand-port site, donor characteristics, preoperative comorbidities, and operative factors were analyzed using binomial logistic regression analysis.

Results: In the univariate analysis, significant differences were identified in sex, smoking history, glucose intolerance, preoperative antibiotic prophylaxis, and subcutaneous drain placement at hand-port site ($p < 0.001$, $p = 0.002$, $p = 0.029$, $p < 0.001$, $p = 0.003$, respectively). In the multivariate analysis, significant differences were identified in sex ($B = 0.726$, $p = 0.012$, Odds ratio 2.066, 95% confidence interval (CI) 1.169 – 3.652), preoperative antibiotic prophylaxis ($B = -3.205$, $p < 0.001$, Odds ratio 0.041 95% CI 0.013 – 0.122), and subcutaneous drain placement at hand-port site ($B = 0.689$, $p < 0.022$, Odds ratio 1.991 95% CI 1.106 – 3.583).
Conclusion: Preoperative antibiotic prophylaxis may decrease the superficial surgical site infection at hand-port site. On the other hand, male LKD and subcutaneous drain placement at hand-port site may increase the superficial surgical site infection at hand-port site.

OP492 CONTROLLED DONATION AFTER CIRCULATORY DEATH: IS THERE A RISK FACTOR OF CULTURE-POSITIVE PRESERVATION FLUID ON SOLID ORGANS FOR TRANSPLANTATION?

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Background: Contamination of organ preservation fluids (PF) may be a mechanism of recipient infection.
We analyzed the influence of the donation process [donation after brain death (DBD) vs donation after circulatory death (DCD)], pre- vs post-mortem cannulation and type of organ, on the prevalence of culture-positive PF; as well as etiology and clinical impact on recipients.
Methods: From January 2018 to June 2019, all solid organ transplants (SOT) performed at our centre were retrospectively included.
Results: A total of 423 SOT episodes (304 DBD; 119 DCD) from 296 cadaveric donors (219 DBD; 77 DCD) were studied. The prevalence of culture-positive PF was 23.4% (99/423). In 42.4% (42/99) of the cases the isolates were considered as "high risk" for pathogenicity. No differences were found between DBD and DCD either in the prevalence of high-risk culture positive PF (both DBD and DCD 10 %), or low-risk microorganisms prevalence (DBD 13% / DCD 15%). However, the prevalence of culture-positive PF was higher in SOT when DCD was performed applying pre-mortem cannulation (33%) compared with post-mortem cannulation (23%) ($p < 0.05$). Moreover, lungs showed a higher prevalence of isolates in PF compared with other SOT ($p < 0.05$).
In both DBD and DCD, the most prevalent high- and low-risk microorganisms were gram-negative bacilli 69% (29/42) [DBD 73.3% (22/30); DCD 58.3% (7/12)] and coagulasenegative staphylococci 82.5% (47/57) [DBD 92.3% (36/39); DCD 61.1% (11/18), respectively.
Only 2 cases (both renal transplants from DCD) developed a PF related infection (one of them due to *Enterococcus faecium* resolved with targeted treatment; and the other caused by *Escherichia coli* requiring transplantectomy).
Conclusions: Donation after circulatory death can be considered a safe procedure, although pre-mortem cannulation seems to increase the risk of PF contamination. The particularly high prevalence of PF contamination in lungs suggests the need for additional measures during retrieval.
Despite the fact that a quarter of preservation fluids cultures in solid organ transplantation were positive, clinical impact is rarely observed, though in affected recipients the consequences are severe.

BUILDING RESILIENCE IN ORGAN DONATION

OP493 THE "CRITICAL PATHWAY" FOR TISSUE DONATION: NEW DEFINITIONS FOR A COMMON AND SYSTEMATIC EUROPEAN APPROACH TO DECEASED DONOR TISSUE DONATION

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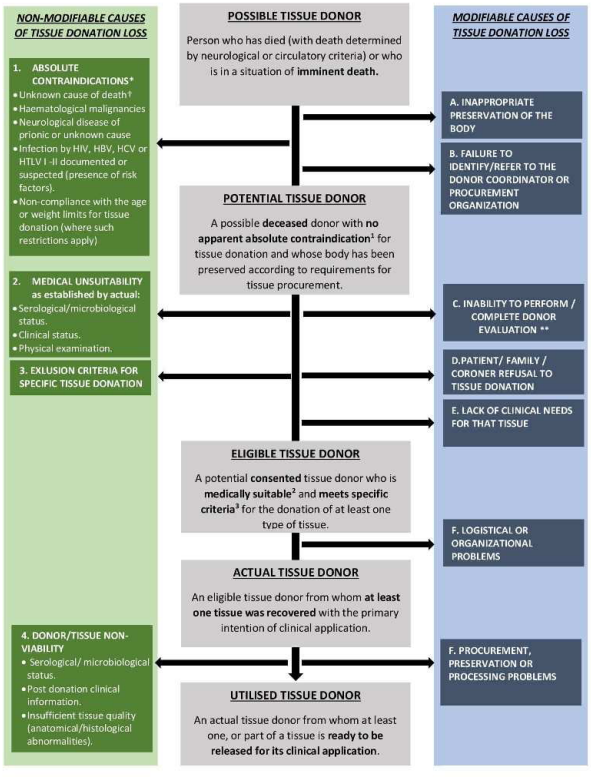
Background: Inspired by a previous initiative regarding organ donation (1), the European Committee for Organ Transplantation of the Council of Europe (CD-P-TO) has recently developed a "Critical Pathway" with the aim of providing a systematic approach to the deceased donor tissue donation process (2).
Methods: The CD-P-TO, made up of representatives of 34 member states and 19 countries and observer institutions, established an ad hoc working group composed of hospital experts and tissue procurement organizations as well as representatives from regulatory agencies, health authorities and European professional societies related to tissue donation. This multidisciplinary group discussed an initial proposal of a Critical Pathway of deceased tissue donation until reaching a broad consensus sensitive to all local and professional realities. The final proposal was finally approved and formally adopted by the CD-P-TO Steering group in October 2020.
Results: The "Critical Pathway" defines the deceased donor tissue donation process from the identification of a "possible tissue donor" until the tissue is released for clinical use ("utilized donor"). It also lists the possible causes of loss, classifying them as "non-modifiable" (related to medical unsuitability or non-viability) and "modifiable" (possible improvement targets). Figure 1
Conclusions: This is to our knowledge the first attempt to define deceased tissue donors according to the donation stage providing a common systematic approach that can be adapted to different scenarios. The "Critical Pathway" for tissue donation can be a useful tool to assess the potential and effectiveness of the tissue donation process, help identify areas for improvement and lay the foundations to build indicators that serve to compare organizations, regions and countries.
(1): Dominguez-Gil B, et al. Transpl Int 2011; 24 (4): 373-8)
(2) Sandiumenge A, et al. Transplant Int 2021 (in press): https://doi.org/10.1111/tri.13841

CRITICAL PATHWAY FOR DECEASED TISSUE DONATION



OP494 HOW DO SPANISH TRANSPLANT COORDINATORS APPROACH RELATIVES FOR CONSENT TO INTENSIVE CARE FOR ORGAN DONATION? RESULTS OF AN EMPIRICAL STUDY

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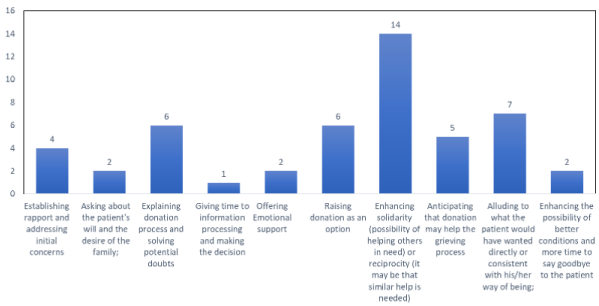
Background: Intensive Care to facilitate Organ Donation (ICOD) is an emergent procedure that can potentially increase deceased organ donation rates. Obtaining family consent for ICOD challenges standard transplant coordinators communication skills, since potential donor relatives have to decide about the maintenance or implementation of procedures directly linked with the possibility of donating before death has been declared. This study represents the first phase of a research program that explores family decision-making in the context of ICOD by means of retrieving Spanish Transplant Coordination Teams' (TCTs) perspectives about this process.
Methods: Semi-structured interviews were performed with a probabilistic sample of 21 TCTs of Spanish hospitals. Sample was stratified by Regions and TCTs were selected by means of random proportional allocation. Interviews were recorded after informed consent and included, among other contents, TCTs' description of their approach to families for consent to ICOD and their perception of those relatives' emotional reactions that are more difficult to manage. Interviews were transcribed and analysed by means of Content Analysis.
Results: Relatives' consent for ICOD is requested in a great variety of circumstances. The most difficult situations for the obtainment of consent for ICOD, labelled here as "Non-controlled" situations, include the confluence of the following circumstances: mechanic ventilation has already not been set up, patient is ubicated outside the Intensive Care Unit and relatives have not been previously contacted. Figure 1 shows which strategies and arguments are more frequently used to approach family consent for ICOD in "Non-controlled" situations.

Figure 1. Strategies and arguments mentioned by Spanish Transplant Coordination Teams (TCTs) as tools for their approach to family consent for ICOD in "Non-controlled" situations (Non-exclusive; N=21)



By other side, relatives' emotional reactions that were mentioned by TCTs as more difficult to be approached included (non-exclusive): Complaints about poor treatment received by healthcare staff (n = 4); Emotional shock or intense crying (n = 6); Anger or aggression (n = 6); Lack of response; and disbelief or denial of the situation (n = 4).
Conclusions: TCTs family approach in the case of CIOD is mainly based on strategies that enhance solidarity and reciprocity of potential donor and relatives, explore potential donor will and provide adequate information and support to relatives. Funding: ISCIII ("PI18/00403"), co-funded by ERDF/ESF, "Investing in your future"

OP495 ITALIAN SURVEY ON THE OPINIONS OF PROFESSIONALS FROM TRANSPLANT AND INTENSIVE CARE AREAS ABOUT COVID-19 AND SOLID ORGAN TRANSPLANTATION ACTIVITY

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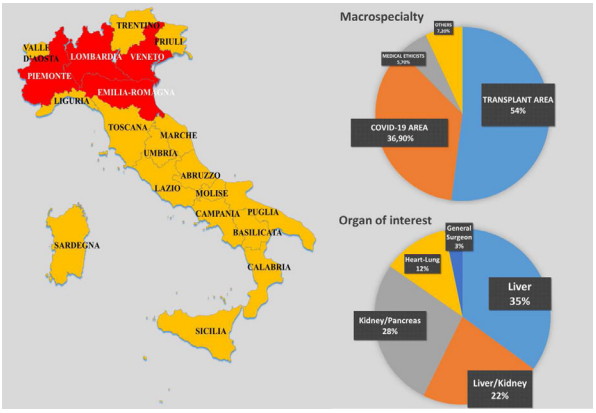
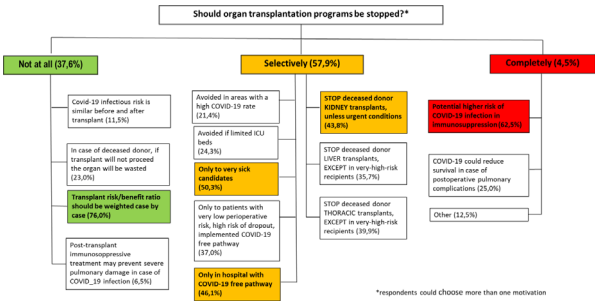
Background: COVID-19 pandemic largely affected Italian area during March and April 2020. The present survey-based study aimed to investigate the optimization of transplant activity during the first COVID-19 lockdown in Italy (March 26-April 18, 2020).
Methods: Respondents were stratified according to their geographical area (red / orange zone, Figure). According to subspecialty stratification, three arbitrary macro-specialty areas (Transplant Area, COVID-19 Intensive Care Area and Ethicists) were defined. A further stratification was made according to the organ of interest (kidney, kidney-pancreas, liver, liver-pancreas, cardiothoracic organs). The main question was related on stopping or not transplant activity. Furthermore, uni- multi-variate analysis about region (red or orange zone) and organ of interest (Liver, Kidney-Pancreas, Liver-Kidney, Thoracic organs) stratification were performed.
Results: We reported 600 participants with a high rate of answers from the red zone (47.3%). Transplant Area (50%) were the most represented, with a 35% of respondents in the liver transplant group. COVID-free ICU for transplant recipients and a specific COVID-19 consent were found to be needed according to 94% and 75% of responses, respectively. Most of the respondents (58%) suggested to selectively reduce the transplant activity, utilizing only COVID-free ICUs and the transplanting most critical recipients (Table). 44% of responders thought that kidney transplantation could be deferrable (44%) and only 4% agreed to completely stop transplant activity in Italy, without differences between red and orange zone. Notably, in multivariate analysis, the daily number of deaths was significantly correlated to the continuation of the transplant activity.
Conclusions: Our survey about transplant activity during pandemic concluded for its selectively continuation, applying COVID-19 free protocols and a hierarchical priority model (heath-lungs, liver, kidney-pancreas).

Figure



Table



OP496 APPLICATION OF THEORY OF PLANNED BEHAVIOR ON ORGAN DONATION BEHAVIOR: A SYSTEMATIC REVIEW

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Background: Organ donation saves lives and improves quality of life. There is a shortage of organ donors worldwide. Behavior theories, such as theory of planned behavior (TPB), help identifying the antecedents of organ donation behavior and designing effective interventions. The TPB suggests that intention is driven by constructs: attitude, subjective norm, perceived behavioral control and intention. TPB can help improving organ donation behavior.

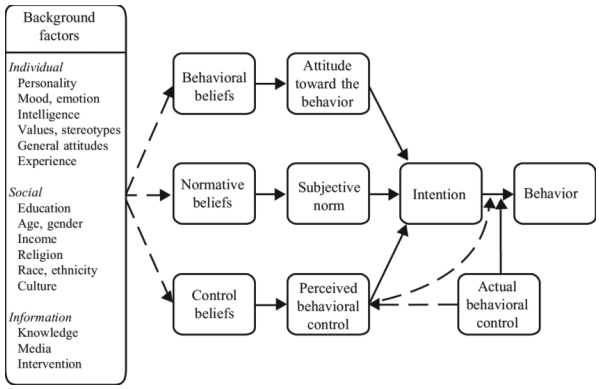

Figure 1 Theory of Planned Behavior

This study aimed to analyze TPB-based interventions on Organ donation.
Methods: this was a systematic review. We conducted a literature search using searching electronic databases, i.e. PubMed, Scopus, Science Direct, and Google Scholar during 1 January 2000 to 30 Feb 2020. We selected studies that using TPB framework for analysis.
Results: 17 studies were assessed as having reasonable methodology design. Structures of TPB were found to be important predictors of donation behavior. Fear, lack of knowledge were the most common barriers. Mistrust and social justice themes, misconceptions about the donation process were infrequently referenced as barriers to becoming a registered organ donor.
Conclusions: Based on the theory of planned behavior (TPB), subjective norms and attitudes toward donation on signing a donor card have a positive effect on organ donation, whereas religiosity and bodily integrity were believed to negatively influence signing a donor card. Plus the main constructs of TPB which affect behavioral intention, background factors of the behavior should be considered as the behavior's pre-factors, including: knowledge, religion, social norms, culture, race and gender. These factors should be considered in any related intervention. Removing barriers and facilitating the behavior, changing attitude, also subjective norms especially family can make interventions more effective.
The result support public education and community campaigns promoting the necessity of sharing donation intentions with others.

OP497 EUDONORGAN: A SUCCESSFUL TRAINING PROGRAM TO IMPROVE ORGAN DONATION KNOWLEDGE IN THE EUROPEAN UNION AND NEIGHBOURING COUNTRIES

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Background: EUDONORGAN was a 36-month service contract awarded by the European Commission on the initiative of the European Parliament. It focused on two main actions: training and social awareness for increasing organ donation (OD) in the European Union and neighbouring countries. Both activities were oriented to healthcare professionals (HCP) and other non-healthcare relevant players (N-HCP). The objective of this study was to improve OD knowledge in the selected group of participants by providing a tailored training program based on an approved curriculum.
Methods: A prospective interventional study was conducted between 2016 and 2019. The Kirkpatrick's four-stages model was partially used to design a tailored training program based on blended learning methodology. It was implemented at 2 different professional levels (HCP and N-HCP) considering 2 different pathways: medical and educational. Pre- and post-intervention evaluation results on knowledge were compared (%) in both groups. Statistical analysis based on T-Student was considered. p value ($p < 0.05$) was seen as statistically significant.
Results: 101 participants enrolled the programme. 95% participants completed the training. Among HCP (n = 79, F = 59.5%/M = 40.5%) the mean age was 40.1 $\pm$ 8.4 years. Among N-HCP (n = 17, F = 76.5%/M = 23.5%) the mean age was 40.8 $\pm$ 11.4 years old.
Pre- and post-tests results showed an improvement of knowledge.
In HCP 72 $\pm$ 13.4 vs 96.2 $\pm$ 5.7 respectively. In N-HCP 64 $\pm$ 4.4 vs 92.82 $\pm$ 1.7 respectively. Statistical differences were found in the variables studied ($p = 0.00$).
Conclusions: Organ donation remains a multicomplex process that affects both healthcare professionals and the entire society. Training is a key enabler in healthcare to increase knowledge and skills. This study proves that the methodology used classically in HCP also applies in N-HCP. We identified a significant increase in knowledge with the trend of higher improvement in N-HCPs vs HCPs. These results underline the need of permanent education at different levels in relation to OD. Seeing the different results of the analysis it might be of value to compare both groups on the different aspects of the study.

OP498 CONDITIONS THAT INFLUENCE FAMILY CONSENT FOR INTENSIVE CARE FOR ORGAN DONATION: THE PERSPECTIVE OF SPANISH TRANSPLANT COORDINATORS

Jorge S. López[1], José Manuel Martínez[2], Elisabeth Coll[3], Mark Beyebach[1], David Uruñuela[3], María Jesús Martín[2], Ricardo Lamelas[2], José Roldán[4], Rubén García-Sánchez[2], Begoña Aramayona[2], Alberto Fernández-Carmona[5], María Soria-Oliver[1]
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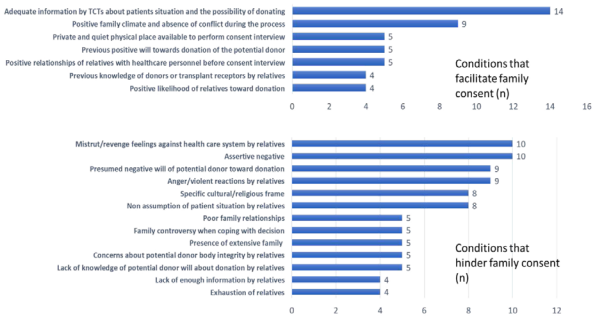
Background: Intensive Care to facilitate Organ Donation (ICOD) implies the initiation or continuation of life-sustaining measures with the purpose of allowing potential organ donation in patients with a devastating brain injury in whom curative treatment has considered futile. The obtention of family consent for ICOD is performed by means of the so called "early interview" and implies differential conditions in relation to standard brain death (BDD) and non-heart beating donation (NHBD), since potential donor relatives cope with the decision about the implementation or maintenance of medical procedures aiming potential organ donation before death has been declared. The present study represents the first phase of an extensive research program that aims to characterize family decision in the context of ICOD by means of retrieving the perspective of Spanish Transplant Coordination Teams (TCTs) about this process.
Methods: Semi-structured interviews were performed with a probabilistic sample of 21 TCTs of Spanish hospitals. Sample was stratified at a national level by Regions and TCTs were selected by means of random proportional allocation. Interviews were recorded after informed consent and included, among other contents, TCTs' perception about those conditions that were more relevant for family consent to ICOD procedure. Interviews were transcribed and analysed by means of Content Analysis.
Results: The obtention of family consent for ICOD takes place in a wide variety of scenarios that involve different degrees of difficulty. The most difficult situations, labelled here as "Non-controlled" situations, include the confluence of the following circumstances: mechanic ventilation has already not been set up, patient is ubicated outside the Intensive Care Unit and relatives have not been previously contacted. Most relevant conditions influencing family consent for ICOD in "Non-controlled" situations on the view of TCTs are exposed in Figure 1. Funding: ISCIII ("PI18/00403"), co-funded by ERDF/ESF, "Investing in your future"

Figure 1. Most relevant conditions that influence relatives' consent to ICOD in "Non-Controlled" situations according to Transplant Coordination Teams (TCTs) (Non-exclusive; N=21)



Conclusions: The obtention of family consent for ICOD procedures involves a great variety of scenarios with different degrees of complexity. However, some key elements conditioning standard BD and NHBD seem to be also relevant factors for the obtention of family consent to ICOD.

OP499 ENLIGHTENING YOUNG MINDS: A SMALL STEP IN THE CURRICULUM, A GIANT LEAP IN ORGAN DONATION - A SURVEY OF 996 RESPONDENTS ON ORGAN DONATION

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Background: Medical students' and junior doctors' awareness about Organ Donation and Transplantation (ODT), may play an important role in mitigating organ donor shortage. This study surveyed the knowledge, attitudes and perceptions of ODT among medical students and junior doctors in a medical college hospital in South India, to ascertain their educational needs.
Methods: A cross-sectional survey was conducted among 1000 medical students and 200 junior doctors. A 30-point questionnaire explored their knowledge, attitudes and perceptions towards ODT.
Results: 996 respondents (83.0%), of which 459 (46.1%) were pre-clinical years (MBBS year 1&2), 453 (45.5%) were clinical years (MBBS year 3&4) and 84 (8.4%) were junior doctors (interns/post-graduates' year 1-3). Only 11.9% had previous exposure to transplant medicine/surgery and only 5% were registered as organ donors. Both of this reflected on their poor knowledge on the transplantable organs and sources of living donor organs. Less than half (49.2%) were aware that next of kin/family consent is required for deceased donation. Only a third (32.8%) accepted brain-stem death (BSD) as being truly death, and the rest either did not accept BSD as true death or were unsure of this. Majority (65.2%) felt happy with their knowledge on ODT, but nearly all respondents (84.0%) felt that ODT should be implemented in their curriculum.
Conclusions: Medical students and junior doctors in India have limited knowledge about ODT, but their perceptions and attitudes towards ODT were favourable. Increasing knowledge and awareness among medical students and junior doctors may help to improve organ donor shortage in India.

OP500 SEIZING THE POTENTIAL RISK OF TRANSMISSION OF OLIGODENDROGLIOMA TO RECIPIENTS

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Background and Aim: Up to 1.5% of organ donors have a past or recent clinical history of primary brain tumors and represent a subgroup with potentially favourable clinical features. Oligodendroglioma accounts for 5% of all primary brain tumors and mainly occurs in the adulthood. According to WHO, it is classified into grade II and III (anaplastic). Donors with a history of this neoplasia, in the absence of other risk factors, are considered to be at low risk of transmission. The aim of this study was to establish which features may predict a higher risk of transmission in this subset of donors.
Methods: We searched PubMed and EMBASE databases for studies reporting oligodendrogliomas with extracranial spreading, and extracted data on the time elapsed between the diagnosis and the onset of metastases, sites of metastases, prior surgery, radiotherapy, chemotherapy and ventriculo-atrial shunt placement.
Results: A total of 88 patients (51 males, 31 females and 6 with undisclosed sex) with metastatic oligodendroglioma were found. Age at metastatic spread ranged between 1.5 to 74 years (mean 44.3; median 46). Fourty-seven percent of patients had anaplastic oligodendrogliomas. Time from the initial diagnosis to metastatic spread ranged between 2 and 325 months (mean: 56; median: 36). In 60 cases patients received radiation therapy before metastases occurred; of these, 29 received both radiotherapy and chemotherapy. Twelve patients did not receive any adjuvant therapy after surgery.
Metastases were mainly localized at the bone (n = 45), followed by bone marrow (n = 29) and lymphnodes (n = 24). The most common visceral metastatic sites were the lung (n = 10), liver (n = 7) and pleural cavity (n = 5). No patients had metastases in the heart or kidneys.
Conclusions: Although rarely, oligodendroglioma may metastasize, independently from the histological grade of the primary tumor. The skeleton and lymphnodes are most commonly involved, while kidneys and heart are always spared. Understanding the preferential patterns and timing of metastatization of oligodendroglioma may help to define the risk profile of donors with a past or recent history of this tumor.

OP501 OUT-OF-HOSPITAL DONORS WITH IRREVERSIBLE CARDIAC ARREST IN RUSSIA: ONE OF THE PROMISING RECOURSE ACCORDING THE FIRST ST PETERSBURG EXPERIENCE

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Background: A worldwide trend in organ transplantation is the development of new strategies to solve the problem of organ donor shortage. The use of organs obtained from those who died "outside the hospital" from sudden circulatory arrest is one of the most promising directions in megacities. In St. Petersburg the model "transfer from ECMO life support of potential donors after cardiac arrest at home - to ECMO life support of deceased donors' organs" has been tested.
Methods: In St. Petersburg, in order to implement the program, a 24-hour ECMO and transplantation team was organized at the inpatient emergency department of the First St. Petersburg Pavlov Medical University, interaction with the city emergency station was established, the first Russian protocol for working with donors delivered from home after irreversible circulatory arrest was developed, approved by the ethical committee, and implemented in clinical practice. Between 2017 and 2020, 62 patients with sudden out-of-hospital circulatory arrest were delivered to the inpatient emergency department. In 6.45%(4) cases, life-saving extended cardiopulmonary resuscitation measures were successful, and 17.74%(11) patients became effective donors.
Results: Liver transplantation was performed in 5 recipients who were severely ill against the background of liver failure. Severe dysfunction of the graft within 33 days with subsequent complete recovery took place in 20% (1) of cases. Kidney transplantation from ASD was performed in 22 patients. Immediate graft function occurred in 45.45%(10) patients. The follow-up period of patients who underwent organ transplantation from ASD was from 12 to 30 months. The survival rate of renal transplant was 86.4%, renal transplant recipients - 95.5%, hepatic transplant recipients - 80%.
Conclusion: The model of work with patients with sudden out-of-hospital circulatory stoppage with the purpose of lifesaving a patient and realization of the transplantation program can be realized on the basis of an in-patient emergency department of a multidisciplinary hospital. The results of liver and kidney transplantation from ASD in the long-term correspond to those of organs from brain-dead donors. Thus, widespread implementation of the new model of asystolic donation will increase the availability of transplantation care.

OP502 WHAT HAPPENS TO UNSPECIFIED KIDNEY DONOR CANDIDATES WHO CANNOT PROCEED TO DONATE: AN INDUCTIVE THEMATIC ANALYSIS FROM THE BOUND STUDY

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Background: Unspecified Kidney Donation (UKD) has expanded dramatically in the UK recently. However, there are little data comparing the experience of those who donate with those who withdraw from the process. We therefore performed a qualitative study of these groups, to determine the psychological and emotional consequences of donating or withdrawing.
Methods: We conducted a qualitative study, interviewing 15 individuals who donated, 11 who had been withdrawn by the transplant team, and 9 who

self-withdrew. Semi-structured interviews were subjected to inductive thematic analysis, which entailed coding 1,050 minutes of interview transcripts, gathering, and reviewing themes, and then refining and labelling them.
Results: The major themes were maximising and sharing benefits; risk-to-motivation analysis; support; self-actualisation; the donor as patient; and relationship with the transplant team. The main finding was that those who had donated found fulfilment in the process, however, many individuals in the withdrawn groups expressed distress and lack of closure linked to inadequate follow-up from transplant teams. Those who were medically withdrawn or self-withdrew generally did not do so because of psychological reasons. For the self-withdrawn group, opposition from loved ones was reported as playing a significant role.
Conclusions: This study provided an in-depth analysis of the UK UKD programme and is currently the largest study of its kind. It is the first study to explore the experiences of withdrawn donors. The key findings were that many individuals in the withdrawn groups experienced significant distress, lack of closure, and family pressure was critical in influencing decisions to withdraw. Our findings illustrate the vital need for a targeted and standardised approach to managing donor expectations from the outset in order to prepare all those who embark on the process for the range of potential outcomes, along with the emotional impacts that may result.

OP503 DECEASED DONOR TRANSPLANTATION DURING COVID TIMES - SUCCESS STORY FROM STATE IN INDIA

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Background: In India, live donor transplantation common than deceased donor transplantations. The enactment of The Transplantation of Human Organ and tissue Act in India in the year 1994 legalized organ donation after brainstem death. The Government of Kerala and KNOS (Kerala network for organ Sharing), in association with Donation and Transplantation Institute (DTI Foundation) of Spain implemented transplant procurement management model (TPM model) in the state in the year 2019.
Methods: Government medical colleges and private transplant centers appointed an in-hospital transplant procurement manager (TPM) to coordinate potential donors at intensive care units. The TPM became actively involved in the deceased organ donation (DDP) process. The cornerstone of the success was early and proactive identification of potential donors.
An educational and international cooperation approach based on the implementation of a specialized program for healthcare professionals according to the DTI Foundation training model started in 2019. It includes on-site training, international internship, hospital visits and DTI´s I experts visiting Kerala hospitals to exchange best practices.
Results: Following the initiation of TPM in various hospitals across Kerala, when compared 2020 Vs 2019, a 60% increase was observed from 30 to 50 organs transplanted in the same period of time even against Covid pandemic effects worldwide.
Conclusion: The collaboration between local and international organization, the hospital-based organ procurement units headed by Transplant procurement managers (TPM) and the role of government-run networking organizations in improving the deceased donor transplantation played a key role for good outcomes of donation and transplant programs. When the COVID 19 pandemic resulted in the suspension of the transplant programs across the country, the deceased donation and transplantation activity in Kerala were going unabated.

OP504 NEW TECHNOLOGIES APPLIED TO MASTER EDUCATION IN THE TIME OF COVID-19

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Background: University of Barcelona together with Donation and Transplantation Institute offer since 2004 a Master degree in Donation and Transplantation. Since 2011, the program had a blended modular structure including: Donation, Transplantation, Management, Tissue Banking and Internship (IS). In 2020, due to COVID-19 restrictions, the program was adapted to be fully online using innovative resources. The aim is to analyse the impact of the pandemics on the grades and the student's satisfaction.
Methods: The syllabus has remained stable in 2020-21 program, although the educational modality has been renewed. Until 2019, face to face training included theoretical sessions, simulations, clinical cases debate and group exercises. IS were face to face in associated centres. Since 2020, theoretical sessions have been included in the virtual classroom and practical simulations have been replaced by live sessions (broadcast sets, case debates and group exercises). New online tools, as immersive training (IT), have been employed to substitute IS and family approach (FA) workshop. For IS, a virtual reality tour to a simulated tertiary Spanish hospital that allows interaction with the staff has been created. In FA experience, students can virtually meet with patient's family and practice their communication skills. In February 2021 only donation module has been completed, therefore data are organized in 2 periods, 2011-2019 and 2020, and the grades obtained in the Organ Donation module and the students´ satisfaction are evaluated.
Results: In 2011-2019, the average grade in Donation was 8.07/10 and in 2020 the score was 8.08/10. In 2011-2019 the Donation module has been evaluated with an average of 9.58/10 considering theoretical, practical sessions and course organization. In 2020 the evaluation was 9.36/10 taking into consideration the theoretical part, live sessions and course organization. Comparative results indicate slight difference in the values, demonstrating stability despite the difficulties caused by the pandemic.
Conclusions: In the face of changes and restrictions caused by the current pandemic the inclusion of new technologies has been essential to keep offering high quality international educational programs. Further exploring of technologies may also improve efficiency.

OP505 IMPACT OF THE SARS-COV-2 PANDEMIC ON TISSUE DONATION IN CATALONIA

Belen Garcés Jimeno[1], Maria Jaume Lliteres[2], Andrés Savío López[1], Andrea Pitarch Serrano[2], Pedro Brillas Fructuoso[2], Magda Quijada Martorell[2], Miriam Castro Villa[2], Maria Teresa Ruiz Gacia[2], Maria Luisa Saez Vizcaino[2], Miguel Montiu Perez[2], Ana Maria Bofill Rodenas[2], Oscar Fariñas Barbera[1], Anna Vilarrodona Serrat[1]
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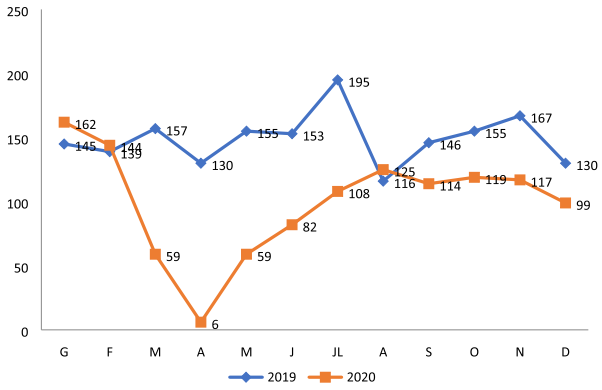
Background: Tissue procurement in Catalonia is centralized in the Donor Center, comprised of a multidisciplinary team. This working group is responsible for the detection, evaluation, acceptance, extraction of tissues, monitoring, and validation of tissue donors. We work together with the transplant coordinators, usually located in the ICUs.
The SARS-CoV-2 pandemic at the end of January 2021 affected 100M people worldwide, being the cause of 2.16M deaths. Many donation programs were affected, significantly reducing their activity. The main causes were: unawareness of the disease, reorganization of infrastructures in the face of the pandemic, relocation of health personnel to provide Covid-19 clinical care, difficulty in mobilization, among others. All of this led to an economic and health crisis that seriously impacted tissue donation activity.
Our objective for this study is to describe and compare tissue donation activity in Catalonia in 2019 and 2020, to evaluate the impact of the SARS CoV-2 pandemic.
Methods: A retrospective observational study of tissue donations in Catalonia during 2019 and 2020. Data are described for each month and type of tissue (corneas, skin, musculoskeletal, valves, and arteries). Activity for each year is analyzed and compared together and separately (for each tissue), with the appropriate statistical method.



Results: In 2019, 1,788 tissue donations were obtained, compared to 1,194 in 2020. This decrease was more pronounced during the months of March, April, May, and June coinciding with the first wave of the pandemic. The worst month was April, with 6 corneas, 1 skin, 2 musculoskeletal, and 1 valve donations procured, and no artery donors. All the differences observed between both years were statistically significant.
Conclusions: The changes to adapt infrastructures and healthcare personnel during the SARS CoV-2 pandemic have had an impact on tissue donation activity in Catalonia with a significant drop in the number of donations, risking the supply of tissues for implantation. The adaptation of logistics, the reintroduction of health personnel to the donation activity, and their training in terms of COVID and donation, have been key to foster the recovery of the tissue donation activity in Catalonia.

OP506 EFFECTS OF THE SARS-COV2 PANDEMIC ON ORGAN OFFERS IN EUROPE

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Italian National Institute of Health, Rome, Italy

Background: On 24 February 2020, WHO notifies the first cases of SARS-CoV2 positive patients in Europe. Since then, the epidemic has directly and indirectly affected many fields of health care, including organ donations and transplants, both in terms of number of reports and of management of donors and organ allocation.
The aim of this work is to analyze the impact of the pandemic on organ exchange between countries.
Methods: We analyzed all the organ offers registered on the IT Foedus portal used by Italy and by other European nations that collaborate for the exchange of organs. It was considered a pre-pandemic period (24/01/2019-23/01/2020) and the pandemic period (24/01/2020-23/01/2021). The number and type of offers made were recorded and related to the preliminary 2020 donation activity data, provided informally by the competent authorities of the main European countries. A comparison was then made between the pandemic and the pre-pandemic period.
For the pandemic period we have also correlated the weekly trend of offers with the pandemic trend in Europe, available on the WHO website.
Results: The pandemic has led to a reduction in donation activity, albeit to varying degrees, in all European nations with an overall average decline of 10.9%. Among the countries that use Foedus, the drop was 11.6%. In the pre-pandemic period 247 organs (heart 69, lungs 65, liver 73, kidneys 33, pancreas 4, intestine 3) were offered from 171 donors compared to the pandemic period in which 282 organs were offered (heart 64, lungs 60, liver 51, kidneys 78, intestine 10, pancreas 19) from 187 donors (+ 9.4% for donors and + 14.2% for organs). No correlations were found between the number of offers and the different phases of the pandemic trend in Europe.
Conclusions: Despite the reduction in donation activity, in the pandemic period there was an increase in the number of organs offered on the European circuit.
This increase was most likely due to logistical and organizational problems related to the health situation of the various nations, and has shown that, despite internal difficulties, all countries have continued to pursue the goal of sharing and not wasting any of the available resources.

OP700 MULTI-OMICS DATA INTEGRATION IN KIDNEY TRANSPLANTATION: THE HIDDEN PATHWAYS OF ANTIBODY-MEDIATED REJECTION

Claire Tinel[1,2], Elisabet Van Loon[1], Jasper Callemeyn[1], Wilfried Gwinner[3], Pierre Marquet[4], Dany Anglicheau[2,5], Maarten Naesens[1]

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Background: Within the European consortium BIOMARGIN (ClinicalTrials.gov, NCT02832661), different omics technologies were used to investigate for noninvasive biomarkers of kidney allograft injury. Each dataset led to the discovery and validation of sets of mRNAs, microRNAs or proteins, with high diagnostic value regarding antibody-mediated rejection (ABMR). Multi-Omics Factor Analysis (MOFA) is a recent innovative and unsupervised computational method for decomposing the sources of heterogeneity in multi-omics datasets.
Methods: In the BIOMARGIN discovery cohort, concomitant blood and urine samples were prospectively collected at the time of 131 kidney allograft biopsies in four European centers. Whole transcriptomic analysis (Affymetrix Microarrays) was performed on blood (N = 120) and biopsy (N = 89) samples, whole miRnome analysis (Taqman Array Cards) on blood (N = 126) and biopsy (N = 88) samples, RNA sequencing (Illumina) on N = 74 blood samples, and expression of gene-candidates (RT-qPCR) was assessed in N = 130 urine samples.
Results: Using MOFA, we integrated BIOMARGIN multi-omics datasets to unravel the causes of heterogeneity in various body fluids and tissue samples. After dimensionality reduction, top features of all six normalized datasets were integrated without any a priori labelling of the samples (Figure 1). Our results identified eight MOFA factors (each explaining > 2% of variance), highly discriminating among the clinical phenotypes including ABMR (N = 32) and no ABMR cases (N = 99). Among these eight factors, the first discriminating one encompassed mostly genes from patients' blood including MYL9 and BCL2A1, two genes previously reported as differentially expressed after kidney transplant and in operative tolerance respectively.
Conclusions: Overall, our multi-omics data integration provides an opportunity to better decipher the kidney rejections pathways, enabling to classify kidney transplant phenotypes into molecularly defined entities that better reflect underlying disease mechanisms than the current clinical classification. It also paves the way to downstream analyses including gene-set enrichment and shared pathways analyses, as well as evaluation of MOFA factors in comparison with conventional diagnostic biomarkers.

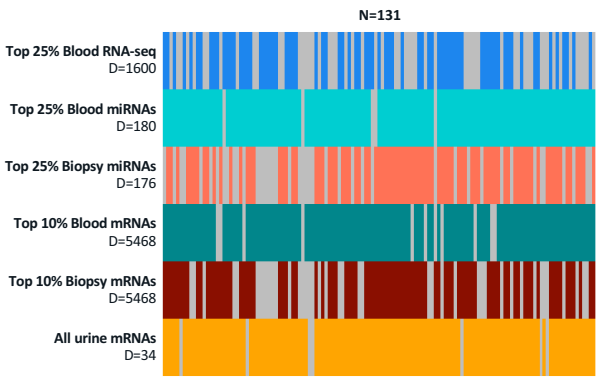

Figure 1 Overview of MOFA integrated datasets. D, number of features per dataset; N, number of samples; grey bars: missing samples

OP701 DEEP PHENOTYPING OF HUMAN KIDNEY TRANSPLANT REJECTION USING SINGLE-CELL TRANSCRIPTOMICS

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Background: How the immune system participates to kidney transplant rejection has not been fully elucidated. Single-cell (sc) genomics techniques are revolutionizing our ability to characterize complex disease processes such as kidney, coupled with the ability to examine transcriptional profiles at single-cell resolution.
Methods: Here, we used sc-RNA sequencing (10x Genomics platform) to define the global immune landscape of human transplanted kidneys. We studied sc-suspensions (N = 35,948 cells) from 16 different kidney transplant biopsies, with a representative mix of clinicopathological phenotypes (3 antibody-mediated rejection (ABMR), 1 mixed rejection, 8 borderline changes, and 4 stable cases).
Results: Unsupervised clustering analysis was performed on the 16 cases, and we identified 25 distinct cell types, including all major immune cell types and most kidney cell types (Fig. 1). Nephron epithelial cells were evident, as well as podocytes, peritubular cells (PTS1-2-3), vascular smooth muscle and pericytes (vSMp) and Loop of Henle (LOH) cells. Immune cell populations included monocytes and macrophages, B cells, CD4 and CD8 T cells, and Natural Killer (NK) cells. Next, we performed subcluster analysis of the myeloid populations and distinguished CD68+ and CD163+ macrophages from CLEC9A+ dendritic cells but also CD14+ and CD16+ monocytes. Pseudotime inference revealed 2 trajectories in myeloid cells: CD14+ monocytes connected to either CD16+ monocytes or to CD68+ and CD163+ macrophages. Myeloid-specific genes analysis according to the clinical groups revealed enrichment in pathways of immune activation and vascular interactions in CD16+ monocytes during ABMR. We also observe different clusters of endothelial cells (EC). Within the endothelial cell cluster, glomerular EC (ECg), afferent/efferent arterioles cells (ECaea), activated EC (ECa) and peritubular capillaries (ECptc) were identified. Gene ontology analysis revealed enrichment in antigen processing and presentation during mixed rejection whereas apoptosis and signalling by TGF-β were enriched in ABMR.
Conclusions: Our study provides new insights of the role of the different myeloid populations and their interactions with the endothelium at single-cell resolution and unravels CD16+ monocytes as key-players during ABMR.

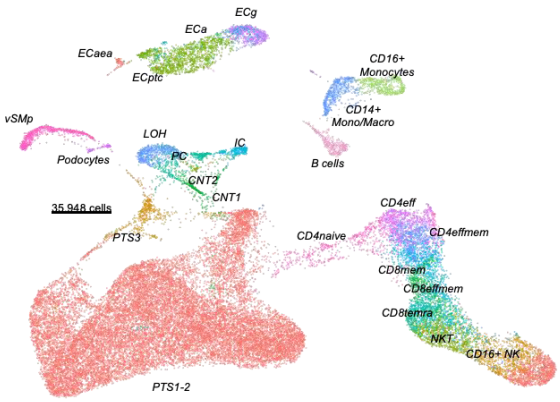

Figure 1

OP702 REAL-WORLD USE AND CLINICAL IMPACT OF EXTRACORPOREAL PHOTOPHERESIS IN HEART TRANSPLANT PATIENTS – RESULTS FROM A EUROPEAN MULTICENTER STUDY

Eric Epailly[1], Cristiano Amarelli[2], Massimo Maccherini[3], Balazs Sax[4], Simon Schopka[5], Andreas Zuckermann[6], Julia Altevers[7], Kathrin Borchert[7], Susanne Behlke[8], Andy Ingram[8], Markus J. Barten[9]
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Background and Aims: Extracorporeal photopheresis (ECP) is recommended as an adjunctive therapy in prevention and treatment of acute cellular rejection (ACR) after heart transplantation (HTx). However, it is also used to treat antibody-mediated rejection (AMR) with and without (+/-) donor-specific antibodies (DSA). The aim of this study was to describe the real-world use of ECP across European heart transplant centres and assess its impact on clinical outcomes.
Methods: This retrospective, explorative, single-arm study included patients who started ECP after HTx in 2015 or later. For this interim analysis, data were extracted from 71 patients' medical charts across four centres from HTx to up to two years after last ECP treatment.
Results: Mean age of patients was 51 years. The main indications to start ECP were ACR (44%), AMR (21%) (+/- DSA), and prevention of rejection (PR) (24%). Median time from HTx to start of ECP was 233 days. At time of analysis, 51 patients had completed ECP and for 20 patients treatment was ongoing. On average, 26 ECP treatments were performed over a mean duration of 9 months. In 51% of patients who completed ECP, severity of rejection was reduced ($\geq$ 1 histological ISHLT grade reduction) and/or graft function improved (measured by echocardiography/MRI). In the PR group, 11 of the 16 patients remained free from any rejection after starting ECP. For 59% of patients who completed ECP, the main reason for stopping was response to treatment. Overall survival was 93%. Five patients died, three with a functioning graft. No deaths were related to ECP. Eight patients (11%) had an ECP-related complication, 6 venous access, and 2 hypotension.
Conclusions: The results of a this pan European ECP study so far, indicate that ECP is a safe and effective treatment for not only ACR but also an option for AMR (+/- DSA) and in rejection prevention.

OP703 EPLETS INCOMPATIBILITY AS A DETERMINANT IN EXPOSURE TO TACROLIMUS

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Background and Aims: Advances in tissue typing include the determination of HLA incompatibility at the epitope and EPLET level. HLA Matchmaker is a computer algorithm that determines HLA incompatibility between donors and recipients by assessing the 3-dimensional molecular modeling of the epitope-paratope interfaces of antigen-antibody complexes.
EPLETs incompatibility can negatively impact graft survival. Knowledge of this level of incompatibility could help us to optimize the level of immunosuppression (IS).
Methods: Retrospective study of 554 recipients of a first kidney transplant (KT) between 2009 and 2019. The IS was based on tacrolimus (TAC), mycophenolate and prednisone. AntiHLA antibodies were determined by Luminex.
They were divided into 2 groups according to TAC trough levels one year after transplantation (mean of three levels): TAC 6-7.9 ng/ml and TAC $\geq$ 8 ng/ml. The HLA Matchmaker software was used to determine the number of incompatibilities in EPLETs DR and DQ. Patients were grouped according to the number of EPLETs mismatch into 2 groups: 1) DR $\leq$ 10 and DQ $\leq$ 17 and 2) DR $>$ 10 and/or DQ $>$ 17.
Graft survival and acute rejection episodes (AR) were evaluated. Subsequently, the relationship between the level of exposure to TAC in the groups was analyzed in terms of graft survival and AR episodes.
Using SPSS version 15.0. Standard Kaplan-Meier methods were applied to determine graft survival rates. Statistical significance was determined by log-rank comparisons of survival rates using p values.
Final Results and Conclusions: We observed better graft survival and less episodes of AR in the group DR $\leq$ 10 and DQ $\leq$ 17 vs DR $>$ 10 and/or DQ $>$ 17 EPLETs mismatch. When grouping patients in DR $\leq$ 10 and DQ $\leq$ 17 vs DR $>$ 10 and/or DQ $>$ 17 and relating them to TAC levels at one year, we observed that the group with the highest EPLETs mismatch and low TAC exposure compared with low incompatibility and low TAC exposure had a higher incidence of AR (33.3% vs 18.0% $p < 0.002$). But if TAC levels remained higher in this risk group, this difference was not observed (Table 1). In contrast, the group with low EPLETs incompatibility (DR $\leq$ 10 and DQ $\leq$ 17) can be managed with less exposure to TAC without representing an increase in AR episodes. We conclude that exposure to tacrolimus has to be planned according the level of eplets' mismatch between donor and recipient.

OP704 CREATING A MODEL FOR KIDNEY-VASCULATURE INTERACTION USING AN ORGAN-ON-CHIP DEVICE

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Background: Induced pluripotent stem cell (iPSC)-derived kidney organoids have proven to be a valuable model to study kidney development and disease; however, the lack of vascularization often leads to a necrotic core and prevents organoids from reaching sequential stages of maturation. Although organoid vascularization can be achieved by implantation into animal models, this technique fails to provide a human-tissue-derived perfusable vasculature. The aim of our research was to culture kidney organoids in an organ-on-chip device with endothelialized microchannels to mimic vasculature and thereby obtain a research model that progresses the differentiation status of kidney organoids.
Methods: The surface of the chip was subjected to plasma ashing, and channels were coated with fibronectin. The chip's microfluidic channels were then seeded with human umbilical vein endothelial cells (HUVECs), and organoids were placed in the upper chamber (Fig. 1).
Results: HUVECs adhered to all surfaces of the microfluidic channels creating an artificial three-dimensional vessel. Culture of iPSC-derived kidney organoids in the chip under continuous fluid flow demonstrated the appearance of glomerular ($WT1^+$) and tubular ($Villin^+$, $E\text{-}Cadherin^+$) structures at day 17. The co-localization analysis of MCAM (CD146) and PECAM (CD31) demonstrated these organoids also display proper endothelial maturation reminiscent of native tissue. Moreover, GFP^+ HUVECs derived from the chip's channels migrated through the pores and proliferated inside the organoid tissue forming tubular structures presenting an open lumen.
Conclusions: To our knowledge, we present the first kidney organoids successfully cultured in a microfluidic organ-on-chip device. We expect that this research will lead to an improvement of kidney organoid maturation by mimicking the interaction of endothelial vessels with kidney tissue and open a new door to translational applications such as pre-clinical drug trials.

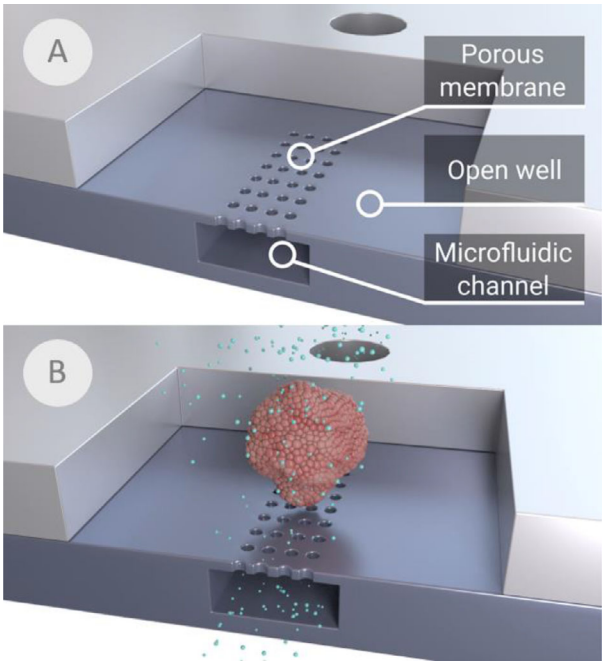

Figure 1 Bi/Ond Organ-on-chip device. (A) Representation of the Bi/Ond organ-on-chip device showing the microfluidic channel in which HUVECs are seeded, the porous membrane and the open well for organoid culturing. (B) Impression of an organoid in the system and medium flow through the channel, reaching the organoid tissue through the pores

OP705 A SINGLE-CELL REFERENCE ATLAS OF THE HUMAN KIDNEY TRANSPLANT UNRAVELS CELLULAR HETEROGENEITY IN BULK ALLOGRAFT TISSUE

Jasper Callemeyn[1], Baptiste Lamarthée[1], Dany Anglicheau[2], Wilfried Gwinner[3], Pierre Marquet[4], Maarten Naesens[1]

[1]KU Leuven, Department of Microbiology, Immunology and Transplantation, Nephrology and Kidney Transplantation Research Group, Leuven, Belgium; [2]Department of Nephrology and Kidney Transplantation, Necker Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [3]Department of Nephrology, Medizinische Hochschule Hannover, Hannover, Germany; [4]U1248 INSERM, CHU Limoges, Université de Limoges, Limoges, France

Background: Single-cell RNA-sequencing studies are powerful tools to chart the cellular landscapes of kidney transplant rejection, but currently lack the sample size of bulk transcriptomics experiments, which may inflate conclusions caused by interindividual variation. Here, we aimed to develop single-cell expression signatures of cell types within the human kidney transplant to untangle the cellular composition in bulk transcriptomics.
Methods: We performed droplet-based single-cell RNA sequencing (10X Genomics) on 16 kidney transplant biopsies, yielding 35,948 single cell transcriptomes. Based on cell type-specific gene expression profiles, a signature matrix for cell types within the kidney transplant was constructed using CIBERSORTx, and applied for deconvolution of cellular composition in an independent microarray cohort of 224 kidney transplant biopsies. High-resolution gene expression imputation was performed to derive cell type-specific gene expression profiles at the sample level.
Results: Single-cell RNA sequencing identified 25 distinct clusters, corresponding to epithelial, endothelial, stromal and immune cells on the basis of canonical expression markers. In the deconvolution analysis, the proportion of immune cells relative to structural cells correlated with severity of acute histological lesions as assessed by the pathologist, and predicted death-censored graft failure after the biopsy (HR 1.71 per 10-percent increase, 95% CI 1.19-2.47). Specifically, microvascular lesions associated mainly with infiltration of NK cells and mononuclear phagocytes (Figure), whereas tubulointerstitial inflammation was hallmarked by CD8+ T cells and mononuclear phagocytes. In addition to higher abundance, NK cells in ABMR biopsies had increased expression of cellular activation pathways compared to NK cells in biopsies without ABMR, identifying potential disease-specific treatment targets.
Conclusions
Single-cell-derived signatures of the kidney transplant can be applied in bulk transcriptomics to uncover cellular composition, absolute immune cell burden and cellular states across different phenotypes.

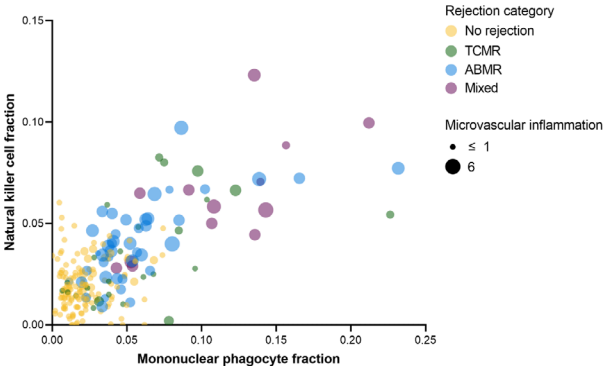

Figure Deconvoluted proportion of NK cells and mononuclear phagocytes relative to structural cells in 224 kidney allograft biopsies. Each dot represents one biopsy.

OP706 PROSPECTIVE EVALUATION OF DONOR-DERIVED CELL-FREE DNA (DD-CFDNA) IN KIDNEY TRANSPLANT RECIPIENTS WITH INDICATION BIOPSY

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[1]Department of Nephrology, Heidelberg University Hospital, Heidelberg, Germany; [2]Transplantation Immunology, Institute of Immunology, Heidelberg, Germany

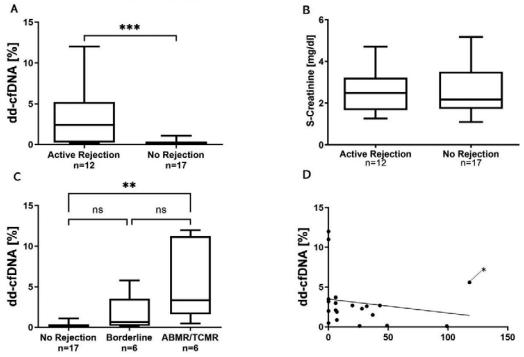
Background: Donor-derived cell-free DNA (dd-cfDNA) has been proposed as a noninvasive biomarker in monitoring allograft injury and rejection in kidney transplantation. Recently, the possibility of evaluating response to therapy by quantifying dd-cfDNA in patients receiving anti-rejection treatment has been discussed.
Methods: In an ongoing prospective single-center study, we evaluate the diagnostic benefit of dd-cfDNA in detection of graft rejection in 100 renal transplant recipients undergoing indication biopsy. dd-cfDNA is quantified in the AlloSeq cfDNA assay (CareDx) at time of biopsy before initiation of therapy and on days 7, 30, and 90 following biopsy. The association of dd-cfDNA levels in peripheral blood with histopathological findings and the course of dd-cfDNA levels after initiation of treatment are assessed.
Results: Since December 2020, 29 patients have been enrolled and 12/29 biopsies (41%) were histopathologically graded as different types of rejection (Table 1). At time of biopsy, patients with active rejection showed significantly higher levels of dd-cfDNA than patients without rejection ($p = 0.0003$; Figure 1A), whereas the serum creatinine was not significantly different in median values between the two groups ($p = 0.91$; Figure 1B). Median dd-cfDNA levels were highest in patients with antibody-mediated rejection (ABMR) or T-cell-mediated rejection (TCMR) (median 3.4%), slightly elevated in patients with borderline changes (median 0.65%) and lowest in patients classified as other than rejection (median 0.18%; Figure 1C).
In patients with graft rejection including Borderline changes, levels of dd-cfDNA were slightly higher at time of rejection (median 2.4%) than in the first week after initiation of treatment (median 1.25%, $p = 0.20$) and tended to decrease further three months after immunomodulation (median 0.61%, $p = 0.22$). When only patients with ABMR and TCMR excluding Borderline changes were considered, we observe decreasing levels of dd-cfDNA following initiation of therapy (pooled slope −0.02; Figure 1D).
Conclusions: dd-cfDNA significantly discriminates active rejection from no rejection at time of indication biopsy. In patients with ABMR or TCMR, decreasing levels of dd-cfDNA may further indicate treatment response.

Table 1. Patient characteristics at time of indication biopsy and before therapy

Clinical Characteristic	Active Rejection	No Active Rejection	P Value
Number of patients	12	17	
Men	9 (75)	14 (82)	0.67
Age at enrollment, years	43.8 ± 16	55.4 ± 14.2	0.05 (*)
Post-transplant, days	1708 ± 2604	892 ± 1399	0.55
Donor type			0.02 (*)
deceased donor	4 (33)	14 (82)	
living donor	8 (67)	3 (18)	
CMV serologic status			0.59
D-/R-	3 (25)	2 (12)	
D-/R+	2 (17)	6 (35)	
D+/R+	4 (33)	6 (35)	
D+/R-	1 (8)	3 (18)	
unknown	2 (17)	0 (0)	
HLA class 1 AB mismatches	2 [1-3]	2 [1-3]	0.97
HLA class 2 DR mismatches	1 [0-1]	0 [0-1]	0.59
S-Creatinine [mg/dl]	2.49 [1.67-3.22]	2.17 [1.73-3.51]	0.91
U-Protein/Creatinine [g/mol]	116.6 [49.12-226]	30.79 [15.46-126.7]	0.02 (*)
dd-cfDNA [%]	2.4 [0.27-5.23]	0.18 [0.13-0.33]	***0.0003***

Data are presented as n (%), mean ± SD or median [IQR]. CMV, cytomegalovirus
For continuous covariates, Wilcoxon rank sum test and for categoric covariates, Fisher exact test was used to generate the *P* values.

Figure 1. dd-cfDNA discriminates active rejection



(A) Fraction of dd-cfDNA in active rejection (n=12) versus no active rejection (n=17). Box and whisker plots; horizontal line represents the median; bottom and top of each box represents 25th and 75th percentiles. Median dd-cfDNA in active rejection 2.4% versus 0.18% for no rejection (*P*=0.0003).

(B) Levels of Serum creatinine [mg/dl] in active rejection (n=12) versus no active rejection (n=17). Box and whisker plots; horizontal line represents the median; bottom and top of each box represents 25th and 75th percentiles. Serum creatinine was not significantly different in median values between two groups (*P*=0.91).

(C) Fraction of dd-cfDNA in ABMR/TCMR and Borderline changes compared to no rejection. Box and whisker plots; horizontal line represents the median; bottom and top of each box represents 25th and 75th percentiles. There was a statistically significant difference between groups as determined by one-way ANOVA (**).

(D) dd-cfDNA in ABMR/TCRM after initiation of treatment. Pooled slope of regression line =-0.02.
*The outlier is linked to a patient not responding to treatment and returning to dialysis five months after initial diagnosis of TCMR.

OP707 REGIONAL DIFFERENCES IN PRIMARY GRAFT DYSFUNCTION IN HEART TRANSPLANTATION: A REPORT FROM THE INTERNATIONAL CONSORTIUM ON PRIMARY GRAFT DYSFUNCTION

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Background and Aims: Primary Graft Dysfunction (PGD) is a leading cause of early mortality after heart transplantation (HT). Regional differences in PGD incidence have not been studied. An international consortium on PGD was developed to identify risks for PGD development in a large patient population and to evaluate regional differences in PGD incidences in the United States (US), Canada and Europe.
Methods: Our consortium includes 10 centers in the US, Canada and Europe. We collected data on all consecutive single-organ HT recipients from 2010 to 2020, including donor and recipient demographics and type and duration of mechanical circulatory support after HT. Severe PGD was defined as need for extracorporeal membrane oxygenation (ECMO) or surgical biventricular assist device (BiVAD) after HT. We calculated the incidence of severe PGD in each region divided into US, Canada and Europe. Baseline characteristic regional differences were identified by chi-squared tests for categorical variables and one-way ANOVA for continuous variables.
Results: We included 2691 HT recipients: 1,628 from the US (60.5%), 330 from Canada (12.3%) and 733 from Europe (27.2%). Recipients from the US were significantly more likely to be obese, have a history of diabetes, and have hypertension. When compared to their European counterparts, North American recipients were more likely to be supported with a left ventricular assist device (LVAD) (Table 1). Donors from Europe were older than donors from North America. There were also significant differences between the regions in HT donor characteristics including ischemic time and sex. In our whole cohort, severe PGD occurred in 211 (7.8%) patients. Absolute incidence of severe PGD was lower in Canada (3.9% vs. 8.7% in US and 7.8% in Europe, $p = 0.014$, Figure 1), but differences amongst the regions disappeared when adjusted for recipient body mass index, sex, pre-transplant LVAD support, and ischemic time (OR: 1.03, 98% CI: [0.85-1.25], $p = 0.76$).
Conclusion: There were no differences in severe PGD incidence between Canada, US and Europe after adjusting for population characteristics. These data will help us identify risk factors for PGD in the current era.

Table 1. Recipient and donor baseline characteristics stratified by region

	United States (n=1628)	Canada (n=330)	Europe (n=733)	p-value
Recipient characteristics				
Age (years)	53.9 ± 12.3	51.7 ± 12.5	54.5 ± 12.1	p=0.79
Female	440 (27.1%)	64 (19.4%)	175 (23.9%)	p=0.01
Blood type O	641 (39.9%)	112 (34.2%)	132 (36.6%)	p=0.06
Etiology of heart failure				
Ischemic	423 (26.4%)	95 (29.2%)	231 (31.5%)	
Non-ischemic	841 (52.4%)	147 (45.2%)	364 (49.7%)	
Body mass index (kg/m^2)	27.4 ± 5.9	26.1 ± 4.9	25.3 ± 3.9	<0.001
Diabetes	511 (33.0%)	76 (23.5%)	183 (25.0%)	<0.001
Hypertension	518 (68.3%)	93 (28.4%)	290 (39.6%)	<0.001
Pre-transplant LVAD	566 (36.6%)	118 (36.5%)	116 (19.7%)	<0.001
Donor characteristics				
Ischemic time (minutes)	171 ± 92	220 ± 63	195 ± 54	<0.001
Donor age (years)	33.9 ± 12.1	38.9 ± 13.9	43.1 ± 12.8	0.002
Female donor	615 (37.8%)	77 (23.6%)	223 (30.6%)	<0.001

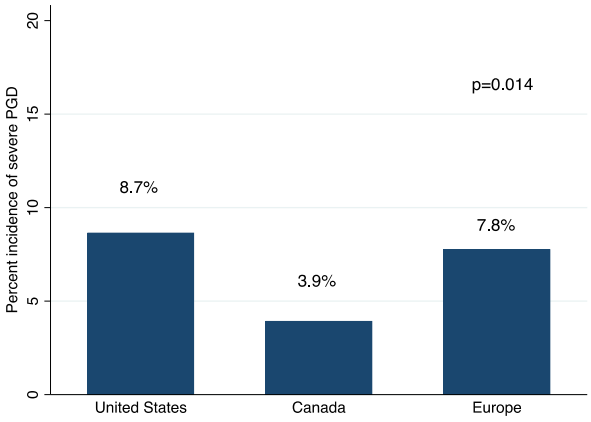

Figure 1 Incidence of severe PGD stratified by region

OP708 RANDOMIZED TRIAL ON HYPOTHERMIC OXYGENATED PERFUSION VS STATIC COLD STORAGE IN LIVER TRANSPLANTATION FROM EXTENDED CRITERIA DONORS: INTERIM ANALYSIS

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Background and Aims: The introduction of hypothermic oxygenated perfusion (HOPE) has radically changed the field of transplants, allowing to mitigate ischemia-reperfusion injury and to improve graft function in extended criteria donors (ECD).
Methods: This is an interim analysis from a currently ongoing randomized clinical trial which compare HOPE and static cold storage (SCS) in liver transplantation with ECD grafts.
HOPE started by flushing the organ at low flow values (30 mL/min) with new oxygenated perfusion fluid during the back-table preparation and successively, the organ was treated with continuous HOPE until transplantation. The minimal perfusion time was one hour. Belzer MPS solution at 4-10°C with continuous oxygenation (paO_2 of 500-600 mmHg) was used. In the control group, grafts are statically preserved in ice-cold perfusion solution.
Results: The first 70 patients enrolled in the study were analyzed: 35 grafts were preserved with HOPE and 35 with SCS. Donor and recipient characteristics were comparable between the two groups and the median follow-up period was 473 days.
ECD criteria were comparable in both groups: donors > 65 years (82% vs. 82%), with BMI > 30 kg/m^2 (14% vs 14%), with micro/macrosteatosis > 40% (20% vs 8%), with transaminases > 3 times the upper limit (11% vs 5%), with serum Na > 165 mmol/l (11% vs. 14%) or with ICU stay > 7 days (5% vs 5%) in HOPE and SCS, respectively. Also, the recipients had similar characteristics, particularly in terms of age (56 ± 11 years HOPE vs. 60 ± 9 SCS) and MELD score (16 ± 6 HOPE vs. 15 ± 8 SCS).
The study group was associated with a significant reduction in EAD rates (14.3% vs. 37.1%, $p = 0.027$), ALT peak (452 U/l vs 707 U/l, $p = 0.05$), ICU stay (4 days vs 5 days, $p = 0.017$) and an increased graft survival at one year (100% vs 86%, $p = 0.028$).
Conclusions: The interim analysis showed that HOPE was related to a significant improvement in functional recovery of the graft and consequently improved graft survival.

Preliminary Results: 9 grafts were perfused for 6 hrs ($n = 5$) and 24 hrs ($n = 4$) in a NMP primed with autologous blood connected to MSCs-b ($n = 6$) Fig 1 or a empty bioreactor ($n = 3$ as control). All grafts showed hemodynamic stability during NMP (PVQ 1.4 L/min;HAQ 155 ml/min) without clotting formation. Lactate significantly decreased over time (t0 13,4 mmol/L, t360 2.6, t24 0,54); bile production started at 1 hr with a mean of 12 ml/h; higher glucose intake was observed in MSCs group after 3 hrs. AST had peak at 3 hrs (2784 UI/l) and remained stable at 6 and 24 hrs. TNFα peaked at 2 hrs in all groups;IL-8 decreased earlier (6 hrs) in MSCs group;IL-10 is released earlier (3 hrs) in MSC group. MSCs at the end of perfusion were vital and proliferated in culture. No circulating MSCs were revealed in perfusion samples At the flow cytometry at the end of perfusion cells preserved MSC markers (CD45-34-31-90+73+29+105+) Fig 2; CD146 was overexpressed (31-56%) compared with static culture (11%).
Conclusion: NMP integrated to MSC-b is feasible and apparently safe for organ perfusion; MSCs seems to express immunomodulatory proprieties also in big animal model of DCD. Further analysis to investigate EV profile are planned.

Figure 1

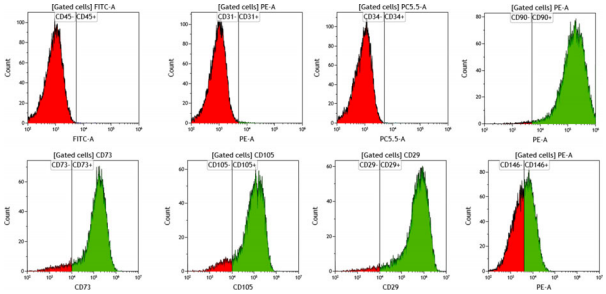

Figure 2

OP709 SET UP OF A DCD PIG MODEL OF NORMOTHERMIC MACHINE PERFUSION ASSOCIATED TO A MESENCHYMAL STROMAL CELL COATED BIOREACTOR TO IMPROVE ORGAN PRESERVATION

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Background: Machines perfusion (MP) are increasingly used in clinical setting especially on grafts from donors after cardiac death (DCD). Livers treated with normothermic-MP (NMP) had lower reperfusion injury. NMP in combination with immunomodulatory strategies may serve to optimize grafts considered too risky for transplantation. Aim of the study was to set in a animal model of DCD the feasibility of a NMP integrated with a mesenchymal cells bioreactor (MSCs-b).
Methods: Swine were used for the study. After heparin administration, left jugular vein was cannulated for blood collection. At 60 min from death declaration, livers were harvested and cold flushed for 20 min. Bile duct, portal vein (PV), celiac trunk (HA) were isolated and cannulated. Livers were connected to an oxygenated dual vessel (PVP 6 mmHg,HAP 30 mmHg) perfusion device set at 37°C.NMP was modified by a loop connected with a bioreactor in which umbilical cord (UC) MSC were previously seeded. Inflammatory cytokines (TNFα,INFγ,GM-CSF,IL-1a/1b,IL-1ra,IL6/2/4/8/10/12/18) were analyzed.

OP710 ESTABLISHING AN IN VITRO 3D MODEL OF FUNCTIONAL HUMAN LIVER ORGANOIDS

Aiste Gulla[1,2], Jaroslav Denkovskij[3], Jekaterina Novikova[3], Audrius Misiunas[4], Dalius Vitkus[4], Rokas Rackauskas[1], Vitalijus Sokolovas[1], Kestutis Strupas[1], Algirdas Ziogas[3]

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Background and Aims: Primary hepatocytes are considered the gold standard human liver cell model; although availability of human liver tissue remains a challenge and difficulties in isolating viable cells potentially limits their use. Three-dimensional (3D) liver tissues reconstituted from liver cells, termed liver organoids, have enormous potential for investigating aspects of liver disorders. The aim of our study was by integration of multiple novel techniques, including state-of-the-art laparoscopic liver resection, engineering of growth factors or morphogens bound to extracellular matrix, direct cell reprogramming to produce functional 3D liver organoids.
Methods: Tissue from 20 anatomical liver sections was used for hepatocyte isolations. Tissue underwent a two-step EDTA/collagenase digestion. Cell viability was determined by ATP luminescence and 7AAD. qPCR, FACS, Western blot, immunofluorescence analysis and biochemical assays were undertaken to ascertain cellular phenotype and function in 3D cultures. Additionally, liver development-associated signaling pathways were tested.

Results: We showed that here is direct correlation between liver status, the number and viability of isolated hepatocytes and their functional properties in 2D and 3D environment. FACS analysis indicated that prolonged cultivation in 2D leads to changes in cell populations. In addition, generated functional liver 3D organoids that maintained viability up to three weeks, produced albumin and expressed liver-specific genes HNF4, CK19, AAT, CYP3A4.
Conclusions: Preliminary results show that we successfully established a protocol to culture human liver organoids in unique 3D environment. These platforms can be used for further translational research, in particularly, liver transplantation.

OP711 MITOCHONDRIAL PERFORMANCE DURING NORMOTHERMIC MACHINE PERFUSION OF THE LIVER PREDICTS CLINICAL OUTCOME AFTER TRANSPLANTATION

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Background: The growing demand for organs promotes the use of extended criteria organs. To assure good clinical outcome, pre-transplantation evaluation of organ quality is needed. We hypothesize, that mitochondrial quality and performance during normothermic machine perfusion (NMP) correlate with organ function after liver transplantation (LTx). Thus, our aim was to determine mitochondrial function (MF) after cold ischemia and during NMP in order to investigate its use for organ quality assessment and as a predictive marker for the clinical outcome.
Methods: In a prospective clinical trial, livers underwent NMP (OrganOx Metra) for up to 24 h before transplantation ($n = 35$). Biopsy and perfusate samples were collected at the end of cold storage, at 1 h, 6 h and end of NMP, and at 1 h after transplantation. Serial histology and real-time confocal imaging were performed in biopsies. MF was characterized in tissue homogenates by high-resolution respirometry (HRR; O2k, Oroboros Instruments) and correlated with clinical outcome (MEAF score). Specifically, succinate-linked coupling control was assessed, and the damage of the outer mitochondrial membrane was monitored by cytochrome c addition.
Results: We observed a considerable variability in mitochondrial respiration between grafts during cold storage, irrespective of the coupling states: OXPHOS (P) 40.8 $\pm$ 14.5, LEAK (L) 7.9 $\pm$ 2.7, ET (E) 71.5 $\pm$ 28.4, (mean $\pm$ SD; pmol s-1 mg wet weight-1). MF correlated with the clinical outcome, specifically, a higher P-L coupling efficiency and lower E-P control efficiency at 1 h NMP predicts a lower MEAF score. AUCs calculated for the above efficiencies during the first 6 h of perfusion show the same trend. Similarly, a higher AUC for cytochrome c control efficiency correlated with higher MEAF. Findings were compared in their predictive capacity with conventional perfusate biomarkers and the predictive power of MF exceeded that of other findings.
Conclusions: Improved indices of ATP production efficiency (P-L coupling efficiency) and mitochondrial outer membrane integrity (cytochrome c control efficiency) during NMP predicts the clinical outcome upon liver transplantation. Mitochondrial respiration assessed by HRR is therefore a promising tool to select optimal grafts.

OP712 THE IMPACT OF NORMOTHERMIC REGIONAL PERFUSION ON SIMULTANEOUS KIDNEY AND PANCREAS TRANSPLANTATION

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Background: Simultaneous pancreas and kidney (SPK) transplantation is the optimum treatment for patients with type 1 diabetes and renal failure and provides survival benefit over deceased donor kidney transplantation alone.
Donation after circulatory death (DCD) SPK transplantation has equivalent long-term results to organs from brainstem dead donors (DBD), but is associated with increased rates of ischemia reperfusion injury and delayed graft function. Normothermic Regional Perfusion (NRP) has emerged as a promising technique to minimise or reverse the additional ischemic insult associated with conventional DCD (sDCD) donation by placing the donor on a modified extra-corporeal membrane oxygenator circuit. To date, little has been published on the outcomes of pancreas transplantation following NRP beyond case reports.
Methods: We performed a retrospective analysis of prospectively collected outcomes our DCD pancreas transplant program and comparing the outcomes of recipients receiving SPK grafts following sDCD and NRP procurement.
Results: 266 patients were included in the study (171 DBD, 77 sDCD, 18 NRP). There was no significant difference between cohorts in terms of serum creatinine, eGFR at 1 year or HbA1c.
There were no significant differences in the potential biochemical markers of graft pancreatitis (CRP, White Blood Count, Neutrophil Count, Albumin, Platelet Count, Amylase, Lipase). There was a significantly lower rate of renal delayed graft function (DGF) in the DBD 41/171 (24.0%) and NRP cohorts 5/18 (27.8%) compared to sDCD cohort 42/77 (54.5%). No differences were seen in the rates of pancreas DGF in DBD 4/171 (2.3%), sDCD cohort 3/77 (3.9%) and NRP cohorts 0/18 (0%).
Conclusions: While there is increasingly strong evidence showing benefit in the setting of liver transplantation, the benefit in the setting of pancreas transplantation is less clear.
We believe this paper represents the largest single centre DCD and NRP series in the setting of SPK presented to date and in it demonstrated that:

- SPK transplantation is feasible after NRP retrieval.
- There was no significant difference in graft pancreatitis in terms of either biochemical markers of injury or delayed graft function.
- Rates of DGF were significantly lower following NRP compared with those that received grafts from sDCD donors.

OP713 DONATION AFTER CIRCULATORY DEATH (DCD) DONORS IN THE EMILIA-ROMAGNA REGION (ERR): OUR FIRST FORTY CASES

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Background and aims: In the face of gap between patients on waiting list and organ supply for transplantation, the ERR, a northern Italy region of 4,459,477, started DCD organ procurement in 2016, according to the DCD National Programme (implemented in Italy in 2015).
All DCD donors were part of category III according to the Maastricht Classification revisited (expected cardiac arrest in ICU; controlled).
Aim of the study was to evaluate organ procurement and transplantation activity from DCD donors from 2016 to 2020.
Methods: We analyzed the first 40 DCD donors in the ERR and related transplants with graft and recipient survival from 2016 to 2020. All data sources were the Italian Informative Transplant System (S.I.T.) and the ERR Informative Transplant System (R.R.T.). Graft and recipient survival at 1 year were assessed by Kaplan-Meier-analysis.
Results: During the study period, 40 DCD controlled donors (Maastricht category III) were procured, 26 males and 14 females, age average 58 years old (range 25-72 years old), median age 59 years old; causes of death were Anoxic Brain Damage (15 cases), Haemorrhagic Stroke (15 cases), Ischaemic Stroke (5 cases), Head Injury (4 cases), and Brain Abscess (1 case). All donors were submitted to veno-arterial extra corporeal life support (ECLS) upon the end of "no touch period" (20 minutes in Italy) and to hypothermic machine perfusion after their removal. 34 out of 40 (85%) donors were utilized, allowing 31 liver transplantations, 37 single kidney transplantations and 9 double-kidney transplantations. Graft and recipient survival at 1 year were as follows: 93.5% for liver graft, 93.5% for kidney graft, 97% for liver recipient and 93.5% for kidney recipient.
Conclusions: Because of organ shortage and age average increment of potential deceased donors (65 years old in ERR), the implementation of DCD organ procurement represents a way to increase the donor pool. Graft and recipient survival rates, even if rather limited, show good results. Further studies and experiences are needed to confirm efficacy and effectiveness of this procedure.

OP714 EARLY IN VITRO DEVELOPMENT OF MESENCHYMAL STROMAL CELLS EXPANDED IN A BIOREACTOR FOR EX-SITU ORGAN PERFUSION

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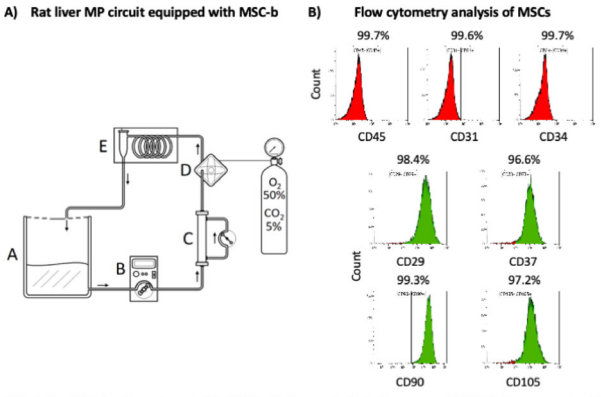
Background: Machine perfusion (MP) provides the opportunity to improve graft function before transplantation. We aim to develop a platform to harness the cytoprotective activity of mesenchymal stem cells (MSCs) during liver normothermic MP (NMP). Here, we report an in vitro feasibility study using MSC-bioreactors (MSC-b) connected to a circuit for rat liver MP.
Methods: Twenty million human CD95+, CD45-, 34-, 31- adipose tissue (AT)-MSCs were seeded into dialysis filters (DyFs) designed for small animal use.
We performed 2 set of experiments: 1) MSC-b ($N = 3$), AT-MSCs-DyFs were incubated for 24 h and then supernatants were collected and cells harvested; 2) NMP+MSC-b ($N = 5$), AT-MSC-b were connected to NMP circuit primed with an Oxyglobin-base fluid, and subjected to 4 h-perfusion at 20 ml/h. Samples of perfusate were collected at time intervals. At the end of MP, AT-MSCs were harvested, tested for viability, and analyzed by flow cytometry.
Results: After 24-h culture in DyF, AT-MSCs showed glucose consumption (MSC-b 18 ± 5 mg/dL vs medium 100 mg/dL) and lactate production (7.0 ± 1.4 mmol/L vs 0.7 mmol/L). Release of inflammatory mediators was observed in the supernatants (IL-8: 66.2 ng; IL-1ra: 6.1 ng). Low apoptotic activity was also detected (CK18: 0.66 U).
Concerning NMP+MSC-b experiments, perfusion pressure was stable pre and post MSC-b (delta: 4.1 ± 0.7 mmHg; trans-membrane: 1.6 ± 0.7 mmHg) throughout NMP. We observed substantial metabolic activity of AT-MSCs, with oxygen (O2) consumption (delta: 10 ± 3 mmHg) and lactate production (delta: 0.7 ± 0.2 mmol/L). Moreover, IL-8 and IL-1ra were detected over the procedure (IL-8: from 237 ng at 1 h to 252 ng at 4 h; IL-1ra: from 26.2 ng at 1 h to 42.4 ng at 4 h). Release of apoptosis markers was likewise observed (from 12.64 U at 1 h to 8.24 U at 4 h). However, no circulating MSCs were revealed in perfusate samples and viability was 98% at the end of MP. Flow cytometry documented preserved expression of MSC-markers CD29, CD73, CD90, CD105, whereas there were no signals related to non-specific markers CD31, CD34, and CD45.
Conclusions: AT-MSCs were metabolically active and showed preserved stem cell marker expression during NMP perfusion. DyFs seeded with MSCs can be integrated in a liver NMP circuit and could serve as a valuable tool to administer cell-based therapies during ex-situ perfusion.



A) Rat liver MP circuit equipped with MSC-b, A, Reservoir; B, Roller pump; C, MSC-b; D, oxygenator; E, bubble trap. **B)** Flow cytometry analysis of MSCs harvested from DyF at the end of MP.

OP715 NORMOTHERMIC MACHINE PERFUSION RECONSTITUTES PORCINE KIDNEY TISSUE METABOLISM BUT STIMULATES INFLAMMATION WHICH IS PARTLY COMPLEMENT DEPENDENT

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Background and Aims: Normothermic machine perfusion (NMP) is a clinical strategy to reduce the effect of renal ischemia-reperfusion injury (IRI), by the clearance of toxic waste products and oxygen reconditioning. Thus, an optimal NMP should restore metabolism and minimize immune activation induced by IRI. Complement is a key component in renal IRI and we aimed to assess its role during NMP.
Methods: Porcine kidneys ($n = 22$) underwent 18 hours (h) of cold static storage (CSS) followed by 4 h of NMP using a closed-circuit system preventing complement activation by air. Kidneys were randomly allocated to receive a complement C5-inhibitor or placebo during CSS and NMP. Perfusion included pressure-controlled pulsatile flow with heparinized oxygenated autologous whole blood.
Results: Perfusion of all kidneys resulted in rapidly stabilized renal flow (100 ± 41.3 mL/minute), low renal resistance (0.8 ± 0.7 mmHg/mL/minute) and urine production (68 ± 78 mL/h). During CSS, tissue microdialysate levels of glucose (Δ-1.6 mM), lactate (Δ-1.4 mM) and pyruvate (Δ-41 μM) decreased significant, whereas glycerol levels (Δ83 μM) increased (all $p < 0.001$). In the first hour of NMP, glucose (Δ4.4 mM), lactate (Δ5.4 mM) and pyruvate (Δ64 μM) increased while glycerol decreased (Δ-265 μM) (all $p < 0.001$). After 4 h, all metabolites settled at *in vivo* levels prior kidney procurement. Inflammatory markers C3a, TCC, TNF, IL-6, IL-1β, IL-8 and IL-10 increased significantly after 60 minutes NMP in plasma and kidney tissue. C5-inhibition completely inhibited plasma and urine TCC ($p < 0.001$; $p = 0.019$), reduced IL-1β, but did not alter the other inflammatory markers or metabolites significantly.
Conclusions: Closed-circuit NMP restores tissue metabolism in renal IRI, but induces inflammation, which is partly C5 dependent. Further research, using additional immune inhibitors, will be an essential next step in optimizing NMP and immediate recipient treatment to prevent IRI-induced immune activation.

OP716 POST-VACCINE IMMUNITY TO COVID-19 VACCINE IN END-STAGE RENAL DISEASE PATIENTS AND KIDNEY TRANSPLANT RECIPIENT

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Background and aims: Immune system alterations in patients with end-stage renal disease (ESRD) and kidney transplant recipients (KTX) predispose to reduced effectiveness of vaccines. Little is known of immune response after COVID-19 vaccination in patients with renal dysfunction. In the study, we aim to examine both humoral and cellular immune response in patients received BNT162b2, Pfizer-BioNTech COVID-19 vaccine. We recruited over 100 patients.
Methods: We included KTX and ESRD patients undergoing dialysis – hemodialysis (HD) or peritoneal dialysis (PD). Sex- and age-matched healthy individuals was a control group. Blood samples were collected before the first and second vaccine dose, and 3 weeks after the latter. Until now, we performed analysis exploring the humoral immune response using chemifluorescence assay in PD and HD patients. To this, in blood serum we measured the level (BAU/ml) of antibodies against viral: S1/S2 (spike) and N (nucleoprotein) proteins. Moreover, we collected PBMCs samples for flow cytometry analysis and cellular tests. Cell-mediated immunity testing using INF-γ release assays (IGRA) is ongoing and plans to finish on July 2021.
Results: We observed that seroconversion rate after first dose of BNT162b2 was significantly ($p = 0.0038$) higher in PD patients (86%) compared with HD individuals (57%). However, we noticed substantial seroconversion after the second dose in both PD and HD subgroups (100% vs. 97%, respectively). Consequently, the level of anti-S antibodies after the first and the second dose of vaccine was remarkably higher in PD patients undergoing hemodialysis. In addition, we noticed higher lymphocytes rate in HD patients.
Conclusions: We conclude that HD patients had lower immune response to BNT162b2 vaccine compared to PD group. Hemodialysis promotes extensive cells activation leading to a chronic inflammation state. We assume that depressed immune response to COVID-19 vaccination in HD patients might be caused by inflammaging process resulting in functional down-regulation of T and B cells. Further tests including KTX and healthy group, as well as cellular components of the immune system, will allow to broad analysis of immune response to BNT162b2 vaccination and will be obtained before the conference commences.

OP717 ACUTE KIDNEY INJURY AFTER HEART TRANSPLANTATION: ROLE OF INTRAOPERATIVE MANAGEMENT

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Background: Acute kidney injury (AKI) is a serious complication after heart transplantation (HT) and is associated with increased early morbidity and mortality. The lack of a univocal definition makes difficult to establish a clear incidence of the AKI and both risk factors and mechanisms remain unclear.
Methods: Herein, we investigated incidence and operative risk factors associated with AKI development after HT, as defined by KDIGO criteria. We hypothesize that hypotension during cardio-pulmonary by-pass (CPB) and during post perioperative setting increases the risk of developing AKI after HT. We included all consecutive HT recipients transplanted between 2008 and 2018 in two medium-large sized European Centres, surviving at least 48 hours after surgery. Primary outcome measure was Incidence of grade $\geq$ 2 AKI development within the first 48 hours after HT. The effect of AKI on one-year mortality was also assessed.
Results: AKI developed in 90(30%) of the 305 patients (51 $\pm$ 12 y, 71% males) included in the study. AKI patients tended to be older (53 $\pm$ 12 vs 50 $\pm$ 10 y; $p = 0.06$), more frequent males (79% vs.67% $p = 0.04$), and treated with pre-HT mechanical circulatory support (MCS) (40% vs. 26%; $p < 0.01$). Of note, pre-HT renal function and etiology of heart failure were not associated with AKI. Longer CPB time was associated with AKI development (205 $\pm$ 80 vs. 167 $\pm$ 50 min; $p = 0.04$). In addition, AKI was more frequent in patients with intraoperative hypotension, i.e. MAP < 50 mmHg for longer than 100 minutes (42% vs 26%; $p = 0.03$), and fluid balance > 1500 ml (38% vs. 25%; $p = 0.04$). Overall, one year survival was 88%. In patients with AKI, however, one year survival was markedly reduced (68% vs. 97%; $p < 0.01$). AKI-related odds for mortality (OR[95%CI] = 13.8[6.1-35.9]; $p < 0.01$) persisted significant also after adjusting for pre-transplant renal dysfunction, which also retained independent association with of post-HT survival (3.9 [1.57-10.1]; $p < 0.01$)
Conclusion: AKI is a major risk factor for post-HT mortality, irrespective of baseline renal function. Overall this study supports the concept that adequate management of intraoperative blood pressure and fluid balance, as well as development of specific management strategies for males and patients with MCS, may reduce the occurrence of AKI after HT.

OP718 METABOLIC OUTCOMES AFTER PANCREAS TRANSPLANTATION FROM DONORS AFTER CIRCULATORY DEATH - THE UK REGISTRY ANALYSIS

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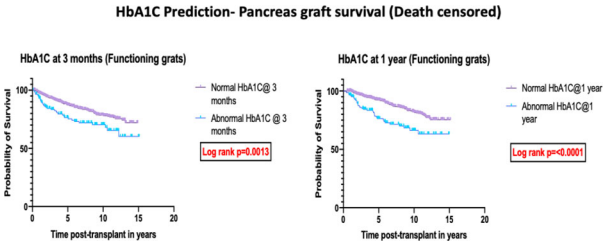
Background: DCD pancreas transplantation is established as a valuable cohort to expand the pancreas donor pool, with equivalent graft & patient survival compared to pancreases from DBD donors, but the metabolic outcomes are unclear. Given the lack of clear metabolic markers, can post-transplant HbA_1C predict long-term graft function, and does it predict function in DBD as well as DCD grafts? We aimed to answer these questions.
Methods: A UK registry analysis of all 2326 pancreas transplants (excluding graft losses < 3 months) performed from January 2005 to December 2018 was done. The primary aim was to compare the HbA_1C between the DBD & DCD grafts and its correlation with graft outcomes. The secondary outcome measures were weight gain, rejection rate (includes the need for steroids) & incidence of secondary diabetic complications post-transplant between the 2 groups. Functioning graft is defined as remaining insulin independent. $HbA_1C \leq 42$ mmol/mol was considered normal. Secondary diabetic complications are defined as any of the following events: myocardial infarction, cerebrovascular accident, limb amputations.
Results: Transplant characteristics as shown in table 1. In univariate analysis, DBD recipients had a higher HbA_1C at 1-year ($p = 0.0004$) & gained more weight at 1- & 3 years post-transplant ($p < 0.0001$, $p = 0.0006$, respectively). Patients who were de novo steroid-free subsequently had a higher rate of steroid usage if they received a DCD graft ($p = 0.0003$). In an adjusted multivariate logistic regression model for predicting metabolic outcomes (HbA_1C & weight gain), increasing donor age in DCD recipients had a higher probability of experiencing worse HbA_1C at 1-, 3-, and 5 years (OR 1.02, $p = 0.0007$/OR 1.03, $p < 0.0001$/OR 0.96, $p = 0.0002$ respectively) & DCD recipients had a higher probability of weight gain at 3 months & 3 years (OR 0.56, $p = 0.02$/OR 0.62, $p = 0.03$, respectively). In both DBD& DCD grafts, a normal HbA_1C at 3 months & 1 year predicts better longer-term pancreas graft survival {p values ≤ 0.001, HR 2.3 & 1.7, respectively, (Fig. 1)}.
Conclusions: Increasing donor age in DCD grafts is associated with a higher risk of abnormal HbA_1C. DCD grafts is associated with a higher risk of weight gain. A normal HbA_1C at 3 months & 1 year predicts better longer-term pancreas graft survival in both DBD/DCD grafts.

Table-1

Transplant characteristics	DBD	DCD	P value
Donor age (Median)	36 years	30 years	<0.0001
Donor BMI in kg/sq. m (Median)	23.40	22.90	0.0003
Donor abdomen girth in cm (Median)	85.00	82.00	0.02
Recipient age (Median)	42 years	42 years	0.95
Recipient BMI in Kg/sq.m (Median)	24.6	24.7	0.50
Caucasian recipients (%)	89.62	89.47	0.92
Non-Caucasian recipients (%)	9.73	9.64	0.95
Recipient HbA1C pre-transplant (mmol/mol), (Median)	71.00	71.00	0.48
Recipient insulin usage (IU/day), (Median)	42	42	0.52
Cold ischemia time in mins (Median)	686	651	<0.0001
% Sensitized recipients (CRF>5%)	30.21% (N=565)	23.46% (N=107)	0.004
% Highly sensitized recipients (CRF>85%)	4.65% (N=87)	2.19% (N=10)	0.01
Proportion of SPK	86.20% (N=1612)	81.79% (N=373)	0.01
Proportion of PAK	7.70% (N=144)	7.67% (N=35)	0.98
Proportion of PTA	6.09% (N=114)	10.52% (N=48)	0.0009
Proportion of re-transplants	3.90% (N=73)	3.72% (N=17)	0.85
0 DR mismatches	10.80% (N=202)	8.55% (N=39)	0.15
1 DR mismatches	55.93% (N=1046)	54.82% (N=250)	0.66
2 DR mismatches	33.26% (N=622)	36.62% (N=167)	0.17
Depleting antibody induction	64.11% (N=1199)	72.24% (N=334)	0.001
De novo Steroid maintenance	41.81% (N=782)	31.35% (N=143)	<0.0001
Incidence of DGF of pancreas graft within first 3 months (Transient insulin use)	2.13% (N=40)	2.63% (N=12)	0.51

Table-1

Incidence of rejection at 3 months	9.19% (N=172)	10.08% (N=46)	0.55
Incidence of rejection at 1 year	13.74% (N=257)	13.15% (N=60)	0.74
Incidence of rejection at 3 years	6.41% (N=120)	7.45% (N=34)	0.42
Incidence of rejection at 5 years	4.75% (N=15)	5.04% (N=23)	0.79
Incidence of secondary complications at 3 months	4.80% (77/1604)	3.0% (12/400)	0.11
Incidence of secondary complications at 1 year	2.20% (32/1453)	1.89% (7/369)	0.71
Incidence of secondary complications at 3 years	1.02% (12/1172)	1.15% (3/259)	0.85
Incidence of secondary complications at 5 years	0.76% (7/919)	1.20% (2/166)	0.56



OP719 PORTABLE GAMMA-CAMERA AS A USEFUL TOOL FOR BRAIN DEATH DIAGNOSIS

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Background: The aim of this study is to correlate the results of transcranial Doppler ecography (TCD) and gamma-camera (GC) using a portable system to establish a reliable diagnosis of brain death (BD).
Methods: A prospective, observational study was carried out. All patients diagnosed with BD by clinical criteria underwent two supplementary tests: TCD and GC using the portable system Sentinella®. Patients were recruited from January 2017 to December 2020. TCD was performed by experienced intensivists; GC, by specialists in Nuclear Medicine using technetium 99 by intravenous administration. The absence of perfusion in the cerebral hemispheres and brainstem was described as a pattern consistent with BD, and typical patterns for TDE were diastolic reverberation and/or systolic peaks.
Results: Ninety-nine patients were studied. 64.7% were men aged 57.9 on average. Causes for BD were haemorrhagic stroke (40.4%), traumatic brain injury (24.2%), ischemic stroke (16.1%), post-cardiac arrest anoxic encephalopathy (13.1%), and subarachnoid haemorrhage (6%). A clinical diagnosis of BD was made in all cases, and both tests were performed on patients. Portable gamma-camera confirmed BD in 100% of the patients. In 21 patients, TCD patterns did not confirm the BD, the absence of an acoustic window being the most frequent cause of failure in this test. 74.5% were donors. No adverse effects were reported when using the portable GC.
Conclusions: Establishing a correct and early diagnosis of BD is important due to its legal and clinical implications, and to its relevant significance in organ donation. A portable GC could be a useful and feasible tool for the diagnosis.

OP720 SPECIFIC URINARY METABOLOMIC PROFILE IN SPONTANEOUS TOLERANT KIDNEY TRANSPLANTED RECIPIENTS

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Background and Aims: Spontaneous operational tolerance is the holy grail in solid organ transplantation. In kidney transplantation, spontaneous tolerance is associated with regulatory mechanisms. Previous reports show that the urinary compartment of operationally tolerant recipients harbor a specific and unique profile. We hypothesized that spontaneous tolerant kidney transplanted recipients (KTR) would have a specific urinary metabolomic profile linked to immune regulatory mechanisms.
Patients & methods: We performed metabolomic profiling on urine samples from healthy volunteers, stable KTR under standard and minimal immunosuppression and spontaneous tolerant KTR using liquid chromatography in tandem with mass spectrometry (UHPLC/MS). Supervised and unsupervised multivariate computational analyses were used to highlight urinary metabolomic profile and metabolite identification thanks to workflow4metabolomic platform.
Results: The urinary metabolome was composed of approximately 2700 metabolites ranging from highly polar to apolar. Raw unsupervised clustering allowed us to separate healthy volunteers and tolerant KTR from others. We identify a specific urinary metabolomic signature in spontaneous KTR of twelve leading ions which was mainly driven by kynurenic acid, a tryptophan-derived metabolite independent of immunosuppressive drugs, serum creatinine and gender. Moreover, both kynurenine and tryptamine pathways were upregulated in tolerant KTR.
Conclusion: For the first time, we could clearly identify a specific urinary signature associated with operational tolerance encompassing tryptophan-derived metabolites from the kynurenine pathway. This profile is independent of any immunosuppressive drugs and serum creatinine level. Kynurenic acid and tryptamine enrichment allowed the identification of putative pathways and metabolites associated with spontaneous operational tolerance such as IDO, GRP35 and AhR signaling and microbiota-derived tryptophan metabolites such as indole alkaloids. Further studies are needed to better decipher the immune mechanisms at play from a long-term therapeutic perspective.

OP721 DESIGN OF STEADFAST STUDY EVALUATING TX200-TR101, A CHIMERIC ANTIGEN RECEPTOR T REGULATORY CELL THERAPY FOR LIVING DONOR RENAL TRANSPLANT RECIPIENTS

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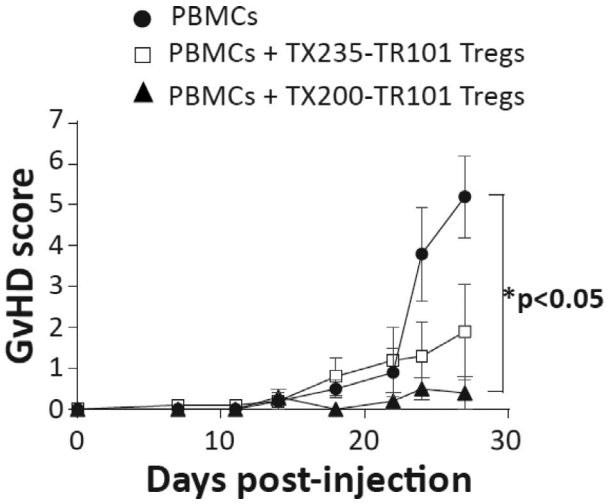
Background: A key priority in transplantation medicine is the induction of immunological tolerance. TX200-TR101 is a first in class therapy consisting of naïve regulatory T cells (Tregs) genetically modified to express a chimeric antigen receptor (CAR). The CAR has a human HLA-A*02 binding site allowing *in vivo* specific recognition of the HLA-A*02 antigen, found only on the allograft in the case of an HLA-A*02 positive renal transplant into an HLA-A*02 negative recipient.
Robust preclinical data in humanised mouse models have been generated assessing the immunoregulatory potential of TX200-TR101 to support its clinical development. In particular, the efficacy of TX200-TR101 was evaluated in a xenogeneic graft-versus-host disease (GvHD) model.
Methods: In a GvHD model, female NOD scid gamma (NSG) mice ($n = 5$ per group) were injected intravenously with 5×10^6 HLA-A*02 positive human PBMC without, or with 5×10^6 HLA-A*02 specific CAR-Tregs (TX200-TR101 Tregs, or Tregs modified with a control CAR bearing a non-signalling endodomain [TX235-TR101]). GvHD score (mean ± SEM) was a total score of 0-15 based on the sum of subscores in 5 categories with 0: no findings, 1: mild, 2: moderate, 3: severe. Statistical significance was determined using 2-way ANOVA.
STEADFAST (NCT04817774, EudraCT 2019-001730-34) is a phase I/IIa, first in human, multi-centre, open label, single ascending dose study evaluating autologous HLA-A2 CAR-Treg safety, mechanism of action and graft-related outcomes in HLA-A*02 mismatched living donor renal transplant recipients. TX200-TR101 will be given as a single infusion to up to 15 transplant recipients. Novel biomarkers will be explored to confirm the localisation of the CAR-Treg cells to the allograft, their activation, immunoregulatory function, and persistence.
Results: In a xenogeneic GvHD model, TX200-TR101 CAR-Tregs actively prevented GvHD by inhibiting the engraftment and expansion of infused proinflammatory human T cells (Figure). TX200-TR101 holds great promise to induce immunological tolerance and prevent graft rejection following HLA-A*02 mismatched renal transplantation.
Conclusions: CAR-Tregs represent a new frontier in cell therapy. The **ST**EADFAST study, the first-ever CAR-Treg clinical study, is currently recruiting patients at several European sites.



OP722 EARLY SAFETY OF SARS-CoV-2 MRNA VACCINES IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Background and Aims: We studied the safety and reactogenicity of SARS-CoV-2 mRNA vaccines in solid organ transplant recipients (SOTRs) because immunosuppressed patients were excluded from vaccine trials.
Methods: We studied SOTRs between September 12, 2020, and January 3, 2021, who received both doses of a vaccine. Self-reported demographics, medical history, and safety information were collected within 7 days after doses 1 and 2 (D1, D2) via an online platform. We identified risk factors associated with symptom development, as well as the association between symptom development and subsequent antibody response using modified Poisson regression with robust error variance.
Results: Among 741 transplant recipients, 400 (54%) received the Pfizer vaccine and 341 (46%) received the Moderna vaccine. The median (IQR) age was 60 (44 -69), with 57% female, and 10% non-white. Organs transplanted included kidney (49%), liver (19%), and heart (15%), with a median (IQR) of 7 (3-14) years since transplant. Immunosuppressive medications included steroids (54%), calcineurin inhibitors (87%), and anti-metabolites (71%). Roughly 82% of SOTRs experienced pain at the injection site, which was the most common local reaction (Figure 1). The most common systemic symptoms were fatigue (36% after D1, 56% after D2) and headache (28% after D1, 42% after D2), with increased incidence after the second dose in almost all systemic adverse symptoms. Severe reactogenicity was low. Younger participants were more likely to develop systemic symptoms after D1 (aIRR per 10 years $= {}_{0.85}0.90_{0.94}$, $p < 0.001$) and D2 (aIRR per 10 years $= {}_{0.91}0.94_{0.97}$, $p < 0.001$). Participants who experienced pain (aIRR $= {}_{1.11}1.66_{2.47}$, $p = 0.01$) or redness (aIRR $= {}_{1.83}3.92_{8.41}$, $p < 0.01$) were more likely to develop an antibody response to D1 of mRNA vaccines (Table 1). No anaphylaxis, incident neurological conditions, or SARS-CoV-2 diagnoses were reported. One patient reported incident acute rejection post D2.
Conclusions: In SOTRs undergoing mRNA vaccination, reactogenicity was similar to that reported in original clinical trials. Severe reactions were rare. These early safety data may help address vaccine hesitancy in transplant recipients.

Figure 1. Development of local and systemic adverse symptoms after each SARS-CoV-2 vaccine dose

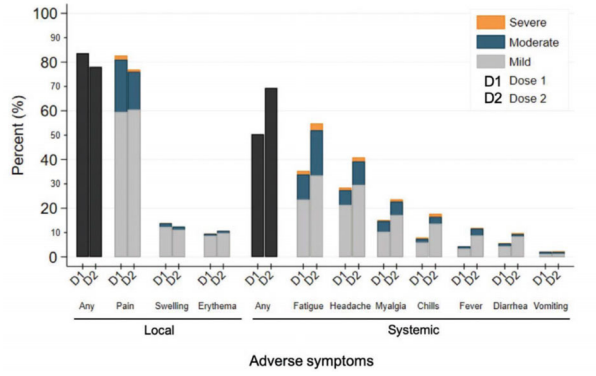

Table 1. Association between local and systemic symptoms and development of detectable antibody response after dose 1 of a SARS-CoV-2 mRNA vaccine.

	Detectable antibody response after dose 1	
	aIRR	P-value
Moderate to severe local symptoms		
Pain	$_{1.11}1.66_{2.47}$	0.01
Swelling	$_{0.39}1.09_{3.07}$	0.9
Redness	$_{1.83}3.92_{8.41}$	<0.01
Moderate to severe systemic symptoms		
Fatigue	$_{0.65}1.19_{2.18}$	0.6
Headache	$_{0.54}1.13_{2.36}$	0.7
Myalgias	$_{0.51}1.11_{2.42}$	0.8
Chills	$_{0.86}2.11_{5.17}$	0.1
Fever	$_{0.09}0.74_{6.28}$	0.8
Diarrhea or vomiting	$_{0.04}0.34_{2.60}$	0.3

N = 557 participants with antibody data after dose 1

Abbreviations: aIRR, adjusted incidence rate ratio; mTOR, mammalian target of rapamycin; Ref, reference

OP723 IDOTCOVID- INTERNATIONAL DATABASE ON ORGAN DONATION AND TRANSPLANTATION - COVID-19

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Background and aims: SARS-CoV-2 virus mortality rate in solid organ transplant recipients (SOTr) is higher than that of the general population (10-35% vs 5-7%, respectively). Unique SOTr characteristics such as type of SOT or immunosuppression (IS) protocols, leads to a significant bias when interpreting the results and translating them into decision-making information. IDOTCOVID was designed as an international online database of SOT COVID19 + aiming to lead to the development of a clinical decision support algorithm (DSA) individualized to this peculiar population which shall be available online, open access.
Methods: A set of variables (demographic, transplant related, epidemiological, clinical manifestation and COVID 19 treatment related) were selected and validated by an external advisory board of transplant physicians. Data entry was done a) individually by each collaborating center; b) automatic incorporation of the data from the Registry of Spanish Society of Nephrology as of August 2020, made available after formalization of the study agreement.
Results: To date, IDOTCOVID has registered 1415 SOTr COVID-19 + from 78 transplant centers in 24 countries. A pre-analysis identified most of the cases are middle-aged men (57.8 years), kidney transplants 72% with 26% liver transplantation and 20 cases of transplants of other organs. Fever (78%), cough (63%), and dyspnea (41%) as most prevalent symptoms. A mortality rate of 21% was detected during follow-up, with significant discrepancies according to transplanted organ (Kidney 25%, liver 15%, heart 20%, lung 50%; $p = .006$). Age at diagnosis was associated with an increased risk of death (OR 1.065 CI95 [1.049-1.081]), a mortality of 62% in those with > 65 yo ($n = 341$), with an increased risk x12 superior to those < 35 yo (OR 12.96 CI95 [3.09-54.3]). On a multivariate analysis, liver transplant risk remained with lower (OR 0.556 CI95 [0.378-0.824]) regardless of age.
Conclusions: These data are being tested to run 5 different supervised learning models to finally build the DSA for supporting the clinical decision making; considering the individualization of patient treatment focussing on clinical management (outpatient vs. hospital admission) and of IS (suspension vs reduction).

OP724 LIMITED IMMUNOGENICITY OF A SINGLE DOSE OF SARS-CoV-2 MRNA VACCINE IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Background: Given substantial challenges with vaccine allocation and evidence for short-term vaccine efficacy after a single dose of SARS-CoV-2 mRNA vaccines, some have proposed prioritizing first dose administration, potentially resulting in delays of second dose administration. However, this evidence is largely based on the early vaccine trials that largely excluded immunocompromised patients. To better understand the immunogenicity of the available SARS-CoV-2 vaccines in immunocompromised individuals, we quantified the humoral response to the first dose of SARS-CoV-2 vaccine in solid organ transplant recipients (SOTRs).
Methods: Transplant recipients across the US were recruited though social media to participate in this prospective cohort; those who underwent SARS-CoV-2 vaccination between December 16, 2020 and February 5, 2021 were included. Participants underwent either at-home blood sampling with the TAPIITM Blood Collection Device (Seventh Sense Biosystems, Medford, MA) or standard venipuncture. TAPIITM samples were tested on the EUROIMMUN enzyme immunoassay (EIA) which tests for antibodies to the S1 domain of SARS-CoV-2 spike protein. Venipuncture samples were tested on the Roche Elecsys® anti-SARS-CoV-2 S EIA which tests for antibodies against the receptor binding domain (RBD) of the SARS-CoV-2 spike protein. Both tests are semi-quantitative, correspond to mRNA vaccine antigens, and consistent correlates of neutralizing immunity. We evaluated the association between demographic/clinical characteristics and positive antibody response using modified Poisson regression with robust variance estimator.
Preliminary Results: We studied 436 transplant recipients who underwent vaccination (Table 1) and did not have a prior polymerase chain reaction-confirmed diagnosis of COVID-19. At a median (IQR) of 20 (17-24) days after the first dose, antibody was detectable in only 76/436 (17%) of participants (binomial exact 95% confidence interval 14-21%). Recipients not on anti-metabolite maintenance immunosuppression were 4.43-fold more likely to develop an antibody response ($p < 0.001$), older recipients were 19% per decade less likely to develop an antibody response ($p = 0.001$).

Table 1. Demographic and Clinical Characteristics of Study Participants, Stratified by Immune Response to the First Dose of SARS-CoV-2 mRNA Vaccine, and Associations with Developing an Antibody Response.

	Overall (n=436)	Detectable antibody (n=76)	Undetectable antibody (n=360)	IRR[a] univariate (95% CI) p-value	IRR multivariable (95% CI) p-value
Age, years median (IQR)	55.9 (41.3-67.4)	46.3 (34.9-64.8)	57.0 (43.8-67.8)	0.81 (0.71-0.93)[b] p=0.003	**0.81 (0.72-0.92) p=0.001**
Female sex, no. (%)	260 (61)	48 (64)	212 (61)	1.12 (0.73-1.73)[c] p=0.6	
Non-white[d], no. (%)	46 (11)	8 (11)	38 (11)	0.99 (0.51-1.94)[e] p=0.9	
Organ, no. (%)					
Kidney	219 (51)	31 (41)	188 (53)		
Liver	78 (18)	28 (37)	50 (14)		
Heart	66 (15)	9 (12)	57 (16)		
Lung	49 (11)	4 (5)	45 (13)	0.68 (0.45-1.04)[f] p=0.07	
Kidney/Pancreas	12 (3)	1 (1)	11 (3)		
Pancreas	5 (1)	1 (1)	4 (1)		
Other multi-organ	2 (1)	1 (1)	1 (0)		
Years since transplant, median (IQR)	6.2 (2.7-12.7)	8.6 (4.5-17.1)	5.8 (2.5-12.0)	1.88 (1.21-2.93)[g] p=0.005	**1.65 (1.09-2.48) p=0.02**
Anti-metabolite[h], no. (%)	320 (73)	28 (37)	292 (81)	4.73 (3.12-7.16)[i] p<0.001	**4.43 (2.92-6.72) p<0.001**
Testing platform, no. (%)					
Roche Elecsys®	330 (76)	64 (84)	266 (74)	1.71 (0.96-3.05)[j] p=0.07	
EUROIMMUN	106 (24)	12 (16)	94 (26)		

[a] IRR: incidence rate ratio
[b] Per 10-year increase in age
[c] Female (versus male)
[d] Race/ethnicity options were defined by the investigators and classified by the participants
[e] Non-white (versus white)
[f] Kidney transplant recipient (versus non-kidney transplant recipient)
[g] ≥6 years since transplant (versus <6 years since transplant)
[h] Maintenance anti-metabolite immunosuppression includes mycophenolate mofetil, mycophenolic acid, or azathioprine
[i] Not on anti-metabolite maintenance immunosuppression (versus on anti-metabolite maintenance immunosuppression)
[j] Roche Elecsys® (versus EUROIMMUN)

OP725 SARS-CoV-2 VACCINATION AND EARLY SPECIFIC IMMUNE RESPONSE IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Background: Current evidence suggests that the immunogenicity of SARS-CoV-2 vaccine is suboptimal in solid organ transplant (SOT) recipients. To date, no study has assessed the relationship between vaccination response and the patient net state of immunosuppression (NSI). We investigated the humoral response to SARS-CoV-2 vaccine in SOT recipients after the 1st vaccination dose, and its relationship with several parameters of patient NSI at baseline.
Methods: Prospective cohort study of SOT recipients vaccinated at our hospital with mRNA-based vaccines. The immune response was evaluated determining the level of anti-receptor binding domain (RBD) of SARS-CoV-2 antibodies at the time of 2nd vaccination dose. In addition, an attempt to investigate the NSI was made at baseline (1stdose) by determining absolute CD4 and CD8 counts, IgG and C3 levels.
Results: We enrolled 323 SOT recipients: 66.4% male, median age 57 (IQR 49-67) years. Of them, 183 were kidney, 106 liver, 26 heart and 8 lung transplant recipients. Overall response to 1st vaccination dose (RBD-antibody titer $\geq$ 0.8 U/ml) was detected in 92 patients (28%). Seroconversion rates across transplant types were 44% in liver, 23% in kidney, 12% in lung, and 7% in heart recipients. The median RBD-antibody titer was 0.4 (IQR 0.4-1.8) U/ml, with little variability between transplant types except for liver recipients where the median titer was 0.41 with IQR 0.40-5.78. The NSI at baseline was available for 178 out of the 323 included SOT patients. Comparison of CD4, CD8, IgG and C3 between patients with and without antibody response showed significant differences for absolute CD4 count 657 (IQR 435-889) vs. 466 (IQR 290-656) $p = 0.002$, and IgG levels 1076 (IQR 89-1239) vs. 937 (IQR 772-1114) $p = 0.009$.
Conclusions: We confirmed a lower seroconversion rate after first vaccination dose in a mixed cohort of SOT recipients. Baseline patient NSI, in particular CD4 count and IgG levels, was associated with the response rate.

OP726 PROSPECTIVE EVALUATION OF HEALTH-RELATED QUALITY OF LIFE, UNCERTAINTY AND COPING STRATEGIES IN ORGAN TRANSPLANT RECIPIENTS DURING THE COVID PANDEMIC

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Background: During subsequent surges of COVID-19 infections, Public Health England advised extremely vulnerable individuals, including solid-organ transplant recipients (SOTR), to 'shield' between March-July 2020 and January-March 2021. The impact of strict self-isolation on health status is unknown. COVID Transplant Survey investigated health-related quality of life (HRQoL), uncertainty, coping strategies and behavioral insights in SOTR.
Methods: A cross-sectional online survey of adult SOTR at a Uk transplant centre was performed in July 2020 and March 2021. Assessment tools are the EQ-5D (HRQoL), short-form Mishel uncertainty-in-illness scale, and Brief Cope. The WHO behavioral insights tool interrogates risk perceptions, public trust, protective behavior and infection rate. EQ-5D scores were compared with age-matched controls from Health Survey England (2017). The first and second survey responses were compared.
Results: 474/790 (60%) respondents completed both surveys. The majority were liver transplant recipients (75%) and > 5 years post-transplant (60%). 18% had a history of mental health illness. COVID infection was experienced by 23/474 (5%), mostly occurring after the first wave. Shielding adherence was high (96%, Table 1). 50% continued to shield after the guidance was lifted in August 2020, and shielding behaviors became less strict over time. Vaccine uptake was 98%, with 86% believing it would provide "some protection against severe disease" and 8% believing it would "completely protect" them.
Compared with normative data, all EQ-5D domains were significantly poorer for those aged 35-65 years. A significant decrease between measurements in all domains of the EQ-5D was identified, with the most notable difference in anxiety and depression (Figure 1). This study showed low levels of uncertainty, which decreased over time (11.4 vs 10.9, $p < 0.01$). The most commonly used coping strategies were acceptance, active coping, planning and self-distraction. Instrumental support was a coping strategy with the most significant increase as the pandemic progressed.
Conclusions: SOTR were highly adherent to shielding recommendations; however, the HRQoL significantly deteriorated during the pandemic. The area with the largest detrimental change was related to mental health.

Table 1

	Measurement 1 July 2020	Measurement 2 March 2021	P Value
Adherance to elements of shielding			
Staying at home at all times			0.1
Yes	339 (72.0%)	345 (72.7%)	
No	6 (1.2%)	29 (6.1%)	
Partially	129 (27.2%)	99 (20.8%)	
Avoiding gatherings			0.05
Yes	457 (96.4%)	438 (92.4%)	
No	6 (1.2%)	16 (3.3%)	
Partially	11 (2.3%)	18 (3.8%)	
Avoiding contact with symptomatic people			<0.01
Yes	468 (98.7%)	442 (93.2%)	
No	3 (0.6%)	23 (4.8%)	
Partially	3 (0.6%)	6 (1.2%)	
Physical distancing between household members			0.85
Yes	186 (39.2%)	149 (31.4%)	
No	198 (41.7%)	259 (54.6%)	
Partially	90 (18.9%)	62 (13.1%)	
Patient reported perception of COVID-19 risk			
What do you consider your probability of getting infected?			<0.01
Extremely likely	39 (8.2%)	36 (7.6%)	
Somewhat likely	80 (16.8%)	119 (25.1%)	
Neither likely nor unlikely	131 (27.6%)	170 (35.8%)	
Somewhat unlikely	148 (31.2%)	125 (26.4%)	
Extremely unlikely	76 (16%)	22 (4.6%)	
How susceptible to COVID infection? [0 to 100 scale (Median IQR)]	80 (57-103)	75 (55-95)	0.02
How severe would COVID be for you? [0 to 100 scale (Median, IQR)]	83 (71-92)	90 (80-100)	<0.01
Confidence in healthcare providers and authorities			
Confidence in healthcare providers and authorities			
Trust in doctor/GP [0 to 100 scale (Median IQR)]	75 (55-95)	76 (56-96)	<0.19
Trust in doctors/nurses of the Transplant unit [0 to 100 scale (Median IQR)]	95 (80-100)	90 (80-100)	<0.01
Trust in local hospital [0 to 100 scale (Median IQR)]	75 (55-95)	75 (55-95)	0.83
Trust in the Government [0 to 100 scale (Median IQR)]	50 (24-76)	50.5 (26-74)	<0.01
Trust in the Department of Health [0 to 100 scale (Median IQR)]	60 (40-80)	70 (54-86)	<0.01
Do you think your access to health care was compromised putting you at risk?			<0.01
Yes	119 (25.1%)	41 (8.6%)	
No	355 (74.9%)	432 (91.1%)	

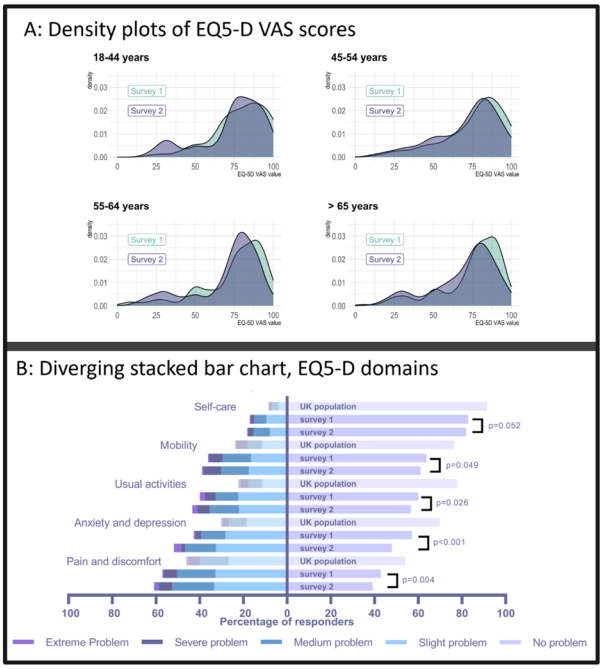

Figure 1 a) Density plots representing the distribution of the EQ-5D visual analogue scores for the two surveys, separated into age brackets b) Diverging stacked bar chart representing the percentage of the responders for each answer and each domain of the EQ-5D questionnaire. The bars to the right of the Y-axis represent responders reporting no problems, the bars to the left of the y-axis represent responders reporting slight to extreme problems.

OP727 MOTIVATION, EXPERIENCES, AND MENTAL HEALTH OUTCOMES OF UNSPECIFIED KIDNEY DONORS IN THE NETHERLANDS: A QUALITATIVE STUDY

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Background and aims: Unspecified kidney donation (UKD) now makes an invaluable contribution to the living donor pool, but has met scepticism about donor motivation and the influence of donation on mental health. Qualitative studies among unspecified kidney donors (UKDs) on experiences and psychological outcomes of donation are scarce.
Methods: All UKDs who donated a kidney in the Erasmus Medical Centre between 2000 and 2016 were invited to participate. Semi-structured interviews were conducted, recorded and transcribed verbatim. Topics were motivation for and experiences with donation, reactions from others, general mental health, and impact of donation on life and mental health. 106 UKDs participated. Interviews were independently coded by 2 researchers in NVivo using an inductive approach.
Results: Themes are divided into donor characteristics, motivation for donation, experiences, and mental health outcomes. Characteristics included: Pushing the boundaries of altruism, and Strong autonomy. Motivations included: Desire to help others, Affinity with kidney patients or donors, Triggered by (social) media, and Psychological gain. Reported experiences were: Satisfaction with donation process, Uncertainty about donor approval, Life on hold during workup, Donation requires perseverance and commitment, Interpersonal stress, Normalization of donation, Becoming an advocate for donation, Appreciation of anonymity, Persistent curiosity about donation outcome, Dissatisfaction about hospital care; and Ample social support. Mental health outcomes included: Donation did not impact mental health, Increased self-esteem and happiness; Donation as a "pat on the back", and Psychological distress after donation.
Conclusions: Results indicate rather positive outcomes of UKD on donors, add to the understanding of motivations and experiences of UKDs, and shed new light on their mental health before and after donation. These findings can help inform transplant professionals, donor education and policy.

OP728 FIVE YEAR HEPATOCELLULAR CARCINOMA RECURRENCE WITH EVEROLIMUS PLUS REDUCED TACROLIMUS VS STANDARD TACROLIMUS AFTER LIVING-DONOR LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) is the optimal curative treatment for hepatocellular carcinoma (HCC); however, post-LT HCC recurrence remains a significant challenge. In this study, HCC recurrence rates up to 5 years were assessed post-LT in living donor LT recipients (LDLTRs) who received either everolimus plus reduced tacrolimus (EVR+rTAC) or standard tacrolimus (sTAC).
Methods: This was a multicenter, non-interventional study (H2406) in *de novo* LDLTRs with primary HCC at LT who were previously randomized to EVR+rTAC or sTAC treatments and completed the 2-year core study (H2307; NCT01888432). Data were collected retrospectively (end of H2307 to the start of H2406), and prospectively (during H2406). Data were analyzed using the intent-to-treat (ITT) and as treated (AT) population.
Results: Of 117 LTRs (ITT) with HCC at LT in study H2307 (EVR+rTAC, $N = 56$ sTAC, $N = 61$), 86 patients (EVR+rTAC, $N = 41$ sTAC, $N = 45$) entered in the study H2406. During the H2406 study period, HCC recurrence was observed in 1 patient each in both treatment arms. The overall HCC recurrence was numerically lower in EVR+rTAC arm (*n* [%], 2 [4.4]) compared with sTAC arm (7 [12.3], (95% CI, −18.4, 2.5) at 5-year post-LT. In patients outside Milan criteria, there was zero (of 14) HCC recurrence in EVR+rTAC vs 6 (of 19) in sTAC arm. No graft loss or chronic rejection was reported during H2406 study, and the incidence of acute rejection (4 [7.6] vs 3 [6.2]) and death (7 [13.8] vs 7 [13.5]) was comparable in EVR+rTAC vs sTAC arms. The mean estimated glomerular filtration rate was higher in EVR+rTAC vs sTAC up to 5 years post-LT (76.8 vs 65.8 mL/min/1.73 m^2). In AT population (H2406), numerically lower adverse events (AEs) (16 vs 23) and serious AEs (3 vs 6) in patients were reported in the EVR+rTAC vs sTAC arms.
Conclusions: Five-year post-LT, EVR+rTAC showed a numerically lower incidence of HCC recurrence, with comparable efficacy and safety and better renal function compared with sTAC treatment.

OP729 PREEMPTIVE KIDNEY TRANSPLANTATION VERSUS NON-PREEMPTIVE KIDNEY TRANSPLANTATION IN ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: Preemptive kidney transplantation (PKT) is performed prior to dialysis initiation to avoid mortality and morbidity associated with dialysis. This systematic review and meta-analysis compared clinical outcomes of PKT versus kidney transplantation after dialysis (nPKT) in adult patients.
Methods: A comprehensive literature search identified studies comparing living (LD) or deceased donor (DD) PKT versus nPKT (PROSPERO registration, CRD42014010565). Study selection, quality assessment and data extraction were carried out by two independent reviewers. Data were combined using the random-effects model. The I^2 statistic was calculated to assess heterogeneity.

Results: Seventy-seven studies met the inclusion criteria. The methodological quality of studies varied (scores ranged from 9 to 20 out of a maximum score of 28). The meta-analyses included a total of 762,846 patients, out of which 157,100 (20.6%) had an LD transplant, and 122,092 (16.0%) received either an LD or DD PKT. LD PKT showed a significantly lower risk of patient death (24 studies; relative risk (RR) 0.75; 95% confidence interval (CI) 0.61-0.92), overall graft loss (21 studies; RR 0.72; CI 0.62-0.83), and delayed graft function (11 studies; RR 0.47; CI 0.41-0.54) compared with nPKT patients. DD PKT patients showed a significantly lower risk of overall graft loss (15 studies; RR 0.80; CI 0.69-0.92) and delayed graft function (11 studies; RR 0.29; CI 0.23-0.38). Substantial levels of heterogeneity were observed, which were explored using mixed-effect analyses. No differences were observed between the two groups in terms of acute rejection.
Conclusions: PKT lowers the risk of patient death, graft loss and delayed graft function compared with nPKT. These results show a need to change clinical pathways to avoid dialysis before transplantation, and promote timely referral to nephrology care, earlier engagement with potential living kidney donors, and timely transplant work up to make PKT the default for end-stage kidney disease patients.

POS001 EFFECT OF OSTEODEX AND CATDEX COMPOUNDS ON THE PRIMARY CULTURE OF HUMAN ARTICULAR CARTILAGE CHONDROCYTES

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Background: Osteodex and Catdex are substances of recent appearance in the market and have clinical applications in osteoporosis and certain genitourinary cancer diseases but have never been exposed to chondral cells, however, they possess inherent properties that could be able to optimize cell growth and expansion of chondral cell culture. The aim of this study was to evaluate the efficacy of this compounds as a supplement for culture medium in human chondrocytes by determining cell viability, cell migration, immunohistochemical analysis and gene expression of specific markers of chondral cells.
Methods: An *in vitro* experimental study will be conducted in which samples of articular cartilage will be obtained from 44 patients undergoing primary TKA due to osteoarthritis with patient approval by informed consent. Subsequently, the samples will be subjected to enzymatic digestion processes to obtain the chondrocytes which will be suspended in a culture medium generating 5 treatment groups per molecule (1 with the OptiMEM commercial kit and 4 with OptiMEM+ the study molecule at concentrations of 0.25, 0.5, 1.0 and 2.0 μm). For each group samples will be obtained at 0, 24 and 48 h of culture to perform total RNA extraction. Cell proliferation will be determined by a colorimetric assay. Cell migration will be assessed by the wound healing assay technique, the immunohistochemical analysis for Collagen type 1, Collagen type 2 and Collagen type 10 and specific hybridization tests for each gene of interest.
Results: With the use of Osteodex at a dose of 0.25 μm, an average of 120370 RLU± was obtained, in the control group an average of 106415 RLU± 701 was obtained, obtaining a significant difference ($p = 0.01$), for which it was determined that that dose increased cell viability. Regarding cell migration quantified by microdensitometric analysis, a higher value was obtained in all Osteodex doses than in the control group, being not significant between doses but significant compared to the control group when compared individually. The genetic expression of ACAN, COL2A1 and SOX9 was significantly higher ($p = 0.001$) in the groups that received Osteodex when compared to the control group.
Conclusions: We consider Osteodex to be a compound that shows encouraging results for improving the supplementation of human chondrocyte culture.

POS002 THE EFFECT OF ANG-3777 ON THE GROWTH OF C-MET-EXPRESSING HUMAN TUMOR CELLS IN IMMUNOCOMPROMISED MICE

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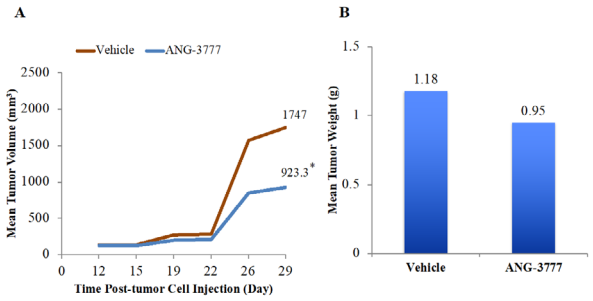
Purpose: In the injured organs, hepatocyte growth factor (HGF) stimulates c-MET, leading to the activation of intracellular pathways involved in tissue repair. ANG-3777 is an HGF mimetic. In a Phase 2 study, renal transplantation patients with signs of delayed graft function treated with ANG-3777 showed renal function improvement relative to placebo up to 1 year post-transplantation. However, uncontrolled activation of c-MET can stimulate tumor growth. The objective of these studies was to assess the potential of ANG-3777 to stimulate tumor growth in human cell lines.
Methods: c-MET-expressing human tumor xenografts (U87-MG glioma cells, HT29 colon cancer cells, and SUIT-2 pancreatic ductal carcinoma cells) were implanted into 20 BALB/c nude mice per xenograft model. The animals were administered an intraperitoneal injection of 2 mg/kg ANG-3777 or vehicle (dimethyl sulfoxide) daily for up to 28 days. Overall survival (glioma transplant model) and tumor growth and weight (colon and pancreatic tumor xenograft models) were assessed.
Results: Overall survival did not differ in animals treated with ANG-3777 vs vehicle. No significant increase in tumor growth or weight was observed with ANG-3777 treatment. ANG-3777 significantly reduced the mean volume of pancreatic tumors (1747 vs 923.3 mm3, $p < 0.01$;), but not the weight of the tumor (Fig. 1 A&B).
Conclusions: Administration of ANG-3777 in human tumor cells expressing c-MET was not associated with increased tumor volume or weight in pancreatic and colon tumor models and did not increase mortality in the glioma model in BALB/c nude mice.
Keywords: ANG-3777, tumor growth, tumor weight, overall survival.

Figure 1. Effect of ANG-3777 on SUIT-2 Pancreatic (A) Tumor Volume and (B) Weight



*p<0.01

POS003 TOTAL RNA FROM BONE MARROW CELLS INDUCES LIVER REGENERATION BY CO-ACTIVATING EARLY APOPTOSIS AND PROLIFERATION PROCESSES

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Background: The cellular mechanisms of activation of recovery processes in the liver while using the total RNA (tRNA) of bone marrow cells (BMCs) on the model of extensive liver resection (ELR).
Methods: Male Wistar rats ($n = 80$) with the model of ELR (70%) were divided into 2 groups: group 1–control with a single injection of saline solution and group 2–experimental with a single injection of tRNA at a dose of 30 μg/100 g of animal weight.
The dynamics of biochemical parameters of liver function and weight were monitored, as well as microstructural changes of hepatocytes in 48 hours after ELR, examining mitotic activity, expression of Caspase–9 and morphometric indices.
Results: It was found that in group 2, compared to group 1, there were a faster normalization of biochemical parameters (by 10–14 days), a higher mitotic index of hepatocytes (23.45% vs. 5.37%), initially a sharper decrease, and then a faster recovery of liver mass (by 10–12 days vs. 18–20 days). In groups 1 and 2, almost total expression of caspase 9 was detected, including in mitotic dividing hepatocytes. In group 1, a decrease in the values of morphometric parameters of single-and double-nuclear cells, a decrease in the number of double-nuclear hepatocytes, and an increase in the total density of hepatocytes compared to an intact liver were revealed. Intraperitoneal administration of tRNA led to an increase in the values of morphometric indices of single-nuclear hepatocytes, did not affect on their number, but increased the area of the nuclei of double-nuclear hepatocytes in comparison with the control.
Conclusions: The proved property of tRNA BMCs to support apoptosis processes in liver cells and simultaneously to induce mitotic activity in them indicates that tRNA is able to switch activated apoptosis to cell proliferation at an early stage of the regeneration process. The detected effect may be

due to the presence in tRNA of regulatory RNA molecules, including numerous protein-non-coding RNAS.

POS004 TOWARD A BIO-ENGINEERED PERIOSTEUM

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Background: Since natural bone healing mostly comes from the periosteum, aiming to restore its function is appealing. Native and processed human periosteum (HP) and fascia lata (FL) were assessed by morphological and mechanical analysis and cytotoxicity testing in the prospect of a bio-engineered periosteum.
Methods: HP and FL were obtained from cadaveric donors and chemically decellularized. Cellular clearance and extracellular matrix (ECM) preservation were assessed by histology (Hematoxylin-Eosin, Masson Trichrome, Sirius Red, Blue Alcian), immunohistochemistry (IHC) for type 1 collagen, DAPI and DNA/Collagen/GAGs quantifications. ECM organization was visualized by electron microscopy (SEM). Immunogenicity was assessed by IHC for major complex of histocompatibility (MHC-1). Stretch tests underscored differences in mechanical properties. Finally, acellular patches were sterilized by γ-irradiation and seeded with $5x10^5$ human fibroblasts. After 7 days culture, they were analyzed with histology, LDH quantification to evaluate the matrix cytotoxicity and Live/dead staining to assess the cell viability.
Results: Histology and IHC brought out similarities (type I collagen fibers, layer organization) and differences (thickness and compaction of fibers, type of cells) between native tissues confirmed by the SEM. FL can support much more load than HP as attested by a distinct stress/strain curve.
Histology and DAPI showed a successful decellularization with a "no man's land" concerning nuclei. DNA concentration statistically fell below the critic threshold (50ng/mg dry weight). Collagen content relatively increased while GAGs one decreased. Immunogenicity derived from nuclei disappeared. The seeded fibroblasts were alive after 7 days as shown by histology and the Live/dead, without significant difference in viability between patches and controls.
LDH quantification confirmed the low cytotoxicity.
Conclusion: HP and FL present morphological differences. Both offer a biocompatible scaffold after processing. FL was confirmed to be more suitable because of its easier harvesting, its integrity and its mechanical stiffness. Whether FL processed scaffold can further hosts periosteal stem cells has still to be demonstrated.

POS005 DONOR-DERIVED CELL-FREE DNA IN UPPER EXTREMITY VASCULAR COMPOSITE ALLOGRAFT RECIPIENTS

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Background/Aims: Diagnosing rejection in vascularized composite allotransplant (VCA) recipients relies on clinical exam and biopsy which are both easily confounded by common causes of skin irritation. Donor-derived cell-free DNA (dd-cfDNA) in recipient plasma originating from injured or apoptotic donor allograft cells is a proven non-invasive indicator of allograft rejection in renal transplant recipients but has not been evaluated in VCA recipients.
Methods: Five VCA patients presenting for evaluation at the outpatient plastic surgery clinic during periods of graft stability without clinical or histologic evidence of rejection, and/or during episodes of suspected clinical and/or biopsy proven rejection were included in this study. dd-cfDNA levels were collected prospectively at each visit with two commercially available kits. Based on established values in renal transplant, a dd-cfDNA level > 1% was considered suggestive of a rejection event.
Results: Five VCA recipients (3 bilateral and 1 unilateral upper limb, 1 lower abdominal wall, penis, and scrotum) were enrolled in this study. One patient had no clinical or biopsy evidence of rejection with dd-cfDNA level <1% and 1 patient had dd-cfDNA levels > 4% at three time points surrounding an episode of biopsy proven BANFF CTA 2007 Grade III rejection. 1 patient with a stable graft and no clinical concern for rejection had a routine dd-cfDNA level > 1% on two different draws one year apart. A final patient with non-specific skin changes but biopsy evidence of severe acute cell mediated rejection had dd-cfDNA level <1%.
Conclusions: These data reflect the first attempt to characterize dd-cfDNA in human VCA recipients. Although these early results are conflicting in the context of baselines established in renal allotransplantation, larger cohorts with careful correlation with biopsy findings are required to fully characterize dd-cfDNA level trends in patients with composite tissue allotransplants.

POS006 THE COVID19 PANDEMIC IMPACT ON TISSUE DONATION, LESSONS LEARNED

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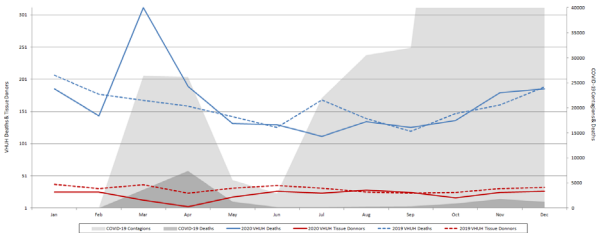
Background: During 2020 the COVID19 pandemic struck and caused an unprecedented number of deaths worldwide. Spain was one of the most affected countries on the planet specially during the first wave. We describe the impact on deceased tissue donation activity of one of the largest centers in Spain as well as the profile of the dead COVID19 patient.
Methods: Retrospective analysis of all death patients reported in Vall d'Hebron University Hospital (VHUH) in 2020 in comparison with 2019.
VHUH is a 1138 bed center attending 450,000 inhabitants. Deceased tissue donation activity is managed by a team of 4 physicians and 5 medical students (1), prospectively evaluating all deaths as possible tissue donors. At the beginning of the pandemic tissue donation was temporarily ceased until adapted and reliable measures were implemented: remote evaluation, telephone family interviews (hospital visits were restricted) and safe retrieval protocols.
Results: Even though only a 3% increase in mortality was reported during 2020, deceased tissue donation activity decreased by 30% (369 real tissue donors in 2019 vs 260 in 2020). Fig 1. A 38.8% of all possible donors were discarded due to COVID19-related contraindication. Family refusals were similar to 2019 figures (41.7% in 2019 vs 42.5% in 2020 of potential donors). Logistical restrictions imposed by the healthcare emergency situation accounted for a marginal loss rate (10.3%).
In order to analyze the lost potential donors we detailed the profile of the dead COVID19 patient, which is a male over 60 years (91.4%) with arterial hypertension (74%), overweight (66%), dyslipemia (51.4%) and heart disease (41.3%); followed by 37.4% respiratory disease. Oncological history was present in 16.8%.
Conclusions: One third of all possible donors were discarded due to SARS-CoV-2 infection.
After the first wave, the application of new protocols allowed us to regain pre-pandemic tissue donation rates.
Strategies tailored to each center characteristics aimed to manage unexpected healthcare crisis such as COVID19 should be planned in order to maintain donation rates.

(1) Transplant Proc. 2015 Oct;47(8):2314–7. https://doi.org/10.1016/j.transproceed.2015.08.027.



POS007 EX VIVO MACHINE PERFUSION TO ASSESS ISCHEMIA REPERFUSION INJURY OF AMPUTATED PORCINE LIMBS

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Background: In limb replantation or -transplantation, reperfusion following ischemia induces a significant, paradoxical, injury to the graft with activation of, among other things, innate immune cells and the plasma cascade systems, leading to severe tissue damage. In this study, we aimed to develop an *ex vivo – in vivo* large-animal model to evaluate and compare the pathophysiology of ischemia/reperfusion (I/R) injury.
Methods: Surgically amputated forelimbs underwent 1h (control) vs. 9h of ischemia and were subsequently reperfused using an extracorporeal perfusion system (*ex vivo*, using whole, anticoagulated pig blood, both forelimbs used) or surgically replanted to the donor pig (*in vivo*, single forelimb used), aiming for 12h of reperfusion. Clinical data as well as blood and tissue samples were collected at different timepoints to analyze markers of muscle damage, endothelial cell and plasma cascade activation, as well as production of cytokines and growth factors.
Results: In the *ex vivo* reperfusion model, both ischemic and control limbs showed a higher pro-inflammatory reaction as compared to the *in vivo* situation (Table 1). Moreover, *ex vivo* average reperfusion times were shorter and activation of coagulation and complement was more prominent, as well as the production of pro-inflammatory cytokines and muscle damage. Additionally, in both models, higher values of vascular growth factors were observed in 9h ischemic limbs as compared to controls and no difference was found for the anti-inflammatory IL-10. Furthermore, higher levels of E-selectin expression were found in controls vs. 9h ischemic limbs.
Conclusions: Our preliminary results suggest that I/R injury can clearly be detected in an *ex vivo* reperfusion setting with whole blood. That this injury was apparently stronger *ex vivo* may be due to the additional pro-inflammatory and pro-coagulant effect of the *ex vivo* perfusion setting itself. As the activation pattern *in vivo* and *ex vivo* is comparable, we conclude that the use of an *ex vivo* system to assess strategies to prevent I/R injury in limb replantation, and potentially also in VCA and organ transplantation, is favorable and has a better 3R profile because both forelimbs of the animal can be used simultaneously.

Table 1 Tabulated summary of changes in clinical parameters and biochemical markers across both reperfusion settings. (*) means P value <0.05 versus control and (-) represents no difference from baseline. Both (↑) and (↑↑) indicate the extent of significant elevation from baseline.

Reperfusion method	Ex vivo		In vivo	
Ischemia time	1h (n=6)	9h (n=6)	1h (n=3)	9h (n=3)
Clinical parameters				
Reperfusion time (h)	12	8.58 (± 3.10)*	12	10.14 (± 3.22)
Limb weight ratio (Endpoint/Baseline)	1.01 (± 0.03)	1.23 (± 0.05)	1.12 (± 0.07)	1.37 (± 0.07)
Biochemical markers (change from baseline)				
Coagulation system (PAI-1-tPA, D-Dimer)	↑	↑↑	–	↑
Complement system (C3a, C5a, sC5b-9)	↑	↑↑	–	↑
Pro-inflammatory cytokines (IL-6, IL-8, IL-1β, TNF-α)	↑	↑↑	–	↑
Anti-inflammatory cytokines (IL-10)	–	–	–	–
Vascular growth factors (PDGF, VEGF, bFGF)	–	↑	–	↑
Muscle damage markers (CKMM, MCP-1)	↑	↑↑	–	↑
Immunofluorescence (difference in intensity at endpoint of control and ischemic groups)				
Complement C3b/c	–	↑	–	–
E-Selectin	↑	–	↑	–

POS008 EVALUATION OF EPIDEMIOLOGICAL FEATURES OF PERMANENT HYPOPARATHYROIDISM PATIENTS WHILE AS A CANDIDATE OF PARATHYROID TRANSPLANTATION

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Background: Permanent hypoparathyroidism causes a significant decrease in quality of life. Data from the field studies indicate that palliative treatment is not sufficient for the symptoms of permanent hypoparathyroidism. National and international guidelines and, literature has no defined guidelines for the etiology of the disease and socioeconomic effects.
Methods: The parathyroid transplantation waiting list was evaluated etiologically, socioeconomically, and retrospectively.
Results: Between January 2013 and December 2020, 304 patients who enrolled for parathyroid transplantation were found eligible and 93 of them transplanted since, with an average waiting time of 48 months. The average duration of hypoparathyroidism before enrolling on the transplantation list was 118 months. Currently, 211 patients were still waiting for parathyroid transplantation. The 178 of these patients (84.4%) were female and 33 were male (15.6%). The 128 patients (61%) were between 30 and 49 years old. Currently, there were 197 people (93%) waiting for their first transplantation, 14 people (7%) waiting for their second transplant, among them six patients had a high PRA (2000>MFI).
The etiology of hypoparathyroidism was iatrogenic in 197 (94%) of the patients, autoimmune in 3%, idiopathic in 1%, and congenital in 2% patients. The mean daily calcium intake was 2448.4mg (highest 15000mg/daily, lowest 500mg/daily), the daily calcitriol intake was 0.98mg (highest 6mg and lowest 0.1mg) and the daily cholecalciferol intake was 2022.9mg (105600mg maximum and 100mg lowest). The 25 (12.8%) of the patients needed regular intravenous (IV) injections of calcium treatment, which means hospitalization.
Conclusions: Permanent hypoparathyroidism has an elevated socioeconomic cost, affecting particularly young people needing daily supplementations of calcium and vitamin D, with the necessity of hospitalizations in 12.8% of the patients. Parathyroid transplantation is the most effective curative treatment option. We suggest that a scoring system may be used for prioritizing patients on the waiting list, estimated from variables including the etiology of hypoparathyroidism, patients' age, oral dose per medicine, frequency, and dosage of IV calcium intake.

POS009 NON-INVASIVE IMMUNE MONITORING OF COMPOSITE TISSUE ALLOGRAFTS IN A TRANSLATIONAL LARGE ANIMAL MODEL

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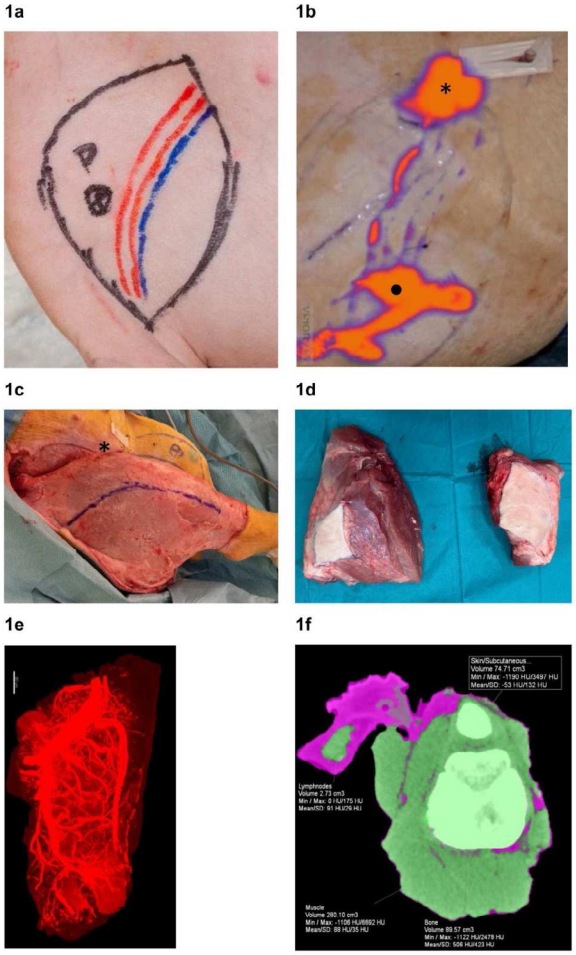
Background: Widespread application of vascularized composite allotransplantation (VCA) is limited by immunosuppressant toxicity. The diagnosis of rejection VCA recipients relies on biopsies which can risk complications and compromise graft integrity. Optical monitoring techniques and skin and serum protein levels can be measured without damaging graft tissue. Analysing non-invasively collected data through computational modelling may generate tissue profiles allowing for improved monitoring and diagnosis of rejection.

Methods: Heterotopic hindlimb transplants were performed in fully mismatched miniature swine. Control animals received no immunosuppression, and tacrolimus-based immunosuppression with consecutive withdrawal, inducing repeat rejection episodes, was administered in a study group. Multimodal imaging techniques including infrared (IR) thermography and 3-charge coupled device (3CCD) were used to monitor tissue perfusion and surface oxygenation, respectively. Raman spectroscopy was used to evaluate the molecular composition of the skin component, and serum Luminex analysis provided trends in cytokine levels.
Results: 3CCD imaging demonstrated decrease in Red minus Blue channel (R-B) intensity from post-recovery value by a mean 24-pixel units at rejection. IR thermography imaging shows decreased temperature at rejection of 4.3°C preceded by a temperature increase, recovering with immunosuppression. Raman spectra of rejecting graft skin show changes in spectral signatures suggestive of increased collagen IV content. Among rejection controls, decreases in serum cytokines IL-12, IL-8, and IFNγ were noted to precede peak of rejection episodes. In animals on pulsed immunosuppression, similar trends were noted with decreases in IL-8, IFNγ, and IL-12 prior to onset of severe clinical rejection requiring rescue with immunosuppression.
Conclusions: Non-invasive imaging techniques detect changes in oxygenation and perfusion of VCA. 3CCD and IR thermography demonstrate enhanced contrast during rejection compared to digital imaging. Potential biomarkers of early rejection have been identified via Raman spectroscopy and Luminex cytokine analysis. Computational modelling of these data may provide insights into less invasive identification strategies for VCA rejection.

Figure 1



POS010 IMPROVING THE TECHNIQUE OF A HETEROTOPIC VASCULARIZED COMPOSITE HINDLIMB ALLOTRANSPLANTATION IN THE PIG

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Background: Although clinically vascularized composite allotransplantation (VCA) has developed rapidly in the last years, numerous unanswered research questions remain. A composite porcine hindlimb flap, heterotopically transplanted into a flank pouch of the recipient, has been described as a VCA model, but it is bulky and does not include relevant immunological tissues. The aims of our study were (1) to adapt this model to reduce bulkiness and (2) to include graft-draining lymph nodes, and compare the two models surgically and anatomically.
Methods: For model development, we conducted an anatomic study by harvesting 11 porcine osteo-myocutaneous flaps, 4 with the conventional and 7 with the modified technique. Flaps were characterized using conventional and angiographic CT scanning. Additionally, *in vivo* heterotopic transplantations were performed in 8 Swiss landrace pigs. Animals were followed up until at least grade 3 rejection. No immunosuppressive treatment was applied.
Results: In the anatomical study, the mean weight of the flaps with the conventional technique was 1710 g (range 1564–1961 g), corresponding to 4.2 $\pm$ 0.38% of total body weight (TBW). The flap weight was significantly reduced with the modified technique with a mean weight of 831 g (range 538 - 1080 g), corresponding to 1.8 $\pm$ 0.18 % TBW (p <0.0001). The muscle/bone ratio was reduced with 2.92 $\pm$ 0.14 (modified) vs. 8.24 $\pm$ 2.71 (conventional) (p = 0.03). Angiography revealed complete vascularization of the tissue including the lymph nodes in the modified flap.
Histologically, graft draining lymph nodes showed no signs of ischemia.
Conclusion: By modifying the surgical technique, the bulkiness of the flap was markedly reduced, without impairing its vascularization and reliably including vascularized graft-draining lymph nodes. Thus our modified VCA model in the pig presents distinct advantages to the previously described model and should be preferred in hindlimb pig VCA.

POS011 AUTOTRANSPLANTATION OF UTERUS ON ANIMAL MODEL PRELIMINARY TO CLINICAL APPLICATION

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Background: Uterus transplantation is a "purpose" transplant, functional to achieve pregnancy in patients with absolute uterine infertility and not a life-saving transplant. Its introduction into the clinic practice requires careful planning that cannot be separated from an experimental phase on an animal model.
Methods: The initial phase of the uterus transplant protocol in the mini-pig that we have developed involves an autotransplant model, to become familiar with the more complex procedure of uterine transplantation. After isolating the internal and external ureters and iliac arteries, we isolated the uterine artery and uterine veins. The vagina and uterine vessels were dissected and the uterus retrieved. During the back table surgery, the uterus was perfused with Celsior's solution and intrauterine circles were evaluated. Trucut uterus biopsies were performed before clamping, at the end of perfusion with Celsior, after 1 hour of cold static storage, and after reperfusion. The uterine vessels and vagina were re-implanted on the resection abutments.
Results: At the reperfusion vessels were patent and the reperfusion was homogeneous. The overall operating time was 11 hours. The first warm ischemia time was 2-minutes. The second warm ischemia was 45 minutes. At the biopsies no relevant histological changes between the various phases.

Conclusions: Surgery on an animal model is preparatory for clinical activity on a human being.

POS012 NEW SURGICAL APPROACH TO USE HUMAN ALLOGRAFT AS BIOLOGICAL DRESSING IN PATIENTS WITH EPIDERMOLYSIS BULLOSA (EB)

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Background: Despite of the progress in the field of surgery and tissue engineering, chronic wounds remain to be the challenge for modern medicine. There is currently no effective treatment for patients with EB. We would like to introduce the new innovative transplantation approach, which is the use of allogeneic human skin graft from cadaveric donors with MSCs in wound healing. The aim of the study it to evaluate of the safety and efficacy of the allotransplant during clinical trials phase I/II study in Patients with EB as the ATMP.
Methods: Preclinical research was conducted on the group of 6 qualified and approved volunteers Patients with EB. BIOOPA is allogeneic, acellular human skin equivalent seeded with Wharton jelly - multipotent stem cells (WJ-MSCs). It is a matrix of decellularized superficial cadaveric human skin layers, which had been seeded with 30 million WJ-MSCs. Currently BIOOPA (grantno.STRATERMED2/269807/14/NCBR/2015) is in the second year of observation as a part of the clinical study. It has been approved by National Authority the Ethics Committee (EduraCT 2018-003890-91).
Results: Preclinical data off all examination techniques has demonstrated allograft infiltration by the host cells and neovascularization of the biological dressing. BIOOPA has been characterized with low immunogenicity. This had been confirmed in immunostaining/histopathology examinations, as well as the in vitro T-cell proliferation tests. BIOOPA dressing indicates to be safe and efficient, which has been observed over the 6-months follow-up period.
Conclusions: Results of the BIOOPA study research, proves this dressing not only to improve the quality of life of the study subjects, but also to be safe and effective. Preliminary results of our clinical trial suggest that BIOOPA might be a promising and alternative method for clinicians in the search for treatment of the chronic wounds especially in the immunocompetent Patients.

POS013 EFFICIENT RECELLULARIZATION OF HUMAN VASCULAR GRAFTS WITH PATIENT DERIVED ENDOTHELIAL CELLS

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Background: In transplant surgery, the endothelial lining is the first barrier between the donor and recipient. Damaged endothelium reveals extracellular membrane (ECM) molecules that can start thrombosis, aggravate inflammation and cause rejection. Endothelial repair strategies may improve transplant outcomes. Re-endothelialization of acellular blood vessels using kidney-vein endothelial cells (EC) was used to establish a research platform for endothelial repair strategies.
Methods: Human common iliac veins (CIV) ($n = 19$) from deceased healthy donors were decellularized by submersion in Triton X-100 (4%), ammonia (1%) and DNase, and used as a scaffold for vascular endothelialization and functional analysis. Efficiency of decellularization was checked by residual DNA content analysis and histology. Decellularized CIV were subsequently repopulated with human umbilical vein endothelial cells (HUVEC) or patient derived kidney-vein EC at concentrations of $2{\cdot}10^5$, $4{\cdot}10^5$ or $1{\cdot}10^6$ cells/cm^2 under static conditions. The re-endothelialised veins were analysed using confocal microscopy for EC confluency. Restoration of the EC barrier was analyzed using trans-endothelial electrical resistance (TEER).
Results: The CIV were fully decellularized, demonstrated by the complete removal of cellular components, and the removal of dsDNA (before: 83.8 ± 29.0, after:13.0 ± 6.5 ng/mg). Histological integrity was preserved, as well as ECM polysaccharides (0.23 ± 0.14 μg/mg wet weight). Confocal microscopy showed the formation of a confluent monolayer of cells as soon as 24 hours after seeding for the highest EC concentration. Repopulated CIV scaffolds remained fully confluent for up to 28 days. After 10 days, the $4{\cdot}10^5$ or $1{\cdot}10^6$ cells/cm^2 concentrations had TEER measurements above background of 5.0 ± 2.9 Ω·cm^2 and 15.1 ± 12.2 Ω·cm^2 respectively ($n = 4$) indicating the maintenance of the barrier function. Vascular remodelling and proliferation associated genes showed a higher mRNA expression in EC on CIV scaffolds compared to EC grown on plastic dishes.
Conclusions: We developed an efficient procedure to decellularize human CIV and generated functional and long-term stable re-endothelialized veins using patient derived kidney-vein EC. This research platform will enable the study of re-endothelialization mechanisms.

POS014 AN ETHICAL FRAMEWORK FOR CONSIDERING LISTING FOR KIDNEY TRANSPLANTATION FOR PATIENTS WHO DECLINE SARS-COV-2 VACCINATION

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Background: As SARS-CoV-2 vaccines have started to be rolled out, a key question facing transplant units has been whether listing for transplantation should be contingent on recipients having received a vaccine. We aimed to provide an ethical framework when considering potential transplant candidates who decline vaccination.
Methods: We convened a working group comprising transplant professionals, lay members and patients, and undertook a literature review and consensus process. This group's work was also informed by discussions in two hospital clinical ethics committees.
Results: Arguments in favour of mandating vaccination prior to transplant listing include:
-A duty to protect patients from avoidable harm
-A duty to protect others
-Consideration of the appropriate use of the scarce resource of donor organs
-Parallels with precedents predicating transplantation listing on aspects of patient choice or behaviour
However, this needs to be balanced against the following arguments against taking such an approach:
-Protecting individual autonomy and respecting patient choice
-As vaccine hesitancy is particularly common in certain patient groups, including those of BAME backgrounds, mandating vaccination may systematically exclude patients who are disadvantaged in access to transplantation, and further undermine trust
-Practical difficulties with adopting a blanket approach, including questions regarding the impact of new variants, and of falling community prevalence of the virus
Conclusions: Rather than mandating that all patients must receive the SARS-CoV-2 vaccine prior to transplant listing, we recommend considering vaccination status as one of a number of SARS-CoV-2-related risk factors in relation to transplant listing. Transplant units should engage in individualised risk-benefit discussions with patients, avoid the language of mandated treatments, and strongly encourage uptake of the vaccine in all patient groups, using tailor-made educational initiatives.

POS015 A SYSTEMATIC REVIEW OF ETHICAL ISSUES IN ORGANOIDS RESEARCH FOR USE IN TRANSPLANTATION

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Background: Organoids are defined as 3D structures, grown from clusters of organ-specific cells derived from pluripotent stem cells taken from human tissue. Organoids are in vitro miniature versions of human organs, that are similar to human organs both in architecture and in physiology. Organoids have the potential to revolutionize biomedical research and clinical care. In the future, organoids may be used as a source of functional tissues and organs for transplantation in human patients. However, organoids should not be seen as morally neutral, because they are grown from human

tissues, and donors may perceive a personal connection with their organoids. Although ethical issues related to potential future clinical applications of organoid technologies have been discussed in 56 scientific articles, a systematic literature review of the ethical issues has not yet been published.
Methods: In this presentation, we present the results of the systematic literature review focused on the ethical issues on the use of organoids in transplantation in humans, which was conducted in the context of the EU-funded VANGUARD project.
Results: A total of 6 scientific peer-reviewed articles have been written about this topic. Multiple articles argue that first-in-human organoid transplantation trials would require a careful examination of specific ethical challenges, such as the balance of risks and benefits, participant selection, trial design and informed procedures. Several articles argue that traditional first-in-human trial designs might expose participants to unnecessary and unjustified risks, due to the invasiveness of organoid transplantation coupled with the lack of in vivo data on humans.
Conclusions: We recommend a proactive interdisciplinary dialogue to stimulate responsible clinical research and innovation in the field of organoid transplantation.

POS016 THE INFLUENCE OF SOCIOECONOMIC FACTORS ON ORGAN DONATION IN IRAN: FINDINGS FROM A SINGLE CENTER STUDY

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Introduction: The shortage of organ donation is a global issue, persisting in all countries. The number of organ donors is insufficient to accommodate the current demand. The purpose of this study was to identify the socioeconomic factors that influence decisions toward organ donation and transplantation from the families of brain-dead patients.
Method and Materials: This retrospective cross-sectional study was performed on 333 actual donors from 2017 to 2019 in Sina Organ Procurement Unit (Sina OPU), Tehran, Iran. Two trained researchers conducted the interviews of all the brain-dead cases' families. The data were analyzed by descriptive and inferential statistics using SPSS ver. 16.
Results: The mean age of the donors were 37.23 $\pm$ 16.59. Most donors had low levels of education, while their families' education levels were reported at moderate levels. More than half of the organ donors were from low socioeconomic status, which nearly half were sole income earners of large families. In addition, significant differences were found in relation to the donors' level of formal education ($p < 0.000$), income (0.000), gender (0.045) and occupation (0.037). Moreover, among the brain dead donors, trauma was the most common cause of death (44.6%).
Discussion: The socio-cultural level of the donor's residency and availability of social services play an important role in organ donation. Consequently, adequate support for the deceased's family after organ donation is imperative.

POS017 QUALITY OF LIFE (QOL) OF RENAL DONORS COMPARED TO FIRST-DEGREE RELATIVES OF HAEMODIALYSIS PATIENTS (THE HIDDEN PATIENT)

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Background: More than 20% of living related transplants are prevented due to the preconception that donating will deteriorate the health of their relative. However, in one study, Sajadi et al concluded that the "family caregivers are considered as hidden patients experiencing physical and mental disorders". We hypothesised that the relatives who donated may have a higher QoL compared to first degree relatives (potential donors) of dialysis patients. The present study is the first in the Middle East to compare the QoL of donors to QoL of relatives of dialysis patients.
Methods: The study was conducted prospectively at Sheikh Khalifa Medical City (SKMC) transplant unit (Group 1: renal donors; 6 months-9 yrs. post donation) and SKMC dialysis unit (Group 2: potential donors, i.e. the first-degree relatives of current dialysis patients), in Abu Dhabi, UAE from July 2019-December 2020. All 40 participants for each group were chosen by convenience sampling. The QoL for both groups was assessed using the short form-36 (SF-36), a validated standardised questionnaire containing eight different scales of measurement. The survey was administered by two researchers independent of the renal transplant team and the dialysis unit.
Results: The median age of Group 1 was 40.5 yrs. (IQR 32.5- 46.5) whereas the median age of Group 2 was 37.5 yrs. (IQR 31.5- 50.5). The median time on dialysis for the affected family member was 3.46 yrs. (IQR 2.0–7.4).
We found that Group 1 reported a better overall QoL when compared to Group 2, regardless of age, gender, or nationality. This was found to be the case for all eight scales of SF-36 ($p < 0.001$; independent t test; See table).
Conclusions: Our findings show that the QoL of dialysis relatives is significantly worse than donors. The dialysis relatives were found to be suffering emotionally and physically due to the stresses associated with caregiving for a diseased family member. On the other hand, the donors enjoyed a better QoL due to minimal surgical complications and comprehensive care from the renal transplant program, which is supported and funded at the federal level by the UAE government.

SF-36 SCALES: GROUP 1 VS GROUP 2

Variable	GROUP 1 (donors)			GROUP 2 (dialysis relative)					
	n	Mean	SD	n	Mean	SD	Difference	95% CI	P [a]
Emotional limitation	40	94.16	16.69	40	63.33	41.89	-30.83	-45.03 to -16.63	<0.0001
Emotional well-being	40	88.80	11.28	40	67.10	21.77	-21.70	-29.42 to -13.98	<0.0001
Energy fatigue	40	84.00	16.61	40	56.62	20.61	-27.37	-35.70 to -19.04	<0.0001
General health	40	90.50	10.90	40	64.18	20.60	-26.31	-33.65 to -18.97	<0.0001
Pain	40	91.31	14.76	40	68.43	26.28	-22.87	-32.36 to -13.38	<0.0001
Physical function	40	96.75	5.83	40	77.37	22.67	-19.37	-26.74 to -12.00	<0.0001
Physical limitation	40	95.62	19.51	40	76.87	31.20	-18.75	-30.33 to -7.16	0.0019
Social Functioning	40	93.68	16.09	40	63.58	23.11	-30.10	-38.96 to -21.23	<0.0001

POS018 CRM AS CRITERIA FOR SELECTING ORGAN PROCUREMENT COORDINATORS

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Background and Aims: Deceased patients with brain or circulatory death are the major sources of transplantable organs. In any country with opt-in system, a family interview is held to seek consent. Even in presumed-consent systems, family approach is recommended. Health care professionals cannot simply break the bad news of someone's death, they must stay to then propose a new request: organ donation. Any communicative mistakes may lead to family refusal (FR). The question is: What are the *modifiable* reasons of FR? With the same level of training, *why* do some of organ procurement coordinators (OPC) have constantly better results in family approach?
Methods: A literature review with advanced search strategies and related mesh terms was done. The study period was limited to past 20 years.
Results: Rates of consent remain suboptimal and FR is the most important reason for one third to half of failures. All the factors with an impact on FR in related articles have been searched and summarized in the Table 1:

Table 1

Authors & country	Positive on consent	Negative on consent	No effect
(Frates & Bohrer2002) USA		Hispanics community	
(Noury et al., 2003) France	Brain death, Donor card, Initial family hesitation	Circulatory death, age, religious beliefs, death etiology, the interviewer	
(Singh et al., 2004) India		Superstitions on reborn with missing organ 40% dead relatives not free from the cycle of life-death-rebirth 26%, delay in funeral 23%, no consensus in family 17%, fear of social criticism 10%, dissatisfaction with hospital 10% unaware of deceased's wishes 6%	
(Frutos et al., 2005) Spain	wishes of the deceased, attitudes of relatives, hospital personnel, stroke	wishes of the deceased, attitudes of relatives hospital personnel brain trauma	
(Andres et al., 2009) Spain	Circulatory death	Brain death	
(Moraes et al., 2009) Brazil	collateral relative (sibling/uncle) or children responsible for the decision	violent death young patient age parental donation	
(Dehghani et al., 2011) Iran		denial of brain death, belief in miraculous recovery, fear of gossip on selling organs, deformation of the body	
(Le Nobin et al., 2014) France		keep body intact, suddenness of death	
(Henon, F., et al. 2016) France		Donor's refusal 39%, integrity of the body 28%, religious order 11%, suddenness of death 9%, denial of death 6%, early age 5%	
(Cheung et al., 2016) Hong Kong		Active intervention at donation process	
(Siminoff et al., 2017) USA			Circulatory or brain death
(Piemonte et al., 2018) Italy	ICU team education	Older age of BD, ICU Lon stay	
(Leblebici, 2020) Turkey		religious concerns distrust in health system	sociodemographic length of ICU stay, decedent's wishes time of interview
(Kananeh et al., 2020) USA	Non African Americans	African Americans Completion of apnea testing	gender, admission diagnosis, number of examinations or completion of a confirmatory test

Different factors mentioned in different studies to affect family consent for Organ donation.

These different factors can be grouped into three categories of situational, family related and coordinators' factors, but no explanation found on the source of different success rates in OPCs. Non-technical skills complement technical skills. The level of situation awareness, decision-making, communication, teamwork, leadership, managing stress and coping with fatigue, are fundamentally different between OPCs. Searching literature with keywords of "organ procurement" and "resource management" revealed as few as 3 papers. At best, they suggested a new model for continuous education and audits.

Conclusion: Many papers have searched the reason of FR. None can explain the individual differences between OPCs in their success rates. Non-technical skills, borrowed from Crew Resource Management (CRM), can elucidate the roots of these differences. CRM training and evaluating agenda can function as screening criteria to help selecting the best suited candidates for procurement coordinator. This new way of viewing CRM as a screening tool for selecting best possible OPCs, can reduce error, avoid stress, increase efficiency, and save more lives.

POS019 WHAT ARE THE PSYCHOSOCIAL FACTORS INFLUENCING ACCESS TO KIDNEY TRANSPLANTATION AND TRANSPLANT OUTCOMES FOR CHILDREN? A SYSTEMATIC LITERATURE REVIEW

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Background and Aims: Kidney transplantation is often seen as the gold standard treatment for children and young people (CYP) with End Stage Kidney Disease (ESKD), in terms of reducing mortality and optimising quality of life (QoL). However, psychosocial factors have been cited as a barrier to accessing a kidney transplant, although it is unclear what these factors are.

This study explores and identifies the range of psychological and social factors that influence how soon a CYP with ESKD can access a kidney transplant using a systematic literature review. This includes factors that influence kidney transplantation outcomes and factors deemed important to patients and their families in terms of their QoL.

Methods: We included quantitative, qualitative and mixed-method studies that were peer-reviewed and included primary data. Medline, PsychInfo, CINAHL and Web of Science were searched for papers published in English between January 1964 and September 2020.

Results: After removing duplicates, a total of 6223 studies were retrieved through database search. A total of 48 studies remained after screening against inclusion criteria. There were 40 quantitative, 6 qualitative and 1 mixed-method study. Most study designs were retrospective longitudinal registry studies. Factors influencing access to transplantation included maternal education, social support network and therapy non-adherence. Race, socioeconomic status and geographic remoteness were often cited as responsible factors. Although factors such as anxiety, depression, avoidant coping strategies were described in the literature with relation to patient family experience and wellbeing, evidence linking these with accessibility or outcomes of a kidney transplant in children was limited.

Conclusions: Longitudinal and prospective studies are needed to fully assess the relationship between psychological factors, its' interplay with social factors and a CYP's subsequent access to or outcomes after kidney transplantation.

POS020 FROM THE WAITING LIST TO TRANSPLANTATION: HOW IS PATIENT'S PERCEPTION OF PROFESSIONALS EVOLVING ALONG THE WAY?

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Introduction: Attitude of professionals as perceived by patients plays an important role in any disease. Perceiving treatments and care givers as qualified enables patients to better cope with their condition.

Methods: Two online questionnaires were developed, one for waitlisted patients, the other for transplant recipients. Specific questions for each target group were designed and organized so as to ensure anonymity, standardization, comprehensibility and adherence to the study goals. The questionnaires feature 19 questions each, also covering patient-perceived professional attitude along care pathway. The questions are mostly closed-ended and multiple-choice, in order to ensure a smoother investigation and a higher completion rate. Three questions are, on the other hand, open. Of these, the last one offers participants the opportunity to express their opinion freely.

Results: From April to December 2020, 3074 participants filled the questionnaires, including 1138 waitlisted patients and 1936 transplant recipients (Table 1). In 53.3% of cases caregivers are perceived as "extremely professional" by transplant patients or "very professional" in 38.7% of cases. Therefore, the overall opinion is very positive (92%). The data are common to all types of transplant. However, the perception reported by waitlisted patients is sharply different. A mere 10.5% consider caregivers to act in an "extremely professional" manner and 33.7% in a "very professional" one. Among them, the positive perception of professionalism drops to 44.2% and even more among kidney patients (37.8%).

Conclusions: A successful transplant meets patient's main need, namely re-gaining health. This aspect alone can positively affect the perception, just as long waiting time can influence negatively the perception by renal waitlisted patients. However, these views, albeit subjective, are also affected by how caregivers approach the patient and by the specific context in which they act. Therefore, such a good perception of professional attitude by transplant recipients has to be acknowledged as a big achievement by transplant centres and their outpatient units and it represents a step forward in improving quality of the donation-transplant process.

Table 1. Perception of professional attitude of caregivers while being treated

Answer	Transplanted recipients		Waitlisted patients	
	n. cases	Ratio	n. cases	Ratio
extremely professional	1031	53,3 %	120	10,5 %
very professional	749	38,7 %	383	33,7 %
moderatly professional	108	5,6 %	398	35,0 %
sufficiently professional	39	2,0 %	143	12,6 %
not professional at all	9	0,5 %	94	8,3 %

POS021 MEDICATION ADHERENCE IN KIDNEY TRANSPLANT PATIENTS: SINGLE CENTRE COMPARISON BETWEEN PATIENTS 12–18 MONTHS AND AT LEAST 7 YEARS POST-TRANSPLANT

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Background: Adherence to immunosuppressive medication (IS) plays an important role in kidney transplant outcome and graft survival. Published research suggests a high prevalence of nonadherence among renal transplant patients. The purpose of this study was to investigate whether IS adherence varies between patients 12–18 months post-transplant and long-term kidney recipients at least 7 years post-transplant.
Methods: Between 01/01/2019-01/02/2020 kidney transplant recipients between 12-18 months post-transplant and all long-term transplant recipients (LTR) attending Transplant Clinic completed screening questionnaires. These included (i) Medicines Adherence Report Scale (MARS) and (ii) Beliefs about Medicines Questionnaire (BMQ).
Results: $n = 52$ transplant recipients between 12–18 months post-transplant completed the questionnaires. Of these 29 (53.7%) were male and 23 (42.6%) were female. The median age was 48.4 years (range 21–72 years). $n = 231$ LTR completed the questionnaires. Of these 148 (64.1%) were males and 83 (35.9%) females. The median age was 53.15 years (range 20–79 years). A Mann-Whitney U test revealed a statistically significant difference in adherence between groups, with patients 12–18 months post-transplant reporting significantly better adherence compared with LTR ($p = .040$). Results are presented in Table 1.
Conclusion: Our comparative analysis identified a statistically significant difference in IS adherence between patients 12–18 months post-transplant and LTR. These findings highlight the need for adherence support for all transplant patients regardless of the time since transplant in order to optimise graft survival. Further interrogation is necessary to identify potential factors contributing to nonadherence.

Table 1 A comparison of characteristics and MARS scores between groups

	12–18 months post-transplant (n = 52)	Over 18 months post-transplant (n = 231)
Gender, *n* (%)		
Male	29 (53.7)	148 (64.1)
Female	23 (42.6)	83 (35.9)
Age in years, M (*SD*); range	48.4 (14.21); 21–72	53.15 (12.71); 20–79
Mean MARS score (range)	29.50 (28–30)*	29.10 (17–30)*
Mean rank	157.19	134.16

Note. *$p < .05$.

POS022 THE FIRST ITALIAN UTERUS TRANSPLANTATION DURING COVID-19: A PSYCHOLOGICAL AND PSYCHIATRIC EVALUATION IN FIVE CANDIDATES

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Background: A uterus transplant is a life-giving transplant. Life with a transplanted uterus is a transactional life stage for both recipients and their partners. In Sweden, the birth of six healthy babies, born to five uterus transplant mothers, recently raised the hopes of thousands of women with absolute uterine factor infertility (AUFI) around the world. In Italy, at the transplant center of Catania (Sicily), in August 2020, during COVID-19, the first uterus transplant from a deceased donor was performed.
In the literature it is described that the main psychological problems can clearly concern various aspects: in vitro fertilization, uterus transplantation, complications with immunosuppressive treatment, embryo transfer, caesarean section, risk of pre-term birth, hysterectomy, etc.
Methods: Five young women with Mayer-Rokitansky-Kuster-Hauser syndrome (MRKH) were given the following tests: Millon Clinical Multiaxial Inventory III (MCMI-III) to evaluate personality characteristics and clinical syndromes; Symptom Checklist - 90 (SCL-90) for the analysis of psychiatric symptoms; Short Form-36 Health Survey (SF-36) to assess perceived quality of life; Machover and Baumtest tests to bring out unconscious contents, not easily verbalizable.
Results: Four out of five patients evaluated showed traits of alienation in interpersonal relationships, self-doubt, mild depression, anxiety and feelings of guilt. All patients showed emotional inhibition and need for support. The prevailing personality trait was the obsessive one. The perceived quality of life did not appear to be compromised. At the post-transplant interview, the woman recalled the most salient moments before and after surgery. A state of emotional balance and good mental compensation emerged, despite the general state of alert and apprehension due to the COVID-19 pandemic.
Conclusions: The role of psychological-psychiatric evaluation in uterus transplantation is to choose those candidates who will be better able to face all unexpected difficulties and complications, including the potential failure of the entire treatment with a seriously negative impact on psychological health.

POS023 EPIDEMIOLOGICAL STUDY OF TRICUSPID REGURGITATION AFTER CARDIAC TRANSPLANTATION. DOES IT INFLUENCE SURVIVAL?

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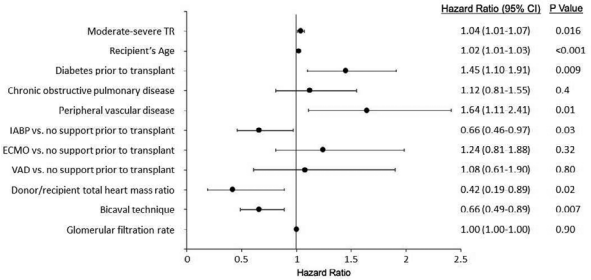
Backgorund: Tricuspid valve disease is the most frequent valvulopathy after heart transplantation (HTx). There is controversy about its relationship with survival. The aim of this study was to analyze its causes and implication in overall mortality.
Methods: this is an observational, retrospective study of all the transplants performed from 2000 to 2019 in two Spanish centers. Retrasplants, pediatric population, combined transplant and deaths in the first three days were ruled out (1009 patients included). Two groups were compared: 1-Patients without tricuspid regurgitation (TR) or mild (809), and 2-Patients with moderate or severe TR (200).
Results: The prevalence of TR was 19.8%. The probability of death was greater when TR was caused by early primary graft failure (PGF) or rejection ($p < 0.05$). The incidence was related to etiology: TR related to PGF showed an early wave while those due to rejection and undefined causes showed a first initial wave (first year), an intermediate one (10–14 years) and a long term one (16–18 years). The variables associated with the development of TR were the age of the recipient (inverse relationship), age of the donor, female donor sex and time of ischemia (direct relationship). In multivariable analysis, TR was significantly associated with mortality/retransplantation (OR: 1.04, 95% CI:1.01–1.07, p:0.0016).
Conclusion: The prevalence of TR after heart transplantation is close to 20%. The annual incidence depends on its severity and etiology. This valve disease in severe degree determines a higher probability of death when it is due to primary graft failure or rejection.

Table. Characteristics of tricuspid regurgitation in transplanted patients according to the etiological types

	Primary Graft Failure (n : 35)	Acute rejection (n : 64)	Undefined (n : 72)	Other (n : 29)	P Value
Prevalence, n (%)	35 (17.5)	64 (32.0)	72 (36.0)	29 (14.5)	0.008
Grading of TR					0.01
Moderate	19 (54.3)	40 (62.5)	58 (80.6)	16 (55.2)	
Severe	16 (45.7)	24 (37.5)	14 (19.4)	13 (44.8)	
Right ventricular dilatation	20 (57.1)	15 (23.4)	11 (15.3)	13 (41.8)	<0.001
Right ventricular dysfunction	31 (88.6)	32 (50.0)	9 (12.5)	14 (48.3)	<0.001
Left ventricular dysfunction	8 (22.9)	21 (32.8)	1 (1.4)	4 (13.8)	<0.001
Echocardiography time course					0.01
Improvement	29 (82.9)	46 (71.9)	58 (82.9)	16 (55.2)	
Stable	6 (17.1)	12 (18.8)	12 (17.1)	8 (27.6)	
Deterioration	0 (0.0)	6 (9.5)	0 (0.0)	5 (16.2)	
Congestive signs	14 (40.0)	42 (65.6)	22 (30.6)	12 (41.4)	0.001
Clinical course of congestive signs					0.005
Improvement	9 (64.3)	23 (54.8)	15 (68.2)	5 (41.7)	
Stable	1 (5.0)	14 (33.3)	6 (27.3)	1 (8.3)	
Deterioration	0 (0.0)	5 (11.9)	1 (4.5)	6 (50.0)	
Number of diuretics					<0.001
0	17 (48.6)	23 (35.9)	47 (65.3)	13 (44.8)	
1	18 (51.4)	29 (45.3)	21 (29.2)	10 (34.5)	
2	0 (0.0)	11 (17.2)	4 (5.6)	3 (10.3)	
3	0 (0.0)	1 (1.6)	0 (0.0)	3 (10.3)	
Treatment					<0.001
No/symptomatic	0 (0.0)	2 (3.1)	71 (98.6)	16 (55.2)	
Etiological	35 (100.0)	61 (95.3)	0 (0.0)	11 (37.9)	
Retransplantation	0 (0.0)	1 (1.6)	0 (0.0)	1 (3.4)	
Coronary stent	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.4)	
Annuloplasty	0 (0.0)	0 (0.0)	1 (1.4)	0 (0.0)	
TR: Tricuspid Regurgitation					

Figure Variables associated with mortality/transplantation



IABC: Intra-Aortic Balloon Counterpulsation; ECMO: Extracorporeal Membrane Oxygenation; VAD: Ventricular Assist Device; MCT: Total Cardiac Mass.

POS024 REDO-STERNOTOMY IN HEART TRANSPLANTATION – OUTCOMES FROM THE SCOTTISH NATIONAL ADVANCED HEART FAILURE SERVICE

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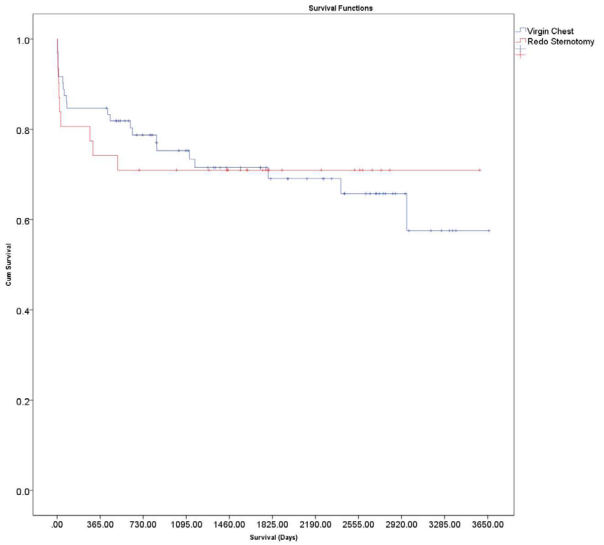
Background: Heart transplant recipients with previous cardiac interventions often have poorer outcomes postoperatively. This could be due to increased technical difficulty, subclinical deconditioning, bleeding and infections. We analysed the results from our institution to ascertain short and long-term outcomes in these patients.
Methods: 103 adults underwent heart transplantation in our institution between January 2011-January 2020. Recipients were divided into 2 groups: Virgin chest (first sternotomy group; $n = 72$(69.9%) and those with at least 1 prior sternotomy (redo sternotomy group; $n = 31$(30.1%). Univariable analysis was performed using T test and Chi-squared test. A time to event analysis was used to depict long-term outcomes between the groups. Outcomes of interest were post-operative ECMO, Length of stay, 30-day mortality and 1-year survival.
Results: There was a trend towards higher number of patients with ischaemic aetiology and mortality within the first 30 days in the redo sternotomy cohort. There was also a trend towards a younger donor age for these recipients, which may partly explain the equivocal findings.

Description	Virgin chest ($n = 72$)	Redo-sternotomy ($n = 31$)	p-value
Recipient Age (years)	46.3 ± 12.2	44.8 ± 11.8	0.570
Preoperative Inotropes (%)	38 (52.8)	18 (58)	0.621
Preoperative IABP (%)	27 (37.5)	7 (22.6)	0.216
Height (cm)	172 ± 10.1	174 ± 8.2	0.376
Weight (kg)	76.9 ± 12.2	77.5 ± 11.7	0.828
Female (%)	23 (31.9)	5 (19.2)	0.076
Ischaemic Aetiology (%)	14 (19.4)	11 (35.5)	0.070
Donor Age (years)	43.3 ± 11.6	37.4 ± 11.5	0.067
Total Ischaemic Time (mins)	188.9 ± 64	194.1 ± 60.5	0.764
Cold Ischaemic Time (mins)	101.4 ± 45.8	117.0 ± 45.9	0.244
Post-operative ECMO	20 (27.7)	10 (32.2)	0.644
Bypass Time (mins)	226.8 ± 69.8	253.0 ± 105.1	0.299
30-day Mortality	6 (8.3)	5 (16.1)	0.101
1-Year Survival	61 (84.7)	23 (74.2)	0.162
Post-operative length of stay (days)	37.6 ± 22.7	33.4 ± 17.8	0.383

The Kaplan-Meier curve shows a steep drop within the first year in the redo sternotomy group but no differences were noted at up to 10 years follow-up (Log Rank $p = 0.974$)
Conclusions: There was no statistically significant increase in post-operative length of stay, mortality or post-operative ECMO rates in the redo sternotomy cohort in our study. This could be due to the preference towards younger donors in this cohort.



POS025 INVASIVE PULMONARY ASPERGILLOSIS AFTER HEART TRANSPLANTATION

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Background: Invasive pulmonary aspergillosis (IPA) is an infrequent but major complication of heart transplantation (HTx) and the aim was to estimate the frequency and to find the risk factors of its development.
Materials/methods: From 2010 to 2019 it was performed 137 HTx (46 ± 14 year-old; male – 113). All patients were managed by immunosuppression (steroids, tacrolimus, mycophenolic acid) plus induction (basiliximab/thymoglobuline). We retrospectively analyzed post-transplant results including laboratory and instrumental investigations.
Results: During the whole follow-up 58 episodes of pneumonia were diagnosed, 16 (28%) of them were IPA (from 33 to 64 year-old). During the first year after HTx the diagnosis was verified in 14 out of 16 patients: an increase in the positivity rate of the Aspergillus antigen in bronchoalveolar lavage from 1.45 to 10.2 was found. Specific changes on CT scans (ground glass opacity) were observed. In two patients, there were no diagnostic criteria for IPA; the diagnosis was based on the results of histological examination after resection of the lower lobe of the lung. All recipients were managed with voriconazole (2–6 months) with positive clinical outcomes in 81% (n = 13) of them. Adjunctive therapies included reduction of immunosuppressive therapy (dose adjustment of tacrolimus and mycophenolic acid) and colonystimulating factors for agranulocytosis. Three patients (n = 2 – in 1 month after HTx) died which was associated with sepsis and right ventricular heart failure, one – 4 months after HTx due to other infectious complications (bacterial causes). All patients had risk factors for the development of IPA: immunosuppression, including steroids (n = 16), prolonged stay in the ICU (n = 14), inotropic support for more than 2 days in the early post-transplant period (n = 10), cachexia (n = 6), leukopenia (n = 9) and neutropenia (n = 14).
Conclusions: In heart transplant patients the incidence of IPA among respiratory tract infections is 28%. The development of IPA was associated with a combination of risk factors: optimal selection of doses of immunosuppressive therapy, prevention of neutropenia. In challenging cases surgical interventions helps to differentiate the disease. Timely diagnosis of IPA allows initiating antimycotic therapy with positive clinical outcomes.

POS026 ARE HEART TRANSPLANT PATIENTS AT HIGHER RISK FOR MORTALITY FOLLOWING SARS-COV-2 INFECTION? SINGLE CENTRE EXPERIENCE

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Background: Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection in heart transplanted (HTx) patients may result in a more aggressive disease, due to the chronic immunosuppressed state of these patients. Aim of the study was to assess the incidence of the infection and the clinical course and outcome of HTx recipients followed at our centre.
Methods: Since February 2020 to February 2021, all patients positive to molecular swab, out of 357 HTx recipients of our HTx program, were enrolled. Testing was performed in case of fever, symptoms or positive contacts. For symptomatic patients, immunosuppressive therapy was modified, reducing basal immunosuppression, holding mycophenolate and introducing steroid therapy, according to ISHLT guidelines.
Results: In the first half of 2020, during nationwide lockdown, no patients have been recognised positive, vice versa in the second half of the year, 24 (7%) HTx recipients resulted to be infected. Only one (4%) became positive during the early post-HTx hospital stay. Twenty-three (96%) patients were male with a mean age of 62 ± 12 years. Most patients had comorbidities transplant- and age-related, as reported in Table 1.
Eight (33%) had an infected family member. Interestingly, 2 patients tested persistently negative despite an affected relative. Sixteen (67%) patients were symptomatic (fever, dyspnoea, cough), 11 (46%) were hospitalized, 7 (29%) required ICU stay and 6 (25%) mechanical ventilation. Three patients (13%) died of pneumonia: 2 of them were > 75 years old and transplanted 22 and 12 years ago, the last one, despite being younger (63 years old) and transplanted 9 years ago, had already a depressed ventricular function and a history of pulmonary infections at last follow-up. The early survivors were in good conditions.
Conclusions: Despite previous reports suggesting an increased incidence and mortality in transplanted patients, in our experience, following appropriate preventive measures and tailoring immunosuppression according to international guidelines, the rate of SARS-CoV-2 infection resulted comparable to the general population with an acceptable morbidity and mortality.

Table 1.

Patients demographics	N=24
Mean Age	62±12
Male	23 (96%)
Hypertension	8 (33%)
Diabetes	3 (13%)
Mean BMI	26±4
Obesity	3 (13%)
Dyslipidemia	11 (46%)
Peripheral vascular disease	4 (17%)
Previous stroke	3 (13%)
Liver disease	1 (4%)
Chronic Renal Insufficiency	9 (38%)
CAV (any grade)	8 (33%)
Neoplasia history	2 (8%)
Mean LVEF	66±7

POS027 COVID-19 AND CARDIAC TRANSPLANTATION. EXPERIENCE IN A TERTIARY HOSPITAL

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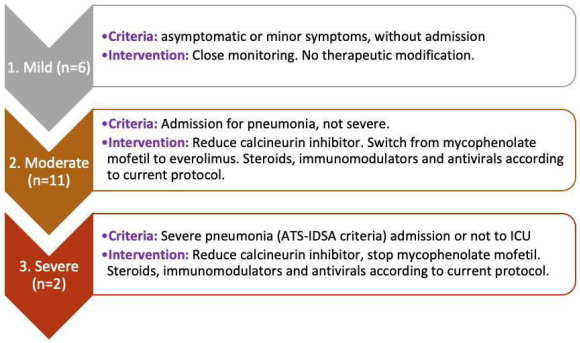
Background: Heart transplant (HTx) patients are a specially vulnerable group to COVID-19 while its treatment is more complex due to the challenge of simultaneously managing infection and immunosuppression to avoid rejection. The aim of this work is to present a series of cases of HTx with COVID-19 in a Spanish third level transplant hospital.
Methods: All consecutive HTx (>16y) with a diagnosis of COVID-19 from February 2020 to February 2021 were included. Patients were classified into 3 groups according to the severity of the disease and recommendations were made for immunosuppressive treatment according to the group (Figure 1).
Results: 19 HTx have suffered from COVID-19 to date (5% of 381 living HTx in our hospital). The first group includes 6 patients (31.6%) with mild symptoms. No change in treatment was made and no incidences have been reported. The second group includes most of the patients (11, 57.9%), all admitted for bilateral pneumonia requiring oxygen therapy in most cases. Mycophenolate mofetil (MMF) was suspended and everolimus was started by extrapolation, as it has shown a protective effect against viral infection due to cytomegalovirus. Their evolution has been favorable, with a mean hospital stay of 14 days, with no deaths. The third group, composed by 2 patients (10.5%) includes those with severe pneumonia criteria. MMF was discontinued. Both patients required mechanical ventilation in a critical care unit and finally died. According to the protocol in force at each time, steroids, immunomodulators or antivirals were associated in groups 2 and 3.
Conclusions: A significant number of HTx have been affected by COVID-19. Management of the infection should be based on a balance between reduction and adjustment of immunosuppression, strict control of the cardiological situation and treatment of the infection. It is necessary to assess and agree on whether these modifications in immunosuppression are associated with better outcomes in these patients.



POS028 SINGLE CENTRE EXPERIENCE OF ORGAN CARE SYSTEM FOR HEART TRANSPLANT

Guido Maria Olivieri, Massimiliano Carrozzini, Bruno Merlanti, Alessandro Costetti, Gaia Loperfido, Michela Cozzi, Mauro Carlo Bosi, Marco Lanfranconi, Aldo Cannata, Michele Giovanni Mondino, Claudio Francesco Russo

ASST Great Metropolitan Niguarda, Cardiothoracovascular Department, Milano, Italy

Background: The Organ Care System (OCS) is an ex-vivo normothermic perfusion device able to prevent the detrimental effects of cold ischemia on donor organs. We reviewed our experience with the use of this device for heart transplant (HTx).
Methods: This is a retrospective, single-centre study. From 2015 to 2020 we included in our analysis all donor hearts transported in the OCS.
Results: During the study period, out of 175 HTx, we applied the OCS in 9 (5%) cases. Organ retrievals and transports were safe, and the donor hearts were all transplanted. Reasons to use the OCS were donor distance, donor clinical conditions (previous cardiac arrest, left ventricle hypertrophy or minor coronary lesions) and recipient features (presence of durable left ventricle assist devices or previous cardiac procedures). Two were peculiar cases: the donor assessment revealed possible malignant lesions, which could not be biopsied at beating heart due to anatomical factors. Therefore, we decided to proceed with the organ retrieval in the OCS, allowing for the necessary time to complete the histological analysis. As both lesions were eventually confirmed negative for malignancy, the transplants were successfully carried out. Overall, the ex-vivo perfusion mean time was 314 minutes (min-max 204–443). In-hospital mortality was 22% (2 cases): a peri-operative hemorrhagic shock and a multi-organ failure 58 days after surgery. Discharged patients showed a 1-year survival of 78%.
Conclusion: In our cohort, the OCS proved safe and effective for heart transport, as all organs were transplanted. This device is extremely helpful in case of distant donors, marginal hearts and complex recipients. Moreover, in our experience, the device was able to preserve the donor organs until fundamental pre-operative exams were completed.

POS029 EARLY EXPERIENCE WITH A NEW STORAGE DEVICE FOR COLD PRESERVATION

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Background: The standard technology for heart preservation for transplantation is cold static storage on ice. No temperature control is performed routinely and change in temperature can lead to graft injury. The SherpaPakTMCardiac Transportation System (CTS) (Paragonix Technologies, MA, USA) can keep temperature stable between 4–8°C. We report our two-year clinical experience in high risk transplants with SherpaPakTM.
Methods: Since November 2018 SherpaPakTM has been used in 19 non-consecutive cases in our institution. The device was used in procurements with either high-risk donors, long ischemic time (>180 minutes) or both. High risk donors were defined as donors with ≥1 risk factor (Age>50, CPR, Hypernatraemia > 160mmol/l, > 0.3μg/kg/min Norepinephrine, ≥1 inotropic drug for hemodynamic support, LVEF≤50%, septum thickness > 12mm). Primary graft dysfunction (PGD) was defined according to ISHLT consensus from 2014.
Results: Transplants had an average of 2.37 ± 1.26 risk factors. 86% of transplants showed long ischemic times (median 201 minutes, 25%-75%: 189–290). 32% of donors had previous CPR, 26% were > 50 years (Median age 40), 21% had high catecholamine support, 16% showed hypernatraemia and hypertrophy respectively. Eleven percent showed LVEF <50%. Recipients were male in 89% and 58% had previous sternotomies (6 VAD). Median recipient impact score was 8 (25%-75%: 5.75–10). Donor hearts were preserved at a median temperature of 5.5°C. Two recipients each showed PGD grade 3 (10.5%) and PGD 2 (10.5%) after weaning from bypass. All patients were supported with ECMO and all grafts recovered to normal graft function within 72 hours post transplant. All patients could be extubated within 7 days post transplant. Overall 1-year survival was 79% in this high risk population.
Conclusions: The Paragonix SherpaPakTM provides consistent temperature during transportation of grafts and could be successfully used with long ischemic times and high-risk donor hearts.

POS030 DISCARDED GRAFTS AFTER CARDIAC EX-VIVO PRESERVATION

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Background: *Ex-vivo* normothermic perfusion (EVP) is a novel procedure of donor beating heart preservation which limits ischemic-reperfusion injuries, allows potential resuscitation of suboptimal organs and permits a real-time monitoring of hemodynamic parameters and evaluation of lactate trend, as marker of organ preservation, with a timely identification of potentially unsuitable hearts. Aim of the study was analyse the grafts discarded after EVP in our centre.
Methods: Since 2018, 65 Heart Transplantation were performed at our centre. Marginal donors were recruited in 45 cases and in 15 the grafts were transported with EVP, with 8 organs discarded. At graft harvesting and just prior to possibly implantation, myocardial biopsies were collected. A pathological evaluation of the discarded organs was done. Clinical and histopathological characteristics were investigated.
Results: Main characteristics are reported in the Table. All discarded grafts were considered not-standard because of age comorbidities or long expected ischemic time. EVP lactate level > 5 mmol/L, venous lactate > arterial lactate, an unfavourable lactate trend or unstable hemodynamic condition during transportation were considered sufficient indicators to reject the organ.
Myocardial biopsies and histopathologic examination revealed signs of severe ischemia in 5 grafts, coronary anomalies in 3 and valve prolapse in 1. However, graft deterioration was not considered EVP related, even if perfusion time > 6–8 hours was shown to increase oedema and haemorrhage.
Conclusions: EVP, allowing continuous evaluation of marginal donor hearts, permits to exclude unsuitable grafts, possibly reducing the risk of early graft failure in recipients.

Table

	Donor characteristics	Cause of graft discarding	Histopathologic examination	Biopsies examination
Case 1	Long expected ischemia	↑ lactate	Post-traumatic dissection of the right coronary artery	Wide haemorrhagic suffusion, with infarction of the epicardial adipose tissue
Case 2	Smoke, NIDD, hypertension	↑ lactate	Biventricular wide haemorrhagic and oedema suffusion.	Myocytes contraction bands necrosis
Case 3	High inotropic support smoke, alcohol and EV drug abuse, hepatic cirrhosis, C hepatitis	Atrial fibrillation, too high inotropic support	Wide oedema suffusion, extended from pericardium to endocardium, severe haemorrhage in sub-endocardium of LV	Myocytes contraction bands necrosis
Case 4	63 years, smoke, dyslipidaemia, LV hypertrophy 14 mm	↑ lactate	Biventricular wide haemorrhagic and oedema suffusion. Presence of atherosclerotic plaque with inflammatory infiltration of the coronary arteries	Replacement/interstitial myocardial fibrosis. Infarction area in LV
Case 5	Long expected ischemia	Abnormal coronary artery	Biventricular wide haemorrhagic and oedema suffusion	Sub-endocardium necrosis
Case 6	61 years, hypertension	Severe aortic valve regurgitation	Atherosclerosis with 60% LAD stenosis	Biventricular oedema suffusion, with sign of myocytes ischemic sufferance
Case 7	62 years	↑ lactate and refractory high AOP	Biventricular haemorrhage in sub-endocardium	Important adipose tissue infiltration in the right ventricle myocardium
Case 8	Obese, hypertension Long expected ischemia	↑ lactate	Biventricular wide haemorrhagic and oedema suffusion	Myocardial replacement with fibrosis (probable previous ischemic damage)

POS031 DISTANCE BETWEEN RECIPIENTS RESIDENCY AND HEART TRANSPLANT CENTER: EFFECT ON LONG-TERM OUTCOME

Andrea Lechiancole[1], Veronica Ferrara[2], Sandro Sponga[1], Igor Vendramin[1], Giorgio Guzzi[1], Chiara Nalli[1], Concetta DI Nora[1], Daniela Piani[1], Ugolino Livi[1,2]

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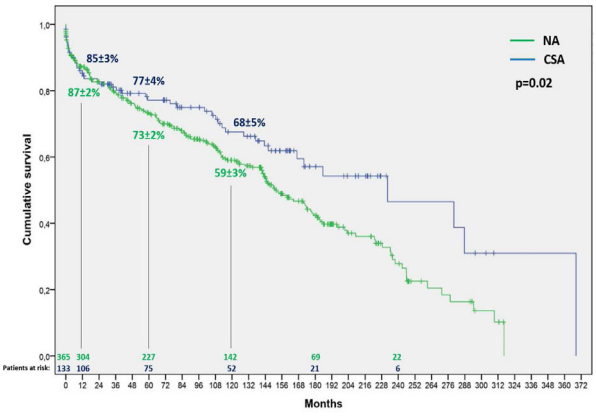
Background: The distance of recipients residency from the heart transplant (HT) Center could condition the treatment received and long-term results. Aim of the study was to verify the impact of the distance from our Center on long-term outcome after HT.
Methods: Adult patients receiving HT at our Centre since 1985 were enrolled. Patients supported with ECMO, VAD, high inotropic support or mechanical ventilation at the time of HT were excluded.
Patients were divided in groups according to the distance from our Center: Northern area (NA, ≤200 mi) and Centre-Southern area (CSA, > 200 mi).
Results: Baseline recipients and donors characteristics are shown in Table 1. During a median follow-up of 90 and 82 months ($p = 0.59$) for NA and CSA groups, survival was worst for patients closer to the HT Center, $p = 0.02$.
Compared to CSA group, NA patients were more frequently affected by neoplasia ($p = 0.03$), and less by ≥grade 2 rejection ($p = 0.03$), with no differences among the incidence of infections and CAV.
There were no differences in immunosuppressive and other medical therapy at 1.5 and 10 years after HT. However, NA group showed higher median creatinine level at 5-year follow-up ($p = 0.03$) and higher median cholesterol level at both 5 ($p < 0.01$) and 10-year follow-up ($p = 0.04$).
Conclusion: Distance of recipient residency from the HT Center seems not to negatively affect the outcome after HT. Other factors, probably related to genetic and lifestyle characteristics typically present in the two Italian areas considered, could have influenced the results.
Further in-depth larger and prospective studies are required to confirm this hypothesis.

Table 1

Recipients data	NA (n=365)	CSA (n=133)	p
Median age	59 (21-75)	58 (18-72)	0.07
Female	73 (20%)	26 (20%)	0.91
Median BMI	25 (21-34)	23 (19-36)	0.49
Hyperlipidemia	133 (37%)	46 (35%)	0.73
DM	88 (24%)	25 (19%)	0.22
HTN	105 (29%)	41 (31%)	0.63
CRF	88 (27%)	34 (27%)	1.00
Dialysis/CRRT	1 (1%)	0	1.00
AF	18 (5%)	11 (8%)	0.16
Previous CCH	97 (27%)	44 (33%)	0.16
Re-HTx	14 (4%)	4 (3%)	0.79
Donors data			
Median age	43 (13-69)	42 (14-69)	0.98
Age ≥55 y	57 (16%)	29 (22%)	0.12
Female	130 (36%)	57 (43%)	0.15
Ischemic time ≥4h	70 (19%)	22 (17%)	0.51
Infection	64 (18%)	32 (24%)	0.11
Cardiac arrest	28 (8%)	14 (11%)	0.32
LVEF<50%	6 (2%)	1 (1%)	0.68
IVS >14mm	3 (1%)	3 (2%)	0.20
CAD	31 (9%)	12 (9%)	0.86
Drug abuse	3 (1%)	3 (2%)	0.20

Figure 1



POS032 TEMPORAL RATES OF CELLULAR REJECTION IN THE FIRST TWO YEARS FOLLOWING HEART TRANSPLANTION IN A CONTEMPORARY COHORT

Paul Callan[1], Mohammed Aboelseoud[1], Steven Shaw[1], Mark Scott[2], Noman Khasati[1], Alpha Diallo[1], Rajamiyer Venkateswaran[1]

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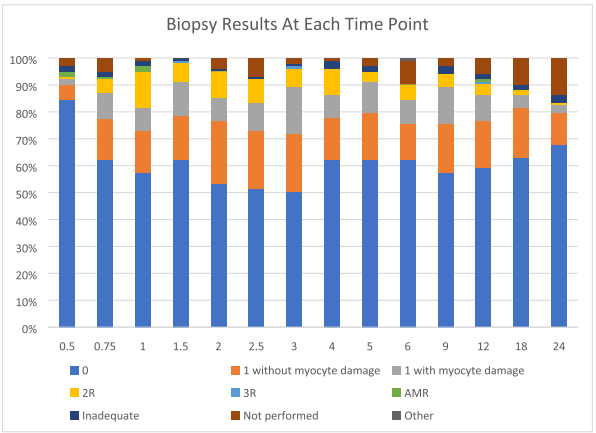
Background and Aims: Endomyocardial biopsy is the gold standard investigation for monitoring rejection following heart transplant (Tx). We schedule 14 biopsies within the first 2 years of transplant. With a recent emphasis on reducing clinic visits due to risk of COVID19 transmission, we assessed temporal rates of rejection in the first 2 years with contemporary post-transplant management. We also analysed factors associated with increased risk of rejection, to see whether we could establish a more personalised biopsy regime.
Methods: Adult Tx between Jan 2013 and Jan 2017, surviving > 1 month post Tx included. Bx result at each timepoint assessed, graded according to 2004 ISHLT criteria. Clinically important rejection (CIR) defined as 1R with myocyte damage or greater. Rates of cellular rejection were assessed at each time point. Multivariate logistic analysis was performed to look for an association between a range of donor and recipient clinical and demographic factors and risk of both CIR, and 2R rejection or greater (2RR).
Results: 103 patients included, 1373 scheduled biopsies, with just 68 (4.9%) not performed for clinical or technical, reasons or inadequate for grading. All received rATG induction, 96% discharged on MMF or azathioprine, 80% Ciclosporin, 20% Tacrolimus. 2 significant complications reported (0.15%). 74/95 patients surviving to 2 years had all 14 scheduled bx. 86/103 (83%) had at least 1 CIR, 55/103 (53%) 2RR. Median proportion of bx showing CIR at a specific timepoint 17.3%, highest at 3 months (25%), lowest at week 2 (3%). Risk of CIR > 12months 10.6% if prior CIR vs 5.6% if no prior CIR. No factors associated with increased risk of CIR on



	n	Odds ratio (CI)	P value
Recipient age	103	0.94 (0.86-1.03)	0.17
CMV +ve donor	45	2.15 (0.4-11)	0.35
CMV +ve recipient	53	0.24 (0.03-1.67)	0.14
Recipient sex	103	1.62 (0.18-22.5)	0.36
Blood Group			
O	50	-	
A	42	0.07 (0.006-0.77)	0.03
B	10	1.28 (0.066-24.6)	0.87
AB	1	1	
Donor age	103	1.01 (0.94-1.09)	0.76
BMI	103	1.82 (1.08-3.07)	0.024
HLA sensitisation pre-Tx	18	1.18 (0.12-11.7)	0.89
Initial CNI	Ciclosporin 82 Tacrolimus 21	2.99 (0.13-68.7)	0.49
Deprivation tertile			
1	42	1	
2	20	0.003 (0.000037-0.22)	0.008
3	34	2.84 (0.34-23.7)	0.33
	7 (unknown)		
Ethnicity	Caucasian 86 Non-Caucasian 17	0.23 (0.023-2.28)	0.21
EGFR <40 at discharge	38	0.20 (0.02 -1.87)	0.16
Aetiology			
Ischaemic Heart Disease	39	1	
Dilated Cardiomyopathy	25	3.2 (0.84-12.9)	0.067
Miscellaneous	39	6.1 (1.82-20)	0.022

Table 1 – Factors associated with 2R rejection or greater, on logistic multivariable analysis. CMV – Cytomegalovirus, BMI – Body Mass Index, EGFR – Estimated Glomerular Filtration Rate, CNI – Calcineurin Inhibitor, HLA – Human Leukocyte Antigen

multivariable analysis; blood group A, social deprivation score within second tertile associated with reduced risk of 2RR, and heart failure aetiology that was not ischaemic or dilated cardiomyopathy associated with increased risk (see table).
Conclusion: Risk of CIR remains high following Tx, underscoring importance of surveillance biopsies, which can be performed safely in high volume centres. The proportion of bx with CIR after 12 months is 11%, suggesting that performing surveillance bx between 12 and 24 months is clinically justified. No clinical factors reliably predicted risk of CIR in this cohort, which makes it challenging to individualise biopsy schedules.

POS033 SAIREITO INDUCED THE SUPPRESSION OF DONOR-SPECIFIC ANTIBODY IN A MURINE CARDIAC ALLOGRAFT TRANSPLANT MODEL

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Background: Saireito could induce the long-term cardiac allograft survival through the generation of CD4+CD25+Foxp3+ cells (regulatory T cells, Treg). However, little is known about the suppression of donor-specific antibody (DSA) by Saireito. We investigated the effect of Saireito on DSA production in the acute phase in a murine model of cardiac allograft transplantation.
Method: CBA mice underwent transplantation of a C57BL/6 heart and received oral administration of 2 g/kg per day of Saireito from the day of transplantation until 7 days afterward. Immunohistochemical study and flow cytometry were performed. Moreover, to investigate the involvement of Treg, anti-interleukin-2 receptor alpha antibody (PC-61) was administered to Saireito-treated CBA recipients on the postoperative day 0, 3, 6, and 9 or 20, 23, and 26.
Results: Flow cytometry studies on the postoperative day 10 showed an increased Treg population in splenocytes and suppression of DSA production. Immunohistochemical study showed more CD4+Foxp3+ cells in the myocardium. DSA production in Saireito-treated CBA recipients was suppressed on the postoperative day 10 even when PC-61 was administrated on day 0, 3, 6, and 9. DSA production was suppressed on the postoperative day 20 when the effect of Saireito was cutting off. Administration of PC-61 on the postoperative day 20, 23, and 26 increased DSA production in Saireito-treated CBA recipients.
Conclusion: Saireito could suppress DSA production in the acute phase through its direct immunosuppressive effect and induction of Treg.

POS034 PREVIOUS CARDIAC SURGERY IN THE HEART TRANSPLANT PATIENTS: A RISK FOR THE LONG-THERM OUTCOME?

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Background: As cardiac transplant medicine is constantly evolving and alongside surgical techniques are improving, more complex patients present today as transplant candidates. It is well proven that REDO cardiac surgery carries higher operative risk than first procedure regardless of the pathology involved. According to the literature up to 45 % of heart transplant candidates had previous cardiac surgery. Also, with the increasing development of LVAD therapy, significant number of patients present with the LVAD implanted at the time of surgery.
The aim was to investigate is previous cardiac surgery independent risk factor for the long-term survival.
Methods: A prospective observational trial has been performed. We studied 44 patients that underwent heart transplant in our institution from 2013 - 2020. The patients were divided in two groups according to presence or absence of previous cardiac surgery. As previous cardiac surgery was considered procedures for congenital heart disease, any cardiac surgery for acquired heart disease or previous LVAD implantation.. During follow-up we analyzed mortality rate as well as reintervention for bleeding rate, transfusion requirements, acute kidney failure and operative mortality.
Results: Median follow-up for our study population was 637.57 days (1 - 2280). The frequency of patients who had previous cardiac surgery was 22.7% in our cohort. REDO group had longer bypass times (204.9 $\pm$ 54.4 vs 148.1 $\pm$ 43.6, $p = 0.002$). Operative mortality was similar between the two groups (3.4 % vs 2.8 %, $p = 0.379$). In the follow-up period survival rate did not differ between the REDO and first surgery group (74.4 % vs 76.5 %, $p = 0.402$). The rate of reintervention for bleeding also was not higher in the REDO group (15.4% vs 12.5%, $p = 0.276$). Transfusion requirements as well as cute kidney failure did not show statistical significance between the groups. Previous cardiac surgery was not found to be an independent predictor of long-term outcome ($p = 0.099$, HR 2.57, 0.84 - 7.86).
Conclusion: Previous cardiac surgery in transplant candidates has not been identified as independent predictor of long-term survival. Although technically challenging, heart transplant after previous cardiac surgery with careful preoperative planning in hands of experienced surgical team do not compromise long term outcome.

POS035 FATE OF IMPLANTED AORTIC SCAFFOLDS- ROLE OF EXTRACELLULAR AND IMMUNE PROTEINS

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Background: Tissue engineering uses both natural and artificial scaffolds, suitable cells and signalling mechanisms, to address the issue of organ shortage particularly for blood vessel disorders.
Methods: (i) develop acellular blood vascular (decellularized) from syngeneic and allogeneic source of rat aorta, (ii) test feasibility of the blood vascular scaffold both cellular and acellular to undergo modulation under *in vivo* condition implanted at different routes and (iii) monitor the changes of the scaffold at protein and gene level using biochemical tools (histology, ddPCR, proteomics and immunohistochemistry).
Results: (i) The histological staining procedure showed successful preparation of a decellularized scaffold with minimum damage to the tissue architecture of both chemically decullarized and acellular scaffold implanted *in vivo*. (ii) Conservation of ECM proteins in the scaffolds and expression of macrophage and T-cell subsets indicated scaffold acceptance and possibility for cell engraftment for developing functional organs
Conclusions: The current work shows the importance of the *ex vivo* preparation of an acellular vascular (chemically decellularized) vis-à-vis acellular scaffold following *in vivo* implantation. The study opens up the possibility to use alternate mechanism for preparation of acellular scaffolds using different sites as potential bioreactors to avoid unfavourable immune responses.
The research was financed by the LUA-ALF, Sahlgrenska University Hospital and Sahlgrenska Academy, University of Gothenburg, Sweden, IngaBritt och Arne Lundbergs Forskningsstiftelse grants to Prof. Michael Olausson and Stiftelsen Professor Lars-Erik Gelins Minnesfond grant to Debashish Banerjee.

POS036 INTESTINAL DONOR CRITERIA: IS THERE ROOM FOR IMPROVEMENT?

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Introduction: Organ shortage is the Achilles' heel of solid-organ transplantation. Extended donor criteria (donation after circulatory death (DCD), advanced age, intensive care unit (ICU) stay > 7 days, ...) are accepted for many organs, due to the high mortality rate on the waiting list. In intestinal transplantation (ITx), however, donor criteria are strict. With improving outcome and new emerging indications, resulting in longer waiting list, it is crucial that the potential donor pool is optimally screened and utilized.

Methods: In this single-center retrospective analysis, theoretical predefined intestinal donor criteria were compared with effectively applied criteria for ITx. All organ donors offered by the University Hospitals Leuven Donor Network to Eurotransplant, between 2014 and 2020, were screened for both predefined and effective criteria.
Results: Twenty-two donors effectively used for ITx were analyzed. In those, predefined criteria were breached in 55% for cardiopulmonary resuscitation, inotropic use and intensive care unit stay. By applying effective criteria to the whole donor pool, an increase of 127% in intestinal organ offering could be obtained. However, it was striking that 70% of the offered intestines were not transplanted. Main reason -provided by Eurotransplant- was the lack of suitable recipients. Subanalysis of the donor criteria in the "no-recipients" versus the transplanted intestines showed no differences.
Conclusion: Effectively used donor criteria were less strict than the theoretical predefined criteria. The intestinal donor pool could be substantially enlarged by applying effective criteria instead of theoretical predefined donor criteria. However, many offered suitable intestines could not be allocated. Creation of a European-wide intestinal donor organ sharing program might increase the proper utilization of suitable intestines, decrease waiting lists, and their associated mortality.

POS037 INFECTIONS IN SMALL BOWEL AND MULTIVISCERAL TRANSPLANT RECIPIENTS IN A UK CENTRE

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Background: Infection is a common complication of small bowel and multivisceral transplantation. We investigated the causes of infection in all adult patients transplanted at Addenbrooke's hospital over a 2-year period.
Methods: A retrospective review was conducted of the electronic records of 19 patients transplanted in 2017 and 2018. Alemtuzumab and methylprednisolone were used at induction, followed by maintenance immunosuppression with tacrolimus, reducing oral prednisolone and an antimetabolite. Patients received broad spectrum antibacterial, antifungal and antiviral prophylaxis in the immediate post-operative period. Infections were recorded for 4 different timepoints: pre-transplant, and early (1–28 days), intermediate (1–6 months) and late (>6 months) post-transplant. Bacterial infections were categorised into 2 groups – bacteraemias and other infection/colonisation. Viraemias were recorded regardless of clinical presentation, along with donor and recipient serostatus for herpesviruses. Positive fungal cultures from all sites were recorded.
Results: 18/19 patients developed infectious complications post-transplant. The period with the most bacteraemias and viraemias was 1–6 months post-transplant. Most positive fungal cultures were seen 1–28 days post-transplant. 12 patients (63%) developed a bacteraemia. In 8 patients, this was due to multidrug-resistant bacteria. The commonest causes of bacteraemia were vancomycin-susceptible and vancomycin-resistant enterococci (32% and 26% of patients, respectively). Infection/colonisation at early timepoints was associated with development of a subsequent bacteraemia with the same organism. 74% of patients developed a viraemia, most resulting from reactivation rather than primary infection. The most prevalent viraemia was with Epstein-Barr virus (EBV; 63% of patients). Primary EBV infection was associated with the development of post-transplant lymphoproliferative disease ($n = 2$). Most positive fungal cultures were of *Candida* sp. One patient developed disseminated *Aspergillus fumigatus* infection.
Conclusions: High rates of infection, including by resistant organisms, were seen in this vulnerable patient population. Further study into methods to reduce colonisation and subsequent bacteraemia is required.

POS038 EXTERNAL VALIDATION OF A CLINICO-HISTOPATHOLOGICAL COMPOSITE SCORING SYSTEM TO PREDICT GRAFT FUNCTION IN MARGINAL DONORS

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Background: Grafts from expanded criteria donors (ECD) and donation after circulatory death (DCD) are frequently discarded. Reasons are often based on variables of low prognostic value.
The clinico-histopathological composite scoring system proposed by Anglicheau et al. shows the higher predictive value described so far (AUC: 0.84). They described a composite score based on three factors (donor serum creatinine, donor hypertension and glomerulosclerosis (GS)) that predicts a low glomerular filtration rate (GFR) at 1 year (GFR< 25 ml/min/1.73m^2). The combination of this variables defines the 4 risk categories: clinical parameters (CP) + GS <10%, CP = 0 + GS≥10%, CP≥1 + GS < 10% and CP≥1 + GS≥10%.
Objective: external validation of the model in a population of ECD and DCD grafts.
Methods: We tested:
-Calibration: OR to predict a low GFR for each risk category was calculated in our population. They were compared with the OR described by Anglicheau et al.
-Discrimination: by ROC analysis.
Results
-Calibration: 27/165 of grafts developed a low GFR at 1 year. OR obtained in our population were different from those observed in the original cohort (Table 1). The model was not well calibrated.
-Discrimination: AUC was 0.54. The discriminatory power was null.

Table 1. % of patients that developed a low GFR and OR by risk category

	Low GFR (at 1 year)				Multivariate analysis			
	Anglicheau et al. cohort		Study cohort		Anglicheau et al. cohort		Study cohort	
Clinico-histopatholigcal score	*n*	%	*n*	% (CI 95%)	OR	*p*	OR (CI 95%)	*p*
CP = 0 + GS< 10%	77	5.2	5	15.6 (5.3–32.8)	1.0	0.003	1.0 (0.2–2.8)	0.733
CP = 0 + GS ≥ 10%	40	12.5	1	7.1 (0.2–33.9)	5.2		0.7 (0.1–3.9)	
CP ≥ 1 + GS < 10%	37	13.5	13	17.8 (9.8–28.5)	5.5		1.4 (0.5–3.9)	
CP ≥ 1 + GS ≥ 10%	37	35.1	8	18.2 (8.2–32.7)	27.5		1.5 (0.5–4.5)	

Conclusions: the model is not valid to predict a low GFR in our population of marginal grafts.

POS039 IMPROVING KIDNEY UTILIZATION IN DEVELOPING COUNTRIES

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Background: Numerous investigations seek to increase organ availability and utilization, using an ex-vivo graft perfusion machine and protocols for using grafts with expanded criteria, among other clinical initiatives (Becker et al., 2020; Kling et al., 2017; Adler et al., 2016; Niemann et al., 2015; Kucirka et al., 2010; Duan et al., 2010). Some articles also focus on process improvement, people training, or technology adoption to improve transplantation process efficiency (Girolami et al., 2020; Sapiano et al., 2019; Kling et al., 2018). However, the literature on the topic is still scarce, and most of the articles are conducted in developed countries. Therefore, this research aims at identifying possible strategies to increase kidney utilization, especially in developing countries.
Methods: We conducted a systematic literature review (SLR) in seven international databases and an international panel of experts between August 2020 and January 2021. The initiatives were classified into four domains: actions directed to people (e.g., training); process improvement; introduction of new technology; and clinical activities. The experts' panel was composed of thirteen specialists in the theme, from Brazil, Argentina, Spain, and the United States.
Results: The SLR returned 241 articles – 75 duplicated. We analyzed the 166 remaining studies, resulting in 22 papers included in the SLR. Most initiatives are related to clinical changes. Few articles focus on improving the transplantation process through people development, new processes, or technologies. Regarding the expert panel, the interviewees mentioned various initiatives that cover the four dimensions analyzed.
Conclusions: Actions to increase kidney utilization have been concentrated on clinical initiatives, while there is space to increase kidney utilization through management initiatives, mainly in developing countries.

POS040 IMPACT OF COMBINED CLINICAL AND HISTOLOGICAL ALLOCATION CRITERIA FOR KIDNEY TRANSPLANTS FROM MARGINAL DONORS

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Background: Although there are still differences for definition and criteria of organs allocation, expanded criteria donors (ECD) are recognized as an effective resource which has leaded to an expansion of the donors pool, in a setting of organ shortage.
As part of the Nord Italian Transplant program (NITp) area, since the early 2000s our Centre adopted a combined clinical and histological allocation algorithm for use of kidneys from ECD (HR).
We retrospectively analyzed the impact of this allocation criteria on the outcome of our kidney transplant (KT) program.
Methods: From 2010 to 2018, we performed 99 HR; of these, 62 were single KT (S-HR) and 37 were dual KT (D-HR). HR group was matched with an equal number of single standard KT (S-LR), performed in the same period.
Results: Preoperative comorbidity, ischemia time, use of thymoglobulin as immunosuppressant, male recipients, and surgical complication were found significantly increased in the HR group.
HR group showed a lower 1- and 5- year graft and patients survivals.
Compared to D-HR group, S-HR showed lower 1 and 5-year graft and patients survivals.
S-HR and D-HR analyzed by biopsy score, showed no significant differences in terms of graft and the patient survivals.
Conclusions: The study confirms the clinical-histological algorithm as an effective tool for allocation of HR, which have shown inferior but acceptable results compared to S-LR.

POS041 URGENCY PRIORITY PATIENTS FOR KIDNEY TRANSPLANTATION, SINGLE CENTER EXPERIENCE

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Background and Aims: Priority urgent kidney transplantation is essential renal replacement therapy way for vascular access failure at the same time failure the perform peritoneal dialysis. Also, vascular access exhausted patients are presumed that shorter graft and life expectancy from other transplant patients due to had multiple comorbid conditions such as diabetes, cardiovascular disease and predisposition of thrombotic events. In this study we aimed that compared patient and graft outcomes between urgency priority kidney transplant (UP-KT) recipients and deceased donor kidney transplant patients.
Methods: We analyzed retrospective data of patients, who performed cadaveric kidney transplantation at our transplant unit from January 2008 to September 2020. We divided two group as PUKT and other cadaveric kidney recipients. Than we compared characteristics and outcomes.
Results: In this period 120 patients underwent deceased kidney transplantation. Seven of them received urgency priority kidney transplantation. The average follow-up were 84 months. There were more woman (%85.7 vs % 48.7, $p = 0.1$) and longer dialysis duration in the UP-KT group (122 vs 103 months, $p = 0.5$). Graft function at 12th months were similar (mean creatinine level 1.03 $\pm$ 03 mg/dL vs 1.33 $\pm$ 0.9 mg/dL, $p = 0.2$). Also, we were not observe increase risk of surgical complications (14.3% vs 24.3, $p = 0.5$), acute rejection episodes (14.3% vs 16.8%, $p = 0.8$) and delayed graft function (42.9% vs 42%, $p = 0.9$). There was not increased graft loss or death at UP-KT group.
Conclusions: UP-KT is a life saving therapy for without access dialysis ESKD patients. This study showed that UP-KT recipients` outcomes comparable with cadaveric kidney recipients from standard organ allocation system.

POS042 MACHINE LEARNING IMPROVES THE ACCURACY OF KIDNEY TRANSPLANT OUTCOME PREDICTIVE MODELS

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Background: Prediction tools have been developed to predict transplant outcomes. The majority of these models are based on regression analysis. More recently models using individual machine learning (ML) algorithms have been published, but 'ensemble' ML methods (combination of individual algorithms) have not been used to predict kidney transplant outcomes.
In this study we used Super Learning, an 'ensemble' of ML algorithms to develop a kidney transplant prediction model.
Methods: Data of 14629 adult patients, from the UK Transplant Registry, who underwent deceased donor kidney transplantation from 1st January 2006 to 31st December 2015 were analyzed. Pediatric donor and multiorgan transplants were excluded.
The SuperLearner package in R was used to develop models to predict 1 year graft survival (GS) and delayed graft function (DGF). Using cross-validation, the performance of different ML models (logistic regression, elastic net and lasso regression, Bayesian regression, random forest, gradient boosting) was evaluated. An 'ensemble' model was built using the combination of the previous algorithms.
Results: The AUC predicting the 1 year GS for logistic regression with all 65 predictors was 0.617, and 0.624 with reduced number of predictors selected. Random forest had a similar AUC of 0.61 and gradient boosting had 0.587. From the individual algorithms used the lasso regression gave the best performance with an AUC of 0.632 equal to the AUC of the 'ensemble' SuperLearner model.
For DGF the SuperLearner gave a prediction with an AUC of 0.647, similar to the one reached by lasso regression (AUC = 0.64) and Bayesian logistic regression (0.63). The AUC for the conventional logistic regression was 0.628.
Conclusions: Lasso regression performed as well as an 'ensemble' SuperLearner ML combination in predicting DGF and 1 year GS; both outperformed slightly conventional regression. Although the difference is small, it could be potentially improved with parameter optimisation.

POS043 ESTIMATION OF HEALTH-RELATED QUALITY OF LIFE IN A GREEK COHORT OF KIDNEY TRANSPLANT RECIPIENTS USING THE KIDNEY TRANSPLANT QUESTIONNAIRE 25 (KTQ-25)

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Background: Kidney transplantation is recognized as the treatment of choice for patients with End Stage Kidney Disease. Improvement in short term patient and graft survival of kidney transplant recipients (KTRs) has shifted interest to the long-term outcomes and Health-Related Quality of Life (HRQoL) estimation.
Method: The Greek version of the recently translated and adapted by our team disease specific tool KTQ-25 and the Greek SF-36 were administered.
Results: 84 KTRs (59 males; mean age 53.45 ± 10.72; mean e-GFR 47.69 ± 15.07; average time since transplantation 55.68 ± 48.26 months) completed the questionnaires. The scores of KTQ-25 were: Physical Symptoms 3.98 ± 1.60, Fatigue 5.30 ± 1.36, Uncertainty/Fear 5.16 ± 1.33, Appearance 6.31 ± 0.94, Emotions 5.03 ± 1.07 and Total Score 5.20 ± 0.87. The mean SF-36 Physical and Mental Component scores were 47.98 ± 8.70 and 46.94 ± 9.70 respectively. Fatigue ($p = 0.009$), Uncertainty/Fear ($p = 0.008$) and Total Score ($p < 0.001$) were better in Male sex. Physical Symptoms ($p = 0.013$) were better in KTRs with children than those with no children. There was positive correlation of e-GFR with Fatigue (p 0.002), Uncertainty/Fear ($p = 0.034$) and Total Score ($p = 0.017$). Hgb was positive correlated with Fatigue ($p < 0.001$), Uncertainty/Fear ($p < 0.001$), Emotions ($p = 0.031$) and Total Score ($p < 0.001$). KTRs who were receiving EPO for anemia had worse scores in all dimension of KTQ-25 (Physical Symptoms $p = 0.001$; Fatigue $p = 0.001$; Uncertainty/Fear $p = 0.021$; Emotions $p = 0.010$; Total Score $p = 0.002$) except Appearance. Appearance was negative correlated with Weight ($p = 0.001$) and BMI ($p = 0.001$). Total number of daily taken pills was also significantly negative correlated with Fatigue ($p = 0.006$) and Total Score ($p = 0.007$). No differences found between different immunosuppressive therapies.
Conclusion: Greek KTRs maximum KTQ-25 score was obtained in Appearance and the minimum in Physical Symptoms. Fatigue, Uncertainty/Fear and Total Score were better for Male sex and for KTRs with higher e-GFR and Hgb levels. Physical Symptoms were better only for KTRs having children. Overweight and high BMI negatively affected Appearance. At this first study using the KTQ-25 for evaluating HRQoL in Greek KTRs, among our significant results is that better graft function is significantly correlated with better HRQoL.

POS044 KIDNEY ALLOCATION RULES SIMULATOR

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Background and Aims: The ability to predict kidney transplant success at organ allocation is essential to leverage if we want to minimize the number of patients who return to an already overcrowded waiting list for transplantation.
Since evidence-based medicine is increasingly used as the standard to define good healthcare practices, we need to develop prognostic tools to use in decision-making. Therefore, the definition of deceased donors' kidney allocation rules on transplantation must be supported by simulations that allow foreseeing, as much as possible, the consequences of these rules.
Here we present the Kidney Allocation Rules Simulator (KARS) application that enables testing different kidney transplant allocation' systems with different donors and transplant candidates' datasets.
Methods: In this application, it is possible to simulate allocation rules implemented in Portugal, in the United Kingdom, in countries within Eurotransplant, and a previously suggested color priority system. As inputs, this application needs three data files: a file with transplant candidates' information, a file with candidates' anti-HLA antibodies, and a file with donors' information. As output, we will have a file with donor-recipient pairs selected according to the kidney allocation system simulated.
Results: With the same candidates' and donors' files, we can have different outputs for each simulation we run. For each output, we will have a resume of the selected donor-recipient pairs as: recipients' blood groups frequencies, mean age, mean time on dialyses, cPRA frequencies, HLA mismatches, and mean transplant score as a measure of good transplant outcome.
Conclusions: When seeking waste reduction while ensuring a fair distribution of organs from deceased donors, the definition of rules selecting donor-recipient pairs in renal transplantation must be based on evidence supported by data. With this purpose, we also need to predict transplant outcomes to define the best allocation rules.

POS045 IMPLEMENTATION OF THE KIDNEY TEAM AT HOME INTERVENTION: EVALUATING GENERALIZABILITY, IMPLEMENTATION PROCESS, AND EFFECTS

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Background: Research has shown that a home-based educational intervention for patients with chronic kidney disease results in better knowledge and communication, and more living donor kidney transplantations (LDKT) compared to care-as-usual. Implementation research in the field of renal care is almost non-existent. The aims of this study were (1) to demonstrate generalizability of the research, (2) evaluate the implementation process, and (3) to assess the relationship of intervention effects on LDKT-activity.
Methods: Eight hospitals in the Netherlands participated in the project. Patients eligible for all kidney replacement therapies (KRT) were invited to participate. Effect outcomes were KRT-knowledge and KRT-communication, and treatment choice. Feasibility, fidelity and intervention costs were assessed as part of the process evaluation.
Results: 332 patients completed the intervention. A significant increase in KRT-knowledge and KRT-communication among patients and invitees was confirmed in practice. 129 out of 332 patients (39%) had LDKT-activity, which was in line with the results of the clinical trials. Protocol adherence was high (4.61 out of 5) and intervention costs were approximately €2750 per intervention. Protocol adherence, knowledge and age were correlated with LDKT-activity.
Conclusions: This unique implementation study shows that the results in practice are comparable to the previous RCTs, and shows that the intervention can be implemented in multiple regions, while maintaining quality. Results from the implementation process resulted in the uptake of the intervention in standard care as of 2021 in the Netherlands. We urge other countries to investigate the uptake of the home-based education as part of standard care.

POS046 COMPARING SCORES FOR PREDICTING KIDNEY TRANSPLANTATION OUTCOMES

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Background and Aims: The development of risk scores that can predict the outcome inherent to the data-recipient pair in transplantation has allowed for better decision-making either in allocating organs or patients' clinical management. The OPTN uses two different scores: an Estimated Post Transplant Survival (EPTS) score (based on patients characteristics) to summarize the fitness of the patient; and a Kidney Donor Percentual Index (KDPI), that combines factors from donors and from the transplant, to summarize the risk of graft failure. Also, Molnar *et al.* proposed the TRANSPLANTSCORE to predict posttransplant outcomes using pretransplant information.
Methods: In this study, we aim to understand how TRANSPLANTSCORE correlates with the scores from OPTN.
Correlations between TRANSPLANTSCORE and OPTN scores were analyzed with Pearson's correlation and tests. Furthermore, TRANSPLANTSCORE performance to predict a good transplant prognostic as defined with EPTS < 40% and KDPI < 40% was analysed with a receiver operating characteristic (ROC) curve (and the area under the curve) and with the

calculation of sensitivity and specificity values for different cutoffs of TRANSPLANTSCORE.
Results: We used data from 140 simulated kidney transplants. To each one of the selected pairs, we computed TRANSPLANTSCORE, EPTS, and KDPI scores. With a rho = 0.59 (p-value < 0.001), we can conclude that TRANSPLANTSCORE is more correlated with EPTS than with KDPI (rho = 0.29, p-value < 0.01). On the other hand, TRANSPLANTSCORE has a good ability to discriminate a good transplant outcome with an AUC = 0.75 (95% Confidence Interval =]0.67; 0.83[).
Conclusions: If we could have a crystal ball at transplantation, we would like to predict time-to-graft failure and/or patient survival. Likewise, the scores presented here are not a crystal ball, but they can help us compare potential donor-recipient pairs and make decisions based on evidence.

POS047 KIDNEY TRANSPLANTATION FROM ELDERLY DONORS – THE EXPERIENCE OF A REFERENCE CENTER IN CROATIA

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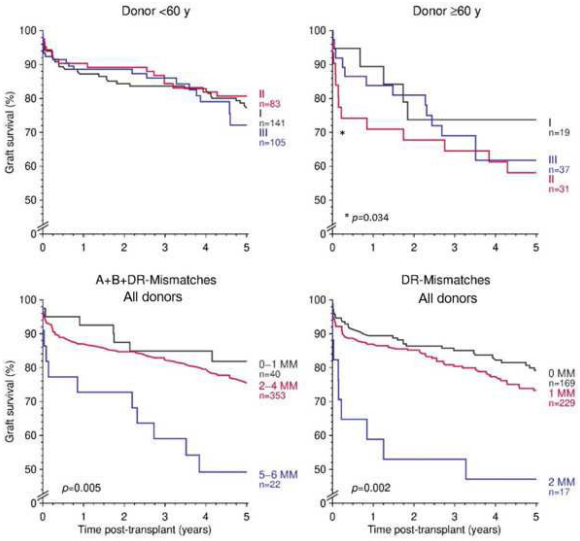
Background: Our country Croatia is among the global leaders regarding deceased donation rates, yet we are facing organ shortage and concurrently a high decline rate of deceased donor kidney offers. To reconsider our organ acceptance policy, we retrospectively analyzed the factors influencing the post-transplant outcome of kidneys from elderly donors at our center during a 20-year span and changes in our organ acceptance criteria during Eurotransplant (ET)-membership.
Methods: We compared all kidney transplantations from ≥60-year-old donors during the first two 5-year episodes of ET-membership between 2007 and 2017 (period II and III) with the preceding decade before ET-membership (period I). Differences in acceptance rates and reasons for the decline of kidney offers between the first two 5-year periods of ET-membership were analyzed.
Results: 14.1% of kidney allografts were obtained from ≥60-year-old donors in period I, as compared to the almost twofold higher 27.0% and 25.7% rates in period II and III, respectively (p = 0.007 and 0.008). During the first 5-year period of ET-membership (period II), we accepted significantly more grafts from marginal donors with higher number of HLA-mismatches than in period I. Consequently, 3-month survival of kidneys from ≥60-year-old donors dropped from 91.1% to as low as 74.2% (p = 0.034). After application of more stringent HLA-matching, especially in HLA-DR, and donor acceptance criteria in period III, graft survival improved again to 91.1%.
Conclusion: Our experience indicates that careful selection and allocation of kidneys from elderly deceased donors to HLA-matched recipients is important to increase the number of transplantations with good outcome.



POS048 MACHINE LEARNING-BASED PREDICTIVE MODEL FOR OUTCOME OF COVID-19 IN KIDNEY TRANSPLANT RECIPIENTS

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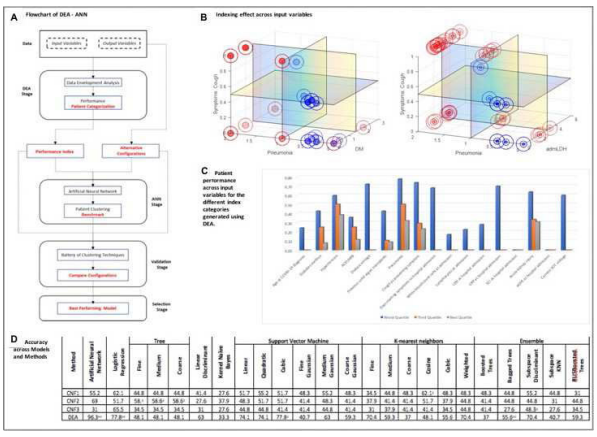
Background: Health systems need tools to deal with COVID-19, especially for high-risk population, such as transplant recipients. Predictive models are necessary to improve management of patients and optimize resources.
Methods: A retrospective study of hospitalized transplant patients due to COVID-19 was evaluated (March 3- April 24, 2020). Admission data were integrated to develop a prediction model to evaluate a composite-event defined as Intensive Care Unit admission or intensification treatment with antiinflamatory agents. Predictions were made using a Data Envelopment Analysis (DEA)-Artificial Neural Network (ANN) hybrid, whose accuracy relative to several alternative configurations has been validated through a battery of clustering techniques.
Results: Of 1006 recipients with a planned or an unscheduled visit during the observation period, thirty-eight were admitted due to COVID-19. Twenty-five patients (63.2%) exhibited poor clinical course (mortality rate:13.2%), within a mean of 12 days of admission stay. Cough as a presenting symptom (p = 0.000), pneumonia (p = 0.011), and levels of LDH (p = 0.031) were admission factors associated with poor outcomes. The prediction hybrid model working with a set of 17 input variables displays an accuracy of 96.3%, outperforming any competing model, such as logistic regression (65.5%) and Random forest (denoted by Bagged Trees,44.8%). Moreover, the prediction model allows us to categorize the evolution of patients through the values at hospital admission.
Conclusions: The prediction model based in Data Envelopment Analysis-Artificial Neural Network hybrid forecasts the progression towards severe COVID-19 disease with an accuracy of 96.3%, and may help to guide COVID-19 management by identification of key predictors that permit a sustainable distribution of resources in a patient-centered model.



POS049 [18F]FDG PET/CT IMAGING DISPROVES RENAL ALLOGRAFT ACUTE REJECTION IN KIDNEY TRANSPLANT RECIPIENTS WITH ACUTE KIDNEY INJURY: A VALIDATION COHORT

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Background and Aims: [^{18}F]FDG-PET/CT has been suggested to predict the absence of acute allograft rejection (AR) in kidney transplant recipients (KTRs) with acute kidney injury (AKI). Such a non-invasive diagnostic approach may help to avoid unnecessary transplant biopsies. Still, the proposed threshold of 1.6 of the mean of mean standardized uptake values ($mSUV_{mean}$) in the renal parenchyma needs validation.
Methods: From March 2015 to December 2019, we prospectively performed 86 [^{18}F]FDG-PET/CT in 79 adult KTRs who underwent *per cause* transplant biopsy. Biopsy-proven polyoma-BK nephropathies ($n = 7$) were excluded. PET/CT was performed 192 $\pm$ 18 minutes after administration of 254.4 $\pm$ 30.4 MBq of [^{18}F]FDG, before any immunosuppression change. The SUV_{mean} was measured in both upper and lower poles of the renal allograft. One-way analysis of variance (ANOVA) and Tukey's studentized range test were sequentially performed. The receiver operating characteristic (ROC) curve was drawn to discriminate "AR" from non-pathological ("normal" + "borderline") conditions.
Results: The mean age of the cohort was 52.5 $\pm$ 13.5 years, with M/F gender ratio of 46/33. The mean eGFR was 31.9 $\pm$ 14.6 ml/min/1.73m^2. Biopsies were categorized in 4 groups: "normal" ($n = 54$), "borderline" ($n = 9$), "AR" ($n = 14$) or "others" ($n = 2$). The median [min; max] $mSUV_{mean}$ reached 1.72 [1.02; 2.07], 1.97 [1.55; 2.11], 2.13 [1.65; 3.12] and 1.84 [1.57; 2.12] in "normal", "borderline", "AR" and "others" groups, respectively. ANOVA demonstrated a significant difference of $mSUV_{mean}$ among groups ($F = 13.25$, $p < 0.0001$). The ROC area under the curve was 0.86. The Youden index reached 2.073 of $mSUV_{mean}$, with a sensitivity of 57.1% and a specificity of 96.8%. The sensitivity and specificity corresponding to the threshold $mSUV_{mean}$ value of 1.6 were 100% and 30%, respectively.
Conclusions: [^{18}F]FDG-PET/CT may help noninvasively prevent inessential transplant biopsies in KTR with AKI and suspected AR.

POS050 PREOPERATIVE NEUTROPHIL TO LYMPHOCYTE RATIO (NLR) PREDICTS DELAYED GRAFT FUNCTION (DGF) IN RENAL ALLOTRANSPLANTATION

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Background: Delayed Graft Function (DGF) undoubtedly affects short and long-term outcomes in renal transplantation. Although, several risk factors contribute to its development, a simple, low-cost and reliable predictive biologic marker is still absent. Neutrophil to Lymphocyte Ratio (NLR) has been shown to represent a reliable marker of systemic inflammation in a variety of pathologic conditions. The aim of our study was to evaluate the value of the pre-transplant NLR as a prognostic marker for DGF development in renal allotransplantation.
Methods: We retrospectively calculated the NLR and recorded the number of DGF cases in a cohort of 94 consecutive deceased-donor renal recipients, who were transplanted between 2011 and 2020 at the University Hospitals of Patras and Ioannina, Greece. 18 recipients were excluded because of the development other complications.
Results: 31 out of the 76 recipients (40.8%) developed DGF. The mean value of NLR was significantly higher in recipients who developed DGF (NLR = 3.67) compared to those who did not (NLR = 2.64) ($p = 0.044$).
Conclusions: Elevated pre-transplant NLR could represent a promising and accurate biological marker for the development of DGF in deceased-donor renal allotransplantation.

POS051 NEW INSIGHT IN THE PREVENTION OF RENAL SUBCLINICAL REJECTION: URINARY EXTRACELLULAR VESICLES MIRNAS

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Background and Aims: The microRNA (miRNA) are short non-coding sequences of RNA (21 – 23 nt) involved in different post-transcriptional gene pathways. The miRNAs are detectable in different types of tissues and biological fluids, such as urine. Particularly in the urine, they seem to be associated with extracellular vesicles, useful to protect them from degradation. Urinary extracellular vesicles (UEVs) are lipid nano bound particles release from cells of the nephro-urological tract. The study of UEVs and their miRNAs content could be helpful to understand the pathophysiological condition of the kidney. For this reason, in this research, we try to identify a miRNAs profile from UEVs samples useful to prevent subclinical kidney rejection in pediatric transplanted patients.
Methods: We enrolled 20 pediatric transplanted patients, with a stable condition or kidney rejection at one-year post-transplantation. Vesicles were isolated from urine samples by the ultracentrifugation method. Their characterization was performed by electron microscopy, whereas the concentration and size were defined by scattering analysis (Nanosight 3000). The miRNAs were extracted from UEVs by a commercial kit and enriched before sequencing with the Illumina sequencer.
Results: The UEVs evaluation show a concentration of 2.79 x 10^{11} – 9.56 x 10^{11} particles with a size diameter of about 197 $\pm$ 7 nm. The miRNAs concentration was between 197 – 907 pg/µl. The sequencing showed about 522 different miRNAs and 48 of them were differentially expressed between patients with subclinical rejection or stable condition (Fig. 1).
Conclusions: These results pave the way to the identification of a UEVs miRNAs profile, useful to prevent the insurrection of subclinical kidney rejection in pediatric transplanted patients.

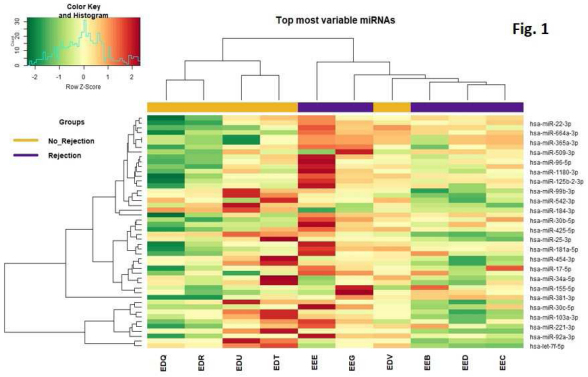

Fig. 1

POS052 URINARY CXCL10 AT 6 MONTHS AFTER KIDNEY TRANSPLANTATION PREDICTS THE HISTOLOGIC FINDINGS OF 1-YEAR SURVEILLANCE BIOPSY

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Background: Routine follow-up of kidney transplant recipients (KdTxR) has traditionally consisted of monitoring serum creatinine, immunosuppressive blood levels, urinary sediment and protein excretion, and, more recently, poliomavirus viremia and donor-specific antibodies. However, some KdTxR can develop significant cellular- or antibody-mediated inflammation, which is detectable only by an invasive test such as a kidney biopsy. Non-invasive biomarkers of alloimmune damage are needed for the precise diagnosis and monitoring of KdTxR. Many studies have reported a relationship between the IFN-gamma-related chemokine C-X-C motif chemokine 10 (CXCL10) and both clinical and subclinical T cell- and antibody-mediated rejection (AbMR), but its ability to predict subsequent subclinical rejection has not been fully analyzed.
Methods: We analyzed the relationship between 41 1-year surveillance biopsies and 41 matched urine samples prospectively collected at 6 months after transplantation. The urinary excretion levels of CXCL10 were measured using a commercial enzyme-linked immunoassay (ELISA) kit. CXCL10 values were divided by urinary creatinine (uCXCL10/Cr) to correct for potential dilution.
Results: Median 6-months uCXCL10/Cr was 7.8 ng/mmol (IRQ 6.2, 15.2 ng/mmol). 6-months uCXCL10/Cr related significantly to some 1-year Banff scores (t: rho = 0.311, $p = 0.048$; i: rho = 0.366, $p = 0.019$; ct: rho = 0.427, $p = 0.004$; ci: rho = 0.370, $p = 0.017$; ptc: rho = 0.390, $p = 0.012$). Moreover, uCXCL10/Cr related to both an "acute" (rho = 0.509, $p = 0.001$) and a "chronic" composite Banff score (rho = 0.370, $p = 0.017$). uCXCL10/Cr at 6 months discriminated 1-year subclinical AbMR (AUC-ROC 0.773, 95%CI 0.596–0.949, $p = 0.008$), whereas neither 6-months creatinine (AUC-ROC 0.641, 95%CI 0.418–0.864, $p = 0.171$) nor proteinuria (AUC-ROC 0.659, 95%CI 0.464–0.854, $p = 0.122$) did it. 6-months uCXCL10/Cr related to 1-year subclinical AbMR (OR 1.122, 95%CI 1.006–1.251, $p = 0.039$) independently of creatinine and proteinuria.
Conclusions: 6-months urinary CXCL10/Cr is a non-invasive biomarker that predicts 1-year histological findings better than creatinine and proteinuria.

POS053 DICKKOPF 3-PRECISELY REFLECTS SUBSEQUENT KIDNEY ALLOGRAFT DETERIORATION

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Background: In the context of kidney transplantation, the increased evidence of tubular atrophy and interstitial fibosis (IF/TA) is prognostically unfavorable and associated with an increased graft loss. In recent years, Dickkopf 3 (DKK3), a profibrotic glycoprotein released by stressed tubular epithelial cells, has been identified in animal experimental and clinical studies to cause tubulointerstitial fibrosis by regulating the Wnt/β-catenin signaling. Furthermore, it seems to engage a profibrotic T-cell response. The aim of our study was to determine on the one hand if a correlation between the DKK3 3 values and graft function over the observation period of 3 years exists and on the other hand if DKK3 could be further developed as a non-invasive marker to identify patients at high risk for a rapid deterioration in transplant function.
Methods: All patients being transplanted at our center between 2016 and 2018 were included ($n = 122$). We analyzed graft function represented by creatinine, eGFR and albuminuria and determined the DKK3 3 values in the urine over the observation period. An analysis of the implemented biopsies to assess histopathological lesions is under progress.
Results: The 12 month DKK3-crea ratio reflected statistically significant the creatinine and eGFR values from month 12 till month 36. This observation was confirmed in a multivariate analysis in which other known factors influencing graft function were included. Patients with high DKK3 scores (highest 25%) also showed worsened creatinine and eGFR in comparison to patients with low DKK3 values (lowest 25%). Patients with an increase in DKK3 between month 3 till 18 of more than 25% had an eGFR that was on average 15.27 ml/min worse than patients with a lower increase.
Conclusion: To conclude, our study shows that Dickkopf 3 correlates significantly with graft function and can thus be further developed as a new predictor of an increased risk for a rapid deterioration in graft function.

POS054 UREMIC TOXIN LEVELS ARE ASSOCIATED WITH GUT MICROBIOME CHANGES IN KIDNEY TRANSPLANT RECIPIENTS

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Backgroud: Chronic kidney disease (CKD) leads to the accumulation of uremic toxins (UT) that have been identified as inducers of oxidative stress, inflammation, and endothelial dysfunction and their circulating levels are correlated with cardiovascular events and mortality in CKD. Disturbances of normal gut microbiome (MB), dysbiosis, are currently recognized in the pathogenesis of CKD. Few studies evaluated the human gut MB in Kidney Transplant Recipients (KTR). It is expected that blood MB also exists, but no information is currently available on the blood MB of KTR, nor their comparison with gut or oral MB.
Methods: A prospective observational study evaluated in KTR before and 3 months after TX ($n = 6$) the MB of stool, saliva, and blood by 16sRNA next-generation sequencing and plasma UT by high-performance liquid chromatography (HPLC) with fluorescence detection.
Results: The habitat-specific MB profiles were dominated by Bacteroidetes and Firmicutes in the gut MB; Proteobacteria, Bacteroidetes, Fusobacteria and Firmicutes in the oral MB; and Proteobacteria, Firmicutes and Actinobacteria in the blood MB. There was a slight increase of the alpha-diversity (Shannon index) for saliva (4.5 to 4.7) and feces samples (4.4 to 4.7) and a decrease for blood samples (3.4 to 3.3) collected before and 3 months after TX, respectively. In the gut MB there was an increase in *Parabacteroides* and certain *Bacteroides* following 3 months; in saliva MB differences were observed in *Escherichia, Granulicatella, Streptococcus* and unclassified Gemellaceae and Bradyrhizobiaceae. In blood MB a reduction was observed in *Leptothrix* and unclassified Micromonosporaceae and an increase was observed in *Parabacteroides* and unclassified Bradyrhizobiaceae in response to the recovery of renal function. Also, we observed a drastic reduction in circulating levels of p-cresol sulfate and indoxyl sulfate after renal function recovery. In parallel with reduction of these UT we observed significant shifts in bacteria known to be p-cresol or indole producers, namely *Bacteroides*, in the gut, but not in oral and blood MB.
Conclusions: This study provides further evidence of a blood MB in KTR, different from the gut and the oral MB profiles, whose dynamics responds to renal function recovery. UT appear to be associated mainly with changes in gut MB.

POS055 IMPACT OF KLOTHO AS A BIOMARKER FOR CANCER SURVEILLANCE IN KIDNEY TRANSPLANT RECIPIENTS

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Background and Aims: It has been reported that klotho is associated with the occurrence of cancer in the general population, but, the association between klotho and the development of cancer in kidney transplant recipients (KTRs) is uncertain. Therefore, we aimed to investigate the impact of klotho as a biomarker for cancer surveillance and the mechanism in KTRs.

Methods: We enrolled 45 non-dialysis chronic kidney disease (ND-CKD) patients, D-CKD patients, and KTRs diagnosed and treated for gastric cancer, thyroid cancer and kidney cancer at Keimyung University Dongsan Hospital from 2009 to 2018. We measured the serum klotho level and expression status in the tissue, the serum levels of MDA, and SOD as oxidative stress markers from the stored samples in the biobank.
Results: The serum klotho level was the lowest in kidney cancer compared to gastric and thyroid cancer, whereas the level of oxidative stress markers was the highest in kidney cancer. In 12 patients diagnosed to kidney cancer, the serum klotho level was the lowest and MDA level was the highest in KTRs, but SOD showed no difference among them. Comparing normal and tumor tissues by western blot analysis, klotho expression was decreased in tumor tissues compared to normal tissues in all three groups, but klotho expression in KTRs only was deceased in tumor tissues compared to normal tissues by real-time PCR. This shows the relationship between the development of kidney cancer and inhibition of klotho gene in KTRs through the mechanism of oxidative stress.
Conclusions: Klotho may play a role as a biomarker for cancer surveillance in KTRs.

POS056 SYSTEMATIC REVIEW OF NON-INVASIVE IMAGING TECHNIQUES USED TO DIRECTLY EVALUATE THE MICROCIRCULATION IN KIDNEY OR LIVER TRANSPLANTATION

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Background: Ischaemia-reperfusion injury has profound effects on the microcirculation during solid organ transplantation. There are currently no non-invasive, imaging techniques in routine use to evaluate the microcirculation. Emerging technologies could provide novel therapeutic targets and facilitate personalised patient care. The aim of the systematic review was to identify imaging technologies that have been applied in the evaluation of kidneys or livers during either experimental ex-vivo machine perfusion or during implantation.
Methods: A systematic search of 4 databases and 1 trials registry was conducted until December 2020. Studies that demonstrated the use of imaging techniques in human studies and experimental pig models were included.
Results: In total, 24 papers were identified. All studies represented case-series (level 4 evidence). In total, 13 human kidney studies, 7 human liver studies and 4 ex-vivo machine perfusion porcine kidney studies wer found. The techniques demonstrated in these studies included: laser doppler, laser speckle, infrared thermal imaging and indocyanine green fluorescence angiograpy. Other techniques that can directly visualise capillaries and erythrocyte velocity include intravital microscopy, orthogonal polarisation spectral and sidestream dark-field imaging. In addition, tissue oxygenation has been assessed using near infrared spectrophotometry and hyperspectral imaging. Four studies applied these imaging techniques in the setting of ex-vivo machine perfusion in experimental pig kidney models. All studies describe useful objective biomarkers of perfusion that have been compared with either transplant factors, graft outcome or machine perfusion characteristics.
Conclusion: These promising preliminary studies require further evaluation in larger clinical trials. Many of the techniques used here have been applied in other surgical specialities, yet remains a poorly researched area in solid organ transplantation.

POS057 LOW INVASIVE SPME TISSUE SAMPLING AS A NEW TOOL FOR GRAFT QUALITY ASSESSMENT

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Background: Solid-phase microextraction (SPME) allows detecting changes occurring in the graft during the transplantation. The small probe's diameter provides minimal invasiveness and permits several samplings from the same organ. Lipidomic analysis using SPME sampling enables a better understanding of the mechanism of ischemia/reperfusion (I/R) grafts injury.
Methods: SPME was used for direct kidney sampling and as a sample preparation method. The porcine renal autotransplantation model was performed to simulate two types of donor scenarios: heart beating donor (HBD) and donor after cardiac death (DCD). Samples were harvested in vivo before retrieval, during perfusion, in vivo after revascularization, and for DCD after 45 min and 2h of warm ischemia (WI). The lipidomic analysis was done using ultra-high-performance liquid chromatography coupled with a Q-Exactive Focus Orbitrap mass spectrometer.
Results: The lipidomic analysis of kidneys enabled determining changes in organs during transplantation and alterations related to WI. Obtained results indicate that grafts injured during WI may be characterized by elevations of glycerophosphoethanolamines and reductions of lyso-glycerophosphocholines and glycerophosphocholines. After reperfusion in the DCD group, triacylglycerols' alterations are mostly related to their acyl chain length and saturation. Obtained results may indicate that membrane remodeling might be transiently inhibited following I/R. Moreover, observed alterations may be associated with affected energy metabolism, cell membrane damage, and the release of pro-inflammatory factors.
Conclusions: SPME sampling might provide an adjunct diagnostic tool to the standard protocol of graft quality assessment in the future. The proposed protocol will help provide a comprehensive assessment of organ quality and characterization of the processes responsible for I/R injury.
Acknowledgment: The study was supported by grant Opus 2017/27/B/NZ5/01013 from National Science Centre

POS058 FUNCTIONAL CATEGORIES DETERMINED BY RNA-SEQ IN URINE OF KIDNEY TRANSPLANT PATIENTS WITH ACUTE REJECTION COMPARED WITH LONG-TERM ALLOGRAFT SURVIVAL

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Background: The molecular mechanisms underlying transplant rejection or long-term acceptance are not well stablished and cellular interactions appear to be insufficient to explain these outcomes. Gene expression and transcription regulation have become important research targets in renal transplantation and urine seems to be a non-invasive sample to study and understand the role of the molecular mechanisms involved in the transplantation immune response, we focus on the search of genes positively regulated in urine of patients with different outcomes to elucidate the signalling pathways implicated in those process.
Methods: Urine was obtained from both acute rejection (pre and post treatment) and long-term allograft survival patient. Sediment was treated with Tri Reagent and RNA was isolated. The RNA-seq was performed at the Macrogen company by Illumina, Novaseq, 100 bp, PE; ~60 M reads. The mapping was done by STAR software and then Differential expression analysis were done by EdgeR software. Transcript interaction networks were constructed implementing ClueGO software (Cytoscape). Functional categories enrichment was defined implementing Gene Ontology tool online.
Results: We found that in the urine of the patient with acute rejection before treatment, compared to that of the long-term survivor, are positively regulated genes related to Th2 immune response, genes associated with the negative regulation of CD8+ T-cell activation as well as genes related to the protection of the NK-cell-mediated response. Similarly, we found that genes related to the humoral immune response are negatively regulated. Interestingly, after treatment, the aforementioned genes are no longer positively regulated.
Conclusion: Our results suggest that in the urine of the patient with acute rejection is reflected an anti-inflammatory immune response that is possibly the result of the control of the inflammatory response as a consequence of the rejection process; this phenomenon has been described in tissue with regulatory genes such as FOXP3. It is important to note that positively regulated genes are involved in both, innate and adaptive immune response. The anti-rejection treatment seems to bring these genes to a homeostasis in their expression.
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POS059 HOW DONOR CYP3A5 EXPRESSION AFFECT TRANSPLANTATION OUTCOMES IN CAUCASIAN POPULATION OF RENAL TRANSPLANT RECIPIENTS

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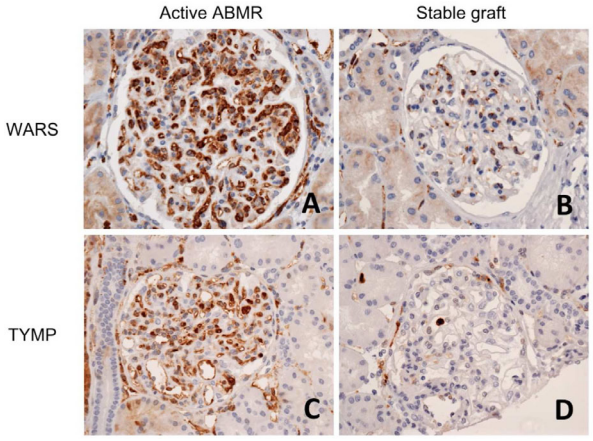
Background: Variability of the CYP3A5 gene in renal transplant recipients has been previously studied for influences on acute rejection and allogenic

kidney function. However, CYP3A5 is also expressed in allogenic renal tissue, the relevance of which has not yet been extensively investigated. The aim of this study was to evaluate the effect of donor CYP3A5 expression on early and long-term transplant outcomes.
Methods: Single nucleotide polymorphisms of CYP3A5 were analyzed in 95 kidney transplant recipients and their corresponding donors. Episodes of biopsy-proven acute rejection, proteinuria and kidney function expressed as estimated glomerular filtration rate, delayed graft function and graft loss were observed during three-year follow-up.
Results: Patients who received a CYP3A5 expressing kidney (n = 16) had a higher risk of biopsy-proven acute rejection (OR [95% CI]; 11.51 [2.41; 55.06] within 1 year and 8.52 [1.98; 36.67] during whole follow-up time), proteinuria (4.03 [1.12; 14.59] within 1 year), and graft loss (26.00 [2.68; 252.68]) compared to donor CYP3A5 non-expressors (n = 79). Multivariate models found donor CYP3A5 expression to be a significant predictor of acute rejection and graft failure. Recipients' *CYP3A5* genotype did not affect transplantation outcomes.
Conclusions: There was a strong correlation between donor CYP3A5 genotype and poorer transplantation outcome, despite controlled exposure to tacrolimus. New insight into the mechanisms of local tacrolimus metabolism may help individualize therapy and prevent graft injury.



POS060 IMMUNOMARKERS OF ENDOTHELIAL INJURIES DURING ACTIVE ANTIBODY-MEDIATED REJECTION IN KIDNEY TRANSPLANTATION REVEALED BY GLOMERULAR PROTEOME ANALYSIS

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Background: Issues remain in active antibody-mediated rejection (aABMR) diagnosis in human kidney transplantation, as the hallmark criteria, the microcirculation inflammation scores and C4d deposits, still lack reproducibility and sensitivity, respectively.
Methods: We used laser microdissection coupled with tandem mass spectrometry-based proteomics from formalin-fixed and paraffin embedded biopsies to characterize the protein profile of active antibody-mediated glomerular injuries compared to stable graft controls. We identified biomarker candidates of aABMR, which were secondarily assessed by immunohistochemistry and four pathologists in an independent retrospective cohort (n = 53).
Results: Overall, 21 patients with aABMR and 8 stable grafts were analyzed. We defined a profile of 82 proteins, characterized by evidence of leukocyte activation, interferon-mediated cellular stress and microcirculation remodeling. Three protein markers of interferons environment, thymidine phosphorylase (TYMP), tryptophan--tRNA ligase, cytoplasmic (WARS) and guanylate-binding protein 1 (GBP1) have been highlighted, that could represent relevant markers of diffuse endothelial stress during aABMR (Image). Using immunohistochemistry in an independent cohort, two of them (TYMP and WARS) displayed promising diagnostic performance of aABMR, with a mean sensitivity of 87.8% and 79.8%, a mean specificity of 85.5% and 81%, and a substantial agreement (kappa = 0.733 and 0.643) respectively.
Conclusions: Using glomerular proteome analysis, this study provides new insights on immunomarkers involved in aABMR, which need to be evaluated in prospective cohorts.

POS061 EARLY PREDICTION OF RENAL GRAFT FUNCTION: ANALYSIS OF A MULTI-CENTRE, MULTI-LEVEL DATA SET

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Background: Long-term graft survival rates after renal transplantation are still moderate. We aimed to build an early predictor of an established long-term outcomes marker, the glomerular filtration rate (eGFR) one year post-transplant (eGFR-1y).
Methods: A large cohort of 376 patients was characterized for a multi-level bio-marker panel including gene expression, cytokines, metabolomics and antibody reactivity profiles. Almost one thousand samples from the pre-transplant and early post-transplant period were analysed. Machine learning-based predictors were built employing stacked generalization.
Results: Pre-transplant data led to a prediction achieving a Pearson's correlation coefficient of r = 0.39 between measured and predicted eGFR-1y. Two weeks post-transplant, the correlation was improved to r = 0.63, and at the third month, to r = 0.76. eGFR values were remarkably stable throughout the first year post-transplant and were the best estimators of eGFR-1y already two weeks post-transplant. Several markers were associated with eGFR: The cytokine stem cell factor demonstrated a strong negative correlation; and a subset of 19 NMR bins of the urine metabolome data was shown to have potential applications in non-invasive eGFR monitoring.

Importantly, we identified the expression of the genes TMEM176B and HMMR as potential prognostic markers for changes in the eGFR.
Conclusions: Our multi-centre, multi-level data set represents a milestone in the efforts to predict transplant outcome. While an acceptable predictive capacity was achieved, we are still very far from predicting changes in the eGFR precisely. Further studies employing further marker panels are needed in order to establish predictors of eGFR-1y for clinical application; herein, gene expression markers seem to hold the most promise.

POS062 MOLECULAR CLASSIFICATION OF RENAL ALLOGRAFT REJECTION BASED ON THE B-HOT GENE PANEL

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Background: Accurate assessment of allograft injury and rejection is critical to improve long-term renal allograft survival and patient outcomes. Gene expression analysis has the potential for precise, objective, and highly reproducible mechanism-based evaluation of allograft biopsy. Numerous microarray studies have defined the molecular phenotypes of rejection. Despite several gene sets being described and validated, molecular assessment of biopsies has yet to be integrated into routine practice.
Methods: The Banff Molecular Pathology Working Group jointly adopted the NanoString platform and established the Banff Human Organ Transplant (B-HOT) consensus gene panel. This technology has the advantage of being performed on the same tissue sample used for routine histology, allowing histo-molecular data integration. We sequenced more than 350 FFPE renal biopsies and developed classification models using an ensemble approach based on differential expression analysis of the B-HOT gene panel. Probabilistic scores were generated for several comparisons: ABMR, TCMR, as well as for histological lesions. These scores are then used in an unsupervised analysis to distinguish rejection from non-rejection.
Results: Differential expression analysis recapitulated gene expression signatures characteristic of each comparison. Biopsies with low predicted probability of rejection had lower average Banff scores than those with high probability. Unsupervised archetypal analysis showed distinct clusters and reflected the associated histological lesion scores.
Conclusions: Augmenting histology-based assessment of allograft injury with continuous and probabilistic molecular interpretation can facilitate the classification of challenging cases, such as borderline, BKV nephropathy, isolated v-lesions, and ABMR without C4d or detectable DSA. Assignment of a level of confidence can enable early diagnosis and intervention by clinicians.

POS063 DEGRADATION OF KEY CYTOSKELETAL AND GLOMERULAR BASEMENT MEMBRANE PROTEINS ASSOCIATE TO SUBOPTIMAL OUTCOMES IN KIDNEY TRANSPLANTATION

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Background and Aims: Deceased after brain death (DBD) donors are the preferred source of donor organs, yet these organs yield inferior posttransplant outcomes compared to living donation. Cerebral injury and subsequent brain death contribute to biological dysregulation including cellular stress adversely affecting graft function. To investigate the biological processes of brain death related injury we profiled the degradome of donor kidneys with suboptimal or good graft function posttransplant, focusing on alterations on glomerular basement membrane proteins.
Methods: Using protein topography and migration analysis platform, we profiled donor kidney degradation profiles. Degradation patterns were further investigated by Immunoblotting and immunofluorescent staining on a separate cohort of deceased and living donor kidney biopsies; with potential mechanisms of injury investigated using in-vitro human immortalised kidney cells and ex-vivo precision cut human kidney sections.
Results: Degradation profiling mapped 135 proteins to glomerulus. A cohort of these showed distinct contrasting degradation patterns in donor kidneys with suboptimal posttransplant compared to good outcome. Key degradation patterns were confirmed in a separate cohort of DBD, DCD and living donor biopsies; demonstrating that the observed protein degradation is associated with brain death. Transforming-growth Factor-ß (TGFß) was investigated as a potential mediator of protein degradation in this cohort. Treatment of our tissue and cell models with TGFß highlighted physiological tissue changes as well as increased activation of Calpain-1 and the subsequent degradation of cytoskeletal proteins. This injury pattern was prevented, in-vitro by the addition of a calpain inhibitor.
Conclusions: Cytoskeletal and basement membrane proteins are degraded in DBD donors, specifically donors with poorer posttransplant outcome. Initial mechanistic investigations suggest a relationship between TGFß and Calpain-1 mediates downstream injury to cytoskeletal proteins.

POS064 PARATHYROID HORMONE (PTH) SERUM LEVEL AS PREDICTOR OF OUTCOME IN RENAL TRANSPLANT: A RETROSPECTIVE STUDY

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Background and Aims: Delayed Graft Function (DGF) harms 20% of patients undergoing kidney transplant. The early recognition of this condition might be extremely useful for a better management of the patient, especially in terms of undertaking the most suitable immunosuppressive therapy. In literature, several biomarkers were suggested to predict the outcome of the grafts. Our aim is to test the predictive values of PTH and calcium serum levels, easily measurable biomarkers, that could potentially be combined with other existing predictive models in order to create a new diagnostic algorithm.
Methods: We considered 257 patients, who underwent kidney transplantation from 2013 to 2018 in our transplantation center. Among them 209 early recover their function (EGF), 41 developed DGF and only 7 grafts never recover. We compared a DGF group (41 patients) and EGF group (209 patients); 7 PNF patients were excluded. For each transplanted patient several clinical variables were considered individually and combined calculating the Irish score: among them we chose as most important
-calcium serum levels, the day before and the average of values in the first eight days after transplant;
-Aspartate aminotransferase (AST) the first day after surgery and the average of values in the first week after transplant;
-PTH levels before and after surgery.
Results: Considering all variables individually, only AST values demonstrated a statistically significant difference between EGF and DGF groups, p value = 0.0001. However, AST is extremely non-specific when considered individually. Mann-Whitney's U test underlines a difference between EGF and DGF groups in PTH serum levels: the value of the medians was not statistically significant, but p value = 0.059 was suggestive of a trend. A linear correlation statistically significant (p value = 0.0338) was observed between PTH serum level and Irish Score in DGF group.
Conclusions: The results of our retrospective cohort suggest PTH as an interesting marker of the function of the transplanted kidney. A larger and prospective study could better define the role of PTH alone and combined with other markers in predicting DGF after kidney transplant.

POS065 CALCIFICATION CT ASSESSED CALCIUM SCORING: EFFECTS OF RENAL TRANSPLANT RECIPIENT OUTCOMES

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Background: Coronary calcification is a known indicator of poor cardiac outcomes. Similarly, iliac and distal vascular calcification has been shown to be an adverse outcome parameter for patients with peripheral vascular disease. There is paucity of evidence around the role of arterial calcification for renal transplant patients. We aimed to assess the impact of iliac calcification on short and long term outcomes of renal transplant patients
Methods: All patients undergoing CT scan within +/- 1 year from the date of transplant who had a CT scan were included between January to November 2013 from a single centre. Patients with dual and multivisceral transplant were excluded. Donor and recipient level parameters were collected retrospectively. Based on morphology (greatest degree of calcification based on appearance and pattern: 0–3), circumference (greatest percentage circumference involvement of arterial segment: 0- 4), length of calcification

(percentage length involvement of arterial segment; 0–4) and internal diameters of the common iliac and external iliac arteries, CT scan based scores were calculated by two senior radiologists independently.
Results: A total of 44 patients were included: M/F (27/17), 29% history of heart disease, 71% hypercolesterolaemic, 34% diabetic, 79% hypertensive, the mean BMI was 27 [range 17.04–36.42]. there was no effects of external iliac calcification morphology, circumference or total score on delayed graft function, creatinine, eGFR, 30 day surgical complications but common iliac artery calcification morphology, circumference and total score significantly predicted high 30-day post op complications and poor 1-year cardiac complications. There were no significant differences on patients and graft survival up to a follow-up of 6 years.
Conclusion: CT estimation of proximal calcification of the iliac vessels predict higher incidence of immediate surgical and longer term cardiac complications but did not affect the longer term graft and patients outcomes in our cohort. Bigger data set will be informative about smaller effect size. Caution needs to be exercised when dealing with patients with significant iliac calcification but should not be a barrier to transplantation.

POS066 LONG TERM OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS WITH CT ASSESSED SARCOPAENIA

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Background: The syndrome of loss of skeletal muscle mass and strength, sarcopenia, has been shown to be a significant risk factor for poor prognosis in cancer patients and liver transplantation. Kidney failure patients usually have significant comorbidities and are considered high risk for short and long-term morbidity and mortality. We aimed to assess the effect of scaropaenia, that has not been studied well in renal transplant population.
Methods: All patients who received a transplant at our centre between January and November 2013 and had a CT scan within a year of transplantation were included. Patients with dual and multivisceral transplant were excluded. Donor and recipient level parameters were collected retrospectively. CT scan images were reviewed by two separate senior radiologists to annotate the skeletal muscle at midpoints of L3 vertebra. Skeletal muscle index was calculated for each individual patient and compared with long term outcomes.
Results: A total of 44 patients were included. Patients were divided into sarcopaenic and non sarcopaenic groups (skeletal muscle index cut offs 41.6 in males and 32.0 in females). Recipient factors including age, gender, diabetes, hypertension and heart disease were similar between two groups. Sarcopaenic patients had a lower mean BMI than non-sarcopaenic patients (23.7 vs 27.9, $p = 0.002$). There was no difference in 3 month, 1, 3, and 5 year graft function, or 30 day complications in each group. There was a significantly increased risk of DGF in the sarcopaenic group ($p = 0.013$). 1-year cardiac complications were significantly increased in male patients with sarcopaenia ($p = 0.01$), but this difference was not seen in females. The long term death censored graft survival was similar while the patient survival was significantly worse in sarcopenic patients ($p = 0.008$). When the outcomes were measured from one year post transplant onwards, there were no differences between groups as majority of the adverse events were within the first year in sarcopaenic patients.
Conclusion: Sarcopaenic renal failure patients who are transplanted may have inferior outcomes, with sarcopaenia an independent risk factor for morbidity and mortality. CT scans performed for other indications can be used as a prognostic tool to risk stratify these patients.

POS067 IS ACCOMMODATION AN UNHARMFUL PROCESS IN ABO INCOMPATIBLE KIDNEY TRANSPLANT?

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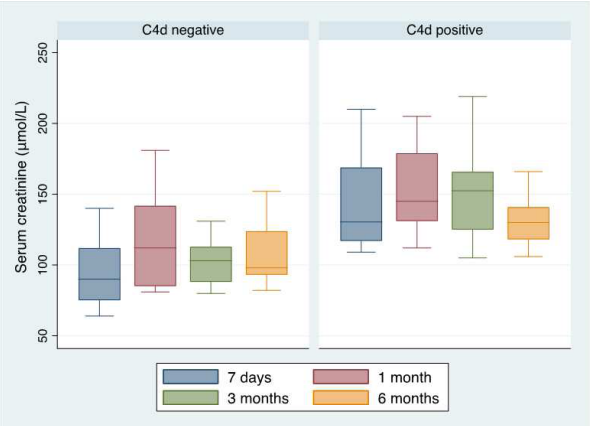
Background: AB0 incompatible (AB0-i) kidney transplantation (KT) is nowadays a well-accepted procedure with similar graft and patient survival rates compared to AB0 compatible KT.
After decreasing isohemagglutinin (IH) titers through antiCD20 and apheresis techniques, the endothelium is able to adapt itself to this new environment and avoid IH mediated rejection through accommodation development. Reduced expression of AB0 antigens and upregulation of regulatory complement factors are suggested to participate in this process. C4d staining has been considered an adaptative and unharmful mechanism, even though it is not a constant feature.
The current study aims at comparing outcomes of KT recipients across AB0 incompatibility by evaluating Banff parameters and complement activation through C4d staining in 10 days KT per-protocol biopsies in a single-centre cohort.
Methods: This is a retrospective study including all AB0-i recipients from 2013 to 2020 with a total of 33 patients included. Clinical and analytical data were collected (Table). Per-protocol 10 days biopsy was performed in 30 patients (2 excluded by negative consent and 1 by immediate artery thrombosis).
Patients were classified according to C4d staining (graded 0- 3) in 10 days after KT biopsy. Intermediate C4d staining intensity (1 -2) were excluded from the analysis in order to characterize 2 pure samples: complete negative (0) and very intense (3) staining.
Results: Two groups were compared depending on C4d - versus C4d +. No significant differences were found in baseline characteristics between both groups (Table).
Microvascular inflammation defined and graded according to Banff scale tend to be more frequently associated to C4d positive staining biopsies.

Table

Characteristic	C4d- (n=7)	C4+(n=14)	P
Recipient sex (men %)	57.14%	85.71%	0.147
Recipient age (years, mean and CI 95%)	56.11 (48.75 - 63.46)	52.73 (45.23 60.22)	0.538
Donor (sex)	28.57%	50.00%	0.350
Donor age (years, mean and CI 95%)	51.39 (43.10 - 59.69)	57.22 (51.64 - 62.81)	0.1984
HLA mismatch (nº of HLA missmatch)	3.86 (1.76 - 5.95)	3.64 (2.78 - 4.51)	0.7974
Cold ischemia time (min)	71.43 (32.43 - 110.43)	63.23 (46.30 - 80.16)	0.6071
Hemagglutinins, IgM titers before rituximab (median, p25 p75)	8, 2 - 16	16, 8 - 16	0.1800
Hemagglutinins, IgG titers before rituximab (median, p25, p75)	64, 16 - 128	32 , 16- 64	0.5462
Hemagglutinins, IgM titers before KT (median, p25, p75)	0, 0 - 1	1, 0 - 1	0.2865
Hemagglutinins, IgG titers before KT (median, p25, p75)	4, 4-4	3, 1 - 4	0.2659
Hemagglutinins IgM at protocol kidney biopsy (median, p25, p75)	0, 0 - 1	2, 0 - 8	0.1604
Hemagglutinins, IgG titers at protocol kidney biopsy (median, p25, p75)	8, 2 - 8	16, 4 - 32	0.2984
cPRA (%, mean, CI 95%)	24.57 (14.60 - 63.75)	33.21 (9.34 -57.09)	0.6592
Induction treatment (without induction/ Basiliximab/Thymoglobuline)	0/6/1	1/10/3	0.687
Blood groups			
A → O (n)	5	9	0.743
B → O (n)	1	3	1.000
AB → O (n)	0	0	1.000
B → A (n)	1	1	0.599
A → B (n)	0	0	1.000
AB → A (n)	0	1	0.469
AB → B (n)	0	0	1.000
Microvascular inflammation (g+v+ptc) median, p25, p75	0 0 0	0 0 2	0.078

Figure



Graft function defined by serum creatinine was significantly better in C4d negative group at 7 days, 1 month, 3 months and 6 months after KT (Figure). No differences were found in proteinuria excretion.
Conclusions: In our cohort, complement mediated endothelial damage evaluated by C4d deposition in per-protocol biopsies predicts worse short and mid-term graft function. Accommodation might not be a uniform process. IH and complement mediated injury could be soften by complement inhibition in order to achieve proper accommodation and further better graft and patient outcomes.

POS068 ANTITHROMBOTIC MANAGEMENT IN KIDNEY TRANSPLANTATION – A PAN-EUROPEAN SURVEY

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Background: In kidney transplantation (KTx), renal graft thrombosis (RGT) is one of the main causes for early graft loss. Although a clear evidence-based international antithrombotic protocol for KTx is absent, antithrombotic prophylaxis is often used in order to prevent RGT. The aim of this survey was to obtain a pan-European view of the different antithrombotic management strategies applied in KTx.
Methods: An online 22-question survey was distributed through e-mail and various platforms of the European Society for Organ Transplantation. Participants were kidney transplant professionals. Questions covered demographic information, whether one would start, continue, or stop specific antithrombotic agents, and which donor and recipient factors influenced their decision.
Results: In total, 75 responses from 21 countries and 51 transplant centers were included: 56 (75%) respondents had over 10 years' experience, 48 (64%) were surgeons and 23 (31%) nephrologists. Availability of a written antithrombotic management protocol was reported by 56 (75%) respondents. In 8 (16%) centers, respondents contradicted each other regarding this. Antithrombotic prophylaxis is preferred by 50 (78%) respondents independent of the available protocol. Vitamin K antagonists (69%), direct oral anticoagulants (79%) and at least 1 agent of dual antiplatelet therapy (85%) were most likely to be discontinued prior to KTx, due to estimated increased bleeding risk (92%). Intraoperatively, 32% administer intravenous unfractionated heparin in selected cases and 18% in all cases. Doses varied between 400 and 10.000 international units. Postoperatively, 50% prescribes subcutaneous LMWH and 19% intravenous unfractionated heparin. Vascular reconstruction (64%), atherosclerosis of the recipient (60%) or history of venous thromboembolism (73%) were the most common reasons to optimize antithrombotic prophylaxis.
Conclusions: Despite the overall preference for antithrombotic prophylaxis in KTx, there is a high variation within Europe regarding type and dosis, most likely due to a paucity of high quality studies. This warrants further research in order to develop better guidelines.

POS069 OPTIMIZATION OF ERYTHROPOIETIN STIMULATING AGENTS FOR POST-TRANSPLANT ANEMIA IN KIDNEY RECIPIENTS: PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Background: Many studies suggested that chronic allograft nephropathy might progress faster in patients with PTA, but whether full correction of anemia improves renal outcomes is unknown. We aimed to assess the impact of full correction of chronic anemia in renal transplant recipients with stable graft function on patient and graft outcome along one year follow-up.
Methods: We enrolled 247 kidney recipients with stable graft function to be assessed for anemia. Eligible patients were randomized to achieve target hemoglobin between 11:12 g/dl (group 1, $n = 183$), or 13:15 g/dl (in group 2, $n = 64$) using erythropoietin receptor stimulating agents (ESA). Monthly clinical and laboratory evaluation of kidney graft function was carried out. Quality of life was assessed at the start and 12 months.
Results: More females were found in group 1(68.9%) vs. (50%) in group 2 ($p = 0.007$), and the original disease was chronic glomerulonephritis (37.5%) followed by diabetic nephropathy (DN) (15.7%)in group2; but DN patients predominate in group 1($p = 0.005$). The studied groups were comparable regarding pre-transplant co-morbidities. Most patients received thymoglobulin as induction and most of them were maintained on cyclosporine. We did not find any significant difference between the two groups concerning post-transplant diabetes, BK viremia or malignancies ($p > 0.05$), however better graft function was observed in group 2 at 6 months ($p < 0.05$). We found that required ESA doses were significantly higher in patients of group 1 from the 6th month. Group 1 showed higher mean blood pressure ($p = 0.003$) while group 2 showed higher mean albumin ($p < 0.05$). Graft outcome was comparable in both groups ($p = 0.125$), but mortality cases were significantly higher in group 1 (16 cases, 8.7%)($p = 0.005$).
Conclusions: Full correction of PTA in renal transplant recipients had no positive impact on graft outcome but it was associated with better patient survival possibly due improved cardiovascular risk.

POS070 A COMPARISON OF CREATIN'S INDEX AND GERIATRIC NUTRITION RISK INDEX IN SHORT-TERM CARDIOVASCULAR MORTALITY RISK IN HEMODIALIZED PATIENTS

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Background: Cardiovascular mortality rates of hemodialysis patients are significantly higher than the general population. In this study, the creatinine index (CI) and the geriatric nutrition risk index (GNRI) were compared in terms of the risk of short-term cardiovascular mortality.
Methods: This retrospective cross-sectional study included 169 patients who had been treated for hemodialysis for over three months in our hospital. The relationship between basal CI and GNRI values determined using demographic and biochemical parameters dated January 2017 and one-year cardiovascular mortality rates were analyzed.
Results: 49.7 % of the patients were female, 15 % were diabetic, the mean age was 57 ± 16 years, and the median hemodialysis duration was 33 (IQR; 23–60) months. Basal CI was 12.6 (11.8 - 13.2) and basal GNRI was 105.9 ± 16.6. Cardiovascular disease caused 8 of 19 patients who died over a 12-month period. Patients in the lower CI percentile had a higher incidence of cardiovascular death than patients with higher percentile ($p < 0.008$). Although patients in the lower GNRI percentile showed a higher incidence of cardiovascular death than patients with a higher percentage, statistical significance remained at the trend level ($p = 0.07$). We observed a significant association with the presence of diabetes mellitus, creatinine, albumin, CRP, CI and GNRI in the multivariate model adjusted for age and sex. Higher CI levels [HR: 0.18 (CI 0.06%, 0.54) $p = 0.002$] and higher GNRI levels [HR: 0.93 (CI 95 0.88, 0.99) $p = 0.03$] were protective for cardiovascular mortality.
Conclusion: CI, a nutritional parameter, is a more reliable and effective method than GNRI to test the risk of short-term cardiovascular mortality in hemodialysis patients.

POS071 ROLE OF DONOR SPECFIC ANTIBODY AND PROTEINURIA IN KIDNEY TRANSPLANTATION AND ALLOGRAFT OUTCOMES

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Background: Antibody –mediated rejection (ABMR) is one of the factors affecting the –long term graft survival after kidney transplantation (KT). Post-transplant porteinuria is common and has mulitple causes. Proteinuria is a sensitive indicator of reduced graft survival.
Methods: We follow-up 530 transplanted patients in our center. We enrolled 85 kidney transplanted patients (-transplanted between 1991–2020) and followed until october 15.2020. We created 3 groups: ABMR group ($n = 19$, biopsy proven ABMR), DSA (donor specific antibody) positive group ($n = 14$), DSA negative group ($n = 52$). Differences in patient, donor and transplant characteristics between DSA positive and negative groups were assessed by Fishers exact test for categorical variables. Death censored graft loss was assessed by Kaplan Meier analysis with log risk statistics.
Results: The majority of DSA pos recipients had either anti HLA class I (47, 37 % in ABMR and 15, 38% in DSA pos group) or II antibodies (AMBR group: 68, 42 %, 92.31 % in DSA + group). Induction therapy was:

antithymocyte globulin (68% in ABMR groups versus 35 % in DSA pos group), basiliximab 21% in ABMR group versus 7.14 % in DSA pos group. The MFI of DSA in ABMR group was: 6700 (MFI:6000–18000) in DSA pos group: mean: 4619 (MFI:3400–17000) before treatment (Wilcoxon rank-sum test: $p = 0.1302$). After treatment DSA decreased MFI: mean:5231 (sd:4099.81) in ABMR group and mean:2012.875(sd:1091,78) in DSA poz group (t-test:0.0071). Proteinuria decrease after treatment in ABMR group ($p = 0.0009$). Graft failure's frequency increase every 10 mg/mmol elevation of porteinuria means 7 % elevation (hazard ration is 1.07%). Estimated 3-year graft survival was 87, 5% in ABMR group, 93 % in DSA pos group, and 100 % in DSA negative group (log-rank probe $p = 0.0666$).
Conclusions: The presence of DSA increases graft loss independent to proteinuria. Decreasing proteinuria can improve outcome our patients reducing their cardiovascular risk.

POS072 IS SAFE OOCYTE DONATION PREGNANCY AFTER KIDNEY TRANSPLANT?

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Background: Oocyte donation enables women with diminished ovarian reserve, premature ovarian failure, genetic disorders, surgical menopause and bilateral tubal ostruction to become pregnant.
Pregnancy after kidney transplant has become possible thanks to the recent surgical and pharmacological breakthrough
Methods: Retrospective study including all women with kidney transplantation and deliveries after oocyte donation. The following variables were analyzed: type of nephropathy, patient age when dialysis started, age at transplantation, time between dialysis and transplantation and between transplantation and baby birth, immunosuppresive theraphy, type of delivery, baby weight, Apgar score, mother and baby follow-up, age of the oocyte donors, numbers and quality of the embryos transferred. Only altruistic oocyte donation were permitted.
Results: We followed up four pregnancies in four patients who were diagnosed with IgA nephropthy and three unknown nephropathy. Three patients received a cadaveric donor kidney, one received a living donor kidney. They were treated with calcium antagonists and alphametildopa for their high blood pressure. Mother complication: preeclampsia (2); Fetal complications: acute distress respiratory syndrome (1) preterm births (two). One baby was admitted to the neonatal intensive care unit. The mother's follow-up showed no acute rejection episodes. Breastfeeding was discouraged due to the transmission of immunesuppressive medications into breast milk. We did not observe significant disease upon child follow-up.
Conclusions: Kidney transplant and oocyte donation are itself independent risk factors for adverse maternal and neonatal outcomes. Patients therefore be referred to highly specialized centres where obstetricians nephrology intesivists and neonatologists provide surveillance and treatment

POS073 TACROLIMUS DOSE AND ETHNICITY: LONG TERM OUTCOMES OF RENAL TRANSPLANT RECIPIENTS

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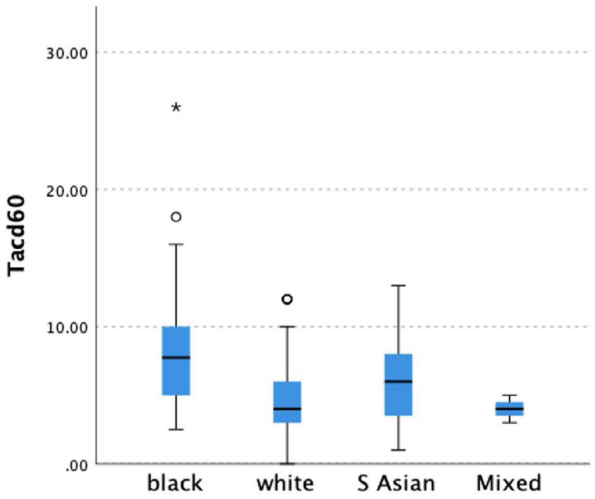
Introduction: Genotypic differences between ethnic groups dictate the need for unique dosing regimens. Cyp3A4/5 plays an important role, with Black population more likely to be homozygous and hence fast metabolisers, thus needing bigger doses. We looked at the tacrolimus dose/level variation across an ethnically diverse population of renal transplant recipients.
Method: A retrospective analysis of 320 renal transplants (living+deceased donor) performed at Royal London Hospital between January 2013 - December 2015. Recipient level data (race, demographics, co-morbidities, primary disease, induction/immunosuppression, long term kidney function) at 3, 12, 24, 48 and 60 months (M) were collected.
Results: Of the 320 transplants, 180 patients were maintained on tacrolimus throughout the study (B:22.5%, W: 45%, SA:28.5%, EA:0.01%, 0.02%).
Mean tacrolimus dose reduced with time post transplant (3M:8.2, 12M:6.49, 24M:6.01, 48M: 6.02, 60M:6.09) but remained similar during the study cohort (7.6–7.8)
Across different ethnicities, tacrolimus dose remains high in Black patients compared to White and South Asian (SA) recipients throughout the follow-up apart from month 60, when dose in Black and White ethnic groups remains significantly different while the difference between Black and South Asian cohorts vanished $p < 0.05$



Tacrolimus levels remained similar across all cohorts throughout the study period.
Serum creatinine was best in SA and remained statistically better than other ethnic groups. At 60 months this difference disappeared between SA and White patients but remains against Black patients $p < 0.05$. 74/302 transplants showed evidence of rejection on biopsy results with no co-relation of biopsy with either tacrolimus dose or levels.
Conclusion
Tacrolimus dose needs to be high in black patients to maintain therapeutic levels, likely due to of genotypic differences. The levels were maintained across all groups with no difference in rejection episodes. Despite similar trough levels, the overall serum creatinine levels declined more rapidly in these patients. Ethnic disparities continue to affect the long term outcomes in transplant recipients. Thus, a multifaceted approach towards improving the outcomes is needed.

POS074 THE CURRENT PRACTICE OF LIVE DONOR NEPHRECTOMY IN TURKEY: RESULTS OF A NATIONWIDE SURVEY

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Background: The availability ofminimally invasive donor nephrectomy has been shown to enhance the willingness of live donation. In this study we evaluated the current preferences regarding the surgical technique of live donor nephrectomy in Turkish transplant centers.
Methods: A questionnaire was sent to 83 kidney transplant centers in Turkey. Questions included the number of donors, techniques used, perceived complication rates, inclusion and exclusion criteria of the technique as well as the training received by surgeons.
Results: Five transplant centers not performing live donor kidney transplants were excluded. Sixty-seven (85.8%) of the centers performing live donor kidney transplantation responded to the questionnaire. In 2019, the median number of kidney transplants was 45 (min = 1, max = 484), and the median number of kidney transplants from living donors was 28 (min = 1, max = 238). Open donor nephrectomy was performed by 19 centers (28.4%), and the minimally invasive technique was performed in 48 centers (71.6%). Among the transplant surgeons 52.2% performed more than 100 donor nephrectomies as primary surgeons, 62.7% had been using their preferred technique for more than 5 years. 41.5 % of surgeons reported to have received a fellowship training.
The rate of having a protocol for a possible technical or surgical problem was significantly higher in centers using minimally invasive techniques ($p < 0.001$). There was no statistically significant difference among the self-reported complication rates ($p > 0.05$). On the other hand, chyle leakage was reported more commonly in centers using minimally invasive techniques ($p = 0.006$). Overall, centers performing minimally invasive donor nephrectomies had higher number of live donor kidney transplantations compared to the centers performing open donor nephrectomy ($p < 0.001$).
Conclusions: Most of the transplant centers in Turkey perform minimally invasive donor nephrectomies with considerably low complication rates and

these techniques have been implemented by experienced transplant surgeons. Centers performing minimally invasive techniques reported to have a protocol for technical or surgical problems.

POS075 DOWN-REGULATION OF INFLAMMATORY SIGNALING PATHWAYS DESPITE UP-REGULATIONOF TOLL-LIKE RECEPTORS; THE EFFECTS OF CORTICOSTEROID THERAPY IN BRAIN-DEAD

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Background: The brain death of a potential organ donor induces a systemic inflammatory response, resulting in inferior organ quality and function. Our study aimed to evaluate the effects of methylprednisolone (MPN) therapy on pattern recognition receptor (PRR) signaling in potential brain-dead (BD) kidney donors.
Material and Methods: To evaluate the effects of MPN therapy on PRR signaling in BD kidney donors we performed a prospective randomized treatment-versus-control study. Fifty-one potential kidney donors were randomly divided into three groups: brain-dead donors (BDDs) who received 15 mg/kg/d of methylprednisolone (group T1, $n = 17$), BDDs who received 15 mg/kg/d of MPN at the time of filling consent for kidney donation and 100 mg/2 h until kidney harvest (group T2, $n = 17$), and normal donors as controls $n = 17$. Gene expression for Toll-like receptors (TLRs) 1–9 and their signaling pathway molecules including MYD88, TRIF, NF-KB1, IRAK, IRF3, and IRF7, as well as the inflammatory cytokines RANTES, IL-1β, TNF-α, IL-6, CXCL8, IL-18, IFN-α, and IFN-β was determined by PCR array. Due to the crucial role of TLRs 2 and 4 in pattern recognition, surface expression of these molecules was analyzed by flow cytometry. Plasma levels of inflammatory cytokines were measured by immunoassay. Finally, serum creatinine and cystatin C were measured in 100 kidney recipients one week and one, three, and six months after transplant.
Result: Polymerase chain reaction (PCR) array gene expression revealed greater expression of TLRs and signalling molecules in group T1 than in the controls. Surface expression of TLRs 2 and 4 were significantly greater in group T2 than in group T1 ($p < .05$). Plasma concentrations of inflammatory cytokines were significantly greater in group T1 than in controls ($p < .05$). The recipients that received kidneys from group T1 had significantly higher levels of creatinine and cystatin C than the recipients of kidneys from both group T1 and controls ($p < 0.05$).
Conclusion: Administration of MPN to BDDs at specified periods until kidney harvest resulted in less systemic inflammation in the BDDs and improved renal function in kidney graft recipients compared with common MPN therapy.

POS076 DECISION MAKING ON ORGAN DONATION: THE REASON OF REFUSING FOR DONATION IN NON-DONOR FAMILIES

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Introduction: the purpose of this study was to determine the factors influencing the relatives' decisions for refusal to consent for organ donation in brain dead donors.

Methods: This cross-sectional study was performed during the year 2019 at the Organ Procurement Unit of Sina, Tehran, Iran. From 166 brain dead potential donors, 139 families accepted donation (group A), while 27 families refused the donation requests (group B . (The data were collected by using a questionnaire via face-to-face. All the participants completed the questionnaires and the relevant data were extracted . Descriptive statistics were performed using t-test, Chi square test and Fisher exact test. The data were analyzed by using SPSS 16 software. Results: The mean age of brain-dead cases were 38.6 ± 17.86 years (range 2–72). There was a significant difference between groups A and B in regards to employment ($p = 0.001$), prior discussion of organ donation with family and friends ($p = 0.001$) and the level of the family's education ($p = 0.003$). The most common causes affecting the relatives' refusal for organ donation included the expectation of a miracle and the unfamiliar concept of brain death. Discussion: Based on our results pertaining to the family's refusal for organ donation, the expectation of a miracle and the lack of awareness about organ donation demonstrates that brain death is not widely accepted and understood by the deceased's family. Therefore, appropriate training techniques in approaching potential donor families is essential for the healthcare staff. Thus, short- and long-term planning is crucial to implement change.

POS077 KIDNEY RE-TRANSPLANT: SINGLE CENTER EXPERIENCE FROM THE MIDDLE EAST

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Background: It has been reported that the long-term survival of second transplants may be similar to that of primary transplants. Reports of re-transplantation outcomes are scarce especially in the middle east region. We aimed to present our experience with second renal transplant in Kuwait and comparing the donor source among our re-transplant recipients.
Methods: Data of kidney re-transplants- under follow-up in Hamed Al-Essa organ transplant center of Kuwait- between 1980 and 2019 were retrospectively analyzed. Out of 3038 kidney transplants (KT), 198 were kidney re-transplants (6.51%). The number of KTs from living donors was 150; from deceased donors, 48 and third transplants represented 15 cases. We compared living donor group (1) with deceased donor group (2) regarding demographics, post-transplant complications and outcome.
Preliminary Results: We observed that episodes of acute antibody mediated rejection (9 cases, 18.7% in group 1 vs. 8 cases, 16.6% in group 2 respectively) and T-cell mediated rejection (14 cases, 9.33 % in group 1 vs.15 cases, 10% in group 2 respectively) were more frequent among patients in group 2 but this did not rank to statistical significance. Concerning 2nd graft outcome, we observed that the percentage of patients with failed grafts was higher among group 2 patients but did not rank to statistical significance during their last follow-up while the two groups were comparable regarding patient outcome.
Conclusions: Both living donor and cadaveric renal allotransplant carry the same risk for graft rejection either AMR or ACR. Meanwhile re- transplants who received their kidneys from either living or deceased donors had experienced similar graft and patients' outcomes. So, re-transplant either from living or deceased donor is considered a good option after first renal allograft loss.

POS078 EFFICACY AND SAFETY OF MARGINAL GRAFTS FROM EXPANDED CRITERIA DONOR (ECD) AND DONATION AFTER CIRCULATORY DEATH (DCD) IN ERDERLY RECIPIENTS

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Background: KT from SCD in erderly patients confers a benefit in survival and an improve in quality of life over remaining on dialysis. However, despite the known benefits of KT, long term and survival outcomes of marginal from ECD and DCD in older recipients are still limited.
The aim of our study was to evaluate the functional outcomes and safety of marginal grafts in recipients aged ≥75y
Methods: We made a retrospective study of a cohort of patients ≥75 y who received a 1°KT from ECD/DCD undergoing hypothermic pulsatile machine perfusion. Description of basal characteristics of donors and recipients was performed. A logistic regression multivariant model was made to analyse the functional results (delayed graft function (DGF), acute rejection (AR) and vascular thrombosis (VT)) and the postoperative complications after KT

(urinary and wound infection, blood transfusion, hemodialysis, lymphocele, urinary leakage and ureterovesical stricture). Recipient survival was estimated by a Cox's regression model. Graft survival was evaluated using an estimative model of survival of competing risks.
Results: 8.9% (32/389) of the KT were performed in ≥75 y. There were no statistically significative differences in the basal characteristics of the patients, except the arteriopaty of the recipients (31.8% vs 17.8% in ≥ 75 and <75y) and tabaquism in donors (18.8% vs 49.6% in ≥ 75 and <75y)
We identified a statistically significant greater number of KT from DCD in the group of <75y compared to ≥ 75y (19.2% vs 0.6%, $p = 0.00$)
There were no differences between groups in AR (OR: 1.12 IC: 0.78–1.6 p:0.5), DGF (OR:0.82 IC:0.31–2.14, $p = 0.68$) and VT (OR: 0.46 IC:0.16–3.5, $p = 0.45$).
Recipient survival at 12 and 24m was 95.5% and 93.8% in <75y vs 100% and 89.6% in ≥ 75y. There were no differences between age groups (HR: 0.85 IC:0.20–3.58; p:0.86).Graft survival at 12 months of KT was 90.2% and 96.6% in <75 y and ≥ 75, respectively. There were no differences between age groups (HR: 0.24 IC:0.03–1.77; p:0.165).
In the analysis of postoperative complications, there were no differences in prevalence and severity between groups.
Conclusions: KT of marginal grafts in ≥75y is a feasible and safe option in the long term. 96.6% maintained the graft at 12m, with an overall survival of 89% at 2y. There were no higher number of post-KT complications compared to <75y.

POS079 KIDNEY TRANSPLANTATION FROM ELDERLY DONORS: SINGLE-CENTER EXPERIENCE

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Background: The shortage of deceased donor kidneys for transplantation has forced the re-evaluation of the limits on donor age acceptability. Thus, marginal donors such as elderly donors have been progressively increasing in recent years for organ transplantation around the world.
Method: In this retrospective cohort study, prospectively recorded data of patients who underwent kidney transplantation between January 1996 and January 2020 were evaluated.
Results: Of the total 392 kidney transplantation, 64 donors met the study criteria. The mean age of the donors was 59 ± 3.86 (SD) years (median 59 years, range 55–69 years). Of these 64 donors, 32 (50%) were female and 32 (50%) were male. The living donors were 40 (87.5%) and the deceased donors were 24 (12.5%). When the relationship between living donors of the recipients was evaluated, 35 (87.5%) donors were first-degree family members of the recipients (mother, father, sibling), 3 (7.5%) donors were second-degree family members of the recipients (aunt, uncle, grandparent) and 2 (5%) donors were spouse, respectively. In living donors, 16 (40%) of the donor nephrectomies performed open, 8 (20%) were laparoscopic, and 16 (40%) were robotic surgery. Twenty-one (87.5%) out of 24 deceased donors and 1 (2.5%) living related recipients presented DGF. There was no mortality in the living donors. There was no follow-up data in 12 (18.8%) donors. Therefore, survey analysis was performed with 52 donors. Overall patient and graft survival for 1, 5, 10 years for this study 84%, 84%, 84% and 90%, 88%, 80% and for living donor 96%, 96%, 96% and 90%, 88%, 80%, for deceased donor 81%, 74%, 74% and 78%, 74%, 67%, respectively.
Conclusion: Transplantation from the donors with age 55 and up, might be related to decreased kidney function and graft survival, compared to the transplantations from the standard donors. However, when the long term graft survival and patient survival is observed, the group of elderly donors cannot be subject to exclusion.

POS080 DECEASED-DONOR INITIATED CHAINS: THREE-YEARS' EXPERIENCE OF THE ITALIAN DECK PROGRAM

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Background: Kidney Paired Donation is a promising innovation in kidney transplantation, consisting in a considerable range of strategies developed for patients with a willing but immunologically incompatible living donor (LD). One third of all potential kidney donors are not suitable for donation to their intended recipients, due to HLA or AB0 incompatibility. The option of using deceased donor (DD) to start a chain of living donor kidney transplants among incompatible pairs had been previously proposed but only in 2018 the first successful experience was performed. In the DECK program, the chain-initiating kidney, selected from DD pool, is allocated to a recipient with an incompatible LD and, at the end of the domino-chain, the LD of the last pair donates to a waiting list (WL) patient. Recipients enrolled in the program gain priority in the allocation of chain-initiating kidney from deceased donor only in the absence of urgent, highly sensitized or combined transplants' candidates, according to the Italian policy for graft allocation.
Methods: From March 2018 to February 2021, 11 kidneys from DD were used to initiate chains allowing to perform 29 kidney transplants, across 11 Italian centers. The program enabled 20 incompatible pairs to achieve a compatible kidney transplant: 11 with HLA incompatibility e 9 with ABO incompatibility.
Results: All LDs are alive, with good renal function. Among recipients no deaths occurred. Mean renal function at 6-months and 1-year after transplantation is 1.35 ± 0.41 mg/dL and 1.65 ± 0.78 mg/dL, respectively. Two graft losses occurred: one in the early post-operative period due to arterial thrombosis and the other, 1-year after transplant, due to humoral rejection. In both cases, it was a chain-ending kidney into a WL recipient. Nine chain-ending kidneys were allocated to sensitized patient on the WL and their mean time on list was 5 years.
Conclusions: After the completion of the current ongoing domino-chain, a multiplying factor of 3 has allowed a significant increase in the number of kidney transplants made available thanks to a DD. Furthermore, the DEC-K program offers an opportunity of transplantation for recipients of incompatible pairs and it benefits the WL's candidates allocating chain-ending kidneys from LDs to them, prioritizing sensitized patients and long waiters.

POS081 THE SURVIVAL OF RECIPIENTS AND RENAL GRAFTS FROM EXPANDED CRITERIA DECEASED DONORS

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The growing demand for transplants has led to an expansion of the criteria for organ donation. The aim: to compare the 1- and 5-year survival of recipients and kidney grafts' from donors with standard and extended criteria after primary kidney transplantation (KTx).
Methods: Out of 1,459 recipients after primary KTx performed from 2007 to 2019, a sample ($n = 196$) was stratified by gender, age and type of donor. In recipients of group I renal grafts were harvesting from standard donors ($n = 134$), in group II – from extended criteria donors (ECD, $n = 62$). ECDs were classified using the UNOS definitions. The recipients of both groups were comparable for most parameters, except of age - 40.4 [32;48] and 46.4 [37;56], $p = 0.0023$. To assess the survival rate, the Kaplan-Meyer analysis method and log-rank criterion were used.
Results: 1- and 5-year survival of recipients in group I was 99% (95% CI 98–100) for both periods, 1- and 5-year survival of recipients in group II was 96% (95% CI 92–99) for both periods, $p = 0.16$ and $p = 0.33$. When comparing the obtained results, no statistical differences had been found.
The 1-year survival rate for renal grafts in group I was 97% (95% CI 94–99), in group II - 91% (95% CI 85–96), $p = 0.035$; 5-year survival rates were 93% (95% CI 89–96) and 78% (95% CI 70–86), $p = 0.023$, respectively. Thus, the 1- and 5-year survival of kidneys from standard donors was significantly better versus ECDs.
Conclusion: The survival rate of renal graft's recipients from standard and extended criteria donors was high and didn't differ. The long-term survival of kidney grafts was lower in ECDs group, but the use of this type of transplants is a perfectly acceptable way to overcome the critical shortage of donor organs.

POS082 CHANGES ON MINERAL METABOLISME AFTER LIVING KIDNEY DONATION. ARE THEY IMPORTANT?

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Background: Living kidney donors (LKDs) experience an acute and important decline in glomerular filtration rate (GFR). During next months after donation it improves until 60–89 ml/min in the most donors.

Modifications on the mineral metabolism that are produced after nephrectomy are controversial and have not been adequately investigated until now. Most important changes that have been descrived are: low serum phosphate levels (sP), low serum calcitriol levels (s1,25OHD) and high serum PTH levels (sPTH).
We retrospectively studied acute and long term mineral metabolism modifications of LKDs.
Material and Methods: From May 2011 to December 2019, we included 124 LKDs. Their clinical and analytical dates were evaluated before donation. Their mineral parameters and renal function (GFR- CKD-EPI) were repeatedly measured at 1, 3, 6, 12 months after donation and after that once a year.
Results: Mean ages of LKDs were 55.49 ± 10.46. 70% women. Baseline clinical characteristics: 18% smokers, 25% high blood pressure,39% dyslipidemia, 3% osteoporosis.
Mean baseline GFR 89 ± 13ml/min. Mean GF after donation: 1-month 58 ± 11ml/min, 3-months 58 ± 13ml/min, 1-year 60 ± 13ml/min, 5-years 68 ± 14ml/min.
Compared to pre-donation, levels of calcium unchanged.
Compared to pre donation, sP levels were lower at all the times until 9 months after donation. The lowest sP levels were 9 months after that (mean sP 1.08 mmol/l, p 0.03).
Compared to pre-donation, sPTH levels were higher at any time. This increasing was highest one month after donation (mean sPTH 70 ± 37 ng/l). This secondary hyperparathyroidism persisted until fives year after donation (p 0.01).
Compared to pre-donation, s1,25OHD levels were lower, and they persisted lower and stable during all the times after that.
Conclusions: Our study confirms that after donation sP levels persist lower until middle term but low levels of s1,25OHD and secondary hyperparathyroidism persists long term. These adaptations differ from those described in CKD patients. Because of these modifications may have a negative impact on bone health of our donors, it could be important to performe studies in this sense.

POS083 THE IMPACT OF PRETRANSPLANT RENAL BIOPSY ON THE EVALUATION OF PROSPECTIVE LIVING KIDNEY DONORS

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Background: Living kidney donation contributes essentially to increasing the donor pool, while offering significant benefits for the recipient. Since safety and excellent long-term outcomes of living kidney donors (LKD) are mandatory, renal biopsy must be part of the pretransplant evaluation in donors with isolated urine abnormalities or other risk factors.
Methods: We retrospectively collected data of potential living donors evaluated in the pretansplant outpatient clinic of Laiko General Hospital of Athens between 2007 and 2021. Demographic, clinical, laboratory and histological data were analyzed for 48 LKD who had undergone pretransplant biopsy. Biopsy indications included isolated microscopic hematuria (IMH), moderate albuminuria and commorbidities suggestive of chronicity. Donors with glomerular diseases and those with chronic lesions were excluded from donation.
Results: We identified 48 potential living donors who had undergone renal biopsy. Of these, 39 (81%) were women. Median age was 58 (IQR 51–63) years, while 19 (40%) were older than 60 years. 38 out of48 (79%) had glomerular hematuria, 8 (22%) had albuminuria (150–300 mg/d). 18 out of 48 (39%) of donors were hypertensive, 4 (2%) had impaired glucose tolerance and 6 (12%) had a BMI> 30 kg/m^2. A total of 30 (62%) potential donors were accepted for donation. The remaining 18 (38%) were excluded based on biopsy findings: 5 (10%) had IgA nephropathy, 5 (10%) TBMD, 3 (6%) secondary FSGS and the remaining 5 (10%) had increased chronicity. There was no biopsy complication in our cohort.
Conclusions: Renal biopsy is a useful tool in the evaluation of prospective LKD. Thorough assessment of donors with isolated urine abnormalities and marginal donors is critical to ensure good long-term post-donation outcomes.

POS084 LONG-TERM OUTCOMES IN OLDER KIDNEY TRANSPLANT RECIPIENTS FROM OLDER DONORS. A PROPENSITY SCORE ANALYSIS

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Background: the age of patients referred for kidney transplantation has increased progressively. However, the precise influence of age on hard outcomes after transplantation is controversial.
Methods: single-centre, longitudinal retrospective study in which graft and recipient survival in a cohort of ≥75 years old kidney recipients were compared with a contemporary younger cohort aged 60–65 years through a propensity score IPTW analysis.
Results: we included 106 recipients between 60–65 and 57 patients of ≥75 years old with a median follow-up of 31 [13–54] months. Unadjusted one- and five-year recipient survival did not significantly differ between the older (91% and 74%) and the younger group (95% and 82%, $p = 0.06$). In the IPTW weighted Cox regression analysis, recipient age was not associated with an increased risk of death (HR 1.88 95% CI [0.81–4.37], $p = 0.14$). Unadjusted one- and five-year death-censored graft survival did not significantly differ between both groups (96% and 83% for the older and 99% and 89% for the younger group, respectively, $p = 0.08$). After IPTW weighted Cox Regression analysis, recipient age ≥ 75 years was no associated with an increased risk of graft loss (HR 1.95, 95% CI [0.65 - 5.82], $p = 0.23$).
Conclusions: recipient age should not be considered itself as an absolute contraindication for kidney transplant. With a judicious selection of the recipient and the donor, kidney transplantation can be safely performed in elderly patients.

POS085 CLINICAL UTILITY AND EVOLUTION OF DONOR SERUM LACTATE DURING NORMOTHERMIC REGIONAL PERFUSION IN UNCONTROLLED DONATION AFTER CIRCULATORY DEATH (UDCD)

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Background: Injury is important in uDCD as a consequence of the inevitable primary ischemic event. We study if lactate, parameter related to ischemia, concentrations and monitoring in uDCD after regional normothermic recirculation (RNP) could be a predictive factor in the viability of organs for transplantation.
Methods: Descriptive, prospective study of a cohort of cases of uDCD in RNP. We study basal lactate, as well as, the evolution of the values of the lactate parameters produced in this uDCD model comparing between the macroscopic appearance of good perfusion will mark the final kidney viability.
Results: Of the 45 possible donor cases, 38/45 (84.4%) arrive to the operating room. No differences found between effective (203.08 ± 59.21) and ineffective 175.43 ± 75.32) organs in lactate (mg/dL) at arrival and serial determinations during RNP. The ability of lactate levels to predict viability outcome at different time points: ROC curve is not useful between the group of valid and invalid organs. Also, lactate value not correlated with the macroscopic poor perfusion of the organs observd.
Conclusion: We believe that for the Udcd in RNP model, the determination of plasma lactate values is not useful to predict the final viability of the kidneys.

POS086 INDIVIDUAL RISK POST-LIVING KIDNEY DONATION: A META-ANALYSIS OF THE EFFECTS OF DONOR DEMOGRAPHIC CHARACTERISTICS

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Background and aim: Living kidney donation risk is likely to differ according to donor's demographics. We aimed to analyse the effects of age, sex, body mass index (BMI) and ethnicity.
Methods: Systematic review and meta-analysis through Ovid (EMBASE, MEDLINE), Web of Science and Cochrane databases. Kidney function and the incidence of end stage renal disease (ESRD), donor survival, proteinuria, hypertension and surgical complications were analysed.
Results: 5129 studies were identified; 34 studies met the inclusion criteria, mainly from USA and Europe. Donors aged > 60 years had a significantly lower eGFR and higher serum creatinine 1-year post-donation; on average their eGFR was < 60 at donation, with higher incidence of surgical complications. Yet, the same findings were not confirmed if using 50 years as a cut-off. Males have higher post-donation blood pressure and a significantly higher relative risk of developing hypertension and ESRD post- donation (RR 1.75–2.24), although still very low in terms of absolute risk, but with higher relative short and long-term mortality, too. BMI>30 was found to significantly lower donor's eGFR one year post donation: on average the eGFR of obese donors was 2.7 lower (95%CI: -3.24 to -2.15) compared to non-obese patients. Obesity was also associated with higher blood pressure both pre- and 1-year post donation and higher proteinuria. BMI had no impact on risk of operative complications. Lastly, no significant difference was found in 1-year donor kidney function in association to ethnicity; however long-term, African donors were more likely to develop ESRD compared to Caucasians, although it is likely that kidney donation does not increase the overall risk of ESRD, compared to the general population.
Conclusion: Age > 60 years and males have higher risk of inferior outcomes after living kidney donation. A higher BMI lowers eGFR post-donation, although its clinical significance is minimal. The role of ethnicity remains to be ascertained.

POS087 THE IMPACT ON RECIPIENT DEMOGRAPHICS ON OUTCOMES FROM LIVING DONOR KIDNEYS

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Background and Aims: Recipient demographics are equally important on outcomes after kidney transplantation to those concerning the donor. The aim of this study was to assess, for kidneys retrieved from living donors, the effect of recipient sex, ethnicity and body mass index (BMI) on delayed graft function (DGF) and one year graft function, incidence of acute rejection (AR), recipient and graft survivals.
Methods: A systematic review and meta-analysis was performed. EMBASE, MEDLINE databases were searched using algorithms through Ovid. Web of Science collection, BIOSIS, CABI, Korean Journal database, Russian Science Citation Index, SciELO were searched through Web of Science. Cochrane database was also searched. Risk of bias assessment was performed using the NHBLI tools. Data analysis was performed using Revman 5.4. Mean difference (MD) and Risk ratio (RR) were used in analysis.
Results: 5129 studies were identified; 24 studies met the inclusion criteria and were analysed. Female recipients were found to have a significantly lower serum creatinine 1-year post-renal transplantation (MD: -0.24 mg/dl 95%CI: -0.18 to -0.29 p <0.01) compared to male recipients. No significant difference in survival between male and female recipients, nor between Caucasians and Africans was observed (p = 0.08). However, Caucasian recipients had a higher 1-year graft survival compared to African recipients (95% CI 052–0.98) with also a lower incidence of DGF (RR = 0.63 p <0.01) and AR (RR = 0.55 p <0.01). Recipient obesity (BMI > 30) was found to have no effect on 1-year recipient (p = 0.28) and graft survival (p = 0.93) compared to non-obese recipients, although non-obese recipients had a lower rate of DGF (RR = 0.65 p <0.01) and AR (RR = 0.81 p <0.01) compared to obese recipients.
Conclusions: Female recipients had a better renal function 1-year post-renal transplantation. Recipient ethnicity (African) and obesity were found not to influence recipient and graft survival, but negatively affecting DGF and AR.

POS088 AGING IN LIVING DONATION. PERIOPERATIVE ANALYSIS

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Background: Live donor kidney transplantation is the best treatment for end stage kidney disease in terms of both, patient and graft survival. However, donors' selection must be done carefully to minimize the risk of nephrectomy. Despite the age of living kidney donors has increased in the last decades, candidates over 70 may not be accepted, as aging is related to comorbidities that implies a higher surgical risk.
Objective: To analyze the basal characteristics and perioperative risk of living donors over 70 compared with a younger group.
Methods: Demographic and clinical characteristics, as well as variables related to perioperative risk were collected of living kidney donors between 2010 and 2017. Two groups (< 70 and ≥70 years old) were established in order to make comparisons between them. Perioperative survival period was measured between nephrectomy and hospital discharge.
Results: Eighty-nine donors over 70 were registered, that accounted for 3.3%. Men accounted for 40.4% with a median age of 72 (range 70–79). The most common first-degree relationship was parents. When both groups were compared, we observed that body mass index was similar. However, the hypertension prevalence was higher in the older group and glomerular filtration rate was 10 points lower as expected due to age difference. The rate of proteinuria (over 150 mg/24 h) was lower, but the difference was not significant. Laparoscopic techniques were widely used and accounted for

Table 1.
Baseline and perioperatoycharacteristics (age <70 vs age ≥70)

BASELINE DONOR CHARACTERISTICS			
	AGE <70 (N=2580; 96,7%)	AGE≥70 (N=89; 3,3%)	p[d]
AGE (years)			
Median (IQR)	51 (44-58)	72 (70-74)	<0,01
Min-Max.	18-69	70-79	
SEX (N, %)			
Male	898 (34,8%)	36 (40,4%)	0,274
Female	1681 (65,2%)	53 (59,6%)	
BLOOD TYPE (N, %)			
O	1436 (55,7%)	43 (48,3%)	
A	943 (36,6%)	39 (43,8%)	0,384
B	171 (6,6%)	5 (5,6%)	
AB	30 (1,2%)	2 (2,2%)	
RELATION DONOR -RECIPIENT (N, %)			
Non related	126 (4,9%)	5 (5,6%)	
First-degree relative	1420 (55,1%)	52 (58,4%)	
Parents	704 (49,6%)	47 (90,4%)	0,934
Siblings	630 (44,4%)	4 (7,7%)	
Other-degree relative.	152 (5,9%)	4 (4,5%)	
Emotional relation (couple)	881 (34,2%)	28 (31,5%)	
BMI (N)	2516	89	0,676
Median (IQR)	26 (23,4-28,7)	25,9(23,9-28,6)	
PROTEINURIA (N, %)[a]			
<150 mg/24h	1694 (87,5%)	59 (92,2%)	0,266
≥150 mg/24h	241 (12,5%)	5 (7,8%)	
PROTEINURIA (N)[b]	241	5	0,770
Median (IQR)	200 (170,5-260)	202 (165-259,5)	
BASAL HYPERTENSION (N, %)			
Yes	260 (10,3%)	21 (23,9%)	<0,01
No	2264 (89,7%)	67 (76,1%)	
HYPERTENSION TREATMENT (N, %)			
One drug	48 (36,1%)	-	0,418
More than one drug	85 (32,7%)	3 (14,3%)	
BASAL CREATININE (N)	2558	89	0,295
Median (IQR)	0,78 (0,67-0,9)	0,78 (0,7-0,9)	
CKDEPI (N)[c]	2579	89	<0,01
Median (IQR)	96,3 (86,3-104,9)	82,3 (74,7-89,2)	
PERIOPERATORY CHARACTERISTICS			
	AGE <70 (N=2580; 96,7%)	AGE ≥70 (N=89; 3,3%)	p[d]
SURGICAL TECHNIQUE (N, %)			0,06
Laparoscopy	1890 (78%)	71 (91%)	0,052
Hand-assisted laparoscopy.	342 (14,1%)	5 (6,4%)	0,530
Transvaginal laparoscopy	96 (4%)	2 (2,6%)	0,100
Open lumbotomy	81 (3,3%)	-	0,551
Minilumbotomy	11 (0,5%)	-	
POST-SURGICAL COMPLICATIONS REPORTED (N, %)	131 (5%)	9 (10.1%)	
Infection	23	1	0,851
Haemorrhage	28	3	
Pain	15	1	
Other complications	65	4	
SURGICAL REINTERVENTION N (%)			
Yes	18 (0,7%)	2 (2,2%)	-
No	2550 (99,3%)	87 (97,8%)	
SURVIVAL AFTER SURGERY (N, %)	2580 (100%)	89 (100%)	-
INPATIENT DAYS (N)	2205	73	0,010
Median (IQR)	4 (3-6)	5 (4-7)	

a. Positive proteinuria if >150 mg/24; b. Median proteinuria estimated when positive proteinuria; c. CKDEPI was estimated assuming that all donors are Caucasian; d. Chi-squared for categorical variables, U Mann Whitney for continuous

100% in the group ≥70. Perioperative survival was 100%. Although a higher number of surgical complications were reported in older donors, they weren't significant, reintervention was only needed in two cases (both due to haemorrhage) and the length of stay in hospital was only one day longer (Table 1).
Conclusions: Old living kidney candidates may be accepted as donors. A cautious assessment of risk factors should be done.

POS089 KIDNEY GRAFTS FROM DONORS AGED ≥80 YEARS, A GOOD ALTERNATIVE FOR PATIENTS ON THE WAITING LIST?

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Background: The acceptance of grafts from donors of 80 years or older is a very complex process due to their older age and comorbidity. Both circumstances can generate doubts about the viability of these organs for kidney transplantation.
Our aim was to show our experience with the use of grafts from donors aged ≥80 years (D> 80) in our center and to compare them with grafts from donors between 70–79 years old (D70–80).
Materials and Methods: Comparative analysis of the evolution of transplantation with kidneys from D>80 versus D70–80 performed in our unit from January-2012 to December-2019. In this period 509 transplants were performed: 21 were D>80 and 122 were D70–80.
Results: Mean follow-up: 35.2 ± 27.2 months. The age of the recipients was higher in D> 80 (69.2 ± 4.3 vs 66.6 ± 5.9 years, p <0.001), without gender differences. Mean age of the donors in D>80 was 82.1 ± 1.8 vs 73.6 ± 2.8 years in D70–80 (p <0.001). We found no differences in donor gender, serum creatinine, HTN, diabetes mellitus or death from cerebrovascular disease (p = 0.97). Cold ischemia time was lower in D>80 (p = 0.01), with no differences in DGF or AR. Renal function measured by serum creatinine was worse in D>80 at first year: 2.3 ± 0.7 vs 1.7 ± 0.6 mg/dl (p = 0.007). First year graft survival was lower in D>80: 65% vs 83%, p = 0.05, without differences in patient survival. Currently, in D>80 group, 10 grafts are functioning and 11 (52.4%) have failed, four of them in the earlier postransplant period (two vascular thrombosis and two primary nonfunction) and four chronic rejections.
Conclusion: The use of kidneys from donors older than 80 years old allowed us the transplantation of older recipients, but with a high rate of early losses and a worse renal function than kidneys between 70 and 80 years. The acceptance of these organs should be individualized and multicenter studies are needed to know their prognostic and risk factors related to it in bigger series.

POS090 MIDTERM OUTCOMES OF LIVE KIDNEY TRANSPLANTATION FROM ELDERLY DONORS

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Background and aim: The rate of living donation from elderly people has been increasing during the last two decades. The outcome of these donations for both the donors and recipients is utmost important to evaluate the trend to accept living donors from elderly population. We have evaluated the outcome of organ donations for donors and recipients of those who had kidney grafts from the living donors aged 60 years or older.
Methods: Between February 2009 and December 2018, 816 living kidney transplantations were performed. The patients were divided into two groups according to the donor age (aged ≥ 60 years, n = 104 and aged < 60 years, n = 712). The demographic characteristics and outcomes of the procedure for both donor and recipient were compared between the two groups. Data were evaluated with independent t-test, Pearson Chi-square, and Fisher's exact tests.
Results: The mean follow-up period was similar in both groups. The demographic characteristics were similar regarding the gender, creatinine level at discharge, follow-up period (49.98 ± 28.40 months) and postoperative complications in donors. Older donors were more obese (28.47 ± 5.08) compared to young group (27.08 ± 4.75 kg; p = 0.006). The creatinine levels were significantly higher at the end of follow-up period in older patient group (1.12 ± 0.24 vs. 1.03 ± 0.23 mg/dL), but in none of the donors required dialysis. There was no significant differences between the groups regarding age, body mass index, follow-up period, hospitalization time, post-transplantation urologic complications and immediate and early graft functions. The number of males were higher in recipient group who received kidneys from younger donors compared to (68.7% vs. 53.8%, p = 0.003). The creatinine levels were significantly higher in those who had older grafts at the end of follow-up period, but graft loss rate was similar at the recipients with older grafts.
Conclusion: Older donors are an important component of living donor pool. Donors with age of 60 and higher can safely donate their kidneys.

POS091 ORGAN DONATION IN A DEVELOPING CARIBBEAN COUNTRY: A SINGLE CENTRE EXPERIENCE IN TRINIDAD AND TOBAGO

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Background: Patients diagnosed with end stage organ failure often benefit from organ transplantation, however, the global shortage of available organs for transplant is unable to meet the demand. In Trinidad and Tobago, Chronic Kidney Disease is the fourth leading cause of death with an estimated 1,800 patients receiving dialysis. The National Organ Transplant Unit (NOTU) was established in 2006 with the aim of providing renal and corneal transplants services. This study assessed the current state of NOTU and the organ donation experience at a single center intensive care unit in Trinidad.
Methods: A review of legal, human and material resources and a retrospective chart review of the current status of organ donation and transplantation in Trinidad and Tobago was conducted. Data were collected from medical records of deceased donors for the period January 2006 to December 2020. The organ donor experience in the Adult Intensive Care Unit at a tertiary care hospital in Trinidad was also evaluated. Data were collected from medical records of all patients in the adult intensive care unit for the period October 2016 to December 2016.
Results: Trinidad and Tobago has 4 donor hospitals, 1 transplant center, 1 surgical team consisting of 3 surgeons, approximately 100 trained Transplant Procurement Managers and 1 trained laboratory technician. There was a total of 27 donors after brain death (DBD) with the first actual deceased donation occurring in 2007. During the period January 1st 2006 to December 31st 2020, there were 195 renal transplants performed. Of these, 46 transplants were from DBD donors. The deceased donation rate was 0.77 donor pmp in 2006, peaked in 2014 at 3.85 and then remained at 1.54 donor pmp. Donor potentiality for the adult intensive care unit was 66.7% with a donation rate of 5.3%.
Conclusions: Organ donation in Trinidad and Tobago mostly relies on living donors. Despite recent increases in donation rates and donor conversion index, there remains a significant discrepancy between the donation potentiality and donation rate resulting in Trinidad and Tobago continuing to rely on living donors to reduce its waiting list. The implementation of a taskforce dedicated to developing action plans to improve organ donation services may assist Trinidad & Tobago in achieving self-sufficiency.

POS092 LONG-TERM OUTCOMES WITH EXPANDED CRITERIA DONORS IN KIDNEY TRANSPLANTATION: 10 YEAR EXPERIENCIA

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Background: Chronic kidney disease is associated with multiple comorbidities and a high cost for the health system. Kidney transplantation is the definitive treatment option. There is a significant gap between donor supply and recipient demand, which is why the use of expanded criteria donor organs (ECD) is a viable therapeutic option.
Methodology: A retrospective cohort of 1002 kidney transplant recipients was analyzed to determine patient and graft survival at 10 years post-transplantation. Kidney and patient survival probabilities were estimated by the Kaplan-Meier Method. A Cox regression model was performed to adjust a multivariate model for each outcome comparing the two groups of expanded versus standard criteria donor.
Results: The analysis included 1002 patients, among 18.8% (n = 189) correspond to the group of transplants with ECD. The group of ECD had lower patient (63.8% vs 48.1%) and graft (74.7% vs 63.3%) survival rates compared with the group of standard criteria donor at 10-year post-transplantation, however, there was no significant association between transplant with

ECD and graft loss or death when adjusted the covariates in a multivariate model. Significant risk factors for graft loss were mismatch (HR 1.1; p 0.019), acute cellular rejection (HR 2.4; p 0.000), acute humoral rejection (HR 2.0; p 0.033), cold ischemia time>14 hours (HR 1.5; p 0.020), and rehospitalization (HR 1.7; p 0.004). Significant risk factors for death were age (HR 1.03; p 0.000), acute cellular rejection (HR 1.5; p 0.018), cold ischemia time>14 hours (HR 1.4; p 0.018) and rehospitalization (HR 1.5; p 0.007).
Conclusion: kidney transplant recipients with ECD had lower survival compared to those who received a standard criteria graft, however, there was no significant association between transplant with ECD and graft loss or death when adjusted the covariates in a multivariate model.

Figure 1. Graft survival in expanded criteria donors compared with standard criteria donors

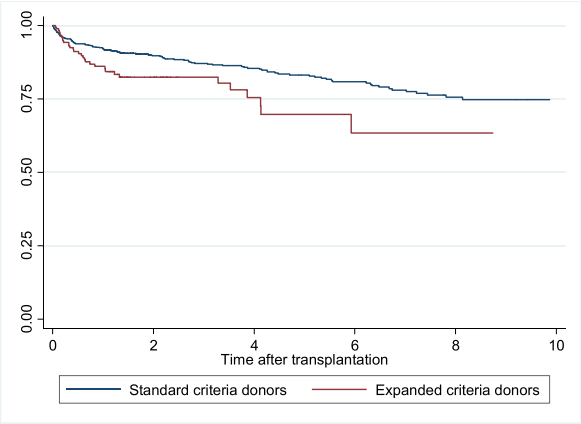

Table 1. Factors associated with Graft loss in kidney transplantation

Variable	HR	p	CI 95%
Mismatch	1.1	0.019	1.02-1.36
Acute celular rejection	2.4	0.000	1.74-3.53
Acute humoral rejection	2.0	0.033	1.06-3.98
Cold ischemia time >14 hours	1.5	0.020	1.07-2.01
Rehospitalizacion	1.7	0.004	1.20-2.60
Expanded criteria donors	1.3	0.178	0.87-2.01

HR: Hazard Ratio; CI: Confidence interval

POS093 LONG TERM RENAL OUTCOMES IN LIVING DONORS WITH ASYMPTOMATIC NEPHROLITHIASIS

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Introduction: Renal calculi can be discovered incidentally during the assessment of a potential living kidney donor. The use of donors with a history of nephrolithiasis is increasing around the world. We aimed to determine if the presence of asymptomatic calculi detected incidentally on CT scans had any effect on long term renal function and the likelihood of developing symptomatic nephrolithiasis after donation.
Methods: We conducted a retrospective analysis of 309 CT scans at centre for the assessment of potential kidney donors between 2012 and 2020. Donors with calculi identified on CT were compared to a random sample of 30 donors with no history of symptomatic nephrolithiasis. Patients were followed up for up to 6 years (1–6 years) years and 6 week, 1, 2, and 3-year mean creatinine were compared. The incidence of symptomatic nephrolithiasis was also assessed.
Results: 3.2% (10/309) donors had calculi identified on CT, ranging from 2–5mm and all of which were non-obstructing. There were no episodes of symptomatic UTIs. There was no difference in mean creatinine 6 weeks, 1, 2, or 3-years (p = 0.11, 0.07, 0.63, 0.23, respectively). None of the donors in either group had symptomatic nephrolithiasis or required any intervention for calculi at 3 years follow-up.
Discussion: The presence of incidental renal calculi did not impact donor kidney function post-donation in our cohort. Our data suggest that the risk of post-donation symptomatic stone episodes is also low. Routinely stone screening in patients who have a history of stones or with calculi identified on CT, may have contributed to the lack of symptomatic nephrolithiasis episodes post donation. Longer term follow-up with a larger population is also required to validate these findings.

POS094 MEETING PATIENT EXPECTATIONS MATTERS MORE THAN UK KDRI SCORE FOR QUALITY OF LIFE OUTCOMES AFTER KIDNEY TRANSPLANTATION

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Introduction: An increasing number of patients in the UK are being transplanted with kidneys from donors with higher UK KDRI scores. The aim of this study was to determine whether recipients of higher UK KDRI kidneys had inferior psychological outcomes.
Methods: All patients receiving a deceased donor renal transplant in 2018 were asked to complete a questionnaire including items on life satisfaction, mood, distress and health-related quality of life (HRQoL). Additional questions on benefit, life improvement, regret and expectations were also asked. UK KDRI was calculated using donor age, height, hypertension, sex, CMV, eGFR at retrieval and hospital stay.
Results: 42 responses were received. 26 were male (61.9%), 20 were white (47.6%) and 22 received a DBD transplant (52.4%). Median age was 60 years (IQR 19). 42.9% of patients received a kidney from a donor with a UK KDRI score > 1.5. The median time since transplant was 15.5 months. Age, gender, ethnicity, or type of kidney (DBD/DCD) had no significant impact on any questionnaire scores. UK KDRI score did not correlate significantly with any of the questionnaires.
The majority of patients felt they benefitted from a transplant (97.6%), that life was better afterwards (90.5%) and demonstrated no regret (97.6%). 83.3% of patients' expectations were met. Where expectations were not met, patients demonstrated significantly more distress (10.4 vs. 18.2; p = 0.018) and significantly worse life satisfaction (13 vs 25; p = 0.011).
Discussion: Patients receiving kidneys from donors with higher UK KDRI scores do not have significantly different psychological or quality of life outcomes after transplantation. Significant differences materialise when patients' expectations of the process are not met. This study has illustrated the importance of detailed discussions about the realities of transplantation, including the likelihood and potential impact of complications, prior to listing and the transplant taking place.

POS095 ESTRADIOL TREATMENT MODULATES ESTRADIOL RECEPTORS EXPRESSION AND REDUCES RENAL INJURY AFTER BRAIN DEATH IN FEMALE RATS

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Background: The impact of female sex hormones (FSH) on the donor state and on the inflammatory process triggered by brain death (BD) is evidenced by reports showing higher cardio-pulmonary injury linked to a reduction in 17β-estradiol (E2) serum levels. Expression of estradiol receptors (ER) are reported to be related to renal protection. This study aimed to investigate the effect of E2 treatment on BD-induced renal injury and ER expression in female rats. A short introduction indicating the rationale of the study
Methods: Female Wistar rats were divided: sham-operation (Sham), brain death (BD), treatment with E2 (50 μg/ml, 2 mL/h, i.v.) 3h after BD (E2). BD was induced by a sudden increase in intracranial pressure by rapid inflation of a balloon catheter in the intracranial space and the rats were maintained for 6 h. Creatinine, urea, and renal injury marker (KIM-1) were evaluated. In parallel, E2 concentration was quantified by ELISA and renal estradiol receptors (ER) expression (ER alpha, ER beta and GPER) were analyzed by immunohistochemistry.
Results: Estradiol concentration was significantly lower after BD and the treatment increased E2 levels (p <0.0001). ER alpha, ER beta and GPER kidney expression were increased by BD and reduced in treated group (p <0.05). The BD group presented higher KIM-1 expression and E2 treatment

resulted in downregulation ($p = 0.0002$). E2 group showed better renal function in comparison to BD group, reducing creatinine levels ($p = 0.04$).
Conclusions: E2 treatment was effective in reducing acute kidney injury and improving renal function in brain-dead female rats. As BD induced E2 reduction was associated with increased kidney ER expression and E2 treatment resulted in ER expression decrease, we could suggest that E2 exerts direct effects in the kidneys by interacting with its local receptors.

POS096 DBD AND DCD SPECIFIC KIDNEY PROTEIN PROFILES ASSOCIATED WITH 12-MONTH POST-TRANSPLANT KIDNEY FUNCTION

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Background and Aims: Organ transplantation is a lifesaving treatment for end-stage kidney disease. The growing demand for transplants has increased utilisation of older donors with comorbid conditions. Transplants from these 'higher risk' donors have increased risk of graft failure or short and long-term suboptimal allograft function. As yet, the molecular processes underlying the donor biological networks that regulate kidney injury progression, with the potential for targeted interventions and pharmaceutical prevention, are unknown.
Methods: Kidney biopsies from 185 deceased donors, taken at the back table, were obtained from the UK QUOD biobank. Kidney biopsies were selected on the basis of paired donor kidney posttransplant outcomes on the continuum of allograft function defined by 12-month eGFR. Using state of the art data independent acquisition (DIA) mass spectrometry techniques, we profiled the proteome of pre-implantation biopsies from $n = 100$ brain death donors (DBD) and $n = 85$ circulatory death donors (DCD). Proteomic profiles were further analysed by bioinformatics to identify the most prevalent biological networks in donor kidneys associated with progression to allograft dysfunction posttransplant.
Results: Mass spectrometry and bioinformatics analysis resulted in the development of a proteomic library of 6,683 proteins that were quantitated across all samples. Proteomic profiles that associated with suboptimal allograft function (eGFR<39ml/min 12-month posttransplant) were significant different between DBD and DCD kidneys. The analysis found 448 proteins in DBDs and 221 proteins in DCDs that significantly discriminated donor kidneys with suboptimal (eGFR<39 ml/min/173mm^2) and good (eGFR>60ml/min/173mm^2) 12-month post-transplant function. Pathway analysis showed that apoptosis and catabolic pathways are key to DBDs and histone modifications and metabolic dysregulation to DCDs.
Conclusion: Our data show that recondition of donor kidneys using pharmaceutical or mechanical prevention of donor kidney injury progression either during donor management or active perfusion should be specific for DBD and DCD donor types.

POS097 EXPERIENCE WITH EXPANDED CRITERIA DONORS IN KIDNEY TRANSPLANTATION IN THE COLOMBIAN CARIBBEAN REGION

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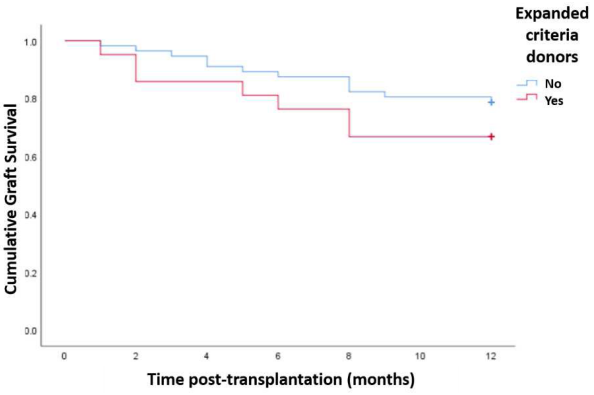
Introduction: In chronic kidney disease (CKD), kidney transplantation (KT) historically provides better benefits and results compared to other options, consolidating itself as the treatment of choice. In the absence of donors, the alternative of kidneys from marginal donors is an option.
Objective: to determine if the exclusive kidney transplant from a cadaveric donor with expanded criteria (ECD) is a valid alternative that presents a therapeutic benefit comparable to kidney transplant from a standard cadaveric donor (SCD) in the Colombian Caribbean Region.
Methods: Non-concurrent cohort study observed from 2013 to 2018 that included all kidney transplant recipients from deceased donors in the Colombian Caribbean region. For the study groups, the magnitude of the association of acute rejection, graft loss and mortality was determined through relative risks. A multivariate analysis was performed exploring the probability of occurrence of acute rejection due to the influence of possibly explanatory co-variables.
Results: 78 transplant recipients were included, corresponding to 57 SCD and 21 ECD, acute rejection at one year of follow-up occurred in 36 patients (46.2%), being for ECD 52.38% and for SCD 43.86% (RR 1.19, 95% CI 0.72–1.97). In ECD grafts there was 18.18% graft loss after acute rejection and for SCD grafts 12% (RR 1.51, 95% CI 0.29–7.83). Graft loss at one year of follow-up was 33.33% for those who received ECD grafts and 12.28% for those who received SCD grafts (RR 2.71, 95% CI 1.08–6.81). Mortality at one year was 6.4%, being among those who received ECD grafts 0% and for those who received SCD grafts 8.77%.
Conclusion: No significant difference was found between ECD and DCS grafts in terms of acute rejection or graft loss after acute rejection, in ECD grafts there was a higher risk of graft loss compared to DCS, however there was no mortality in said group at one-year to follow-up of kidney transplantation. The low number of patients limits the results, therefore more studies are required to account for the dynamics of kidney transplantation in the Colombian Caribbean Region in terms of acute rejection, graft survival, and recipient mortality.

Figure 1. Graft survival in expanded criteria donors compared with standard criteria donors



POS098 ANTI-HLA-DP ANTIBODIES POSITIVE - A RETROSPECTIVE REVIEW OF OUTCOMES IN RENAL TRANSPLANTATION- SINGLE CENTRE EXPERIENCE

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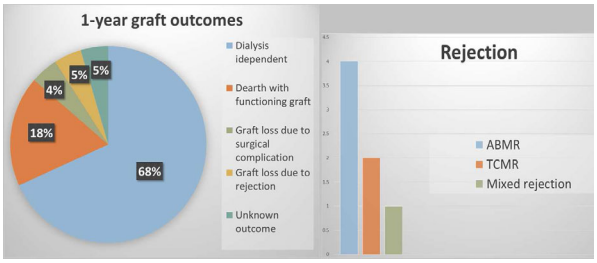
Background: Data on the role of HLA-DP antibodies on graft outcome are not precise. Some studies have suggested that the presence of donor-directed HLA-DP antibodies correlate with reduced allograft survival and increased risk for ABMR among recipients of a kidney transplant. In this single-centre retrospective study, we have investigated the one -year graft outcomes of patients with donor-directed HLA-DP antibodies who have received a renal transplant. Our primary outcomes included dialysis independence at one-year post-transplant and rejection ABMR, TCMR or mixed
Methods: Retrospective data were collected on 22 Kidney Transplant recipients who had donor-directed HLA-DP antibody at the time of transplantation between 2009 and 2019
Results: We identified 22 patients. Induction IS: Basiliximab 6; Alemtuzumab 11 Unknown 5 Maintenance IS: Myfortic, and Tacrolimus or Myfortic, Tacrolimus and Prednisolone.19 patients had deceased donor, and 3 patients had a live donor transplant. Most of our patients were highly sensitised (cRF>85%) pre-transplant 81% ($n = 18$). 18% ($n = 4$) patients were not mismatched at HLA A, B, and DR. 68% were at their 2nd or 3rd transplant. At 1-year post-transplant, 68% had a working graft (defined as dialysis independent regardless of eGFR). Of those with graft loss, four died with a functioning graft, one due to surgical complications, one due to rejection; no information is available on the remaining two patients. A majority of 13 (59%) had delayed graft function, and six patients had a kidney biopsy in the first-week post-transplant (acute tubular necrosis- 5 and acute vascular rejection-1). 72% ($n = 16$) had donor-directed HLA-DP antibody MFI > 5000 at the time of transplantation;63% ($n = 14$) had a positive FCXM at the time of transplantation. 32% ($n = 7$) had a biopsy-proven rejection. The majority 5 out of 7 being ABMR.
Conclusions: Most of our patients were highly sensitised and at their 2nd or 3rd transplant. Even though 63% had positive FCXM at the time of transplantation, the rejection rate was 32%. Most rejections were ABMR. At 1-year post-transplant, 68% of the patients were dialysis independent. Our centre experience suggests that KTx across DP DSAs with +/-ve FCXM could be a feasible option for carefully selected, highly sensitised patients who otherwise may not find a compatible donor.



POS099 ATHENA – IMPACT OF PRIMARY IMMUNOSUPPRESSION ON DEVELOPMENT OF DE NOVO DONOR SPECIFIC ANTIBODIES WITHIN 12 MONTHS POST-KIDNEY TRANSPLANTATION

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Background: In the ATHENA trial [NCT01843348], safety and efficacy of everolimus co-administered with tacrolimus [EVR/TAC], tacrolimus plus mycophenolic acid [MPA/TAC], or everolimus with cyclosporine A [EVR/CsA] was analyzed in *de novo* kidney transplant [KTx] recipients. In the present post-hoc analysis the effect of the primary immunosuppressive regimen on the development of *de novo* donor specific antibodies [DSA] as well as on the clinical outcome, within the first 12 months [M] after KTx, was investigated.
Methods: ATHENA was a 12M prospective, open-label study with 612 patients [pts] randomized 1:1:1 at time of KTx to either EVR/TAC, the control arm MPA/TAC, or EVR/CsA; all in combination with steroids. As part of a post-hoc analysis the role of HLA and non-HLA antibodies was investigated on the per-protocol population [PP] (n = 337). Here, we report initial results on the development of *de novo* DSA within the first 12M after KTx.
Results: The PP included n = 110 pts in EVR/TAC, n = 147 pts in MPA/TAC, and n = 80 pts in EVR/CsA arm. Within the first 12M after KTx, development of *de novo* DSA was observed in only seven pts across all three treatment groups: n = 1 in EVR/TAC, n = 2 in MPA/TAC, and n = 4 in EVR/CsA arm. From these seven pts only two experienced a clinical event in form of BPAR during the first 12M: n = 1 in EVR/CsA and n = 1 in MPA/TAC group; no events occurred in the EVR/TAC group. Neither graft loss nor death were observed in this subset.
Conclusions: In this post-hoc analysis of the as to date largest randomized European KTx study ATHENA, initial findings reveal that development of de novo DSA seems not to be impacted by the primary immunosuppression selected. Moreover, within the first 12M after KTx development of de novo DSA does not appear to have a direct influence on the resulting clinical outcome. Further analyses on de novo DSA as well as on non-HLA antibody (ETA & AT1) development and outcomes are currently ongoing.
In memoriam Duska Dragun, our dear friend and always inspiring colleague, who passed away much too early.

POS100 CLUSTERS OF ANTI HLA CLASS II LUMINEX RESPONSES REVEALED BY SIMPLE MACHINE LEARNING ALGORITHMS. IMPLICATIONS FOR DSA STUDIES

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Background: Antibody response against HLA is one of the most important factors determining the immunological risk for graft loss. Anti-HLA antibody responses present cross-reactivity and are even directed against HLA not presented by the graft. Antigenic distance between donor and recipient is crucial for predicting the transplantation outcome and finding a way to objectively measure it, thus improving the transplantation prognosis.
Methods: In this study, pre and post-transplantation anti-HLA class II responses of 1748 patients were analyzed. The analysis was performed through the application of machine learning algorithms using as input the raw Mean Fluorescence Intensities as measured by Luminex platforms. Dimensionality reduction analysis was performed in R with a FactoMiner package. To avoid statistical bias, only one serum sample per patient was included.
Results: In a previous work (1), we showed that the major variance explaining projection shows a strong correlation of anti DR and DQ responses while anti DP responses are almost orthogonal to the previous ones when a large population is studied. In this study we performed single locus antigen response decomposition through Principal Component Analysis (PCA) in order to detect intra locus antigen similarities in the aforementioned cohort.
Intra-locus PCA projections revealed a major correlation pattern for anti HLA-DR responses divided into DR51/52/53 groups with minor exceptions. Anti-HLA-DQ responses formed four major distinct groups explaining the majority of variance of the antibody response while for anti HLA- DP responses a strong sub clustering effect of DPA antigens is observed.
This analysis reveals new correlations and provides robust representations of antigenic distances to be used for the prediction of harmful immune responses in pre and post transplantation settings.
Conclusion: We conclude that unsupervised modeling of antibody responses can be another weighing tool for evaluation of the immunological risk especially for previously immunized patients. The implications of these findings for the prediction of Donor Specific Antibody responses are discussed. (1) *Vittoraki A. et al Patterns of 1,748 Unique Human Alloimmune Responses Seen by Simple Machine Learning Algorithms, Front. Immunol. (2020) 11:1667*

POS101 DETECTION AND QUANTIFICATION OF IMMUNOLOGICALLY RELEVANT ALLOANTIBODY-HLA INTERACTIONS USING MICROFLUIDIC ANTIBODY AFFINITY PROFILING

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Background: Detection and characterisation of donor human leukocyte antigen (HLA)-specific antibodies (Abs) is essential for patient evaluation, immune monitoring and risk assessment in solid organ transplantation. Currently used immunoassays rely on HLA surface immobilisation and do not enable determination of fundamental properties of Abs in solution, namely their affinity (K_D) and concentration [Ab]. We aimed to overcome these limitations to enable in depth profiling of HLA-specific Abs directly in patient sera and provide insights into its clinical translation.
Methods: Using a microfluidic diffusional sizing-based strategy, we developed microfluidic antibody affinity profiling (MAAP), a novel in-solution immunoassay that simultaneously determines K_D and [Ab] in patient sera without the need for antigen immobilisation or purification. Human monoclonal Ab reactivity was characterised at various concentrations using Single Antigen Beads (SAB), SAB-C1q, flow cytometry (FC) and complement dependent cytotoxicity (CDC). Interaction kinetics were quantified with MAAP and Biolayer Interferometry (BLI). HLA Ab incompatible (HLAi) transplant patient sera were characterised using MAAP and Luminex SAB.
Results: Abs exhibited the highest affinity for their sensitising HLA enabling its distinction from other interactions with cross-reactive HLA. SAB and SAB-C1q outputs correlated poorly with K_D due to effects of avidity and [Ab]. FC and CDC outputs were dependent on [Ab] and K_D. The degree of CDC kill was proportional to Ab-HLA K_D when the same HLA cell target was used. Micromolar Ab-HLA interactions could generate high SAB and SAB-C1q signals but were consistently CDC negative, even at high [Ab]. Affinity analysis using purified samples was consistent between BLI and MAAP, however MAAP also enabled reliable analysis in human serum. Importantly, MAAP enabled biophysical quantification of immunologically relevant Ab-HLA interactions in HLAi transplant sera, not previously attainable using currently available immunoassays (Figure 1).
Conclusions: This work provides evidence for the importance of antibody abundance and affinity in clinically relevant humoral alloresponses and, through development of MAAP, outlines a path towards in depth profiling of antibody responses in patient sera.

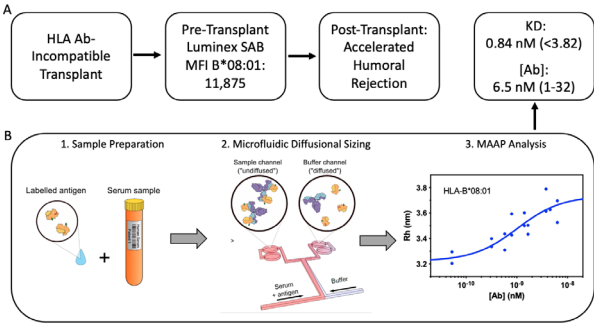

Figure 1. Microfluidic Antibody Affinity Profiling to determine both antibody concentration and affinity in human patient serum. A) An example of a patient that underwent HLA antibody incompatible transplantation. Pre-transplant serum showed donor-specific antibody with a Luminex SAB MFI of 11,875 against HLA-B*08:01. The transplant proceeded following desensitisation but the patient went on to suffer accelerated humoral rejection. B) Retrospective MAAP analysis of this pre-transplant serum sample showed the presence of donor specific antibody with high affinity to HLA-B*08:01.

POS102 HIGH CHOLESTEROL AND AGING NEGATIVELY INFLUENCE RENAL CAPILLARY DENSITY AND TUBULE VILLIN EXPRESSION BY DECREASING CAPILLARY VEGF AND NITRIC OXIDE

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Background: The role of aging and high cholesterol (HC) on endothelial cells (ECs) is not well defined. Aged ECs might produce less nitric oxide (NO) and VEGF, resulting in reduced glomerular capillaries (GCs) and peritubular capillaries (PTCs). To understand whether the capillary loss was due to changes in angiogenic factors affected by age and cholesterol, we investigated the impact of age and HC on the density of GCs and PTCs.
Methods: Among 150 patients, 63 (42%) had HC. HLA-DR and CD31 stained to determine the mean number of GCs and PTCs. PCNA, VEGF, and NO expression of GCs and PTCs examined. EC proliferation index (PI) of GCs and PTCs assessed by PCNA. Villin expression and PI of tubules examined.
Results: The mean capillary numbers were 38.4 ± 15.2 and 27.6 ± 14.4 for GCs and PTCs, respectively. VEGF and NO expression of both GCs and PTCs and the PI of all capillaries decreased with increasing donor age and cholesterol (p <.001). The PI index of ECs showed a negative correlation with VEGF and NO expression of both GCs and PTCs (p <.001). The number of PTCs correlated with PTCitis (r = -0.73, p <.001), PTC-VEGF expression (r = 0.73, p <.001), PTC-NO expression (r = 0.86, p <.001), tubular villin (r = -0.83, p <.001), proteinuria (r = -0.5, p <.001), hypertension (r = -0.48, p <.001), IF (r = -0.74, p <.001), graft loss (r = -0.57, p <.001). GC loss was significantly associated with GC inflammation (r = -0.68, p <.001), GC-VEGF expression (r = 0.76, p <.001), GC-NO expression (r = 0.86, p <.001), tubular villin (r = -0.76, p <.001), proteinuria (r = -0.64, p <.001), hypertension (r = -0.43, p <.001), GS (r = -0.53, p <.001), graft loss (r = -0.46, p <.001).
Conclusion: Loss of capillary VEGF and NO associated with aging and HC resulted in a significant loss of GCs and PTCs. Loss of PTCs and GCs correlated with the severity of the tubular injury, proteinuria, hypertension, IF, and GS. We suggested that donor age and HC influenced graft survival negatively by impairing the microvasculature and tubular integrity.

POS103 CLINICAL IMPLICATION OF C1Q DEPOSITION IN KIDNEY TRANSPLANTATION

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Background and Aims: C1q nephropathy is an uncommon type of glomerulonephritis and is characterized by an extensive and dominant C1q mesangial deposition in the absence of systemic lupus erythematosus. However, there are limited studies about C1q deposition in renal allograft.
Methods: Between January 2005 and December 2018, a total of 1742 kidney transplantations were performed in Seoul National University Hospital. C1q deposition was detected in 104 of these cases. 28 cases had intense (≥2+) C1q-dominance and were reviewed in this study.
Results: Among the 28 cases, 10 cases were detected in the post-reperfusion biopsy and 18 cases were detected in the post-operative periods, which includes both indication and protocol biopsy. In the post-reperfusion biopsy group, C1q depositions either disappeared (n = 9, 90%) or diminished (n = 1, 10%) in the follow-up biopsy. 3-year graft survival rate was 89.5% and 3-year mean eGFR was 57.4 ± 22.35. There were 9 cases (32.1%) of borderline acute T-cell mediated rejection (ATMR) and 3 cases (10.7%) of ATMR. Also, 3 cases (16.7%) of BK nephropathy and 5 cases (26.8%) of IgA nephropathy co-existed with C1q depositions in the post-operative biopsy group. In the follow-up biopsies (n = 5) of the post-operative group, C1q depositions disappeared in 80% (n = 4) and diminished in 10% (n = 1).
Conclusions: Nearly half of the C1q deposition cases detected in the post-operative periods were accompanied by t-cell mediated rejection or IgA nephropathy. Conversely, C1q depositions in the post-reperfusion group disappeared and graft survival were relatively good. Further studies to identify the natural history and the clinical significance of C1q deposition in renal allograft outcome are needed.

POS104 SINGLE KIDNEY TRANSPLANT USING ORGANS WITH KARPINSKI/REMUZZI SCORE 6 OR HIGHER: A TABOO TO DISPEL?

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Background: The weight to attribute to the morphological biopsy of the pre-transplant kidneys, compared to the functional parameters and clinical data, for choosing if performing single or dual kidney transplantation, in the case of an elderly or marginal donor, is debatable.
In the original Karpinski/Remuzzi (K/R) score, the limit for performing a single transplant was fixed at 3 and kidneys with score 4 to 6 were indicated for dual grafting. Currently, the majority of transplant centres who take into consideration the K/R score, accept score 4 (some of them also score 5) kidneys for single transplantation. We present a series of single kidney transplants performed with kidneys classified K/R score 6 or 7, at the pre-transplant biopsy.
Methods: In the period 2011–2019, 6 transplants were performed with organs from 4 donors (3 male and 1 female) with a mean age of 71.5 ± 5.2 years, mean BMI of 26.9 ± 0.91 kg/m2, mean serum creatinine of 0.59 ± 0.05 mg/dl with an estimated GFR of 118.5 ± 8.61 ml/min. Three donors were hypertensive, one was type 2 diabetic, one died from a stroke and three from head trauma. Pre-transplant kidney biopsy was K/R score 6 in 4 kidneys and 7 in 2 kidneys. The survival of the graft, the number of rejections and the last creatinine value were evaluated.
Results: Recipients were on dialysis and had an average age of 61.8 ± 4.1 and a BMI of 24.3 ± 1.4 kg/m2. The postoperative course was regular and the renal function recovery was immediate for all of them. After a median follow-up of 107.2 ± 38.6 months, all grafts are functional with a median creatinine of 1.3 ± 0.24 mg/dL. No episodes of rejection were recorded.
Conclusions: In selected donors and recipients, single kidney transplantation with an K/R biopsy score of 6/7 appears feasible. A good balance of biopsy morphology, functional and clinical parameters is mandatory. A careful selection and matching of donor/recipient characteristics, in term of age, gender, BMI and immunological parameters make it feasible to dispel the score 6/7 taboo.

POS105 RESEARCH BIOPSIES IN KIDNEYS FOR TRANSPLANT: AUDIT TO COMPARE CLINICAL SAFETY WITH TISSUE QUALITY

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Background: Tissue biopsies obtained from organs pre-transplant provide valuable information about donor kidneys and can be used for research. The Quality in Organ Donation (QUOD) biobank has collected > 6000

kidney biopsies and has provided research samples for > 35 projects designed to improve clinical outcomes. Minimising biopsy size reduces the risk of complications such as bleeding, but may jeopardise tissue quality. We set out to assess the optimal biopsy size needed for adequate quality tissue.
Methods: 3 transplant surgeons each performed two sets of 2mm, 3mm, 4mm punch biopsies and a core needle biopsy from two separate pig kidneys. One set of biopsies taken by each surgeon was bisected longitudinally: half placed in formalin and half in RNAlater (standard practice for QUOD samples). Data on tissue processing, tissue quality and histology along with surgeon observations on biopsy retrieval were captured.
Results: All surgeons reported difficulties obtaining 2mm biopsies; 2 biopsies were inadequate and needed to be repeated. Cutting the 2mm biopsy in half longitudinally was frequently not possible and preparation for analysis was challenging with damage to tissue and a reduction in usable material. The average biopsy size and total protein recovered from each biopsy is shown in table 1. Size and weight of 3mm and 4mm biopsies had better reproducibility between surgeons and kidneys compared to 2mm and core needle, shown by coefficient of variation (table 1). Coomassie blue staining is a standard technique scientists use for visualising and potentially isolating proteins in complex biological samples and showed no significant difference in Coomassie bands between biopsy size or surgeon.
Conclusions: 2mm biopsy acquisition was technically challenging and frequently provided too little tissue for certain molecular techniques. 4mm biopsies provided the largest amount of useable material and 3mm biopsies were the smallest size that reliably obtained tissue adequate for molecular analysis and histology, and were straightforward to perform.
We recommend using 3mm punch biopsies for kidney research.

Sample ID	Size mm^2 (mean ± SD)	Coefficient of variation (%)	Total protein mg (mean ± SD)
2mm	4.67 ± 3.7	57	0.317 ± 0.13
3mm	10.48 ± 5.2	34	0.695 ± 0.48
4mm	14.50 ± 3.2	16	2.111 ± 0.41
Core biopsy	12.00 ± 9.4	55	2.451 ± 0.46

Table 1.

POS106 PREIMPLANTATION BIOPSY EFFECTIVENESS IN EXPANDED CRITERIA DONORS AND KDPI>95%

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Background: Nowadays in Transplant Centres, Kidney grafts coming from expanded criteria donors acceptance, depends mainly of preimplantation biopsy. Recent biography discloses the great controversy that exists about the utility of the biopsy, as the variability of the biopsy depends of several factors like pathologist training, the way of obtaining the sample and sample processing, that is why donors clinical aspects and macroscopic evaluation of the kidney graft are getting more relevance.
Currently and despite the efforts made, the differences of time spent on the waiting list depends on the ABO group, being for O group much longer than for the others. Official recommendations in our region recommend to perform a biopsy if expanded criteria donor and to discard the graft if the score is higher than 7. In 2015 we decided to discard kidney grafts from O groups donors only if the score was higher than 9, and pay special attention to macroscopic evaluation and renal function.
Methods and Results: We analyse the results of group O recipients that received a graft with a score higher than 7 since 2015 until 2019.

Table 1

Transplant date	Donor age	Donor biopsy score	Recipient age	Delayed renal function	Creatinine	Rejection	BK/CMV
06/11/2015	64	8	54	YES	1.5	NO	NO
09/08/2015	73	8	67	NO	1.5	NO	NO
09/08/2015	73	9	60	NO	2	YES. CAR IIA	CMV ILLNESS
04/02/2016	73	8	71	NO	1.1	NO	NO
02/05/2017	71	8	75	YES	2.3	NO	NO
04/08/2018	68	9	68	NO	1.3	NO	URINE BK
05/20/2018	69	9	69	YES	1.9	YES. CAR IIA	CMV
08/02/2018	70	8	70	NO	1.3	NO	BK/CMV
08/20/2018	70	8	70	NO	1.5	NO	BK/CMV

Conclusions: Regarding to the lack of grafts we need to upgrade ours protocols in order to no discard grafts that could be profitable for some recipients. Our data show up grafts that have an acceptable evolution even though the biopsy score was higher than 7, making possible to decrease the time on the waiting list and the comorbidities associated.
Therefore, the number of cases examined corroborate that preimplantation biopsy should not be the only factor to discard an organ. Measuring thoroughly renal function and the macroscopic evaluation could be enough to predict an acceptable evolution of the graft

POS107 EXPANDED CRITERIA DONORS, IS IT BIOPSY NEEDED?

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Background: One of the main causes to reject expanded criteria donors for kidney transplantation is the preimplantation kidney biopsy, although latest research gives prominence to clinical aspects of the donor and macroscopic evaluation of the graft. In order to minimize grafts lost we decided in our Hospital to perform biopsies only when donor KDPI is over 95% or unknown creatinine. We analyze our initial results.
Methods: Descriptive and retrospective study of kidney transplants performed between 2015–2018. Every graft was biopsied previous the implantation but the result was not known at the time the transplant was performed. We evaluated kidney function at 1st, 6th, 12th months, rejection ratio and infections (CMV/BK), and recipient/graft survival. Furthermore we compared results between grafts with a favorable preimplantation biopsy score (less than 7) vs unfavorable (more than 7).
Results: 145 kidney transplant were performed, 9 of then showed a biopsy score > 7. Table 1 displays both groups evolution, becoming evident a slightly higher median of creatinine if score > 7, but only significant at 1st month. 15.2% showed active rejection (33% if biopsy score>7). 64% CMV infection (only 2% presented illness) vs 55.6% if biopsy score was > 7. 16.6% showed up BK infection (4.4% BK nephropathy) vs 11% infection and nephropathy if biopsy score was > 7. The biopsy score > 7 group showed up a kidney graft that never worked (11.1%). Graft survival was similar in both groups.
Conclusions: Our study shows similar graft survival and function regardless of biopsy. No differences in rejection ratio or infections were showed up. Our data support the poor implication of biopsy results regarding graft function or survival. Otherwise between every donor only a few showed up a biopsy score > 7, this fact could justify that clinical data are sufficient to evaluate graft viability, decreasing time on waiting list and comorbidities.

POS108 A DEEP LEARNING SOFTWARE FOR THE HISTOPATHOLOGICAL EVALUATION OF PRE-TRANSPLANTATION RENAL GRAFT BIOPSIES

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Introduction: The aim of the project was to create a machine learning system based on Deep Neural Networks (Deep Learning) to accurately identify the glomeruli from digitized images of human renal biopsies. The system should aid the pathologist during the evaluation of the morphological parameters of renal grafts for transplantation.
Methods: Fifty cases of wedge biopsies from deceased donors renal grafts were selected. PAS and Masson Trichrome stained sections (Whole Slide Image) were scanned using Ventana DP200 scanner producing around 3 -4 gigabite for each slide.
The maps were annotated by skilled pathologists using the QuPath software. Around 70 glomeruli were found from each wedge biopsy. Three classes of glomeruli were established: (i) normal glomeruli, (ii) glomeruli with global sclerosis, (iii) glomeruli with partial sclerosis. The images were then evaluated through a custom-made "Deep Learning" analysis software for kidney tissue images segmentation.
Results: The software was able to discriminate the three classes. The second phase of this project will be a progressive training of the software, in order to reach a sensitivity and specificity similar to those of a skilled pathologist.

Conclusions: This study demonstrates the feasibility of Deep Learning approach for assessing complex histologic structures from digitized human renal biopsies to become a standard support for pre-transplantation diagnostics.

POS109 FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS AFTER KIDNEY TRANSPLANTATION

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Background and Aims: Focal and segmental glomerulosclerosis (FSGS) is the leading cause of end-stage renal disease among primary glomerulopathies. Its recurrence after kidney transplantation is a major risk factor for graft loss. Aim of the study is to evaluate allograft function in the long term, incidence and potential risk factors for recurrent FSGS among a cohort of kidney transplants recipients with idiopathic FSGS.
Methods: All adults who performed a kidney transplant at our Unit between January 2005 and December 2018 for idiopathic FSGS were included in the retrospective study. Data about donor, recipient and transplant characteristics, allograft function and the presence of FSGS recurrence were recorded.
Results: 22 patients were included in the analysis and were followed for a median time of 50 months. At the end of follow-up all patients were alive with a functioning graft. FSGS recurrence was diagnosed in 4 patients over 22 (18%). Serum creatinine (SCr) and estimated glomerular filtration rate (eGFR) median values did not show a statistically significant difference between patients with or without recurrence (Fig. 1). Younger age at the time of transplantation was associated with recurrence ($p = 0.017$). Recurrent patients had also a higher incidence of CMV infection ($p = 0.03$) and of acute cellular rejection ($p < 0.001$).
Conclusions: Kidney allograft function (SCr and eGFR) isn't different between patients with or without recurrence and the presence of recurrence seems not to negatively impact graft survival. Younger age at the time of transplantation is a risk factor for recurrence.

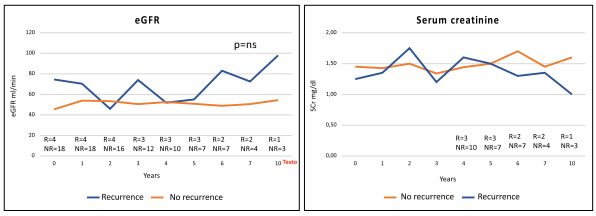

Figure 1 eGFR and SCr during follow-up in patients with and without recurrence. eGFR = estimated glomerular filtration rate. SCr = serum creatinine.

POS110 DESENSITIZATION TREATMENT AS AN OPTION FOR HIGH IMMUNOLOGICAL RISK RENAL TRANSPLANT CANDIDATES: SINGLE CENTER EXPERIENCE

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Background: Desensitization protocols based on HLA donor specific antibodies (DSA) removal either by plasma exchange or immunoadsorption combined with low dose intravenous immunoglobulins and rituximab have been employed to allow renal transplantation from deceased or living donors in high immunological risk patients. We analysed our series of patients with preformed DSA who received a pre-transplant (living donor) or a peri-transplant (deceased donor) desensitization protocol and were monitored by surveillance biopsies.
Methods: From 2012 to 2019 we performed 19 renal transplants with preformed DSA who received pre-transplant ($n = 9$) or peri-transplant ($n = 10$) desensitization. Patients with an immunodominant DSA (iDSA) MFI > 6000 were managed with 5 sessions of immunoadsorption ($n = 6$) and patients with an iDSA < 6000 were managed with 7 sessions of plasma exchange ($n = 13$). All patients received low dose IVIg (0.2 g/kg after each treatment) and rituximab (one dose of 375 mg/sqm). All patients received treatment with 3–6 doses of thymoglobulin at the time of transplant and maintenance immunosuppression was based on tacrolimus, MMF and steroids. Surveillance biopsies at 3 and 12 months were performed.
Results: Ten first transplants and 9 re-transplants with a mean age of 45 ± 12 years were included. Mean donor age was 51 ± 12 years. Mean DR-HLA mismatch was 1.1 ± 0.7 and mean A+B-HLA mismatch was 2.5 ± 1.4. cPRA before transplant was 89 ± 24% (class I 65 ± 39% and class II 81 ± 26%) and after desensitization treatment 75 ± 30% (class I 47 ± 37% and class II 64 ± 35%). MFI of the iDSA before treatment was 6093 ± 4092 and 2681 ± 5500 after treatment. After transplant two patients suffered from active antibody-mediated rejection (ABMR) at 75 days and 170 days while 2 patients suffered from T cell-mediated rejection at 15 and 330 days. Subclinical active ABMR was observed in 3 patients (16%) and chronic active ABMR in 5 patients (26%). One patient lost her graft due to chronic antibody-mediated rejection at 3 years and serum creatinine was 1.7 ± 1.1 mg/dL and proteinuria 0.6 ± 0.8 g/g at 48 ± 31 months of follow-up.
Conclusions. Our desensitization protocol allowed to transplant highly sensitized patients and despite the high prevalence of subclinical ABMR, graft survival and graft function at the end of follow-up is acceptable.

POS111 FREQUENCY OF HLA-SPECIFIC IGE ANTIBODIES IN SOLID ORGAN TRANSPLANTATION ANALYSED BY SINGLE-ANTIGEN BEADS-BASED IMMUNOASSAY

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Background: While immunosuppressive drugs could significantly improve short-term graft survival, long-term outcome still needs to be improved. Donor specific antibodies (DSAs) are either pre-existing before transplantation (TX) or develop *de novo* and especially those of the IgG isotype may affect graft survival. Our research group detected donor-specific as well as third-party anti-HLA antibodies of the IgE isotype in a subset of highly sensitized kidney recipients. Here, we performed a prospective pilot study measuring the frequency of HLA-specific IgE antibodies in a cohort of 60 kidney transplant recipients.
Methods: HLA-specific IgE was measured using a single antigen bead assay for HLA class I/II based on multiplex technology adapted (One-Lambda, LabScreen Single Antigen HLA class I and II). Serum samples were collected from healthy controls at one time point and from transplant recipients at baseline, three- and 12 months post-TX.
Results: 10% ($n = 6$ from 60) of all kidney transplant recipients had pre-existing anti-HLA IgE, with 5% against HLA class I and 8.3% against HLA class II. 3.3% ($n = 2$ from 60) had pre-existing IgE DSA. After three-month post-TX 8.8% ($n = 5$ from 57) had anti-HLA IgE antibodies, 5.3% HLA class I and 7% HLA class II. After one year, 8.2% ($n = 4$ from 49) had anti-HLA IgE, 6.1% HLA class I and 6.1% HLA class II. After three months post-TX, 1.8% developed *de novo* anti-HLA IgE. In most instances IgE developed against the same HLA specificities against which IgG was also present. However, anti-HLA IgE was present in several patients without the presence of IgG against the same HLA specificity.
Conclusion: HLA-directed IgE antibodies occur before transplantation and develop *de novo* in a small subset of kidney transplant recipients. Due to its unique effector mechanism, the potential pathophysiological role of IgE DSA deserves further investigation.

POS112 PRETRANSPLANT NATURAL KILLER CELLS LEVEL IS INVOLVED IN REJECTION AND OPPORTUNISTIC INFECTION ONSET WITHIN THE FIRST YEAR AFTER KIDNEY TRANSPLANTATION

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Background: Longitudinal analysis has revealed strong links between the proportion of lymphocytes cells and the appearance of events such as rejection, opportunistic infection or presence of DSA after kidney transplantation. These results have identified those immune profiles during the time of transplantation whereas the choice of immunosuppressive therapy has already been decided. Our study identifies pretransplant lymphocyte profiles associated with such complications.
Patients and Methods: B, T lymphocytes subsets and NK cells were analyzed in kidney allograft recipients from 01/2016 to 12/2018 not treated with rituximab the day of transplant and three months after. Within 12 months after transplant, three groups were defined : rejection, opportunistic infection (OI) and OI- rejection-free (control group).
Results: Among 175 patients, 21 belonged to rejection group, 24 to OI group and 96 to control group. OI were represented by viral (n = 9), bacterial (n = 10) and fungal (n = 5) infections. Rejection group experimented significantly lower pretransplant NK cells than control group and OI group (p = 0.03 and p = 0.01 respectively). Patients with pretransplant DSA suffering from allograft rejection had significantly lower pretransplant NK cells (p = 0.031) than those without rejection. Pretransplant serum levels of NK cells in patients with OI within 3 months after transplant (n = 15) were significantly higher than in control group (p = 0.035). However, patients with OI after 3 months of transplant had significantly lower pretransplant CD4 T cells than control group (p = 0.016). Analysis of B and T cells' different populations were comparable between the 3 groups.
Conclusion: Our study suggested association between pretransplant NK cells' level and acute rejection or OI onset within the first year after kidney transplantation and acute rejection episode in pretransplant DSA patients. Whether NK cells could be a key player in the development of tolerance or help to adapt the immunosuppressive treatment needs to be further analyzed.

POS114 DECLINE IN CD4+ T CELLS EXPRESSING T CELL IMMUNORECEPTOR WITH IG AND ITIM DOMAINS UNDERLIES DONOR-SPECIFIC HYPORESPONSIVENESS POST TRANSPLANTATION?

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Background: Development of T-cell hyporesponsiveness to donor antigen may explain the substantial decreased risk for acute rejection in the years following kidney transplantation. This study tested the hypothesis that donor-specific recipient T cells become hyporesponsive due to exhaustion from continuous stimulation by donor antigen.
Methods: Peripheral blood mononuclear cells (PBMCs) of stable kidney transplant recipients (n = 17) before and 3–5 years after kidney transplantation were stimulated with CD3-negative donor or third-party PBMCs for 18–24 hours. Donor-specific T cells (identified by CD137 expression) were characterized for multiple exhaustion markers by multi-parameter flow cytometry. Expression data were clustered using Flow Self-Organizing Map (FlowSOM), a dimensionality reduction technique, allowing for unsupervised and unbiased analysis. The statistical method, edgeR, via diffcyt identified FlowSOM clusters containing cells of a particular expression profile with significant differential abundance after transplantation.
Results: No increase in donor-specific T cells with an exhausted phenotype were observed 3–5 years post kidney transplantation. Instead, a significant decrease in abundance of donor-specific CD137+ CD4+ T cells expressing the co-inhibitory receptor T cell immunoglobulin and ITIM domain (TIGIT) was detected following transplantation. Detailed characterization of these cells revealed a predominant central as well as effector memory phenotype and high potential to produce multiple cytokines when compared to donor-specific CD137+ CD4+ T cells not expressing TIGIT.
Conclusions: This study has identified TIGIT as a marker for a previously undescribed polyfunctional donor-specific CD4+ T cell population whose decline after kidney transplantation may underlie the phenomenon of donor-specific hyporesponsiveness. Prospective clinical studies will help determine whether a low frequency of donor-specific TIGIT-expressing CD4+ T cells could guide lowering of immunosuppressive drugs.

POS115 THE HLA-DR4-DQ8 PHENOTYPE OF THE RECIPIENT IS ASSOCIATED WITH INCREASED MORTALITY AFTER KIDNEY TRANSPLANTATION

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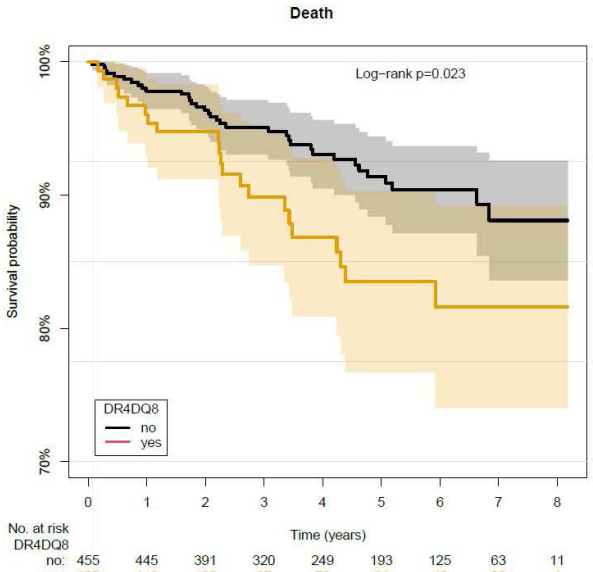
Background: The importance of the human leukocyte antigen (HLA) system in kidney transplantation is well-known, but it remains unexplored if recipient HLA antigens constitute independent risk factors in complications after transplantation. We hypothesized that specific HLA class II phenotypes associated with immune-mediated disease (HLA-IMD) predispose to immunological activity and/or complications after kidney transplantation.
Methods: Based on the literature we defined HLA-DR2-DQ6 (n = 138); -DR3-DQ2 (n = 156) and -DR4-DQ8 (n = 152) as HLA-IMD phenotypes. We investigated associations between HLA-IMD phenotypes in recipients, biomarkers of systemic chronic inflammation at the time of transplantation, and the outcome after kidney transplantation in a retrospective cohort study of 611 kidney transplanted recipients in from 2009 to 2015.
Results: The HLA-IMD phenotypes were all associated with higher levels of interleukin (IL)-6, whereas HLA-DR2-DQ6 and -DR3-DQ2 ware associated with higher levels of C-reactive protein (CRP). Correspondingly, HLA-DR4-DQ8 were associated with lower levels of IL-10. The HLA-DR4-DQ8 phenotype was associated with mortality after transplantation (figure 1) in Cox analyses adjusted for age at transplantation, sex, pre-transplant DM, pre-transplant MACE, hsCRP and HLA immunization status, with a hazard ratio: 1.89, 95% confidence interval: 1.04–3.42, p = 0.04.
Conclusions: The HLA-IMD phenotypes were associated with higher levels of biomarkers of systemic chronic inflammation at the time of transplantation. The HLA-DR4-DQ8 phenotype was associated with mortality after transplantation. Our findings support the hypothesis that specific HLA class II phenotypes affects immunological pathways, that determine the midterm clinical outcome of kidney transplantation. These novel findings demonstrate that the HLA system of the recipient is important from more perspectives than just matching and should be taking into consideration in clinical risk estimation.

Figure 1. Kaplan-Meier plot of recipients expressing the HLA-DR4-DQ8 phenotype, compared to recipients negative for the HLA phenotype.



POS116 CLINICAL OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS WITH C1Q-BINDING DE NOVO DONOR-SPECIFIC ANTIBODIES: A SINGLE-CENTER EXPERIENCE

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Background: Donor-specific antibodies (DSA) are associated with an increased risk for antibody-mediated rejection (AMR) and reduced allograft survival. Studies evaluating the clinical significance of complement-binding DSA are limited. The aim of the present study was to investigate the clinical outcomes of kidney transplant recipients with C1q-binding de novo (dn) DSA followed in our center.
Methods: The presence of dnDSA was identified in 116 out of 1325 kidney transplant recipients who were screened between 2015–2019. The C1q-binding capacity was retrospectively assessed in 69 patients with dnDSA and MFI values > 2000. Sera were tested for HLA class I and/or II DSA using Luminex IgG single antigen beads (SAB) and C1q-SAB assays (One Lambda). Renal graft biopsies were performed in patients with new-onset proteinuria and/or increased serum creatinine.
Results: C1q-binding dnDSA were identified in the sera of 32/69 (46.4%) kidney transplant recipients. Significantly higher MFI values were observed in C1q-positive DSA (mean 18978 vs 5840, $p < 0.001$). Renal graft biopsy was performed in 43 patients (62.3%) with allograft dysfunction in a median time of 12 months (IQR 3–60) after DSA identification. Patients with C1q-binding DSA were more likely to undergo a graft biopsy (OR: 2.8, $p = 0.046$). AMR was detected in 29/43 (67.4%) of these patients. The incidence of AMR was similar between patients with C1q-binding and non-C1q-binding DSA (51.7% vs 48.3%, $p = 0.523$). Graft loss occurred in 30/69 (43.5%) of patients at a median time of 82.5 months (IQR 45–135) from DSA detection; 68.2% of them had biopsy-proven AMR. C1q-binding DSA correlated with an increased incidence of graft loss (53.1% vs 35.1%, $p = 0.152$) without statistical significance.
Conclusions: Higher MFI values and inferior clinical outcome were shown in most kidney transplant recipients with C1q-binding dnDSA. Larger clinical trials are required to establish the C1q assay as a predictive tool for allograft survival.

POS117 ANTI-HLA ANTIBODIES – A CONTINUOUS CHALLENGE IN RENAL TRANSPLANTATION

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Background: Anti-human leukocyte antibodies (HLA) play a major role in any post-transplantation graft survival. Preformed donor-specific and de novo anti-HLA antibodies can induce graft rejection. This study aimed to investigate the occurrence post-transplant of anti HLA antibodies and relation to rejection episodes in patients with kidney transplantation.
Methods: A total of 1012 patients (517 males, 495 females) with kidney transplantation between 2001 and 2020 were enrolled in this study and monitored for one year. Screening and Identification of anti-HLA antibodies were done using Luminex-based assays.
Results: At one-year, anti-HLA antibodies were detected in 33.39% ($n = 438$) of recipients. Among non-sensitized recipients ($n = 233$), de novo anti-HLA class I antibodies were detected in 21% recipients; anti-HLA class II in 63.07% recipients; and both anti-HLA I and II antibodies in the remaining 15.93% recipients. Among pre-sensitized recipients ($n = 205$), de novo anti-HLA class I antibodies were detected in 34% recipients; anti-HLA class II in 54.07% recipients; and both anti-HLA I and II antibodies in the remaining 11.93% recipients. 9.87% ($n = 23$) of the pre-sensitized recipients had experienced graft loss during thirst year post kidney transplantation. However, none of the recipients with no preformed HLA antibodies had graft loss. There were no significant differences between sensitized males and females regarding the appearance of HLA antibodies and graft loss. Also, we have observed that patients on Tacrolimus and MMF had a lower rate of anti HLA antibodies production in time, compared with Cyclosporine and MMF regimen.
Conclusions: In some patients, non-donor specific HLA antibodies may develop after organ transplantation and induce rejection through multiple mechanisms including activation of the complement cascade with the formation of the MAC complex and inflammatory anaphylatoxins and transduction of intracellular signals with the proliferation of graft vasculature. Knowing this, the histocompatibility and immunogenetics centres need to continue the monitoring of recipients for a long period of time. Thus, clinicians will be able to predict the risk of graft failure and they will consider adjustment of immunosuppressive treatment according to the anti- HLA antibodies status.

POS118 THE BALANCE BETWEEN EFFECTOR AND REGULATORY CELL POPULATIONS IN KIDNEY TRANSPLANT RECIPIENTS WITH OPERATIONAL TOLERANCE AND CHRONIC REJECTION

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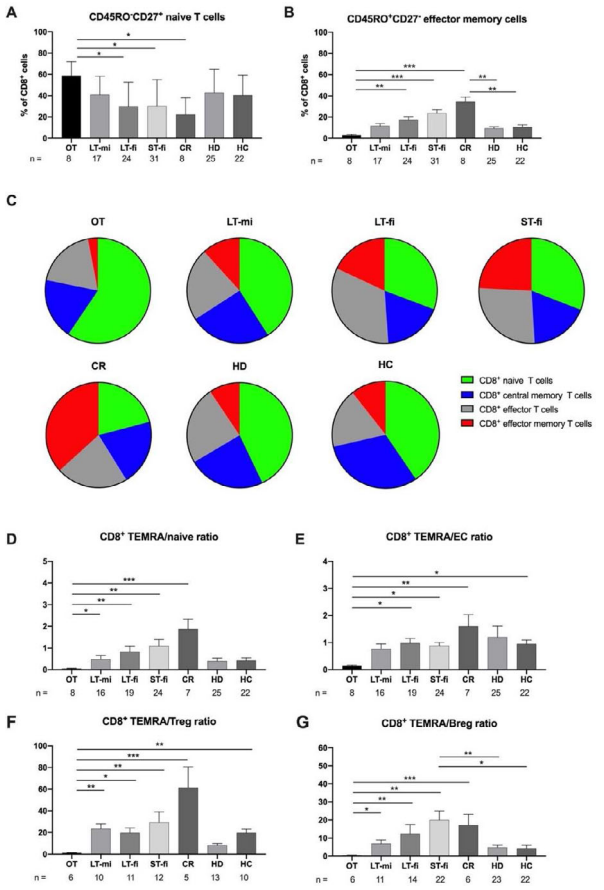
Background: Donor-reactive memory cells represent a barrier to long-term kidney graft survival. A better understanding of regulatory mechanisms that counterbalance alloreactive immune responses may help to identify patients with operational tolerance (OT) or chronic rejection.
Methods: The prospective, bicentric BALANCE study enrolled 147 patients from two different transplant centers in Heidelberg ($n = 82$) and Medellin ($n = 65$). We investigated the equilibrium between regulatory T or B cells (Tregs, Bregs) and effector or memory T cell subsets in peripheral blood of kidney transplant recipients with OT ($n = 8$), chronic rejection ($n = 8$), and different immunosuppressive treatment regimens ($n = 81$). Patients on hemodialysis and healthy individuals served as controls ($n = 50$). In addition, the expression of Treg- and Breg-associated molecule genes was analyzed.
Results: Patients with chronic rejection showed a disrupted memory T cell composition with a significantly increased frequency of circulating $CD8^+$ terminally differentiated effector memory T cells (TEMRA) compared to patients with OT, patients on hemodialysis, or healthy controls ($p < 0.001$; Figure 1A-C). Compared to all other transplant recipients, the lowest ratios between $CD8^+$ TEMRA and naïve T cells or EC and the highest frequency of Tregs and transitional Bregs were found in OT patients (for all $p = 0.001$; Figure 1D-E). Consequently, OT patients showed, as compared to all other transplant recipients, the lowest ratios between $CD8^+$ TEMRA cells and Tregs or Bregs (for both $p < 0.001$; Figure 1F-G). Furthermore, OT patients displayed a specific peripheral blood transcriptional pattern with an increased expression of regulatory B and T cell genes *CD22* and *FoxP3* and a decreased *FcγRIIA/FcγRIIB* transcript ratio (for all $p < 0.001$), as compared to all other transplant recipients).
Conclusions: Monitoring the balance between circulating $CD8^+$ TEMRA T cells and regulatory cell subsets and their transcripts may help to distinguish transplant recipients with operational tolerance from recipients at risk of graft loss.

Figure 1



POS119 DIMINISHED TREG CELLS IN PERIPHERAL BLOOD IS ASSOCIATED WITH LATE ANTIBODY MEDIATED REJECTION AFTER FIRST YEAR POST KIDNEY TRANSPLANT

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Background: Treg cells play a major role in maintaining immune tolerance. Late antibody mediated rejection is a major problem in kidney transplant (KT). Immunosuppressant medication non adherence is present in a high number of patients. The objective of this study was to identify differences in Tregs cell populations in stable KT patients vs late active antibody mediated rejection (ABMR).
Methods: A cross-sectional study was conducted in a cohort of 21 KT recipients (11 stable KT vs 10 late ABMR). Stable KT was defined as steady serum creatinine <1.5 mg/dL for more than 3 years without rejection, tacrolimus trough level variability < 25% and adherence to immunosuppressants. Late ABMR was defined by Banff 2019 classification after 3 months post KT. A standarized eight color antibody panel proposed by the Human Immunophenotyping Consortium was used to analyze Treg population in peripheral blood samples.
Results: Baseline clinical characteristics were comparable except for age, delayed graft function, immunosuppression adherence and serum creatinine. Patients with late ABMR were younger (31 ± 4.4 vs 48 ± 2.0 years, $p = 0.02$) non-adherent to immunosuppressants (66% vs 0%, $p = 0.01$) and had higher serum creatinine (2.4 ± 0.8 vs 1.1 ± 0.3, $p = 0.001$) . Absolute lymphocytes and CD4T cells number were decreased in ABMR compared with stable KT. Additionally, Treg cells were decreased in patients with late ABMR compared to stable KT (9 cells/mL IQR[6–17] vs 57 cells/mL IQR [26–93], $p = 0.01$) (Table 1). CD4T and Treg cells count were normal in stable KT patients according to age. Percentage of Treg cells in CD4 population was similar in both groups.
Conclusions: T cell population is altered in late ABMR compared to stable KT. CD4 and Treg cells are decreased in late ABMR, which can explain the lack of inhibition of immune system.

Table 1. T Cell population in peripheral blood of stable kidney transplant versus late antibody mediated rejection

	Stable KT n= 11	Late ABMR n= 10	p value
Leucocytes/mL, median (RIQ)	5705 (5220-8300)	5930 (4650-7830)	0,525
Lymphocytes/mL, median (RIQ)	1624 (1224-1848)	799 (501-1059)	0,02
% T Cell, median (RIQ)	35,3 (20,8-60,3)	66,5 (57-71,3)	0,002
% T CD4, median (RIQ)	98,8 (91-99,5)	36 (28-43)	0,002
%Tregs, median (RIQ)	4 (2,8-5,7)	4 (3,2-5,6)	0,31
%memory Treg, median (RIQ)	86 (78-93)	80 (58-94)	0,91
% activated memory Treg , median (RIQ)	5,1 (3,6-9,9)	12 (3,3-26,3)	0,38
% naive Treg, median (RIQ)	13,6 (6,8-21,9)	19,2 (5,5-41,1)	0,97
% activated naive Tregs, median (RIQ)	1,48 (0,06-1,8)	7,3 (0,99-21,7)	0,28
T Cell/mL, median (RIQ)	675 (270-1158)	535 (359-650)	0,41
T CD4/mL, median (RIQ)	1346 (841-1646)	298 (135-420)	0,00
Tregs/mL, median (RIQ)	57 (26-93)	9 (6-17)	0,01
Memory Treg/mL, median (RIQ)	50 (20-69)	6 (4.2-16.3)	0,03
Activated memory Treg/mL, median (RIQ)	2,8 (1,14-5)	0,69 (0,43-1,08)	0,099
Naive Treg/mL, median (RIQ)	5,5 (2,9-8,5)	2 (0,7-3,4)	0,016
Activated naive Tregs/mL, median (RIQ)	0,04 (0,03-0,1)	0,05 (0,01-0,71)	1

Late ABMR: antibody mediated rejection after 3 month, KT Kidney Transplant, RIQ Interquartile range.

POS120 VALIDATION OF C3, IC3B, C3D, C4D, PROPERDIN C5 AND C5B-9 ASSAYS TO MONITOR COMPLEMENT ACTIVATION IN KIDNEY TRANSPLANT PATIENTS

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Introduction: Several assays have been developed to identify clinical relevant complement activation markers, but they have not been standardized and validated for diagnostics yet. In addition, assays for iC3b are completely lacking. In this study, we have validated enzyme-linked-immunosorbent (ELISA) C3d, C3, C5, C4d, soluble (s)C5b-9 assays and novel iC3b assay that can be used to monitor disease progression.
Methods: Serum C3, iC3b C3d, C4d, properdin, C5 and sC5b-9 were measured in a cross-sectional cohort of 130 kidney transplant recipients (KTR) at a median [interquartile range] 5.3 (1.8–12.2) years after transplantation.
Results: Statistical significant correlations (p <0.05) with a correlation coefficient R>0.70 were found between sC5b-9 and C3d (p <0.001; R = 0.70), sC5b-9 and C3/C3d ratio (p <0.001;R = 0.708), C3d and iC3b (p <0.001; R = 0.761), C3d/C3 and iC3b (p <0.001;R = 0.751), sC5b-9 and iC3b (p <0.001;R = 0.725) and C3d/C3 and C3/iC3b (p <0.001;R = 0.775). Properdin correlated significantly with C5 (p <0.005;R = 0.278). We found comparable results between the validated iC3b and validated C3d assay, therefore these assays could both be utilized in complement related diseases. Correlations of C4d with C3d, C3d/C3, iC3b and sC5b-9 did not reach R>0.70. In addition we showed that C4d did not reach high correlation coefficients when compared to C3d, C3d/C3, iC3b and sC5b-9, suggesting that the alternative pathway explain complement activation in RTR. In a clinical sense, the major finding was the negative association between serum C3 protein and proteinuria (p <0.03;R = 0.46). Further, there was a negative association between serum iC3b protein and proteinuria (p <0.02;R = 0.22). Also, an association between properdin and proteinuria during was observed (p <0.04;R = 0.21).
Conclusions: Our findings point towards a potential role for systemic alternative complement C3 and iC3b activation in the pathogenesis of allograft failure whilst correlating with the amount of proteinuria. Systemic iC3b and C3 might be useful biomarkers for complement activation.

POS121 HUMAN PODOCYTE INJURY OF KIDNEY ALLOGRAFTS IN ANTIBODY-MEDIATED REJECTION

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Background: Kidney podocytes form the filtration barrier and translate the signals. The change of podocytes in antibody-mediated rejection (ABMR) remains unclear. The aim of the study is to examine the podocyte-specific changes in ABMR.

Methods: 33 renal transplant recipients were diagnosed as ABMR from 2018 to 2020 by Banff 2017 revised criteria. 13 subjects were excluded for diabetic nephropathy and graft nephropathy. 20 recipients were divided into acute ABMR (AABMR), chronic active ABMR (CAABMR), and chronic ABMR (CABMR) with estimated glomerular filtration rate (eGFR) and proteinuria. Control group comprised 6 healthy volunteers. The expression of nephrin and synaptopodin was detected by immunostaining. RT-qPCR was used to determine mRNA of Nphs1 and Synpo. The urine mRNA from podocytes were measured. Transmission Electron Microscope was used to evaluate the podocyte morphology.
Results: AABMR group comprised 8 cases (eGFR 46 ± 28 mL/min/1.73 m^2) with 1 case accompanied by proteinuria. CAABMR group comprised 7 cases (eGFR 29 ± 19 mL/min/1.73 m^2, 4 allografts loss) with 5 case proteinuria. The CABMR group comprised 5 cases (eGFR 27 ± 12 mL/min/1.73 m^2, 4 allografts loss) with 5 cases proteinuria. In the rejection group, the expression of nephrin at the plasma membrane and synaptopodin along actin fibers in a punctate pattern was significantly decreased, especially in CABMR, compared with the control group. The mRNA of Nphs1 and Synpo indicated a significant reduction in the ABMR group compared with the control group. The podocyte detachment rate (nephrin mRNA-to-creatinine ratio) from podocytes appeared in urine samples with glomerular disorders showed a higher expression. The TEM micrographs showed the foot processes had a broken arrangement and podocyte detachment from the GBM.
Conclusions: Nephrin and synaptopodin are related to the pathological changes and functional properties of human podocytes along with ABMR, and play a pathogenic role in the development of ABMR.

POS122 MICROVASCULAR INFLAMMATION IN NO-DSA MEDIATED CHRONIC REJECTION AFTER KIDNEY TRANSPLANTATION

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Background: Antibody-mediated rejection (AMR) is the main immunological challenge for the long-term graft survival after kidney transplantation. Microvascular endothelium is the common target of injury in AMR that appears histologically as microvascular inflammation (MVI), characterized by glomerulitis and/or capillaritis. MVI is one of the diagnostic cornerstones of the 2017 Banff classification in association with C4d and detection of "Donor Specific Antibodies" (DSA). However, some patients with MVI do not express DSA. The purpose of this study was to evaluate the impact of MVI in patients with immunological related graft disfunction.
Methods: We conducted an observational, retrospective study of 80 renal transplants, between 2014 and 2019 with post transplant impaired renal function. The evaluation was assessed with an ultrasound-guided graft biopsy. All specimen were reviewed by two skilled pathologists and reclassified according to Banff 2017 criteria, in association with the detection or not of class I/II HLA antibodies (DSA or not).
Results: 65 patients (81%) had grade 2–3 MVI, 31/65 patients (48%) had no DSA and only 8/65 patients (16%) had DSA. The presence of MVI was the only variable that affects significantly the graft survival ($p = 0.018$).
Conclusions: MVI is present in a significant percentage of cases without DSA detection. Contrary to what was expected, the percentage of patients with DSA was low. According to some authors, in these cases the immunological damage could be mediated by "missing self-induced NK cell activation" which promotes the expression of (MVI) intra-graft. This immunological mechanism appears unresponsive to calcineurin inhibitor therapy.

POS123 ANGIOTENSIN II TYPE-1 RECEPTOR (AT1R) ANTIBODIES ARE ASSOCIATED WITH INFERIOR RENAL ALLOGRAFT SURVIVAL

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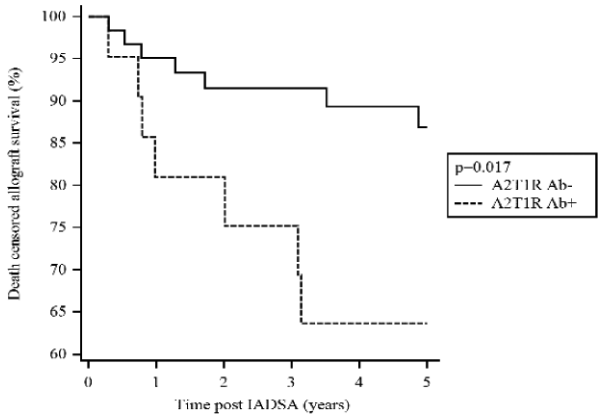
Background: AT1R-antibodies have been implicated in antibody-mediated vascular rejection in the absence of detectable HLA DSA, in addition to cardiovascular diseases. Transplant renal artery stenosis (TRAS) or macrovascular disease has also been shown to be associated with rejection. We aim to investigate the prevalence of AT1R antibodies and associated outcomes in patients undergoing angiography for suspected TRAS with biopsy proven rejection.
Methods: 78 patients with no HLA DSA were identified and serum at the time of angiography was tested for AT1R-Abs using an enzyme-linked immunosorbent assay technique. A threshold of > 17u/ml was considered a positive result. Prospectively collected outcomes up to 5 years were obtained from our unit's transplant registry.
Results: The prevalence of AT1R-Abs was high at 21/78 (27%). 46/78 (59%) of patients were found to have significant TRAS at the time of angiography, 13/46 (28%) of TRAS+ patients had Abs compared with 8/32 (25%) of TRAS- patients, $p = 0.88$. Median time from transplantation to IADSA was 0.46 years.
There was no difference in gender, ethnicity, donor type, cause of ESKD, total HLA mismatch in the Ab+ versus Ab- groups. However, Ab+ patients were more likely to be younger than Ab- patients at the time of angiography 46.95 ± 12.2 versus 55.1 ± 11.812.0 respectively, $p = 0.009$.
AT1R-Ab+ patients at the time of angiography had an inferior 5-year allograft survival compared with Ab- patients, $p = 0.017$(figure 1). Outcome by TRAS and Ab status, showed that TRAS+Ab+ patients had significantly worse outcomes than either TRAS+Ab- and TRAS-Ab+ patients, $p = 0.008$



Conclusions: In a highly selected patient population, we found a high prevalence of AT1R-Abs. Although we found no association with TRAS, further work is underway to compare the prevalence in patients with normal renal artery imaging. Importantly, we did find a negative association with allograft survival, which highlights the potential importance of AT1R-Abs in renal transplantation which warrants further investigation.

POS124 THE ROLE OF T LYMPHOCYTES SUBPOPULATIONS IN KIDNEY TRANSPLANTATION

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Background: Disturbances in T cell immunity are frequently seen in patients with CKD-5 eligible for renal transplantation and they are not readily reversed by a well functioning graft, as alloreaction and immunosuppressive regimen cause additional T-cells phenotypic changes. In the present study we assessed T cell subpopulations and the effect of graft function on relevant changes of these lymphocytes after transplantation.
Methods: Flow cytometry analysis was performed in 61 recipients of kidney transplant (47 deceased) before and three months after transplantation, in order to estimate CD3+, CD4+, CD8+, CD4CD28null, CD8CD28null and Natural Killers (NK) subtypes. Patients were classified into two groups regarding renal function at three months, with a cut-off value for eGFR of 50ml/min/1.73m^2.
Results: In all 61 patients there was an increase, three months after transplantation of lymphocyte count, both percentage 21.5(15.9–31.2)% vs. 18.8 (14.8–23.7)%, $p = 0.017$ and absolute number 1700(1200–2300) μ/L vs. 1200(1000–1700) μ/L, $p < 0.001$ as well as an increase of CD4+ (47.8 ± 9.9% vs. 44.1 ± 10%, $p = 0.005$) and CD8+ cell frequencies (28 ± 8% vs. 25.8 ± 7.9%, $p = 0.002$) and total numbers, 783(524–1223)

μ/L vs. 528(375–718) μ/L, p <0.001 and 443(323–636) μ/L vs. 308(226–408) μ/L, p <0.001, respectively. Natural Killer (NK) cells reduced as percentage 9.4(5.7–14)% vs. 17.8(13.2–22.1)%, p <0.001 and number 138(83–234) μ/L vs. 191(161–315) μ/L, p = 0.002 while the proportion of CD4CD28null cells decreased, 3.3(1.5–8.5)% vs. 5.4(2.4–9.8)%.
Twelve patients (20%) were included in the group of lower eGFR. Patients with higher eGFR had a significant increase in total lymphocyte (p = 0.035) and CD4+ percentage (p <0.001) and number (p <0.001) and a decrease in NK number (p = 0.014) and CD4CD28null proportion (p = 0.008) while in the group of lower eGFR there were no significant differences regarding these subtypes.
Conclusions: Three months after kidney transplantation many alterations of T cell subpopulations noticed in CKD are restored and this might be mediated by recovery of adequate renal function.

POS125 CHANGES OF REGULATORY T LYMPHOCYTES IN KIDNEY TRANSPLANTATION

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Background: T regulatory lymphocytes (Tregs) are CD4+CD25+ T cells expressing the transcriptional factor FoxP3, and they have a vital role in immune response homeostasis and the induction of graft tolerance. As CD25 is the therapeutic target of basiliximab and anti-thymocyte globulin (ATG) depletes T lymphocytes, the induction immunosuppressive protocols might affect Tregs as well.
Methods: Subpopulations of CD4+CD25+ και CD4+CD25+FoxP3+ T lymphocytes were measured, by flow cytometry, in 42 CKD-5 patients before (T0) renal transplantation (32 from deceased donors) as well as at three (T3) and six (T6) months after transplantation. All patients received either basiliximab or ATG as induction therapy, and triple immunosuppressive regimen as a standard therapeutic protocol.
Results: Patients retained a well-functioning graft with eGFR of 62 ± 19ml/min/1.73m^2 at T3 and 62 ± 21ml/min/1.73m^2 at T6, respectively. Before transplantation the proportion of CD4+CD25+FoxP3+ T cells was 4.2 ± 2.3% of the CD4$^+$ lymphocytes while it reduced at T3 and significantly increased again at T6 (4.1 ± 2 vs. 3.2 ± 1.4, p = 0.009). Absolute numbers of Tregs were 22(15–32) μ/L at T0, remained stable at T3, and significantly increased at T6, 31(22–54) μ/L vs 23(16–32) μ/L, p = 0.004.
Six patients (14.3%) received ATG while 36 (85.7%) received basiliximab as induction immunosuppression. Patients who received basiliximab had their proportion of CD4+CD25+ cells reduced at T3, compared to T0, 4.9 (3.9–6.6)% vs 6.7(5.3–9)%, p = 0.019. However, they retained stable their absolute numbers of Tregs at T3 and increased them at T6 (p = 0.023).
Conclusions: Despite immunosuppression therapy affecting CD25+ helper T cells early at renal transplantation, the absolute numbers of Tregs remain stable 3 months later and are increased 6 months after transplantation and this may have a positive effect on the graft function.

POS126 PATTERNS OF IGG REBOUND AFTER IMLIFIDASE TREATMENT

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Background: Imlifidase is a cysteine protease which cleaves all subclasses of IgG to a F(ab')$_2$ and dimeric Fc fragment and is conditionally authorised in the EU for kidney transplant desensitization. To elucidate the rebound of relevant IgG groups after imlifidase dosing, we report on the patterns and timing of rebound for anti-drug antibodies (ADA IgG), immunodominant donor specific antibodies (DSA IgG), vaccine antigen-specific IgG (VIgG) compared to the total IgG pool in immunosuppressed kidney transplant recipients.
Methods: Ten patients in the phase 2, 13-HMedIdeS-03 study were analyzed. Immunodominant DSA IgG (MFI ≥1,000) were measured by single antigen beads, ADA IgG were measured with IdeS-ImmunoCAP, V IgG to test antigens in Pentavac® and Total IgG were measured using Meso Scale Diagnostic (MSD) technology. Relative IgG was calculated as level of IgG at each time point compared to the maximum IgG level for each individual for each analysis (Table 1).
Results: Following imlifidase dosing, IgG rebound generally occurred between 3 and 14 days, with substantial interpatient variability. Initial DSA IgG appearance was faster than the rebound of total IgG and thereafter DSA IgG maintained a steady state at or below its' predose (T = 0) level. ADA IgG rebounded in a similar rate as DSA IgG but to a higher magnitude compared to DSA IgG. The reappearance of V IgG was concurrent with the rebound of total IgG (Figure 1A, 1B).
Conclusions: The patterns of IgG rebound are consistent with expectations. IgG which have active antigen presentation during the period of IgG rebound (i.e. DSA, ADA) reappear faster than general IgG. The patterns of ADA IgG and DSA IgG rebound suggest that V IgG can rebound at the same level if antigen is present.

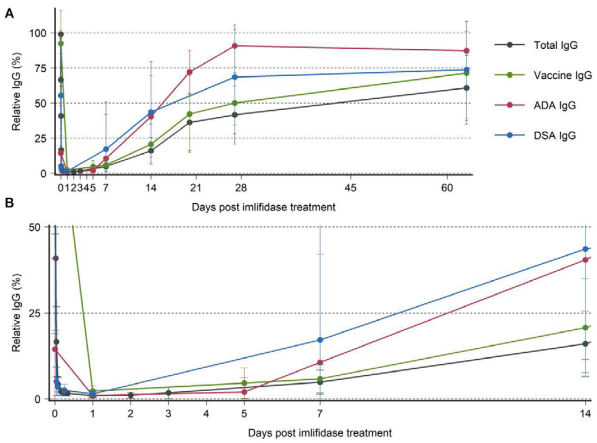

Table 1. Characteristics of Subjects, and relative (to max) IgG Levels

% IgG Level (mean [SD])	Pre-dose	Post-dose, 24h	Post-dose, day 14	Post-dose, day 64
Total IgG (n = 10)	99 (3)	1.0 (0.4)	16 (9)	61 (23)
Vaccine IgG (n = 10)	93 (24)	2.3 (1.6)	21 (14)	71 (37)
ADA IgG (n = 10)	14 (26)	1.0 (1.2)	40 (29)	87 (14)
Immunodominant DSA IgG [only DSA positive (MFI ≥ 1000)] (n = 8)	55 (36)	1.5 (1.1)	44 (36)	74 (34)

POS127 MUSEKAL - A MULTI-CENTRE NON-INTERVENTIONAL STUDY TO ASSESS THE TOLERABILITY AND EFFECTIVENESS OF ENVARSUS IN DE NOVO KIDNEY TRANSPLANT PATIENTS

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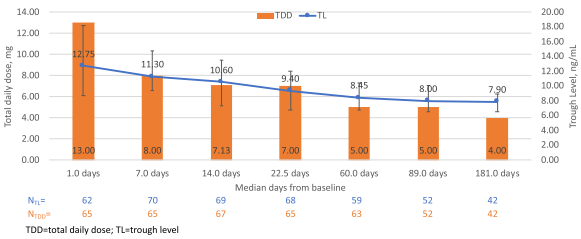
Background: Tacrolimus (tac) is prone to substantial inter- and intra- individual variability in absorption and metabolism, requiring frequent dose adaptations to achieve target trough levels (TL). Envarsus was shown to achieve target TL faster and at lower total daily dose (TDD) for TL maintenance compared to other tac formulations. The present analysis aimed to assess tolerability and effectiveness of Envarsus in de-novo kidney transplant patients in real-life.
Methods: The study was conducted in adult (≥18 years) patients in Austria and the Czech Republic. Patients received Envarsus according to local daily clinical routine and per approved indication. Written informed consent was provided. Safety and effectiveness were assessed during six months of observational. Variables relevant to de novo patients are presented here, i.e. tac TL, tac TDD from day 1 to 6 months, number of dose adjustments; time (days) to standard reference range; kidney function rapidly improved and remained stable at 50 ml/min/1.73m^2 at day 60 and beyond. Adverse

drug reactions (ADRs) were summarized using the MedDRA dictionary. The data collection period was 07/2016 to 08/2019.
Results: A total of 34 de novo kidney transplant patients were analysed; patients were predominantly male and < 65 years old (Table). The mean time to achieve target TL was 3.7 days after a mean of 8.5 dose adjustments; TDD decreased consistently over time from 13 mg at day 1 to 4 mg at day 181 (Figure). Kidney function continuously improved over time. Envarsus was well tolerated with 3 ADRs in 2 patients, none serious (Table).
Conclusions: After Envarsus initiation in de novo kidney allograft recipients, TL were consistently maintained within target, while the TDD could be reduced over time. Kidney function rapidly improved. Envarsus was well tolerated in this population.

Table. Baseline characteristics and treatment outcomes

Parameter	De Novo (N=34)
Male sex, n (%)	22 (64.7)
Age <65 years, n (%)	26 (76.5)
Trough level, ng/mL	Consistently above 5 ng/mL
Total daily dose, mg	Consistently reduced over time from 13 mg at day 1 to 4 mg at day 181
Mean (SD) time to standard trough level, days	3.7 (5.0)
Mean (SD) number of dose adjustments	8.5 (6.0)
Kidney function	eGFR consistently increased after transplant and then remained stable at 50 ml/min/1.73m^2 at day 60 and beyond
Adverse drug reactions	3 events in 2 patients (bacterial pyelonephritis, CMV infection, diarrhoea)
Serious adverse drug reactions	None reported

Figure. Trough levels and total daily dose over time



TDD=total daily dose; TL=trough level

POS128 MUSEKAL - ASSESSING TOLERABILITY AND EFFECTIVENESS OF ENVARSUS IN KIDNEY TRANSPLANT PATIENTS CONVERTED FROM OTHER TACROLIMUS FORMULATIONS

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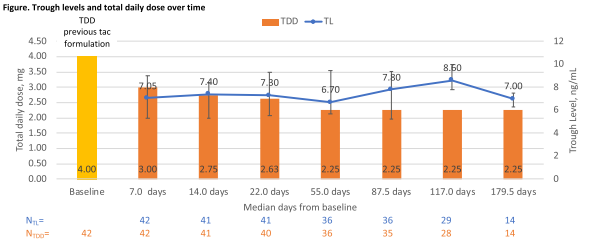
Background: Available tacrolimus (tac) formulations exhibit substantial inter- and intra- individual variability in absorption and metabolism leading to various difficulties in long-term maintenance of immunosuppression. Envarsus was shown to maintain stable target trough levels (TL) at reduced total daily dose (TDD) compared to other tac formulations. This study assessed tolerability and effectiveness of Envarsus in kidney transplant (Tx) patients (pts) converted from other tac formulations in real-life.
Methods: The study was conducted in Austria and the Czech Republic. Adults received Envarsus per approved label and local clinical routine. Written informed consent was obtained. Safety and efficacy were assessed during 6 months of observation. Variables relevant to conversion pts are presented, i.e. tac TL, tac TDD and C/D ratio over time, number of dose adjustments and kidney function. Adverse drug reactions (ADRs) were summarized using the MedDRA dictionary. Data collection period was 07/2016 to 08/2019.
Results: A total of 42 pts were analysed before and after conversion; pts were predominantly male and <65 years old (Table); 31 pts had no pre-existing abnormalities, 6 experienced tremors. After conversion to Envarsus, TDD decreased over time from 4 mg at baseline to 2.25 mg at day 55 and beyond while TL remained stable (Figure). C/D ratio improved from 1.76 ng/mL*1/mg at day 7 to 2.75 ng/mL*1/mg at day 117. Kidney function remained stable throughout the study. Envarsus was well tolerated with 6 ADRs in 4 pts; one serious ADR was reported (Table).
Conclusions: After conversion to Envarsus, target TL were maintained while the initial TDD could be reduced during the first 3 weeks with few dose adaptations and remained stable thereafter. Improvements in C/D ratio also indicate a higher bioavailability of Envarsus. Excellent tolerance, minimal dose adjustments and robust kidney function after conversion to Envarsus indicate both practicability and safety of this strategy in renal Tx pts.

Table. Baseline characteristics and treatment outcomes

Parameter	Switch patients (N=42)
Male sex, n (%)	28 (66.7)
Age <65 years, n (%)	33 (78.6)
Mean (SD) time since transplantation, days	554.9 (1444.5)
Trough level, ng/mL	Consistently above 5 ng/mL
Total daily dose, mg	Constantly decreased over time from 4 mg at baseline to 2.25 mg at day 55 and beyond
C/D ratio, ng/mL*1/mg	Increased from 1.76 at day 7 to 2.75 at day 117
Kidney function	eGFR remained stable at 50 ml/min/1.73m^2 throughout
Adverse drug reactions	6 events in 4 patients (leukocytopenia, otitis media, diarrhoea [n=2], CMV reactivation, febrile pulmonary infection)
Serious adverse drug reactions	1 event of febrile pulmonary infection

Figure. Trough levels and total daily dose over time



Tac=tacrolimus; TDD=total daily dose; TL=trough level

POS129 EFFECT OF TACROLIMUS EXPOSURE ON EVEROLIMUS-BASED IMMUNOSUPPRESSION IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS: A 24-MONTH ANALYSIS FROM TRANSFORM STUDY

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Background: Long-term use of calcineurin inhibitors including tacrolimus (TAC) has been associated with nephrotoxicity and infections. Here, we evaluated the efficacy and safety of everolimus+reduced-dose TAC (EVR+r-TAC) versus mycophenolic acid+standard-dose TAC (MPA+sTAC) by TAC subgroups, from TRANSFORM (NCT01950819) study.
Methods: Patients were stratified within treatment arms, based on mean TAC trough levels (C_0) from week 1 to month (M) 2, into below (<4 & <8 ng/mL), within (4–7 & 8–12 ng/mL) and above (>7 & > 12 ng/mL) the target range in EVR and MPA arms, respectively. Composite of treated biopsy-proven acute rejection (tBPAR)/graft loss/death and individual components, renal function estimated glomerular filtration rate (eGFR), and infections were evaluated up to M24.
Results: Incidence of composite efficacy failure was higher in EVR+rTAC versus MPA+sTAC arm (p = .125) among patients above TAC target C_0. In EVR+rTAC arm significantly higher incidence of tBPAR (p = .016), acute rejection (p = .003), and acute antibody-mediated rejection (p <.001) was observed in patients with TAC C_0 above target range. In patients within TAC target C_0, all efficacy endpoints were comparable in EVR+rTAC versus MPA+sTAC arm. Incidences of BPAR and tBPAR were significantly lower (p <.001) in EVR+rTAC versus MPA+sTAC arm in patients below TAC target

Table: Efficacy, renal function and AE outcomes

Parameters*	Below-target TAC C_0				Within-target TAC C_0				Above-target TAC C_0			
	EVR+TAC N=22	MPA+TAC N=170	% Difference (95% CI)	*P value*	EVR+TAC N=533	MPA+TAC N=631	% Difference (95% CI)	*P value*	EVR+TAC N=347	MPA+TAC N=99	% Difference (95% CI)	*P value*
tBPAR, graft loss or death	3 (13.6)	28 (17.0)	−3.3 (−18.8, 12.1)	.673	82 (17.1)	77 (16.1)	1.0 (−6.4, 8.5)	.791	56 (17.6)	11 (11.4)	6.1 (−1.7, 14.0)	.125
tBPAR	0 (0.0)	18 (11.0)	−11.0 (−15.8, −6.2)	<.001	57 (11.9)	58 (12.4)	−0.5 (−7.5, 6.5)	.897	45 (14.2)	6 (6.2)	8.0 (1.5, 14.4)	.016
tBPAR	0 (0.0)	19 (11.7)	−11.7 (−16.6, −6.7)	<.001	60 (12.5)	62 (13.1)	−0.6 (−7.6, 6.6)	.870	48 (15.1)	6 (6.2)	8.8 (2.3, 15.4)	.008
Graft loss	2 (9.1)	4 (2.6)	6.5 (−5.8, 18.8)	.298	17 (3.3)	13 (2.1)	1.2 (−0.7, 3.1)	.225	7 (2.0)	2 (2.2)	−0.1 (−3.5, 3.2)	.938
Death	1 (4.5)	8 (4.9)	−0.3 (−9.6, 9.0)	.947	17 (3.9)	17 (3.6)	0.3 (−2.6, 3.2)	.836	9 (3.0)	3 (3.1)	−0.2 (−4.2, 3.9)	.938
AR	3 (14.9)	29 (17.6)	−2.7 (−19.4, 13.9)	.747	77 (15.9)	87 (19.6)	−3.8 (−12.7, 5.2)	.409	63 (19.4)	8 (8.3)	11.1 (3.8, 18.4)	.003
Acute ABMR	3 (14.9)	15 (9.1)	5.8 (−10.4, 22.0)	.485	37 (7.2)	42 (12.4)	−5.2 (−13.3, 3.0)	.213	28 (9.1)	1 (1.1)	8.0 (3.8, 12.3)	<.001
Chronic ABMR	0 (0.0)	1 (0.6)	−0.6 (−1.8, 0.6)	.316	7 (1.4)	11 (1.8)	−0.5 (−1.9, 1.0)	.543	3 (1.8)	1 (1.1)	0.6 (−2.7, 4.0)	.708
Treated acute rejection	3 (14.9)	26 (15.2)	−0.3 (−18.8, 18.3)	.973	65 (15.4)	74 (17.3)	−3.9 (−12.5, 4.7)	.371	59 (18.0)	8 (8.3)	9.6 (2.4, 16.9)	.009
	EVR+TAC N=22	MPA+sTAC N=170	Mean difference (95% CI)	*P value*	EVR+TAC N=533	MPA+sTAC N=631	Mean difference (95% CI)	*P value*	EVR+TAC N=347	MPA+sTAC N=99	Mean difference (95% CI)	*P value*
Serum creatinine (µmol/L), Mean ± SD	124.9 ± 62.04	124.4 ± 0.23	0.42 (−28.50, 29.35)	.977	128.4 ± 50.33	124.9 ± 43.04	3.53 (−2.99, 10.05)	.288	138.2 ± 49.25	137.1 ± 62.96	−8.97 (−25.02, 7.28)	.280
eGFR by MDRD-4 (mL/min/1.73m^2), Mean ± SD	61.76 ± 22.15	61.15 ± 19.99	0.61 (−10.74, 11.96)	.915	58.60 ± 19.20	58.77 ± 19.52	−0.17 (−2.91, 2.56)	.902	58.36 ± 21.06	57.99 ± 17.42	0.37 (−5.22, 5.96)	.897
	EVR+TAC N=22	MPA+sTAC N=170	Risk ratio (95% CI)	*P value*	EVR+TAC N=531	MPA+sTAC N=631	Risk ratio (95% CI)	*P value*	EVR+TAC N=343	MPA+sTAC N=99	Risk ratio (95% CI)	*P value*
Any infection as AE	13 (59.1)	128 (75.3)	0.10 (0.06, 0.18)	<.001	374 (70.4)	484 (78.3)	0.76 (0.68, 0.84)	<.001	248 (72.3)	73 (73.7)	3.39 (2.65, 4.34)	<.001
BKV infection	0	13 (7.6)	0	<.001	32 (6.0)	74 (11.7)	0.43 (0.29, 0.65)	<.001	21 (6.1)	12 (12.1)	1.76 (0.86, 3.53)	.116
CMV infection	0	19 (11.2)	0	<.001	15 (2.8)	93 (14.7)	0.16 (0.09, 0.28)	<.001	12 (3.5)	10 (10.1)	1.20 (0.52, 2.76)	.672
Any viral infection[†]	3 (13.6)	56 (32.9)	0.05 (0.02, 0.17)	<.001	110 (20.7)	238 (37.7)	0.46 (0.37, 0.57)	<.001	74 (21.6)	27 (27.3)	2.74 (1.78, 4.21)	<.001
BKV	0	12 (7.1)	0	<.001	28 (5.3)	61 (9.7)	0.46 (0.30, 0.71)	<.001	13 (3.8)	10 (10.1)	1.30 (0.57, 2.95)	.532
CMV	0	26 (15.3)	0	<.001	25 (4.7)	103 (16.3)	0.24 (0.16, 0.37)	<.001	14 (4.1)	12 (12.1)	1.16 (0.54, 2.51)	.697
dnDSA												
Anti-class I	0	4 (2.4)	-	-	5 (0.9)	7 (1.1)	-	-	5 (1.5)	2 (2.0)	-	-
Anti-class II	0	4 (2.4)	-	-	11 (2.1)	10 (1.6)	-	-	10 (2.9)	2 (2.0)	-	-
Anti-class I + Anti-class II	0	1 (0.6)	-	-	11 (2.1)	4 (0.6)	-	-	1 (0.3)	0 (0.0)	-	-

*All data are n (%). Data are represented as n (%) unless specified. †Infections were confirmed by micro-organisms.
Note: Only significant differences between groups have been bolded. All incidences were reported for all the endpoints. 95% CI and P value for difference is to test for no difference (EVR+TAC) − (MPA+TAC) = 0.
ABMR, antibody-mediated rejection; AE, adverse event; AR, acute rejection; BKV, BK virus; BPAR, biopsy-proven acute rejection; C_0, trough levels; CI, confidence interval; CMV, cytomegalovirus; dnDSA, de novo donor specific antigen; eGFR, estimated glomerular filtration rate; EVR, everolimus; MDRD4, 4-variable modification of diet in renal disease; MPA, mycophenolic acid; rTAC, reduced TAC; sTAC, standard TAC; TAC, tacrolimus; tBPAR, treated BPAR.

C_0. At M24, no significant difference in creatinine or eGFR was observed across TAC subgroups. Cytomegalovirus and BK virus infection rates were significantly lower among patients below and within TAC target C_0 (p <.001) in EVR+rTAC arm. Incidence of de novo donor specific antigen was comparable in both arms across TAC subgroups (Table).
Conclusions: Better anti-rejection efficacy could be achieved with lower TAC exposure in EVR arm while higher TAC exposure was required with MPA. EVR+rTAC offered comparable renal function and lower viral infections versus MPA+sTAC regimen up to M24 posttransplant among subgroup of patients within TAC target C_0.

POS130 COVID-19 INFECTION CAN LEAD TO AN INCREASE OF TACROLIMUS LEVEL IN RENAL TRANSPLANT PATIENTS: AN OBSERVATIONAL COHORT STUDY

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Background: Transplant patients are at high risk of adverse outcomes once infected with COVID-19. The aim of this observational study was to evaluate the effect of COVID-19 infection on serum tacrolimus (Tac) levels in these patients.
Methods: A prospective database of transplant patients cared for by the Cardiff Transplant Unit and diagnosed with COVID-19 infection between March-December 2020 was maintained. 59 patients were infected, 53 of them on Tac. We identified 20 transplant patients with raised trough serum Tac levels at the time of diagnosis. Analysis was performed using a paired sample T-test to compare levels at diagnosis to their pre-infection levels, both to their 2 year historic levels (method 1) and their three most recent levels prior to infection (method 2).
Results: Mean age at diagnosis was 52 ± 14.2 years. 38% of the COVID-19 infected cohort (57.1% of those with available trough levels close to diagnosis) presented with raised Tac levels (20 of 53 Tac patients). 12 (60%) of these patients presented with 'classic COVID-19 symptoms', 5 (25%) had diarrhoea at presentation. 17/20 patients (85%) with high levels required hospital admission (compared to 46% of the rest) with 2 of them (12%) requiring intensive care. 13 patients (65%) suffered graft dysfunction and one patient (2%) graft failure. 4 patients (20%) died during admission due to COVID-19 infection. The mean serum Tac level at diagnosis was 15.3 μg/L (with a target range 5–8 μg/L), while the patients' mean historic value prior to infection was 7.7 and 6.6 μg/L respectively with the 2 methods used (p <0.0001).
Conclusions: Tacrolimus has a narrow therapeutic range. Tac levels are elevated in a high percentage of COVID-19 transplant patients compared to their baseline and is associated with a higher admission rate. We suggest measuring Tac levels in transplant patients at diagnosis of COVID-19 to enable reduction in cases with elevated serum levels. It's unclear whether diarrhoea, decreased small-bowel transit time or decreased Pgp expression play the main role in the raised Tac levels.

		Range	Mean ± SD	Median	Statistical Significance (95% CI)
Historic Mean Serum Tacrolimus level (μg/L)	Method One	3.6–16.2	7.7 ± 2.6	7.6	p < 0.0001
	Method Two	2.8–8.9	6.6 ± 1.8	6.8	p < 0.0001
Serum Tacrolimus level at diagnosis (μg/L)		8.2–23	15.3 ± 4.5	16.2	

Table 1. Summary of results

POS131 PAIRED STUDY OF KIDNEY DONORS COMPARING TWO FORMULATIONS OF PROLONGED-RELEASE TACROLIMUS (ADVAGRAF® VS ENVARSUS®)

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Objective: To analyze the results after deceased donor kidney transplantation (DDKT) comparing two formulations of prolonged-release tacrolimus (Advagraf® versus Envarsus®).
Material and methods: We performed a prospective study with a paired analysis of DDKT using Advagraf® for the first transplant undertaken from the same donor if the date was even and Envarsus® if it was odd. Data were collected during one year post-transplant.
Results: The study included 108 kidney transplants; 54 patients received treatment with Advagraf® and 54 with Envarsus®.The mean age of the donors was 57 ± 11 years and 63% were male;40% had hypertension and 8% diabetes. No differences were found between the groups in the recipient characteristics. In 13 patients it was necessary to change the formulation to Prograf® (7 in the Envarsus group (EG) and 6 in the Advagraf group (AG)). We found no differences between the AG and EG in any of the results, except for the tacrolimus levels during the first week and the dose needed during the follow-up (Table).
The percentage of acute rejections was 14% in the AG versus 10% in the EG (p = 0.5).
In 23 patients (13 EG and 10 AG) a protocol biopsy was performed in the third month post-transplant, observing data of subclinical rejection in 61% of the patients EG and 80% AG (p = 0.04).
Censored graft survival was significantly greater in the EG (100% versus 91% for AG; p = 0.04) and patient survival was 100% versus 95% (p = 0.1).
Conclusions: Envarsus® enables higher tacrolimus levels to be achieved during the first post-transplant week despite receiving lower doses. This could explain the tendency to a greater immune dysfunction in the AG and the better graft survival. Other parameters of safety and efficacy were similar between the two formulations

	ENVARSUS (n = 47)	ADVAGRAF (n = 48)	p
Cold ischemia time (hours)	13.1 ± 4.1	13 ± 3.6	0.9
Delayed graft function (%)	29	35	0.5
Hypersensitized (PRA>50%)	16	18	0.7
Creatinine 6 months (mg/dl)	1.6 ± 0.7	1.7 ± 0.9	0.5
Creatinine 12 months (mg/dl)	1.5 ± 0.4	1.6 ± 0.7	0.7
Tacrolimus levels day 2 (mg/dl)	8.4 ± 5.1	6 ± 2.8	0.007
Tacrolimus levels day 7 (mg/dl)	10.9 ± 4.6	8.8 ± 4	0.04
Tacrolimus levels month 12 (ng/ml)	8 ± 2.4	8 ± 2.2	0.9
Tacrolimus dose day 7 (mg/kg)	0.09 ± 0.02	0.13 ± 0.02	<0.001
Tacrolimus dose month 12 (mg/kg)	0.04 ± 0.02	0.08 ± 0.05	<0.001
Coefficient of variation	28	25	0.3

POS132 SENSITIVITY TO TACROLIMUS NEPHROTOXICITY AND LONG-TERM GRAFT OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Tacrolimus (TAC) is cornerstone immunosuppression after kidney transplantation, but TAC nephrotoxicity may impair graft survival. Short-term sensitivity to TAC nephrotoxicity may vary between individuals and its long-term implications are unclear. Here, we quantified short-term sensitivity to TAC nephrotoxicity and assessed its association with long-term graft outcome.
Methods: Longitudinal cohort study in kidney transplant recipients (KTRs) receiving TAC-based immunosuppression with stable kidney function at baseline (6 months post-transplant). Short-term individual sensitivity to TAC nephrotoxicity was defined as the slope of the association between TAC trough levels and serum creatinine (SCr) from 6 months onwards (Figure 1). Multivariable Cox regression was used to study the association between short-term sensitivity to TAC nephrotoxicity and long-term graft outcome, defined as a composite of sustained doubling of SCr, start of dialysis or re-transplantation, censored for death.
Results: We included 362 KTRs (48 ± 18 yrs, 58% male, eGFR 52 ± 15 mL/min/1.73 m^2). Sensitivity to TAC nephrotoxicity was 1.6 (IQR 0.7–2.8) μmol/μg, indicating that each 1 μg/L increase in TAC trough level was associated with a 1.6 μmol/L rise in SCr. Sensitivity to TAC nephrotoxicity was higher in recipients from a female donor (1.7 (0.8–3.0) μmol/μg) vs. a male donor (1.5 (0.6–2.7) μmol/μg, p = 0.04). A higher sensitivity to TAC nephrotoxicity was independently associated with a lower baseline eGFR, a lower mean TAC level and donor female sex.
After 3.3 yrs follow-up, 52 (14%) participants had reached the endpoint. Sensitivity to TAC nephrotoxicity was associated with a higher risk of the primary graft outcome (HR 1.28, 95% CI 1.11–1.48, p = 0.001), independent of potential confounders (Table 1).
Conclusions: Short-term sensitivity to TAC nephrotoxicity, which is more pronounced in recipients from a female donor and in patients with lower eGFR, is associated with poor long-term graft outcome.

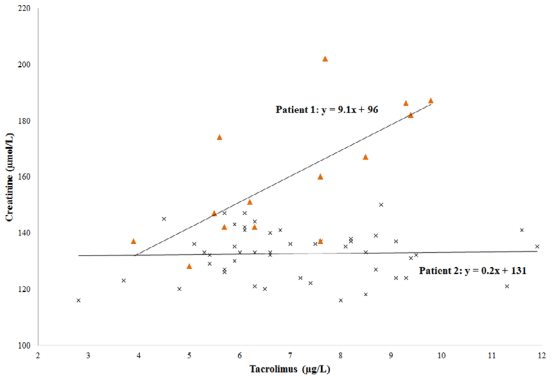

Figure 1 Two patient examples of serum creatinine levels (µmol/L) plotted against the corresponding tacrolimus (TAC) trough levels (µg/L). Tacrolimus sensitivity is defined as the slope of the trend line. Patient 1 (triangles) has a sensitivity to TAC nephrotoxicity of 9.1 µmol/µg. Patient 2 (crosses)has a sensitivity to TAC nephrotoxicity of 0.2 µmol/µg.

Table 1 Univariate and multivariate cox regression analysis.

Model	HR	95% CI	P-value
1	1.27	1.15 – 1.41	**< 0.001**
2	1.30	1.17 – 1.44	**< 0.001**
3	1.25	1.12 – 1.40	**< 0.001**
4	1.26	1.13 – 1.41	**< 0.001**
5	1.28	1.11 – 1.48	**0.001**

Model 1: crude analysis;
Model 2: adjusted for recipient sex and recipient age;
Model 3: model 2, additionally adjusted for eGFR at baseline and mean tacrolimus trough level;
Model 4: model 3, additionally adjusted for donor age, sex and CMV status;
Model 5: model 4, additionally adjusted for recipient BMI, systolic blood pressure, proteinuria and CMV status;
eGFR – estimated glomerular filtration rate; BMI – body-mass index; CMV – cytomegalovirus.

POS133 COMPARISON OF BASILIXIMAB VS NO INDUCTION ON 24-MONTHS RENAL FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS IN THE TACROLIMUS ERA

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Background: IL2-RA (Interleukin 2 receptor antagonist) are recommended for the induction immunosuppression of kidney transplant recipients in patients with low immunological risk. Studies showing the effectiveness of these substances have often been performed in patients taking cyclosporine. We aimed to find out whether the induction immunosuppression with basiliximab led to improved kidney graft function at 12 and 24 months in tacrolimus era.
Methods: Induction immunosuppression using IL2-RA basiliximab in all patients undergoing kidney transplantation has been routinely used in our transplant center since April 1, 2018. We retrospectively compared outcomes of kidney transplantation of the last 80 patients before introduction of induction and the first 80 patients after the induction (monitored period of analysis is May 2016 to February 2021). All patients in each group received baseline immunosuppression of tacrolimus, corticosteroid and mycophenolate. We selected patients with low immunological risk (1st transplant, panel reactive antibodies up to 20%, without donor specific antibodies, donation after brain death) in both groups and evaluated their renal outcomes (serum creatinine and estimated glomerular filtration rate/eGFR) at 12 and 24 months after transplantation.
Results: Renal transplant function at 12 months was analyzed in 49 patients with and 41 patients without basiliximab induction and renal transplant function at 24 months was analyzed in 23 patients with and 38 without basiliximab induction. The patients who received basiliximab inductive immunosuppression did not have better graft function compared to patients without basiliximab administration at 12 months and also at 24 months: median serum creatinine level at 12 months 121 µmol/L vs. 123 µmol/L ($p = 0.773$) and eGFR 0.84 ml/s vs. 0.77 ml/s ($p = 0.297$); median serum kreatinine level at 24 months 118 µmol/L vs. 114 µmol/L ($p = 0.565$) and eGFR 0.90 ml/s vs 0.83 ml/s ($p = 0.391$).
Conclusions: At our transplant center, the introduction of basiliximab induction in patients with low immunological risk did not improve graft function at 12 or 24 months.

POS134 CORRELATION BETWEEN NON MELANOMA SKIN CANCER AND BLOOD LEVELS OF TACROLIMUS IN KIDNEY TRANSPLANT RECIPIENTS: A RETROSPECTIVE COHORT STUDY

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Background: Renal transplant patients undergoing immunosuppressive therapy are at high risk of developing non-melanoma skin cancers (NMSC), especially basal cell (BCC) and squamous cell (SCC) carcinomas, conflicting and rare reports exist about the blood levels and the coefficient of variation of tacrolimus and the risk of NMSC.
Patients and methods: Retrospective cohort study, including a consecutive series of patients followed up between 2013 and 2019. For each patient age, sex, BMI, rejection and presence of one or more NMSC recorded. Tacrolimus blood levels (trough level) were measured every three months, and coefficient of variation was calculated. Univariate analysis was performed with $\chi 2$ and Fisher's exact test, and Student's t test for continuous variables. Logistic regression was used for multivariate analysis.
Results: 166 patients (103 males and 63 females) were included. 23 patients (13.9%) developed NMSC (15 SCC and 8 BCC). In univariate analysis risk factors for NMSC were age ($p = 0.0014$) and male sex (19/23 men and 4/23 women in the NMSC group vs. 84/143 men and 59/143 women in the control group; $p = 0.036$). Trough levels of tacrolimus were not significantly different between patients with and without NMSC, and before and after the diagnosis of NMSC ($p = 0.6468$). No differences existed in variation coefficients of tacrolimus between patients with and without NMSC, and no correlation between NMSC risk and patients who maintained drug levels within the therapeutic range during the observation period and over immunosuppressed patients. In logistic regression, including age, sex, coefficient of variation and acute rejection, only age and male gender predicted the occurrence of NMSC ($p = 0.0001$ and $p = 0.030$).
Discussion and conclusions: The main risk factors for NMSC in the present study were age and male gender, and no correlation existed with the blood levels of tacrolimus or with the coefficient of variation. One possible explanation is the low number of over-immunosuppressed patients included in our cohort, due to accurate clinical and laboratory monitoring of our cohort.

POS135 COMPARISON OF BASILIXIMAB AND R-ATG ON ACUTE REJECTION RISK IN HIGH IMMUNOLOGICAL RISK RENAL TRANSPLANT RECIPIENTS

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Introduction: High PRA level has been widely accepted as a marker for acute rejection risk following kidney transplantation. PRA>/ = 20% is considered a high immunological risk renal transplant. The aim of our study was to assess the risk of acute rejection in kidney transplant recipients (KTR) following Basiliximab induction compared to R-ATG maintained on tacrolimus and mycophenolate mofetil maintenance immunotherapy.
Methods: This was a retrospective observational cohort study using data from the United States Organ Procurement and Transplantation Network, all KTR's with PRA = /> 20%, who were maintained on tacrolimus and mycophenolate mofetil between September 2017 and September 2019 were included. Follow-up was until September 2020. The cohort were divided into 2 groups; living and deceased donor renal transplants. The groups were further divided by PRA level, each group was divided into 3 subgroups: Group A (low PRA level: PRA range from 20% to 49%), Group B (moderate PRA level: PRA range from 50% to 79%), and Group C (High PRA level: PRA range from 80% to 100%). Multivariable logistic regression models were constructed to assess the effect of induction therapies (Basiliximab versus R-ATG) on acute rejection episodes at 6 months post-transplant.
Results: Among living donor KTR's, there was no difference between Basiliximab and R-ATG in acute rejection episodes in any of the three groups, Group A (low PRA level, $n = 717$, OR = 1.17, $p = 0.79$, 95%CI:0.34–3.95), Group B (moderate PRA level, $n = 618$, OR = 1.51, $p = 0.58$, 95%CI:0.33–6.92) and Group C (high PRA level, $n = 401$, OR = 1.17, $p = 0.85$, 95% CI:0.21–6.56) respectively. In contrast, among deceased donor KTR's R-ATG was associated with lower risk of rejection compared to Basiliximab in all three groups, group A (low PRA level, $n = 1895$, OR = 0.52, $p = 0.03$, 95%CI: 0.28–0.94), group B (moderate PRA level, $n = 1618$, OR = 0.41, p

<0.01, 95%CI: 0.22–0.78) and group C (high PRA level, $n = 3973$, $p < 0.01$, 95%CI: 0.28–0.70).
Discussion: This study shows that risk of acute rejection is no different with Basilximab induction compared to R-ATG in high immunological risk living-donor KTR's at all levels of PRA in the current tacrolimus-mycophenolate mofetil immunosuppression era. However, risk of acute rejection seems to be lower in deceased donor KTR's having R-ATG induction at all levels of PRA.

POS136 ASSOCIATION OF TACROLIMUS TROUGH LEVEL AND DAILY DOSE RATIO WITH OUTCOMES IN A PROSPECTIVE PREVALENT COHORT OF KIDNEY TRANSPLANT RECIPIENTS

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Background: After solid organ transplantation tacrolimus remains the immunosuppressive treatment of choice. Due to its narrow therapeutic window, it requires serum trough level (C0) monitoring and dose adjustment. Both high and low serum levels may have harmful effects regarding overall mortality and graft survival due to increased risk of cardiovascular diseases, malignancies, new onset diabetes and rejection. C0 and total daily dose ratio (CD) has recently been suggested as a potential predictor of worse graft outcome in the early period after transplantation, however, long term prospective studies are lacking. We hypothesized the association between lower CD ratio and increased risk of death with functioning graft (DWFG), graft loss (GL) and overall death (D) in our prospective cohort study.
Methods: Our study included 386 prevalent kidney transplant recipients (205(53%) males, median and IQR age of 47.5 (13.2) years, eGFR 53.5 (22.5) ml/min/1.73m2, time since last transplant 51 (26–79) months) out of a total of 993 enrolled between 2006–2007. Sociodemographic, past medical history, clinical and laboratory data were collected and CD was recorded at baseline and 1 year after the enrollment. The associations between CD and CD2 ratios and above mentioned outcomes were examined using survival models.
Results: The median and IQR of CD was 2.1(1.4–3.2) at baseline and 2.0 (1.3–3.0) 1 year later (CD2). There was 46 (11.9%) DWFG, 79 (20.5%) GL and 68 (17.6%) D, respectively. After adjustment for important confounders (age, gender, eGFR, Charlson score, dialysis duration, donor age, rejection), neither CD (DWGL: HR 0.56(0.30–1.03) $p = 0.06$; GL: HR 0.82(0.50–1.36) $p = 0.46$; D: HR 0.79(0.48–1.32) $p = 0.38$) nor CD2 (DWGL: HR 1.12 (0.54–2.31) $p = 0.74$; GL: HR 0.76(0.61–1.97) $p = 0.78$; D: HR 1.19(0.64–2.20) $p = 0.59$) found to be predictors of the outcomes.
Conclusions: CD ratio was not associated with increased risk of death with functioning graft, graft loss or overall death in our prevalent kidney transplant recipients.

POS137 AN EFFECT OF DONOR-RECIPIENT CYP3A5 GENOTYPE COMBINATION ON TACROLIMUS EXPOSURE IN RENAL TRANSPLANT RECIPIENTS

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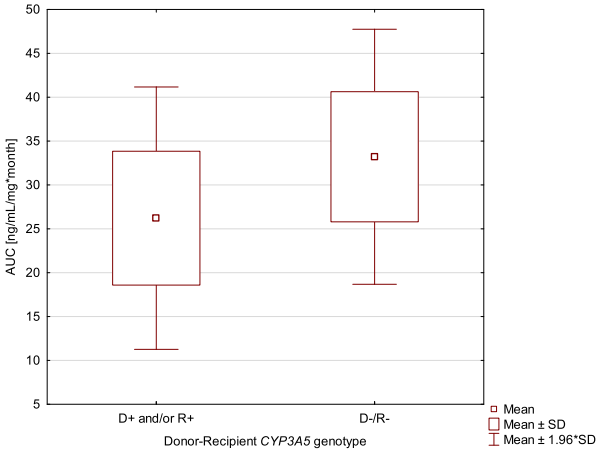
Background: Previous reports established that *CYP3A5* allelic variability may be the most important genetic contributor to inter-individual variation in exposure to tacrolimus in renal transplant recipients. CYP3A5 protein is expressed in allogenic kidney tissue but little is known of the significance of this phenomenon. We aimed to investigate the role of a donor CYP3A5 expression in pharmacokinetics of tacrolimus.
Methods: A cross-sectional study on 90 renal transplant recipients and their respective donors evaluated an effect of CYP3A5 single nucleotide polymorphisms on tacrolimus exposure. Area-under-the-curve (AUC) for tacrolimus concentration-to-dose ratios within three-years follow-up was calculated.
Results: Subjects were assigned to four groups due to the donor-recipient CYP3A5 genetic combination: donor (D) and recipient (R) expressors (+) ($n = 2$), D+/R- ($n = 10$), D-/R+ ($n = 11$), D-/R- ($n = 67$). A significant effect of CYP3A5 expression variants on tacrolimus exposure was observed [$F(2, 85) = 6.36$, $p = .003$]. Then new groups were created: the group in which at least one of the pair, donor or recipient, expressed CYP3A5 ($n = 23$) and the group of non-expressors ($n = 67$). AUC was significantly lower in the group of expressors (26.2 ± 7.6 vs. 33.2 ± 7.4, respectively, $p < .001$).
Conclusions: Intrarenal tacrolimus metabolism may affect both local and systemic drug exposure. Non-expressors receiving kidney with CYP3A5*1 allele may benefit from higher tacrolimus doses to shorten the time to achieve target drug concentrations.



POS138 IMPACT OF POLYCLONAL ANTI-T-LYMPHOCYTE GLOBULIN ON THE RECURRENCE OF IGA NEPHROPATHY AFTER KIDNEY TRANSPLANTATION: THE PIRAT STUDY

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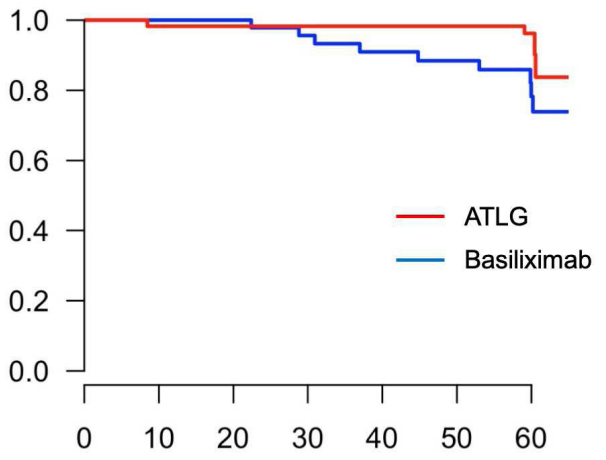
Background: IgA Nephropathy (IgAN) often recurs on kidney transplants. Polyclonal anti-T-lymphocyte globulin (ATLG) immunosuppressive induction has been shown to be associated with a lower rate of IgAN recurrence compared to basiliximab in a retrospective study. The aim of the PIRAT study was to compare an induction by ATLG *vs.* basiliximab by the mean of a randomized controlled trial.
Method: Adults with primary IgAN, first transplantation, panel reactive antibody <50% could be included in the study. Patients were randomized 1:1 prior to transplantation to receive either ATLG (Grafalon, 4mg/kg for 3 days, then 2 days 3mg/kg) or basiliximab (20mg twice). Both groups received methylprednisolone followed by oral corticoids for at least one year, tacrolimus and mycophenolic acid. Primary outcome was the clinico-histological recurrence defined by both IgA deposition on transplant biopsy and albuminuria>300mg/d during 5 years post-transplantation. Protocol biopsy at 5 years was highly recommended.
Results: A total of 117 patients were finally included, with 60 patients in the ATLG group and 57 in the basiliximab control group. Both groups were similar (median, ATLG vs. basiliximab, $p > 0.05$) in term of recipient age (47.9 vs. 47.7 years), dialysis vintage (26.2 vs. 24.6 months), age at IgAN diagnosis (35.0 vs. 42.2 years), living donors (33% vs. 25%).
A trend in favor to the protection by ATLG from the occurrence of a clinico-histological recurrence was found (HR 0.35 [0.11–1.1], $p = 0.082$).
Biopsy proven histological recurrence was significantly lower after ATLG induction (HR 0.34 [0.16–0.76], $p = 0.0079$). ATLG group experienced more infections (40 vs. 28 $p = 0.06$), a lower number of graft losses (3 vs 9, $p = 0.07$), a lower number of biopsy-proven acute rejections (5 vs 10, $p = 0.17$). Similar rates of cytomegalovirus and BK virus infections were found.
Conclusion: ATLG for immunosuppressive induction was found protective from the recurrence of IgA deposition during the first 5 years after

transplantation, compared to basiliximab. A similar trend, although not significant, was found about the clinico-histological recurrence which was the predefined primary outcome.

Figure:



POS139 THE BURDEN OF GASTRO-INTESTINAL COMPLAINTS IN KIDNEY TRANSPLANT RECIPIENTS USING TACROLIMUS WITH AND WITHOUT MYCOPHENOLATE MOFETIL

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Background: Tacrolimus (TAC) combined with mycophenolate mofetil (MMF) is the immunosuppressive regimen in the majority of solid organ transplant recipients. Gastro-intestinal complaints are frequent, which is considered predominantly a side effect of MMF. However, systematic research in this field is lacking. The aim of this study is to systematically investigate the burden of gastro-intestinal complaints in tacrolimus treated kidney transplant recipients with and without MMF.
Methods: In a single-center, open-label, randomized controlled trial, low immunological risk recipients were randomized to either TAC and MMF or to TAC monotherapy from 6 months after kidney transplantation onwards [NTR4672, www.trialregister.nl]. They filled in the Gastro-intestinal Symptom Rating Scale questionnaire, covering 5 dimensions (abdominal pain, reflux, indigestion, constipation and diarrhea) 6, 12 and 15 months after transplantation. This questionnaire makes use of a seven-point graded Likert scale, where 1 represents the absence of symptoms and 7 represents very troublesome symptoms. A score of ≥3 is considered troublesome.
Results: 79 Recipients were randomized of which 72 completed all questionnaires (34 TACmono and 38 TAC/MMF). At baseline, mean age was 59 years with 72% male, BMI 28 kg/m^2, eGFR 55 ml/min, mean daily dose of MMF 1200 mg and TAC 5.8 mg, with trough levels of 2.1 mg/L and 7.4 ug/L respectively. Six months after transplantation, 75% of the recipients reported troublesome symptoms. Diarrhea was the most troublesome (mean 3.3) and discontinuing MMF significantly reduced diarrhea (mean Δ score between 6 and 15 months TAC/MMF -0.9 vs TACmono -1.8, $p = 0.03$). In recipients with troublesome symptoms abdominal pain (2.7 to 1.8, $p = 0.003$), indigestion (2.8 to 2.3, $p = 0.012$) and reflux (2.9 to 1.7, $p = 0.007$), significantly decreased over time, independent of MMF use.
Conclusion: The majority of kidney transplant recipients with TAC and MMF experienced troublesome gastrointestinal symptoms six month after transplantation. While constipation remained troublesome, indigestion, abdominal pain and reflux improved over time by month 15. Diarrhea only improved after discontinuing MMF.

POS140 IMMUNOREGULATION AFTER RITUXIMAB INDUCTION IN BLOOD GROUP INCOMPATIBLE LIVING-DONOR RENAL TRANSPLANTATION – 2 YEAR DATA OF A PROSPECTIVE PILOT STUDY

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Background and Aims: An increased frequency of severe infectious diseases has been described in the first year after ABOi renal transplantation. As rituximab induction may alter immunoregulation in these patients, we analyzed clinically relevant immune parameters in a prospective renal transplant study.
Materials and Methods: Mononuclear cell subsets (peripheral blood; lymph nodes taken during transplant surgery), intracellular cytokine responses, CD4 helper function and in-vitro B cell responses were assessed pretransplant and up to 2 years posttransplant in 85 renal transplant recipients (living donation: $n = 25$ ABO incompatible (ABOi) and $n = 30$ ABO compatible (ABOc); deceased donation (DD): $n = 30$, all ABO compatible).
Results: Severe infectious diseases occurred more often in ABOi than ABOc recipients (11/24 (46%) versus 6/30 (20%), $p = 0.046$). After rituximab induction in ABOi recipients and 2 years of follow-up, B cell repopulation reached only 50% of the B cell counts observed in the blood of ABOc und DD recipients ($p = 0.001$; memory B cells, $p < 0.0005$). CD4+ T cell counts were significantly lower in ABOi compared to ABOc recipients at 3 and 6 months posttransplant ($p = 0.025$ and $p = 0.046$, respectively). In regional lymph nodes of ABOi patients, CD20+ B cell counts were vigorously downregulated at the time of transplantation ($p < 0.0005$) whereas counts of CD19+ B cells and CD4+ T cells were not altered. T-dependent B cell responses were significantly impaired in ABOi patients (2 years: $p = 0.01$; T-independent B cell responses $p = 0.137$).
Conclusion: An increased frequency of severe infectious diseases in ABOi renal transplant recipients may be explained by significantly downregulated CD4+ T cell counts and delayed B cell repopulation after rituximab induction, most pronounced with regard to memory B cells. Whether HLA antibody formation in ABOi recipients is suppressed by the impaired T-dependent B cell responses despite unaffected CD19+ B cell counts in regional lymph nodes at the time of transplantation, would be of considerable clinical interest.

POS141 LONG- TERM OUTCOMES OF ABO INCOMPATIBLE LIVING KIDNEY TRANSPLANTATION IN GREECE

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Background: ABO incompatible (ABOi) kidney transplantation (KT) has been established to overcome the immunological barrier of blood group incompatibility thereby increasing the living donor pool. We evaluated the long-term outcomes of the sole institution in Greece conducting ABOiKT.
Methods: A total of 71 patients, 5 of them highly sensitized, who had undergone ABOiKT between June 2005 and June 2020, were included. They were compared to a matched group of 71 ABO compatible (ABOc) non sensitized kidney transplant recipients transplanted during the same period. Our desensitization protocol consisted of a single dose of rituximab, sessions of immunoadsorptions or double filtration plasmapheresis to remove the anti-A/B antibodies to a titer less than 1:16 and intravenous immunoglobulin. Double oral immunosuppression with tacrolimus (TAC) plus everolimus or mycophenolate acid (MPA) was initiated 2 weeks before surgery. The ABOc recipients received TAC or CsA and MPA. All patients were transplanted with negative CDC and T/B FCXM and received induction therapy with IL-2Rmab and corticosteroids from the first day of KT. Most of ABOiKT recipients additionally underwent three plasmapheresis sessions every other day after surgery.
Results: The median follow-up period was 55 months (range, 6–203). A mean of 4.6 ± 3.06 apheresis sessions pre-KT were required. Mean serum

creatinine is 1.75 ± 0.86 mg/dl and 1.70 ± 0.57mg/dl in ABOi and ABOc KT at the time of last follow-up.
There was no significant difference between biopsy proven acute rejection episodes, bacterial and viral infections in two groups with the exception of an increased risk of BK virus associated nephropathy in the ABOiKT group. The 1,5,10 year patient survival rates were 100%, 95.6%, 91.9% in the ABOi and 100%, 97.4 %, 93.7% in the ABOc KT ($p = 0.646$) while graft survival rates were 97.2%, 92.8%, 75.6% in the ABOi and 98.5%, 86.1%, 79.4% in the ABOcKT respectively ($p = 0.856$).
Conclusions: Our desensitization protocol in ABOiKT is safe, providing excellent patient and graft survival, comparable to that of ABOcKT.

POS142 COVID-19 AND THE KIDNEY: SINGLE-CENTER EXPERIENCE FROM TURKEY

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Background: A special action plan is required for the COVID-19 infected dialysis patients, renal transplant recipients, and patients with progressive kidney disease as most of these patients are immunosuppressed.
Materials and Methods: The present study was conducted at the nephrology and transplantation clinic of Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, between March-May 2020. The frequency and clinical outcome of nephrology patients infected with COVID-19 were reviewed.
Results: Eighty-two patients were hospitalized at the nephrology clinic during the study period. Of the 82 patients, 21 were positive for COVID-19. The mean patient age was 65.33. Seven patients were on hemodialysis (33.3%), whereas 12 had a kidney disease not requiring dialysis. Among the twelve, seven patients had chronic kidney disease (33.3%), and 5 had acute kidney injury (23.8%). Two patients with COVID-19 positivity were renal transplant recipients (9.6%). Cough and dyspnea were detected in 16 patients (76.2%) and constituted the most common COVID-19 symptoms. Diarrhea was recorded as an atypical symptom in six of the patients (28%). During follow-up, leukopenia was detected in three patients (14.3%). Nine patients demonstrated lymphopenia (42.9%), and ten thrombocytopenia (47.6%). The most common finding on computed tomography scans of the thorax was lung consolidation with ground-glass appearance ($n = 15$, 71.4%). After the medical treatments, sixteen (76.2%) patients were discharged. Five patients were transferred to the intensive care unit. Two of these patients were intubated and died due to acute respiratory failure (9.5%). One of whom was a kidney transplant recipient (postoperative day 30).
Conclusion: The symptoms and course of COVID-19 vary depending on the primary kidney disease. Despite the low numbers in our study, we observed that the clinical course of COVID-19 was milder in the hemodialysis patients compared to the renal transplantation patients. Considering, one of the two deceased patients had a diagnosis of acute kidney injury, and the other was a recent kidney transplant recipient, it can be contemplated that kidney involvement has a predictive value for morbidity and mortality in nephrology patients infected with COVID-19.

POS143 RECURRENT URINARY TRACT INFECTIONS AMONG RENAL TRANSPLANT RECIPIENTS: RISK FACTORS AND OUTCOME WITH DEVELOPING RESISTANCE

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Background: Urinary tract infection (UTI) is the most common type of bacterial infection among kidney transplant recipients, with adverse effects on graft and patient survival. We aimed to assess risk factors and outcome of renal transplant recipients with recurrent episodes of urinary tract infection.
Methods: Out of 2000 kidney transplant recipients who are followed up in Hamed Al-Essa organ transplant center of Kuwait, 122 were suffering recurrent episodes of UTI. Cases with clinically evident pyelonephritis (PN represented group 1, $n = 33$) while cases without PN represented group 2 ($n = 89$). Along the previous 6 months of the study, we assessed these patients regarding risk factors and their outcome.
Preliminary Results: The two groups were comparable regarding their demographics. Group 1 showed positive gallium scan in 60.6% of cases (vs. 25.8% of group 2, $p = 0.001$), vesico-ureteric reflux was noted in 63.6% of cases in group 1(vs. 21.3% in group 2, $p = 0.001$), but the two groups were comparable regarding gender, diabetes and immunoglobulin levels. *E coli* and *Klebsiella Pn.* were isolated in the majority of patients in the 1st and 2nd episodes of UTI with increasing risk of resistance after the 3rd episode onwards (up to > 60% in the 4th episode.
Conclusions: Recurrent UTI is not uncommon among renal transplants and gallium scan support the clinical diagnosis of PN in most of cases. VU reflux was found the main risk factor for recurrent UTI with PN. Resistant bacterial strain were found to increase after the 3rd episode onwards.

POS144 CARBAPENEMS PROPHYLAXIS AND EXTENDED-SPECTRUM CEPHALOSPORINS-RESISTANT ENTEROBACTERALES URINARY TRACT INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Extended-spectrum cephalosporins-resistant (ESC-R) Enterobacterales (EB) urinary tract infection (UTI) has frequently been mong KT recipients. We investigated the effectiveness of carbapenems as perioperatively prophylactic antibiotics during KT surgery with cefuroxime to prevent ESC-R EB early UTI in KT recipients.
Methods: A retrospective study was conducted between 1 January 2016 and 31 December 2019. We performed 1:1 nearest neighbor propensity score matching without replacement prior to the analyses. Risk factors of ESC-R EB early UTI, including carbapenems peri-transplant prophylaxis were analyzed by Cox proportional hazards models.
Results: We included 620 KT recipients which 37% were female, and the mean age (±SD) was 43 ± 11 years. The 64% and 76% received deceased-donor allograft (DDKT) and induction therapy, respectively. There were 65 (10%), and 555(90%) received carbapenems and cefuroxime peri-transplant prophylaxis, respectively. There were 65 well-balanced matched pairs. During a 14-day follow-up period, the cumulative incidence of ESC-R EB early UTI was estimated by Kaplan-Meier methodology revealed 5% and 28% in carbapenems and cefuroxime group, respectively (log-rank test = 0.003). Peri-transplant carbapenems prophylaxis was a protective factors of ESC-R EB after KT (HR 0.19; 95% confidence interval [CI], 0.05–0.64, $p = 0.008$). Clinical and allograft outcomes were not significantly different between the two groups.
Conclusions: ESC-R EB UTI is common among KT recipients. Using carbapenems peri-transplant prophylaxis could provide a protective effect against the occurrence of early ESC-R EB UTI after KT.

POS145 EFFECT OF MYCOPHENOLIC ACID AND TACROLIMUS ON THE INCIDENCE OF INFECTIONS AFTER KIDNEY TRANSPLANTATION IN CONTRAST WITH ACUTE KIDNEY REJECTION

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Background: Goal of effective immunosuppressive treatment (IS) must be balanced between the decreasing incidence of acute kidney rejection (AKR) by maintaining effective levels of IS and avoiding the incidence of infections caused by dose-dependent toxicity of IS.
Methods: The aim of our analysis was to identify the risk of fixed daily doses (DD) of mycophenolic acid (MPA) and levels of tacrolimus (TAC) in the development of a single, recurrent infection after kidney transplantation (KTx) and AKR.

Results: Our analysis consisted of 100 patients after KTx (66 males, 34 females). DD of MPA>1080 mg was a RF for recurrent infection in general (OR 1.2964; $p = 0.0277$), recurrent bacterial infection (BI) from 1st-6th month (OR 1.2674; $p = 0.0151$), recurrent BI (OR 1.2574; $p = 0.0436$), single viral infection (VI) (OR 1.2640; $p = 0.0398$) from 6th-12th month after KTx. Incidence of mycotic infection in 1st month after KTx correlated with average TAC level ($p = 0.0300$) and with average MPA DD ($p = 0.0203$). Correlation between the average DD of MPA and the incidence of BI ($p = 0.0161$) and VI ($p = 0.0161$) from 1st-6th month after KTx were found. We confirmed correlation between the incidence of BI and the average DD of MPA from 6th-12th month after KTx ($p = 0.0479$). We confirmed correlation between TAC levels and the incidence of BI, mycotic infection (MI) and multidrug-resistant infection (MDRi), correlation between the DD of MPA and the incidence of MI in 1st month after KTx. We found correlation between TAC levels and MDRi and DD of MPA and the incidence of BI, MI and MDRi from 1st-6th month after KTx and between DD of MPA and the incidence of MDRi from 6th-12th month after KTx. We did not confirmed statistical significance between TAC levels, DD of MPA and the incidence of AKR and were not found as an independent RF for the incidence of AKR.
Conclusion: Lowering the DD of MPA <1080mg 1 month after KTx can lead to lowering the risk of infections without increasing risk of AKR.

POS146 TUBERCULOSIS IN KIDNEY TRANSPLANT RECIPIENTS IN A UNIVERSAL ISONIAZID PROPHYLAXIS SETTING

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Background: A little is known regarding universal INH prophylaxis's role to prevent TB in KT recipients in an endemic setting.
Methods: A retrospective cohort study was conducted among all adult KT recipients from January 2016 to August 2019. All patients received INH after KT regardless of their LTBI status. Patients who received INH less than one month were defined as a non-INH group. Differences in occurrence of TB between those who received INH and did not were assessed. Association between INH therapy and occurrence of TB was assessed with logic regression analysis.
Results: Of 613 KT recipients included, 62.2% were male, and a mean ± SD age was 43 ± 11 years. Of those, 64.6% underwent deceased-donor KT, and 5.2% received anti-thymocyte globulin for induction therapy. There were 557 (90.9%), and 56 (9.1%) patients classified into INH and non-INH groups, respectively. The most common reason for INH discontinuation was transaminitis (51.6%). During a mean follow-up of 35.89 months, 5 (0.8%) patients developed TB after KT, with 3 cases in INH group (0.5% vs 3.6%, $p = 0.02$). Clinical spectrums included 2 pulmonary-limited TB (40%), and 3 disseminated TB (60%). The median duration of onset was nine months (IQR 7–11). There was no difference in TB rate among those who received at least 6 (but less than nine months)-month course vs. 9-month course (1.64% vs. 0.44%, $p = 0.25$). A shorter INH therapy duration was associated with TB after KT (OR 0.84; [95% CI 0.70–0.99], $p = 0.04$). Allograft failure and mortality were significantly greater in KT recipients who developed TB ($p < 0.05$).
Conclusions: Isoniazid prophylaxis is generally well tolerated after KT. TB is less prevalent among KT recipients who receive INH. This universal prophylaxis could potentially prevent TB among KT recipients who live in endemic areas regardless of their LTBI status.

POS147 COVID-19 POSITIVE KIDNEY TRANSPLANT RECIPIENTS BEHAVE DIFFERENTLY DURING THE UNREMITTING STAGE WITH OPTIMIZED ANTICOAGULATION AND IMMUNOSUPPRESSION

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Background: COVID-19 is a briskly developing disease that has altered our lives especially kidney transplant recipients. We aimed to report the largest number of COVID-19 positive kidney transplants and discuss their demographics, management, and evolution.
Methods: Out of 2000 kidney transplants that were followed up in Hamed Al-Essa Organ transplant center in Kuwait, we collected data of all COVID-19-positive kidney transplants till the end of July 2020. Clinical features, management details, and both patient and graft outcomes were reported.
Preliminary Results: Most of cases were males aged 49.3 ± 14.7 years, 82 patients were hospitalized, 31 needed intensive care unit. Comorbidities included hypertension (64.4%), diabetes (51%), and ischemic heart (20.2%). Therapeutic management included anticoagulation (56.7%), antimetabolite withdrawal (54.8%), calcineurin inhibitor withdrawal (33.7%), antibiotics (57.7%), tocilizumab (8.7%), and antivirals (16.3%). Within 30 days follow-up, we reported acute kidney injury happened in 28.7%, respiratory failure requiring oxygen therapy in 46.2 %, overall mortality rate 10.6% (hospital mortality was 13.4% and ICU fatality 35.5%).
Conclusions: Better outcome of covid-19 positive KTR during this unremitting stage could be due to younger age together with early optimized anticoagulation, immunosuppression, and prompt treatment of secondary bacterial infections. Mild cases can successfully be managed at home without a change in immunosuppression.

POS148 ACUTE KIDNEY INJURY AMONG COVID-19 POSITIVE PATIENTS IS ASSOCIATED WITH HIGHER MORTALITY: SINGLE CENTER EXPERIENCE

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Background: Despite the lungs are the major targets of COVID-19, other organs as kidneys are affected. Renal complications of COVID-19 are not yet well studied. We aimed to study the prevalence of acute kidney injury (AKI) among positive COVID-19 cases that were managed in the intensive care unit in an isolation hospital in Kuwait.
Methods: This retrospective study included 616 patients with COVID-19 who were managed in the ICU in an isolation hospital, from February to December, 2020. AKI was defined according to criteria of KDIGO guidelines. Among the 616 patients, 40.2% developed AKI (group 1, $n = 248$) and were compared with the patients without AKI (group 2, $n = 368$).
Results: Most of cases in the 2 groups were males (73% vs. 70.7%), aged (60.8 ± 14 vs. 51.7 ± 16 years) respectively. The 2 groups were comparable regarding chronic kidney disease (2% vs. 0.8%), and chronic pulmonary disease. Other factors were significantly predominating among group 1 as diabetes mellitus (63.7 vs. 40.5%), hypertension (74.2% vs. 40.5%), ischemic heart disease (26.2% vs. 12.5%). Fever, cough shortness of breath and dehydration were the significant presentations among patient of group 1 who had radiological findings synchronized with COVID-19 (89.5% vs. 50.8%). Moreover, sepsis, dehydration, shock, arrhythmias and ARDS predominated among the AKI group. Number of cases who were managed by therapeutic anticoagulation was significant in AKI patients (89.9 % vs. 51.9%); cases who received vasopressors, convalescent plasma transfusion and steroid were significant in the same group. Other therapeutic modalities as antivirals and tocilizumab were comparable. Acute respiratory failure requiring mechanical ventilation was significant among AKI group (66.8% vs. 29.4%), and the overall mortality rate was significant in AKI group (62.5%. vs. 32.8%).
Conclusion: The prevalence of AKI in patients with COVID-19 was 40.2%, and it was associated with poor prognosis among ICU covid-19 positive cases.

POS149 CRITICALLY ILL COVID-19 POSITIVE KIDNEY TRANSPLANT RECIPIENTS BEHAVE DIFFERENTLY COMPARED TO NON-TRANSPLANT PATIENTS: SINGLE CENTER EXPERIENCE

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Background: COVID-19 is an ongoing pandemic that has altered our lives especially that of kidney transplant recipients (KTR). We aimed to compare the of COVID-19 positive kidney transplant recipients with non-transplant positive cases that were managed in the intensive care unit (ICU) during the pandemic.
Methods: Out of 2000 KTR that were followed up in Hamed Al-Essa Organ transplant center in Kuwait, we collected data of all COVID-19-positive KTR (group 1, $n = 79$) till the end of January 2021. Clinical features, management details, and both patient and renal outcomes were reported and compared with (group 2, $n = 445$) non-transplant cases admitted during the same period in the ICU of a single isolation hospital in Kuwait during the pandemic.
Preliminary Results: Most of cases were males (74% vs.73%), aged 51.7 ± 16 and 60.8 ± 14 years in the 2 groups respectively. Both groups were comparable regarding patients with diabetes mellitus (50.6 vs. 55.2%), hypertension (62% vs 57.1%), ischemic heart disease (20% vs 19.8%) and chronic kidney disease (1.3% vs 1.6%). Fever, cough, body aches and gastrointestinal symptoms were the most frequent presentation among KTR. Meanwhile, complicated cases with sepsis, volume depletion, shock, and ARDS predominated among the non-transplant group ($p < 0.05$). Therapeutic management included anticoagulation (81 %) in both groups, while steroid and tocilizumab were used frequently among the non-transplant group (8.7%). Within 30 days follow-up, non-transplant group showed significantly higher number of cases with acute kidney injury (47.8% vs. 26.7%), respiratory failure requiring mechanical ventilation, and mortality rate (54.4%. vs. 22.8%).
Conclusions: we reported better outcome of ICU admitted COVID-19 positive KTR in comparison with the non-transplant patients possibly due to younger age modified immunosuppression.

POS150 PRIMARY-INFECTED RENAL ALLOGRAFT: CLINICAL OPTIONS AND OUTCOMES

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Background and Aims: In some cases the KG's storage solution turns out to be contaminated. This asymptomatic donor's bacteremia can threat to recipient's health and life, because of leading to various infectious complications. Moreover, primary graft infection is detected several days after surgery. The aim: to explore options for the clinical course and outcomes after primary-infected kidney transplantation.
Methods: we analyzed 1633 KTx. 72 cases of primary-infected renal allograft (PIRAG) transplantation were identified. All PIRAG's recipients were initially prescribed immunosuppressive therapy (IST) and antibacterial prophylaxis with 3d gen of cephalosporins. The bacteriological research results were obtained on the 3–7 day after KTx. Having a positive result, the therapy was immediately adjusted according to the individual sensitivity of infection to antibiotics.
Results: In 47.2% cases, the Gram+ or - flora had been detected. Mixed infection - in 4.2% cases. Yeast fungi - in 1.4% cases. There were no any infectious complications in 72.2% of PIRAG cases. In 16.7% the development of local and/or generalized purulent-septic complications with the development of sepsis had been noted immediately (on 2–5 days after KTx). In such cases, emergency nephrotransplantectomy, revision, sanitation and drainage of infected areas were performed. Antibiotic therapy was prescribed, IST was canceled, and intravenous administration of human immunoglobulin was used. In cases of arrosive bleeding from the vessel's anastomoses we performed the recipient's external iliac artery and vein resection with simultaneous cross-iliac-femoral shunting. In 11.1% delayed complications with satisfactory graft's function had been manifested.
Conclusion: PIRAG is an undoubted factor of septic complication's development in kidney recipients. While PIRAG detected, the immediate antibacterial therapy maximization is necessary, with its correction according to microflora's sensitivity to antibiotics.

POS151 GENDER AND AGE DISPARITY IN INFECTIOUS COMPLICATIONS AFTER KIDNEY TRANSPLANTATION

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Background: Number of older patients with end stage kidney disease has been increasing, therefore there are increased number of older kidney transplant recipients (KTR). Potent immunosuppression (IS) used in patients after kidney transplantation (KTx) lowered the incidence of acute kidney rejection (AKR) but increased the risk of post-transplant infection and sepsis. Older adults are at high risk of infections due to functional impairment and multiple comorbidities. Nowadays, no change in IS or prophylactic therapy is recommended based on the age of a KTR. Female gender may be risk factor (RF) for infection after KTx due immunomodulatory effect of sex hormones.
Methods: The aim of our analysis was to find whether there are sex differences in the incidence of single and repeat infection and whether there is increased incidence of single and recurrent infectious complications in older KTR.
Results: Our analysis consisted of 100 patients after KTx (66 males,34 females), average age 47.5 ± 12.6 years. Male gender was a protective factor (PF) for the incidence of following infections in the 1st month after KTx: infection in general ($p = 0.0054$), recurrent infection ($p = 0.0239$), bacterial infection (BI) ($p = 0.0125$) and mycotic infection (MI) ($p = 0.0103$), recurrent BI ($p = 0.0258$). From the 1st-6th month after KTx, male gender was identified as a PF for the incidence of infection in general ($p = 0.0218$), BI ($p = 0.0186$) and MI ($p = 0.0318$), repeat infection ($p = 0.0216$), recurrent BI ($p = 0.0368$). From 6th-12th month after KTx, male gender was found as a PF for the incidence of BI ($p = 0.0144$), single infection ($p = 0.0355$), recurrent infection ($p = 0.0007$), single BI ($p = 0.0309$). Age > 60 years was not found as a RF for the incidence of single, repeat infection regarding its etiology. In our analysis we did not found correlation between gender and the incidence of single or recurrent infection of any etiology, we did not find significant differences in the severity of infections neither in gender, nor in older patients. In our study we did not confirm gender or age as a RF for the AKR.
Conclusion: In our analysis, we found significant sex differences in the incidence of BI, MI, viral, single and repeat infections in different time intervals after KTx, while we did not confirmed age > 60 years as a RF for the infectious complications after KTx.

POS152 BENEFITS OF VACUUM THERAPY IN THE MANAGEMENT OF SURGICAL CITE INFECTION AFTER KIDNEY TRANSPLANTATION: A RETROSPECTIVE SINGLE-CENTRE STUDY

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Background: Surgical cite infection (SSI) is one of the main reasons for the renal graft loss and the recipient death after surgery. Its development is associated with the technical features of the operation, concomitant pathology and the immunosuppressive status of the recipient. One of the most advanced methods of treating SSI is the use of vacuum-assisted closure (VAC) therapy.
Methods: From June 2018 to November 2019 at the Transplantation Department of the Botkin hospital performed 75 kidney transplants from a deceased donor. Wound complications were recorded in 7 patients. We retrospectively divided them into two groups and evaluated the effectiveness of VAC therapy in comparison with standard methods for the treatment of infected and long-term non-healing wounds. Group I included 3 patients (1 with a wound infected with Klebsiella pneumonia and 2 with long-term non-healing wound), group II - 4 patients (3 with infected wounds (Escherichia coli - 1, Klebsiella pneumonia - 2) and 1 with long-term non-healing wound). To treat infected and long-term non-healing wounds, standard methods were used, including daily dressings using modern materials (group I) and VAC therapy (group II). Average wound healing time was evaluated for each group.
Results: The average time between the start of treatment and the imposition of secondary sutures in the first group of patients was 33.11 ± 5.43 (28 - 37) days, in the second group 15.01 ± 3.15 (13 - 17) days ($p = 0.031$).
Conclusions: The use of VAC-therapy in patients with SSI after kidney transplantation, in comparison with standard methods of treatment, makes it possible to achieve rapid wound cleansing, relief of acute inflammation and acceleration of maturation of mature granulation tissue, thereby improving the results of treatment of this category of patients.

POS153 EARLY URETERAL STENT REMOVAL AFTER KIDNEY TRANSPLANTATION: A RETROSPECTIVE SINGLE-CENTRE STUDY

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Background: Urological complications (UC) are currently one of the main reasons for the renal graft loss and the recipient death in the early and late periods after surgery. Routine ureteral stent placement reduces the incidence or UC but at the same time leads to concomitant rise in urinary tract infections (UTI). The risk of UTI after kidney transplantation reducing achieves by early ureteral stent removal.
Methods: From June 2018 to March 2020 in the department of organ and/or tissue transplantation of the Botkin Hospital performed 89 kidney transplantation from a deceased donor with the internal double-J ureteral stent placement. Depending on the timing of stent removal, the patients were retrospectively divided into 2 groups: the first group included 54 patients who had the stent removed on day 21, and the second group - 35 patients who had the stent removed on day 14. Incidence of UC and UTI was assessed in both groups.
Results: No urological complications were recorded in both groups. Urinary tract infection in the first group was recorded in 8/54 patients (15%), in the second group - in 1/35 patient (3%) ($p = 0.01$).
Conclusions: Removal of the internal ureteral stent on the 14th day after surgery safely and reliably reduces the incidence of developing a urinary tract infection, improving the immediate results of kidney transplantation.

POS154 MAY ROUTINE BIOMARKERS FOR THE SEVERITY OF COVID-19 PNEUMONIA DIFFERENCE SARS-COV-2 INFECTION TO OTHERS INFECTIONS IN KIDNEY TRANSPLANT RECIPIENTS?

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Background: Coronavirus disease (COVID-19) is associated with high mortality rates in kidney transplant (KT) recipients. COVID-19 is diagnosed based on a polymerase chain reaction assay using nasal and/or pharyngeal swab specimens, and the treatment is based on the patient's clinical status and levels of inflammatory biomarkers. However, the comparative activity of these biomarkers in KT patients with pneumonia from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and non-SARS-CoV-2 aetiologies is unknown. This study compares the clinical presentation and inflammatory parameters at admission of KT patients with COVID-19 pneumonia and those with non-COVID-19 pneumonia over the same period.
Aim: To compare the clinical presentation and inflammatory parameters at admission of KT patients with COVID-19 pneumonia and those with non-COVID-19 pneumonia over the same period.
Methods: Leukocyte, neutrophil, and lymphocyte counts, haemoglobin levels, red blood cell distribution (RDW), and d-dimer, ferritin, C-reactive protein (CRP), interleukin-6 (IL-6), lactate dehydrogenase (LDH), and procalcitonin levels were measured and compared between KT patients with COVID-19 pneumonia ($n = 42$) and non-COVID-19 pneumonia ($n = 18$) from March to November 2020.
Results: Both groups showed comparable demographics. The COVID-19 KT patients had fewer neutrophils (4,650 [2,925–9,498] vs. 9,100 [7,170–11,150], $p = 0.01$) than the non-COVID group, although there was no significant difference in the lymphocyte count. Non-COVID-19 pneumonia was associated with a higher d-dimer (962 [427–1,448] vs. 1,704 [868–2,481], $p = 0.09$) and IL-6 (37 [23–10] vs 254 [53–602], $p = 0.006$)) levels. The ferritin level was higher in the COVID-19 pneumonia group (908 [496–1,377] vs. 340 [264–785], $p = 0.008$).
Conclusions: COVID-19 pneumonia in KT recipients shows a different presentation of inflammatory biomarkers than other non-COVID pneumonias. It could be usefully to identify KT patients with SARS-CoV-2 infection. More detailed studies are necessary to understand the presentation of biomarkers in immunosuppressed patients with COVID-19.

POS155 NOVEL AGENTS FOR ERADICATING HEPATITIS C VIRUS IN RENAL TRANSPLANT RECIPIENTS

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Background: Treatment of HCV infection after renal transplantation has been a problem because of contraindications associated with IFN-based and Ribavirin therapies. The direct-acting antiviral agents have revolutionized HCV treatment. We aimed to evaluate the effectiveness and safety of Sofosbuvir/Velpatasvir (SVR) vs Glecaprevir/Pibrentasvir (GP) in renal transplant recipients.
Methods: This is a prospective analysis of 13 renal allograft recipients with HCV treatment-naive infection. 10 patients self-administered a combined SVR (400–100 mg) tablet once daily for 12 weeks and 3 patients self-administered a combined GP (300–120 mg) tablet once daily for 8 weeks. The primary efficacy endpoint was sustained virological response (HCV RNA less than 15 IU/mL at 12 or 8 weeks after the treatment). The primary safety endpoint was the proportion of renal toxicity events (Crs > 30% over baseline, increased of 24 hour urine protein) and others adverse events (headhache, respiratory tract infection, astenia). Patients were monitored for trough levels of CNI.
Results: All patients showed a positive HCV RNA infection without cirrhosis, genotype 1(60%), 2(40%). All recipients were treated with CNI. All patients completed the full treatment course. Twelve patients exhibited a rapid virological response within 4 weeks (HCVRNA concentration below the lower limit of quantification), the other one within 8 weeks. The mean baseline e-GFR was 56 ± 9 ml/min/1.73m2, the mean baseline 24 hour urine protein was 480 ± 120mg. We didn't observe significant worsening of renal function in 10/13 patients (e-GFR 57 ± 9 ml/min/1.73m2, $p < 0.01$) and 24 hour urine protein in any patients (410 ± 120 mg, $p < 0.01$) within 12/8 weeks of SVR/GP use. A worsening of renal function was observed in the three patients on GP therapy during the last week of treatment (e-GFR< 35 ml/min), but at the end of therapy the e-GFR improved. Dose adjustments for CNI were not necessary. The most common adverse events were asthenia (9/13) and headache (5/13). Nobody developed infectious complications. At three years the patients have sustained remission from HCV infection.
Conclusion: We conclude that the novel agents are effective in renal transplant recipients for eradicating hepatitis C virus. SVR12 would seem more safe for renal transplant function than GP8.

POS156 RISK FACTORS FOR MORTALITY IN KIDNEY TRANSPLANT PATIENTS INFECTED BY SARS-COV-2 IN SOUTH OF SPAIN

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Purpose: To determine risk factors related to infection and mortality from Covid-19 in kidney transplant (KT).
Methods: We included 53 KT who had PCR-confirmed COVID-19 infection between march 21st and november 24th, from a total of 2030 KT. Outcomes related to patient survival were analyzed.
Results: 39 (73%) patients were men, with a mean age of 56 ± 15 years old. Median time after KT where the infection took place was 104 months (IQR: 55–160). One patient was infected 40 days after transplant. 90% were on Tacrolimus therapy and 79% on MMF.
81% of patients were hypertensive, 36% diabetic and 19% had ischemic heart disease.
Clinical presentation consisted on pneumonia (64%), fever (55%), cough (70%), dyspnoea (45%), lymphopenia (66%) and gastrointestinal symptoms (36%). 21% required intubation and admission in ICU. 8 patients were asymptomatic.
18% received Hydroxychloroquine therapy plus Azithromycin, 11% Tocilizumab, 11% Ritonavir-Lopinavir, 59% steroids, 7.7% Remdesivir and 13.5% convalescent plasma. Immunosuppression was reduced in all symptomatic patients.
10 patients (19%) died. Table 1 compares the characteristics of these patients with those who survived.
Conclusions: We concluded that mortality in KT is very high, more than reported in general population. Risk factors are patient age, time after KT, baseline renal function, the presence of pneumonia, as well as higher CRP levels at the time of diagnosis. More experience is needed to optimize our protocols and therapy for Covid-19 in KT.

Table 1. Comparison between the characteristics of patients who live and die.

	Alive (n = 43)	Dead (n = 10)	p
Age (years)	53 ± 15	67 ± 6	0.01
Time alter KT (months)	178 ± 157	93 ± 75	0.04
BMI (Kg/m^2)	28 ± 6	27 ± 3	0.7
HTA (%)	76	100	0.09
DM (%)	34	44	0.6
ARAII (%)	66	61	0.9
Tacrolimus (%)	88	100	0.5
MMF (%)	80	77	0.8
mtorI (%)	7	30	0.03
Pneumonia (%)	55	100	0.09
Gastrointestinal (%)	35	40	0.8
Fever (%)	58	66	0.9
Basal Creatinine (mg/dl)	1.4 ± 0.3	1.9 ± 0.7	0.01
Ferritin (ng/ml)	858 ± 577	1113 ± 752	0.4
Lymphocytes	0.8x10^9 ± 0.3 x10^9	0.6x10^9 ± 0.3x10^9	0.2
CRP (mg/l)	54 ± 38	132 ± 62	0.006
Dimero D (ng/ml)	1.772 ± 2500	90.009 ± 270.799	0.05
Tozilizumab (%)	7	33	0.04
Ritonavir/Lopinavir (%)	2.3	33	0.02
Steroids (%)	52	100	0.02
Hydroxychloroquine + Azithromycin (%)	14	40	0.05
Convalescent plasma (%)	14.3	10	0.7
Remdesivir (%)	0	10	0.1

POS157 CLINICAL PREDICTORS OF COVID-19 DISEASE SEVERITY IN KIDNEY TRANSPLANT RECIPIENTS

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Background and Aims: Kidney transplant recipients (KTR) have a higher rate of severe and critical COVID-19 disease and related death. We aimed to identify risk factors, namely transplant specific ones, associated with disease severity.
Methods: All KTR with COVID-19 infection (assessed by polymerase chain reaction) diagnosed at our center till December 31, 2020 were included. COVID-19 was classified as severe (including critical) and non-severe (including asymptomatic, mild and moderate) disease.
Results: Fifty-one out of 1084 KTR followed in our center were diagnosed with COVID-19. Median age was 55 years (IQR 50–63), 25.5% older than 60 years and 60.8% male. Majority (94%) were on triple immunosuppression with low-dose steroids and a calcineurin inhibitor (84% tacrolimus), with either mycophenolate (86%) or azathioprine (6.0%) or everolimus (8.0%). Six patients had < 1 year of transplant, 3 a rejection episode in the last 6 months and 2 a treated cytomegalovirus (CMV) infection in the previous year. Most frequent comorbidities were hypertension (76.5%), estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73m2 (51%), cardiovascular disease (23.3%) and diabetes (25.5%). Chronic respiratory disease was present in 3 patients. Antimetabolite was withdrawn in 60.8%, including all KTR with severe disease. Disease presentation was severe in 26 KTR (51%), 9 (17.7%) required mechanical ventilation and 2 died (3.9%).
Except for eGFR < 60 ml/min/1.73m2 (OR 2.163, 95% CI 1.16–4.04), we found no association between age, sex and other comorbidities with disease severity. Noteworthy everolimus was negatively associated with disease severity (0/4 (0%) vs 26/47 (55%), p = 0.034). Any correlation was noticed with the other immunosuppressive drugs. Time since transplantation (< 1 year), acute rejection (< 6 months) and treated CMV infection (<1 year) were not associated with disease severity.
Conclusions: In our cohort eGFR <60 ml/min/1.73m^2 was identified as a potential risk factor for disease severity in KTR. Our study suggests that everolimus may lessen COVID-19 severity, probably through its antiviral properties. Multicenter studies analyzing the effect of mammalian target of rapamycin inhibitors in different immunosuppressive regimens are urgently needed and may further clarify this association.

POS158 WILLINGNESS OF KIDNEY TRANSPLANT RECIPIENTS TO RECEIVE COVID-19 VACCINE

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Background: Organ transplant recipients are considered clinically extremely vulnerable to coronavirus disease (Covid-19). Acceptance of vaccination is essential for them to maintain health.
Methods: A cross-sectional survey about attitude towards vaccination was conducted using telephone interviewing between January 21 to February 15, 2021.
Results: Out of 129 recipients (mean age 53 ± 13 (23–83) years, 53% male, mean 5.7 ± 4.6 years since transplantation) 50.4% stated that they are going to accept Covid-19 vaccine, 31.8% had not decided and 17.8% refused the vaccine. 41% would like to receive a vaccine as soon as available, 9% would consider it in the future. Characteristics associated with willingness to receive a Covid-19 vaccine were acceptance of other prior vaccinations (p <.001), Latvian as a spoken language (p <.001), transplantation from living donor (p = .005), younger age (50.6 ± 13.7 vs 55.5 ± 12.4 years, p = .035) and higher education (p = .04). Furthermore, these patients were more likely to wash their hands more frequently during the pandemic (p <.004). Gender, employment status, living in a city, retransplantations, wearing a face mask and use of hand sanitizers, prior SARS-CoV-2 infection to themselves or member of their household showed no statistically significant association with the willingness to receive Covid-19 vaccine. Most common reasons for refusal and hesitation included fear of side effects, potential harm to transplant and belief that "vaccines are not well-studied yet".
Conclusions: A half of the studied kidney transplant recipients are undecided or unwilling to receive a Covid-19 vaccine. Publications about vaccination results in transplant population and delivery of information to patients may be critical for increasing Covid-19 vaccine uptake among kidney transplant recipients.

POS159 IMMUNOSUPPRESSION MANAGEMENT IN KIDNEY TRANSPLANT RECIPIENTS WITH SARS-COV-2 INFECTION: A SINGLE CENTER EXPERIENCE

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Background: The coronavirus disease of 2019, also known as COVID-19, has become a global health care crisis.
Having a weakened immune system might increase the risk of severe illness from COVID-19. Significant controversies exist regarding the optimal treatment modalities for this novel disease, especially in immunocompromised, as renal transplant recipients.
Methods: Data were collected on all kidney transplant recipients tested positive for SARS-CoV-2 between September 1, 2020, and January 31, 2021. Thirty-five transplant patients tested positive for SARS-CoV-2 during the study period from a total cohort of 980 kidney transplant recipients under follow-up in our transplant centre.
Preliminary Results: Thirty-five transplant patients tested positive for SARS-CoV-2 during the study period from a total cohort of 980 kidney transplant recipients under follow-up in our transplant unit. Fifteen patients required hospital admission, of whom 5 required intensive care and 3 died. The mean age was 53.02 ± 12.60 years. There were 21 male and 14 female patients. The most prominent symptoms were fever (69%), cough (69%), asthenia (20%) and anosmia (20%). All patients were managed with reduction of immunosuppression with cessation of antiproliferative agents and continuation of calcineurin inhibitors either at the same or reduced dose

along with continuation of corticosteroids. In all hospitalized patients, at the admission, we observed elevated levels of calcineurin inhibitors. The drugs used for COVID-19 such as azithromycin show significant interaction with tacrolimus, causing toxicity. We avoided macrolides, where possible and, if used, tacrolimus levels were monitored closely. Patients with a worst course and fatal outcome were obese. BMI of the patients in ICU was 30.46 ± 2.22.
Conclusions: The choice of immunosuppressive drugs in renal transplant recipients with COVID-19 infection remains unclear. Early modulation of immunosuppressive therapy can influence prognosis.

POS160 REMDESIVIR IS USEFUL AND SAVE IN KIDNEY TRANSPLANTATION WITH COVID-19 PNEUMONIAE

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Background: Remdesivir is the only treatment that has been shown to be useful against SARS-CoV-2 infection. It shorts hospitalization time compared to placebo. Kidney transplant (KT) patients were not included in these studies, therefore, its effects in this population is limited to some published cases.
Methods: We performed a retrospective observational study that included all KT patients admitted with SARS-CoV-2 pneumonia who received treatment with remdesivir. Patients received a 200mg loading dose followed by 100mg/day maintenance dose for 5 days.
Aim: To describe the experience of a cohort of KT patients treated with remdesivir.
Discussion: A total of 36 KT patients developed SARS-CoV-2 infection, 6 of them received treatment with remdesivir. The rest of the patients did not receive the drug due to either CKD-EPI less than 30mL/min or they did not present clinical criteria. In addition to remdesivir, all patients received dexamethasone and anticoagulation therapy. Immunosuppression was suspended in all patients, maintaining only dexamethasone. 50% were men, the median age was 58.5 (52.75–68) years. 67% had unknown underlying kidney disease, 83% were hypertensive and 33% had diabetes. All patients received KT from deceased brain donor and 50% received thymoglobulin as induction treatment. Median time from transplantation was 49 (20.5–135.5) months, with median glomerular filtration at admission of 47.5 (42.25–63.25) mL/min. The most frequent clinical manifestation was dry cough and dyspnea (83%), followed by tachypnea and fever (67%). Chest X-rays of all patients showed pulmonary infiltrates and required low oxygen flow therapy upon admission, requiring high flow nasal therapy in 33% of cases during admission. Only 17% of the cases presented deterioration of the graft function, not requiring hemodialysis in any case, and all recovered renal function at hospital discharge. No patient died or required admission to the critical care unit. Median days of admission was 12 (10–18) days.
Conclusions: KT patients with SARS-CoV-2 pneumonia under treatment with remdesivir have a good clinical course, with few cases of renal function deterioration and a low mortality rate. Additional studies are necessary with a larger number of patients to improve the knowledge of remdesivir in KT with SARS-CoV-2 infection.

POS161 EXTERNAL URETERIC STENT VS. INTERNAL DOUBLE J STENT IN RENAL TRANSPLANTATION: OCCURRENCE OF URINARY TRACT INFECTIONS AND UROLOGIC COMPLICATIONS

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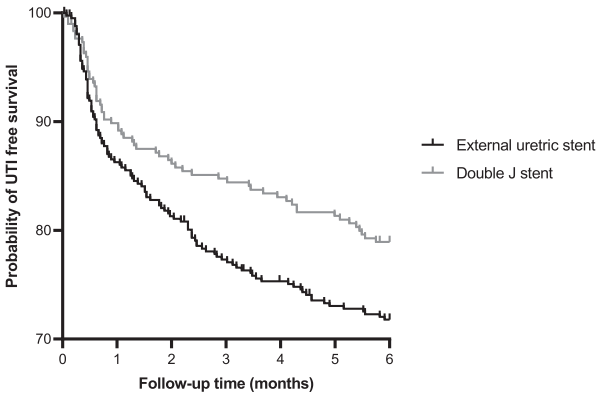
Background: urinary tract infections (UTIs) and urologic complications (UC) are common after renal transplantation. Catheter and stent placement are important risk factors for developing UTIs. Intraoperative stent placement reduces the risk of UC. In September 2014 our protocol changed from external ureteric stent (ES) to internal double J stent (DJ). We analysed the incidence of UTIs and UC between ES and DJ.
Methods: we performed a retrospective study of 711 kidney recipients, transplanted between 09-2012 and 12-2016 (2 years before and after protocol change, 3 months overlap). Vesicoureteric anastomosis was done by the Lich-Gregoir technique, ES was removed 7-12 days and DJ 3–4 weeks after transplantation. Induction immunosuppression consisted of basiliximab, a calcineurin inhibitor, mycophenolate mofetil and steroids. Follow-up period was 6 months. UTI was defined as clinical suspicion/leukocyturia and/or positive urine culture ($\geq 10^5$ CFU/ml) and need for antibiotic treatment. UC were defined as urinary leakage, ureter stenosis or urinary retention requiring an intervention.
Results: in 412 (57.9%) patients an ES was used and in 299 (41.2%) a DJ; median age was 55 years and ± 40% were women. In the ES group more patients had an pre-emptive transplantation (33.3% vs. 22.4%; $p = 0.002$). There was an equal distribution regarding living and deceased donor kidneys. In the ES group, 114 (28.6%) patients had ≥1 UTI within the first 6 months compared to 62 (21.3%) in the DJ group ($p = 0.029$). Also, the cumulative incidence over time of a first UTI was higher in the ES vs. DJ group (Figure 1). The frequency of urological complications was comparable (Table 1).
Conclusions: intraoperative use of an ES compared to a DJ is associated with a higher incidence of UTIs within 6 months following renal transplantation. There is no difference in UC between ES and DJ. The change in protocol is therefore justified.

Table 1. Urologic complications requiring intervention

Variable	ES $n = 399$	DJ $n = 291$	p-value
Total of UC	50 (12.5)	29 (10.0)	0.296
Urinary leakage	12 (3.0)	3 (1.0)	0.079
Ureter stenosis	28 (7.0)	17 (5.8)	0.537
Urinary retention	15 (3.8)	10 (3.4)	0.823
UC without urinary retention	35 (8.8)	20 (6.9)	0.363

Figure 1. Kaplan-meier curve of the probability of UTI free survival for ES vs DJ; HR 1.40 (95% CI 1.04–1.89), $p = 0.031$.



POS162 OUTCOMES OF THE COVID-19 PANDEMIC ON THE TRANSPLANT AND WAITING LIST POPULATION OF WALES – IS IT SAFE TO CONTINUE TRANSPLANTATION?

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Background: Transplant and waiting list patients have been severely affected by COVID-19 as they face a significant risk of contracting the infection and potentially worse outcomes. The aim of this study was to assess the impact of COVID-19 on kidney transplant and waiting list patients in South Wales during the 1st 2 phases of the pandemic.
Methods: Data of all South Wales transplant follow-up (Tx FU) and waiting list (WL) patients who were diagnosed with COVID-19 infection between 1st March and 31st December 2020 were prospectively collected and analysed in 2 separate periods (March-September, October-December) corresponding to the disease surges. The Welsh transplant program was suspended from March until July 2020. A series of measures designed to reduce risk (regular staff and patient testing, strict infection control measures including restriction of movement of non-transplant patients to the transplant unit) were implemented.
Results: During the period 88 patients were diagnosed with COVID-19 infection (Tx = 61, WL = 27). Median age was 54.5 years (24–78), BMI was 29.1 kg/m^2 (20.4–42.8) and time from transplant to infection was 122 months (1–465). 34 transplant (2.3% of Tx FU) and 11 WL (7.9% of WL) patients were admitted to hospital. 8 (9.1%) required escalation to an Intensive Care Unit (ICU). 7 transplant died (0.46% of Tx FU; 4 (0.26%) in the 1st and 3 (0.2%) in the second surge, $p = 0.7$). 2 WL patients died (1.42% of WL). Death to admission ratio went from 33.3% in the first period to 13.6% in the second period ($p = 0.173$) for the Tx FU patients.

Conclusion: The impact of the COVID-19 pandemic on transplant and WL population has been significant. The outcome on transplant and waiting list patients has improved in the second surge of the pandemic. This, along with implementation of strict in-hospital precautions, provides reassurance for the continuation of transplant programs.

POS163 KIDNEY TRANSPLANTATION ACTIVITY DURING COVID PANDEMIC - A SINGLE CENTER EXPERIENCE

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Background: The COVID-19 pandemic during 2020 has significantly impeded solid organ transplant activity nationally. This has considerably affected transplant patients and prolonged their morbidity. There is also risk of immunosuppressed patients being at increased risk of acquiring COVID-19 resulting in increased morbidity and mortality. We aimed to review the clinical activity during the pandemic year of 2020. We also aimed to review the outcomes of patients transplanted in 2020 and acquired COVID-19.
Methods: One year outcome data were collected at our institution. This included review of new patient referrals received for transplant evaluation. We also reviewed the incidence, treatment patterns, and outcomes of COVID-19 infection in patients transplanted in 2020.
Results: There was significant decrease in number of new patients evaluated monthly from beginning of March 2020 (Figure 1). 121 patients received kidney transplant between July 2019 and December 2020. Five patients (4%) were COVID-19 infected with in one year of transplant. 4 patients required hospitalization and ICU stay. Three (2%) patients died because of COVID within one year from transplant. Table 1 describes the treatment offered to all five patients diagnosed with COVID-19.
Induction therapy for all patients was thymoglobulin (4.5mg/kg) and maintenance therapy was tacrolimus, mycophenolate and steroids.
Conclusions: COVID-19 pandemic has significantly impacted patient evaluation and listing for transplant in resource limited and medically underserved populations. It is also associated with significant morbidity and mortality in transplanted patients.

Table 1. Treatment and Outcome of patient's infected with COVID-19 within one year of transplant.

	Patient 1	Patient2	Patient 3	Patient 4	Patient 5
Age	45	63	55	50	44
Gender	M	F	M	M	M
Race	AA	AA	AA	C	H
Allo-graft	Deceased Donor	Deceased Donor	Deceased Donor	Living Donor	Deceased Donor
Time since transplant (months)	5	3	6	2	8
Hospital Stay	Yes	Yes	Yes	No	Yes
ICU Stay/ Mechanical ventilation	Yes	Yes	Yes	No	Yes
Treatments	Plaquenil, Tocilizumab, Convalescent Plasma	Steroids	Plaquenil, Tocilizumab	None	Dexamethasone, Remdesevir,
Dialysis	Yes	Yes	No	No	No
Outcomes	Recovered	Deceased	Deceased	Recovered	Deceased

M: Male, AA: African American, C-Caucasian, H-Hispanic

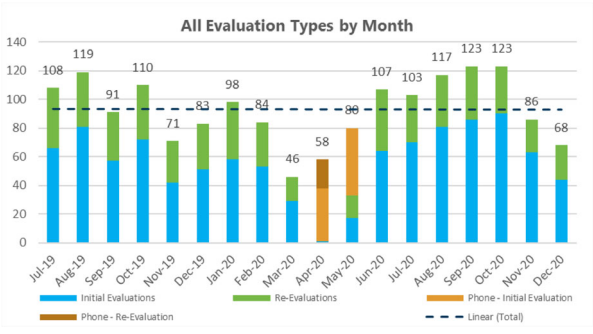

Figure 1

POS164 FERRITIN AND LDH ARE THE BEST MARKER TO DIFFERENTIATE SARS-COV-2 INFECTION VS OTHER INFECTION IN KIDNEY TRANSPLANT PATIENTS

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Background: Kidney transplants recipient (KT) are a high risk of SARS-CoV-2 infection but their symptoms are nonspecific and very common in other diseases. Analytical markers of severity in COVID-19 could help to differentiate SARS-CoV-2 infection from other infectious processes in KT.
Material and Methods: We included all KT patients with suspected SARS-CoV-2 and in whom the analytical severity markers for COVID-19 were performed. The patients were classified according to the result of the PCR for SARS-CoV-2: positive vs negative (2determinations).
Objective: To study the behavior of COVID-19 severity markers in other diseases that could lead to suspicion of SARS-CoV-2 infection.
Discussion: 80 KT patients have been admitted with clinically suspicious of COVID-19. SARS-CoV-2 infection was confirmed in 31 patients. In the 49 negative cases the diagnoses were: 18 with non-COVID-19 pneumonia, 17 with urinary tract infection, 4 with gastroenteritis, 6 with fever from other causes. Four patients were excluded due to the diagnosed of heart failure. The analytical markers are shown in the table. The best cut-off points to differentiate COVID-19 were LDH 225 (AUC0.68;sensitivity:82%;specificity:63%) and ferritin 400 (AUC:0.73;sensitivity:82%; specificity: 0.73%)
Conclusions: Ferritin and LDH could be the best biomarker to identification of patients with COVID-19 in KT.

	Positive COVID-19 (31)	Negative COVID-19 (45)	*p*
Leukocytes/μL	5.400 (3.900–8.700)	9.900 (7.150–14.200)	0.001
Neutrophils/μL	4.470 (2.300–8.500)	8.160 (6.110–11.750)	0.001
Lymphocytes/μL	800 (400–1.140)	900 (500–1.393)	0.62
Monocytes/μL	400 (300–600)	700 (320–1.275)	0.004
Hemoglobin (g/dL)	12.7 (11–13.7)	11.6 (10.1–13.8)	0.15
RDW%	14.8 (13.6–16.1)	15.8 (14.2–17)	0.02
Plateletsx10^3/μL	164 (130–192)	169 (135–228)	0.14
Neutrophil-lymphocyte-index	5.1 (2.6–11)	9.7 (6.1–17)	0.05
Monocyte-lymphocyte-index	0.46 (0.33–0.88)	0.85 (0.43–1.23)	0.08
Platelet-lymphocyte-index	203 (128–295)	201 (126–350)	0.90
D-Dimer (μg/mL)	688 (387–1.235)	1.420 (909–2.480)	0.02
LDH (UI/L)	258 (187–361)	200 (157–282)	0.03
CK (U/L)	89 (59–165)	47 (30–104)	0.18
PCR (mg/L)	77 (22–136)	63 (18–149)	0.87
IL-6 (pg/mL)	36 (23–72)	175 (54–520)	0.05
Ferritin (ng/ml)	991 (570–1.512)	175 (54–520)	0.002

POS165 RISK FACTORS FOR HOSPITAL ADMISSIONS AFTER MONOCLONAL ANTIBODIES FOR COVID-19 INFECTION IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Background and aims: Symptoms of COVID-19 tend to be more severe in patients with uncontrolled hypertension, diabetes, chronic kidney disease, and other chronic health problems [1]. Two monoclonal antibody (mAb) treatments are authorized by the FDA for the outpatient treatment of mild to moderate COVID-19 in patients at risk for progressing to severe disease [2,3]. We followed solid organ transplant (SOT) recipients with COVID-19 after receiving monoclonal antibody infusion, to identify possible risk factors leading to hospital admission post-treatment.
Method: In this retrospective study, we identified 17 solid organ recipients diagnosed with mild SARS-CoV2 infection in the outpatient setting and have received mAb. Patients were followed for 3 weeks after the infusion to detect complications and need for hospitalization. Basic characteristics, comorbidities, COVID-related symptoms, immunosuppressive agents, and baseline absolute lymphocyte count (ALC) were collected, and then analyzed using T-test and Fisher's exact test.
Results: Out of the 17 patients, 4 were admitted. Three out of those 4 patients were black males (75%) when compared to 15% in the non-admitted group. Patients requiring hospitalization tended to report fever (75%),

headache (75%), and myalgia/arthralgia (75%) more when compared to 23.1%, 30.8%, and 46.2% respectively in the non-admitted group. Most recent ALC prior to COVID-19 infection was 700 (K/uL) in hospitalized group, comparing to 1120 (K/uL) in the other group. The non-admitted group was farther out of transplant at the time of COVID-19 diagnosis, 1844 days (58 – 9538d) vs 833 days (53 – 1758d). All 17 patients were alive at the end of follow-up. No statistical significance was found.
Conclusion: While none of the study variables were statistically significant due to small sample size; black race, male gender, lower ALC, recent transplant, and symptoms consistent with fever, headache, and myalgia/arthralgia at the time of mAb infusion were more common in patients ultimately admitted for COVID-19 illness. A larger study is needed to better determine risk factors for COVID-19 related admission after receiving mAb in SOT recipients.

POS166 TRANSPLANT RELATED RISK FACTORS ANALYSIS OF MORTALITY IN RENAL TRANSPLANT RECIPIENTS WITH COVID-19 - A SINGLE CENTER-BASED RETROSPECTIVE STUDY

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Background: COVID-19 in solid organ transplant recipients (SOT) is associated with increased mortality; however, transplant-related risk factors associated with mortality have not been clearly defined in renal transplant recipients (RTR). We describe transplant-related risk factors associated with mortality in RTR with COVID-19 at our center.
Methods: A Single center-based retrospective study of RTR diagnosed on nasopharyngeal swab RT-PCR to have COVID-19 between April 2020 to Jan 2021 was conducted; data were collected from electronic medical records, case files, and a dedicated COVID-19 teleconsulting helpline. RTR who died due to COVID-19 were compared with the control arm of RTR who recovered from COVID-19 for transplant-related risk factors.
Results: Of the 63 RTR with COVID-19, 13 died. Our study population crude case fatality rate (20.6%) correlates with the reported COVID-19 mortality rate in SOT. On univariate analysis, factors independently associated with mortality in COVID-19 RTR were the presence of coinfection, ongoing graft dysfunction, lymphopenia at presentation, CNI withdrawal, biopsy-proven acute rejection during COVID-19, requirement of hemodialysis, oxygen supplementation, and mechanical ventilation requirements with CO-RADS 4 or 5 radiological images at the time of hospital admission for COVID-19. There were no significant difference for RTR age, live vs. deceased transplantation, time since transplant, depleting induction, prior therapy for rejection, comorbidities (diabetes or hypertension), baseline serum creatinine at the time of presentation; though mean serum creatinine increased in both groups post-COVID-19 infection censored to death. However, serum creatinine returned to baseline in the majority of the recovered control group. Coinfection at the time of presentation or acquired during the hospital stay and mechanical ventilation requirement for COVID-19 is an independent risk factor for mortality due to COVID on multivariate analysis.
Conclusions: Transplant-related factors themselves were not associated with mortality. Early and aggressive treatment of coinfection may reduce the mortality in RTR.

POS167 THE SERUM LEVELS OF ANTI-SARS-COV-2 ANTIBODIES REMAIN DETECTABLE AT 9 MONTHS POST COVID-19 IN SYSTEMATICALLY SCREENED KIDNEY TRANSPLANT RECIPIENTS

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Aims and Background: The kinetics of serum anti-SARS-CoV-2 antibody concentration following COVID-19 remains unclear in kidney transplant recipients (KTRs). Furthermore, a comparative follow-up between asymptomatic versus symptomatic patients has not been done thus far.
Methods: Systematic screening for SARS-CoV-2 antibodies using the DIASORIN chemiluminescence immunoassay SARS-CoV-2 S1/S2 IgG was performed in KTRs from June, 1st to October, 1st 2020. Patients diagnosed with RT-PCR-proven COVID-19 via a nasopharyngeal swab were similarly included and tested. The serum concentration of antibodies was prospectively followed in each patient at different time-points: at 3 ± 1; at 6 ± 1; and at 9 ± 1 months. Patients were further classified as symptomatic (Group S) or asymptomatic (Group aS) upon clinical criteria.
Results: Serology was prospectively tested in 525 KTRs. Among them, 28 KTRs had anti-SARS-CoV-2 IgG (>15 UA/ml), including 7 asymptomatic patients (25%). Their median (interquartile range [IQR]) age was 50 years [40; 63], and 7 (25%) were women. In Group S, 3 patients (14%) showed no serologic conversion. During the follow-up, anti-SARS-Cov-2 IgG were detectable in 84% at M3, in 76% at M6, and in 70% at M9 in Group S. In 3 patients of Group S, anti-SARS-CoV-2 IgG disappeared during the study period (2 at M6 and 1 at M9). In Group aS, all patients remained seropositive at the last follow-up. In the whole population, the serum levels of anti-SARS-CoV-2 IgG showed a non-significant decrease from a median [IQR] value of 51 UA/ml [22; 127] at M3 to 39 UA/ml [8; 70] at M9 ($p = 0.08$ for the Wilcoxon test).
Conclusions: Our prospective and systematic cohort suggests that the serologic response against SARS-CoV-2 in KTRs persists at 9 months post COVID-19 in most cases in both symptomatic and asymptomatic patients.

POS168 CLINICAL CHARACTERISTICS AND OUTCOMES OF COVID-19 IN ADULT FILIPINO KIDNEY TRANSPLANT RECIPIENTS

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Background: Year 2020 was the mark of another global pandemic caused by the novel corona virus known as Coronavirus Disease 2019 (COVID-19). Kidney transplant (KT) recipients are a particularly vulnerable population because they are maintained on immunosuppression to prevent graft dysfunction.
Methods and Materials: To describe the clinical characteristics, management and outcome of KT recipients diagnosed with COVID-19 infection admitted at the National Kidney and Transplant Institute (NKTI) from April 1 to December 31, 2020. A retrospective observational study among 28 post-KT recipients with COVID-19 infection. Descriptive statistics was used to summarize the general, clinical characteristics and outcomes of the participants.
Results: The mean age was 50 years with 54% male and 75% chronic glomerulonephritis as primary renal disease. Common presentations were fever (58%), cough (62%), and dyspnea (50%). The average graft age was 57.2 months with 4 (17%) who were on the first 6 months post-transplant. One (4%) had acute kidney injury (AKI) during admission and 4 (17%) presented with graft loss on admission requiring renal replacement therapy (RRT). Treatment was mainly immunosuppression reduction (54%) particularly mycophenolate dose. All patients who died presented with graft loss and had critical COVID-19 infection. The overall patient and graft survival rate were 89% and 86% respectively.
Conclusion: Our experience shows that the clinical characteristics and mortality rate among KT recipients is comparable with other foreign studies.

POS169 COVID-19 INFECTION RATES/OUTCOMES IN CLINICALLY EXTREMELY VULNERABLE RENAL REPLACEMENT THERAPY PATIENTS ADMITTED FOR PROCEDURES DURING THE PANDEMIC

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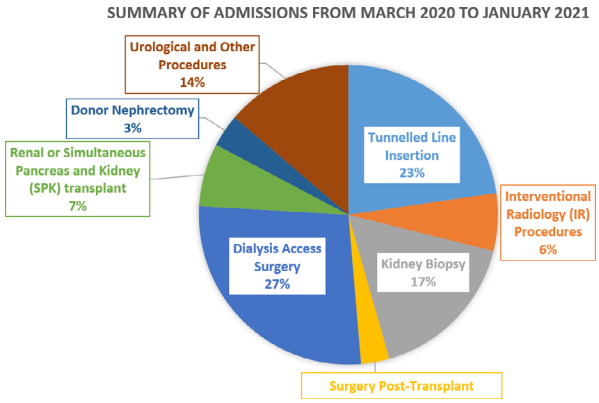
Background: The COVID-19 pandemic has had an enormous impact on provision of healthcare. Patients admitted to hospital for procedures may be at increased risk of contracting nosocomial COVID-19 infection. Patients with renal failure and/or on immunosuppression appear to be at higher risk. A number of evolving measures were put in place to minimise this risk. We assessed COVID-19 infection rates for patients admitted for urgent elective and emergency procedures at our centre.
Methods: Patients admitted for transplantation, renal replacement therapy or other procedures from 01/03/2020 to 31/01/2021 were retrospectively identified from the Nephrology and Renal Transplant database and Electronic Patient Record. SARS-CoV-2 swab results were analysed to identify rate of COVID-19 infection, and sub-categorised to analyse whether COVID-19 infection arose from the community or during hospital stay (diagnosis of COVID-19 ≥8 days after admission defined as probable healthcare associated transmission)
Results: There were 851 admissions and 954 procedures performed (Figure 1). Of the 851 admitted patients, 52 (6.1%) tested positive for COVID-19 (Table 1). 18/851 (2.1%) were diagnosed with COVID-19 ≥8 days after admission: of these 6 (33.3%) had severe infections (admission to ITU and/or death).



Total number of admissions	851
Total number of patients who tested positive for COVID-19	52 (6.1%)
Patients admitted with known COVID-19	19 (2.2%)
Patients who tested positive on the day of admission	5 (0.6%)
Patients who tested positive within 1-7 days after admission	10 (1.2%)
Patients who tested positive within 8-14 days after admission	7 (0.8%)
Patients who tested positive within 15-30 days after admission	11 (1.3%)

Conclusions: We describe a low incidence of COVID-19 infection in patients admitted for renal replacement and associated procedures at our centre - both community related and healthcare associated infections. We continue to monitor this closely. The low rate of community related infections is testament to patients adhering to self-isolation advice, and low healthcare associated COVID-19 rates relate to organisational admission pathways and infection control measures. When infections were acquired, there was a high rate of severe infection. Knowledge of these rates is vital to consent patients effectively, and has significant decision-making implications for increasing operational capacity.

POS170 INFECTIONS IN RENAL TRANSPLANTATION - EIGHT–YEAR EXPERIENCE IN OUR UNIT

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Introduction: Infections among renal transplant recipients are more frequent in comparison to general population as a result of immunosuppression, the presence of foreign bodies as well as the prolonged hospital stay.
Aim: To record infections in our renal transplant unit during the last eight years (2013–2020).
Material-Methods: Our study included all renal transplant recipients who presented with bacteriuria or bacteremia during their hospitalization, between 2013 and 2020. For the purpose of our study, the patients were divided in two groups: Group A included all renal transplant recipients between 2013 and 2016 and group B all renal transplant recipients between 2017 and 2020. Patients in group A received prophylactic treatment with cefuroxime and ciprofloxacin as opposed to patients in group B who received upgraded prophylactic treatment with meropenem and vancomycine.
Results: Out of 96 patients in group A, 52(54%) presented with at least one episode of bacteriuria and 22(23%) presented with bacteremia. The most common pathogens in urine were E coli (42%), Klebsiella pneumoniae (26%), Enterococcus Faecalis (17%) and Pseudomonas aeruginosa (10%). The most common blood pathogens were E coli (27%), Klebsiella pneumoniae (22%), Pseudomonas aerogunosa (13%), Staphylococcus epidermidis (12%), Acinetobacter baumanni (12%)and Enterococcus faecalis (12%).
Out of 80 patients in group B, 48(60%) presented with at least one episode of bacteriuria, while 10(13%) presented with bacteremia. The most common urine pathogens were Enterococcus Faecium (49%), Enterococcus Faecalis (21%), E coli (18%), Klebsiella pneumoniae (5%), Pseudomonas aeruginosa (4%) and Proteus mirabilis (0.5%). The most common blood pathogens were Klebsiella pneumoniae (35%), E coli (25%), Pseudomonas aeruginosa (22%), Proteus mirabilis (11%) and Enterococcus faecalis (2%).
Conclusions: The upgrade of prophylactic antibiotic treatment resulted in multi-sensitive bacteria which were easier to treat with simple, non toxic antibiotics, with absolutely no effect on mortality or rejection episodes. The appearance of more primitive types of bacteria resulted in no asymptomatic urine infections treatment, whereas oral antibiotics can be used for bacteremias.

POS171 THE USE OF ANTIBIOTICS FOR ASYMPTOMATIC BACTERIURIA IN RENAL TRANSPLANT RECIPIENTS

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Introduction: Asymptomatic bacteriuria (AB) is defined as the presence of bacteria in urine without symptoms or signs of urinary tract infection (UTI). It is present in 17 to 51% of renal transplant recipients. The use of antibiotic treatment does not seem to prevent an ongoing UTI or acute pyelonephritis. It does not also seem to affect graft survival.
Aim: To present our centre's experience in the treatment of AB from January 2015 to August 2019.
Methods-Material: Our study included renal transplant recipients with AB during their hospitalization, from January 2015 to August 2019. The patients were divided into two groups: Group A ($n = 43$) included renal transplant recipients from January 2015 to December 2016. Group B ($n = 50$) included patients from January 2017 to August 2019. All patients in group A received antibiotic treatment, whereas patients in group B did not receive antibiotic treatment.
Results: Out of 43 patients in group A, 23(54%) presented with AB. The most common pathogens were E.coli (42%), Klebsiella pneumoniae (26%), Enterococcus faecalis (17%) and Pseudomonas Aeruginosa (10%). Treatment included Ciprofloxacin in 49%, meropenem in 25%, cefoxitime in 14%, tygecycline in 8% and colistin in 4% of patients. The mean duration of treatment was 20 days, until the patients had negative urine cultures. Ten patients (23%) had increased serum creatinine, three (6.9%) had increased liver enzymes and three patients (6.9%) had increased serum amylase.
Out of 50 patients in group B, 32(64%) presented with AB. The most common pathogens were Enterococcus faecium (48%), Enterococcus faecalis (21%), E coli (12%), Pseudomonas aeruginosa (6%) and Proteus mirabilis (5%). No patient received antibiotics. Five patients (15%) eventually needed antibiotic treatment, due to UTI in 2, due to bacteremia in 2 and due to acute pyelonephritis in one patient. The rest of patients had negative urine cultures following removal of the ureter –bladder anastomotic catheter (pigtail).
Conclusions: The use of antibiotics does not seem to have better results in the treatment of AB. On the contrary, they could be related to increased side-effects. However, there are still limited data concerning the use of antibiotic treatment which need further investigation.

POS172 PREDICTIVE FACTORS AND OUTCOMES OF URINARY TRACT INFECTIONS AFTER KIDNEY TRANSPLANTATION: A RETROSPECTIVE COHORT STUDY

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Background: Urinary tract infection (UTI) is one of the most common infectious complications in kidney transplant recipients. However, the risk factors for and the impact of UTIs remain controversial.
The aims of our study were to identify possible predictive factors for UTI and associated outcomes after kidney transplantation (KT).

Methods: All patients who underwent KT between November 201' and december 2019 were retrospectively analyzed. Patients who had urinary symptoms and positive urine culture were diagnosed with UTI. The types of urinary bacteria causing UTIs were also examined.
Results: The study population consisted of 86 kidney transplant recipients; 95% were living donor transplants. Thirty four patients developed at least one episode (45.3%), and the median of onset time was 30 days after the surgery (range: 7–320). Among all infectious complications, UTI was the most frequent (52.1). Most of episodes occurred in the three first months (74.4%). The most common causative agent was Escherichia coli (52.2%), followed by Klebsiella pneumonia (36.5) and Enterococcus faecalis (10.5%). The variables that were independently related to a UTI were female gender ($p = 0.002$, OR 4.19, 95% CI 1.36–31.27), donor age > 50 ($p = 0.032$, OR 3, 95%CI 1.6–10.808) and mismatche HLA>3 ($p = 0.001$ OR 95%CI 1.16–1.96). Graft function did not correlate with post-transplant urinary tract infection ($p = 0.8$).
Conclusion: UTI degrades the health-related quality of life and can impair graft function, potentially reducing graft and patient survival as reported by other authors but not confirmed in our study.

POS173 THE MAIN RISK FACTORS OF ADVERSE OUTCOME OF COVID-19 INFECTION IN KIDNEY TRANSPLANT RECIPIENTS-OUR EXPERIENCE

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Background and Aims: In the Transplant Center of Vojvodina, Serbia, we control 210 patients (pts) who had a kidney transplant in our or the other transplantation center. The goal was to see the frequency and outcome of the infection of COVID-19 within these patients.
Methods: We analyzed kidney transplant patients who was monitored at our center and who had a COVID-19 infection in the period from March 2020 to February 2021.
Results: In the period from March 2020 until February 2021, out of all of our patients with the kidney transplant, 21 pts contracted COVID-19 (10%). The average age of the infected was 46,43 years old (the youngest being 26 and the oldest being 70 years old). All of the infected were on triple immunosuppressive therapy (calcineurin inhibitor, antimetabolite, corticosteroid). In only 14.28% of patients during COVID-19 infection the immunosuppressive therapy did not change.
Because of poor clinical prognosis with radiographically proven pneumonia 10 (47.62%) pts have been hospitalized. Only 1 (10%) patient did not require supplemental oxygen, 70% pts needed high-flow nasal cannula (HFNC) oxygen or noninvasive positive pressure ventilation (NIPPV), and invasive mechanical ventilation was needed in 20% of patients. 20% of patients received tocilizumab.
Out of all infected, death occured in 5 pts (23.81%), average 8.6 days since diagnose of the infection. The death cause was severe acute respiratory syndrome in 3 pts (14.28%), and cardiac arrest in 2 pts (9.5%). All the patients that have passed away have had serious comorbidities (congestive heart failure 60%, diabetes mellitus 20%, liver failure 20%). All of the patients that had been treated in home conditions had not received antimetabolites, CNI dose was reduced by 25–50%, and corticosteroid was increased to 20mg per day. After stabilization of inflammatory parameters and normalization in lymphocyte numbers immunosuppressive therapy was brought back. With only one patient (4.76%) continuous renal replacement therapy (CRRT) was applied, within the rest of the patients the worsening of the graft was not noticed during the infection and a month after a full dose of immunosuppressive therapy.
Conclusions: The main risk factors of adverse outcome of COVID-19 infection in kidney transplant recipients were serious comorbidities.

POS174 URINARY TRACT INFECTIONS AND LONG TERM OUTCOMES AFTER PEDIATRIC RENAL TRANSPLANTATION

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Introduction: Renal transplantation is the best option for treatment of children with end-stage renal disease and it provides a long-term survival. However, the chronic immunosuppression exposes children to multiple complications and side effects such as infections. We aimed to analyze retrospectively long term outcomes and urinary tract infections of 184 pediatric renal transplant recipients at our centers.
Materials and Methods: In 1975, we performed the first living-related renal transplant in Turkey which was also a pediatric kidney transplant. Since 1975 we have performed 3175 kidney transplantation at our transplant centers, 370 of them were pediatric kidney transplantation. Medical records of the pediatric patients who underwent renal transplantation between 1999 to 2021 were retrospectively analyzed at our centers. A hundred and eighty-four pediatric renal transplant recipients were defined as study group.
Results: A hundred and two of 184 pediatric transplant patients were male and 82 were female. Mean age of the patients was 13.8 ± 6.7 (range: 1.5–21years). The follow-up period ranged from 6 to 245 months (mean, 69.1 ± 38.8 months). Donor types were living-related in 77% (141 patients) and deceased donor in 23% (43 patients). Immunosuppressive medications were tacrolimus in 122 patients, cyclosporine-A in 56 patients, sirolimus in three patients, and everolimus in three patients. Induction treatment was administered to 51of the subjects. When we assessed urinary tract infections that require hospitalization, were recorded in 27 (14.6%) patients. CMV was determined in five, BK virus in seven patients and severe bacterial urinary tract infections were observed in 15 patients. We did not see graft loss and mortality due to severe bacterial urinary tract infections. The 1, 3, 5, 10, and 15-year graft survival rates were 99%, 92%, 86%, and 76%, respectively, and the 1, 3, 5, 10, and 15-year patient survival rates were 100%, 98%, 95%, and 92%, respectively.
Conclusion: Our study showed that, kidney transplantation in pediatric patients have successful long term results with no graft lost and mortality due to severe bacterial infections.

POS175 ROUTINE TRANSPLANT URETERIC STENT CULTURE - UTILITY IN IDENTIFYING PATIENTS AT HIGHER RISK OF URINARY TRACT INFECTION

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Background: Urinary tract infection (UTI) represents one of the most common infections in renal transplant recipients. Routine placement of ureteric stents in kidney transplantation reduces the incidence of major urological complications, however may result in an enhanced risk of UTI by acting as a nidus for microbial colonisation. The aim of this study was to investigate the correlation between results of routine stent culture with concurrent (time of stent removal) and subsequent urine culture and UTI.
Methods: A retrospective single centre study of all patients undergoing cystoscopic removal of transplant ureteric stents from November 2018 to January 2021 was undertaken. Data were collected on patient demographics, stent and urinary cultures, and clinically significant UTI (defined as treatment required) within a 6-month follow-up period.
Results: 418 patients underwent stent removal during the study period, 374 (89.5%) patients had routine stent cultures. 197 (52.8%) patients had a concurrent urine culture, yielding 48 (24.3%) positive cultures. 186 (49.7%) patients had positive stent cultures with concurrent urine culture available in 97 (52.1%). Positive stent cultures were predominantly bacterial (88.8%), the remainder accounted for by yeast (8%) or mixed bacteria & yeast (3.2%). In patients with positive stent culture, 36 (37.1%) exhibited positive concurrent urine culture with fully concordant culture profiles in both samples in 19 (52.7%) patients. 301 patients who had routine stent culture achieved 6-month follow-up. The rate of subsequent clinically significant UTI during follow-up was 22.9% and 10.1% following a positive or negative stent culture respectively ($p = 0.003$). In patients with a subsequent UTI, culture results were concordant with stent and concurrent urine culture in 37.1% and 55.6% respectively ($p = 0.2$).
Conclusion: Our data demonstrate a significant correlation between positive stent culture and clinically significant UTI within six months. Positive stent culture may be underestimated by the culture technique used in this cohort, as newer technologies such as sonication fluid culture have been demonstrated to increase yield. Routine stent culture therefore warrants further investigation in identifying patients at higher risk of UTI following transplantation.

POS176 ASYMPTOMATIC BACTERIURIA IN KIDNEY TRANSPLANT RECIPIENTS - TO TREAT OR NOT TO TREAT?

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Background: Screening and treatment of asymptomatic bacteriuria (ASB) after kidney transplant (KT) is a widely disseminated, but controversial, practice. Several studies have been recently conducted to evaluate its usefulness.
Methods: A retrospective study included patients admitted for KT between January and December 2018, with systematic presentations for routine care for one-year post-KT. Were eligible those who had acute graft pyelonephritis (AGP) and/or ASB and were > 2 months post-KT. Patients with indwelling catheters, graft loss, who underwent urological procedures or perform catheterization were excluded.
We compared whether the occurrence of AGP in the first year post-KT, particularly after 2 months post-KT and double J/urinary catheters removal, was influenced by previous episodes of treated and untreated ASB. Secondary endpoints included, among others, hospitalization, bacteriemic AGP, acute kidney injury (AKI) and if the species isolated in AGP were previously isolated in ASB.
Results: 95 patients were enrolled, 71 excluded. AGP occurred in 6 of 24 eligible patients (25%), and 33.3% of ASB received treatment. Median follow-up time until the 1st episode of AGP was 108.33 ± 68.67 days (26–214). We found no statistically significant differences in age, sex, immunosuppression regimen, donor type, serum creatinine (sCr) at one-year follow-up, total number of ASB or treated ASB between the AGP and Ø AGP groups. Treatment of ASB was not significantly related to the occurrence of AGP ($p = 0.808$), AKI ($p = 0.582$), bacterimic AGP ($p = 0.207$), hospitalization ($p = 0.499$) or sCr at one-year follow-up ($p = 0.194$). Most AGP causative agents were previously isolated in ASB ($p < 0.05$). *K. Pneumoniae* was the most common.
Conclusions: Current guidelines do not recommend a screen-and-treat strategy for ASB beyond the 2nd month post-KT. Although this study has limitations, our results suggest that ASB treatment has no benefit in the occurrence of AGP (and other secondary outcomes).

POS177 SARS-COV-2 IGG SEROPREVALENCE AND FACTORS AFFECTING ITS LEVELS IN KIDNEY TRANSPLANT RECIPIENTS DURING SECOND PEAK OF COVID-19 PANDEMIC

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Background: Data on immune response to SARS-CoV-2 in kidney transplant recipients are scarce.
Methods: We conducted a single-centre prospective observational study to assess the SARS-CoV-2 neutralizing IgG antibody seroprevalence in outpatient kidney transplant recipients ($n = 1002$) and healthcare workers (HCW $n = 512$) between Oct 1st and November 30th 2020. Antibodies against S1 and S2 subunit of SARS-CoV-2 were evaluated using chemiluminescent assay. Variables affecting antibody levels were determined in the study population which was enriched by another 54 covid-19 symptomatic patients in whom SARS-CoV-2 IgG antibodies were evaluated outside of study period.
Results: SARS-CoV-2 IgG seroprevalence was lower in kidney transplant recipients than in HCW (7% vs. 11.9%, $p = 0.001$) during the study period. Four kidney transplant recipients with previous SARS-CoV-2 infection did not develop neutralizing antibodies. The covid-19 patients were younger ($p = 0.001$) and received CNI-based immunosuppression more ($p = 0.029$) than seronegative patients. SARS-CoV-2 IgG positive symptomatic patients had higher BMI ($p = 0.04$) than SARS-CoV-2 IgG positive asymptomatic patients. Interestingly, SARS-CoV-2 IgG levels were higher in patients than in HCW (median 31 AU/ml, IQR 17–84 vs median 15 AU/ml, IQR 11–39, $p < 0.001$). The presence of moderate to severe covid-19 symptoms in kidney transplant recipients was found to be only independent factor affecting IgG levels (beta coefficient = 37.36, 95% CI = 19.94; 54.77, $p < 0.001$) in multivariable model.
Conclusions: Kidney transplant recipients exhibit well preserved humoral response to SARS-CoV-2.

POS178 THE BITTER 'SWEET' ENEMY OF RENAL TRANSPLANT RECIPIENTS–A DEMI DECADE EXPERIENCE OF POST RENAL TRANSPLANT GRAFT OUTCOMES IN DIABETIC KIDNEY DISEASE

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Background and Aims: Diabetes is the leading cause of end stage renal disease (ESRD). As the diabetic pandemic is on the rise, so are the cases of diabetic kidney disease (DKD) for which renal transplantation is the therapeutic modality of choice. This is a retrospective, cross sectional study aimed at identifying the clinical profile of patients with ESRD due to DKD who underwent renal transplant at our centre & to analyse the spectrum of infectious complications along with their one year graft outcome.
Methods: In this retrospective cross sectional observational study, all patients with DKD who underwent renal transplant between January 2015-January 2020 were included & their one year graft outcomes and infectious complications were analysed from data collected from the medical records department
Results: A total of 192 patients who underwent renal transplant over 5 years were analysed of which only 27 patients (14%) had diabetic kidney disease as the cause of ESRD. Mean age of the study population was 49 years. 18 out of 27 had documented infections. Most common infection was UTI (51%) (& the most common uropathogen identified was Klebsiella Pneumoniae) followed by wound sepsis (33%)> CMV (18.5%) > varicella zoster (7.4%). One patient each had an episode of fungal wound sepsis, fungal rhinitis, and acute pyelonephritis. Pertaining to graft outcome, at the end of one year follow-up, 13 patients (48.1%) retained good graft function, while 10 patients (37%)went into chronic graft dysfunction, 3(27%) patients died due to infections leading onto MODS and shock and 1 patient suffered graft loss & went into maintenance hemodialysis. Graft loss was secondary to biopsy proven acute cellular rejection.
Conclusion: Despite being the most common cause of ESRD worldwide as well as in India, only 14 % of the renal transplants at our centre had DKD as the cause of ESRD. Regarding infectious complications, UTI was the most common infection seen post-transplant followed by wound sepsis. The fact that around 50% of these patients retained good graft function at the end of one year follow-up should prompt primary care physicians to refer patients with diabetic ESRD for renal transplant work up as it can tremendously improve the QOL of these patients in comparison to dialysis.

POS179 NOVEL CORONAVIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENTS (A SINGLE-CENTER EXPERIENCE)

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Background: The novel coronavirus infection is a life-threatening medical condition in kidney transplant (KT) recipients. Optimizing the treatment regimen determines the survival of the patients and the KT.
Methods: Since April 2020 to February 2021 a SARS-Cov-2 were infected 61 (29.2%) KT recipients from 209 recipients, taken care in Leningrad Regional Clinical Hospital: male 39 (63.9%), female 22 (36.1%). Median age 46.6 years, the average time after kidney transplantation 7 years.
Real-time polymerase chain reaction (RT-PCR) testing of SARS-Cov-2 were positive in 50 cases, negative tests 8 cases, in 3 cases was not performed. A chest CT scan was also performed. Mild COVID-19 has 33 (54.1%) recipients, moderate – 18 (29.5%), severe – 10 (16.4%). The patients with moderate and severe COVID-19 were hospitalized. In most cases the immunosuppressive therapy were modified: reduced dose once-a-day tacrolimus (Tac 3–4 ng/ml) or cyclosporine (30–50 ng/ml), increased dose of methylprednisolone (8–16 mg/day), temporary withdrawal mycophenolic acid or everolimus. Some recipients taken i.v. dexamethasone. In 2 cases with severe and moderate COVID-19 were prescribed baricitinib. All patients

were taken umifenovir, anticoagulants and 16% recipients interferon alfa-2b. Those patients who had bacterial infection prescribed antibiotics.
Results: In KT recipients had taken antiviral, steroids, anticoagulants therapy in addition of minimization of immunosuppression. 55 (90.2%) recipients recovered, 6 (2.8%) patients with severe COVID-19 and comorbidity factors were died. Most of recipients had mild and moderate COVID-19. We registered a positive effect of the therapy of baricitinib without adverse effects in 2 patients. The function of KT is preserved in 57 (93.5%) recipients.
Conclusion: The priority treatment of SARS-Cov-2 infection in KT recipients are complex therapy, transfer to the optimal regime of immunosuppression and early access to medical care.

POS180 INFLUENCE OF VITAMIN D STATUS ON THE PROGNOSIS OF COVID 19 IN PATIENTS WITH KIDNEY TRANSPLANT

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Background: The protective role of Vitamin D as an immunomodulator has been demonstrated in different viral pathologies. This effect has been described by different mechanisms: acting as an immunoprotein inducer, participates in growth and cell differentiation and acts as a mediator of apoptosis. Some evidence suggests that it could influence the SARS-COV 2 infection and its prognosis.
Kidney transplant (KT) patients are more susceptible to 25 (OH) VitD (Calcidiol) deficiencies.
The purpose of this study is to evaluate the Vitamin D status in KT who have been diagnosed with COVID-19 and its possible correlation with prognosis.
Methods: It is an observational, retrospective, cross-sectional and descriptive study that includes kidney transplant patients with COVID-19 and with serum 25 (OH) Vit D.
Results: From 134 KT with COVID-19 in our center, 79 were evaluated. The mean age was 58 years, 60.8% were men. 86.1% were KT, 11.4% were simultaneous pancreas and kidney transplant (SPK), 1.3% were renal- liver and renal-heart transplant. The most prominent clinical presentation was: 39 (48%) presented pneumonia, 22 (28%)flu-like syndrome. 14 (17%) asymptomatic and 2(2.5%) fever. From this patient 39,2% had not changes in the anti-inflammatory therapy, 20.3%, required increased dose of corticosteroids, and 40.5% required methylprednisolone bolus or initiation and/or anti-interleukin therapy. The mean of Vit D was 21.41+/- 11 ng/dl; we found that 52% has Vit D <20 ng/dl. 25% between 20 -30 ng/dl and 21,51% > 30 ng/dl. In 32 patients who required intensification of treatment we found that 73% had Vit D levels <20 ng and regarding the presentation, patients with low vitamin D have a higher risk of pneumonia and being statistically significant with a p <0.015 and 0,001 respectively. 11 patients need a critical care unit, of these 62.5% had levels below <20 ng/dl. There were 12 deaths. 66% of deaths had vitamin D values <20 ng/dl. being statistically significant the correlation in both cases.
Conclusions: We were able to observe that vitamin D levels could influence in the prognosis of SARS-COV 2 infection. Vitamin D deficiency was found in a high percentage of transplant patients with COVID 19. Low levels of 25 OH Vit D were evidenced in patients who required greater intensification of treatment and in deaths.

POS181 EFFECTS OF OXYGEN DURING HYPOTHERMIC MACHINE PERFUSION IN AN EXPERIMENTAL PORCINE MODEL OF KIDNEY DONATION AFTER CARDIAC DEATH. ADDED CONTROVERSIES

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Background: The efficacy and safety of employing high concentrations of oxygen during hypothermic machine perfusion (HMP) has not been fully elucidated to date. This study investigates the impact on renal function of administering high concentrations of oxygen during HMP in a porcine donation after circulatory death (DCD) model, as well as the metabolic and biochemical effects of this method.
Methods: A randomized non-blinded prospective cohort study was established in a porcine transplant model mimicking Maastricht type III DCD under oxygen-supplemented HMP (Ox-HMP) compared with non-supplemented (nOx-HMP) (LifePort® kidney transporter) conditions. The primary endpoints lipid peroxidation as a measure of oxidative stress and *in vitro* ATP generation in primary cultures of proximal tubule cells. Finally, renal function and survival were measured.
Results: ATP generation and oxidative stress, as measured by lipid peroxidation, both increased simultaneously after warm ischaemia in the Ox-HMP group. Ox-HMP did not exhibit a significant effect on kidney function or animal survival. It was observed a clear increase of lipid peroxidation in the Ox-HMP group which also resulted in a greater expression of the genes responsible for SOD-1 and catalase oxygenation enzymes. Respiratory chain dysfunction was maintained in the Ox-HMP group with a decrease in ATP production, increased proton leakage and a decrease in respiratory reserve. Regarding epithelium-mesenchymal transition an increase in the expression of vimentin, fibronectin and collagen genes was also observed. Finally, the expression levels of miR-101 and miR-126 related to characteristic functions of the tubular epithelium were significantly modified.
Conclusions: The effect on renal function of utilizing oxygen addition during HMP still needs to be elucidated. An increase in lipid peroxidation levels calls into question the safety of oxygen supplementation. At present, Ox-HMP cannot be considered a standard practice.

POS182 PREDICTORS OF DEVELOPMENT AND DURATION OF DELAYED GRAFT FUNCTION (DGF) IN MARGINAL KIDNEYS WITH HYPOTHERMIC PULSATILE MACHINE PERFUSION (HPMP)

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Background: DGF is associated with an increased risk of acute rejection rates and worse longterm graft outcomes. The aim of our study was to evaluate the risk factors that impact in the development and duration of DGF (>7d) in marginal grafts.
Methods: Retrospective study of KT from ECD/DCD undergoing HPMP between 2012–2019.DGF was defined as no decrease in creatinine>10% of baseline in the first 48h after KT.Local grafts received a completed HPMP vs imported grafts (parcial HPMP).Description of basal characteristics of donors&recipients was performed by Chi2, T-Student & U-Mann Whitney's test.A multivariate logistic regression model was developed to assess the factors that influence in the development and duration>7d of DGF. Performance of the statistical prediction model was quantified in terms of calibration (Hosmer-Lemeshow's test) and discrimination (AUC).
Results: 389 KT were performed. 92(24.86%) developed DGF. We identified a statistically significative difference in the following basal characteristics: DCD (6.3% in no-DGF vs 20.8% in DGF, p = 0.00), imported graft/parcial HPMP (55.8% in no-DGF vs 75.8% in DGF, p = 0.01) and type of renal replacement therapy's (RRT) prior to KT, with a higher percentage of hemodyalisis in the DGF group (71.9%)vs no-DGF group (50.9%), p = 0.001. In the multivariate predictive model, we observed that DCD (OR:4.3, p = 0.00), imported origin/parcial HPMP (OR:1.83; p = 0.024) and type of RRT's recipient prior to KT (hemodialysis vs predialysis) (OR:2.17; p:0.02) were associated with the developement of DGF. The model presented a good calibration (Hosmer-Lemeshow's test:0.77) and discrimination (AUC:0.7). 54/389(13.88%) presented a duration of DGF>7d. In the multivariate predictive model, we observed that DCD (OR 2.25; p = 0.021) and imported origin (OR:5.04; p = 0.00) were associated with a duration>7d.The model presented a good calibration (HL's test = 0.36) and discrimination (AUC:0.7).
Conclusions: We observed a higher risk of development of DGF in marginal grafts from DCD, imported origin and hemodialysis as RRT, and a longer DGF's duration in DCD grafts and parcial HPMP. Both models are simple with a good calibration and discrimination.The identification of the grafts and recipients with a higher risk of developing DGF could help us to optimize them.

POS183 DELAYED GRAFT FUNCTION; DOES IT REALLY BURDEN FOR DECEASED DONOR KIDNEY TRANSPLANTS?

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Background: The frequency of DGF varies from 5 to 50% in deceased donor kidney transplants. DGF increases morbidity after transplantation, prolongs hospitalization and may lead to premature graft failure. We aimed to asset outcome of DGF in deceased donor kidney transplantation
Methods: Totally 92 deceased donor kidney transplantations were performed since Jan 2006 in Gazi University Transplantation Center, Ankara/Turkey. Data retrospectively collected from patients who have received first deceased donor kidney transplants' charts and hospital files. All patients received calcineurine based triple immunosuppression protocol. As induction therapy all received IL-2r blockers. ATG was given in case of DGF from dose of 2–3mg/kg/IV infusion until the serum creatinine (Cr) decreased spontaneously 50% or Cr < 3mg/dL.
Results: DGF has detected in 79 (86%) deceased donor kidney transplants. There were 40 female and 39 male recipients. In patients with DGF, mean cold ischemic time was found as 21 ± 6.1 hours. Mean mismatch was 3 ± 2.1. Mean donor age was 41 ± 19 years. The duration of ATG administration was 9.4 ± 4 days (median 10 days, 8–15 days). The mean length of follow-up was 98 ± 59 months (range, 6–173 weeks; median of 113 months). Totally 8(10%) acute rejection (ARx) episodes were seen during follow-up. Three out of 8 were antibody mediated rejections (AMRx). All ARx treated successfully with pulse steroids. AMRx episodes were treated successfully by plasmapheresis and IVIg. Totally 5 viral infections (3 BK,1 CMV,1 parvo) were detected during follow-up. Totally 22 grafts were lost during median 113 months of follow-up;12 chronic allograft nephropathy, 3 BKV, 2 HUS, 2 sepsis, 1 dual kidney, 1 CMV, 1 unknown reason. We have not seen any PDLD or malignancies during follow-up. Twelve out of 79 patients (15%) were lost due to sepsis 7, aorta dissection 1, and traffic accident during follow-up. Patient and death-censored graft survivals for 1, 5 and 10 years are 100%,97%,91% and 89%,86%,79% respectively.
Conclusion: Renal populations continue to be negatively impacted by DGF. Patients with DGF seem similar patient and death censored graft survival compared with, literature. However, they experienced increased viral infections during the first year after transplantation.

POS184 HYPOTHERMIC MACHINE PERFUSION CAN BE SAFELY USED TO PROLONG COLD ISCHEMIA TIME IN DECEASED DONOR KIDNEY TRANSPLANTATION

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Background: in deceased donor kidney transplantation (KT), a prolonged cold ischemia time (CIT) is a negative prognostic factor for KT outcome, and the efficacy of hypothermic machine perfusion (HMP) in prolonging CIT without any additional hazard is highly debated.
Methods: retrospective study on a cohort of 154 single graft deceased donor KTs, in which a delayed HMP, after a preliminary period of static cold storage (SCS), was used to prolong CIT for logistic reasons. Primary outcomes were postoperative complications as well as 1 year graft survival and function.
Results: 73 cases (47.4%) were managed with HMP and planned KT, while 81 (52.6%) with SCS and urgent KT. The median CIT in HMP group and SCS group was 29h:57min [27h - 31h:45min] and 11h:25min [9h - 14h:30min], respectively (p <0.001). The period of SCS in the HMP group was significantly shorter than in the SCS group (10h vs 11h:25min, p = 0.02) as well as the prevalence of expanded criteria donors was significantly higher (43.8% vs 18.5%, p <0.01). After propensity score matching for these two baseline characteristics, the HMP and SCS groups showed comparable outcomes in terms of delayed graft function (HMP vs SCS, 17% vs 12.2%, p = 0.75), vascular (0% vs 2.4%, > 0.99) and urologic (14.6% vs 12.2%, p > 0.99) complications, infections (21.9% vs 9.7%, p = 0.22), and episodes of graft rejection (7.3% vs 2.4%, p = 0.61). At one year follow-up, serum creatinine levels were comparable between the groups (1.3 [1.1–1.8] vs 1.7 [1.6–2.0], p = 0.19).
Conclusions: The use of HMP to prolong the CIT and convert KT into a planned procedure seems to have an adequate safety profile, with outcomes comparable to KT managed as an urgent procedure and a CIT nearly three time shorter.

POS185 IMPACT ON KIDNEY TRANSPLANTATION OF THE PERCENTAGE OF T LYMPHOCYTES ISOLATED FROM HEPATIC PERFUSATE OF MULTI-ORGAN DECEASED BRAIN DONORS

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Background: Hepatic interstitial T-lymphocytes (T-Li), Natural Killer (NK) and NK-T cells play an important role in both innate and adaptive immunity and contribute to the regulation of ischemia/reperfusion injury (IRI) after transplantation of abdominal organ.
Methods: The cellular concentrations and phenotypes of NK, T-Li, NK-T were analyzed retrospectively in a consecutive series of hepatic perfusates after surgical removal of whole livers on the bench previously collected from adult multi-organ donors after brain death. (DBD), and compared with the demographic and pathological characteristics of the patients transplanted at our Institute with kidneys taken from the same donors. The liver interstitial cells were purified from the perfusate by density gradient centrifugation and the phenotype was determined by flow cytometric investigation using the following immunological markers: CD3, CD4, CD8 and CD56 in order to determine the relative percentage of T-Li, NK-T and NK cells.
Results: The perfusates of 46 DBDs, and the related clinical outcome of kidney transplant recipients from 2010 to 2020, were analyzed. T-Li were significantly associated with the time in days of delayed functional recovery of transplanted kidneys (DGF) (p = 0.02), to onset of secondary infection from Cytomegalovirus (p = 0.03). On COX analysis, percent cell concentration of T-Li and time to DGF were significantly associated with an increased relative risk (HR) of organ survival (HR = 1.038, p = 0.04; and HR = 1.029, p = 0.01, respectively). The specificity of the NK and NK-T cell proportions were not associated with any relevant clinical outcomes in kidney transplant patients.
Conclusions: The present study points to a new potential role of T-Li cells detected in the context of liver perfusate DBD, and could detect potential impacts in organ allocation, surgical harvesting techniques and in the analysis of IRI pathophysiological events after kidney transplants from multi-organ DBDs.

POS186 DOES OXYGENATION AT PO2 21% DURING HYPOTHERMIC MACHINE PERFUSION (HMP) IMPROVE THE CLINICAL OUTCOME OF DECEASED DONOR KIDNEY TRANSPLANTATION?

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Background: in deceased donor kidney transplantation (KT), the use of hypothermic machine perfusion (HMP) has been acquiring the status of best practice in the pre-transplant management of kidney grafts. Two types of HMP are currently available, oxygenated HMP and non-oxygenated HMP. However, data on the real clinical impact of oxygenation on KT outcome are still limited.
Methods: retrospective study on a cohort of 103 patients transplanted with a single kidney graft that was randomly managed either with oxygenated HMP (O2 group, Waves Machine, n = 51, 49.5%) or non-oxygenated HMP (no-O2 group, Life Port Kidney Transporter Machine, n = 52, 50.5%), during the period January 2016-December 2020. Oxygenation was performed at PO2 21%.
Results: the median cold ischemia time was 29h:20 min [IQR 26h:40min - 31h:5min] and the prevalence of grafts from expanded criteria donors was 45.6%. The study groups were homogeneous in terms of recipient characteristics, ischemia times and donor characteristics. Moreover, O2 and no-O2 groups showed comparable outcomes in terms of delayed graft function (O2 vs no-O2, 20.4% vs 25%, p = 0.58), vascular complications (0.2% vs 0.2%, p > 0.99), urologic complications (13.7% vs 11.5%, p = 0.77), infections (32.7% vs 25%, p = 0.31), and episodes of graft rejection (11.7% vs 7.7%, p = 0.52). At 6 months follow-up, even serum creatinine levels were comparable between the groups (1.5 [1.3–2] vs 1.6 [1.3–2.1], p = 0.53).
Conclusions: Oxygenation at PO2 21% during HMP seems not to significantly enhance the KT outcome in terms of postoperative complications or graft function.

POS187 FROSTBITE LESIONS OF KIDNEYS RETRIEVED FROM DECEASED DONORS AND FAILED USE: A NATIONAL APPROACH BY THE ITALIAN NATIONAL TRANSPLANT CENTER

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Background: Although organ packaging, storage and transport procedures are regulated by national legislation (State-Regions Conference 55/2015) and by European guidelines (EDQM 7 °, 2018), in the last 5 years the Italian National Transplant Center (CNT) recorded 18 adverse events characterized by partial or total freezing of cadaveric donor kidneys. In 7 cases, the organ was no longer usable for transplantation.
Methods: In November 2020, the CNT launched a national survey on the kidney packaging procedures in use at transplant centers, conducted by sending a request to the regional centers (CRT). Once the procedures were acquired, the common elements and the peculiar differences were analyzed in terms of packaging methods, type of used containers, chemical-physical characteristics of the ice used for storage, temperature monitoring during transport.
Results: 19 procedures were received (100% of CRTs). In all procedures the kidney is placed in 3 cellophane, air-tight, single-package bags, with cold perfusion liquid in the first bag, in variable quantities. 8 out of 19 (42%) procedures involve the addition of cold physiological solution and/or crushed ice in the second bag while in 15 out of 19 (79%) the third one is empty. In all procedures, rigid isothermal box with flake ice inside are used for transport. Ice temperature and quantity/size ratio of the container are not uniform. In one procedure a temperature detection system in the transported container is provided.
Conclusions: According to the results, the CNT has deemed it useful to set up a working group made up by coordinators, procurement surgeons and physics engineers, which could draw up a shared national procedure for the packaging and transport of the kidneys, which includes the minimum requirements of safety and reliability with the aim of minimizing the risk of frostbite and failure to use organs.

POS188 DUAL AND OPPOSITE COSTIMULATORY TARGETING WITH A NOVEL HUMAN RECOMBINANT PROTEIN PREVENTS RENAL WARM IRI AND ALLOGRAFT REJECTION IN MURINE MODELS

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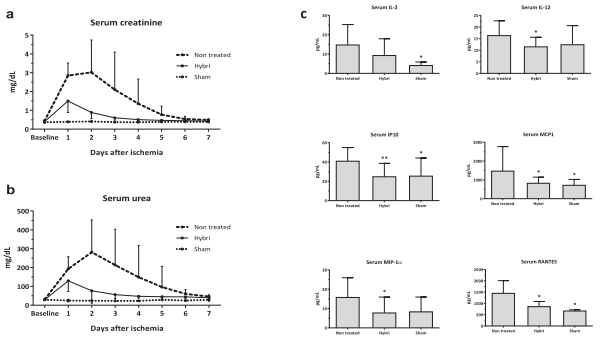
Background: Many studies have shown both the CD28—CD80/86 costimulatory pathway and the PD-1—PD-L1/L2 coinhibitory pathway to be important signals in modulating or decreasing the inflammatory profile in ischemia-reperfusion injury (IRI) or in a solid organ transplant setting. The importance of these two opposing pathways and their potential synergistic effect led our group to design a human fusion recombinant protein with CTLA4 and PD-L2 domains named HYBRI.
Methods: Determine the HYBRI binding to the postulated ligands of CTLA4 (CD80) and PD-L2 (PD-1) using the Surface Plasmon Resonance technique and to evaluate the in vivo HYBRI effects on two representative kidney inflammatory models: rat renal IRI and rat allogeneic kidney transplant.
Results: The Surface Plasmon Resonance assay demonstrated the avidity and binding of HYBRI to its targets. Affinity constants reflected a high affinity for both CD80 and PD1 bindings (Table). Kinetics analysis revealed rapid association (Ka) and dissociation (Kd) as well as a consistent affinity constants (KD) for both CD80 and PD1. HYBRI treatment in the models exerted a high functional and morphological improvement. HYBRI produced a significant amelioration of renal function on day one and two after bilateral warm IRI (Figure) and on days seven and nine after transplant, clearly prolonging the animal survival in a life-sustaining renal allograft model. In both models, a significant reduction in histological damage and CD3 and CD68 infiltrating cells was observed. HYBRI decreased the circulating inflammatory cytokines and enriched the FoxP3 peripheral circulating, apart from reducing renal inflammation.
Conclusions: The dual and opposite costimulatory targeting with that novel protein offers a good microenvironment profile to protect the ischemic process in the kidney and to prevent the kidney rejection, increasing the animal's chances of survival. HYBRI largely prevents the progression of inflammation in these rat models.

	Steady state	Kinetics		
		ka (1/Ms)	kd(1/s)	KD (M)
CD80	3.72×10^{-6}	1.57×10^{5}	5.68×10^{-1}	3.62×10^{-6}
PD-1	5.29×10^{-5}	6.37×10^{4}	3.19	4.91×10^{-5}



POS189 FUNCTIONAL MRI ASSESSMENT DURING EX VIVO NORMOTHERMIC PERFUSION: THE FIRST EXPERIENCE WITH DISCARDED HUMAN KIDNEYS

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Background: The upsurge of using high-risk renal grafts for transplantation mandates optimisation of pre-transplant organ assessment strategies. Current decision-making methods to accept an organ for transplantation lack overall predictive power. Normothermic machine perfusion (NMP) has the potential to improve pre-transplant kidney viability assessment. While renal NMP is gaining increasing interest, it remains in its infancy. Functional magnetic resonance imaging (fMRI) is a class of imaging methods developed to demonstrate regional, time-varying changes in metabolism. To broaden our understanding about the physiological processes throughout NMP, we combined fMRI with ex-vivo renal perfusion. As a proof of concept, we applied several fMRI sequences during NMP of discarded human kidneys.
Methods: Five discarded human kidneys were preserved with either static cold storage or hypothermic machine perfusion. Kidneys underwent NMP for 3 hours at 37°C in an MRI compatible circuit. Vital parameters, blood gasses, and perfusate and urine samples were acquired during NMP. Two fMRI sequences, arterial spin labelling (ASL) and T2* mapping, were longitudinally applied to assess renal microcirculation and oxygen delivery, respectively. Regions of interest were drawn in the renal cortex and medulla to specify regional signal intensity.
Results: During NMP, all kidneys showed a gradual shift in corticomedullary flow distribution from medulla to cortex. Average ASL C/M ratios at 30, 90, and 180 minutes were 0.6, 4.1, and 7.6, respectively. Kidneys with a lower overall C/M ratio showed diminished urine production and higher levels of ASAT and lactate. The kidney with the lowest medullary T2* signals, representing a higher fraction of deoxyhemoglobin, showed a high urine production and creatinine clearance. This observation corresponds with the relative hypoxic environment in which the medulla functions in-vivo.
Conclusions: This pilot study provided the first evidence for the feasibility of assessing renal integrity during NMP by means of fMRI in discarded human kidneys. Combining non-invasive measurement strategies with conventional biochemical tools paves the way to better understand functional processes during NMP and might eventually serve as an add-on quality assessment tool during NMP.

POS190 COMPARISON BETWEEN KIDNEY TRANSPLANTATION AFTER CIRCULATORY DEATH AND AFTER BRAIN DEATH:A MONOCENTRIC RETROSPECTIVE STUDY AFTER TWO YEARS OF FOLLOW-UP

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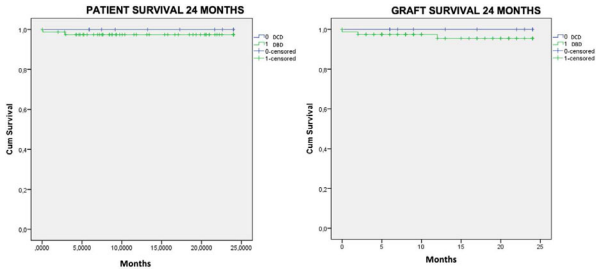
Background: Kidney transplantation (KTX) is the best therapy for patients with end-stage renal disease. Donors after cardiac death (DCD) are used worldwide to expand the donor pool, with encouraging results. DCD KTX is increasing in Italy, despite an initial scepticism due to the 20 minutes asystole time prescribed by law for death declaration. We report a single centre experience in DCD KTX activity at the University Hospital of Modena.
Methods: This is a single-centre retrospective study. We considered Donor after Brain Death (DBD) and DCD (controlled only, with normothermic in situ perfusion (ECMO) followed by ex situ hypothermic oxygenated perfusion (HOPE)) KTX performed from 1/11/17 to 31/12/19. We described donor/recipient characteristics and clinical data. The primary endpoint of the study is 2 years DCD vs DBD survival, stratified for: standard/expanded criteria, single/double, KDPI, renal function. We also compared DCD vs DBD frequency of complications. Descriptive statistics reported mean/median values with standard deviation (SD) for continuous variables, frequencies of categorical ones; comparison with t-test, Chi-square, Fisher Test; survival analysis with Log-Rank (Mantel-Cox) method, plots according to Kaplan-Meier, multivariate correlation with Cox regression.
Results: Of 91 KTX 78 were DBD, 13 DCD, with similar demographic variables. Survival analysis at two years did not show any significant difference ($p > 0.05$) between groups (patient survival: DBD 97.4% (1 circulatory arrest, 1 sepsis), DCD 100%, overall 97.8%; Death censored graft survival: DBD 96,2%, DCD 100%, overall 96.7%), before and after stratification. Primary Non Function (PNF) rate in DCD 0%, in DBD 1,28%; Delayed Graft Function (DGF) rate in DCD: 46,15%, in DBD 24,36%.

	DBD (n=78) donors	DCD (n=13) donors	DBD (n=78) recipients	DCD (n=13) recipients
Sex-M (n)	32 (41,02%)	8 (61,53%)	54 (69,23%)	10 (76,92%)
Age (years) ± SD	60,76 ± 17,19	57,7 ± 6,4	55,2±13,2	57,5 ± 5,8
Cause of death (n)				
Cerebral Hemorrhage	46 (58,97%)	2 (15,38%)		
Head trauma	15 (19,23%)	3 (23,08%)		
Ischemic stroke	8 (10,26%)	1 (7,69%)		
Post-anoxic encefalopathy	8 (10,26%)	7 (53,85%)		
Meningitis	1 (1,28%)	0 (0%)		
BMI (kg/m²) ± SD	24,69±3,64	25,95±6,72	25,03±3,59	24,8 ± 4
Ipertension (n)	33 (42,31%)	5 (38,46%)	59 (75,64%)	12 (92,31%)
Diabetes (n)	8 (10,26%)	1 (7,69%)	14 (17,95%)	0 (0%)
Creatinine (mg/dl) ± SD	0,87 ± 0,27	0,84 ± 0,33		
KDPI %± SD	85,50 ± 27,83	79 ± 16,53		
KDRI ± SD	1,48±0,57	1,35±0,25		
Caucasian ethnicity (n)			66 (84,61%)	11 (84,61%)
Months in tx waiting list (months) ± SD			33,4±34,25	20,6±31
Months of dyalisis (months) ± SD			59,56±39,35	33,15±32,83
Cardiopaty (n)			23 (29,49%)	4 (30,77%)
Creatinine 1 month (mg/dl) ± SD			1,61± 0,86	1,6±0,5
Creatinine 1 year (mg/dl) ± SD			1,66±0,84	1,60±0,37
Creatinine 2 years (mg/dl) ± SD			1,60±0,56	1,33±0,22
eGFR 1 month (ml/min) CDK EPI ± SD			54,97±23,15	49,69±19,49
eGFR 1 year (ml/min) CDK EPI ± SD			53,33±22,84	51,38±15,34
eGFR 2 years (ml/min) CDK EPI ± SD			51,30±22,00	63,3±16,09
DGF			24,36%	46,15%



Conclusions: TX outcomes from DBD and controlled DCD are comparable. ECMO and HOPE allow optimal graft recovery, without differences in renal function and complications rates in the first two years of follow-up.

POS191 VALIDATION OF THE PRECLINICAL MODELS FOR RENAL ISCHEMIA REPERFUSION INJURY: A SYSTEMATIC REVIEW

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Background: Ischemia and subsequent reperfusion (IR) is inevitable during organ transplantation. IR injury, the paradoxical increase of tissue damage following reperfusion, is a major contributor to early graft dysfunction and compromises long-term outcomes. Despite decades of intense research and numerous preclinical successes, no intervention has been successfully translated to the clinic, an observation that implies a profound translational gap.
We recently identified metabolic failure as the mechanism underlying clinical renal IR injury (delayed graft function (DGF)). Similar conclusions were also reached for acute kidney injury following major surgery. These clinical leads now provide an opportunity to evaluate preclinical models. We therefore performed a systematic review of the preclinical studies that reported on metabolic aspects in the context of renal IR injury, in order to identify parallels and incongruences between preclinical models and clinical context.
Methods: Systematic literature searches were performed in PubMed, EMBASE and Web of Science.
Results: The systematic searches identified 34 preclinical studies that reported (aspects of) the post-reperfusion metabolome. Most studies were performed in rats or mice, four in pigs, and one in dogs. A systematic inventory of these preclinical studies pointed to a series of translational hurdles (summarized in Table 1).
Conclusions: This systematic review identified profound methodological inadequacies in preclinical studies of IR injury. Altogether, inconsistencies amongst preclinical studies as well as profound translational gaps between preclinical and clinical studies provide a rationale for the failure to translate preclinical successes. Optimisation of the experimental models and consensus on optimal methodological practices is urgently needed.

Table 1. Overview of the identified translational problems in the included 34 preclinical studies.

Translational problem	#studies/ #applicable studies
No discrimination between ischemic injury and IR injury	34/34
No discrimination between prerenal and renal injury	19/34
Short follow-up (≤24 h)	24/34
Single end point	10/34
Reliance on urine for liquid biomarkers	10/34
Reliance on peripheral blood instead of renal blood	24/26
Incomplete reporting of metabolome	19/34
Translatable model	0/34

POS192 THE EFFECT OF THE KETOGENIC DIET ON MITOCHONDRIAL FUNCTION IN PORCINE PRECISION-CUT KIDNEY SLICES

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Background and aims: Kidneys derived from Donation after Circulatory Death (DCD) donors suffer from ischemic injury. When reperfusion occurs, the formation of Reactive Oxygen Species (ROS) in mitochondria contributes to the development of ischemia reperfusion injury (IRI). Preoperative fasting is known to be protective against renal IRI. During fasting or a ketogenic diet, the metabolic substrate switches from glucose to fatty acids, which then becomes the main energy source. Precision-cut kidney slices (PCKS) is an *ex vivo* model to study intra- and extracellular mechanisms. Here, we used PCKS to evaluate the effect of a ketogenic diet on mitochondrial function.
Methods: Porcine kidneys were obtained from a local abattoir. After 30 min of warm ischemic time (WIT), kidneys were preserved for 3 hours with hypothermic machine perfusion (HMP) with University of Wisconsin Cold

Storage (UW-CS) solution. Thereafter PCKS were made and incubated at 37°C with 80% oxygen. The incubation medium consisted of Roswell Park Memorial institute (RPMI) 1640 medium without glucose supplemented with either 2mg/mL glucose (control) ($n = 5$) or 2 mg/mL (±)-sodium 3-hydroxybutyrate (BHB) ($n = 5$) or 1,5 mg/mL SMOFlipids® (SMOF) ($n = 5$). Directly after slicing and after 24, 48 or 72 hours of incubation, tissue and medium samples were taken to analyse mitochondrial, oxidative stress and injury markers.
Results: No differences were found in mitochondrial respiratory control rates. After 72 hours ATP levels were significantly higher in the control group compared to the BHB group. In the first 48 hours a significant increase in thiobarbituric acid reactive substances (TBARS) levels was seen in the SMOF group. Over time significantly less lactate dehydrogenase (LDH) was seen in the SMOF group compared to the BHB group.
Conclusions: A ketogenic diet has no beneficial effect on mitochondrial function in the PCKS model. As seen by less LDH release, dietary modification as a preconditioning strategy is promising, but more in-depth research must be performed.

POS193 EVALUATION OF SEX DIFFERENCES IN ACUTE KIDNEY INJURY AFTER BD USING AN ISOLATED PERFUSED RAT KIDNEY MODEL

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Background: Clinical evidence correlates female donor kidneys with poor outcomes in male recipients. Brain death (BD) induces hemodynamic and immunologic alterations impacting organ viability. After BD, female rats present higher renal inflammation associated to female sex hormones reduction. In this study, we aimed to investigate differences between sexes in the renal function and injury generated by BD using isolated perfused rat kidney (IPK).
Methods: Male and female Wistar Rats (8 weeks) were maintained after BD for 4h. Sham-operated (S) rats were used as controls. Left kidneys were procured and preserved in cold saline solution (30 min). Normothermic IPK (90 min) was carried on with Williams Medium E (WME) perfusion fluid. Renal function and injury were assessed by monitoring creatinine clearance, perfusate flow, renal morphology analyses, staining of complement system components and inflammatory cell markers.
Results: After IPK, both sexes presented increase in complement system formation/deposition (C5b-9: Pglom = 0.0166, Pint<0.0001; C3d: Pglom = 0.0008, Pint = 0.0105), myeloperoxidase (Pglom = 0.0043, Pint<0.0001) and perfusate IL-6 ($p = 0.0126$). Analysis of relative gene expression in perfused kidneys from BD rats revealed a similar upregulation of inflammatory profile in both sexes (IL-1β, IL-6 and eNOS - $p < 0.0001$), however P-selectin ($p = 0.0001$), iNOS ($p = 0.0002$), Caspase-3 ($p < 0.0001$) and BCL-2 ($p = 0.0153$) increased in BD-female kidneys and KIM-1 ($p = 0.0191$) in BD-male kidneys.
Conclusions: Our data showed that the inflammatory response is present in both sexes similarly. Since normothermic IPK allows graft assessment and therapeutic drug delivery under physiologic environment, these findings support further studies focusing in anti-inflammatory therapeutics to improve renal graft quality.

POS194 CONTROLLED OXYGENATED REWARMING PROTECTS MITOCHONDRIAL FUNCTION IN DCD PORCINE RENAL GRAFTS

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Background: Warm reperfusion after previous cold storage has been shown to have a negative impact on mitochondrial function of organ grafts. Here, we wanted to investigate, if a more gentle warming up of the cold graft by ex vivo machine perfusion with gradually elevated temperature from cold to near normothermia prior to implantation would be effective in preventing mitochondrial dysfunction upon reperfusion.
Methods: All experiments we conducted on porcine kidneys retrieved 15 min after cardiac arrest. After 18h of cold storage in HTK solution, half of the kidneys ($n = 6$) were subjected to 2 hours of reconditioning machine perfusion starting with a short hypothermic period followed by a gradual increase in perfusion temperature up to 35°C (controlled oxygenated rewarming- COR). The other kidneys ($n = 6$) were left untreated and served as controls.
Functional recovery of all grafts was then observed upon normothermic reperfusion in vitro.
At the conclusion of the experiments, tissue specimens were taken for immediate isolation and analysis of renal mitochondria.
Results: COR resulted in a significantly and more than 3-fold increased glomerular filtration rate upon reperfusion (8.7 ± 4.3 vs 1.96 ± 0.49 ml/min; $p = 0.038$) along with a significant higher tubular sodium reabsorption (8.2 ± 17.1 vs 74.9 ± 8.9 %; $p = 0.031$) and lesser but not significant loss of glucose in comparison to the controls (72.1 ± 27.6 vs 38.1 ± 24.8 %; $p = 0.09$). Enzyme release (AST) was also massively reduced during the reperfusion period (131 ± 93 vs 839 ± 268 I.U.; $p = 0.0023$). Specific analysis on the mitochondrial level revealed significantly better electron transport and coupling efficiency in the COR group compared to the cold storage group (88.9 ± 2.2% vs 68.8 ± 15%; $p = 0.0022$).
Interestingly, additional experiments revealed that the omission a hypothermic perfusion period did not deteriorate any of the results after COR, provided that the instant temperature increase from 10 to 35°C was effectuated in the same, controlled manner.
Conclusion: Controlled rewarming after extended cold preservation effectively improves mitochondrial recovery upon reperfusion and early functional outcome of kidney grafts.

POS195 INFRARED THERMAL IMAGING: A NON-INVASIVE, REAL-TIME, BIOMARKER FOR PREDICTING EARLY GRAFT FUNCTION IN KIDNEY TRANSPLANTATION

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Introduction: Ischaemia-reperfusion injury (IRI) during kidney transplantation has profound effects on cortical microcirculation. There are currently no tools in routine practise to evaluate this, nor targets to ameliorate its effects in real-time. The aims of this study were to evaluate the use of modern infrared (IR) thermal imaging to objectively quantify the renal cortical microcirculation during transplantation, and to correlate this with short and mid-term outcomes.
Methods: IR images of the exposed surface of the kidney were captured using a FLIR E75 camera at seven time points, from removal from ice up to 15 minutes after re-perfusion. From each image, the mean (average) and standard deviation (heterogeneity) of temperature measurements across the surface of the kidney were recorded, which were subsequently pooled across the time points. Associations between the average and heterogeneity of temperature and transplant outcomes were then assessed using ROC curves or Spearman's (rho) correlation coefficients.
Results: Delayed graft function (DGF) developed in 49% (35/71) patients. DGF was significantly more common in those with greater heterogeneity of IR temperature (AUROC curve: 0.74, $p = 0.001$). IR heterogeneity remained significant on multivariable analysis, with an adjusted odds ratio for DGF of 1.37 per 0.1°C increase ($p = 0.011$). For a cut-off heterogeneity value of 1.16°C, DGF rates increased from 30% to 79%, yielding 63% sensitivity and 83% specificity. eGFR levels on both day 7 and at 6 months were significantly positively correlated with the average temperature (rho: 0.278; 0.285) and significantly negatively correlated with the heterogeneity of temperature (rho: -0.342; -0.246).
Conclusion: IRT is a feasible, non-invasive method to objectively assess graft microcirculation. IR heterogeneity is a good predictor of DGF and provides a potential therapeutic target to ameliorate IRI and to tailor patients' care.

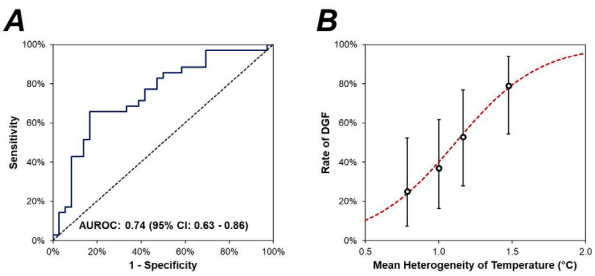

Figure Association between IR heterogeneity and DGF

POS196 COMPARISON OF EARLY POSTTRANSPLANT OUTCOMES IN KIDNEYS PRESERVED BY HYPOTHERMIA MACHINE PERFUSION AND STATIC COLD STORAGE

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Background: Early posttransplant complications impact late outcomes in kidney transplantation. Improvement in donor kidney preservation by means of machine perfusion (MP) may help to achieve better results. The aim of this study was to evaluate MP impact on early posttransplant outcomes.
Methods: This study included all consecutive cases of use of MP for donor kidney preservation and transplantation ($n = 23$) cases (donations from deceased donors after brain death (DBD) - MP group, donors: male/female = 11/12, mean age 51.5 ± 11.2 (35–74) years, ECD criteria met in 11 cases; recipients: male/female (n) = 11/12, mean age 54.6 ± 10.6 (31–77) years). Mean cold ischemia time was 21.4 ± 4.6 (15–34) hours).
Results of kidney transplantations were compared with cases, transplanted between 2004 and 2010, matched for DBD and recipient age (>35 and > 30 years, respectively) and cold ischemia time (CIT > 15 hours) - control group (CG, $n = 134$, donors: male/female (n) = 75/58, mean age 50.3 ± 9.2 (35–68) years, ECD criteria met in 65 cases; recipients male/female = 79/55, mean age 50.6 ± 10.5 (30–72) years, CIT 18.6 ± 2.8 hours.
Groups were compared for early posttransplant complications, such as delayed graft function (DGF), surgical complications (SC: vascular, urological, lymphocele), acute rejection (AR) and graft losses and patient deaths during 12 posttransplant months.
Results: In postoperative period MP group still had higher CIT ($p < .001$) showed lower frequency of vascular and lymphocele SC, delayed graft function and acute rejections ($p < .05$ for all). Other postransplant complications, graft losses and patient survival showed no statistical differences.
In cases of ECD donors DGF and AR rates were also lower in MP group ($p < .05$), other postransplant complications, graft losses and patient survival showed no statistical differences.
Conclusion: Use of machine perfusion provides better early posttransplant outcomes regarding DGF and AR rate even in cases of longer CIT.

POS197 IS VITAMIN D DEFICIENCY RELATED TO REJECTION AND CHRONIC ALLOGRAFT NEPHROPATHY?

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Background: One the important modifiable factors post-transplant is the serum vitamin D level. This plays a significant role in keeping calcium and phosphate levels at balance. Additionally, vitamin D has a wide range of effects on the immune, renal, and cardiovascular systems.
Methods: This single-centre retrospective cohort study was performed at Diskapi Research and Training Hospital. Patients with a follow-up of less than one year were omitted. Patients included in this study received vitamin D replacement therapy, as recommended in KDIGO guideline. Demographic characteristics, past medical history, donor type, immunosuppressive medications, biopsy results, and serum vitamin D levels at the time of graft biopsy were collected.
Results: Review elucidated 130 adult kidney transplant recipients. Among these patients, 52 met the eligibility criteria. The mean age of these patients was 41 ± 11.9 years. The mean post-transplant follow-up duration was 5.91 ± 1.83 years.
Histopathologic results of graft biopsies revealed rejection in 25 recipients (48%). Acute T-cell-mediated rejection (TCR), acute antibody-mediated rejection (ABMR) and chronic active ABMR were detected in 6 (11.5%), 10 (19.2%) and 9 (17.3%) patients, respectively. Chronic allograft nephropathy was diagnosed in 19 (36.5%) cases.
Study population was divided into two groups based on serum vitamin D levels. Patients with 25 (OH) vitamin D levels higher than 15 ng/ml were clustered in Group 1, and other patients with inadequate vitamin D levels were clustered in Group 2. Group 1 included 14, and Group 2 included 38 recipients. There was no significant difference between the groups in terms of recipient age and comorbidities ($p > 0.05$). There was no significant difference between groups in terms of CAN ($p > 0.05$). However, the biopsy-proven rejection rate presenting with low serum vitamin D levels was significantly higher in Group 2 ($p < 0.001$).
Conclusions: Low vitamin D levels were associated with increased rate of biopsy-proven allograft rejections. Prospective clinical studies should be designed to evaluate the impact of vitamin D on allograft rejection rates.

POS198 IMPACT OF STRUCTURED DIABETES EDUCATION ON SELF-CARE DIABETES MANAGEMENT OF KIDNEY TRANSPLANTS WITH POST-TRANSPLANT DIABETES: KUWAIT EXPERIENCE

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Background: Diabetes knowledge among kidney transplant recipients with post-transplant diabetes (PTDM) is not assessed exhaustively. We aimed to evaluate the impact of structured diabetes education on lifestyle knowledge and self-care diabetes management of kidney transplant patients.
Methods: In this prospective randomized controlled study, 210 renal transplants with PTDM were categorized in 2:1 groups according to type of diabetes education. Group 1 ($n = 140$) received structured education while group 2($n = 70$) received conventional education. Patients' data were collected through patient identification form, metabolic control parameters form and diabetes self-care scale questionnaire (with score between 0–7).
Results: Most of patients in the two groups (1&2) were Kuwaiti (60.7 vs. 58.6%), men (57.9 vs. 68.6%), with high school education level (43.6vs.48.6%). The minority was smokers (12.9 vs.8.7%) but chronic glomerulonephritis was the original disease in 36.4 vs. 35.4% of cases. Most of patients (72.8 vs. 78.6%) were hemodialyzed pre-transplant. At the start of the study, low mean scores (<50%) were reported in the majority of patients of both groups regarding healthy diet (>75% of cases), practicing exercise (>85%), blood sugar monitoring at home (nearly 20%), and caring feet (> 86% of cases). At the end of the study, patients of groups 1 showed significant improvement of the mean scores (to > 75%) of the same variables as follow: > 80.5, > 32%, 96.6%, 69.4% respectively. Moreover, most patients of the 2 groups were lacking advices about sharp disposal; diet regimen; logbook use; hypo-and hyperglycemia, sick day management; and the importance of HbA1c. By the end of the study, patients who received structured education showed significant improvement of their knowledge regarding the same parameters ($p < 0.001$).
Conclusions: Lifestyle knowledge and self-care diabetes management have improved significantly among kidney transplant recipients with PTDM after receiving structured diabetes education program. It is highly recommended to be delivered to all diabetic kidney transplant recipients.

POS199 T- CELLS COMMANDS CHIEF ORCHESTRAS FOR POST-TRANSPLANT DIABETES

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Background: Post-transplantation diabetes mellitus (PTDM) is a serious metabolic complication. Cytokines are involved in the inflammation of islet β-cells in diabetes; however, few studies have studied this in PTDM. We aimed to assess susceptibility to PTDM through screening of transplants that developed diabetes compared with those who did not.
Methods: A total of 309 renal transplant recipients (RTRs) were included in this study. The association was examined between the development of diabetes in a PTDM cohort compared with those without diabetes (non-PTDM). We have selected cytokines T cell or macrophage derived ones with well-stablished functionality in protein level. Interferon-γ T (+874) A gene (IFNG) (TH1), IL-4 C (-590)T (TH2), TGF-β1 T (29)C (TH3) and IL-6 G (−174) C (macrophage derived) . The genes were amplified using well-established techniques in our laboratory. Allelic and genotype frequencies of IFNG, IL-4 C(-590)T, TGF-β1 T (29)C and IL-6 G(-174)C were calculated for PTDM versus non-PTDM RTRs using SPSS system.
Results: IFNG TT, high producer of IFNG protein was significantly more in PTDM than non-PTDM, $p = 0.005$, while AA, low producer of IFNG, was predominant in the control group ($p = 0.004$). In IL-4 the CC genotype, low

producer of IL-4 protein level, was more in PTDM than non PTDM, $p = 0.02$, on the other hand TT which corresponds to high producer of IL-4 was more in non PTDM than PTDM cohort, $p = 0.003$. However, GG of IL6 and TT of TGF-β1 which corresponded to high protein levels of both cytokines were significantly more in PTDM with $p = 0.002$ and $p = 0.03$.
Conclusions: Inflammation of the islet β-cells- through TH1 cell-mediated variations of IFNG, IL-4, TGF-β1 and IL-6- may play a crucial role in the pathogenesis of PTDM. Further larger studies are required to confirm our findings.

POS200 EFFECT OF PHYSICAL ACTIVITY AND LIFESTYLE CHANGES ON INSULIN RESISTANCE IN PATIENTS AFTER KIDNEY TRANSPLANTATION

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Background: Insulin resistance (IR) at the time of kidney transplant (KT) is the most significant risk factor for the development of post-transplant diabetes mellitus (PTDM) and is a strong predictor of cardiovascular morbidity and mortality in patients after KT. It is possible to improve long-term survival of grafts and patients by influencing just modifiable risk factors, including obesity and the associated IR. The aim of this work is to determine the effect of precisely determined physical activity and lifestyle changes on IR in patients after KT.
Methods: The primary goal was to complete at least 150 minutes of moderate intensity physical exertion per week. Study group ($n = 22$) performed an aerobic or combined (aerobic + strength) type of sports activity. Monitoring was provided by a sports tracker (Xiaomi Mi Band 4 compatible with Mi Fit mobile application). Control group was consisted of 22 stable patients after KT. Patients in both groups have the same immunosuppressive protocol. The duration of follow-up was 6 months.
Results: There were significantly better graft function ($p = 0.0036$, $p = 0.0137$), lower value of fasting blood glucose ($p = 0.0016$, $p = 0.0003$) and C-peptide ($p = 0.0447$, $p = 0014$) in the observed group compared to the control group in the 3rd and 6th month of monitoring. IR was statistically significantly lower at 6 months ($p = 0.0202$) and fasting blood glucose at 3 and 6 months ($p = 0.0227$) in the observed group confirmed in a multivariate model. There was found no additional effect of combined sports activity on IR and fasting blood glucose.
Conclusion: In our study, we confirmed a significant effect of regular physical activity in preventing the development of IR and impaired fasting glucose in patients after KT. It is necessary to perform at least 150 minutes of medium-intensity aerobic or combined sport effort per week to achieve this goal.

POS201 EFFECT OF STRUCTURED DIABETES EDUCATION ON DIABETIC ANGIOPATHIES AMONG KIDNEY TRANSPLANTS WITH POST-TRANSPLANT DIABETES: KUWAIT EXPERIENCE

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Background: Diabetes knowledge among kidney transplant recipients with post-transplant diabetes (PTDM) is not assessed exhaustively. We aimed to evaluate the impact of structured diabetes education on the development of diabetic micro-and macro-angiopathies in kidney transplant patients with post-transplant diabetes.
Methods: In this prospective randomized controlled study, 210 renal transplants with PTDM were categorized in 2:1 groups according to type of diabetes education. Group 1 ($n = 140$) received structured education while group 2($n = 70$) received conventional education. Patients' data were collected through patient identification form, and metabolic control parameters form.
Results: Most patients in the two groups (1&2) were Kuwaiti (60.7 vs. 58.6%), men (57.9 vs. 68.6%), with high school education level (43.6vs.48.6%). The minority was smokers (12.9 vs.8.7%) but chronic glomerulonephritis was the original disease in 36.4 vs. 35.4% of cases. Most of patients (72.8 vs. 78.6%) were hemodialyzed pre-transplant.
At the start of the study, the percentage of patients with diabetic neuropathy was comparable in both groups (32.4 vs. 27.6% in the two groups respectively) and after 24 months follow-up EMG/NC did not show significant difference between the studied groups ($p > 0.05$). Similarly, the number of patients with fundus imaging showing retinopathy was comparable in both groups at the start and at the end of the study ($p > 0.05$). Also, macroangiopathic events were higher in group 1 but did not rank to significance ($p > 0.05$).
On the other hand, although the percentage of patients with nephropathy was comparable in both groups at the start of the study but the percentage decreased significantly in group 1 after 24 months of the study compared to group 2 and to the basal value in the same group ($p = 0.016$).
Conclusions: Structured diabetes education is associated with reduction of diabetic nephropathy but without significant impact on other micro- or macroangiopathy. It is highly recommended to be delivered to all diabetic kidney transplant recipients.

POS202 FLUDROCORTISONE AMONG RENAL TRANSPLANT RECIPIENTS WITH PERSISTENT HYPERKALEMIA: SINGLE CENTER EXPERIENCE

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Background: Calcineurin inhibitors (CNI) is the cornerstone of immunosuppression following solid organ transplantation. However, it may cause hyperkalemia by multiple mechanisms. Hyperkalemia is commonly observed in renal transplant recipients. Our cohort study aimed to evaluate impact of fludrocortisone in the management of CNI-induced hyperkalemia after renal transplant.
Methods: Our cohort study evaluated the newly transplanted patient who developed hyperkalemia or those attending the outpatient renal transplant clinic in Hamed Al-Essa organ transplant center of Kuwait with hyperkalemia. Patients were evaluated clinically and by laboratory investigations during their follow-up visits. All follow-up parameters were collected before starting fludrocortisone (Basal) and then at 1,2,4,8 weeks. Drug history was assessed with special stress on possible drugs which induce hyperkalemia that were discontinued (as spironolactone) otherwise essential drugs like prophylactic agents (sulfamethoxazole trimethoprim) were kept. Dose of oral anti-hyperkalemic agents (bicarbonate, resonium calcium, and fludrocortisone) were collected.
Results: 26 patients were included in the study. Most of cases were males, aged (45.8 ± 15 years). Body weight showed no significant change basal and after introduction of fludrocortisone (73.3 ± 19, 72.8 ± 18.8, 71.1 ± 18, 69.4 ± 16, and 69.4 ± 16 Kilograms). Systolic and diastolic blood pressure also do the same (129.3 ± 18.6, 129.1 ± 15.3, 129.3 ± 20, 127.4 ± 18, and 127.2 ± 18), (76.3 ± 11, 75.8 ± 9.1, 76.5 ± 7.5, 73.8 ± 12, and 73.2 ± 12 mmHg). The steroid doses (prednisolone) were significantly reduced over one month (15.7 ± 12.4, 14.1 ± 10.19, 12.6 ± 8.7, 9.5 ± 5.2, and 9.5 ± 5.2mg per day). Fludrocortisone doses did not show any significant change between starting and follow-up doses (0.1211 ± 0.07, 0.1158 ± 0.07, 0.116 ± 0.07, 0.115 ± 0.08, and 0.115 ± 0.08). Serum potassium levels were significantly improving (5.18 ± 0.58, 4.9 ± 0.49, 4.8 ± 0.54, 4.8 ± 0.65, and 4.4 ± 0.72). Serum creatinine was significantly improving by the end of 8 weeks (129.3 ± 50, 129.5 ± 54, 116.7 ± 48, 114.5 ± 28, and 114.5 ± 28). Serum bicarbonate did not show any significant differences.
Conclusions: Fludrocortisone was safe and effective option in management of CNI-induced hyperkalemia among renal transplant recipients.

POS203 DETERMINANTS OF SECONDARY HYPERPARATHYROIDISM RESOLUTION AFTER KIDNEY TRANSPLANTATION

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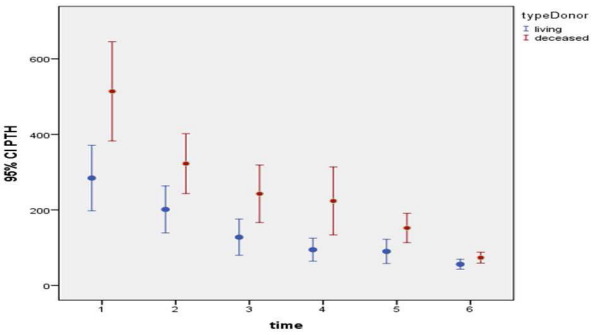
Background: Spontaneous remission of secondary hyperparathyroidism after kidney transplantation requires time to occur. The aim of the present

study is to investigate factors that may be related to the reduction of parathyroid hormone (PTH) after transplantation as well as the rate of its reduction.
Methods: We studied 91 kidney transplant recipients of the transplantation unit of our center, between January 2014 and September 2016. The relationship between parathyroid hormone values, during the first year after transplantation, with renal function, type of kidney graft origin (deceased or living) as well as delayed renal graft function (DGF) was examined. Moreover, we determined the correlation of the rate of PTH reduction within the first year with the value of PTH prior to transplantation.
Results: Out of the total of 91 recipients, 32(35.1%) were women and 59 (64.8 %) were men, with a mean age 47 $\pm$ 11.87years. There was a gradual decrease in PTH values throughout the first year after transplantation, with the exception of the period between the 3rd and 6th month, when PTH reaches a plateau (PTH = 194 $\pm$ 24.). At the same time, there is a decrease of PTH by 33% in the first half of the first year after transplantation and by 57% in the second. In addition, a statistically significant correlation of PTH with renal function was found (p = 0.001), with PTH values decreasing as the glomerular filtration rate increases. In contrast, the age of the recipient does not seem to affect the value of PTH, nor is DGF related to PTH (p = 0.001). Finally, it was found that transplants from deceased donors are associated with higher values of parathyroid hormone, than those from living, while the value of parathyroid hormone before transplantation is positively correlated with the value after it (p = 0.001). A summary of the results of the research
Conclusions: Secondary hyperparathyroidism, which accompanies end-stage chronic renal failure, usually resolves adequately after transplantation. However, the rate at which this will occur and the values that parathyroid hormone will receive, in the first year after transplantation, are related to the recipient's renal function, the kidney graft origin (deceased/living) and the pre-transplant parathyroid hormone values.



POS204 THYROTOXICOSIS AFTER KIDNEY TRANSPLANT: AN EARLY POST-OPERATIVE COMPLICATION

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Background: Thyroid disorders (TD) are frequent in end stage renal disease but data after kidney transplant (KT) are conflicting. Many reports highlight the high incidence of thyroid cancer during the follow-up of KT recipients but few data are available about TD in the early post-operative period.
Methods: We analyzed thyroid function in 60 consecutive patients who underwent KT from deceased donors from July 2020 to February 2021 at our Centre. 17 patients had a history of TD (Table 1). All patients had normal levels of thyroid stimulating hormone (TSH) at the time of KT. After 2 weeks from KT, TSH, FT3 and FT4 were measured.
Results: 7 patients developed impaired thyroid function (Table 1). Interestingly, all of them had hyperthyroidism with low TSH and high levels of FT4. One patient experienced symptom (atrial fibrillation), while the others were asymptomatic. No patients had antithyroid antibodies. 5 patients had pre-existing TD: 3 had an euthyroid goiter and 2 had Hashimoto's disease. 5 patients were still anuric at the time of thyroid hormones measurement, because of delayed graft function (DGF). In the 2 patients without DGF, ioduria was high. 2 patients had received iodinate contrast medium. All patients were exposed to iodinate antiseptic agents. Patients were successfully treated with the limitation to iodine exposure. The symptomatic patients also received methimazole.
Conclusion: In our early KT cohort, we found a high prevalence of thyrotoxicosis, which may be caused by iodine overload. In fact, in these patients, exposure to iodinated agents (especially contrast medium and topical antiseptic solutions) may result in iodine poisoning. In addition, immunosuppressive therapy may contribute to TD. Thus, a screening of thyroid function should be performed even in the first weeks after kidney transplant, especially in patients with pre-existing TD. A prompt diagnosis of this condition is necessary to avoid hemodynamic complications that may delay graft function.

Tab.1

	KT recipients (n=60)
Age (median, years)	60 (IQR 46-67,3)
Gender (F/M), n (%)	25/35 (42/58)
Pre existing TD (n,%) - Goiter, n(%) - Thyroid nodules, n(%) - Hypothyrodism, n(%) - Hyperthyroidism, n(%)	17 (28) - 8 (47) - 2 (11) - 6 (2) - 1 (5)
	KT recipients who developed TD (n =7, 11,6%)
Age (median, years)	62 (IQR 54,5-70)
Gender (F/M), n (%)	3/4 (43/57)
Pre existing TD, n(%) - Goiter (n,%) - Thyroid nodules , n(%) - Hypothyrodism, n(%) - Hyperthyroidism, n(%)	5 (79) - 3 (42) - 0 - 2 (28) - 0
TD developed - Hyperthyroidism -TSH (median, microU/ml) - FT4 (median, pg/ml) - Ioduria (microg/dl)	7 (100%) - 0,09 (IQR 0,05-0,14) - 14,6 (IQR 11,4-16,8) - 400 (IQR 200-600)
Dialysis need, n	5 (79%)
Exposed to iodinate contrast medium, n(%)	1 (14%)
Exposed to iodine antiseptic agents, n(%)	7 (100%)

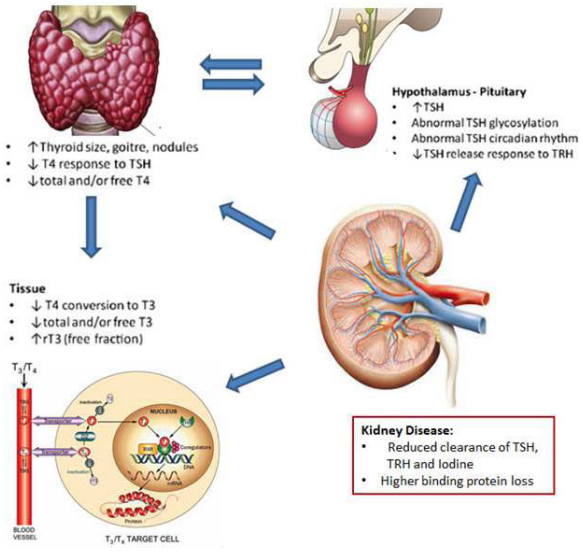

Fig.1 Effects of chronic kidney disease on thyroid function

POS205 DIABETES AFTER TRANSPLANTATION AMONG KIDNEY TRANSPLANT RECIPIENTS: INCIDENCE AND OUTCOMES

Amal Ouni, Wissal Sahtout, Awatef Azzebi, Mayssa Hadj Brahim, Aicha Ben Aicha, Sanda Mrabet, Raja Boukadida, Asma Fradi, Ferdaous Sabri, Dorsaf Zellama, Samira Ben Amor, Yossra Geudri, Achour Abdeltif
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Background: Diabetes after transplantation (DAT) is a common complication after kidney transplantation. It increases the risk of cardiovascular

disease. The aim of this study is to examine its effect on the outcomes of kidney transplantation.
Methods: This study included non-diabetic renal allograft recipients, transplanted from 2008 to 2019 in our department. Demographic and clinical data at transplant time and clinical events during the study period were collected. Patient and graft survival rates were analyzed. Patients with or without DAT were compared.
Results: Our study included 257 patients, the overall incidence of DAT was 21,8 %. The median age was 36 years with a male predominance (sex ratio = 3). Laboratory data such as serum cholesterol, serum creatinine at discharge and 24-hour proteinuria, as well as systolic and diastolic blood pressure, were similar in those with and without DAT.
There was no significant difference in cardiovascular diseases and infectious complications rates between the group of patients with DAT and the group without. There was no significant difference in graft survival at 5 years between the patients with DAT and those without (p = 0,459). The 5-year patient survival in the patients with DAT was 87,5%. There was no significant difference in survival between the group with DAT and the group without (p = 0,589).
Conclusion: DAT affects graft and patient survival, and increases the incidence of post-transplant cardiovascular disease. The incidence and impact of DAT can be minimized through pre- and post-transplant screening to identify patients at higher risk.

POS206 SODIUM-GLUCOSE COTRANSPORTER 2 INHIBITORS (SGLT2I) SHORT-TERM OUTCOME IN DIABETIC KIDNEY TRANSPLANT RECIPIENTS

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Introduction: The emergence of positive data on the use of sodium glucose co-transporter inhibitors (SGLT2i) in the last several years, begged the question of whether their positive outcomes can be seen in kidney transplant recipients, as they have the same and even more pronounced cardiovascular risk factors than the general population and in addition, we have a better short term graft and patients survival, but we lack the tools to improve long term patients and graft survival where so many patients die from cardiovascular disease with a functioning graft or lose their graft from chronic changes with difficult to control blood pressure and proteinuria
Patients and Methods: We collected data retrospectively from transplant records of patients with type II diabetes (T2D) (n = 79) or post-transplant diabetes mellitus (PTDM) (n = 56) receiving SGLT2i agents plus standard of care [SOC] management comparing them to similar diabetic patients who were only on SOC.
Results: The two groups were comparable in age, sex, donor type, diabetes type (T2D PTDM), post-transplant period, induction immunosuppression and CNI use. Though HbA1c improvement was not significant between them, patients on SGLT2i showed better drop in HbA1c compared to the SOC (0.7% versus 0.5% respectively). Reduction of BMI was equal between the two groups(-1.1%) and there was no significant difference in the number of blood pressure medications (average 2 drugs per patient). Kidney function was assessed by eGFR using CKD-EPI and urine albumin/creatinine ratio (ACR). The eGFR was calculated at start then at 1,3,6 and 12 months. In SGLT2i group, eGFR showed a dip at 3 months (from 66 to 63.35 ml/min) then improved gradually by the end of the year and maintained at a level close to baseline (65.44 ml/min). The SOC group showed gradual drop in eGFR over the year from 65.76 to 63.19 ml/min. uACR reduced in the SGLT2i group from 48.79 to 23.79 mg/mmol creatinine and increased from 42.84 to 63.16 mg/mmol creatinine in the SOC group. The incidences of graft rejection, urinary tract and genital infection, cardiovascular outcomes were not different between the groups.
Conclusion: Use of SGLT2i in managing diabetic patients post kidney transplantation is safe and has better short-term outcomes on renal function with comparable safety to standard of care.

POS207 RISK FACTORS OF DIABETES AFTER KIDNEY TRANSPLANTATION: A TUNISIAN SINGLE CENTER STUDY

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Background: Kidney transplant recipients who had diabetes after kidney transplantation (DAT) have been reported to be at increased risk of cardiovascular complications. The aim of this study is to estimate the incidence of DAT, and to determine its risk factors in our population.
Methods: Retrospective data collection of 272 renal transplant recipients over a 12-year period was performed to record presence of DAT. Demographic (gender, age), and clinical (origin of graft, body mass index at transplantation time and 3, 6 and 12 month after, causes of kidney failure) data were analysed. Patients with or without DAT were compared.
Results: DAT incidence was 20,6%. Risk of DAT was highest in the first year of post-transplantation (69,6%). The majority of patients (65,9%) were receiving an immunosuppressive regimen associating Tacrolimus, Mycophenolate Acid and Prednisolone. Risk factors for DAT included: oldest age at transplant (p = 0,001), origin of graft (p = 0,06) and higher body mass index at transplant time (p = 0,009), 3 month (p = 0,013) and 6 month after (p = 0,06). None of gender (p = 0,150), smoking (0,082) and causes of kidney failure (p = 0,551) was found to be significantly associated with the risk of DAT. The group of patients with DAT had a highest rate of hospitalisation (p = 0,017).
Conclusion: NODAT was common in renal transplant recipients. Some risk factors predate transplant and could be used to risk-stratify patients to determine appropriate risk-reduction strategies.

POS208 HIGHER OBESITY CLASSES (II/III) ARE ASSOCIATED WITH INCREASED PERI-OPERATIVE SURGICAL COMPLICATIONS IN KIDNEY TRANSPLANT RECIPIENTS

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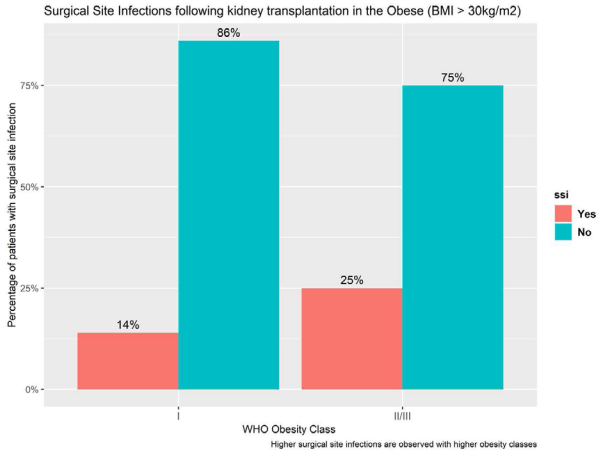
Background: Patients with a body mass index greater than 35 kg/m^2 are considered to have severe (WHO Class II) or if above 40 kg/m^2 morbid (WHO class III) obesity. These patients are often included with moderately (WHO class I) obese patients with a BMI 30–35 kg/m^2 when reporting transplant outcomes. Collectively they are associated with worse post-transplant outcomes attributed to a higher rate of early complications that account for a disparity in longer-term outcomes when compared to other weight categories. This study aimed to determine the complication rate following kidney transplantation according to obesity class and assess the impact on early post-transplant outcomes.
Methods: We conducted a retrospective review of consecutive cases identified from a prospectively collected clinical database in the 18 months from Feb 2019-July 2020. Included patients, underwent transplantation within our network collaboration involving two UK transplant units. Identified cases were classified by WHO BMI class, the transplant characteristics and peri-operative outcomes were reported.
Results: We identified 67 Obese patients in the study period with an overall complication rate of 38.8% (Clavian-Dindo classification > 2). A comparison of transplant characteristics and post-transplant outcomes of Class I patients to Class II/III is shown in Table 1. Surgical complications were

		WHO Obesity Class			
Table 1	**levels**	**I**	**II/III**	**Total**	**p**
Total N (%)		43 (64.2)	24 (35.8)	67	
Surgical Site Infection	Yes	6 (14.0)	6 (25.0)	12 (17.9)	
	No	37 (86.0)	18 (75.0)	55 (82.1)	
Superficial wound drain	Yes	19 (44.2)	18 (75.0)	37 (55.2)	0.021
	No	24 (55.8)	6 (25.0)	30 (44.8)	
Length of Hospitalisation	Median (IQR)	4.0 (1.5)	6.0 (2.0)	5.0 (3.0)	0.054
Recipient Diabetes	No Diabetes	30 (69.8)	16 (66.7)	46 (68.7)	
	Diabetes Mellitus	13 (30.2)	8 (33.3)	21 (31.3)	
Recipient Age	Median (IQR)	56.0 (12.5)	52.0 (15.0)	55.0 (13.5)	
Donor Type	DCD	17 (39.5)	12 (50.0)	29 (43.3)	
	DBD	26 (60.5)	12 (50.0)	38 (56.7)	
Recipient BMI	Median (IQR)	32.2 (2.5)	36.9 (3.3)	33.5 (4.4)	<0.001
Induction Immunosuppression agent	Alemtuzumab	19 (44.2)	16 (66.7)	35 (52.2)	
	Basiliximab	24 (55.8)	8 (33.3)	32 (47.8)	
6-9 month GFR	Median (IQR)	47.0 (30.0)	45.0 (35.5)	45.0 (31.2)	
Clavian-Dindo Complication (>2)*	Yes	14 (32.6)	12 (50.0)	26 (38.8)	
	No	29 (67.4)	12 (50.0)	41 (61.2)	

***complications included: Perinephric haematoma, post-operative ileus, Hospital acquired pneumonia and hernia.**



higher in Class II/III (25%) relative to Class 1 (14%) despite a significantly greater use of superficial wound drains ($p = 0.021$) in the Class II/III. Recipient diabetes, donor type and induction immunosuppression had no impact on complication rate.
Conclusions: Obesity is associated with a high perioperative complication rate, which is greater in higher obesity classes (II/II). These patients experience more wound complications and longer hospital admissions despite a greater use of surgical drains. Reducing surgical complications in Class II/III recipients may be important in improving long term outcomes.

POS209 FUNCTIONAL OUTCOMES OF END-ISCHEMIC HYPOTHERMIC MACHINE PERFUSION

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Background: In clinical trials expanded criteria donors (ECD) grafts preserved with continuous hypothermic machine perfusion (cHMP) show better survival and lower delayed graft function (DGF) compared to simple cold storage.
In daily practice imported grafts are frequently end-ischemic machine preserved (eHMP) and local grafts are cHMP preserved.
Objective: To compare outcomes in ECD grafts cHMP and eHMP preserved.
Methods: Prospective study.192 recipients of a first kidney transplant (KT) were included. Minimum follow-up was 12 months.
Primary outcomes: DGF, 1 and 3-year graft survival (yGS).
Secondary outcomes: Acute rejection (AR), Vascular Thrombosis (VT) and Primary Non-function (PNF).
A multivariate logistic regression model was applied to estimate the influence of eHMP in DGF, AR, VT and PNF. A multivariate Cox proportional hazards model was applied to estimate the influence of eHMP in GS.
Results: 74 cHMP and 118 eHMP preserved grafts.
There were differences in these baseline characteristics: donor age (67.9 vs 76.9 years), cold ischemia time (16.3 vs 18.5 h), time HMP preservation (14.4 vs 7.8 h) and recipient age (56.7 vs 61.3 years) in cHMP vs eHMP group, respectively.
DGF occurred in 13 patients (18.1%) in the cHMP group and in 32 patients (28.8%) in the eHMP group. eHMP did not increase the risk of DGF, OR: 1.8 (CI 95%: 0.7–4.5, $p = 0.23$).
1 and 3yGS was 93.2% and 90.3% in the cHMP group and 85.9% and 77.4% in the eHMP group. eHMP did not influence GS, HR: 1.8 (CI 95%: 0.6–5.4, $p = 0.31$).
AR occurred in 9 patients (12.3%) in the cHMP group and in 12 patients (9.8%) in the eHMP group. Adjusted OR: 0.8 (CI 95%: 0.3–1.9, $p = 0.59$).
VT occurred in 4 patients (5.4%) in the cHMP group and in 7 patients (5.9%) in the eHMP group. Adjusted OR: 1.1 (CI 95%: 0.3–3.9, $p = 0.89$).
There was no cases of PNF.
Conclusions: We did not find any differences in outcomes between cHMP and eHMP preserved grafts. eHMP could be enough to get acceptable outcomes in ECD grafts. This could minimize the costs of machine transportation.

POS210 DELAYED MACHINE-PERFUSED KIDNEY IMPLANTATION IN COMBINED LIVER AND KIDNEY TRANSPLANT: EARLY SINGLE CENTER EXPERIENCE

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Background: Data regarding the feasibility and efficacy of delaying the kidney transplant (KT) as a part of the combined liver and kidney transplantation (CLKT) are currently emerging.
We report our preliminary experience in delayed machine-perfused kidney implantation in CLKT.
Methods: A retrospective analysis was performed in all 29 adults who underwent CLKT at our centre between 2003 and 2020. Kidneys were preserved by cold-static storage until 2018 and perfused via hypothermic pulsatile machine perfusion from 2019. We compared outcomes of 21 patients (72.4%) who underwent simultaneous KT during CLKT (sCLKT) with 8 patients (27.6%) who received delayed machined-perfused KT (dCLKT).
Results: Median follow-up was 16.5 months (IQR:1.97–92.2). Median lab-MELD score was 22 (IQR:21–24) for sCLKT, and 21 (IQR:16.5–24) for dCLKT ($p = 0.276$) respectively. A large percentage of dCLKT recipients had polycystic liver disease (PLD) as primary diagnosis (75% vs 28.6%, $p = 0.038$). As expected, median kidney CIT was significantly longer for dCLKT recipients (52.85h vs 10h, $p < 0.001$). Perioperative data demonstrated a greater median requirement for packet red blood cells (11 vs 4, $p = 0.05$) and fresh frozen plasma (18 vs 3, $p = 0.008$) in sCLKT patients. Median intensive care unit length of stay (LOS) and hospital LOS were not statistically longer in sCLKT (12d vs 7d and 31d vs 28.5d respectively).
The median CCI was not statistically greater in sCLKT (49.85 vs 38.2). The rate of kidney DGF was 6/21 (28.6%) in sCLKT, but no DGF was observed in dCLKT.
In sCLKT 5 patients (21%) showed renal allograft futility (RAF) (death or continued need for haemodialysis within 90d posttransplant) but none of the dCLKT recipients showed RAF.
Patient, liver, and kidney survival were greater in dCLKT at 1-year post-transplantation, although the difference was not statistically significant (figure1).
Conclusions: All strategies to avoid kidney allograft futility in CLKT should be evaluated and, if feasible, adopted, especially in patients with PLD with an increased risk of perioperative mortality.
Despite an admittedly short follow-up, the results of our early experience with dCLKT compared to sCLKT seem encouraging.

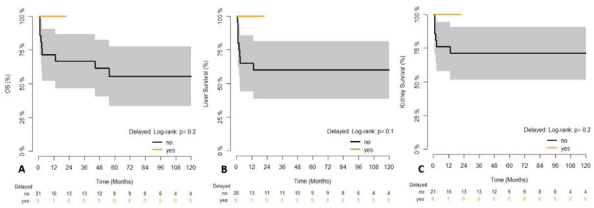

Figure 1. Patient and grafts survival curves in CLKT. (A) Overall survival. (B) Liver graft survival. (C) Kidney graft survival.

POS211 PROTOCOL FOR RECONDITIONING OF EXPANDED CRITERIA DONOR GRAFTS BY EX-SITU OXYGENATED HYPOTHERMIC MACHINE PERFUSION IN DONORS AFTER BRAIN DEATH

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Introduction: Kidneys from Expanded Criteria Donors (ECD) are more likely to develop Delayed Graft Function (DGF). Currently more than 50% of deceased donor transplants in Tuscany region, Italy, come from ECD. The efficacy of Hypothermic Machine Perfusion (HMP) in ECD donors has been previously demonstrated. There is also evidence from animal models and

from the experience with grafts from Donors after Cardiac Death (DCD) that an additional benefit can be achieved with the addition of oxygen (OHMP, Oxygenated Hypothermic Machine Perfusion).
Methodology: We propose a prospective, observational, randomized, multicenter study focusing on the benefit of HMP and OHMP in ECD donors in Tuscany. The 2 kidneys from ECD donors will be randomized one to HMP and the other to OHMP, comparing the HMP arm and the OHMP arm with a retrospective cohort of transplants performed with ECD grafts preserved with SCS (Static Cold Storage). The primary end point will be the incidence of DGF between perfused kidneys and kidneys preserved with SCS, and the secondary end points will be the incidence of PNF (Primary Non Function), renal function (measured with eGFR) at one year, graft and patient survival, length of hospital stay, incidence of acute rejection.
Results: Based on the impact of HMP in previous studies, a reduction in DGF in the recipient population in Tuscany was hypothesized from the current 55% to 30%. According to this hypothesis, to demonstrate a statistical difference between HMP and SCS, a recruitment of about 44 - 50 patients (88 – 100 grafts) was calculated.
Conclusions: Considering the advantages of OHMP on kidney from DCDs, we plan to use this method to improve the long-term outcome of kidney transplants from ECDs.

POS212 KIDNEY TRANSPLANTATION IN PATIENTS WITH CAKUT AND NON- CAKUT CAUSES OF CHRONIC KIDNEY DISEASE: DO THEY HAVE THE SAME OUTCOMES?

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Background: Congenital abnormalities of the kidney and urinary tract (CAKUT) represent the main cause of pediatric end-stage renal disease. However, its contribution to adult chronic kidney disease (CKD) is less well characterized. We here report our experience on adult with CAKUT who underwent kidney transplantation. We compared the adverse outcomes between CAKUT and non-CAKUT patients after KTx.
Methods: We retrospectively reviewed all patients who underwent kidney transplantation (KT) in our center between December2007 and December 2020 (258 patients). Patients were divided into those with CAKUT and those with non-CAKUT as the cause of CKD. Our aim was to compare delayed graft function (DGF) rate, acute rejection, complication's rates, and graft loss between groups.
Results: All KTx performed between 2008 and 2019 were included ($n = 272$). The cause of CKD was CAKUT in 62 patients (22,8%) KTx and non-CAKUT in 210 (77,2%). There was no difference in age between the groups, with a mean age of 32,1 $\pm$ 13,9 years in the CAKUT group and 33,2 $\pm$ 13 years in the non-CAKUT group ($p = 0,594$).
The most common CAKUT-related cause of CKD was primary vesicoureteral reflux (80,6%). In non-CAKUT patients, chronic interstitial nephropathy was the underlying cause of CKD in 34,7%.
Recipients non CAKUT showed male preponderance ($p = 0,027$), were more likely to be seropositive for both CMV and EBV. However, recipients with CAKUT have greater access to a pre-emptive transplant.
For both groups, living donor was more frequent (96,4% vs 94,5%, $p = 0,976$), and there was no difference in cytotoxic PRA (21% vs 19%, $p = 0,695$) or number of compatibilities (2,86 vs 2,98, $p = 0,693$).
The post transplant hypertension was significantly higher in CAKUT recipients than in those with non-CAKUT ($p = 0,002$).
Patients with CAKUT had more Vesicoureteral reflux after kidney transplantation compared to the non-CAKUT group ($p = 0,021$). Compared to non CAKUT-group, CAKUT patients had more urinary tract infection ($p = 0,013$). There was no difference in DGF (10,9% vs 19,6%, $p = 0,278$), Acute rejection (16,4% vs 17,8%, $p = 0,493$) or graft loss (6% vs 6,8%, $p = 0,571$).
Conclusion: Graft survival in CAKUT is favourable ; however, recipients with CAKUT had an increased risk of urinary tract infection.

POS213 CLINICAL EFFICACY OF DUAL-KIDNEY TRANSPLANTATION FROM PEDIATRIC DONORS TO ADULT RECIPIENTS

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Background and Aims: Pediatric-donor kidneys are an important source for expanding the donor pool. With more experience in assessment, improved surgical techniques and refined peri-operative management, dual-kidney transplantation from pediatric donors to adult recipients can achieve good long-term outcomes through rational matching, and therefore increasing the utilization of low age and low weight pediatric donor kidneys. Our center is an early pioneer in exploration and has achieved good clinical outcomes.
The aims of our research were to investigate the clinical efficacy of dual-kidney transplantation from pediatric donors to adult recipients.
Methods: The clinical data of 27 dual kidney transplantations from pediatric donors to adult recipients were retrospectively analyzed. The 1,3,5-year survival rates of recipients and grafts was calculated, the recovery of kidney function after operation and the adverse events were also observed.
Results: The 1,3,5-year survival rates of 27 recipients were 96.2%, 96.2% and 84.1%, respectively; the 1,3,5-year graft survival rates were 88.2%, 88.2%, 77.2%, respectively; the 1,3,5-year death-censored graft survival were 88.2%. One patient died due to acute myocardial infarction, and one patient died due to hemorrhage from duodenal ulcer 4 years after surgery. Three grafts lost function due to thrombosis or ureter stenosis and urinary fistula. The estimated glomerular filtration rates at 1, 2 and 3 years post-transplant were (99.34 $\pm$ 21.78)ml/(min*1.73m2), (103.11 $\pm$ 29.20)ml/(min*1.73m2) and (114.99 $\pm$ 28.55)ml/(min*1.73m2), respectively.
Conclusions: The overall outcomes in adult recipients with dual-kidney transplantation from donations after children 's death is excellent. Choosing proper recipients, standardization of donor acquisition and surgical procedures, and strengthening the perioperative management can improve the long-term outcome of adult recipients, and can be an important way to expand the donor pool.

POS214 ASSESSMENT OF CYSTINOSIS IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS: CASE CONTROL STUDY FROM KUWAIT

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Background: Cystinosis is an autosomal recessive lipsosomal storage multisystem disease characterized by deficient cystenosin that result in cystine accumulation in the lysosomes. It can lead to end stage kidney disease in most of cases before 20 years' age.
We aimed to evaluate the outcome of renal transplantation in pediatric renal transplant with cystinosis.
Methods: Data of renal transplant recipients with Cystinosis ($n = 15$) in Hamed Al-Essa organ transplant center were retrospectively evaluated against matched control cohort ($n = 128$). Demographic data in both groups were compared and post-transplant complications and both graft and patients outcomes were assessed.
Results: Most of cystinosis patients (53.3%) were Kuwaiti males in their second decade of life with their mean age 13.3 $\pm$ 3.9 vs. 68% and mean age of 14 $\pm$ 3.1 years in the control group. The two groups were comparable regarding type of donor, pre transplant comorbidities ($p > 0.05$). The percentage of cystinosis cases with immediate graft function was significantly higher than the control ($p = 0.024$), and this was reflected by relatively lower basal creatinine but did not rank to significance (>0.05), and they received significantly less induction therapy ($p = 0.002$). The two groups were maintained on comparable immunosuppressive regimen and we did not find any significant difference between the two groups regarding post-transplant complications like post-transplant diabetes, viral infections, graft function at 1,3,5,10 years and the both graft and patient outcomes were comparable ($p > 0.05$).
Conclusion: Under standard immunosuppression therapy with steroid calcineurin inhibitors, mycofenolate mofetil, renal transplant is safe with good long term outcome in patient with cystinosis.

POS215 LOVER URINARY TRACT DYSFUNCTION AND TRANSPLANTATION OUTCOME:A SINGLE CENTER EXPERIENCE

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Background: Renal transplantation to patients with lower urinary tract dysfunction (LUTD) remains challenging in the field of pediatric transplantation.
Method: LUTD origin was five (5,6%) out 89 pediatric transplantation recipients since 2006. Videourodynamic tests were performed on all patients

preoperatively, and postoperatively if required. The causes of urological disorders were: Posterior urethral valve (PUV) (n = 3), PUV with a neurogenic bladder (n = 1), and a meningiomyocele plus a neurogenic bladder (n = 1). Continual intermittent catheterization (CIC) was required by three patients for bladder emptying. Three patients received kidneys from deceased donors and two patients received kidneys from living donors (mother and father). All patients underwent calcineurine-based triple immunosuppressive therapy. No patient underwent pre-transplantation augmentation. Only one patient (with PUV and a neurogenic bladder) underwent an augmentation operation during transplantation surgery. We used the Haberal corner-saving suture technique for ureteral stenting combined with ureteroneocystostomic anastomosis.
Results: The mean age at transplantation was 12.2 $\pm$ 1.6 years (10–14 years). The median follow-up duration after transplantation was 101 months (68 to 110 months). Two of the five recipients developed BK virus nephropathy (BK). One of the grafts was lost to BK but the other retained normal functioning. No recipient developed urological or surgical complications after transplantation. Three grafts were lost [BK (n = 1); chronic allograft nephropathy (n = 2)] but the remaining two patients are doing well with median creatinine levels 1.1 mg/dL. The 1-, 3-, and 5-year patient and graft survival rates were: 100%, 100%, 100% and 100%, 100%, 60% respectively.
Conclusion: Renal transplantation in children with a LUTD may yield long-term successful outcomes comparable to those in children with non-LUTD. Because of the high complication rates associated with these transplants, careful evaluation, surveillance, and management of pre/post-transplantation periods are essential to optimize these outcomes.

POS216 KIDNEY TRANSPLANTATION IN CHILDREN: POSTRANSPLANTATION CHALLENGES AND MANAGEMENT. SINGLE CENTER EXPERIENCE

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Aim: Understanding the aspects of transplantation immunology is essential for the personalized management of pediatric renal graft recipients.
Methods: We anlyzed retrospectvely data from kidney transplanted children, between 2013–2019 in Fundeni Clinical Institute, Bucharest.Using Hippocrates, our hospital information program, their post-transplant evolution was monitored for a year checking for post-transplant complications, acute or chronic rejection and transplant-related mortality.The p values were calculated following a paired student T-test. A p-value less than 0.05 was considered statistically significant.
Results: Of the 26 haploidentical patients, there were 20 males and 6 females. The mean age at transplantation was 12 years. The most common diagnosis was congenital anomalies of the kidney and urinary tract in 53%. Of the 26 children, five had an episode of acute or chronic rejection. And of these 5 children with an episode of acute or chronic rejection, 3 were younger children and two older children. There was a statistically significant difference in acute rejection between the 5-year-old and over-5-year-old patients (p = 0.001). Acute rejection was more common in 5-year-olds. Regarding the type of donor (related donor versus cadaveric donor) no statistically significant difference was found in terms of rejection. Instead, there were statistical differences between the type of donor in terms of the rate of post-transplant complications. Surgical complications were more common in cadaveric donor transplantation than in related donor transplantation (p = 0.0001). Detection of anti-HLA antibodies was performed at the time of registration on the waiting list and then after transplantation every three months. All the patients had negative antibodies to class I and class II throughout the follow-up period posttransplantation. No patients died during the follow-up period. Cross-match tests were negative for all patients.
Conclusions: Understanding the clinical features of transplant immunology in children who have received or are about to receive a renal graft is essential for the proper management of post kidney transplantation follow-up. Although our pediatric kidney transplant program is a young program it has had successful patient outcomes.

POS217 A THIRD OF CHILDREN AND THEIR FAMILIES HAD SIGNIFICANT FEAR ABOUT RENAL TRANSPLANTATION DURING THE COVID PANDEMIC

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Background: Current SARS-CoV-2 pandemic has brought a lot of anxieties for patients with end stage renal disease particularly as they were identified as a vulnerable group. Many transplant programmes were closed and reopening brought new concerns for patients and professionals. We report patient experience on receiving a kidney transplant in childhood during pandemic.
Methods: In the first 6 months of reopening of our transplant programme, we transplanted 13 paediatric patients. One patient refused transplant and one lacked social support to proceed with transplant. An anonymous online questionnaire was sent to patients and their families.
Results: All transplanted patients felt that all their questions were answered before the transplant and 85.7% felt well informed about the SARS-CoV-2 effects on transplantation. 57.1% reported feeling nervous, 42.9% were anxious, 28.6% scared and 14.3% felt relaxed about transplantation during the pandemic. The majority of participants reported surgical complications being their biggest fear; only one participant was worried about catching SARS-CoV-2. More than 85% felt that care was delivered safely in inpatient and outpatient setting. 85.7% of participants found shielding easy and important. Overall, 100% of patients were glad to have received a kidney transplant during the pandemic with one patient feeling vulnerable when leaving the hospital.
Conclusions: Receiving a kidney transplant can be a stressful experience, particularly during a pandemic. Our results show that significant number of patients felt scared, that detailed counselling of patients/families about risks and addressing their concerns related to SARS-CoV-2 contributed to a good patient and family experience on transplantation during the pandemic. Further studies are needed to look into the long term effects of the pandemic on this vulnerable group of patients and strategies in addressing the same.

POS218 KIDNEY TRANSPLANTED PATIENTS FROM PEDIATRIC TO ADULT TRANSPLANT CENTRE: TRANSITION DIFFICULTIES AND MANAGEMENT

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Background: Kidney transplantation (KTx) in pediatric ages is successful, leading to optimal patients and graft survival with indication, in adolescent age, to transition toward an adult transplant facility. To date, the transition process of adolescents and young adults with KTx is not well defined. Transfer to a different medical facility is a discontinuation of care and marks a vulnerable phase with an increased risk for non-adherence and allograft failure reported as high as 24%–42% within 3 years after transfer.
Methods: We enrolled patients transited from the pediatric to the adult transplant Centre (2017–2020). Data of KTx, baseline renal disease, post-transplant medications and post-transplant renal function and complications were recorded.
Results: Data of 19 patients (pts) (6 males, 31.6%) were analysed. The cause of renal dysfunction was malformations (10; 52.6%), glomerulonephritis (GN) (5; 26.3%) and genetic syndromes (4; 21.1%). Median age at KTx was 12 years [IQR 10–18]. Median age at transition was 31 years [IQR 30–33].
Seven pts (36.8%) had a history of PTLD. All patients were receiving steroids, 11 pts (57.9%) CyA and 8 pts (42.2%) tacrolimus; only 9 pts (47.4%) were receiving MMF or AZA.
The median follow-up at the adult Transplant Centre was 1 year [IQR 1–2]. After transition, 5 pts experienced complications: 2 pts developed PTLD de novo, 2 pts had a recurrence of native GN after reduction of immunosuppression for PTLD and pregnancies (one pt underwent re-tx), 1 pt experienced an acute cellular rejection after transition to another Centre. The median eGFR slightly decreased from baseline at transition (80 ml/min/1.73m2) to the last follow-up (74 ml/min/1.73m2) (p = 0.127).
Discussion: Our results confirm that transition from pediatric to adult medical care is not a simple process. Several factors linked to the patient and to the kidney have to be considered in the development of post-transplant complications: the long term immunosuppression; infections typical of pediatric ages that may develop in adulthood, such as EBV; the exposure to different immunological stimuli and physiological events such as pregnancies in female patients. Defining effective practices for recipient transition are essential to optimize the KTx patients outcome.

POS219 COMPLEX BENCH SURGERY DID NOT INCREASE THE RISK OF VASCULAR COMPLICATIONS AFTER PEDIATRIC KIDNEY TRANSPLANTATION

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Background: One of the most threatening adverse events after pediatric kidney transplantation (KT) concerns vascular complications, especially bleedings and graft thrombosis. We aimed to investigate whether a complex bench surgery could affect the graft outcome.
Methods: Data from pediatric KTs, consecutively performed from 2015 to 2019 at Padua University-Hospital, were collected. The population was grouped into the following categories according to the complexity of the bench surgery (BS): arterial anomalies, venous anomalies, elongation of the vein and standard BS. Surgical tips about vascular procedures during BS were reported. Outcomes of KT, the overall rate of survival and the rate of vascular complications were reported and compared among the groups.
Results: Eighty KTs, with median age 11 (IQR 4.3–14) years and median body weight 24 (IQR 13–37) kg, were performed. Thirty-nine donor kidneys (49%) needed a complex BS due to anomalies of renal veins in 12 (31%) and renal arteries in 16 (41%). The remaining 11 grafts (28%) underwent an elongation of the vein. There was no difference in the rate of primary graft non function ($p = 0.97$), delayed graft function ($p = 0.72$), overall survival ($p = 0.27$). The rate of vascular complications, including bleedings and venous graft thrombosis was similar (respectively $p = 0.51$, $p = 0.59$, $p = 0.78$). No arterial thrombosis or stenosis was reported.
Conclusions: Complex BS, performed by well-experienced surgical teams, especially by using microsurgery, did not compromise survival of the graft and did not put the allograft at risk of vascular complications, such as bleedings or thrombosis.

POS220 UTILISING THE HEMIAZYGOS VENOUS SYSTEM IN LIVING AND DECEASED DONOR PAEDIATRIC KIDNEY TRANSPLANTATION

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Background: Although kidney transplantation (KT) is the gold standard treatment for children with end-stage kidney disease (ESKD) complex venous anomalies may present challenging surgical barriers.
Methods: Two recipients presented for KT. Preoperative imaging showed inferior vena cava (IVC) or iliac vein occlusion. The left external iliac vein (EIV) and drainage through the left ascending lumbar and hemiazygos system were patent. A multidisciplinary transplant team, was approached for surgical planning.
Results: Case 1. A 14 year old, 58 kg patient presented with severe rejection following a previous living donor KT at the age of 3 years for congenital nephrotic syndrome. Receiving a deceased donor kidney, with a cold ischaemia time (CIT) of 07:35 hrs and a warm ischaemia time (WIT) of 43 minutes and was anastomosed to the leftcommon iliac artery (CIA) and EIV. 3-year post-KT creatinine was 138umol/L (eGFR 46ml/min/1.73m2)
Case 2. An 8 year old,8.5kg patient with ESKD secondary to hypoplastic kidneys presented for KT consideration but had IVC thrombosis (secondary to repeated vascular lines). This patient had the option of a living donor. As the EIV was short and narrow, thesuperior mesenteric vein was considered as an alternative vessel for venous anastomosis (using a deceased donor, blood group compatible vein graft). Recipient surgery was performed first establishing feasibility to proceed with donation. The patient had successful implantation onto the left CIA and EIVwith a CIT of 2hrs and a WIT of 33 minutes. 5 months post-KT creatinine was 50 umol/L (eGFR 99ml/min/1.73m2)
Both had negative thrombophilia screens further treated with 50U/kg subcutaneous heparin, twice a day, until discharge. Thereafter, they were given aspirin.
Conclusion: We demonstrate the successful utilisation of the hemiazygos system for venous drainage in these two KT recipients. We believe a multidisciplinary approach including a liver transplant team is essential for planning.

POS221 PEDIATRIC KIDNEY TRANSPLANTATION: A SINGLE STUDY IN TUNISIA

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Background: Kidney transplantation (KT) is the gold standard for renal replacement therapy in pediatric patients with end-stage renal disease (ESRD). Precise surgical techniques and modern protocols for immunosuppression provide excellent long-term patient and graft survival. The aim of this study is to evaluate the clinical characteristics of pediatric KT and its outcomes.
Methods: We conducted a retrospective study, from 2008 to 2019, including kidney transplant recipients aging below 17 years transplanted in our center.
Demographic data, renal function, rejections, and other complications recorded were noted. Patient and graft survival rates were analyzed.
Results: A total of 259 living donor kidney transplants were done till 2019. Thirty nine (15%) were ≤17 years (56,4% male), aged 7–17 (median 14) years. Cause of end stage renal disease (ESRD) was chronic interstitial nephropathy in 21 patients, Median weight was 52.7 kg [32.8–65.2]. Histories of hemodialysis prior to kidney transplantation were present in 71.1 % of the patients. Three had received a preemptive transplant.
Twenty four (61.5%) donors were female, 14 (35.9%) were mothers. Mean donor age was 42.7 ± 11.3 years.
Overall incidence of hypertension was 46.1%, and diabetes after transplantation occurred in 17.9%.
A total of 51 episodes of infections occurred in these children. Leading were 35 episodes of urinary tract infections, 5 episodes of upper respiratory tract infections, and 4 episodes of gastroenteritis.
Three patients (7.7%) had biopsy-proven acute cellular rejection. One had de novo membranous nephropathy.
Patient and graft survival at 5 year were 92.3% and 89.7%, respectively. One patient died because of Post-transplant lymphoproliferative disorder.
Conclusion: Successful pediatric KT requires a multidisciplinary approach with effective interagency coordination between pediatric nephrologists, urologists, and transplantation surgeons.

POS222 FABRY DISEASE SCREENING IN KIDNEY TRANSPLANT PATIENTS

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Background and Aims: Fabry Disease is a congenital defect of the glycosphingolipid metabolic pathway. Mutations in the GLA gene cause pathological depositions in tissues. Most patients develop chronic kidney disease. The limited number of screening studies in kidney transplant patients have shown that the incidence is much higher than reported. The aim of this study is to determine the frequency of Fabry Disease in our kidney transplant patients.
Methods: 126 patients were included in the study. In male patients, firstly α-GAL-A enzyme activity (by dry blood drop method) was evaluated. GLA gene mutation screening was performed in those with ≤ 2.5 nmol/mL/hour. Since the sensitivity and specificity of the enzyme activity measurement in women were low, mutation analysis was performed directly in the GLA gene.
Results: 89 (70.6 %) of 126 patients were male. The mean age was 48.75 ± 10.24 years and the mean time after transplantation was

10.10 ± 6.78 years. One year prior to the study, a male patient was diagnosed with Fabry Disease [c.264C> G (p.Tyr88)] and enzyme therapy was initiated. Angiokeratomas of the patient's abdominal skin, left ventricular hypertrophy on cardiac imaging and cornea vertisilata on ophthalmological examination were associated with disease. No mutation was found in the mother, father and sister of the case. It was thought that the Fabry-related mutation developed as *de novo*. In another 1 male patient, a-GAL-A activity was detected at the lower end of the reference range. No mutation was detected in the gene analysis. Gene analysis of 1 female patient revealed c.937G> T (p.D313Y) heterozygous mutation. There were no cardiological, ophthalmological, dermatological or neurological findings suitable for the disease. Lyso-Gb_3 level was within normal limits. The disease prevalence determined in our study is 0.79 % (1:126).
Conclusions: Screening studies are extremely important to determine the prevalence of Fabry disease in kidney patients. Some of the multisystemic effects of the disease can be prevented with specific treatments initiated in diagnosed patients. Among the new cases, the rate of individuals who have not yet developed clinical symptoms or life-threatening complications increases. With genetic counseling given to more patients, transmission rates to future generations can be reduced.

POS223 MANAGEMENT OF COVID-19 CASES IN HEMODIALYSIS PATIENTS: A SINGLE-CENTER EXPERIENCE

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Background: Patients with chronic diseases have been shown to have a higher risk for both COVID-19 infectivity and mortality. The aim of this study is to show the management and follow-up strategies, as well as short-term outcomes of COVID-19 in our hemodialysis center.
Methods: Characteristics and treatment strategies of COVID-19 patients who were receiving hemodialysis treatment in our center at the time of infection were examined and a database was formed after adjoining medical records during inpatient care.
Results: As of January 2021, 30 out of a total of 116 hemodialysis patients were diagnosed with COVID-19. 4 of them had intensive care requirements, 3 had received outpatient treatment, and 23 patients have had inpatient care in the COVID unit. The average length of hospital stay was found to be 12,3 ± 6,3 days. The survival rate of COVID-19 in our hemodialysis unit was 90%. Initial symptoms in infected patients were most commonly coughing (63.3%) and dyspnea (66.7%), followed up by fever and gastrointestinal system complaints. Ground-glass opacification (70.0%), thickened interlobular and intralobular lines (50.0%), and pleural effusion (46.7%) were the most common findings in the chest computed tomography (CT) scans.
Conclusions: Hemodialysis patients are considered in the high-risk group for COVID-19. Even as this patient group mostly requires commuting to a health clinic thrice a week, therefore yielding them vulnerable to droplet transmission at the time, they are also constantly under close surveillance by healthcare personnel as they receive renal replacement therapy, enabling prompt diagnosis and inpatient care that led to relatively low mortality rates in this study. Hence, it could be deduced that developing new strategies that protect patients, prevent interpersonal transmission, and augments early diagnosis and treatment in hemodialysis centers is of vital importance.

POS224 RENAL TRANSPLANTATION IN HUMAN IMMUNODEFICIENCY VIRUS (HIV)-INFECTED PATIENTS

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Background: Prognosis of human immunodeficiency virus (HIV) infection improved with the introduction of highly active antiretroviral therapy (HAART), no longer being a contraindication to transplantation (KT).
HIV-associated nephropathy (HIVAN) is the main cause of end-stage renal disease (ESRD) in HIV-infected patients worldwide. Its prevalence in Europe is lower and the main cause of ESRD is glomerulonephritis.
Selection criteria of HIV patients for KT are multidisciplinary: no opportunistic infections; CD4 > 200 cells/L; undetectable viral load.
Methods: Clinical chart review of 14 HIV-infected primary renal allograft recipients (January 2001-June 2019). Inclusion criteria met the American and Spanish guideline recommendations.
Immunosuppressive protocol consisted of tacrolimus, mycophenolate mofetil and steroids (routine practice in Spain). HAART was started in the immediate post-KT period (same regimen in previously treated patients).
Results

Age (median; IQR)	49.0 (14.3)
Male	12 (85.7%)
ESRD aetiology	
Glomerulonephritis	6 (42.9%)
HIVAN	4 (28.6%)
Thrombotic microangiopathy	2 (14.3%)
Interstitial nephritis	2 (14.3%)
Dialysis type	
Hemodialysis	10 (71.4%)
Peritoneal dialysis	3 (21.4%)
Pre-emptive	1 (7.1%)
Co-infection	
P HCV	10 (71.4%)
P HBV	0
CD4 (median; IQR)	458 (666)
Viral load	<1.6 log
HAART	13 (92.9%)
Donor type	
Standard	12 (85.7%)
Expanded criteria	2 (14.3%)
Living donor	0

Two patients underwent early transplantectomy due to venous thrombosis and cortical necrosis. The remaining patients were followed for a median of 61 months (range 3.7–106.2).
Delayed graft function rate: 58.3% (7/12).
Acute rejection rate: 33.3% (4/12).
Median creatinine at 3 months and last follow-up: 1.35 mg/dL (IQR 0.85) and 2.05 mg/dL (IQR 7.16).
Graft survival at 1 and 3 years: 100%, 100%. Patient survival at 1 and 3 years: 100%, 89.9%.
Conclusions: KT can be safe and effective in selected HIV-infected patients in the short and medium term, with patient and graft survival rates similar to HIV-negative recipients.

POS225 KIDNEY TRANSPLANTATION DURING THE COVID-19 PANDEMIC PERIOD: A SINGLE CENTER EXPERIENCE

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Background: Beginning of this year, when the Covid-19 pandemic has first started, it had the immediate effect of severely reducing living and deceased organ donation and transplantation activity worldwide. Our early experience showed that neither hemodialysis nor transplant patients have got infected with Covid-19 higher than the normal population.
While it seems obvious that life-saving transplant activity should not be stopped, it should be tailored with careful selection of both donors and recipients within transparency and considering ethical and legal aspects.
Materials and Methods: With the declaration of COVID-19 as a pandemic, many studies have indicated that elective surgeries including transplantation should be postponed. However, according to our study results, we decided to continue our transplant activities in a controlled manner at our centers located in 3 different cities. From March 1 2020 to December 30, 2020, we performed 69 kidney transplants (58 adults, 11 pediatrics). All recipients were given a routine immunosuppressive protocol. We reviewed the medical records of both recipients and donors, PCR tests have been carried out twice before transplantation, and they were screened with thoracic CT.
Results: Kidney transplants were performed from 67 living related and 2 deceased donors with an average length of hospital stay 8.3 days. Mean serum creatinine values of the recipients were 0.93 mg/dL, 0.84 mg/dL, and

0.76 mg/dL at post-operative day 7, 30 and 90 respectively and all recipients were discharged successfully. Out of 69 kidney transplants, 68 patients are alive with normal kidney function and 1 patient died to due to cardiac problem.
During this period, no patients died due to Covid-19 pandemic, both recipients and donors were discharged successfully. Only one patient has got infected with Covid-19 and has recovered.
Conclusions: Our results show that when precautions are taken, transplant does not pose a risk to patients during the pandemic period. The safety and success of our transplantation activities lies in our newly developed protocol in response to the COVID-19 pandemic.

POS226 ANALYSIS OF FACTORS FOR ENROLLMENT OF HEMODIALYSIS PATIENTS TO THE NATIONAL DECEASED DONOR WAITING LIST

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Background: As of 2020, 86% of those awaiting organ transplantation is made up of kidney transplantation (KT) candidates in Turkey. Although KT is the gold standard in the treatment of end-stage renal disease (ESRD), it is yet to reach an adequate frequency that could fulfill the demand, specifically due to the shortage of non-living donors. The aim of this study is to analyze the views towards KT and enrollment status of hemodialysis patients to the National Deceased Donor Waiting List (NDWL).
Methods: 116 chronic hemodialysis patients receiving treatment in our center were interviewed about their views regarding KT and health-related quality of life. Age, nationality, etiology for end-stage renal disease, NDWL registration, insurance, and refugee status data were retrieved and evaluated from the medical records system. The characteristics of hemodialysis patients were compared using non-parametric statistical methods. A Cox Proportional Hazards Regression analysis model was appropriated to compute potential risk factors for rejecting KT.
Findings: 62 (53.4%) out of the total of 116 patients were found to be registered to the NDWL. The mean waiting duration was 40.4 $\pm$ 52.4 months. Being a refugee was the most common cause for not considering kidney transplantation, making up 20.7% of the unregistered patients, followed up by refusal due to personal reasons with 18.1%, and being previously deemed unsuitable for kidney transplantation with 16.4%. Age was a statistically significant risk factor ($p < .05$). The mean age of the registered candidates was 51,1 $\pm$ 14,8 years whereas it was 59,2 $\pm$ 15,1 for unregistered and reluctant patients.
Conclusion: Refugee status and advanced age, together with the comorbidities it brings, constitute a statistically significant foundation for KT refusal in hemodialysis patients. Education about KT and ensuring follow-ups for these vulnerable groups and their caretakers is of great importance for their health-related quality of life.

POS227 INFLUENCE OF DIFFERENT TRENDS ON RESULTS OF KIDNEY TRANSPLANTS AT A SINGLE CENTER

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Background: The long term follow-up of the initial and later stage of kidney transplants (KTx) program implementation at our Center showed that the conditions of our work were constantly changing. We evaluated the influence of different factors on the outcome of KTx and transplant activities in order to optimize a regional system of transplant services.
Methods: Between April 1986 and January 2021 were performed 735 kidney transplants from deceased (518 - 70.5%) and living (217 - 29.5%) donors. Among all KTx we classified 103 as a high risk (children, diabetics, repeated transplants and other). Modern standard immunosuppressive protocols were provided after surgery.
Results: World progress and own experience of KTx led to the gradual resolution of many issues and improved results. Currently patient and graft survival rates from our Center are similar to those described in great databases. One-year survival of high risk recipients was 92,2 %. The maximum term of satisfactory function of the cadaveric kidney transplanted is more than 31 years. Furthermore, the monitoring continues. The maximum time after kidney transplants in our Center with favorable pregnancy outcomes is actually 11 years. Obviously, that the ensuring of successful living by the recipient of his biological cycle is an achievable goal. However, there is a limitation in the availability of transplants. A significant improvement of the results of kidney transplants, with a paradoxical combination of insufficient transplant activity, causes social tension and requires coordinated actions of politicians, health workers, patients and society as a whole to resolve the conflict that has arisen. The later improvement is related to expanding transplant activities through education and multidisciplinary strategies. Transplantology included in the academic curricula of medical students starting in 2017. Priority for optimization of the Center's work is the improvement of logistics and administrative correction of the regional model of organ donation taking into account demographic, mental, personnel, geographic and other features.
Conclusions: Patient and kidney graft survival defined by personnel professional experience and skills. Level of transplant activity depends on public worldview and administrative support.

POS228 CHILDBIRTH AFTER KIDNEY TRANSPLANTATION COMPARING DIFFERENT DECADES IN THE HISTORY OF OUR UNIT. BUDAPEST EXPERIENCE

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Background: Renal transplantation restores fertility. The heightened maternal and fetal risk is a challenge for nephrologist and obstetrician alike.
Methods: Between 2010–2019 data of all childbirth following kidney transplantation were collected. We compared the results with our previous periods, between 1973–2000 and 2000–2010.
Results: Out of 1688 transplantations 22% were female in childbearing age (15–49 y) and 13 of them had delivery. The median age at transplantation was 27 years and 32 years at birth. Three women gave birth with a second transplant. The average duration of the pregnancy was 35 weeks (28–37.7 weeks).
Immunosuppression was tacrolimus-steroid in 11 cases, cyclosporine-steroid and tacrolimus monotherapy in 1–1 cases.
Se-creatinine values did not rise significantly due to pregnancy and birth. However, the rate and frequency of proteinuria increased significantly around the time of delivery. Average value was 840 mg/l (207–5124 mg/l).
Caesarean section was performed in all 13 cases.
The average weight-age percentile at the time of birth was 6,2% with 2292 g and 46 cm.
The mean hospital stay was 21 days. There were no birth defects, kidney diseases or other abnormalities. The current weight-age percentile of the children is 55,4%.
Conclusion: During the three periods the average age increased from 29 to 30, then 32 years. The time between the kidney transplant and delivery has also increased from 2 to 4 years. The duration of pregnancy decreased from 37 to 35 weeks. The percentage of caesarean sections changed significantly, from 60% to 78%, then 100%. The average weight of newborns was markedly less than their peers. Rejection, graft loss, or birth defects were not observed.
Having children should be advised after 1–2 years of a successful organ transplant with good graft function, at a relatively young age.

POS229 DIGITAL MATURITY OF UNITED KINGDOM RENAL TRANSPLANT CENTRES

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Background: The complexity of care for patients undergoing renal transplantation involves voluminous and heterogenous clinical data, which can be difficult to manage. Information technology (IT) and electronic medical records (EMRs) have the potential to improve this by enabling information sharing and automating administration. However, it is currently unclear how IT supports workflow in transplantation. This study aims to establish the use of IT during transplant referral and determine the level of digital maturity of United Kingdom (UK) renal transplant centres.
Methods: We conducted a telephone survey among transplant coordinators of all 23 UK transplants centres to capture information on local workflow and use of IT. A topic guide was developed based on the National Health Service Digital Maturity Index to include themes on interoperability,

readiness and infrastructure. Results were analysed along the Healthcare Information and Management Systems Society EMR Adoption Model (HIMSS-EMRAM) to provide a score (1–7) for each centre; higher scores reflected more digital maturity.
Results: All centres described comparable workflow with referrals for transplantation from regional renal units in the form of paper letters ($n = 7$), email attachments ($n = 5$) or both ($n = 11$). No centre had a transplant-specific IT solution and thus relied on manual processes to summarise clinical information for decision-making. Most centres had a hospital-wide EMR in place ($n = 15$), however, no centre could readily exchange all necessary clinical data with referral units. This meant that they depended on either paper-based notes ($n = 8$), scanning of documents onto EMRs/shared drives ($n = 8$), or manual transcription of data onto local IT systems ($n = 7$). Transplant departments' HIMSS-EMRAM scores were low (1 ($n = 11$); 2 ($n = 6$); 3 ($n = 6$)).
Conclusions: Clinical workflow and data management across transplant centres is relatively uniform, however IT support is varied and generally of poor maturity, highlighting the need for digital transformation. Key priorities for future solutions include: (1) interoperability of systems across organisational boundaries in line with the regional nature of transplantation (2) specific single-screen views of relevant clinical data to meet the needs of transplant workflow not provided by existing EMRs.

POS230 EXERCISE INTERVENTIONS IN RENAL TRANSPLANT PATIENTS: A FULL REVIEW

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Background: While kidney transplantation still stands as the golden standard in the treatment of chronic kidney disease (CKD), there is an increased frequency of cardiovascular disease in these patients, compared to their healthy counterparts. The goal of this literature review is to study the impact of exercise interventions in renal transplant patients.
Methods: Using the keywords "renal transplant recipient exercise" on PubMed search engine, 334 results came back. After checking the abstract, there were 101 published papers related to the topic. The study of these papers provided 12 more papers as references. Out of these 113 publications, 49 had experimental data.
Results: A variety of researchers have implemented exercise interventions in renal transplant patients. Fifteen aerobic exercise interventions, of various lengths, were performed, improving VO_{2max}, lowering fat mass, normalising creatinine and lipid values and reducing anxiety. Seven resistance training interventions have been performed, improving bone mineral density, glycose control and VO_{2peak}, while stabilising weight and improving quality of life. Finally, eighteen mixed interventions were performed. These mixed interventions have consistently improved VO_{2peak}, heart rate variability, ejection fraction, glomerular filtration rate (GFR), muscle strength and quality of life, while normalizing lipid and creatinine values.
Conclusions: While the implemented exercise interventions have various lengths, intensities, and types, it is evident that exercise can improve the overall health of kidney transplant recipients. Especially mixed exercise programmes, that are more prominent during the last decade, can improve cardiovascular and musculoskeletal health, while upgrading quality of life. It would be interesting for future researchers to use more standardised methods, in order to conclude on the exact attributes of the best-fitting exercise programme for renal transplant patients.

POS231 PROTECTING SURGICAL PATIENTS DURING THE COVID-19 PANDEMIC; ADVANTAGES FROM THE ESTABLISHMENT OF A REGIONAL CLINICAL NETWORK

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Background: The indirect effects of COVID-19 on healthcare have been recognised. Significant increases in cancer deaths are predicted as a result of suspension of routine services. The effect on transplantation is less well characterised. We have previously reported an increase in activity at the Oxford Transplant Centre during the pandemic, aided by location at a COVID-free site. A clinical network (COxNET) has been established between Coventry (CV) and Oxford (OX) enabling the sharing of resources, logistics and improving patient access to transplant. Here, we report how COxNET enabled maintenance of transplantation throughout the pandemic.
Methods: Transplant activity, patient movements and outcome data were collected prospectively 16/02/20 – 01/01/21 and compared to an historical cohort of transplants performed at the same centres 12 months prior and to national activity.
Results: The pandemic cohort consisted of 171 deceased-donor renal transplants. Transplantation in OX continued throughout the pandemic; in CV it was suspended in April 2020 before reactivation of CV wait-listed patients at the OX site. Transplantation resumed in CV in August 2020. 171 DD renal transplants were performed in OX (OX historical $n = 108$) and 10 in CV (CV historical $n = 34$). 38 CV patients were transplanted in OX (historical $n = 16$) and 2 OX patients transplanted in CV (historical $n = 5$). This resulted in continued access to transplantation throughout for CV patients, and minimisation of cold-ischaemia time despite suspension of overnight operating (13h53 pandemic vs 12h47 comparator). There were no cases of in-hospital COVID transmission in this cohort, aided by robust screening measures (4 cancellations due to CT chest appearances; 2 further with positive swabs once rapid testing became available). Patient and graft-specific outcomes have been maintained (patient survival 98.8% 2020 vs 96.3% 2019 as of 01/02/21; 3-month eGFR 48 vs 49 ml/min/1.73m^2).
Conclusions: Regional clinical networks can facilitate exchange of expertise and sharing of resources. This enables at least one site to continue working in situations such as pandemics or disasters, to the benefit of patients throughout the network. The flexibility and resilience imbued by our network has enabled continued access to transplantation despite a major global stressor.

POS232 A SINGLE-CENTER ANALYSIS OF UNPLANNED HOSPITAL READMISSIONS AFTER KIDNEY TRANSPLANTATION: INCIDENCE, CAUSES AND RISK FACTORS

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Background: Hospital readmission (HR) after kidney transplantation is an important metric for health care quality, which associated with increased morbidity, costs and transition-of-care errors. It is influenced by population demographics and the comprehensiveness of the healthcare system.
The aim of this study was to evaluate incidence causes risk factors associated with HR within the first year after transplantation and its associated outcomes.
Methods: All patients undergoing kidney transplantation at a single center over a ten-year period were analyzed *via* retrospective chart review .A multivariable logistic regression analysis was performed to identify associated factors.
Results: In 86 patients, the incidence of unplanned readmissions within the first year was 68.6% ($n = 59$). The main reasons for HR were infection (33%), renal events (32%), surgical complications (16%), and metabolic disturbances (9%). In univariate analyses, HR was associated with medical history of cardiomyopathy ($p = 0{,}011$;$OR = 6.4$, 95% CI: 5.4–7.54), dyslipidemia ($p = 0.04$; $OR = 4.8$; 95% CI: 1.3–18.5), anemia ($p = 0.011$; $OR = 4.5$, 95% CI: 1.3–15.6), hemodialysis ($p = 0.012$; $OR = 10.462$, 95% CI: 1.355–80.748), and new onset diabetes after renal transplantation (NODAT) ($p = 0.05$; $OR = 3.5$, 95% CI: 1.6–13.88). While independent risk factors were NODAT, hemodialysis vintage and cardiomyopathy. There were no difference in One-year patient survival and death-censored graft survival in HR group and non-HR group but the first one was associated with more graft dysfunction and impaired graft function.
Conclusion: Unplanned readmissions severely affect a patient's physical and mental well-being after kidney transplantation (KT), which is also independently associated with morbidity. Our study showed that risk factors associated with hospital readmission often reflect pretransplant comorbidity.

POS233 EMOTIONAL INTELLIGENCE, PSYCHOPATHOLOGY, AND THERAPEUTIC ADHERENCE IN KIDNEY TRANSPLANTATION DURING COVID-19

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Background: Non-adherence to therapy in transplant patients represents one of the main problems related to the loss of the transplanted organ. Psychopathology aspects and a low level of intrapersonal and interpersonal emotional intelligence with difficulty in managing "change" are associated with an increased risk of non-adherence to medical prescriptions. This study aimed to explore these aspects during a particularly stressful period, such as that of the COVID-19 pandemic.
Methods: We tested 80 kidney transplanted subjects with the Emotional Intelligence Test (EIT) to evaluate emotional capacity in dealing with stressful situations, the Symptom Checklist-90 (SCL-90) for the analysis of possible psychological symptomatology, and the Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS) to evaluate therapeutic adherence.
Results: Individuals with a higher level of education and with more years of transplantation showed greater mental stability ($r = 0.59$; $p < 0.05$; $r = 0.61$; $p < 0.05$). Their level of education negatively correlated with anxious aspects ($r = -0.49$; $p < 0.05$), but positively correlated with depression ($r = 0.67$; $p < 0.05$).
Regarding gender difference, women seem to be less adherent to therapy ($r = 0.56$; $p < 0.05$), while years after transplantation negatively affect correct pharmacological intake ($r = 0.44$; $p < 0.05$). Regarding emotional skills, poor management of emotions negatively affects adherent behavior ($r = 0.54$; $p < 0.05$).
Conclusions: Our study was carried out, during COVID-19 and highlighted difficulties in management of self-perceived emotions and psychopathology aspects that negatively influence individual adaptation processes and therapeutic adherence in post-transplantation. Psychosocial rehabilitation interventions are desirable to plan strategies to strengthen the patient's resources, especially during this pandemic, in order to positively influence final transplant outcomes.

POS234 TIMING AND DURATION OF PRE-TRANSPLANT SCREENING FOR RENAL TRANSPLANTATION: REASONS FOR DELAY AND ROOM FOR IMPROVEMENT?

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Background: Transplant eligibility is assessed via a range of medical examinations. Since patient survival after renal transplantation is significantly improved with a shorter duration of pre-transplant dialysis, it is recommended to start the transplant workup in a timely fashion.
Methods: This study is a retrospective analysis of the chronology of actions taken during the care for patients with CKD stage 5 who were registered on the renal transplant waiting list of the Antwerp University Hospital between 2016 and 2019. We assessed how often patients started the transplant evaluation before they started dialysis and identified potential explanatory factors by multiple logistic regression analysis. We subsequently analysed the time spent on the transplant workup and identified influencing factors by multiple linear regression analysis.
Results: Of the 161 patients included, only 43% started the transplant workup before starting dialysis and only 33% started the transplant evaluation before their first dialysis access procedure. Multiple logistic regression analysis identified the number of hospitalisation days (OR 0.79), language barriers (OR 0.20) and a shorter nephrology follow-up time before CKD stage 5 (OR 0.99) as factors having a significant negative impact on the probability of starting the transplant screening before dialysis. We observed a median screening time of 8.6 months (IQR 5–14). In a multiple linear regression analysis only the number of hospitalisation days appeared significantly related with the duration of the transplant workup.
Conclusion: Transplant screening was often started too late to be completed before the start of dialysis. We should be planning the transplant workup prior or simultaneously with planning the dialysis access procedure and not afterwards. The time needed to complete the workup was also very long. By starting the transplant screening in a timely fashion and reducing the time spent on the screening examinations, we should be able to register patients on the waiting list before or at least at the start of dialysis. We estimate that such an internal audit could be of value for every transplant centre and that we should perform it regularly to permanently monitor our results.

POS235 COUNSELLING ON CONCEIVING: CONSIDERATIONS OF PROFESSIONALS IN TRANSPLANTATION

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Introduction: Pregnancy after kidney transplantation (KT) conveys higher risks of adverse pregnancy outcomes (APO). Guidelines and consensus statements sketch ideal circumstances for pregnancy after KT. Little is known about pre-pregnancy counselling after KT, especially in less ideal situations. Therefore, this study aims to gain understanding of the current status on pre-pregnancy counselling in the Netherlands.
Methods: A cross-sectional survey on pre-pregnancy counselling after KT was conducted between March 2020 and February 2021. This web-based survey consisted of socio-demographic and general questions on counselling, and 5 clinical vignettes were presented. These vignettes were based on known risk factors for APO after KT such as proteinuria, hypertension and poor kidney function. The survey was distributed by email to nephrologists and gynecologists in the Netherlands. Positive versus negative attitudes towards pregnancy after KT were examined per vignette, including factors influencing this attitude and estimation of outcomes.
Results: 57 professionals participated: 20 (35%) gynecologists and 37 (65%) nephrologists. 35 (61%) participants work in an academic hospital. Participants had median experience in KT of 10 years (IQR 12). One third of the participants had no experience in treating pregnant KT recipients. 63% of the participants felt a large responsibility for influencing the decision to become pregnant after KT.
100% consensus on a positive pregnancy advice was only achieved in the vignette with optimal kidney function, good blood pressure and no proteinuria. In the vignettes where only one of these three risk factors were present, the advice on pregnancy was mixed, although the majority was positive. In general nephrologists had a more negative attitude towards pregnancy than gynecologists.
Conclusion: Generally, pregnancy after KT was positively reviewed, even in less ideal situations. Most important factors influencing advice were pre-pregnancy kidney function, proteinuria and blood pressure. Although pregnancy after KT is rare, it is important that woman after KT receive good quality counselling. Therefore, expert opinion consensus statements to inform specialists are needed.

POS236 ENHANCED RECOVERY AFTER SURGERY AFTER KIDNEY TRANSPLANTATION: FEASIBILITY AND PREDICTIVE FACTORS IN THE ERA OF EXTENDED CRITERIA DONORS

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Background: The experience of "Enhanced recovery after surgery" (ERAS) program in kidney transplantation (KT) is limited and there are no consensus or guidelines published. The aim of this study is to evaluate the feasibility and identifying predictive factors for discharge home within 5 according to the ERAS protocol.
Methods: Monocentric retrospective study involving all patients underwent KT from 2011 to 2019. Data of donors, recipients, surgical procedures and post transplantation outcomes were analyzed.
Results: Out of 459 patients [Male:296(64.5%); Age:57(19–77) years] undergoing KT, with median follow-up 41months (1–120), 216(47%); age:57 (19–77) were enrolled in the ERAS group with discharge within 5 days after

KT. These patients were compared with 243(52.9%) patients no-ERAS group (discharge > 5 days). Patients in the ERAS-group were significatively younger [55 years (19–77) vs 58 years (23–74), $p = 0.0029$]. Also, donor age was lower in the ERAS group 53 years (11–88) vs 60 years (15–83), $p = 0.001$]; and 40% of ERAS patients received graft from extended criteria donor vs 51.4% in the comparative group ($p = 0.0191$). Other variables analyzed are comparable between groups without statistically significant difference. Incidence of re-admission after 1 and 3 months after KT between ERAS and no-ERAS group were comparable (15% vs 20%, $p = 0.1425$) and (25% vs 32%, $p = 0.0806$) respectively. Complication rate after KT was similar (19% vs 24%, $p = 0.2578$). Otherwise, incidence of delayed graft function was lower in the ERAS group (17% vs 53%, $p = 0.0001$).
Conclusions: ERAS approach showed feasibility and safety in KT without increasing risk of re-admission or complications after transplantation. ERAS approach should be routinely applicated in all recipients receiving graft from standard donors and early graft function recovery, with excellent recovery for patients and reducing health costs.

POS237 SUBJECTIVE CHANGES IN LOWER URINARY TRACT SYMPTOMS AFTER RENAL TRANSPLANTATION

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Background: Many patients with end-stage renal failure (ESRF) require renal replacement therapy (RRT) prior to renal transplantation (RTX). During this time, the amount of urine is often reduced, leading to changes in the functioning of the lower urinary tract (LUT). After successful RTX, LUT gradually adapts to variable urine volumes. However, in some patients lower urinary tract symptoms (LUTS) develop or worsen. The aim of the study was to determine the subjective changes in LUTS reported by patients after RTX.
Methods: Study included patients who visited the Outpatient Clinic of Nephrology and Renal Transplantation from 12.2019 to 01.2021. They were asked to fulfill 2 Core Lower Urinary Tract Symptoms Score (CLSS) questionnaires, assessing LUTS before and after RTX. Exclusion criteria included age ≤ 18 years, presence of a urinary catheter or stoma, active urinary tract infection, ≥2 RTXs and pre-transplant anuria. Of the 139 patients who completed the questionnaire, 84 met criteria. The Wilcoxon signed rank test was used to compare patients' CLSS score (CLSSs) before and after RTX. LUTS were diagnosed when the patient received ≥ 1 point for a question, with the exception of question 2, where the cut-off point was 2. To evaluate the influence of RTX on the CLSSs the McNemar test was used. Prognostic factors increasing the CLSSs were determined using multivariable generalized linear model (mGLM).
Results: 84 patients (39 Female/45 Male) met criteria. Hemodialysis was the most common type of RRT (84.52%). The mean time of RRT was 21.53 months. The most common LUTS was slow urinary stream before RTX (47.62%) and nocturia after RTX (65.79%). It was shown that the change the CLSSs was not statistically significant. Detailed analysis showed that RTX significantly affected the CLSSs in 3 out of 10 symptoms. In the case of a slow stream and straining, the result increased, and in the case of nocturia, it decreased (Table). In mGLM hemodialysis was found to be an independent factor associated with increase in CLSSs after RTX.

Table Influence of RTX on the CLSSs

Symptom	Before RTX	After RTX		p
		N	Y	
Daytime frequency	N	53	15	0.42
	Y	10	6	
Nocturia	N	35	29	**<0.01**
	Y	9	11	
Urgency	N	47	17	0.17
	Y	9	11	
Urgency incontinence	N	68	10	0.18
	Y	4	2	
Stress incontinence	N	73	5	0.45
	Y	2	4	
Slow stream	N	48	6	**0.05**
	Y	16	14	
Straining	N	64	0	**<0.01**
	Y	16	4	
Incomplete emptying	N	57	16	0.15
	Y	8	3	
Bladder pain	N	74	2	0.45
	Y	5	3	
Urethral pain	N	76	1	0.45
	Y	3	4	

Y – yes; N - no

Conclusions: Patients after RTX often experience LUTS, particularly nocturia. Despite statistically significant changes in the CLSSs for nocturia, slow stream and straining, RTX does not significantly affect overall CLSSs. Hemodialysis is an independent factor associated with increase in CLSSs after RTX.

POS238 ADHERENCE AND PATIENTS´ ATTITUDE TO IMMUNOSUPPRESSIVE THERAPY AFTER KIDNEY TRANSPLANTATION

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Background: Non-adherence to immunosuppression increases the risk of graft loss. We hypothesized that patients who have been on home dialysis modalities have higher kidney health literacy, thus are more adherent with their treatment after transplantation
Methods: 103 incident kidney transplant patients participated in the survey. Patients' attitude was evaluated with the Q-methodology, consisting of statements on issues potentially associated with non-adherence. Factor analysis was applied to uncover patterns in the ranking of statements. The patients also answered the BAASIS and health-related quality of life surveys. We retrieved data on demographics, previous dialysis modality, comorbidity score, number of medications and pills, and graft survival.
Results: 94 out of 103 patients completed the Q sort table. From them, 72 patients provided complete answers and suited to a certain factor, therefor included in the analysis. 26 % have been on home HD, 26% in-center HD and 48% on PD. Mean time elapsed from transplantation to the survey was 4,9 years. We chose 3-factor analysis because differentiated patient´s attitudes the best. All cohorts were similar in terms of age, comorbidities, time on dialysis, graft function, immunosupressives concentrations, and HRQoL. After mean 5,3 years of follow-up, cohort 3 had the poorest graft survival (figure 1) and they were identified by having complains about side effects, worried about rejection, needed more information, felt limitations because of the transplant, sometimes forgot medication, challenged doctor´s understanding. Cohort 3 had significantly the highest number of meds (mean 13,4, $p = 0,007$)) and pills (mean 18,4; $p = 0,027$). Cohort 1 was the most

adherent evaluated with BAASIS. Previous dialysis modality had no impact on adherence
Conclusions: Self-dialysis has no effect on patients' adherence after transplantation. High meds & pills, complains about side effects and insufficient information are related to less adherence and worse graft survival.

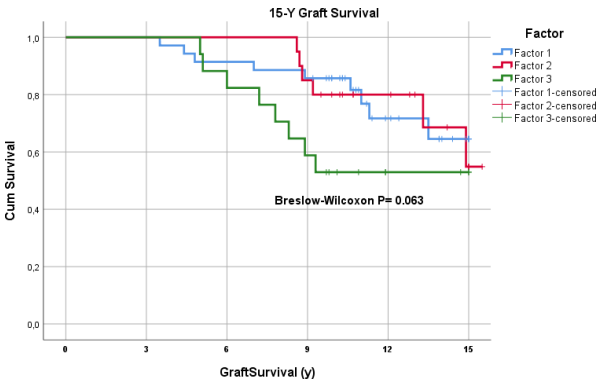

Figure 1

POS239 ESTABLISHING A KIDNEY- PANCREAS TRANSPLANTATION CENTER IN SRI-LANKA-SUPPORTED BY THE ISN-TTS SISTER TRANSPLANT PROGRAM

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Background: The leading cause for chronic kidney disease in Sri Lanka is diabetes mellitus. Currently nearly 2.8 million are diabetic. Approximately 7000 patients are in end stage renal disease and dialysis where more than 40% of those due to diabetic nephropathy. The long-term treatment for most of these patients is a kidney transplant, with better results of renal graft survival if is done simultaneous kidney- pancreas or pancreas after kidney transplant. PT is not well established In Sri -Lanka. The Sri Jayewardenepura General Hospital (SJGH) is willing to establish the first kidney pancreas transplant (KPT) program in the country. To reach this goal, SJGH entered a partnership in 2020 through an ISN-TTS Sister Transplant Centers Program with the University of Barcelona (UB), Hospital Clinic of Barcelona (HCB) and DTI foundation.
Methods: A preliminary study was carried out to evaluate the current practice of the KT and to explore the possibility of establishing a combined KPT program. A specific program on theoretical and hands-on training was designed. An online series of 12 webinars will be conducted during 2021; focusing on deceased donation and PT.
An evaluation tool to assess the learning of the participants will be applied pre- and post-each webinar. Communication channels between the experts of partner centers have been established facilitating rapid consultation and clinical opinions in given cases.
Results: A report was elaborated out of the preliminary study that served as the ground to build further actions. The evaluation tool compiled by specific questions regarding different topics covered in each webinar is created and already on disposal to be delivered virtually.
Conclusions: The collaboration between local and international organization, sharing clinical skills and expertise in KPT much knowledge will be gained facilitating SJGH to become a role model organization in optimizing care for patient in end stage renal failure due to diabetes.

POS240 CONSOLIDATION OF KIDNEY TRANSPLANT PROGRAM IN THE REGION OF MINDANAO (PHILIPPINES) UNDER ISN SISTER RENAL CENTER (SRC) PROGRAM. 5 YEARS' EXPERIENCE

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Background: Chronic kidney disease is the 4th leading cause of death in the Philippines, and the number of patients with End Stage Renal Disease undergoing dialysis has increased to about 40 000; meanwhile the number of kidney transplant (KT) patients is only 500 and only 6% of those performed from decease donors (DD).
Under this background, South Philippines Medical Center (SPMSC) got into engagement with- DTI foundation, the University of Barcelona, Hospital Clinic of Barcelona (HCB) in the ISN-TTS Sister Transplant Centers Program aiming to maximize the odds of prompt donor identification, referral, and management to lead in efficient organ retrieval and successful transplantation.
Methods: Actions were focused on: engaging experienced collaborating institutions to support and train the health care professionals; align the procedures of OD program in SPMC with the national standards; designing a program for professional and public education; establishing SOP and follow-up protocols for KT; training physicians and staff in the identification and management of potential donors, and faculty and staff to organize, lead, and operate a hospital-based organ procurement organization.
Results: 203 professionals were trained in different modalities; internships at HCB were made and online trainings are being performed since June 2020. A kidney transplant symposium was done in December 2018.
Awareness campaigns were organized at regional and national level. The in-hospital activity has been improved. The number of referrals increased from 2 in 2016 to 389 in 2019.The first effective DD was performed in December 2019; 2 kidneys and cornea were successfully transplanted.
Conclusions: The collaboration between local and international organization, proper trainings, awareness, protocolized and structured hospital clinical activity are necessary for the improvement of D&T program. Sustainability and leadership by hospital administration, governmental agencies are continuously needed.

POS241 DONOR BLOOD TYPE O IS A RISK FACTOR FOR BK POLYOMA VIREMIA IN KIDNEY TRANSPLANT RECIPIENTS

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Background: There is a well-known correlation between blood types and susceptibility to certain viral infections. In this study we sought to investigate whether there is an association between the blood groups of the kidney transplant recipient and donor and BK Polyoma viremia.
Patients and Methods: This is a retrospective study using the Rabin Medical Center transplant registry and the serum and urine *quantitative* PCR BK Polyoma results that were collected monthly during the first six months and every three months thereafter during the first year following kidney transplantation. Uni and multi-variate analysis was used in order to test the correlation between the blood groups of the kidney donor, the recipient and BK viremia.
Results: 708 consecutive kidney transplant recipients transplanted between 1/1/2015 and 1/5/2019 were included in the study. During the follow-up period, 139(19.6%) patients had BK viremia. By Cox analysis, blood group O of the kidney donor was associated with an increased risk for BK viremia by univariate (HR 1.83, 95% CI 1.26–2.85, $p = 0.001$) and multivariate Cox analysis (HR 1.69 for O type donor, 95% CI 1.15–2.48, $p = 0.007$). Non-O recipients transplanted with O donors had a significant risk compared to non-O recipients with non-O donors (HR 1.82, 95% CI 1.04–3.18, $p = 0.034$)
Conclusions: There is an association between donor blood type O and the risk of BK Polyoma viremia . Additional studies in additional patient populations are needed for the generalization of these finding.

POS242 TRANSPLANT IN TIMES OF A SARS-COV2 PANDEMIC, EXPERIENCE IN REFERENCE CENTER PUBLIC HOSPITAL IN MEXICO

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Introduction: The new coronavirus disease 2019 (COVID-19) had an impact on the health system worldwide after being declared a pandemic, causing the stoppage of solid organ transplants in various countries. In Mexico, once the pandemic was declared, the National Transplant Center for government proclaimed the cessation of activities at the national level, continuing for the following 6 months.
Material and Methods: Retrospective cohort, included transplant patients at Hospital General de Mexico, from January 2020 to January 2021, with follow-up for a period of 3 months. Descriptive statistics were performed.
Results: 9 patients with deceased donor Kidney Transplant were included, mean age 31.32 ± 7.8 years, 60% male, the main cause of Kidney Disease was undetermined in 77.7%, one of glomerulate basal membrane, and one with nodular diabetic glomerulosclerosis. One patient with preformed DQ7 ADEs, all receive induction with Thymglobulin, and maintenance with triple scheme. During the follow-up there was one hyper acute rejection secondary to non-HLA humoral rejection plus venous thrombosis due to protein S deficiency, a second patient presented an event of acute kidney injury AKIN3, secondary to gastroenteritis due to C. difficile, with complete recovery, the 3rd patient presented Hypovolemic shock, secondary to sub aponeurotic hematoma. 44.4% of patients presented delayed graft function, with stable renal function during follow-up.
Conclusions: During the pandemic, kidney transplantation was safe in our center, compared to keeping patients with replacement therapy with improvement in quality of life and mortality. No cases of receptors with COVID -19 disease was found.

POS243 CALM AFTER THE STORM: RESUMING TRANSPLANTATION SAFELY AFTER PEAK OF FIRST WAVE PANDEMIC

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Background: Combination of muli-morbidity, prior organ failure and thraputic immunosuppression makes renal transplant recipients extremely vulnerable group in the face of COVID-19 pandemic.
We aimed to assess the outcomes of the acute transplants performed after the resumption of activity in the face of new safety measures.
Methods: 50 consecutive kidney transplants done from April 2020 to December 2020 (immediately following the peak of pandemic in London), were compared with 50 consecutive transplants done after April 2019 at the Royal London hospital. Both live and deceased donors were included in the study. Detailed clinical donors and recipient parameters, preoperative and post operative course were studied.
Results were analysed using SPSS version 26.0
Results: Recipient demographics were similar in both cohorts. Donors in 2020 were younger (44.6 yrs) compared to 2019 group (48.2 yr) .8 kidneys from the extended donors were transplanted in 2020 group compared to 15 kidneys in 2019 group (*p* value). One patient in 2020 transplant group had anti-thymocyte globulin (ATG) induction compared to 8 patients 2019 group (p). was this change in induction policy per protocol or changed due to covid? need to give av cr, dgf rates and graft and pt survials in one sentence
Higher number of extended donors were accepted in 2019 compared to 2020.This reflects causious approach at the time of accepting kidney offers during COVID pandemic.Statistically significant difference in ATG induction is due to fear of heavy immunosuppression during COVID and lack of experience in the 1st wave.Because of increased donor scrutiny in 2020, there was lower incidence of delayed graft function compared to 2019 group *p* value. One patient broke shielding protocol and contracted mild COVID-19 in 2020 group.
Conclusion: Present study shows that transplant centres can continue to have safe and successful transplants by adhering to strict testing, modifying patients pathways, patient and staff education stringent scrutiny of donor offers.Continuing experience with more transplants will only inform us more of how best to adapt transplantation to ensure safety while resuming high risk trnasplants.

POS244 CALM AFTER STORM-RESUMING TRANSPLANTATION SAFETY AFTER PEAK OF FIRST WAVE PANDEMIC

Vikrant Thakur, Laura Clementoni, Benjamin Lindsey, Vassilis Hadjianastassiou, Rajesh Sivaprakasam, Raj Thuraisingham, Minahi Ilyas, Olga Manolitsi, Ravindra Rajakariar, Muhammad Khurram, Ismail Mohamed
Royal London hospital, London, United Kingdom

Background: Combination of multimorbidity, prior organ failure and therapeutic immunosuppression makes renal transplant recipients extremely vulnerable group in the face of covid 19 pandemic.We aim to access the outcomes of the acute transplants performed after the resumption of activity in the face of new safety meaures.
Methods: 50 consective kidney transplants done from April 2020 to December 2020 immediately following the peak of pandemic in London were compared with 5o consectives transplants done after April 2019 at the Royal London Hospital.Both live and deceased donors were included in the study.-Detailed clinical profiles of donors and recipients parameters, preoperative and post operative course were studied.Results were analysed using SPSS version 26.0
Results: Donors in 2020 were younger (44.6 years) compared to 2019 group (48.2 years).8 kidneys from the extended donors were transplanted in 2020 group compared to 15 kidneys in 2019 group (p value < 0.050) .One patient in 2020 transplant group group had anti thymocyte globulin ATG induction, compared to 8 patients in 2019 group.Was this change in induction policy as per protocol or changed due to covid?Higher number of extended donors were accepted in 2019 compared to 2020.This reflects cautious approach at the time of accepting kidney offers during covid pandemic .Stastically significant difference in ATG induction is due to fear of heavy immunosuppression during Covid and lack of experience in the first wave .Because of increased donor scrutiny in 2020 there was a lower incidence of delayed graft function compared to 2019 group *p* value.One patient broke shielding protocol and contracted mild covid 19 in 2020 group.
Conclusions: Present study shows that transplant centres can continue to have safe and successful transplants by adhering to strict testing, modifying patients pathways, patient and staff education, stringent scrutiny of donor offers.

POS245 DOES PRE-EMPTIVE TRANSPLANTATION VERSUS POST START OF DIALYSIS TRANSPLANTATION WITH A KIDNEY IMPROVE OUTCOMES AFTER TRANSPLANTATION?

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Background: Preemptive renal transplantation (PRT), is defined as transplantation before the initiation of dialysis. By avoiding complications associated with dialysis, preemptive renal transplantation offers significant benefits in terms of societal cost-saving. The aim of this study is to measure the outcomes of these patients in terms of death and graft loss rates, and adverse events (infection, cancer, major adverse cardiovascular events).
Methods: 272 renal transplantation (22 PRT, 250 non PRT) recipients were included in our study. Demographic (gender, age), and clinical (comorbidities, adverse effects, graft loss and patient death rates) data were analysed. PRT and non PRT groups were compared.
Results: There was no difference in age between the groups, with a mean age of 35,3 ± 15,9 years in the PRT group and 32,7 ± 13,2 years in the non-PRT group ($p = 0,4$). Diabetes after transplantation rates were similar in the two groups ($p = 0,157$). Cardiovascular diseases rates were 4,7 % and 1,3% in the group of patients with PRT and the group without, respectively ($p = 0,294$). Urinary tract infections were significantly higher in PRT recipients than in those with non-PRT ($p = 0,018$).
There was no significant difference in graft loss at 5 years between the patients with PRT and those without ($p = 0,625$). There was no significant difference in death rate between the two groups ($p = 0.458$).
Conclusion: Avoidance of dialysis-associated comorbidities, diminished immune response, and cardiovascular complications are the main benefits of PRT.

POS246 TIME DEPENDENT BLOOD EOSINOPHILIA COUNT CORRELATE WITH WORSE IMMUNOLOGICAL OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS

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Background: There are growing evidences that type 2 immunity effectors (immunoglobuline E, eosinophils, mast-cell/basophils) play a role in auto-immune disorders but also in solid organ transplantation. The aim of this study was to evaluate the impact of blood eosinophil count (BCEo) during follow-up of kidney transplanted recipients with a stable graft function at 3-months on immunological outcome.
Material and Methods: We performed a survival analysis (cause specific Cox model) between the occurrence of immunologic events (transplant rejection and/or the appearance of *de novo* DSA) and time dependent variation of BCEo on a retrospective cohort of 1013 kidney transplanted patients in which common causes of increase in BCEo were excluded. The cause-specific Cox model was performed considering BCEo, Calcineurin inhibitors and systemic corticoid at each measurement as time dependent explicative variables.
Results: Our data showed that BCEo > 0,3G/L was associated with a 2-time higher risk of immunological event and 3-time higher risk of rejection during follow-up independently of immunosuppressive regimen.
Conclusion and Clinical Implication: Our data revealed that BCEo > 0,3G/L threshold could be an interesting and routine biological maker to monitor for immunological outcome along with other routine parameters (serum creatinine, proteinuria, DSAdn) in kidney transplantation at steady state (ie. 3 months after transplantation) after eliminating common causes of BCEo increase (PTLD, allergy/atopy, parasitic infections, drug induced hypersensitivity). These observation thus clearly open new perspectives and directions. Not only they clearly suggest that eosinophil count may be of clinical relevance when detected in blood as surrogate markers of rejection but they also raise the question of the involvement of eosinophils and type 2 immunity in kidney rejection.

POS247 RAPID VS. LATE RE-TRANSPLANTATION FOR EARLY KIDNEY GRAFT LOSS

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Background and Aims: Early graft failure (EGL) is a devastating kidney transplant complication. These patients have of up to 12 times a higher mortality risk than patients with grafts surviving beyond 30 days. Moreover, their cPRA can increase if they become sensitized to the failed graft. The issue is that the measurement antibodies to the donor's HLAs may not be reliable until several weeks after transplantation. Thus, if rapid re-transplantation occurs, the recipient's immunological status will remain uncertain, theoretically increasing their immunological risk and potentially reducing the new graft's survival.
Methods: We performed a retrospective observational study of re-transplanted EGLs (defined as graft loss before 30 days from transplant) between January 1977 and November 2019 in our centre and analysed the outcomes of rapid re-transplantation (within 30 days of EGL) vs late re-transplantation (beyond 30 days).
Results: There were 82 re-transplants after EGL. Their median patient survival was 32 years with 8 patients dying within the first year and with a death censored graft survival of 89% both at 1 and 5 years after re-transplantation. There were 73 late and 9 rapid re-transplants with a 5-year death censored graft survival of 69% and 89% respectively. There were fewer deaths in the rapid re-transplantation than late re-transplantation group, but this difference was not statistically significant. There was also no association between the re-transplantation timing and the graft failure risk (HR 0.30 [0.04 – 2.2]). Four rapid re-transplants shared at least one HLA type I incompatibility, and one shared both and HLA class I and class II incompatibility. There were no T-cell mediated rejections (TCMR), and there was only one AMR in the rapid re-transplantation group, whereas there were 6 TCMRs and 15 AMRs in the late re-transplantation group ($p = 0.03$ and $p = 0.4$, respectively).
Conclusions: Rapid re-transplantation appears to be safe and does not entail increased rejection risk, nor it diminishes long-term graft survival when compared to late re-transplantation.

POS248 GENE EXPRESSION ANALYSIS USING QRT-PCR IN THE DIAGNOSIS OF ANTIBODY-MEDIATED REJECTION IN RENAL TRANSPLANT BIOPSIES

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Background: The diagnosis of antibody-mediated rejection (AMR) is reached using the Banff Classification for Allograft Pathology, which now includes gene expression analysis. In this study, we investigate the application of "Increased Expression Of Thoroughly Validated Gene Transcripts/Classifiers Strongly Associated With AMR" as a diagnostic criteria.
Methods: We used qRTPCR for 10 genes associated with AMR on a retrospective cohort of 297 transplant biopsies, including biopsies that met criteria for AMR, even without molecular data (AMR, $n = 27$); biopsies that showed features of AMR, but that would only meet criteria for AMR with increased transcripts (AMRsusp, $n = 49$) and biopsies that would never meet criteria for AMR (No-AMR, $n = 221$). Gene expression levels were transformed using Z-Score normalisation. The sum of these 10 genes Zscores was our 10-gene AMR socre.
Results: A 10-gene AMR score trained by receiver-operator curve to identify AMR identified amongst AMRsusp cases a group with a high score (AMRsusp-high) ($n = 16$) that had significantly worse graft survival than those with a low score (AMRsusp-low) ($n = 33$) (Figure 1). In a Cox regression analysis, the AMR 10-gene score was significantly associated in both univariate and multivariate analysis with an increased hazard ratio for graft loss in the AMRsusp group, but not in the whole cohort. Finally, logistic regression models were performed, and Net reclassification index analysis showed improved risk classification when gene expression was added to histology and serology.
Conclusions: This study provides evidence that use of an AMR gene score may provide significant additive benefit for the prediction of allograft failure in the AMRsusp subgroup.

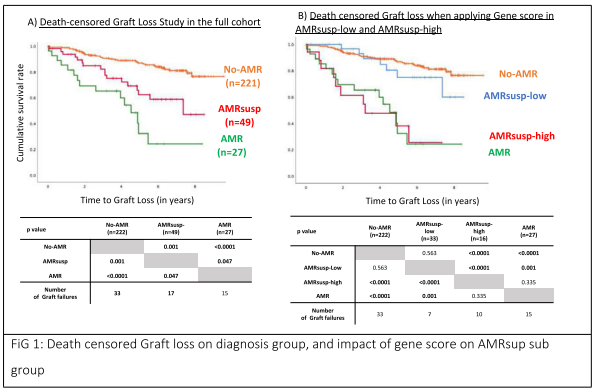

FiG 1: Death censored Graft loss on diagnosis group, and impact of gene score on AMRsup sub group

POS249 IMPACT OF DE NOVO DONOR SPECIFIC ANTIBODY ACCORDING TO THE TRANSPLANT TYPE IN KIDNEY TRANSPLANTATION

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Background: Repeated blood loss, volume overloading or infection according to hemodialysis can increase mortality. For this reason, it has been reported that preemptive living donor kidney transplantation (P-LDKT) has a better prognosis than non-preemptive living donor KT (NP-LDKT) or deceased donor KT (DDKT). However, the impact of de novo donor specific antibody (dnDSA) according to KT type is uncertain.
Methods: We enrolled 1,114 patients performed KT at Keimyung university Dongsan hospital between 1994 and 2020. We investigated the incidence of delayed graft function (DGF), acute rejection within 1 year, risk factors associated with allograft failure, allograft survivals, and the interaction between dnDSA and KT type.
Results: Mean follow-up duration was 131.5 ± 89.5 months. Mean recipient age and HLA mismatched number were significantly higher in the DDKT group than P-LDKT and NP-LDKT groups (47.2 ± 11.9 vs. 41.4 ± 12.7,

41.1 ± 11.1, p <0.001: 3.6 ± 1.7, vs. 3.1 ± 1.6, 3.0 ± 1.6, p <0.001). The incidence of DGF was significantly higher in the DDKT group than P-LDKT and NP-LDKT groups (18.1% vs. 1.4%, 2.4%, p <0.001). There were no significant differences of the incidence of dnDSA, and acute rejection within 1 year among them. Death-censored graft survival rate was significantly higher in the P-LDKT group than DDKT group (p = 0.030), but there was no significant difference between P-LDKT and NP-LDKT group, or NP-LDKT and DDKT group, respectively. Acute rejection within 1 year was an independent risk factor for allograft failure (HR 9.605, 95% C.I. 1.329–69.403, p = 0.025), but not dnDSA. Nevertheless, there was a significant interaction between KT type and dnDSA (p <0.001).
Conclusions: There was no significant difference of the incidence of dnDSA based on KT type, but NP-LDKT and DDKT with dnDSA showed poor prognosis in the allograft survival compared to P-LDKT with dnDSA. Therefore, continuous and rigorous surveillance of DSA needs in the NP-LDKT and DDKT.

POS250 PRE-TRANSPLANT DONOR-REACTIVE IL-21 PRODUCING T CELLS CAN HELP PREDICT PATIENTS AT RISK FOR ACUTE REJECTION

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Background: Pre-transplant screening focuses on the detection of anti-HLA alloantibodies determined by complement-dependent cytotoxicity assay. This strategy, however, does not account for the presence of donor-reactive memory T cells. Previous studies have shown that both pre-transplant IFN-g and IL-21 producing T cells are associated with the development of acute rejection (AR). The aim of this study, was to assess whether pre-transplant donor-reactive T cells and/or B cells are associated with increased rejection risk.
Methods: Peripheral blood mononuclear cell (PBMC) samples from 114 kidney transplant recipients (transplanted between 2010–2013) were obtained pre-transplantation. The number of donor-reactive IFN-g and IL-21 producing cells was analyzed by ELISPOT assay. Patient serum was measured to determine donor specific antibodies (DSA) by Luminex technology before transplantation. The incidence of AR within the first 6 months after transplantation was assessed.
Results: Out of 114 patients, 30 (26.3%) patients experienced one or more rejections within the first 6 months after transplantation. First rejections were scored as 24 TCMR, 3 ABMR and 3 mixed TCMR and ABMR. Numbers of donor-reactive IFN-g producing cells were comparable in patients with or without AR whereas those of IL-21 producing cells were higher in patients with AR (p = 0.03). The presence of DSA was higher in patients with AR [6/30(20%)] compared to patients without AR [5/84(5.9%), p = 0.03]. Multivariate logistic regression showed that donor age (OR 1.06, CI 1.01- 1.10), pre-transplant DSA (OR 5.6, CI 1.2- 25.9) and positive IL-21 ELISPOT assay (cut-off of 37 spots determined by ROC analysis) (OR 2.8, CI 1.0–7.4) were independent indicators of an increased risk for the development of AR in the first 6 months after transplantation.
Conclusions: The number of pre-transplant donor-reactive IL-21 producing T cells is an independent predictor for the development of acute rejection within the first 6 months after kidney transplantation. Additionally, advanced donor age and the presence of pre-transplant DSA were indicators of an increased risk for the development of AR. Our data underline the added value of monitoring pre-transplant donor-reactive IL-21 T-cells for assessment of immunological risk.

POS251 TOCILIZUMAB IN THE TREATMENT OF ACTIVE CHRONIC HUMORAL REJECTION RESISTANT TO STANDARD THERAPY

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Background: There is no consensus on the most appropriate treatment for chronic active antibody -mediated rejection (cABMR). Recent studies suggest that treatment with Tocilizumab (TCZ) may stabilize graft function, decrease the intensity of donor-specific HLA antibodies (DSAs) and reduce microcirculation inflammation.
Methods: Observational study with renal allograft recipients with cABMR (n = 6) who did not response to the traditional treatment based on the combination of plasma replacements, immunoglobulins, and Rituximab. Patients were received TCZ as compassionate treatment in six doses per month (8mg/kg/month). Renal function, proteinuria, histology, and the intensity of DSAs were monitored during follow-up.
Results: Six patients, average age 56 ± 17 years, three male and two re transplants (cPRA average 55%) with preformed DSAs. Treatment with TCZ was initiated within 41 ± 24 days of biopsy. In two cases treatment was discontinued after the first dose, due to severe bicitopenia with cytomegalovirus viremia and graft failure, respectively. In four patients that completed treatment, renal function deteriorated (serum creatinine from 2.2 ± 1.4 to 2.0 ± 0.5 mg/dL, e-FGR 38 ± 16 to 33 ± 13 ml/min), proteinuria increased (2.3 ± 2.8 to 4.6 ± 8.3 g/g) and the intensity of DSAs was stable (Figure 1). No changes were observed in the degree of microcirculation inflammation (g +ptc 4.3 ± 0.8 vs. 4.0 ± 1.0) or in the degree of transplant glomerulopathy (cg 1.2 ± 0.4 vs. 1.8 ± 1.0), or in the interstitial fibrosis/tubular atrophy (ci +ct 2.3 ± 1.4 to 2.8 ± 1.0) (Figure 2).
Conclusions: TCZ therapy does not appear to be effective in modifying the natural history of chronic active antibody-mediated rejection since it does not improve the degree of microcirculation inflammation and does not reduce the intensity of DSAs.

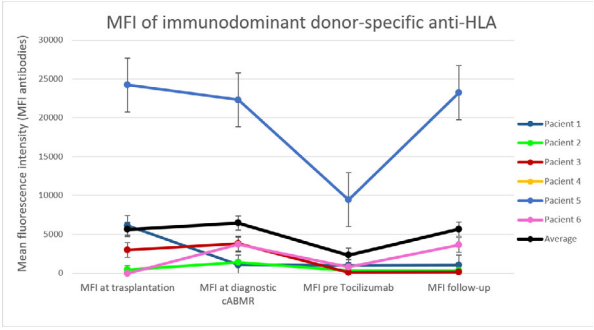

Figure 1. Evolution of the MFI of immunodominant donor-specific anti-HLA the patients included in the study. Patient 4 is not represented in the graph, as it did not develop specific donor antibody.

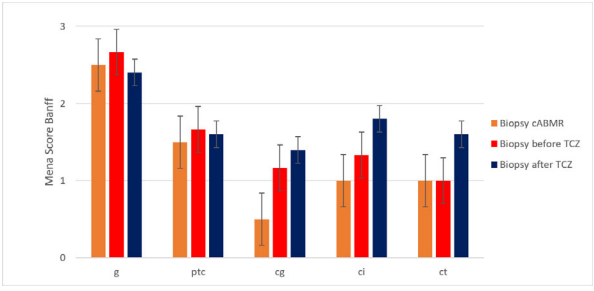

Figure 2. Histology of the biopsies with cABMR, before treatment with TCZ and after treatment with TCZ. G, glomerulitis; ptc, peritubular capillaritis; cg, chronic glomerulopathy, ci, interstitial fibrosis; ct, tubular atrophy; TCZ, tocilizumab.

POS252 CD68+ URINARY CELLS AS A SURROGATE MARKER OF REJECTION IN KIDNEY TRANSPLANTATION AND CLINICAL-PATHOLOGICAL CORRELATION

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Background: Chronic rejection is known to be the main cause of graft loss, the gold standard for diagnosis being kidney biopsy. Proteomics and cell-free DNA researches are giving promising outcomes in finding alternative rejection diagnosis approaches, but they are not yet final. This study is aimed to test if the presence of CD68+ cells in urinary sediment is a marker

of graft rejection. Up to 60% of infiltrating leukocytes in kidney biopsy during rejection are macrophages, with interstitial, perivascular and/or glomerular distributions. Immune-histochemical analysis of urinary macrophages might help to study the possible correlation between CD68 and kidney rejection, in order to use it as a diagnostic tool.
Methods: 166 kidney biopsy performed for cause, from 2011 to 2019, have been analyzed along with the corresponding cytologic tests. Urinary CD68 (total 47/166) presence has been evaluated with urinary cytology through immune-histochemistry.
Results: There is a statistically significant correlation between cellular rejection and CD68 distribution (glomerular $p = 0.006$, interstitial $p = 0.003$, and peritubular $p < 0.0005$). Statistical significance has not been found in the case of humoral rejection (glomerular $p = 0.073$, interstitial $p = 0.24$, and peritubular $p = 0.203$). An association between urinary CD68 and the main histologic diagnosis of rejection (total 125/166) has been excluded.
Conclusions: Macrophages have been confirmed to infiltrate the graft during rejection. The presence of CD68+ cells in the urine, either as a categorical and as a continuous variable does not seem to be accurate enough to diagnose rejection. The results of this study stimulates us to selecting specific effector macrophages differentiation clusters (like CD163, CD14, CD16) to look for an association with rejection.

POS253 BIOPSY FINDINGS AFTER DETECTION OF DE NOVO DONOR-SPECIFIC ANTIBODIES IN RENAL TRANSPLANT RECIPIENTS - A SINGLE CENTER EXPERIENCE

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Background: Development of de novo donor-specific antibodies (DSA) is associated with an increased risk of antibody-mediated rejection and a substantial reduction of allograft survival. We hypothesized that detection of DSA should prompt a biopsy even in the absence of proteinuria and loss of eGFR.
Methods: Single center retrospective analysis on biopsy findings after detection of de novo DSA. One-hundred-thirty-two kidney and pancreas-kidney transplant recipients with de novo DSA detected between 2014 and 2018 were included. Eighty-four of these patients (63.6%) underwent allograft biopsy. At the time of biopsy $n = 50$ (59.5%) had a protein/creatinine ratio (PCR) > 300 mg/g creatinine and/or a loss of eGFR $\geq$ 10 ml/min in the past 12 months, whereas 40.5% did not. Diagnosis of rejection was performed according to Banff criteria.
Results: De novo DSA were detected after a median of 44 months (interquartile range, IQR 3.0–94.3) post-transplant, in those subjects undergoing biopsy. Seventy-seven (91.7%) of the biopsies had signs of rejection (47.6% ABMR, 13.1% cellular, 20.2% combined, 10.7% borderline). Among those subjects without proteinuria or loss of eGFR $\geq$ 10 ml/min/a ($n = 34$), 29 patients (85.3%) revealed rejection (44.1% ABMR, 14.7 % cellular, 11.8% combined, 14.7% borderline). Prevalence of rejection tended to be higher in those subjects with proteinuria or deterioration of eGFR ($p = 0.08$).
Conclusion: The majority of subjects with de novo DSA have histological signs of rejection, even in the absence of proteinuria and deterioration of graft function. Thus, it appears reasonable to routinely perform allograft biopsy after detection of de novo DSA in order to detect subclinical rejections.

POS254 TOCILIZUMAB TREATMENT IN DSA POSITIVE ANTIBODY MEDIATED REJECTION AMONG KIDNEY TRANSPLANT RECIPIENTS

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Background: Pretransplant or de novo donor specific antibodies (DSA) may lead to active or chronic active antibody mediated rejection (a and cABMR) as leading cause of graft loss after kidney transplantation. There is no treatment protocol approved for ABMR. Anti Il-6 tocilizumab (TCZ), inhibitor of DSA production, is a potential approach to stabilize kidney allograft function, however, evidence based results are not available so far. Changes in DSA (MFI) and eGFR during and at the end of treatment period with TCZ were assessed in our single center, retrospective case series analysis.
Methods: In our single center case series analysis, 10 kidney transplant patients with biopsy proven ABMR (aABMR 6, cABMR 4, age 43 $\pm$ 10.5ys, 6 males, time since transplantation 18(2–119)months, 7 first transplant, serum creatinine 224 $\pm$ 80 umol/L at baseline) were studied between January 2017 – June 2019. Total plasma exchange (PE) (5x) was followed by TCZ (8 mg/kg, 1x monthly for 6 months) in case of a and cABMR. Intravenous immunoglobulin (IVIG, 1gr/kg) was added in case of aABMR. Routine laboratory parameters and DSA were reported retrospectively.
Results: 6 aABMR patients completed the treatment protocol. Class I DSA decreased significantly (MFI 4457(635–14084) vs. 877(595–5678); $p = 0.007$), but Class II DSA remained the same during the treatment (MFI 4725 (586–17615) vs. 8097 (671–14636) p = NS). eGFR of aABMR patients and 1 cABMR patient were stabilized. 3 cABMR patients returned to dialysis. Reversible elevation of liver transaminases was detected in three patients. There was no any serious adverse event recorded.
Conclusions: TCZ seems to be effective in reducing Class I DSA and stabilize graft function in patients with aABMR. Further studies are needed to prove the long-term efficacy and the exact role of TCZ in cABMR among kidney transplant patients.

POS255 CD56BRIGHT CD16DIM NK CELLS PRESENT INCREASED PHENOTYPIC ACTIVATION AND PRO-INFLAMMATORY CYTOKINE SECRETION DURING KIDNEY REJECTION

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Background: Circulating CD56^{bright} CD16^{dim} NK cells may play a role during kidney allograft rejection through their ability to release either pro-inflammatory or immunosuppressive cytokines and their potential to induced cytotoxicity depending on specific microenvironment instructions.
Methods: Deep phenotypic analysis of circulating CD56^{bright} CD16^{dim} NK cells using 25-color spectral flow cytometry was implemented in 67 kidney transplant recipients (KTx): (i) 17 donor specific anti-HLA antibody (DSA) free of antibody-mediated rejection (ABMR), (ii) 17 DSA+ biopsy-proven mixed ABMR, (iii) 17 stable free of DSA/rejection, (iv) 16 T-cell mediated rejection (TCMR) and 17 healthy controls (HC). Samples were analysed at the time of rejection, or DSA occurrence, or at matching timepoints in stable patients. Functional assays were performed in 8 patients from each group consisting of 4-hour IL-15 cytokine stimulation or 6-hour cytotoxicity assay against T2 lymphoblastic cells.
Results: The frequency of CD56^{bright} CD16^{dim} NK cells was significantly increased in KTx as compared to HC. An unsupervised clustering analysis revealed a specific cellular cluster uniquely present during ABMR and TCMR. This cluster was characterized by elevated levels of the β chain receptor for IL-2/IL-15 and IL-7Rα, cytokines that promote NK cell survival and activation, and of the activating receptors NKG2D and NKp46. Moreover, this cluster was induced to express the cytotoxic marker CD160, previously described as restricted to activated CD56^{dim} CD16^{bright} NK cells. CD56^{bright} CD16^{dim} NK cells from both ABMR and TCMR patients were functionally more potent, but during ABMR these cells displayed increased polyfunctional (IFN-γ and TNF-α) pro-inflammatory potential in response to IL-15 or during cytotoxicity.
Conclusions: CD56^{bright} CD16^{dim} NK cells display higher activation and pro-inflammatory state during ABMR with high IL-15 responsiveness, cytokine that could potentially be a therapeutic target to mitigate this inflammatory profile of NK cells during rejection.

POS256 RETRANSPLANTATION, A GOOD OPTION IN RECIPIENTS OLDER THAN 65 YEARS

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Background: The number of patient candidates for a new kidney transplant after the graft failure of a previous one has gradually increased. The complexity of retransplantation increases in elderly patients.
Our objective was to analyze the evolution of retransplanted patients aged $\geq$65 years in our center.

Material and Methods: Retrospective study of a series of 258 transplant patients aged ≥ 65 years performed from November-1996 to December-2019. We compared demographics, evolution and survival of a group of patients who received a second transplant (RTx) to the recipients of their first one.
Results: Mean follow-up 55.5 months. In this period, 20 patients (7.7%) received a second graft. Graft failure during the first transplantation was chronic rejection in 12 (60%), vascular thrombosis or primary non-function in five patients (25%), followed by BK nephropathy, late recurrent disease and acute rejection.
In the comparative analysis, we did not observe differences in recipients´ demographics such as age, gender, pre-transplant comorbidity: HTN or DM. Percentage of sensitization was higher in RTx (18.8% vs 3.2%, $p = 0.003$). No differences were found in donor characteristics: age (RTx 64.5 ± 15.9 vs 68.4 ± 11.7 years, $p = 0.21$), HTA, serum creatinine. The percentage of grafts from donors older than 75 years was lower in RTx (4.8% vs 28.7%, $p = 0.01$) and the number of HLA-matches was higher (2.4 ± 0.98 vs 1.8 ± 1.0, $p = 0.04$). No differences were found in DGF or acute rejection. We did not find differences in renal function or in the number of readmissions due to infections. Graft and patient survival were similar in both groups.
Conclusions: In our experience, retransplantation in recipients older than 65 presented similar results as those obtained after the first transplant, with excellent graft and patient survivals in our series. So, retransplantation must be considered as an alternative in selected older recipients with selected older donors too.

POS257 ACUTE HUMORAL REJECTION IN THE IMMEDIATE POST-TRANSPLANTATION IN PATIENTS WITH STANDARD IMMUNOLOGICAL RISK

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Background: The diagnosis of acute humoral rejection (AHR) in the immediate post-transplant phase is increased in high immunological risk patients. However, in standard risk patients this diagnosis could be conditioned by factors related to the donor and the transplant procedure.
Our objective was to find which factors were related to the biopsy-diagnosed AHR in standard-risk patients during the immediate post-transplant period.
Methods: In a series of standard immunological risk patients transplanted from January-2014 to March-2019, we compared those who developed AHR in the immediate post-transplant to patients who did not (no -AHR). High immunological risk patients were excluded.
Results: Of the 271 patients, 13 (4.8%) patients had AHR. In the AHR group, none were retransplanted and 38.5% were women. Twelve donors were brain dead and one was controlled circulatory arrest. Donor Mean age was 68.3 ± 10, and in recipients 61 ± 10 years, cold ischemia time was 16 ± 7 hours. No patient became positive for anti-HLA antibodies. Eight grafts (53.3%) did not work after a mean follow-up of 20 ± 21 months, the causes of failure were: chronic rejection 2, primary dysfunction 4 and one death. Of the 8 patients with graft failure, 3 patients received a second transplant, without post-transplant AHR.
When comparing the AHR group with the non-AHR group, we observed an older age of the donor (68 ± 13 vs 56 ± 18 years, $p = 0.02$) and a history of HT (100% vs 64, $p = 0.008$) in AHR without differences in the age or sex of the recipient, cold ischemia, vascular anastomosis or induction. The AHRs presented more delayed graft function (57 vs 16%, $p = 0.05$) and more thrombotic microangiopathy (38.5% vs 8.9%, $p = 0.01$). Renal function was worse in the AHR group ($p > 0.05$). First year graft survival was lower in the AHR group with no differences in patient survival.
Conclusions: AHR in patients with standard immunological risk had a negative impact on graft survival in our series. However, none of them had positive anti-HLA antibodies and none of the retransplants developed AHR to date. Therefore, non-immunological factors such as older age and the donor's comorbidity could have conditioned the immune activation of the graft and the consequent development of AHR in these patients with standard immunological risk.

POS258 LONG TERM OUTCOMES AFTER ACUTE REJECTION IN KIDNEY TRANSPLANT RCIPIENTS

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Background: Acute rejection (AR) is a common complication in kidney transplantation, it occurs within the first three to six months after kidney transplantation. The aim of this study is to estimate the incidence of AR and to evaluate the clinical outcomes.
Methods: Retrospective data collection of 272 renal transplant recipients over a 12-year period was performed to record presence of AR. Demographic, pathological and clinical data were analysed. 5-year death and graft loss rates were analysed.
Results: Our study included 49 AR episodes experienced by 46 patients (69.6% male, median age 31 years old), including 22 biopsy-proven AR episodes (44.9%), and 17 cellular AR episodes (77.3%). Chronic interstitial nephropathy were the main causes of ESRD (43.5%). Living donor was more frequent (97.8%). Median HLA mismatches was 3 [1.25–4]. The majority of patients had received an induction therapy by thymoglobulin (71.7%). The majority of patients (69.6%) were receiving an immunosuppressive regimen associating Tacrolimus, Mycophenolate Acid and Prednisolone. Pulse steroids were the most commonly reported therapy, used in 30 (65.2%) participants, 6 (13%) received other therapies, including lymphocytedepleting antibodies, IVIG, and plasmapheresis.
As compared with recipients without AR, those with AR were more likely to experience graft loss at 5-year post transplant (7.6% vs 26 respectively with $p = 0.001$). Those with AR experienced higher rates of death (17.4%) ($p = 0.043$).
Conclusion: AR is associated with increased risks of longer-term graft failure and death, particularly death from cardiovascular disease and cancer.

POS259 ROBOTIC LIVING-DONOR KIDNEY HARVESTING. DOES LONGER WARM ISCHEMIC TIME AFFECT THE TRANSPLANT OUTCOME?

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Background: Warm Ischemia Time (WIT) has been proven to be detrimental for graft recovery after transplantation. We herein report the outcome of kidney transplants from living donor according to different WIT in our robotic harvesting setting.
Methods: In our institution, since November 26th 2009, all kidneys harvesting from living donors have been performed using the Da Vinci robot. Different surgical techniques, different surgical teams and different instruments like, for example, the vascular stapler devices have been used. This is the reason why we experienced wide range of WIT. We finally relate the kidney transplant function to the Graft WIT in order to find out if our longest WIT has somehow affected the transplants outcome.
Results: From November 26th 2009 to December 27th 2020 we performed 168 kidney transplants from living donors. WIT varied from 120 to 943 seconds (median 235). WIT has been divided in three different time intervals: A) Tertile: 1) up to 210 seconds (31.8%), 2) from 210 to 260 seconds (35.7%), 3) more than 260 seconds (32.5%); B) Median: less than 235 seconds (49%) and more than 235 seconds (51%); C) Deciles: first 9 deciles <360 seconds (89.2%), last deciles > 360 seconds (10.8%). At statistical analysis we did not find any statistically significant correlation between the WIT of our series and the kidney transplants outcome as far as creatinine at discharge, delayed graft function, acute rejections, thrombosis, urinary fistula, lymphorrea and overall complications are concerned.
Conclusions: Although WIT should be kept as short as possible in organ transplantation, WIT up to 943 seconds in living donor kidney transplant doesn't seem to have any detrimental effect on the kidney recovery after transplantation. This finding can be useful to the surgeon who will not have to rush while staplering perhaps in difficult conditions or in presence of multiple vessels.

POS260 ANALYSIS OF RISK FACTORS AND LONG-TERM OUTCOMES IN KIDNEY TRANSPLANT PATIENTS WITH IDENTIFIED LYMPHOCELES

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Background: One of the most frequently occurring complications after renal transplantation is lymphocele with an incidence of 0.6% to 51%. In fact,

Lymphocele is a significant adverse event, which may cause acute graft dysfunction or venous obstruction. There are no consistent risk factors reported in literature.
We aimed to analyze incidence, risk factors for lymphocele formation and outcome of post-transplant lymphocele.
Methods: We analyzed 86 consecutive renal transplant recipients from 2010 to 2019. All recipients had undergone protocol screening ultrasound scan at first week after surgery and 3 months post-transplant. We analysed risk factors for lymphocele formation. Comparison between lymphocele and no-lymphocele groups was made with linear logistic regression analyses.
Results: Fifteen of 86 (17.4%) transplant recipients developed lymphocele on average 30 days after kidney transplantation (extremes: 30–330 days). The diagnosis was done before 3 months in 10 patients (66.7%) and between 3 months and 1 year in 5 patients (33.3%). Fourteen recipients (93.3%) were asymptomatic, while ipsilateral lower limb lymphedema was the mode of discovery in a single patient (6.7%). Treatment was required in four patients: Sclerotherapy was used in 3 recipients and sclerotherapy with percutaneous drainage was performed in one patient.
Unifactorial analysis identified six predictive factors related to the incidence of lymphocele. They were the age of the donor ($p = 0.011$), the duration of warm ischemia time greater or equal to 40 minutes ($p = 0.007$), acute rejection ($p = 0.010$), peritoneal dialysis ($p = 0.032$), immunosuppressor treatment with Cyclosporine ($p = 0.019$) and Calcineurin Inhibitor Toxicity ($p = 0.015$). The independent risk factors significant in multifactorial analysis were acute rejection and duration of warm ischemia.
Renal function was comparable between no-lymphocele and lymphocele group at one year. But lymphocele group had more infectious ($p = 0.031$) and surgical ($p = 0.000$) complications within the first year post tranplantation.
Conclusion: Our study shows that a better management of surgical procedure and immunosuppressant treatment would be associated with fewer incidences of lymphoceles and better renal transplantation outcomes.

POS261 RETROSPECTIVE AND DESCRIPTIVE STUDY OF INCISIONAL HERNIA PREVALENCE ON KIDNEY TRANSPLANT AND RISK FACTORS ASSOCIATED

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Introduction: Incisional Hernia (IH) incidence is stablished between 5% and 18%. This high incidence rate is caused by many factors as surgical incision placement, immunosuppressants use, and all comorbidity associated to terminal kidney disease. In addition, IH reparation is complex due to anatomical and functional factors, and it makes necessary a review of factors which could avoid the apparition of IH.
Objectives: To discover actual IH prevalence on patients with Kidney Transplant (KT) and to analyze different variables which could influence on its apparition.
Material and Methods: Retrospective and descriptive study on KT patients in our Medical Center between 2016 and 2019 with 2 years tracing. Analysis of different variables described on literature which could be related to IH.
Results: 130 transplant patients were analyzed. All of them were subjected to pararectal Gibson incision approach and surgical closure was made with Vicryl® suture in more than 95% of patients. Immunosuppression regimen included tacrolimus, mycofenolate mofetil and prednisone. Most frequent complications were Urinary Tract Infection (16.7%) surgical site infection (13.3%) and hematoma (9.2%). Patients were followed up for a mean of 32.86 months and clinical IH prevalence was 12.5% and it rose to 25.5% in the subgroup of patients who underwent CT scanning due to any other reason. On multivariant analysis the following risk factors were identified: hospitalization, surgical site infection, surgical reoperation, and urinary leak.

	Hazard ratio	95% CI	*p*-value
Hospitalization duration	1.020	1.003–1.038	0.023
Surgical site infection	6.262	1.952–20.081	0.002
Surgical reoperation	3.558	1.115–11.353	0.032
Urinary leak	7.820	1.729–35.360	0.008

Conclusions: IH prevalence reached 25.5% and they were related to surgical complications occurrence. As it has been demonstrated in midline laparotomy, prophylactic mesh use at surgical closure could be valuable and merits prospective investigation.

POS262 THE EVOLUTION OF LIVING DONOR NEPHRECTOMY PROGRAM AT A HELLENIC TRANSPLANT CENTER. LAPAROSCOPIC VS OPEN DONOR NEPHRECTOMY: SINGLE-CENTER EXPERIENCE

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Background: Laparoscopic nephrectomy has emerged as the preferred surgical approach for living donor nephrectomy. As it is an elective operation on otherwise healthy individuals, it is imperative to ensure appropriate preoperative risk stratification and anticipate intraoperative challenges. Aim of the present study was to compare outcomes of living kidney donors (LD) who had undergone laparoscopic (LDN) and open nephrectomy (ODN).
Methods: Data from 252 LD from a single transplant center from March 2015 to December 2020 were analyzed retrospectively. In total, 117 donors in the LDN and 135 in the ODN group were assessed. Demographics, type of transplantation, BMI, duration of surgery, length of hospital stay, peri- and postoperative complications, renal function at discharge and QoL were recorded and compared between the two groups.
Results: There was no difference in baseline characteristics, nor in the prevalence of peri-and postoperative complications (16%, mostly minor). Duration of surgery was significantly longer in the ODN group (240 vs 160 min in LDN, $p < 0.01$), warm ischemia time was longer in the LDN group (6 vs 2 min in ODN, $p < 0.01$) and length of hospital stay shorter in the LDN group (3 vs 7 days in ODN). Conversion rate from laparoscopic to open surgery was 2.5%. There was a drop in eGFR at discharge of 36 ml/min in the LDN and 32 ml/min in the ODN group respectively ($p = 0.03$). No death, readmission or reoperation were recorded. There was a significant difference in favor of LDN group for all eight items of the questionnaire (SF1-SF8). While the total physical component summary (PCS) score was comparable between the two groups (57.87 in the LDN and 57.07 in the ODN group), the mental component summary (MCS) score was significantly higher (62.14 vs 45.22, $p < 0.001$) in the LDN group.
Conclusions: Minimally invasive surgery can be performed safely, providing several benefits for the living kidney donor, thereby contributing to expanding the living donor pool, especially in countries with deceased-donor organ shortage.

POS263 ROUTINE ULTRASOUND FOLLOWING TRANSPLANT URETERIC STENT REMOVAL – DOES IT ALTER PATIENT MANAGEMENT?

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Background: Ureteric stent placement in kidney transplantation reduces the incidence of major urological complications. Imaging post stent removal may aid early identification of urological complications that become apparent following stent removal. The aim of this study was to examine the utility of routine ultrasound following stent removal in identifying patients with clinically significant urological complications.
Methods: We conducted a retrospective review of all patients undergoing transplant ureteric stent removal since the introduction of a routine imaging protocol in our centre from October 2019 to January 2021. Patients undergoing ultrasound imaging within 30 days of transplant ureteric stent removal were included. Data were collected on the indication for imaging (routine or urgent/clinically indicated), imaging findings and need for intervention.
Results: 245 patients underwent stent removal during the study period. 200 (81.6%) patients had ultrasound imaging within 30 days of stent removal. 147 (73.5%) patients had routine ultrasound at a median (IQR) of 4 (3–7) days post stent removal. 53 (26.5%) patients had a clinically indicated ultrasound at a median (IQR) of 7 (3–15) days post stent removal. Prompts for clinically indicated scans included graft dysfunction and review of known collections. A clinically significant urological finding requiring intervention was observed in 1 (0.7%) and 3 (5.7%) patients undergoing routine and clinically indicated imaging respectively ($p = 0.03$). The one patient requiring intervention in the routine imaging group underwent nephrostomy insertion 4 months following an initial finding of mild pelvicalyceal prominence that progressed on serial imaging. An incidental, non-clinically significant urological finding was observed in 27 (18.4%) and 13 (24.5%) of routine and clinically indicated imaging respectively ($p = 0.3$).

Conclusion: This single centre study demonstrates that routine imaging post-stent removal results in a significantly low yield of clinically relevant findings and involves unnecessary resource utilisation.

POS264 IMPACT OF PREOPERATIVE ABDOMINAL ADIPOSE TISSUE ON SURGICAL COMPLICATIONS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

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Background: Computed tomography (CT) analysis permitted accurate evaluation of abdominal adipose tissue. We aimed to evaluated whether adipose tissue distribution has an impact on surgical complications after simultaneous pancreas-kidney transplantation (SPK).
Method: This retrospective study included 115 adult patients undergoing SPK between January 2015 and January 2020. Relationships between adipose parameters, including adipose area at umbilical level, adipose volume of pelvic, and surgical complications were investigated. The risk factors for surgical complications were identified using univariate and multivariate analyses. The graft and patient survival rates were compared between surgical complications group and non-surgical complications group.
Results: Postoperative surgical complications were documented in 20 (17.4%) patients, which had a higher BMI, subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT) VAT/SAT total adipose tissue (TAT), visceral adipose tissue volume of pelvis (VATP) and total adipose tissue volume of pelvis (TATP) before surgery. On multiple logistic regression analyses, VAT/SAT>1.016 and SAT>245.93 cm^2 were significant predictor for surgical complications ($p = 0.003$, $p = 0.029$), while BMI was not. Non-surgical complications group had better patients and kidney/pancreas survival rate than surgical complications group ($p = 0.029$, $p = 0.00021$, $p < 0.0001$).
Conclusions: Surgical complications of SPK are better predicted by adipose parameters than by the BMI, especially VAT/SAT and SAT. This study has provided new elements for discussion on the impact of visceral and subcutaneous adiposity in SPK.

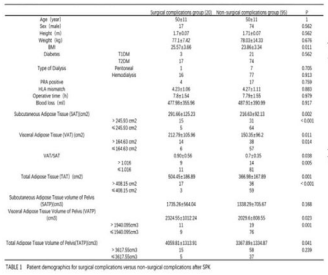

TABLE 1 Patient demographics for surgical complications versus non-surgical complications after SPK

	OR	CI	P
SAT>245.93 cm2	6.681	1.216–36.71	0.029
VAT>164.63 cm2	0.37	0.057–2.407	0.298
VAT/SAT>1.016	11.739	2.249–61.259	0.003
TAT>408.15 cm2	4.349	0.655–28.862	0.128
VATP>1940.09 cm3	0.865	0.187–3.993	0.852
BMI	1.044	0.823–1.323	0.724

TABLE 2 Multiple logistic regression analysis to determine predictors of surgical complications after SPK

Surgical complications	N=20
Pancreatic leakage	3
Intestinal leakage	1
Urine leakage	1
Wound split	4
Intestinal hemorrhage	2
Allograft vascular thrombus	6
Allograft vascular thrombus+Intestinal hemorrhage	1
Intestinal hemorrhage+Wound split+Urine leakage	1
Intestinal hemorrhage+Wound split	1

Table 3 Surgical complications in SPK patients

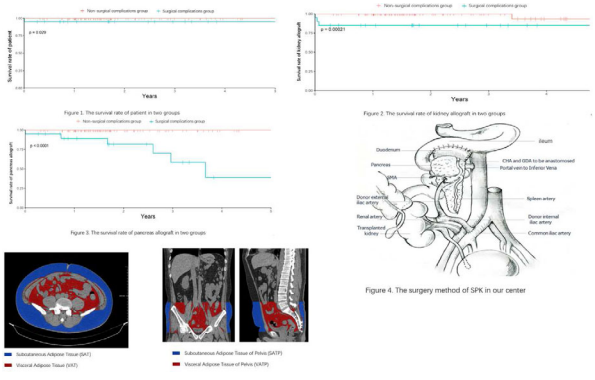

Figure 1. The survival rate of patient in two groups

Figure 2. The survival rate of kidney allograft in two groups

Figure 3. The survival rate of pancreas allograft in two groups

Figure 4. The surgery method of SPK in our center

Subcutaneous Adipose Tissue (SAT)
Visceral Adipose Tissue (VAT)

Subcutaneous Adipose Tissue of Pelvis (SATP)
Visceral Adipose Tissue of Pelvis (VATP)

POS265 PRETRANSPLANT MANAGEMENT OF PATIENTS WITH POLYCYSTIC KIDNEY DISEASE

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Background: Preparation for kidney transplant patients with polycystic kidney disease (PKD) includes resolving a significant number of problems, which has an impact on the outcome. The use of laparoscopy for nephrectomy of native kidneys significantly reduces surgical risks. The aim of this research was to study the results of kidney transplantation in patients with PKD, depending on the pre-transplant preparation option
Methods: In the period from 2003 to 2019, kidney transplantation was performed in 46 patients with renal failure due to PKD. The sample was divided into 2 groups. The study group consisted of 23 patients who underwented polycystic-altered kidneys (PAK) nephrectomy at the pre-transplantation stage. The control group was formed of 23 patients who had PAK preserved at the time of transplantation.
Results: Time period of post-operative observation has been substantially different between study group 3.6 $\pm$ 2.5 years and control group 5.3 $\pm$ 3.08 years ($p > 0.05$). The frequency of episodes of bacteriuria, leukocyturia and (or) hematuria was in the study group 0.24 $\pm$ 0.3 cases per year, in the control group – 1.49 $\pm$ 0.54 ($p < 0.05$). Due to cysts infection or severe pain syndrome, PAK nephrectomy at various times after transplantation was required in 5 (21.7%) patients. 28 (61%) patients with PKD who underwent kidney transplantation had to have their PAK removed for medical reasons during their lifetime. Five-year graft survival in the study group was 84.6%, in the comparison group – 79.8%. Due to the small time of observations, it was not possible to estimate the 10-year survival rate in the study group. In the comparison group after 10-year transplant survival was 46.3%. The study group patient survival was 100%. 5 and 10-year survival of patients with preserved PAK was 87.8% and 73.3% respectively. There was a lethal outcome due to severe sepsis caused by cysts infection of PAK 6 years after transplantation.
Conclusion: More than 60% of patients with PKD need a PAK nephrectomy during their lifetime for medical reasons, including after transplantation on the background of immunosuppressive therapy. Application of the surgical pretransplant preparation of patients with PKD will help reduce the incidence of infectious complications and minimize the risk of kidney transplantation in this category of patients.

POS266 USE OF BOVINE PERICARDIAL PATCH IN LIVING AND DECEASED DONOR KIDNEY TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE ON 14 ARTERIAL RECONSTRUCTIONS.

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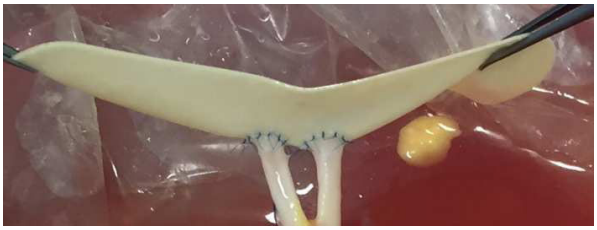
Background: Multiple renal arteries and a donor-recipient vascular mismatch, in the setting of living donor transplantation, or a damaged aortic patch from marginal deceased donors, represent common scenarios for kidney transplant surgeons. Several techniques of vascular reconstruction at the time of bench surgery have been described. Aim of our study was to evaluate the safety and efficacy of bovine pericardium for arterial reconstruction in both living and deceased donor kidney transplants.
Methods: Between April 2017 and December 2020, we carried out at our center 14 arterial reconstructions on back-table using a 9 $\times$ 2 cm bovine pericardial patch, cross-linked with glutaraldehyde, 11 were living donor grafts while 3 were deceased donor grafts. In 8 kidney grafts bovine pericardium was used to anastomose multiple arteries on a single patch, whereas in 6 allografts a single renal artery with a diameter <5 mm was anastomosed to the bovine pericardial patch. All arterial reconstructions were fashioned end-to-side with interrupted 7/0 polipropilene sutures.
Results: At a mean follow-up of 29.4 months (range 5–46) 13 recipients have a well-functioning kidney graft with a mean serum creatinine of 1.3 mg/dL (range 0.8–1.9). One intra-parenchymal kidney thrombosis, without involvement of the arterial anastomosis, happened in our series. No early or late anastomotic arterial thromboses or infectious complications were recorded. One recipient with severe arterial vasculopathy, bilateral common iliac artery stents and thromboendoarterectomy during transplantation, presented 6 months after surgery with a non-significant TRAS (about 50%).
Conclusions: Bovine pericardium appears to be a safe and effective bioprosthetic material for arterial reconstructions in kidney transplantation.

Besides, its implementation as a patch for single small-size arteries of living donor grafts helps to ease the arterial anastomosis in the recipient.



POS267 MECHANIC IN SITU ELONGATION PATCH IN RIGHT KIDNEY TRANSPLANTATION

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Background: One of the difficulties linked to right kidney transplantation is the shortage of the renal vein, which is commonly elongated with an inferior vena cava patch during bench surgery. In a previous article we have presented our technique of in situ elongation during the harvesting, through the cold ischemia period. We propose a further development of the technique, employing a mechanic stapler.
Methods: From January 2018 to December 2020, we have performed a mechanic in situ elongation patch in 8 cases. During the perfusion phase of the harvesting, we have used a three line vascular mechanic stapler to achieve the elongation patch, with an inclination from the lower corner of the left renal vein ostium, up to the upper part of the right margin of the vena cava.
Results: The 8 kidneys procured with this technique have been successfully transplanted and the venous anastomoses have been easily and safely executed, without vascular complications. Moreover, we did not found a higher complications rate or graft loss when compared to kidneys with continuous suture patches.
Conclusions: The use of the mechanic stapler for the extension of the right renal vein during the perfusion allows a faster and safer harvesting, also with a reduction of bench ischemia time and of warm ischemia time. It is not linked to increased risks of complication, however resulting in higher costs. The benefits of this mechanic in situ elongation patch the long period should be further investigated with a greater number of patients.

POS269 INNATE IMMUNE INTERACTION WITH REENDOTHELIZED VEIN SCAFFOLDS

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Background: The limited supply of organs for transplantation and substantial organ discards rates remain key problems in transplantation. Both issues have driven the usage of expanded criteria donor organs. These organs often suffer from poor quality vasculature which is the interface between donor tissue and the recipient immune system. To repair the vasculature of donor kidneys, recellularization of injured blood vessels with healthy endothelial cells (Ecs) could provide a solution. However, whether reendothelized vein scaffolds evoke an immune response has not been explored. This study focuses on how innate allogeneic immune cells interact with extracellular matrix (ECM) scaffolds and recellularized ECM scaffolds.
Methods: Common iliac veins, intended as tool kits, were obtained from liver donors and stored for two weeks at 4°C. After that period, the veins became rest material and could be used for research purposes with written consent from next of kin. The veins were decellularized using Triton-X-100 and Dnase solutions and the resulting ECM was recellularized with Ecs from renal transplant derived veins (Figure 1) and afterwards co-cultured with monocytic THP-1 cells.
Results
Decellularization led to a complete removal of cells and decreased dsDNA content (before 83.8 ± 29.0 after 13.0 ± 6.5 ng/mg). Three days after seeding Ecs on the ECM scaffolds the cells formed a confluent Ecs monolayer. The addition of monocytes to the ECM scaffolds was visualized via immunohistochemistry and confocal microscopy, which showed that THP-1 cells adhere to both the ECM scaffolds and the reconstructed ECM scaffolds in a time dependent manner. Activation of the reconstructed Ecs layer with TNF-α, to mimic inflammatory conditions, mediated an increase in monocyte adhesion. We are currently examining the transmigration of THP-1 cells across the reconstructed Ecs monolayer.
Conclusions: Our findings indicate that both ECM and recellularized ECM scaffolds deploy an innate immune response possibly triggered by the ultrastructure of the ECM of the scaffolds and presence of immunogenic proteins. Further understanding of these immune reactions could bring recellularization techniques closer to clinical use.

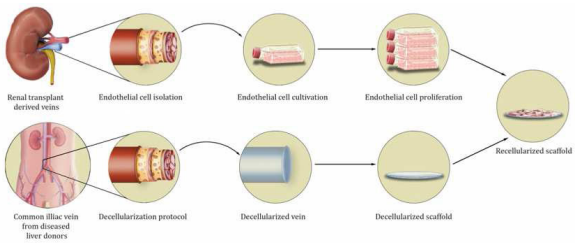

Figure 1 Graphical representation of the human endothelial cell decellularization and recellularization procedure

POS270 POST-TRANSPLANT MALIGNANCY: CLINICAL PROFILE AND RISK FACTORS

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Background: Malignancy in kidney transplant (KT) patients are diagnosed late and presents with mortality and renal graft failure. Identifying patients at risk for malignancy is important for screening, prevention and early diagnosis and treatment. This study determined the clinical profile and risk factors for Post-transplant Malignancy (PTM) among Filipino patients from the National Kidney and Transplant Institute.
Methodology: A retrospective case-control study with 1:2 matched-pair analysis of 78 KT patients with post-transplant malignancies from 1983 to 2018.
Result: The incidence of PTM was highest among KT recipients done during 2000–2009 which accounted for 53.7% of the total cases. Breast, renal and gastro-intestinal malignancies were the most common PTM. No significant difference was seen based on the presence and type of induction and maintenance immunosuppression between cases and controls in PTM development. The odds of having Hepatitis B among cases is 3-fold greater than compared to controls.
Conclusion and recommendation: Seventy one percent were diagnosed within the 1st decade post-KT. Upon diagnosis 48% were already at late stage resulting to 50% mortality within 5 years. Induction therapy, maintenance immunosuppression and rejection treatment were is not associated with increased risk of PTM. A vigilant cancer screening in the 1st 5 to 10 years post-KT regardless of age is advised.

POS271 MALIGNANCY AFTER RENAL TRANSPLANTATION, AN ENTITY THAT MUST KEEP EXPERTS ALERT.

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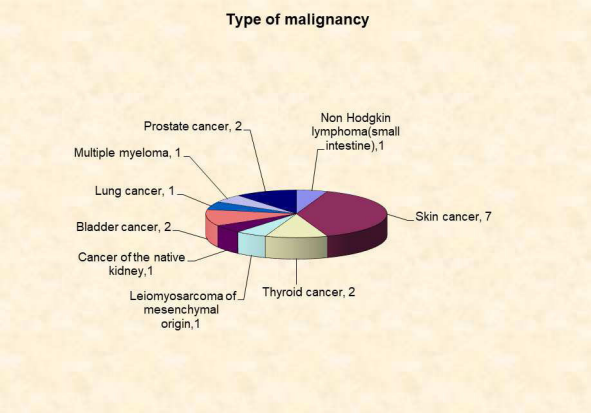
Background and Aims: Renal transplantation is the most common procedure among solid organ transplantations. The high incidence of cancer, which is the second cause of morbidity and mortality in this specific population, is related with certain risk factors, traditional and transplantation-related ones.
The aim of this study is to analyze data from the Transplant Unit at "Evangelismos" General Hospital regarding malignancy after renal transplantation and its relationship with specific risk factors.

Method: A retrospective cross-sectional study was carried out regarding patients who underwent kidney transplantation in our center during the period 2012–2018.
Results: Data were collected from a total of 126 recipients (75% male and 25% female) whose mean age was 50.44 ± 12.17 years. The transplant allograft was from a deceased donor in 75% and from a living donor in 25% of cases. Patients had a mean hemodialysis time of 5.64 ± 4.22 years. Eight percent (8%) of them had a personal history of malignancy and 32.5% had a family history of malignancy. Tobacco smoking included the 45% of patients, while a 11% of them reported sun exposure. An acute graft rejection episode was developed in 12% of patients, whereas in 48% of patients a statin was prescribed and 14.3% had received immunosuppression before transplantation.
Male patients demonstrated a 3.3 times greater probability for malignancy compared to women ($p = 0.162$). For every one year added to a patient's age, cancer probability increases by 5% ($p = 0.054$). Moreover, patients with a cancer family history had 3 times greater probability for malignancy ($p = 0.089$). Furthermore it was found that patients with history of cancer had 15.3 times greater probability of malignancy ($p < 0.001$), whereas patients taking statins demonstrated 4.5 times greater probability of cancer after a kidney transplantation ($p = 0.021$).
Conclusion: Our study confirms the well-known association of age, sex and personal history of cancer with the development of malignancy. Regarding the association of statins with cancer, there are consistent data in the literature. Knowledge about malignancy incidence after kidney transplantation and its relationship with different risk factors provide us with the ability to follow-up and care this vulnerable population with greater effectiveness.

Figure.



POS272 MALIGNANCY AFTER KIDNEY TRANSPLANTATION – A SINGLE CENTRE OBSERVATIONAL STUDY

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Background: Kidney transplantation (KT) provides a better quality of life and greater survival for patients with end-stage kidney disease, making it the preferable treatment. However, it is also associated with a greater risk of de novo-malignancies when compared to the general population, affecting graft and patient survival. Thus, we intended to on-alc the incidence and risk factors of malignancies after KT, and their impact on graft and patient survival.
Methods: Retrospective analysis that included adult patients that underwent isolated KT, between 1983 and 2017 in a transplant department of a single-centre.
Results: In the referred period, 2273 patients, with a mean age of 43.4 ± 12.8 years, underwent KT. During a median follow-up of 11.3 ± 7.8 years, 234 patients developed 270 de-novo malignancies, 88 of those corresponding to non-melanoma skin cancer (NMSC), with an overall incidence of de-novo malignancies of 10.7/1000 patients/per year (95% CI: 9.5–12.0).
The risk factors for developing NMSC were age at the time of transplant, male-sex, immunosuppressive induction therapy including antithymocyte globulin (ATG) and acute rejection in the first year; for the remaining tumors the risk factors were age at the time of transplant and deceased donor, when compared with living donor.
Regarding the types of malignancies post-transplant, the most common were NMSC ($n = 88$), followed by haematological tumors, including post-transplant proliferative disorders ($n = 31$), renal cell carcinoma ($n = 16$), breast cancer ($n = 14$), stomach cancer ($n = 14$), colon cancer ($n = 14$), lung cancer ($n = 13$) and bladder cancer ($n = 13$).
The cumulative incidence of mortality at 3 years is 40.1% in patients with other tumors than NMSC, and is higher than NMSC ($p < 0.001$).
Conclusions: The incidence of malignancy after KT is considerable, being associated with important morbimortality. Awareness of this problem in the posttransplant period, along with timely screening, are crucial in managing KT recipients.

POS273 NO DIFFERENCE IN ASSOCIATION OF SKIN CANCER WITH THE USE OF MYCOPHENOLATE OR AZATHIOPRINE

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[1]University Hospital Coventry & Warwickshire, on-alco, United Kingdom; [2]Coventry University, Coventry, United Kingdom; [3]University of Warwick, Coventry, United Kingdom; [4]University Hospital Coventry & Warwickshire, Coventry, United Kingdom

Background: Renal transplant is associated with increased risk of skin cancer. Renal transplant patients are usually on triple immunosuppression including steroids, calcineurin inhibitors and antiproliferative agent. Of all the risk factors, the use of azathioprine has been traditionally associated with skin cancer. In this study we try to identify if the use of azathioprine is associated with skin cancer.
Methods: This is a retrospective analysis of renal transplant data done at our center from 1st January 1998 to 31st December 2018. We included patients with renal transplant only.
Results: The number of patients included in the study was 862 patients. The incidence of skin cancer was 0.08% ($n = 74$ patients). Skin cancer was more commonly seen in the Caucasian race. Of the 74 patients who developed skin cancer 48 (64.9%) were males whereas 26 (35%) were females. The mean duration for the onset of skin cancer in was 78 months while it was 60 months in the Myocphenolate group and 88 months in the Azathioprine group. The incidence of skin cancer in the mycophenolate group was 12.3% (32 of 261 patients) whereas in the Azathioprine group it was 12.6% (22 of 174 patients). By statistical analysis there is no difference in incidence of skin cancer with the use of mycophenolate versus azathioprine.
Conclusion: This is one of the largest retrospective analysis of single centre data on skin cancer in renal transplantation. The use of Azathioprine is not associated with higher risk of skin cancer. Further randomized controlled trials are required to establish the conclusion of the study.

POS274 DONOR-TRANSMITTED MELANOMA – THE NEED FOR CONTINUOUSLY UPDATED GUIDELINES

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Introduction: Donor-derived melanoma has previously been described in solid organ transplant recipients. Previous SABTO guidelines considered some cancers, including superficial spreading melanomas, to have low risk of transmission. We describe a case of donor-transmitted superficial spreading melanoma which resulted in the recipient's death.
Case presentation: A 50 year old male received a kidney from a 57 year old donor with a history of superficial spreading melanoma (Breslow thickness <1.2 mm, fully excised 8 years prior, and discharged after 5-year cancer free follow up) who died from an intracerebral haemorrhage. Based the SABTO guidelines at the time, this falls under "low risk of cancer transmission" (0.1–2%). Two recipients at another centre received the contralateral kidney and islet cells. 8-months post-transplant, the islet cell recipient was diagnosed with donor-derived melanoma. Our patient was still asymptomatic and management including imaging, immunosuppression withdrawal and graft explant was planned. He was admitted two weeks later with a malignant pleural effusion. He was unfit for a surgical nephrectomy, hence an IR embolization of the kidney was performed. A CT-PET showed FDG uptake in the lungs, liver, left adrenal, and pancreas. Immunotherapy to treat the melanoma was considered, but he was unfit for this and died 1-month later.

Outcome: All three recipients from this donor died of donor-derived melanoma.
Discussion: Donor-transmitted melanoma is a rare complication of organ transplantation. Previous SABTO guidelines for "low risk of transmission" melanoma potentially included melanoma ranging from stage IA to IIIB, and corresponding 10-year melanoma survival probabilities between 98–77%. SABTO guidelines have since been updated to only include pT1a tumours, reflecting the latest evidence. It is important to ensure guidelines are kept updated in line with new evidence.

POS275 IMBALANCE OF RESOURCES, AN HYPOTHESIS FOR A NEW WAY OF ALLOCATING LIVERS NOT USED IN THE DONATION REGION

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Italian National Transplant Center, Italian National Institute of Health, Rome, Italy

Background: Due to the country's shape, liver allocation in Italy has to be managed through national programs, at the macro-area (MA) level: northern (NMA) and southern (SMA). Livers, which are not used by the donation region (DR) are first offered to the regions of the same MA and then to those of the other. The data analysis of these programs has, on several occasions, highlighted an imbalance in the two Mas, in terms of procurement and ability to use existing resources. This study aimed at analyzing the livers not used by the DR and transplanted in other regions, highlighting any imbalances between the two Mas and postulating a better way of distributing the resources.
Methods: All livers not used by the DR but transplanted in the other regions during the 2018–2019 two-year period were evaluated. An overall and per year data analysis was performed: we analyzed the rejection causes, the outcome and the follow-up of the liver transplants performed. The organ flow between the two Mas was also quantified. All data were collected through the transplant information system, the Italian registry of all donation and transplantation activities.
Results: In the study period, 344 livers (150NMA e 194SMA) were not used by the DR. Out of these, 169 (49%, 58NMA e 111SMA) were transplanted in another region. In particular, 11 (19%) livers from NMA were transplanted in the SMA and 37 (33%) from the SMA were transplanted in the NMA. Liver transplants with organs not used in other regions represented 6.8% of total liver transplants in the two-year study period (2498, 1.963NMA/535SMA), in particular 4% of those of the NMA (79 / 1.963) and 16.8% of those of the SMA (90/535).
Conclusions: Livers not used by other regions represent an extra resource, lost by the DR and gained by the transplanting one. A fair distribution of these resources could be obtained by allocating the liver to the patient who would best benefit from the transplant, on a national list.

POS276 EVOLUTION OF WAITING LIST FOR LIVER TRANSPLANTATION OVER 20 YEARS IN ONE SINGLE CENTRE IN ROMANIA

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Background: In 2000, the first successful LT (with whole graft) was carried out by the surgical team led by Professor Popescu, followed by the first living donor liver transplantation (LDLT) later the same year. Waiting list for LT was constantly increasing since 2000, with 162 patients on the WL for LT at the end of 2005 and then at the beginning of year 2011 with 427 patients; at the end of year 2019 there were 468 patients on the WL for LT in our Center.
Methods: We analysed 2415 liver cirrhosis patients included on the WL for LT since 2000 in the Gastroenterology and Hepatology Center from Fundeni Clinical Institute.
Results: In relation to the number of LT performed we divided the analysis of the mortality on the WL in 3 periods 2000–2010; 2011–2016; 2017–2020 as follows: one year mortality of 25.3%, 13% and 18.6% respectively (log rank test with p value <0.0001). The 3 year mortality on the waiting list was 46.5%; 23.5% and 29% respectively according to the 3 periods and number of LT performed. This is in accordance with the increase of donors during years 2011–2016. There was a statistically significant different time to LT between the 3 time periods ($p = 0.00002$, shortest time to LT was between years 2011–2016. The evolution of the aetiology of liver cirrhosis on the WL during the 3 periods was: HCV (31.3% vs 31.5% vs 17.1%, $p = 0.0008$); HBV+HDV (25.2% vs 30.3% vs 37%, $p = 0.0002$); alcohol (14.2% vs 19.8% vs 23.6%, $p = 0.0001$). There was a significance increase in the rate of LT for alcohol related cirrhosis (9.3% vs 23.7% vs 27.8%, $p < 0.0001$), as well as a higher death rate on the WL for these patients (17.6% vs 19.4% vs 35.1%, $p = 0.01$). Death rate on the WL was significantly higher among HBV and HDV coinfected patients and significantly lower for HCV infected patients during the 3 time periods. Hepatocellular carcinoma significantly increased both as indication for inclusion on the WL and for LT in the period 2017–2020.
Conclusions: In Romania, the main indication for LT is still viral coinfection HBV and HDV; in addition alcohol-related diseases also increased as indication for LT similar to other European Countries. Number of liver donors should be increased due to high mortality on the waiting list.

POS277 LIVER TRANSPLANTATION FOR T2 HEPATOCELLULAR CARCINOMA IN THE COVID-19 PANDEMIC: A NEW MODEL BALANCING INDIVIDUAL BENEFIT AGAINST HEALTHCARE RESOURCES

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The COVID-19 pandemic caused temporary drops in the supply of organs for transplantation, leading to renewed debate about whether T2-HCC patients should receive priority during these times. The aim of this study is to provide a quantitative model to aid decision-making in liver transplantation for T2-HCC. We propose a novel ethical framework where individual transplant benefit for a T2-HCC patient should outweigh the harm to others on the waiting-list determining a "net benefit" to define appropriate organ allocation during a pandemic. This ethical framework was then translated into a quantitative Markov model including Italian averages for waiting-list characteristics, organ arrival, mortality, and transplant rates obtained from a national prospective database ($n = 8,567$ patients). The net benefit of transplantation in a T2-HCC patient in a usual situation, varied from 0 life months with MELD 15 to 34 with MELD 40, while it progressively decreased with acute organ shortage during a pandemic (i.e. with a 50% organs decrease the net benefit varied from 0 life months with MELD 30 to 12 with MELD 40). Our study supports the continuation of transplantation for T2-HCC patients during COVID-19 like crises, however the focus needs to be on those T2-HCC patients with highest net survival benefit.

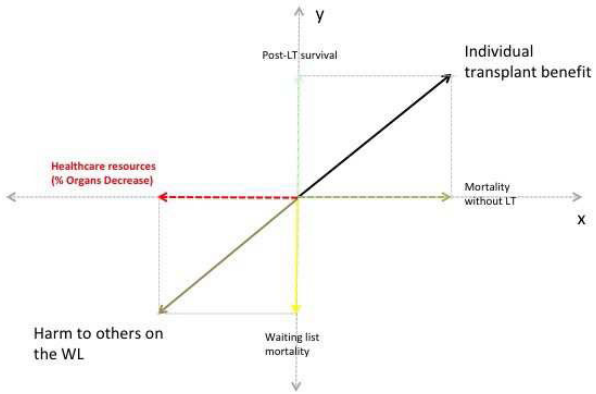

Figure 1. Ethical model for decision-making in organ allocation for liver transplantation in T2-HCC patients.

POS278 LIVER TRANSPLANTATION IN THE ELDERLY: PROPOSAL FOR AN INNOVATIVE PATIENT SELECTION PROTOCOL

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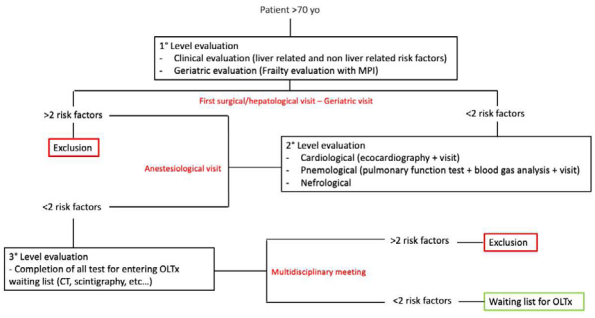
Introduction: Despite European and international guidelines don't pose a specific contraindication to liver transplantation (LT) in elderly patients, and invite to take into account physiological rather than chronological age, an upper age limit (65 or 70 years old) has been widely adopted by most transplant centers and regulatory institutions.
We sought to evaluate the outcome of patients who exceeded 70 years while waiting for LT in our centre in the last 10 years in order to develop a prospective pre-listing selection protocol for over-seventy patients.
Methods: We enrolled consecutive patients aged between 70 and 75 years old who received LT from deceased donor at our center for chronic end-stage liver disease or hepatocellular carcinoma in the last ten years. Primary endpoint was 5 year post-LT survival in over-seventy compared to that of younger adult recipients. Moreover, in order to correct for all biases in the comparison between groups, propensity score values and inverse probability weights (IPW) were calculated.
This retrospective study represents a preliminary analysis to design a prospective protocol for the selection of elderly patients for LT,
Results: We evaluated 805 liver transplantations from deceased donor performed at our center between 01/01/2010 and 31/12/2019. Among them we found 27 patients aged ≥70 years old receiving LT. Five-year patient and graft overall survival rates were respectively 92% and 88% for patients 70–75 years old, 88% and 84% for patients aged <70 years old ($p > 0.05$). Even the survival analysis performed comparing the two IPW adjusted populations demonstrated the absence of statistically significant differences between groups.
Based on these results, we developed a prospective protocol in the fashion of a decision algorithm; this can be used to super-select a population with high prevalence of comorbidities, in order to prevent a waste of resources.
Conclusions: Post-transplant outcome in over-seventy patients seems acceptable, provided that extreme care is used in the evaluation of comorbidities and functional status of the recipient, according to objective and widely accepted protocols focused on sparing donor and healthcare resources.

1° level evaluation (1° surgical/hepatological visit + geriatric evaluation)		
Risk factors		
Liver related (1 pt)	**Non liver-related (1pt)**	**Frailty (MPI)**
- MELD-Na >25 - Prior laparotomic liver surgery - Complete/incomplete portal thrombosis	- Diabetes - BMI >30 - Cardiac disease - Pulmonary disease - Renal disease - Tumor (<5 yrs) - Debilitating osteoporosis	- Low risk (MPI <0.33) – 0pt - Medium risk (MPI 0.33 – 0.66) – 1pt - High risk (MPI > 0.66) – 3pt
2° level clinical-instrumental evaluation		
- Cardiological evaluation (ecocardiography + ECG + visit) - Pnemological (pulmonary function test + blood gas analysis + visit) - Nefrological - Anesthesiological		
3° level clinical-instrumental evaluation		
- Completion of all test for entering OLTx waiting list (CT, scintigraphy, etc…) - Multidisciplinary discussion		



POS279 MODIFICATION OF DROP-OUT RATES AFTER FOUR YEARS FROM ITALIAN SCORE FOR ORGAN ALLOCATION INTRODUCTION AT A SINGLE CENTRE: A COMPETING RISK ANALYSIS.

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Background: Organ allocation remains a significant challenge in liver transplantation (LT). In 2016, a new organ allocation system based on the transplant benefit principles, the Italian score for organ allocation (ISO), was introduced. The main objective of the analysis is to compare both drop-out (DO) and LT rates before (Era 1) and after (Era 2) ISO introduction. Secondly, risk factors of DO are identified.
Methods: We retrospectively analysed the patients with end-stage liver disease (ESLD) that left the waiting list (WL) between 2012 and 2019 due to LT or DO. We considered the patients with chronic ESLD that received an organ from the deceased-donor pool. The re-LTs and the patients that waited less than 30 days for LT were excluded from the analysis. Uni and multivariable competing-risk regressions using DO and LT respectively as failure and competing event were performed to determine DO risk factors. The cumulative incidence functions of LT and DO between Era 1 and Era 2 were compared using Pepe and Mori's test.
Results: Six-hundred ninety-five patients were selected. Among these, 209 (30%) left the WL due to DO, while 486 (70%) left due to LT. Three hundred fifty patients left the WL during era 1, while 345 during Era 2. A-hundred-thirty-four (38.3%) and 75 (21.7%) Dos were observed respectively in Era 1 and 2 ($p < 0.001$). In the univariate competing risk analysis, ISO (sHR: 0.528) and HBV (sHR: 0.601) resulted as protective from DO, whereas complete portal vein thrombosis (sHR: 2.431), Child-Pugh B (sHR: 1.833), age at enlisting (sHR: 1.015) and waiting time (sHR: 1.011) positively affect DO. The multivariate analysis confirmed ISO (sHR: 0.544), HBV (sHR: 0.642), CPVT (sHR: 1.771), Child-Pugh B (sHR: 1.538), age at enlisting (sHR: 1.025), waiting time (sHR: 1.010) to be significantly related to DO. DO probability at one year from listing was computed by a cumulative incidence function and decreased from 21 to 14% between Era1 and Era 2 ($p = 0.044$).
Conclusions: Among other factors, the introduction of ISO score seemed to be protective of DO in patients with ESLD awaiting LT.

POS280 PROPENSITY SCORE MATCHED ANALYSIS OF POST-TRANSPLANT OUTCOMES IN LIVING DONOR LIVER TRANSPLANTATION FOR OLDER ADULT RECIPIENTS

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Background: The impact of increasing recipient age on morbidity and mortality following living donor liver transplant (LDLT) remains controversial. The study aims to analyse the impact of recipient age on outcomes following LDLT.
Methods: Adult LDLTs performed between November 2009 to February 2020 were retrieved from a prospectively maintained database. Patients were stratified into two groups based on recipient age: 18–65 years (younger adults) and >65 years (older adults). Propensity score matching (PSM) using nearest-neighbour matching was used to match each older recipient with upto two younger adult recipients using multiple pre-operative parameters. Outcomes evaluated were duration of ventilation, need for reintubation, tracheostomy, intensive care unit (ICU) readmission, length of ICU and hospital stay, post-operative complications, re-operation within 90 days, and patient survival.
Results: A total of 801 adult LDLT recipients were included in the study – 751 (93.7%) were younger adults and 50 (6.3%) were older adults. Older recipients were more likely to be diabetic (60.0% vs. 39.7%), hypertensive (44.0% vs. 20.4%), with pre-existing cardiac disease (28.0% vs. 11.2%). However, their pre-transplant MELD was significantly lower (14.5 vs. 17.7) and they were more likely to be transplanted for HCC (38.0% vs. 17.7%). Older recipients had longer duration of ventilation post-LT both before (3.7 vs. 1.9 days) and after PSM (4.0 vs. 1.5 days). After PSM, the 30-day (13.0% vs. 2.4%), 90-day (15.2% and 2.4%) and overall mortality (21.7% vs. 7.1%) was significantly higher for older recipients, when compared to younger recipients. There was no difference between the younger and older recipients, with respect to other post-operative outcomes.
Conclusions: This propensity score matched study shows that the older LDLT recipients have higher 30-day, 90-day and 1- and 5-year mortality, when compared to matched younger counterparts.

POS281 EVALUATING THE EFFICIENCY OF A NATIONAL ADAPTIVE ALLOCATION SCORING SYSTEM FOR LIVER TRANSPLANTATION: A PRELIMINARY BENCHMARKING ANALYSIS.

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Background: After a 4 year consensus conference process and public appraisal, since 2015 a new liver allocation scoring system (ISO score, ISOs) was set in Italy. The score was aimed at dynamically equalizing the risk of death/dropout while waiting among different diseases leading to transplant. Italian ISOs official onset was on July 1, 2019. Centers were not mandate to transplant the first ISOs listed patient to favour donor-recipient matching. When not transplanting the first ISOs patient, Centers were asked to provide a written explanation. Our study aimed at preliminarily evaluating the efficiency of such an introduction.
Methods: we on-alco the waiting list (WL) for liver transplantation (LT) from July 1, 2019 to June 30, 2020 (period2-P2) and compared it to the WL of the same period of the previous year (period1-P1). Prospectively collected Data were on-alco retrospectively through CNT information transplantation system. A comparative analysis of drop-out (DO) and LT probabilities in the three main categories of indications to LT, liver cirrhosis (LC), hepatocellular carcinoma (HCC) and MELD exceptions (MELD-ex), was performed in the two study periods. DO and LT probabilities were on-alco both as crude rates and as competing risk time dependent events.
Results: 2089 listings across the two periods were evaluated. They included 608 (29.1%) LC, 924 (44.2%) HCC and 557 (26.7%) MELD-ex. There were 931 (45.2%) LTs with 231 (11.2%) DO in P1, and 992 (47.5%) LTs with 150 (7.2%) DO in P2 ($p = 0.000$). Using HCC as reference group, competing risk of DO in P1 was higher in LC (HR 1.70, $p = 0.000$) and lower in MELD-ex (HR 0.57, $p = 0.034$), whereas in P2 the difference between HCC and LC disappeared (HR 1.20, $p = 0.309$). Competing risk of LT was lower in LC and MELD-ex than HCC groups in both P1 (HR 0.68, $p = 0.000$, and HR 0.29, $p = 0.000$), and P2 (HR 0.50, $p = 0.000$ and HR=0.81, $p = 0.004$) but in P2 a higher LT probability in MELD-ex group was observed
Conclusions: Provided the potential biases related to COVID19, national introduction of ISOs was associated with an improved balance in DO risk between HCC and LC groups and in a more homogeneous distribution of DO risk at competing risk regression among general categories. This scoring system, open to donor-recipient matching flexibility, looks promising even though requiring further study

Table 1

PERIODS	Groups	LT Number (%)	Competing risk HR (95% CI), p value	Drop-out Number (%)	Competing risk HR (95% CI), p value
Period 1	HCC	530 (55.4%)	reference	90 (9.4%)	reference
	LC	332 (44.2%)	0.68 (0.59-0.78), 0.000	124 (16.5%)	1.70 (1.30-2.23), 0.000
	MELD-ex	69 (19.6%)	0.29 (0.23-0.38), 0.000	17 (4.8%)	0.57 (0.34-0.96), 0.034
Period 2	HCC	509 (55.1%)	reference	70 (7.6%)	reference
	LC	204 (33.6%)	0.50 (0.42-0.59), 0.000	56 (9.2%)	1.20 (0.84-1.70), 0.309
	MELD-ex	279 (50.1%)	0.81 (0.70-0.93), 0.004	24 (4.3%)	0.54 (0.34-0.86), 0.010

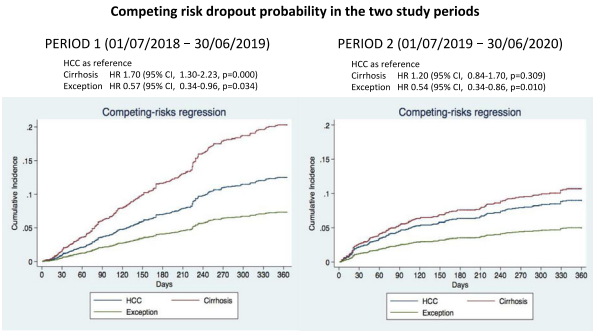

Figure 1

POS282 LIVER TRANSPLANTATION IN PATIENTS >70 YEARS RESULTS IN GOOD LONG-TERM OUTCOME – A EUROTRANSPLANT REGISTRY ANALYSIS

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Background: Life expectancy has steadily increased over the last decades in the western hemisphere. Consequently, the number of older patients waiting for liver transplantation (LT) is growing. However, because of an increasing number of co-morbidities associated with advanced age, elderly recipients need to be selected carefully for LT in order to achieve good long-term outcome.
Methods: In this retrospective study, outcome of 1846 patients receiving a LT between 2006–2015 at the age ≥65 in a member country of Eurotransplant were analysed. Two age groups were defined (Group 1: ≥65, $n = 1536$ and Group 2: ≥70 years, $n = 310$) and differences regarding graft and patient survival were analysed.
Results: 1536 Patients were transplanted at the age of 65–69 years, 293 were between 70–74 years old and 17 recipients between 75–78. There was no statistically significant difference between the two age groups (≥65 vs. ≥70 years) regarding 1-,3- and 5-year graft survival (70% vs 75%, 60% vs 60%, 51% vs 47%, $p = 0.71$, respectively) and patient survival (73% vs 77%, 62% vs 62%, 54% vs 50%, $p = 0.61$, respectively). Cold ischemic time and MELD score were independent risk factors for patient survival in univariate and multivariate analysis (HR=1.041, CI: 1.003–1.080, $p = 0.03$ and HR=1.016, CI: 1.002–1.030, $p = 0.03$, respectively). Multivariate cox regression analysis identified donor leucocytes as predictive factor for graft loss ($p = 0.01$) and donor lipase for patient death ($p = 0.001$). Furthermore, acute liver failure as the indication for LT was a strong independent risk factor for poor graft (HR=1.852, CI: 1.245–2.755, $p = 0.001$) and patient survival (HR=1.761, CI: 1.177–2.630, $p = 0.01$).
Conclusion: In conclusion, recipient age of ≥70 years is not associated with worse outcome compared to recipients aging between 65 and 69 years. Therefore, recipient age is not a contraindication for LT after appropriate screening for co-morbidities.

POS283 ROLE OF OSTEOPONTIN IN THE MONITORING OF LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Background: Osteopontin (OPN) is a multifunctional phosphorylated glycoprotein of the extracellular matrix involved in several carcinogenic and angiogenic processes, such as cell invasion, inflammation, tumor progression and metástasis. The aim of this study is to test whether pre-transplant osteopotin levels in patients with HCC correlate with alpha-fetoprotein (AFP), an established marker of the disease, as well as with the number of tumors, vascular invasion, tumor necrosis, recurrence after transplantation and death. Likewise, we also want to observe whether these osteopontin levels decrease significantly after transplantation, specifically at 1, 2 and 3 years post-transplantation.
Methods: Peripheral blood was obtained from 39 patients with HCC before transplantation, at 1 year, 2 years and 3 years post-transplantation. Plasma OPN levels were determined by ELISA (Enzo Life Sciences®). Serum AFP levels were obtained in Cobas e601 (Roche Diagnostics®). Spearman's rho test was used to determine the correlation between pre-transplant markers and between OPN and number of tumors, while the Mann Whitney U test was used to determine the association between OPN and qualitative clinical variables. The Wilcoxon test was used to determine the variation of OPN before and after transplantation.
Results

	AFP before LT	OPN before LT	OPN 1 year after LT	OPN 2 years after LT	OPN 3 years after LT
Median	6	19.44	19.13	10.37	5.32
IR	3.75–8	14.87–29.26	13.09–27.56	6.98–14.28	3.87–6.92
Wilcoxon			Z= −0.417	Z= −3.657	Z= −3.920
			p = 0.677	p = 0.000	p = 0.000

Regarding the association between OPN and the other parameters, we did not obtain any statistically significant association or correlation.
Conclusion: OPN levels experience a statistically significant decrease at 2 years and 3 years post-transplant, so this biomarker could play an important role in the monitoring of the patient transplanted for hepatocarcinoma, complementing AFP.

POS284 PROTEOMICS IN LIVER TRANSPLANTATION: BIOMARKERS BEYOND GENOMICS. A SYSTEMATIC REVIEW

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Background: Although proteomics has been employed in the study of several models of liver injury, proteomic methods have only recently been applied not only to biomarker discovery and validation but also to improve understanding of the molecular mechanisms involved in transplantation.
Methods: The study was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology and the guidelines for performing SLR in bioinformatics (BiSLR). The PubMed, ScienceDirect, and Scopus databases were searched for publications through April 2020. Studies aimed at the identification of proteomic biomarkers for liver transplant outcomes, including ischemia-reperfusion injury (IRI), rejection, or operational tolerance in human or rat samples that applied methodologies for differential expression analysis were considered.
Results: The analysis included 22 studies after application of the inclusion and exclusion criteria. Among the 497 proteins annotated, 68 were shared between species and 10 were shared between sample sources. Among the types of studies on-alco, IRI and rejection shared a higher number of proteins. The most enriched pathway for liver biopsy samples, IRI, and rejection was metabolism, compared to cytokine-cytokine receptor interactions for tolerance.
Conclusions: Proteomics is a promising technique to detect large numbers of proteins. However, the experimental variability between studies and the low number of samples have not helped to identify potential biomarkers specific to certain conditions such as IRI, rejection, or tolerance. The future of proteomics lies in its integration with other techniques such as genomics and metabolomics to obtain a global view of the interactome for a particular biological process.

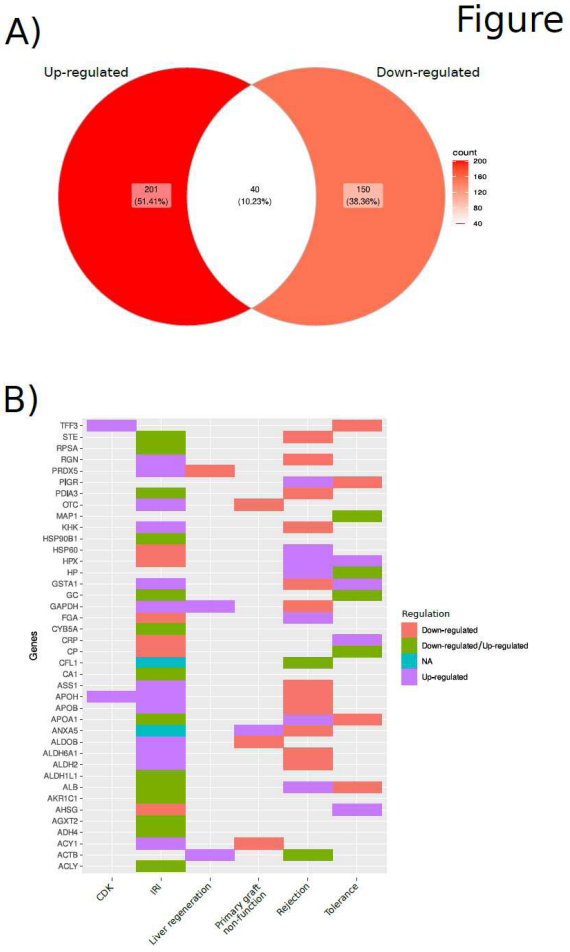

Figure. Differential pattern of protein expression. (A) Comparison of differential expression patterns observed for proteins among all selected studies expressed as a Venn diagram. (B) Heat plot of the list of proteins that had evidence supporting both types of expression changes.

POS285 C-REACTIVE PROTEIN AND UREA BLOOD LEVELS DISTINGUISH PRIMARY NON-FUNCTION FROM EARLY ALLOGRAFT DYSFUNCTION AFTER LIVER TRANSPLANTATION

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Background: A spectrum of graft dysfunction occurs following liver transplantation (LT), ranging from early allograft dysfunction (EAD) to primary non-function (PNF). EAD is common and requires organ support until graft function improves, whilst emergency re-transplantation is required for cases of PNF. The aim of this study was to determine whether serum markers can distinguish PNF from EAD early after liver transplantation.
Methods: This was a retrospective study of adults that underwent deceased donor LT between January 2010 and April 2020. PNF was defined as graft dysfunction resulting in death or retransplant within 14 days, not explained by any other cause. EAD was defined as bilirubin ≥177 umol/l on day 7, and/or AST or ALT >2000 IU/L within the first 7 days. Individuals with PNF were also grouped according to whether they died or survived within 90 days, with or without a re-transplant. Biochemical results

were compared between EAD and PNF patients, then between the PNF subgroups.
Results: Out of 1907 LTs performed, $n = 341$ (17.9%) and $n = 34$ (1.8%) patients developed EAD and PNF, respectively according to our definition (Table 1). In the first 2 postoperative days, urea, CRP, fibrinogen and platelet values were significantly lower in the PNF group (Table 1), while day 1 levels of bilirubin and ALT did not discriminate well between the two groups. The absence of an increase in urea levels between day 1 and day 2 was significantly apparent in PNF compared to the EAD group. The change in urea from day 1 to day 2 distinguished PNF non-survivors from the survivors ($p = 0.02$).
Conclusions: Differences in urea and CRP are evident earlier than the commonly used measures of ALT and bilirubin. Therefore, clinicians should also consider taking these markers into account when making treatment decisions for patients on the liver allograft dysfunction spectrum.

Table 1

	PNF ($n = 34$)	EAD† ($n = 341$)	p
CRP (mg/l)			
Day 1	25 (12–41)	37 (18–63)	0.021*
Day 2	28 (15–50)	73 (50–106)	<0.001*
Day 3	33 (16–67)	61 (38–89)	<0.001*
Day 2:1	1.2 (0.8–1.8)	1.9 (1.2–3)	<0.001*
Urea (mmol/l)‡			
Day 1	4.9 (3.2–7.4)	6.6 (5.0–8.5)	0.002*
Day 2	3.5 (2.4–8.6)	9.1 (6.4–12.7)	<0.001*
Day 2:1	0.8 (0.5–1.0)	1.4 (1.1–1.8)	<0.001*

Median (IQR). Mann-Whitney test. *Significant at $p < 0.05$ level. † EAD defined as per Olthoff KM et al. 2010. ‡Minimal day 3 data available.

POS286 PROGNOSTIC VALUE OF PIVKA-II LABELLING IN LESIONS OF HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

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Background: Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the third most common in terms of mortality. It has an increasing incidence with a poor prognosis unless diagnosed early. Today, the use of biomarkers such as alpha-foeto protein is well established. Serum des-γ-carboxy prothrombin (DCP), also known as protein induced by vitamin K absence-II (PIVKA-II), has also been validated for several years as a biomarker for the diagnosis of HCC.
Aim: The main objective of the study is to evaluate the accuracy DCP serum levels and liver immunohistochemistry as a prognostic marker of hepatocellular carcinoma (HCC) after liver transplantation (LT).
Method: This is a prospective monocentric study including patients between 2016 and 2018, who have all undergone liver transplant for cirrhosis complicated by a radiological and histological diagnosis of HCC within Milan criteria.
Results: Thirty-nine patients were enrolled. Median follow-up was 21 months. Alcoholic cirrhosis was the most frequent aetiology (59%), followed by HCV (25.6%). HCC lesions were stratified into three groups according to DCP immunohistochemistry labelling: negative, focused positive and diffuse positive labelling.
Serum levels of DCP at diagnosis were significantly higher in focal positive labelling (258 mUA/ml) and diffuse positive labelling (257 mUA/ml) compared to negative labelling (47.5 mUA/ml) ($p = 0.005$). At the time of LT, the serum level of DCP was significantly higher in the diffuse positive group (220 mUA/ml) compared to the other groups.
Examining the situation in each individual lesion, we observed a significant difference in the presence of microvascular invasion in the diffuse positive lesions compared to the negatively marked group (58.8% vs. 19% $p < 0.001$). Lesion size was also significantly correlated with DCP marking, with a maximum median diameter of 20 mm in the diffuse marking group versus 12 mm in the other groups ($p = 0.002$).
All recurrences in the negatively labelled group occurred within the first 3 months after transplantation, reflecting inadequate pre-transplant selection. Late recurrence occurred only in the other two groups.
Conclusion: DCP labelling in liver lesions correlated with serum levels. DCP expression correlates with larger and more aggressive tumour profile.

POS287 TUMOR-DERIVED EXOSOMAL MIR-21 INDUCES RECURRENCE IN LIVER CANCER

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Background: The early detection of hepatocellular carcinoma (HCC) recurrence presents a challenge because of the lack of specific biomarkers. Exosomal microRNAs (miRNAs) can discriminate HCC patients with poor prognosis from others. We aimed to identify and evaluate recurrence-associated exosomal miRNAs originating from the liver as early biomarkers for detecting HCC recurrence.
Methods: Blood samples were collected from 48 Hepatocelular cancer (CC) patients undergoing Liver transplantation. Exosomes were isolated from each individual using the ExoQuick solution. Three hundred eighty-six different miRNAs were analysis using RT-PCR.
Results: Recurrence was observed in 8 patients within 5 years after liver transplantation. We investigated among the 386 different miRNAs, upregulation of miR-21 was determined significant in HCC blood samples with poor prognosis (10.2-fold, $p = 0.004$). In additional, we found that high expression level of miR-21 associated with shorter disease free survival (Long Rank, $p = 0.0001$).
Conclusions: Our results show that the expression of exosomal miR-21 can induce HCC recurrence after Liver transplantation. We suggest that the formation of recurrence may be prevented by decreasing the expression of miR-21.

POS288 LONG NON-CODING RNA HULC OVEREXPRESSION PREDICTS TUMOR RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

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Background: Long-non coding RNA play role in many solid tumors and associated with cancer metastasis and recurrence. However, its role in hepatocellular carcinoma (HCC) remains poorly understood. In our study, we aimed to determine the prognostic importance of LncRNAs in tumor recurrence of HCC following LT.
Methods: In the present study, we evaluated the expression of 15 different LncRNAs by quantitative real-time PCR in 3 liver cancer cell lines and 226 HCC cases i who received liver transplantation (LT) with complete follow-up data. Moreover, small interfering RNA (siRNA) was used to inhibit HULC expression to investigate its biological role in tumor progression.
Results: We found that HULC was up-regulated in both cell lines and clinical tissue samples. Patients with high expression level of HULC had a significantly increased risk of tumor recurrence after LT, particularly in patients who exceeded the Milan criteria. On multivariate analysis, HULC was an independent prognostic factor for predicting HCC recurrence (hazard ratio, 3.112, $p = 0.0001$). In addition, inhibition of HULC in HepG2 and Huh-7 cells could effectively reduce cell viability, motility, invasiveness, and increase the sensitivity to apoptosis
Conclusions: Our data suggest that lncRNA HULC play an important role in tumor progression and could be a novel biomarker for predicting tumor recurrence after LT and serve as a promising therapeutic target.

POS289 DONOR CHARACTERISTICS CAN BE PREDICTIVE OF THE HEPATIC ARTERY THROMBOSIS IN LIVER TRANSPLANTATION

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Background: Hepatic artery thrombosis (HAT) is one of the most severe complications after liver transplantation. For this reason, an early finding of arterial complications, through clinical surveillance of high-risk cases can improve the transplant outcome. The detection of predictive factors for HAT can have significant repercussions on the survival of the graft. Our work aims to investigate the correlation of donor-related factors with the onset of post-transplant HAT
Methods: Consecutive liver transplants performed in our Center from November 2006 to July 2020 were retrospectively investigated. The donor parameters considered as predictive factors for HAT were 14: age, gender,

body mass index (BMI), alcohol or tobacco abuse, diagnosis of diabetes, hypertension, dyslipidaemia, pre-mortem hypotension or cardiac arrest, pre-mortem use of high-dose (nor) epinephrine, cause of death, cold ischemia time (CIT). The donors were divided according to the post-transplant development of HAT. Categorical variables were compared with the Pearson chi-square test, while continuous variables were analyzed with Student's T test. Predictive features were analyzed with a binary logistic regression
Results: In the considered period, 359 liver transplants were performed in our center. The incidence of HAT in the population was 4.1%. The recipients showed no demographic or clinical differences. Examining the factors related to the donor, a relationship of HAT was found with death from anoxia ($p = 0.036$), with the over-50 age ($p = 0.037$), with a positive history of cardiovascular disease ($p = 0.044$) or diabetes mellitus ($p = 0.038$). Multivariate analysis of significant parameters showed a strong correlation with post-transplant development of HAT ($p < 0.0001$).
Conclusions: HAT is one of the most major complications after liver transplantation, resulting in a primary non-function of the graft. The development of predictive factors is a good strategy to optimize the search for arterial complications. Our data indicated a good reliability of the donor's cardiovascular risk factors (age over 50, heart disease, diabetes mellitus, death from anoxia) on the transplant outcome, more reliable when present together. Through the transplant, the graft is moved in the recipient together with its pre-existing history.

POS290 LIVER TRANSPLANTATION AND ISCHEMIC CARDIOPATHY: OUTCOMES OF PRE-TRANSPLANT CORONARY STENTING

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Background: Liver transplant is a high-risk surgery for cardiac events, with an estimated 30-day major cardiac adverse event rate of more than 5%. Nowadays we are observing an increase in the number of patients being listed with end-stage liver disease from on-alcoholic steatohepatitis (NASH) that parallels an increasing cardiovascular disease (CVD) risk profile for liver transplant candidates due to shared risk factors between NASH and CVD.
Methods: We report our experience with pre-transplant coronary stenting to reduce the risk of post-operative complications by reviewing our series of liver transplants for any indication between January 2017 and December 2020.
Results: Among 236 patients that underwent liver transplant in the study period in our Center, 5 were pre-operatively treated with percutaneous coronary interventions (PCI). Mean age in this cohort is 59.4 years, with a mean BMI of 28.36 (range 23.5–36.8). They were transplanted in one case for NASH, 2 for HCV and 2 for Alcohol related cirrhosis, and 3 out of 5 had HCC. One patient received a double aortocoronary bypass, 2 were treated with percutaneous transluminal coronary angioplasty (PTCA) plus + left anterior descending artery stenting LAD, one was treated with stenting for three-vessel disease and one received PTCA plus anterior interventricular artery stenting. 4 out of 5 were diagnosed with coronaropathy during the pre-transplant screening. After a mean follow-up of 12.99 months (range 1.87–26.7) all patients are alive. One patient had two heart-failures during LT and was successfully resuscitated.
Conclusions: With the limitation of a small case series, we reported no mortality in a cohort of patients underwent liver transplant with coronary disease. Our experience demonstrates that an aggressive pre-transplant screening and treatment of coronary disease, in particular if previously unknown, result in good post-operative outcomes after liver transplantation.

POS291 CLINICAL APPLICATION OF EXTRACORPOREAL PHOTOPHERESIS AS AN ALTERNATIVE STRATEGY IN POSTTRANSPLANT IMMUNOSUPPRESSIVE THERAPY

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At present, the use of extracorporeal photopheresis (ECP) is one of the possible methods for correcting immunological reactivity after liver.

The aim of the present work was to evaluate clinical efficiency and safety of extracorporeal photopheresis in the prevention of liver transplant rejection in the early post-transplant period.
Materials and methods. The study design called for prospective comparison with patients (control group) on full dosage calcineurin inhibitors (CNI) immunosuppression. Inclusion criteria: patients after orthotopic liver allotransplantation with contraindications to the prescription of calcineurin inhibitors due to acute renal damage, nephrotoxicity or chronic renal failure. The study group included 17 patients who underwent extracorporeal photopheresis sessions (on day 4 and 8 post- liver transplantation) on the background of a reduced dosage of tacrolimus. The control group consisted of 17 patients.
Results and discussion. No adverse events associated with extracorporeal photopheresis have been identified. The incidence of infectious, hemorrhagic and biliary complications was comparable in the study groups. Immunological dysfunction of the graft developed in 3 patients in the main group and in 3 patients in the control group. In the ECP group, on the background of delayed CNI immunosuppression, there was an early recovery of renal and liver functions recovery, which made it possible to reduce the duration of the hospital stay from 20 days to 14 days ($p = 0.04$; Wilcoxon Matched Pairs Test).
Conclusion. The research data indicate that the clinical application of ECP can safely reduce the dosage of CNI, which favorably affects the restoration of renal function.

POS292 MULTICENTRIC DONOR SURVEY 20 YEARS AFTER DONOR HEPATECTOMY

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Background and Aim: The main concern of living donor liver transplantation is the risk for donor morbidity and impaired life quality in long-term. We implemented an interview with the living donors to investigate the health related quality of life their thought living donation in long-term.
Methods: Donors between 1998–2014 who were still available to answer a questionnaire, were identified. Data were retrospectively evaluated. Each donor was asked to fill a standardized survey (Table 1). Complications were defined in Clavien-Dindo classification.
Results: There were total of 272 donors. Postoperative major complications (grade 3a or 3b) occurred in 26 patients (10%). Majority (90%) of the donors answered that they are in excellent or good overall all health. Seventy donors (26%) reported some or major psychological problems after donation. Return to baseline functionality occurred within 6 months after donation for 177 (65%) of the donors, 11 (4%) donors responded that they never returned to their baseline functionality. The vast majority reported positive or no impact of donation in professional life ($n = 262$, 96%) while 10 (4%) responded negative impact. Seventy-five donors (28%) reported unsure or no to donate again.
Conclusions: This report represents the longest follow-up liver donor quality of life data to the best of our knowledge. We conclude that, while overall results seem positive, 28% of negative response to donate again is high. Life long effects of living liver donation should be further explored.

Questions	Answers (n = 272)					Missing data
How would you rate your health now?	**Excellent**	**Good**	**Neutral**	**Bad**	**Very bad**	
	n = 94	n = 150	n = 25	n = 3	n = 0	
	35%	55%	9%	1%		
How would you rate your overall physical condition now?	**Excellent**	**Good**	**Neutral**	**Bad**	**Very bad**	
	n = 66	n = 161	n = 36	n = 6	n = 2	
	24%	59%	13%	2%	0.7%	
Did you have psychological problems after donation?	**Yes, many**	**Yes, some**	**No problems**			n = 2
	n = 9	n = 61	n = 200			
	3%	22%	74%			
When did your life return to baseline normalcy?	**<3 months**	**3–6 months**	**6–12 months**	**>12 months**	**Never**	
	n = 95	n = 82	n = 58	n = 26	n = 11	
	25%	30%	21%	10%	4%	
How did donation impact your professional life?	**Very positive**	**Positive**	**No impact**	**Negative impact**	**Very negative**	
	n = 0	n = 28	n = 234	n = 6	n = 4	
		10%	86%	2%	1%	
Would you make the decision to donate again?	**Yes**	**Unsure**	**No**			n = 3
	n = 194	n = 58	n = 17			
	71%	21%	6%			

POS293 SIMILAR POST-TRANSPLANT OUTCOMES USING DONORS AFTER CARDIAC DEATH WHEN APPLYING STRICT SELECTION CRITERIA

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Background: Outcomes of liver transplantation (LT) with donors after cardiac death (DCD) have been considered suboptimal due to a higher rate of ischemic cholangiopathy, especially when super-rapid recovery (SRR) technique is used. This study aimed to compare the incidence of complications between recipients receiving DCD vs those receiving donors after brain death (DBD) in a large-volume liver transplant centre.
Methods: We performed a retrospective cohort study from January 2015 to December 2018 of recipients who underwent a LT with DCD compared with a control group of LT with DBD, matched 1:1 without replacement by propensity score matching that included the following variables: indication for LT, recipient sex, recipient age, donor age and MELD score.
Results: 51 recipients with DCD-LT (29 SRR, 22 normothermic regional perfusion [NRP]) were matched with 51 DBD-LT recipients.
Results are shown in table 1. Biliary complications were more frequent in DCD and SRR technique, 10%(n = 5) vs 2%(n = 1) in DBD group, (p:NS). Two patients (4%) suffered primary graft non-function in the DCD group (1 SRR and 1 NRP) versus zero in the DBD group (p:NS). Postoperative bleeding and reinterventions were also higher in the DCD group: 7 (13.7%) vs 1 (1.95%) and 8 (15.7%) vs 2 (3.9%) respectively (p = 0.06 and 0.09).
The 1st postoperative day AST/ALT peak was higher in DCD (p≤0001). The incidence of rejection, vascular complications, renal injury, hospital stay and readmissions were similar in both groups.
Cumulative 1-, 2-, 3- and 4-year graft and patient survival were also similar (Figure 1).
Conclusions: DCD donors are an adequate strategy to increase the donor pool in LT, achieving similar long-term graft and patient survival rates to those achieved with DBD donors, especially when NRP technique is used.

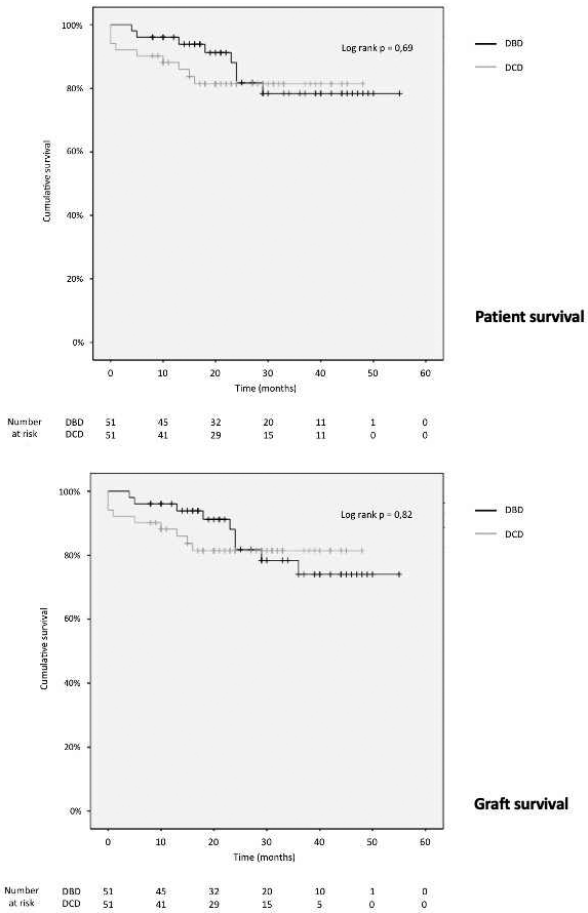

Figure 1. Patient and graft survival.

Table 1. Results

	DBD (n=51)	DCD (n=51)	p value
Transfusion in surgery			
RBC	1 (0-2,5)	2 (0-4)	0.16
Platelets	1 (0-2)	2 (0-2)	0.03
FFP	1,5 (0-2)	2 (0-3)	0.22
AST day 1 (UI/L)	694 (349-1026)	1369 (749-2311)	0.000
ALT day 1 (UI/L)	529 (279-914)	885 (749-2311)	0.001
Bilirubin day 7 (mg/dL)	3.6 (1,9-6,2)	7.1 (2.6-9.4)	0.024
PNF	0 (0%)	2 (3.9%)	0.49
Acute cellular rejection	3 (5.9%)	2 (3.9%)	1
Postoperative bleeding	1 (1.95%)	7 (13.7%)	0.06
Reinterventions within 6 mos.	2 (3.9%)	8 (15.7%)	0.09
Vascular complications within 6 mos.	2 (3.9%)	2 (3.9%)	
Hepatic artery stenosis	0	1 (1.95%)	
Hepatic artery thrombosis	1 (1.95%)	0	1.3
Hepatic artery pseudoaneurysm	0	1 (1.95%)	
Portal vein thrombosis	1 (1.95%)	0	
Biliary complications within 6 mos.	1 (1.95%)	5 (9.8%)	
Bile leak	0	3 (5.9%)	
Ischemic cholangiopathy	0	2 (3.9%)	0.2
Biliary stenosis	1 (1.95%)	0	
eGFR 1st month (mL/min/1.73m²)	83.04 ± 19.7	80.04 ± 23.96	0.4
Hospital stay (days)	13 (9-18)	14 (10-19.5)	0.55
Readmissions within 6 mos.	0 (0-1)	0 (0-1)	0.85
Follow-up (months)	27.4 ± 13.6	23.2 ± 12.6	0.1

DBD, Donation after Brain Death; DCD, Donation after Cardiac Death; RBC, Red Blood Cells; FFP, Fresh Frozen Plasma; AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; PNF, Primary Non-Function; eGFR, estimated Glomerular Filtration Rate; LT, Liver Transplantation.

Values expressed as mean (± standard deviation), median (interquartile range) or number (percentage) as appropriate.

POS294 COMPARISON OF ANTE-MORTEM VS POST-MORTEM CANNULATION IN LIVER DONATION AFTER CIRCULATORY DETERMINATION OF DEATH

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Background: In controlled donation after determination of circulatory death (cDCD) the normothermic regional perfusion (NRP) rescue livers to be suitable for transplantation by reducing biliary complications. However, there are no studies that evaluate the difference between the ante-mortem (amC) vs the post-mortem cannulation (pmC). The aim of our work is to compare both techniques.

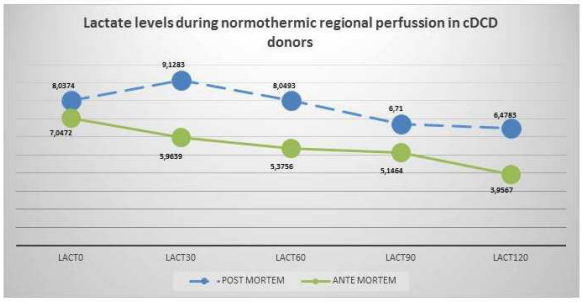
Methods: We performed a longitudinal prospective study from August 2013 to November 2019. We exclude the first six because we performed super-rapid recovery. We collect demographic data of organ donors, the disease that leads to withdrawal of life sustaining therapy (WLST), the records of the total warm ischemia time (TWIT), the functional warm ischemia time (FWIT), the agonic time (AT), the blood analysis data during the NRP and the validity of procured liver. Chi square test were performed for categorical data and t test for quantitative data. $p < 0.05$ were considered statistically significant.

Results: We include 45 cDCD donors with NRP, 23 with pmC and 22 with amC. Demographic characteristics between groups were similar (Table). The TWIT and FWIT differed between groups being in pmC and amC of 27.3 ± 8.1 minutes and 20.8 ± 6.2 minutes compared with 19 ± 5.3 minutes and 12.4 ± 4.5 minutes respectively. The AT was similar (13.5 ± 7.4 vs 12.8 ± 5.1) which means that the technique did not influence the WLST protocol. Also, we observed a higher lactate concentration during NRP in pmC compared with the amC (Figure). The lower levels of lactate in the amC at 30 minutes (9.12 ± 3.9 vs 5.9 ± 2.4 $p < 0.05$) and 60 minutes (8.04 ±2.5 vs 5.37 ± 2.4 $p < 0.05$) were statistically significant compared to pmC. The lactate levels in pmC the were clearly higher at 90 and 120 minutes but there were not statistically differences. Finally, the viability of liver was higher in DCD donors with amC, however we did not find statistically differences. (Table)

Conclusions: The amC reduces the TWIT and FWIT without affecting WLST protocols. Also, it improves the functionality of livers according to the lactate concentrations during the NRP. Finally, with amC the recovery of livers was higher. Future randomized research is warranted to investigate the benefits of amC compared with pmC. Also, other benefits such as reducing the graft dysfunction or graft failure should be assessed.

Table

	Total (45)	Post-mortem (23)	Pre-mortem (22)	p
Age	53 ± 12,1	53,9 ± 12	53,8 ± 12	0,97
Sex	Male 75,6%	M 87%%	M 63,6%	0,16
Body mass index	27 ± 0,8	26,7 ± 3,9	27,3 ± 4	0,61
Smoking	33,3%	30,4%	36,4%	0,45
Alcohol	20%	17,4%	22,7%	0,47
Drugs	11,1%	13%	9,1%	0,52
Hypertension	28,9%	39,1%	18,2%	0,111
Diabetes	17,8%	17,4%	18,2%	0,62
Dyslipemia	37,8%	34,8%	40,9%	0,45
Cardiopathy	13,3%	17,4%	9,1%	0,35
TWIT	23 ± 8,0	27,3 ± 8,1	19 ± 5,3	<0,001
FWIT	16,7 ± 6,8	20,8 ± 6,2	12,4 ± 4,5	<0,001
AT	13,2 ± 6,3	13,5 ± 7,4	12,8 ± 5,1	0,69
Lactate 0´	7,5 ± 3,7	8,03 ± 4,6	7,04 ± 2,5	0,43
Lactate 30´	7,5 ± 3,5	9,12 ± 3,9	5,9 ± 2,4	<0,05
Lactate 60´	6,5 ± 2,8	8,04 ± 2,5	5,37 ± 2,4	<0,05
Lactate 90´	5,8 ± 2,3	6,7 ± 2,6	5,1 ± 1,9	0,87
Lactate 120´	5,3 ± 3,5	6,4 ± 4,3	3,9 ± 1,3	0,11
Validity of liver	44,4%	39,1%	50%	0,333



Figure

POS295 PROSPECTIVE HISTOLOGICAL ANALYSIS OF DONOR AND RECIPIENTS' HEPATIC ARTERY IN LIVER TRANSPLANTATION.

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Background: Arterial complications in liver transplantation (LT) represent the most dangerous complications with great impact both for the patient and the graft survival. The main aim of this prospective study is to determine the incidence of histological lesions in the arteries of both donors and recipients

in the LT. The secondary endpoint is to determine if histological injuries lead to an increase in arterial complications.
Methods: The hepatic arteries of 65 consecutive LT (5 cases of retransplantation) were analyzed. Histological injuries were classified as atherosclerosis, detachment of the intima and fibrosis, and were detected in the vessel tract close to the vascular anastomosis site.
Results: The 60 recipients presented a median age of 57.5 years (IQR: 52.25–64) and a median lab MELD-Na of 16.75 (IQR: 11.25–27). Among these 60 recipients, 34 patients (52.3%) had HCC and 15 (23.1%) were subjected to the pretransplant transarterial chemoembolization (TACE). The 65 donors (61 donors after brain death and 4 donors after cardiac death) had a median age of 64 years (IQR 49–71), higher to the median european age of 54 years. The Cardiovascular accident was the main cause of death (58.5%). The histological analysis documented the following arterial injuries: 16 donors' arteries and none of the recipients presented atherosclerosis ($p < 0.001$); 12 donors' arteries and 3 recipients presented detachment of the intima ($p = 0.013$); 29 donors' arteries and 22 recipients presented fibrosis ($p = 0.23$). 5 arterial complications have been reported (4 thrombosis and 1 dissection) and none statistical correlation with the presence of histological injuries was found ($p = 0.23$ for donors and $p = 0.25$ for recipients, respectively). Among the 15 cases of pretransplant TACE, 9 presented histological injuries ($p = 0.67$).
Conclusions: The advanced age of the donors should justify the greater incidence of histological injuries on the arteries of the grafts. Pre-transplant TACE did not lead to a greater incidence of histological injuries. In our experience histological lesions seem to not increase the risk of arterial complications, in contrast with what has been expressed so far in the literature.

POS296 ERG IN SITU EXPRESSION AS A MARKER OF ENDOTHELIAL STRESS IN EXTENDED CRITERIA DONORS BEFORE AND AFTER GRAFT REPERFUSION.

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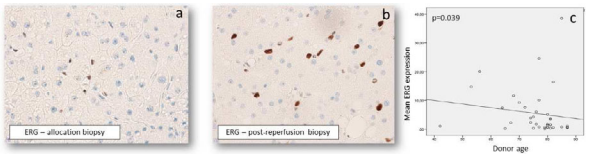
Background: Different reperfusion strategies have been proposed in the last years to preserve grafts from extended-criteria donors (ECD) prior to liver transplantation (LT), but the implications on cellular level are unknown. The aim of our study was to analyse *in situ* the endothelial preservation and activation in liver grafts before and after hypothermic oxygenated perfusion (HOPE) and static cold storage (SCS).
Methods: Forty-one consecutive ECD liver were prospectively enrolled, 28 (68.3%) preserved with HOPE and 13 (31.7%) with SCS. Enrolment criteria included two surgical biopsies, (i) one allocation biopsy for graft suitability before LT, and (ii) one post-reperfusion biopsy, performed after implantation. Tissue was routinely formalin-fixed, paraffin embedded and processed for histopathological analysis.
In all biopsies, immunohistochemistry was performed for CD34 (sinusoidal endothelization and arterial endothelial preservation), ERG (endothelial activation) and Nestin (marker of endothelial immaturity and neoangiogenesis). CD34 and Nestin were semi-quantitatively evaluated; ERG was quantitatively analysed counting the positive nuclei. Standard livers were used as controls.
Results: CD34 and Nestin expression in allocation biopsies was very similar to controls, and significantly increased in post-reperfusion biopsies ($p = 0.004$ and $p = 0.001$ respectively); Nestin increase in post-reperfusion biopsy was proportional to cold ischemia time ($p = 0.027$), indicating a response to a higher ischemic stress.
In allocation biopsies, ERG expression was very low compared to controls, indicating a depressed endothelial trophism in donors (Figure 1a), and it was even lower with age ($p = 0.039$, Figure 1c). In post-reperfusion biopsies ERG expression significantly increased ($p = 0.035$, Figure 1b), despite donor age.
Conclusion: The ischemic and inflammatory stress in donors cause a depression of ERG activity, activating endothelial-to-mesenchymal transition and neoangiogenesis.



POS297 EXTRAHEPATIC MANIFESTATIONS IN PATIENTS WITH LIVER TRANSPLANTATION DUE TO AUTOIMMUNE LIVER DISEASE

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Puerta de Hierro Majadahonda University Hospital, Majadahonda, Spain

Background: Autoimmune liver diseases (AILD) (primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), autoimmune hepatitis (AIH), and overlap syndrome (OS)) can present extrahepatic autoimmune (AI) manifestations, the most frequent being inflammatory bowel disease (IBD), autoimmune thyroid disease (ATD) and Sjögren's syndrome (SS). The evolution of extrahepatic manifestations is independent of the evolution of liver involvement, and the evolution after liver transplantation (LT) is highly variable. There are not enough studies that analyze the appearance and evolution of extrahepatic manifestations in patients who have undergone LT.
Methods: Retrospective study of LT patients with post-LT follow-up of at least 2 years. Descriptive analysis of clinical variables and overall and graft survival using Kaplan-Meier curves.
Results: AILD was an infrequent indication for LT (68/835, 8%), 39 PBC, 17 AIH, and 12 PSC.
56 were women. The mean pre-LT MELD value was 17 ± 5.4. The mean age of LT recipients at the time of LT was 40 ± 21 years.
27 patients presented some type of extrahepatic AI. The most frequent was inflammatory bowel disease (IBD) in 7 patients – preferentially in patients with PSC (10/12) -, followed by SS (5 patients), and ATD (4 patients).
IBD was present in 12 patients: 8 ulcerative colitis (UC) (6 PSC, and 2 AIH-OS), 2 Crohn's disease (CD) both PSC, and another 2 PSC patients and IBD without conclusive diagnosis (neither for UC nor CD).
5 presented IBD de novo post-LT, the other 7 debuted prior to LT. In 3 of these 7 patients with pre-LT IBD, the disease went into remission after LT, and in the remaining 4 there were flares. Colectomy was necessary in 3 of the patients with IBD due to poor evolution of IBD. None of the patients developed colon cancer during the follow-up period.
In the survival analysis, no statistically significant findings were found among IBD patients versus patients without IBD.
Conclusions: AILD is an infrequent cause of liver transplantation. Extrahepatic AI diseases are associated in these patients, with IBD being the most frequent one. IBD presents a torpid post-LT course but does not impact overall survival.

POS298 PERIPHERAL BLOOD TREG:TH17 RATIO IN LIVER TRANSPLANT RECIPIENTS WITH ACUTE REJECTION: ASSESSMENT UTILIZING MAXPAR IMMUNE PROFILING ASSAY.

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Background: Acute T-cell mediated rejection (TCMR) is a common cause of morbidity following liver transplantation. Regulatory T-cells (Tregs) have the ability to abrogate alloimmune responses. The balance of tolerance inducing Tregs and effector T-helper plays a crucial role in acute rejection. The aim of this study was to determine if the Treg: effector T cells ratio has an impact on the severity of acute TCMR in liver transplantation.
Methods: Peripheral blood samples were collected from patients suspected of having early acute rejection at the time of liver graft biopsy. These samples were collected whilst the patients were taking routine maintenance immunosuppression but prior to the commencement of anti-rejection, high dose corticosteroid therapy. Patients with biopsy proven TCMR were included and whole blood immunophenotyping performed via mass cytometry. Treg:T_h17 ratios were determined and compared to the rejection activity index (RAI) score from the graft biopsy specimen.
Results: The demographic and transplant characteristics of the four patients included are demonstrated in table 1. The median post-operative day the blood and liver biopsy were obtained was 7 (range 6–8). All patients were taking triple therapy maintenance immunosuppression (tacrolimus + prednisolone + Azathioprine OR Mycophenolate mofetil). The proportion of $CD4^+$ subsets are demonstrated in Figure 1° with Tregs and Th17 comprising 2.1–10.5% and 0.9–5.9% of $CD4^+$ cells respectively. A low Treg:T_h17 ratio was associated with a higher severity of rejection, as indicated by the RAI (Figure 1B).
Conclusions: These findings suggest that an imbalance between Treg and T_h17 cells, that favours a predominance of T_h17, is associated with increased severity of rejection. These findings need further investigation in a larger cohort but suggest therapies that aim to augment Treg frequency may be of benefit in the management of acute TCMR following liver transplantation.

Table 1

Case	Age	Gender	Indication	Post op biopsy	Immunosuppression	RAI	Total Treg	Total Th17	Treg:Th17
1	63	Male	ArLD and HCC	Day 6	Tac + Aza + Prednisolone	7	325	209	1.56
2	48	Male	Ischaemic cholangiopathy	Day 8	Tac + MMF + Prednisolone	6	86	37	2.32
3	58	Male	Cryptogenic cirrhosis	Day 7	Tac + Aza + Prednisolone	6	545	388	1.4
4	61	Female	Primary sclerosing cholangitis	Day 6	Tac + MMF + Prednisolone	9	22	65	0.33

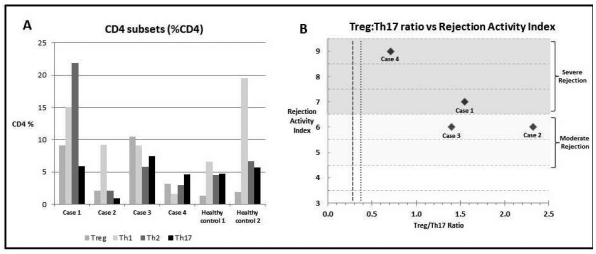

Figure 1
Legend: 1A) Demonstration of $CD4^+$ subsets in the four transplant recipients with acute rejection and two healthy controls. 1B) Treg:Th17 ratio appears to demonstrate a trend towards increased severity of rejection with a lower Treg:T_h17 ratio. The dotted lines represent the Treg:Th17 ratio in two healthy volunteers.

POS299 MUSEKAL – A MULTI-CENTRE NON-INTERVENTIONAL STUDY TO ASSESS THE TOLERABILITY AND EFFECTIVENESS OF ENVARSUS IN DE NOVO LIVER TRANSPLANT PATIENTS

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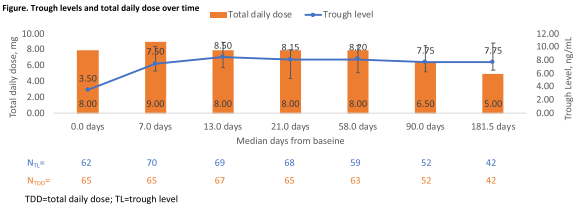
Background: Available formulations of tacrolimus (tac) exhibit substantial inter- and intra-individual variability in absorption and metabolism. In clinical trials, Envarsus achieved target trough levels faster and reduced the total daily dose needed to maintain therapeutic levels compared to other tac formulations. The present non-interventional study aimed to assess tolerability and effectiveness of Envarsus in de-novo hepatic allograft recipients in real-life.
Methods: The study was conducted in Austria and the Czech Republic. Patients ≥18 years received Envarsus per approved label and local daily clinical routine. All participants signed informed consent. Tolerability and effectiveness were assessed in seven clinical visits during six months observational period. De novo patients are presented here with relevant clinical variables, i.e. tac trough level (TL), tac total daily dose (TDD) from day 1 to 6 months, number of dose adjustments; time (days) to standard reference range; kidney and liver function. Adverse drug reactions (ADRs) were summarized using the MedDRA dictionary. The data collection period was 07/2016 to 08/2019.
Results: A total of 70 de novo liver transplant patients were analysed; patients were predominantly male and < 65 years old (Table). The mean time to achieve tac target TL was 6.4 days after a mean of 4 dose adjustments; TDD decreased from 9.00 mg at Day 7 to 5.00 mg at day 180 (Figure). Liver function continuously improved, while kidney function remained stable until the end of the study period. Envarsus was well tolerated with 21 ADRs in 5 patients; two serious ADRs were reported (Table).
Conclusions: After Envarsus initiation in de novo liver transplant-patients, tac target TL were rapidly achieved while initial TDD was reduced after day 60 with few dose adaptations. Liver function rapidly improved, while kidney function remained normal. Envarsus was well tolerated in this population.

Table. Baseline characteristics and treatment outcomes

Parameter	De Novo (N=70)
Male sex, n (%)	51 (72.9)
Age <65 years, n (%)	60 (85.7)
Trough level, ng/mL	Stable around 8 ng/mL after 7 days
Total daily dose, mg	Stable at around 8 mg between days 1 to 60, then drop to 5 mg at 180 days
Mean (SD) time to standard trough level, days	6.4 (4.6)
Mean (SD) number of dose adjustments	4.0 (3.9)
Kidney function	eGFR stable at around 60 mL/min/1.73m²
Liver function	Consistently improving over time
AST	Rapidly decreasing until day 21, then stable at around 25 U/L
ALT	Rapidly decreasing until day 14, then stable at around 20 to 25 U/L
GMT	Increased between day 1 and 7 then steady decrease to around 40 to 50 U/L
Adverse drug reactions	21 events in 5 patients (mostly mild renal insufficiency and haematological adverse events)
Serious adverse drug reactions	2 events (moderate atrial flutter, severe abnormal hepatic function)

Figure. Trough levels and total daily dose over time



TDD=total daily dose; TL=trough level

POS300 MELTDOSE® TECHNOLOGY PROLONGED RELEASE TACROLIMUS IN DE NOVO LIVER TRANSPLANT RECIPIENTS: MID-TERM EVALUATION OF THE SAFETY AND EFFICACY

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Background: Tacrolimus (TAC) is the backbone of immunosuppression (IS) after liver transplantation (LT), but its use is associated with varied toxicities. MeltDose® TAC (LCP-TAC) is a novel formulation resulting in increased dissolution and better absorption. However, scanty evidence is available on safety of LCP-TAC in de novo LT with regard to neurologic toxicity. This study aimed to evaluate the safety of LCP-TAC compared to twice-daily (TD-TAC).
Methods: This was a retrospective analysis on 272 patients transplanted from January 1, 2018 thru December 31, 2019: 166 LCP-TAC patients were compared to 106 TD-TAC. Both groups received delayed-TAC in the setting of triple/quadruple IS with basiliximab (BAX), steroids (S), and mycophenolate mofetil (MMF). TAC target range was 6–10 for the first 6 months and 3–8 thereafter. Data were censored at death, graft loss or latest follow-up.
Results: At latest follow-up, graft and patients survival were 94% and 95% in LCP-TAC group, both 90.5% in TD-TAC group (log rank $p = 0.448$ and $p = 0.424$). The treated biopsy proven acute rejection (t/BPAR) rate was 3.6% vs 3.8% (P = ns). Renal dysfunction (as per eGFR <60 mL/min) was 9.5% in each group (P = ns). The incidence of new onset diabetes mellitus was 14.5% for LCP-TAC versus 6.7 for TD-TAC group ($p = 0.089$). Neurological complications were 6.0% for LCP-TAC and 9.5% for TD-TAC ($p = 0.201$).
Conclusions: To the best of our knowledge, this is one of the largest series of de novo use of LCP-TAC in LT. LCP-TAC is safe and effective with a numerical reduction of neurological adverse events versus TD-TAC.

POS301 DIFFERENT EFFECTS OF TACROLIMUS, MYCOPHENOLATE MOFETIL AND RAPAMYCIN ON APOPTOSIS IN HUMAN HEPATOCYTES CULTURES

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Background: Liver transplant (LT) recipients have higher hepatic apoptotic markers in comparison to non-transplanted subjects. This is due to the immunosuppression agents used after LT with cytotoxic and proapoptotic effects. The aim of our study was to assess the apoptotic effects of immunosuppressive agents used in the post-LT setting, in human hepatocytes cultures isolated from cirrhotic livers.
Methods: Human cirrhotic hepatocytes have been isolated from liver explant fragments by the collagenase perfusion technique described by Seglen et al. Cirrhotic hepatocytes have been cultured in low glucose DMEM culture medium and have been treated for 24 hours with 1 μM tacrolimus (TAC), rapamycin (RAP), mycophenolate mofetil (MMF), or combinations (TAC+SIR, MMF+TAC). At 24 hours apoptosis and necrosis was assessed using Tali™ Apoptosis Kit – Annexin V Alexa Fluor™ 488 & Propidium Iodide (Thermo Scintific). Gene expression has been assessed by qRTPCR using a microarray of 19 genes significant for apoptosis.
Results: Cytometry analysis has indicated the lowest apoptotic cells percentage in human cirrhotic hepatocytes cultures treated with MMF (5%) and TAC+MMF (2%) whereas the highest apoptosis percentage was registered for the TAC alone (11%). The highest toxicity indicated by apoptosis and necrosis was registered for the association of TAC+RAP (17%). Gene expression analysis has suggested a marked antiapoptotic effect of MMF in

human cirrhotic hepatocytes cultures, mediated by a significant decrease in the gene expression of membrane receptors mediating apoptosis (TNFRSF1A and 10°, CD40 and FAS), the down regulation of genes mediating mitochondrial apoptosis (BAK1, BAX, RIPK1, ASK1, SMAC, HTRA2), of apoptosis specific effector proteins, especially DFFB-CAD, parallel by a significant decrease in the expression of the transcription factor NFkB1. The gene expression results are concordant to cytometry study results, indicating the lowest apoptotic effect for MMF and MMF+TAC immunosuppressive regimens.
Conclusions: MMF based immunosuppressive regimens have a favourable anti-apoptotic profile in vitro, in human cirrhotic hepatocytes cultures, as suggested by cytometry and gene expression studies, supporting its use in case of liver transplants recipients at high risk for liver graft fibrosis.

POS302 IMPACT OF SARS-COV-2 PANDEMIC ON TRANSPLANTATION ACTIVITY IN ITALY: THE REPORTING AT THE END OF THE YEAR

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Background: Despite the SARS-CoV-2 pandemic and the two peak periods recorded in Italy in March and November 2020, the transplantation activity (TA) continued uninterrupted. The Italian National Transplant Center, the competent authority in this field, supported the transplant network by issuing guidelines, that would allow the activity to continue safely, and by promoting and coordinating collaboration between transplant centers. This study aimed to assess whether these efforts have been effective and the extent to which the pandemic has impacted TA.
Methods: TA was monitored throughout the year through the information transplant system, the Italian registry of all donation and transplantation activities. The results obtained were compared with the TA of the previous year.
Results: from 01/01/2020 to 31/12/2020 3441 solid organ transplants (SOTs from deceased and living donors) were performed, 9.7% less compared to 2019 (3813 SOTs). In particular, we recorded a reduction by 10.8% in kidney TA, by 7.8% in liver TA and a consistent heart TA (−2.5%). A greater decrease was obviously recorded in lung TA (−24.2%)
Conclusions: In Italy, where SARS-CoV-2 infection had a strong impact in terms of positive cases and deaths, TA continued overall with minimal inflection compared to last year. This was an excellent team result of the Italian national transplant network.

POS303 PNEUMOCYSTIS JIROVECII PNEUMONIA IN LIVER TRANSPLANT RECIPIENTS IN AN ERA OF ROUTINE PROPHYLAXIS

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Background: Pneumocystis jirovecii pneumonia (PCP) is an opportunistic infection in solid organ transplantation recipients. We investigated the incidence rate (IR) of PCP, the related hospitalization, ICU-admission, and 180-days all-cause mortality in liver transplant recipients who received routine PCP prophylaxis the first six months post-transplantation.
Methods: We used data from the Knowledge Center for Transplantation database at Rigshospitalet. We included 343 adult liver transplant recipients transplanted between January 1st, 2011 and October 1st, 2019. Microbiology data were obtained from the Danish Microbiological Database (MiBa) which is a national database containing all data on microbiological samples in Denmark from both hospitals and general practice. The 95% confidence intervals (CI) of Irs was calculated using Byar's approximation to the Poisson distribution.
Results: Among the 343 included liver transplant recipients, seven (2%) recipients were diagnosed with PCP infection during a total follow-up of 1153 person-years. The IR of PCP in the first five years post-transplantation was 6.1 (95% CI 2.7–12) per 1,000 person-years of follow-up (PYFU). The IR in the first 6 months post-transplantation (during PCP prophylaxis) and in the months 7–12 post-transplantation (after discontinuation of PCP prophylaxis) were 6.2 (95% CI 0.56–29) and 9.6 (95% CI 2.7–26) per 1,000 PYFU, respectively. Six of seven (86%) liver transplant recipients diagnosed with PCP were admitted to hospital, but none required admission to ICU or died (Table 1).
Conclusions: Despite more intensive immunosuppression, the IR of PCP the first six months post-transplantation and during PCP prophylaxis was lower than the following six months after discontinuation of prophylaxis, underpinning the importance of PCP prophylaxis. Most liver transplant recipients with PCP were hospitalized, underlining the need for randomized clinical trials to determine the optimal duration of prophylaxis.

Table 1: Characteristics, clinical outcomes, and treatment-related variables in seven liver transplant recipients who had PCP.

Variable	The liver Tx recipient's number						
	1	2	3	4	5	6[!]	7
Gender	Male	Male	Female	Female	Female	Female	Male
Age (at time of Tx, years)	44	64	54	47	59	63	34
PCP prophylaxis	No	Yes	Yes	Yes	Yes	Yes	Yes
Time of PCP infection since Tx (days)	123	458	192	332	471	353	426
Diagnostic method	Microscopy in BAL	Microscopy in BAL	Microscopy in BAL	PCR in BAL	PCR in sputum	Microscopy in lung biopsy	PCR in BAL
Treatment of infection	TMP-SMZ	TMP-SMZ	TMP-SMZ	TMP-SMZ, clindamycin + primaquine*	TMP-SMZ	TMP-SMZ	Clindamycin + primaquine
Rejection (number of days prior (-) to or after (+) PCP infection)	Yes (-103)	No	Yes (-184, -71)	No	No	Yes (228)	No
Rejection treatment	Large standard methyl-prednisolone **	-	Large standard methyl-prednisolone**	-	-	Small standard methyl-prednosolon***	-
Hospital admission	Yes	Yes	Yes	Yes	Yes	No	Yes
X-ray verified pneumonia	Yes	Yes	Yes	Yes	No	No	-
ICU admission	No	No	No	No	No	No	No
Mechanical ventilation therapy	No	No	No	No	No	No	No
Dead	No	No	No	No	No	No	No

* patient was initially treated with TMP-SMZ but later switched to clindamycin + primaquine.
** 1g of solumedrol for five days followed by recycling.
*** 1g of solumedrol for three days followed by recycling.
! This patient was lobectomized.
Abbreviations: Bronchoalveolar lavage, **BAL**; Intensive Care Unit, **ICU**; *Pneumocystis jiroveci* pneumonia, **PCP**; Transplant, **Tx**; Trimethoprim/sulfamethoxazole, **TMP-SMZ**.

POS304 STUDY THE EFFECT OF POSITIVE BLOOD CULTURE IN DECEASED DONORS ON THE RESULTS AND COMPLICATIONS OF LIVER TRANSPLANT

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Background: Positive blood culture in deceased donors is one of the possible barriers for organ donation. In this situation, the recipients probably are at increased risk of infection following transplantation. The aim of this study was to determine the effect of positive blood culture on the results and complications of liver transplant.
Methods: In this cross-sectional study, demographic data gathered from database registry of liver transplant patients between 2016–2018 in Mashhad. According to the protocol, blood culture was done in all deceased donors. Cases with positive blood culture without clinical sepsis were treated with sensitive antibiotics. If the second blood culture (24 hours later) was negative, transplant surgery was performed, but with the second positive blood culture test, we rejected the case. In all recipients, sensitive antibiotics were used at least for five days. The results of liver transplantation and complications were compared between the groups (negative versus positive blood culture of the donor).
Results: Results from 137 recipients (18 cases with positive blood culture and 119 with negative blood cultures) were compared. The most common

pathogens cultured were as follows: staphylococcus aureus (33.5%), and enterococcus faecalis (16.7%). The study showed that there was no significant relationship between the results of positive blood culture in the donor and the rate of in-hospital complications including post-transplant infections (p-value=0.22), vascular events (p-value=0.39), acute rejection (p-value=0.13) and biliary complications (p-value=0.43). The rate of first year complications didn't have significant difference including post-transplant infections (p-value=0.13), vascular events (p-value=0.79), rejection (p-value=0.08) and biliary complications (p-value=0.06). The hospital stay were comparable between the groups (p-value=0.25). As well, the 1-year survival rate did not have significant difference between the groups (p-value=0.18).
Conclusions: The results of this study indicate that the donor blood culture in the absence of clinical or laboratory sepsis does not affect the complication and survival rate of liver transplantation and these organs can be used safely.

POS305 TENOFOVIR ALAFENAMIDE FOR HEPATITIS B VIRUS PROPHYLAXIS POST-LIVER TRANSPLANTATION: A REAL-WORLD STUDY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background: Antiviral treatment is recommended to prevent Hepatitis B Virus (HBV) re-infection of the graft in patients after liver transplantation (LT). Tenofovir alafenamide fumarate (TAF) was shown equally efficacious in suppressing HBV but with less renal toxicity than tenofovir disoproxil fumarate (TDF). The aim of this real-world study was to evaluate renal function in post-LT patients that changed TDF with TAF.
Methods: The TAF group ($n = 17$) included patients who switched to TAF mainly (14/17, 82%) due to low (<60 ml/min/1.73 m^2) Glomerular Filtration Rate (GFR) (TAF is reimbursed in Greece only in patients with GFR <60 ml/min, serum phosphorus levels <2.5 mg/dl or DEXA T-score <−2.5). The control group included patients that remained on TDF ($n = 30$), although some ($n = 14$) had low GFR (TDF-Chronic Kidney Disease [CKD] group). GFR was assessed using: (i) MDRD-6 variable; (ii) CKD-EPI formula and (iii) radionuclide technique (rGFR).
Results: The follow-up period was significantly shorter and diabetes mellitus was significantly more common in the TAF group as compared with the TDF group (13.7 vs. 35.5 months, $p < 0.001$ and 35% vs. 10%, $p = 0.03$, respectively). At the end of follow-up there were no significant changes in any marker of renal function between the TAF and the TDF group or TDF-CKD group, although the numerical change in rGFR in the latter comparison was greater in the TAF group (ΔrGFR 3 vs. −2.14 ml/min, $p = 0.26$). The changes remained non-significant when the patients were divided according to age (>65 vs. <65 years) or current CNI use. The use of everolimus was associated with improvement in renal function (ΔrGFR 2 vs. −7.75 ml/min, $p = 0.06$ [TAF vs. TDF group]; 2 vs. −12 ml/min, $p = 0.01$ [TAF vs. TDF-CKD group]). There were no TAF-related side effects or cases of HBV recurrence.
Conclusion: Conversion to TAF in post-LT patients who develop CKD does not lead to improvement of kidney function after a period of approximately one year.

POS306 COVID-19 IN 823 TRANSPLANT PATIENTS: A SYSTEMATIC SCOPING REVIEW

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Background: Management of COVID-19 in transplant patients is a big challenge. Data on immunosuppression management, clinical picture, and outcomes are lacking. Therefore, we summarized the primary research on COVID-19 in transplant patients regarding the immunosuppression protocols, clinical presentation, and clinical outcomes.
Methods: Search strategy: We performed a systematic search of MEDLINE, EBSCO, CENTRAL, CINAHL, LitCovid, Web of Science, and Scopus electronic databases. Besides, we searched the references of the relevant studies.
Selection Criteria: Primary reports of solid organ transplant patients who developed COVID-19 were included with checking for overlap of cases.
Data collection and analysis: We provided a descriptive summary of immunosuppression therapy (before and after COVID-19), clinical presentation (symptoms, imaging, laboratory, and disease severity), management (oxygen therapy, antiviral, and antibacterial), major outcomes (Intensive care admission, invasive mechanical ventilation, acute kidney injury), and mortality.
Main results: We identified 74 studies reporting 823 cases of solid organ transplantation with COVID-19. Among 372 patients with sufficient data, 114 (30.6%) were mild COVID-19, 101 (27.2%) moderate, and 157 (42.2%) severe or critical.
Major outcomes included intensive care unit admission, invasive ventilation, and acute kidney injury, which occurred in 121 (14.7%), 97 (11.8%), and 63 (7.7%) of patients, respectively. Mortality was reported in 160 (19.4%) patients.
Conclusion: COVID-19 in solid organ transplant patients probably has a more disease severity, worse major outcomes (Intensive care admission, invasive ventilation, acute kidney injury), and higher mortality than in non-transplant patients.
Figure 1: Study flowchart.

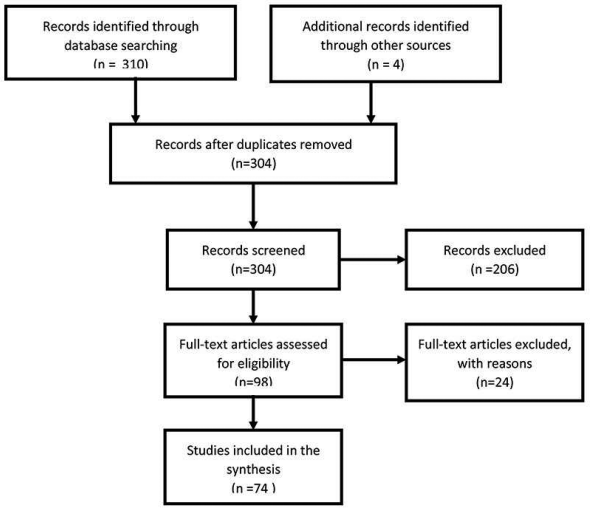

Table 3. Distribution of illness severity and organ transplant

Organ	Mild	Moderate	Sever or Critical	Total
Kidney	44	35	90	169
Liver	26	7	29	62
Heart	11	1	11	23
Lung	4	1	9	14
Combined	-	2	2	4
Non-specified	29	55	16	100
Total	114	101	157	372

POS307 BILE MICROBIOTA IN LIVER TRANSPLANTATION: PROOF OF CONCEPT USING GENE AMPLIFICATION IN A HETEROGENOUS CLINICAL SCENARIO

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Introduction: Historically, bile in the biliary tract has been considered sterile. Most of the series are based on patients with biliary tract diseases or the bile has been obtained with procedures susceptible to contamination.

Methods: We evaluated the bile in a heterogeneous cohort of liver donors and recipients patients, with samples obtained in a sterile way, directly from gallbladder and the common bile duct.
Results: We assessed the bile microbiota in six liver donors and in six liver recipients after whole or split liver procedures in adult or pediatric recipients. Bile samples were studied using PCR sequencing of the 16S ribosomal RNA gene amplification (rDNA).
Conclusion: We demonstrated that the bile is sterile thereby ruling this out as a source of contamination following transplant.

POS308 LIVER TRANSPLANTATION RESULTS IN THE ERA OF MODERN ANTIVIRAL THERAPY OF HEPATITIS C

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Background: Appearance of direct antiviral drugs (DAAs) are a new potential treatment of chronic hepatitis C (CHC) in patients with decompensated liver cirrhosis, who previously didn't have another alternative like liver transplantation (LT). However, there is the question of the optimal timing of antiviral therapy (AVT). The aim of the study was researching of a spectrum of clinical outcomes in patients with HCV cirrhosis, who received or not AVT DAA in waiting list.
Methods: 49 patients with HCV-related cirrhosis in waiting list were selected. The data were divided into 2 groups: 1–40 patients who received AVT DAA before LT, 2–9 patients without.
Results: In most cases MELD-Na was less 20 points and six patients had MELD-Na > 20 and didn't exceed 25. At the time of analysis 38 patients reached 12 weeks after AVT. 35 of them (92.1%) had a sustained virologic response (SVR). Among them in 51.4% ($n = 18$) of cases MELD-Na got decreased. There were no changes in 22.9% ($n = 8$), while in 25.7% ($n = 9$) observed increasing of MELD-Na. In 42.8% ($n = 15$) sustained elimination of HCV infection led to delisting. Among patients without SVR the increasing of MELD-Na was detected in all cases ($n = 3$). In the non-AVT group one patient showed improvement in liver function (11.1%), in the rest - MELD-Na either remained stable or continued to grow in equal proportions – 44.5% ($n = 4$). Statistically significant differences were obtained in frequency of deaths in patients with or without AVT ($p < 0.001$, $V = 0.728$). Chances to die on waiting list in patients without AVT were higher in 66.5 times (95% CI: 7.99–554).
Conclusion: Our study showed significant advantages of the AVT DAA for patients on waiting list with MELD-Na less than 25 points.

POS309 INFLUENZA IN LIVER TRANSPLANT RECIPIENTS: INCIDENCE AND OUTCOMES

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Background: Influenza virus is a common cause of infection in liver transplant (LTX) recipients and may have an aggressive course. We determined the incidence of influenza in eight seasons in a cohort of Danish LTX recipients and described risk factors and outcomes after influenza infection.
Methods: *The Centre of Excellence for Personalized Medicine of Infectious Complications in Immune Deficiency (PERSIMUNE) data repository* contains information on nationwide influenza PCR results on LTX recipients transplanted from 2010 to 2017. *The Knowledge Center for Transplantation database* includes data on influenza vaccination, laboratory confirmed influenza PCR results, comorbidities and outcomes following influenza in LTX recipients transplanted in 2010–2019. Incidence of influenza were estimated as number of cases per 1000 person-months. Multivariate cox regression model was used to asses risk factors.
Results: In 323 LTX recipients from the PERSIMUNE data repository the cumulative incidence of influenza 1 year and 5 years post-LTX was 1.2% (CI 0.03%–2.4%) and 3.2% (CI 1.1%–5.2%), respectively (Figure 1). The incidence rates 1 year and 2–5 years post-LTX were 1.1 (CI 0.38–2.7) and 0.38 (CI 0.14–0.83) per 1000 person-months. The incidence rates for the seasons 2010/2011–2017/2018 varied from 0 to 5.2 (CI 2.3–10.3) per 1000 person-months. In 378 LTX recipients from the Knowledge Center for Transplantation database, we found the most common outcome after influenza was hospital admission (61%). We found no significant effect of same-season influenza vaccination or any other risk factors.
Conclusion: The incidence of influenza in LTX recipients was subject to seasonal variation. Only few cases of influenza were identified, and the first year post-LTX did not have a significantly higher rate of infection compared to later years. Most LTX recipients with influenza required hospital admission, and same-season influenza vaccination was not associated with lower risk of influenza.

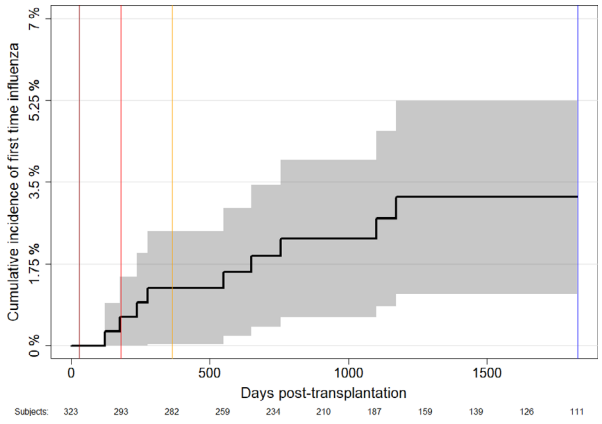

Figure 1. Cumulative incidence of influenza with 95% confidence interval. Vertical lines marks 1 month (maroon), 6 months (red), 1 year (yellow) and 5 years (blue) post transplantation.

POS310 EARLY LIVER GRAFT DYSFUNCTION IS A RISK FACTOR FOR A RELAPAROTOMY FOR HEMOPERITONEUM (WITH NO APPARENT SOURCE OF BLEEDING).

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Background: Relaparotomies after liver transplantation (LT) have an important impact on the overall result and are performed in 17–34% [HPB Surgery 2014; Transplantation 2018]. Depending on the cause and other factors, relaparotomy after liver transplantation can play both a positive and a negative role, provoking septic complications, while the most unfavorable prognosis is typical for patients who have undergone relaparotomy for peritonitis [Liver Transpl 2019].
Methods: A retrospective analysis was performed for 690 consecutive patients undergoing LT from 2008 to 2019; 131 (19%) of which underwent relaparotomy postoperatively. Relaparotomy indications were hemoperitoneum (in 50% cases), peritonitis (in 25% cases), biliary leakage (11%), pancreatitis (5%) vascular complications (2%) and others (7%).
Results: Recipients with hemoperitoneum without an obvious source on relaparotomy were characterized by higher ALT level on the first postop day (1137 [646; 1337] vs 644 [343; 927], U/L, $p = 0.07$) and a higher rate of early allograft dysfunction (EAD) (53% versus 28%; $p = 0.07$). The most unfavorable indication for relaparotomy was peritonitis: 90-day mortality in this group was 49% versus 20% ($p = 0.001$) in the group of patients with other indications. Recipients who underwent relaparotomy and died within 90 days were characterized by significantly higher MELD (26 [20; 36] versus 19 [15; 25]; $p < 0.001$), higher rate of performed relaparotomies (4 [2; 9] versus 1 [1; 3], $p = 0.001$), higher frequency of urgent transplantations (33% versus 8%, $p < 0.001$). No differences in cold and warm ischemia time, donor age, blood loss were found.
Conclusions: An unfavorable prognosis after relaparotomies was associated with the severity of the recipient's condition (urgent status, multi-resistant flora contamination). The main cause of death in recipients who

underwent relaparotomy after LT was sepsis. EAD was a risk factor for relaparotomy for hemoperitoneum with no apparent source.

POS311 STRESS BURDEN RELATED TO POSTREPERFUSION SYNDROME MAY AGGRAVATE HYPERGLYCEMIA WITH INSULIN RESISTANCE DURING LIVING DONOR LIVER TRANSPLANTATION

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Background: We investigated the impact of postreperfusion syndrome (PRS) on hyperglycemia occurrence and connecting (C) peptide release, which acts as a surrogate marker for insulin resistance, during the intraoperative period after graft reperfusion in patients undergoing living donor liver transplantation (LDLT) using propensity score (PS)-matching analysis.
Methods: Medical records from 324 adult patients who underwent elective LDLT were retrospectively reviewed, and their data were analyzed according to PRS occurrence (PRS vs. non-PRS groups) using the PS-matching method. Intraoperative levels of blood glucose and C-peptide were measured through the arterial or venous line at each surgical phase. Hyperglycemia was defined as a peak glucose level >200 mg/dL, and normal plasma concentrations of C-peptide in the fasting state were taken to range between 0.5 and 2.0 ng/mL.
Results: After PS matching, there were no significant differences in pre- and intra-operative recipient findings and donor-graft findings between groups. Although glucose and C-peptide levels continuously increased through the surgical phases in both groups, glucose and C-peptide levels during the neohepatic phase were significantly higher in the PRS group than in the non-PRS group, and larger changes in levels were observed between the preanhepatic and neohepatic phases. There were higher incidences of C-peptide levels >2.0 ng/mL and peak glucose levels >200 mg/dL in the neohepatic phase in patients with PRS than in those without. PRS adjusted for PS with or without exogenous insulin infusion was significantly associated with hyperglycemia occurrence during the neohepatic phase.
Conclusions: Elucidating the association between PRS and hyperglycemia occurrence will help with establishing a standard protocol for intraoperative glycemic control in patients undergoing LDLT.

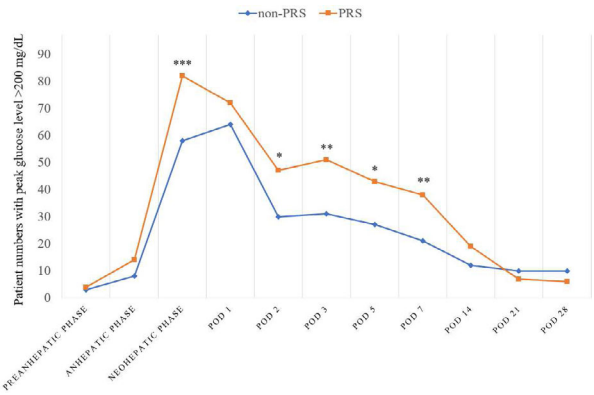

Figure 1. Comparison of intra- and postoperative hyperglycemia occurrence (peak glucose level > 200 mg/dL) between propensity score-matched patients with or without postreperfusion syndrome (PRS). $*p < 0.05$, $**p \leq 0.01$, and $***p \leq 0.001$. POD, postoperative day.

POS312 LIVER GRAFTS FROM CONTROLLED AND UNCONTROLLED DONATION AFTER CIRCULATORY DEATH IN ITALY: PRESERVATION PROTOCOL AND RESULTS

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Background: Donation after circulatory death (DCD) in Italy, with its 20-min stand-off period, provides a unique high-risk cohort. In the last few years, we have observed a progressive reduction in the number of uncontrolled (uDCD) donors mainly due to logistical challenges of this practice, which was paralleled by an increase in controlled (cDCD) donors. Nevertheless, 30% of the Italian DCD transplants come from uDCD.
Methods: We present the results of a multicenter Italian cohort with 19 uDCD and 44 cDCD donors. The uDCD donors were patients unsuccessfully resuscitated after out-of-hospital cardiac arrest. Cardiopulmonary resuscitation was maintained during transport, and death was declared at arrival in the hospital. The cDCD donors were patients with devasting brain injury not fulfilling brain death criteria, where the decision to withdraw treatment was based on futility. Normothermic regional perfusion (NRP) was used in all cases. Hypothermic oxygenated machine perfusion (HOPE) was added after transport and back-table surgery.
Results: The utilization rate was found with 73.1% and 86.5% for uDCD and cDCD, respectively. Patients receiving uDCD grafts experienced more frequently acute kidney injury requiring dialysis (28% vs. 5%, $p = 0.015$). Primary nonfunction was more frequent among uDCD transplants, although the difference was not statistically significant (16% vs. 5%, $p = 0.16$). Two recipients (1 in each group) developed hilar biliary strictures that were managed with endoscopic stenting, and no relisting was required during 27- and 33-months follow-up.
Conclusions: The cDCD-group did well despite the high-risk profile resulting from the prolonged warm ischemia. The inferior results of the uDCD-group appear in line with earlier outcomes in other countries with shorter warm ischemia and are therefore considered acceptable, mainly in the context of the applied preservation protocol with NRP+HOPE and the balance between posttransplant survival and waitlist mortality in Italy.

POS313 COMBINED INFRARED THERMOGRAPHY AND MICRODIALYSIS AT THE END OF STATIC COLD STORAGE FOR ASSESSING LIVER GRAFT QUALITY – PILOT CLINICAL STUDY

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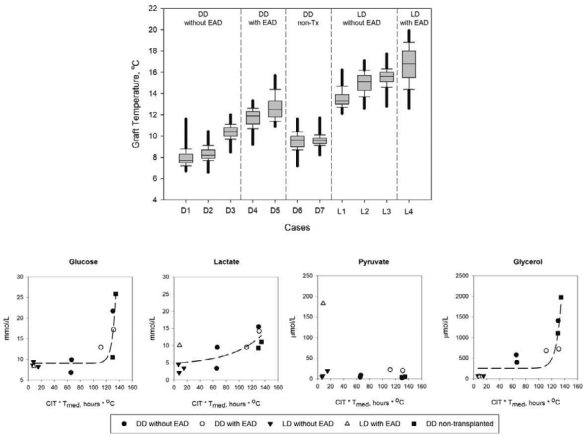
Background: Choosing an adequate control method for donor organ static cold storage is a complex issue. In this pilot study infrared thermography and interstitial microdialysis have been simultaneously used to determine the association among graft temperature, its metabolic state, and initial function in actual clinical practice.
Methods: We evaluated four right lobe liver grafts from living donors (LDs) and seven grafts from deceased donors (DDs). Thermography and microdialysis were performed at the end of cold ischemia time (CIT). Glucose, lactate, pyruvate, and glycerol (Glyc) levels were determined in interstitial fluid samples.

Results: The median graft temperatures were significantly higher than the target value of 4°C and varied widely (LD: 13.4–16.8°C; DD: 7.7–12.4°C). The temperatures of DD grafts with normal initial function were significantly lower than those in grafts with early allograft dysfunction (8.5°C (range, 6.6–12.0°C) vs. 12.1°C (range, 9.2–15.7°C), $p = 0.005$). Only Glyc was significantly different between DD and LD grafts (723 μmol/L (range, 397–1973 μmol/L) vs. 70 μmol/L (range, 53–75 μmol/L), $p = 0.006$).
The associations between [cold ischemia time * graft temperatures] and metabolic parameters (Glucose, Lactate, Pyruvate, and Glycerol) were investigated. The dotted lines on the graphs are the best results of dynamic fitting using the equation: f = y0+a*exp (b*x). The R2 values for Glu, Lac, and Glyc were 0.80, 0.60, and 0.81, respectively.



Conclusions: Not only the CIT but also the graft temperature affects the state of metabolism and initial function. Thus, temperature monitoring combined with microdialysis can be used for assessing graft quality and improving static cold storage technology.
This study was supported by the Russian Science Foundation (grant number: 19-75-10040).

POS314 LIVER DONOR BOARDING PASS FOR USING THE MACHINE PERFUSION

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It has been worldwide showed that the machine perfusion (MP) offers many benefits in liver transplantation, but it has still some grey area: costs are still high, not all perfused grafts are implanted, the discard frequency after MP preservation can be up to 12% and it is still reported PNF and EAD rate that might be patient life threatening. The aim of the study is to assess the donor risk factors of grafts, perfused with whatever MP, that would predict an ineffective MP setting up and those would trigger a EAD post-transplant.
Data from donors of all MP-perfused grafts have been analysed, whether they were implanted or discarded after perfusion. First endpoint was the negative events after perfusion (NegE), that is the number of grafts discarded plus those were implanted but lost after the transplant. A risk factor analysis was performed for NegE and marginal grafts for MP were identified. Finally, the risk of EAD was investigated, considering only implanted grafts.
From 2015 to September 2019, 158 grafts were perfused with MP: 151 grafts were implanted and 7 discarded. Of 151, 15 grafts were lost after transplant, therefore, the NegE group was of 22 donors. In the univariate analysis, the donor risk index>1.7, the presence of hypertension in the past medical history, the S-CIT and the moderate or severe macro-vesicular steatosis were the significant factors for NegE. The multivariate analysis confirmed the macro-steatosis>30% as an independent risk factor for NegE (odd ratio 5.643, $p = 0.023$, 95%CI : 1.27–24.98).
Of 151 transplanted patients 34% of recipients experienced a EAD and had a worse 1- &3-year-survival, comparing with those who don't faced with EAD (NoEAD), respectively 96% & 96% for EAD vs. 89% & 71% for NoEAD, $p = 0.03$. No one of the donor/graft characteristics was associated to EAD even if the graft was form aged donor, or moderately steatotic or fibrotic or with elevated transaminase.
For the first time, this study shows that macro vesicular steatosis > 30% might be a warning factor involved in graft lost risk or a graft discard cause after the MP treatment. From the other side, the MP seems to be useful to reduce the donor and graft weight in developing a EAD. More studied needed to investigate other EAD factors to better prevent this fatal complication.

POS315 PERIOPERATIVE RISK FACTORS OF ACUTE KIDNEY INJURY POST LIVER TRANSPLANTATION: A MONOCENTRIC RETROSPECTIVE COHORT STUDY OF 260 PATIENTS

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Aims and Background: Acute kidney injury (AKI) is a major risk factor of poor outcomes after liver transplantation (LT). AKI is usually attributed to post-LT events and drug toxicity. Peri-operative risk factors of LT-associated AKI remain poorly documented, which hampers the development of personalized preventive strategies.
Methods: AKI was assessed by KDIGO criteria based on creatinine changes from baseline to day 5 post LT. 260 single first full-size LTs without any pre-existing renal replacement therapy (RRT) were performed from 2003 to 2018. Incidence of AKI was assessed. Logistic regression determined the risk factors of KDIGO I and II-III AKI.
Results: Incidence of AKI KDIGO I and II-III was 30% (78/260) and 25.7% (67/260), respectively. Preoperatively, patients with AKI had higher lab-MELD and Child-Pugh scores, lower serum fibrinogen and albumin levels. Donor type, donor hepatectomy and cold ischemic time were similar between groups. AKI was more frequent in case of marginal donors. LT surgery was longer in the AKI groups. Needs for per-operative blood transfusions were higher in the AKI groups. Rate of post-reperfusion syndrome was higher in AKI groups. Postoperatively, lower hemoglobin levels and higher INR from day 1-5 were associated with AKI. Peak of transaminases were not different between AKI versus non-AKI groups. AKI was associated with longer length of hospital and ICU stays. After multivariate analysis, blood transfusions and post-reperfusion syndrome were risk factors to develop KDIGO I AKI. Pre-operative serum levels of fibrinogen and albumin were risk factors for KDIGO II-III AKI. Finally, "marginal donors" was the only risk factor for both KDIGO I and II-III AKI.
Conclusions: LT-associated AKI occurs in >50% of cases. Per-operative hemorrhage and post-operative reperfusion syndrome represent risk factors, particularly in cases of marginal donors.

POS316 EX-VIVO LIVER SPLITTING DURING HYPOTHERMIC OXYGENATED PERFUSION : A NOVEL PROCEDURE TO OPTIMIZE GRAFT PRESERVATION IN SPLIT LIVER TRANSPLANTATION

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Background: Split liver transplantation increases organ availability. However, split grafts from deceased donors have prolonged ischemic times leading to inferior outcomes compared to whole grafts. Hypothermic

Oxygenated Perfusion (HOPE) has been shown to improve outcomes of marginal liver grafts and may also benefit split grafts. This study establishes a standardized technique for ex-vivo liver graft splitting during HOPE.
Methods: We included all single-center split liver transplantations from deceased donation performed from 2018–2020. In 2020, we developed and prospectively used *HOPE-Split*, an ex-vivo liver splitting technique with simultaneous HOPE. The local ethics committee approved the study.
Results: From the 13 ex-vivo splits during the study period, four partial grafts were obtained after *HOPE-Split*. After hilar plate division, 2 whole grafts underwent HOPE through the main portal vein during the entire parenchymal transection which lasted for 62 min and 75 min, respectively (Figure 1). Respective partial grafts were perfused through a single portal cannula until recipient hepatectomies were completed. With HOPE static cold storage was shortened but total ex-vivo preservation times were similar compared to the standard split technique (Table 1). The 4 *HOPE-Split* grafts were successfully transplanted in 2 adult and 2 pediatric recipients. We observed no early allograft dysfunction or graft loss.
Conclusion: We present a step-by-step liver graft splitting technique during HOPE. Our preliminary results confirm feasibility and suggest improved preservation notably reduction in static cold storage for both partial grafts. A prospective trial is currently ongoing to validate *HOPE-Split* as a promising preservation strategy in split liver transplantation.

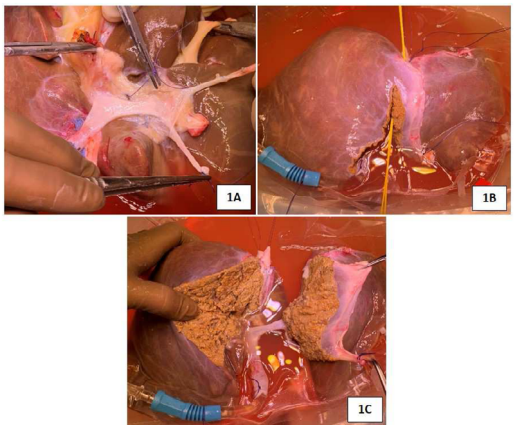
Table 1. Clinical data of HOPE split

		Split				Transplantation
	Recipient	*HOPE (min)*	*Total split (min)*	*Static Cold Storage (min)*	*Ex-vivo preservation (min)*	*L-Graft7 (risk, %)*
HOPE Split ***n*** **= 4**	56 y Cirrhosis Hepatitis B- HCC	165	275	378	543	2.8
	3 y – 13 kg Alagille syndrome Second LT			475	640	10.8
	45 y Hepatitis B– Auto-immune	152	240	368	520	2.6
	3 months – 5 kg Acute Liver Failure			296	448	2.3

HCC: hepatocellular carcinoma ; L-Graft7 score expressed as individualized risk of allograft dysfunction according to Agopian et al.

Figure 1: Technical aspects of the HOPE-Split procedure

Vessel dissection and hilar plate division (1A) were performed during static cold storage. Parenchymal transection was performed during HOPE using a "split hanging manoeuvre" (1B). Both partial grafts remained perfused through the main portal trunk until hepatectomies in both recipients were carried out (1C).



POS317 CERIUM OXIDE NANOPARTICLES ADMINISTRATION DURING EX-SITU NORMOTHERMIC PERFUSION OF DISCARDED HUMAN LIVER GRAFTS.

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Background: The combined approach of ex-situ normothermic machine perfusion (NMP) and nanotechnology represents a new potential strategy to mitigate the severity of ischemia-reperfusion injury (IRI) in liver transplantation. This study evaluated incorporation, distribution and effects of antioxidant cerium oxide nanoparticles conjugated with albumin (Alb-NC) delivered during NMP of discarded human livers.
Methods: Nine human liver grafts deemed not suitable for clinical use were randomized in two groups: 5 were treated with Alb-NC added to the perfusate (study group, SG) at the beginning of NMP (T0) at a final concentration of 50 μmol/L, and compared to 4 untreated grafts (control group, CG). A self-assembled machine and a blood-based solution were used for perfusion. Vascular flows and pressures were continuously monitored. Blood gas analysis was evaluated every 30 minutes, while liver biopsies and perfusate samples were obtained at T0 and after 4 hours NMP (T1) for electron microscopy (TEM), antioxidant activity and transaminases concentration evaluation. Cerium was quantified in perfusate and tissue samples by ICP-MS.
Results: Seven DBD and 2 DCD grafts were considered. Liver were all discarded on histology evaluation: necrosis>10% (2 in each groups), macrosteatosis>30% (1 in each groups), stage 3 fibrosis as per Ishak's classification (2 in SG, 1 in CG). Median donor age and cold ischemia time were 75 years (63–77) and 850 minutes (720–951) in the SG versus 86 (79–88) and 595 (445–799) in the CG ($p = 0.207$ and 0.145 respectively). All grafts were successfully perfused with stable blood flows. At T1, TEM analysis showed transcytosis as mechanism of Alb-NC internalization, a rescue of mitochondrial phenotype and a decrease of peroxidated lipid droplet in SG (11% (T1) *vs* 38% (T0), $p < 0.0001$) compared to CG (68% (T1) *vs* 81% (T0), $p = 0.372$. Liver tissue levels of glutathione increased in SG (2.6 ± 1.1 μg/mg protein at T1 *vs* 0.85 ± 0.1 μg/mg protein at T0, $p = 0.027$) whereas were unchanged in CG (1.4 ± 0.3 μg/mg protein *vs* 1.5 ± 0.36 μg/mg protein at T0, $p = 0.108$). Alb-NC uptake at T1 was confirmed both by a decrease of cerium in the perfusate solution (−80%±6%) and accumulation in hepatic tissue (4.8 ± 1.04 ppm).
Discussion: The use of Alb-NC during ex-situ NMP has the potential to counteract the oxidative stress induced by IRI.

POS318 IL-6 LEVEL AFTER LIVER TRANSPLANTATION IN PATIENTS DEVELOPING ACUTE KIDNEY INJURY

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Background: Pathogenesis of Acute kidney injury (AKI) post-liver transplantation (LT) is multifactorial. Beyond the classical pre-transplant risk factors, the hypoxia of the graft and the ischemia-reperfusion injury (IRI) have recently been recognized to exert a pathogenetic role with specific mechanisms.
The ischemic tissues put in place protective mechanisms in response to hypoxia mediated by the expression of factors induced by hypoxia (HIF)-1-alpha, that promotes cell survival under hypoxic conditions by several reactions, including the activation of inflammatory cytokines responsible for systemic inflammatory response syndrome (SIRS). Tumor necrosis factor-α, IL-1 and IL-6 are the most important cytokines released in IRI and seem to play a pivotal role in the onset of AKI in SIRS and sepsis.

Aim of the study is to evaluate AKI occurrence among liver transplanted patients and its relationship with IRI and cytokines systemic release.
Methods: Data of 78 patients (62 males, 79.5%) undergone liver transplantation (2007–2011) were retrieved. Data on pre and post-LT liver and renal function were retrieved. IL-6 were evaluated at transplant, 1- and 12-days post- LT.
Results: AKI developed in 40 patients (51.3%) [30 pts with AKI stage 1, 5 pts AKI stage 2 and 5 AKI stage 3]. Patients with AKI stages 2&3 presented more deteriorated pre-LT liver function as suggested by higher MELD score (AKI2&3 20 vs no AKI-AKI1 15; $p = 0.008$), higher bilirubin (AKI2&3 5.7 mg/dl vs no AKI-AKI1 2.8 mg/dl; $p = 0.009$) and INR (AKI2&3 1.9 vs no AKI-AKI1 1.4; $p < 0.0001$) at LT, despite superior renal function (serum creatinine in AKI2&3 0.7 mg/dl vs no AKI-AKI1 0.9 mg/dl).
Patients with AKI2&3 experienced greater IRI based on functional recovery of the transplanted liver (higher peak AST in the first 7 days post-LT $p = 0.029$, and higher peak ALT level $p = 0.062$).
AKI patients demonstrated a progressive increasing of IL-6 after liver transplantation (AKI 34.4–37.8–88.2 ng/ml vs no AKI 30.5–21.6–23.3 ng/ml).
Conclusions: Patients who experienced greater ischemia-reperfusion injury of the liver graft developed more frequently AKI. Patients with AKI experienced an increased release and circulation of IL-6, that probably is involved in AKI development with interesting implications in future therapy.

POS319 PROTECTION OF MITOCHONDRIAL MACHINERY IN HYPOTHERMIC STATIC ISCHEMIA PRESERVATION: A ROLE FOR IGL2 SOLUTION

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Background: Static cold preservation using preservation solutions is still the most common way to preserve livers for transplantation, and their composition has a deep impact in the outcome of transplantation. The oncotic agent is a key element in the composition of a preservation solution. Polyethylene glycol 35 (PEG35) is a stable and non-toxic polymer, and it is the oncotic agent of IGL-1 solution. Reduced glutathione, another critical component used in preservation solutions as natural antioxidant, is essential for graft preservation. Furthermore, ALDH2 has been described to be involved in liver injury prevention against ischemia. In this study we show the benefits of a novel IGL2 solution which is characterized by augmented concentrations of both PEG35 and glutathione compared to IGL-1, which has become widely used in liver transplantation. The aim was to reinforce mitochondrial machinery preservation through aldehyde dehydrogenase 2 (ALDH2) and antioxidant capacity during hypothermic fatty liver graft storage. In this communication, we evaluated and compared the benefits of increasing PEG35 and glutathione content, on mitochondrial ALDH2 and antioxidant capacity as well as other biomarkers important on ischemic protection.
Methods: Fatty livers from male Zücker obese rats were conserved for 24 h at 4°C in the following solutions: IGL-0 (PEG 0 g/l, GSH 3 mM), IGL-1 (PEG 1 g/l, GSH 3 mM) or IGL-2 (PEG 5 g/l, GSH 9 mM). After organ recovery and rinsing of fatty liver grafts with Ringer Lactate solution, liver injury, mitochondrial damage, lipoperoxidation, oxidative stress and cytoprotective regulators were measured.
Results: PEG35 and GSH dependently on their amount prevented liver injury (AST/ALT), mitochondrial damage (GLDH) and lipoperoxidation (AOPP, MDA, 4HNE), and concomitantly augmented antioxidant capacity (GSH/GSSG), mitochondrial ALDH2, and constitutive eNOS.
Conclusions: Increased PEG35 and glutathione in IGL-2 solution are determinant factors for preserving mitochondrial integrity and increasing the antioxidant capacity to better protect the graft against cold ischemia insult.

POS320 IGL2: A SOLUTION FOR LIVER HYPOTHERMIC OXYGENATED PERFUSION (HOPE) STRATEGIES.

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Background: The lack of optimal organs for transplantation has been a reality for so many years. In this context, machine perfusion (MP) has shown benefits in improving graft cold preservation as compared to static cold storage. Nevertheless, MP needs to use a perfusate and until now the one used is the Belzer-MPS and analogues (PerfGen) which were initially designed for kidney perfusion by Belzer et al. by the seventies. Therefore, a preservation for MP specifically designed for liver is still needed. Belzer-MPS contains HES as oncotic agent, which promotes erythrocytes hyperaggregation problems during liver perfusion. This is an issue that can be avoided by using a different oncotic agent, such as polyethylene glycol 35 (PEG35). In this study we compared commercially available Belzer-MPS analog solution (PerfGen) versus an IGL-2 solution (modified IGL-1 solution with an increased dosage of PEG35) on rat livers subjected to HOPE.
Methods: Sprague Dawley rats 11 weeks old were used. Livers were extracted and preserved (8 hours; 4°C), followed by HOPE (4 hours at 4 °C) either in IGL-2 or PerfGen solution. After organ recovery, liver injury (AST/ALT), mitochondrial damage (GLDH), and ALDH2 activity were assessed.
Results: Levels of AST/ALT and GLDH with the IGL-2 solution were reduced while there was an upregulation of mitochondrial ALDH2.
Conclusion: In this communication we present for the first time a perfusate designed for liver using PEG35 that contributes to increase the mitochondrial integrity, as a determinant factor for liver preservation in HOPE.

POS321 THE RELEASE OF EXTRACELLULAR VESICLES DURING LIVER NORMOTHERMIC MACHINE PERFUSION: A POTENTIAL SOURCE OF VIABILITY MARKERS

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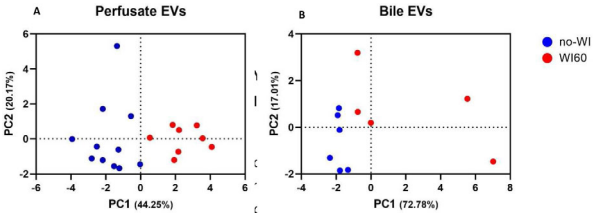
Background: Normothermic Machine Perfusion (NMP) allows assessment of hepatocellular and cholangiocytes viability makers of high-risk livers. However, their validity is still unclear and there is yet no consensus on the best set of markers. Extracellular Vesicles (EVs) are paracrine mediators involved in physiological and pathological processes released by all cells. EVs store microRNA (miRNA) selected in response to stressors and carry a signature of the functional state of the parental cells. We observed that EVs-associated miRNAs change in response to Warm Ischemia (WI) and here we investigated their potential as additional viability markers.
Methods: Porcine livers exposed to 60 min WI (WI60, $n = 5$) or not (no-WI, $n = 5$) underwent 6 h NMP. Perfusate and bile were sampled at 1, 3, and 6 h. The concentration of transaminases, lactate, perfusate pH, vascular resistances, bile volume, biliary concentration of lactate, glucose, bicarb, and pH were measured and compared between groups. EVs were characterized and RNA isolated at the same timepoints. RNAseq identified transcripts differentially expressed in WI60 in both perfusate and bile EVs. A principal component analysis explored if differentially expressed miRNAs can be used as viability markers. Mean (±SD) is given.
Results: In WI60, overall perfusate transaminases levels were 6-fold higher ($p < .001$), whereas lactate was higher only at 1 h NMP [7.8 (±2.9) mmol/L vs 1.7 (±2.7), $p = .004$]. Perfusate pH was higher in WI60 at 3 and 6 h ($p < .05$). There was no difference in vascular resistance or bile volume during NMP. The biliary concentration of lactate, glucose, bicarb, and biliary pH was also similar. In WI60, 5 miRNAs were downregulated in perfusate EVs (miR-92a-2, miR-145, miR-148b, let-7a-1, miR-451, all adj. $p < .001$), whereas in biliary EVs 23 miRNAs were upregulated (all adj. $p < .001$). In principal component analysis, combining perfusate EVs miRNAs with other perfusate markers discriminated the experimental groups perfectly, where perfusate markers alone did not. In contrast, biliary EVs miRNAs discriminate the experimental groups less precisely (Fig.1).
Conclusions: EVs released in perfusate and bile during NMP are a potential source of novel viability biomarkers which merit further investigation to assess viability of high-risk livers during NMP



POS322 CALL FOR AN INTERNATIONAL STUDY TO IDENTIFY TRAJECTORIES TO EARLY ALLOGRAFT FAILURE AND ASSESS HOW EARLY RETRANSPLANT MAY IMPACT ON PATIENT SURVIVAL

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Background: Early Allograft failure Simplified Estimation (EASE) score has been recently developed using a multicenter retrospective Italian liver transplant database (1609 patients).1 The EASE score predicts the Early Allograft Failure (EAF, defined as graft failure or death due to any cause) with an accuracy of 87%. In addition, the EASE score allows identifying a class of cases (EASE score > 0) with a very high risk of failure and need of prompt retransplant. The EASE score has been validated on a UK liver transplant cohort of 538 cases.1
Methods: We call transplant Centers to participate in a large multicenter international observational study to 1. identify trajectories to EAF; 2. assess how early retransplant may impact on patient survival; 3. validate previous prognostic indices.
The study design includes two arms: a prospective arm (for Centers that perform at least 40 transplants in 6 months, so qualified as high volume Centers) and a retrospective arm (for intermediate and low-volume Centres). High volume Centers will be requested to register data from donor biopsy, frailty and sarcopenia evaluation, heart and kidney function, infection, and sepsis during the early postoperative period. Intermediate and low volume Centers will be requested only general descriptive data and the data for the calculation of prognostic scores.
An EASE-score calculator, available on smartphones and computers, will be offered.
The Center volume effect will be managed, allowing in both arms, enrolling for each Center the same number of cases: 40 cases (prospective arm) or 100 cases (retrospective arm).
The enrolment period will be April 1- September 30 (plus 90-day follow-up for each case) for the prospective arm and April and April 1-May 31 (for the retrospective arm).
Each Center will be recognized in the Author line (1 author) and in the study group (1 author).

1. Avolio AW, Franco A, Schlegel A, Lai Q, Meli S, Burra P, e al. Development and Validation of … **JAMA Surg 2020** Oct28:e204095

POS323 PROLONGED COLD STORAGE PRIOR TO NORMOTHERMIC MACHINE PERFUSION ALTERS THE MOLECULAR PROFILE OF DONOR LIVERS: INSIGHTS FROM 'BACK TO BASE' LIVER NMP.

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Background: Continuous liver normothermic machine perfusion (NMP) is a novel technology associated with safe extension of organ preservation time, increased organ utilisation and reduced early graft injury. Increasingly, NMP is utilised as a 'Back to Base' application with static cold storage (SCS) for organ transport and NMP initiated at the implanting centre prior to transplantation. This study aimed to evaluate the impact of prolonged cold ischaemia (>6 hrs) on the proteomic and molecular profile of NMP livers.
Methods: Liver tissue samples ($n = 57$) representing the end of cold storage (LT1), the end of NMP/total preservation (LT2) and in situ organ reperfusion (LT3), were analysed from a prospective clinical trial of 'Back to Base' NMP. Following homogenisation and protein extraction, samples were digested and analysed by quantitative label-free LC-MS/MS (timsTOF Pro, Bruker). Differential proteome expression analysis was performed comparing tissue from livers that had short (<6 hr), and long (>6 hr), SCS period prior to NMP (Student's-test, $p < 0.05$) at LT2 ($n = 7$ vs $n = 14$) and LT3 ($n = 6$ vs $n = 9$). Protein–protein interaction (PPI) networks and functional enrichment analysis were performed using the STRING database.
Results: A total of 170 proteins were identified as present in all samples and of these proteins, expression of 3 proteins at LT2 and 7 at LT3 proteins were significantly different in these conditions. Proteins involved in maintaining cellular homeostasis and removal of damaged or misfolded proteins were significantly downregulated at LT2 in livers with long SCS compared to short SCS. The differentially expressed proteins at LT3 were associated with autophagy and cell-cycle regulation.
Conclusions: These findings suggest that the length of SCS prior to NMP influences the molecular profile of the liver at the end of preservation (LT2) and following reperfusion (LT3). The length of SCS prior to NMP is an important consideration in 'Back to Base' NMP.

POS324 INTRODUCING NORMOTHERMIC MACHINE PERFUSION (ORGANOX) INTO CLINICAL PRACTICE – THE EDINBURGH EXPERIENCE

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Edinburgh Transplant Centre, Edinburgh, United Kingdom

Background and Aims: Here we describe the introduction of *ex situ* Liver Normothermic Machine Perfusion (NMP) into routine clinical practice in a centre with previous experience of NRP. The objective was to increase organ utilisation by overcoming logistical challenges and by the addition of dynamic functional assessment of marginal grafts.
Methods: A pre-intervention period included on-site training with the OrganOx team, construction of local standard operating procedures and discussion with every patient on the liver transplant waiting list for informed consent. Three new Advanced Perfusion and Organ Preservation Specialist posts were created with the objective of sustaining a 24/7 rota to support NMP alongside the established local Normothermic Regional Perfusion (NRP) programme for DCD organ retrieval. The outcomes of all NMP perfusion undertaken in the first year were collected prospectively.
Results: Over 12 months from February 2020, 23 livers were perfused with NMP and 15 proceeded to transplantation (comprising 20.3% of all liver transplant activity during this period). Indications for NMP included logistics (fast track offers / sequential transplants – 52%), change of recipient (COVID +ve / unfit – 9%), difficult recipient hepatectomy (13%) and functional assessment of the donor liver (22%). Of the 15 transplanted livers, two developed hepatic artery thrombosis (HAT) over 30 days after transplant and required relisting, three developed acute rejection that was successfully treated and three livers developed focal parenchymal ischaemia (pressure effect) with no long-term adverse effect. In three cases, NMP was undertaken sequential to NRP. Five grafts were declined after NMP on the basis of poor function or perfusion.

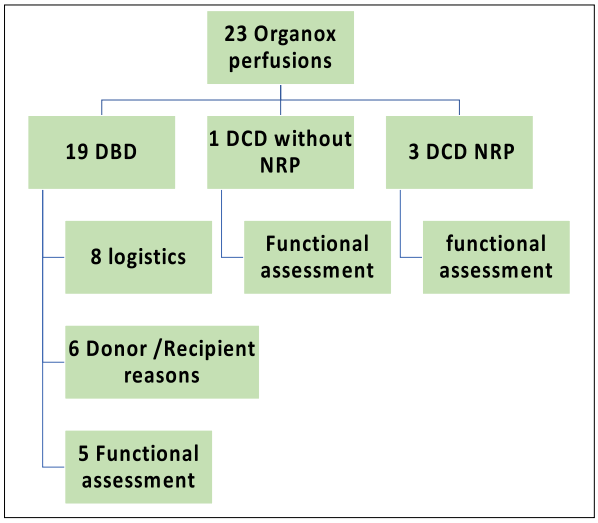

Figure 1: Indications for NMP (OrganOx) in first 12 months since introduction to clinical practice in Edinburgh

Conclusions: NMP can safely be introduced in clinical practice to increase organ utilisation in liver transplantation. Previous experience with NRP shortened the learning curve. In our unit, it has served as a complementary technology to NRP and has been an invaluable tool for negotiating the added logistical complexities of transplantation during the COVID-19 pandemic.

POS325 "HISTOPATOLOGICAL GRADE OF ISCHEMIA REPERFUSION INJURY ON SHORT- AND LONG-TERM OUTCOMES IN LIVER TRANSPLANTATION USING DCD GRAFTS."

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Background: To assess the impact of ischemia reperfusion injury (IRI) on DCD outcomes in liver transplantation.
Methods: Between 2002–2017, 455 DCD transplant were performed at our institution, of which 248 had post reperfusion biopsy that were graded for IRI into four categories (0-no necrotic hepatocytes, 1-scattered foci of single cell necrosis/ drop-out, 2-perivenular zonal necrosis, 3-broader necrosis).
Results: Grade 0, 1, 2 and 3 were 20.7%, 44.5%, 23.4% and 11.3% respectively. In univariate analysis, grade 3 was significantly associated with donor functional warm ischemia>30 minutes ($p = 0.036$) and donor bilirubin>30 mmol/l ($p = 0.014$). IRI grade was also associated with MELD>20 ($p = 0.024$), recipient coagulopathy (INR>2, PLT<70, $p = 0.011$) and portal vein reperfusion, rather than artery ($p = 0.012$). Longer Donor ICU stay and heavier Graft weight was associated with IRI 3 on DBD. Patient and graft survival were significantly associated with the grade of IRI ($p = 0.05$). Patient survival at 1, 5, 10 years was: grade 0= 97.5, 94.7, 72.2%; grade 1= 96.0, 78.6, 69.1%, grade 2= 91.2, 79.8, 67.1%, and grade 3= 82.8, 77.6, 57.7%. Similarly graft survival at 1, 5, 10 years were in group 0 97.8, 94.3, 80.9%, group 1 94.9, 84.3, 72.4%, group 2 91.2, 83.0, 73.4%, and group 3 83.1, 73.3, 68.6%, respectively. The incidence of PNF, HAT and re-transplantation was not associated with the grade of IRI. Patient with IRI had higher rates of re-laparotomies for bleeding ($p = 0.016$) and higher peak AST in the first seven postoperative days ($p = 0.013$). However, no association was observed between IRI and early allograft dysfunction, biliary complications, grade of rejection, viral and malignant recurrence post-transplant.
Conclusion: IRI is an independent risk factor for graft and patient survival. The exact reasons for this are unclear. This grading system might be of use to predict outcome post-liver transplantation. Efforts to minimize IRI are important at a time of organ shortage and increasing use of marginal grafts.

POS326 EX SITU ISCHAEMIA REPERFUSION MOBILISES PASSENGER LEUKOCYTES INTO THE CIRCUIT DURING LIVER NORMOTHERMIC MACHINE PERFUSION

Fungai Dengu[1], Tamsyn Clark[2], Hussain Abbas[1], Ann Etohan Ogbemudia[1], Faysal Elgilani[1], Richard Dumbill[1], Georg Ebeling[1], Carlo Ceresa[1], David Nasralla[2,3], James Fildes[4], Peter Friend[1]
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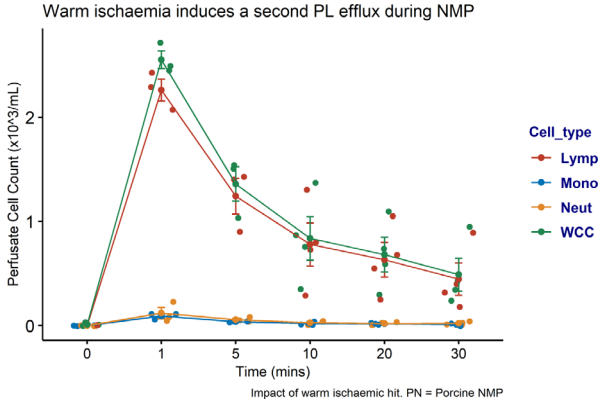
Background: Passenger Leukocytes (PLs) are donor derived cells transferred to the recipient during transplantation. PLs are implicated in both the direct and semi-direct pathways of allorecognition and consequently, are key components in the process of acute allograft rejection. Depletion of PLs has been shown in kidney, lung and vascularised composite allografts to reduce early allograft damage and abrogate ejection. Normothermic machine perfusion is a novel organ preservation strategy that could facilitate PL depletion. In this study, we aimed to explore the impact of ex situ ischaemia reperfusion on the kinetics of PLs during NMP.
Methods: Porcine livers ($N = 4$) procured in a donation after circulatory death (DCD) model were preserved with sequential static cold storage then NMP. During NMP, livers were subjected to repeated 20 min warm ischaemic hits (IHs) separated by 30 mins of NMP. The perfusate was autologous leukodepleted red cells re-suspended in colloid. PLs in the perfusate were quantified using the Sysmex®cell counter system and samples stored for detailed flow cytometric analysis. Cell counts are presented as medians with the range.
Results: 3.4 (1.5–4.5) x10^6 PLs were effluxed into the circuit immediately after ex situ reperfusion and then fell rapidly to 1.35 × 10^6 (1.22 × 10^6–9.9 × 10^7) by 30 mins. After the first (warm) IH during NMP, a further efflux of PLs occurred, with a peak of 3.74 × 10^6 (1.36 × 10^6–1.01 × 10^8range) detected in the circuit (Fig 1). The second (warm) IH also induced an efflux of cells 1.61 × 10^6 (9.3 × 10^6–2.0 × 10^6) with lymphocytes representing the predominant PL sub-type detected.
Discussion: During NMP, there is an inducible and reproducible efflux of PLs into the circuit that occurs in response to ischaemia reperfusion and is composed of predominantly lymphocytes with unexpectedly low numbers of monocytes. PL depletion during NMP may be feasible using an in-line leukocyte-filter upon ex situ reperfusion of donor livers.



POS327 NO DIFFERENCE IN OUTCOMES OF LIVER TRANSPLANTATION USING ELDERLY DONOR GRAFTS VERSUS YOUNG DONOR GRAFTS IN THE SETTING OF SHORT COLD ISCHEMIA TIMES

Mlran Bezjak[1], Stipislav Jadrijevic[1], Branislav Kocman[1], Anna Mrzljak[2], Tajana Kaniza[2], Miro Antonijevic[3], Bojana Dalbelo Bašić[4], Danko Mikulic[1]
[1]University Hospital Merkur, Department of Surgery, Zagreb, Croatia; [2]University Hospital Merkur, Department of Medicine, Zagreb, Croatia; [3]Koncar Electric Traction and Engineering, Zagreb, Croatia; [4]Faculty of electrical engineering and computing, Zagreb, Croatia

Background and aims: Liver transplantation using elderly donor livers is expected to yield results that are inferior to transplantation using young donor grafts. Cold ischemia time is one of the major predictors of postoperative liver function and has a significant influence on short-term and long-term outcomes. In this study, we compared the outcomes of transplantation using young (<45 y) and elderly (>75y) liver grafts in the setting of short cold ischemia times (<8 h).
Methods: A group of 87 recipients of elderly donor liver grafts was compared to a group of 124 recipients of young liver grafts. The groups were matched with regard to age, MELD score and etiology of liver disease. Both groups had mean cold ischemia times of less than 8 hours. Parameters studied included graft and patient survival rates, biochemical markers of early liver injury and function, and the incidence of postoperative complications.
Results: When cold ischemia times are kept relatively short (mean<8 hours), transplantation using elderly grafts showed similar early graft function, similar graft and patient survival rates and no significant difference in the incidences of postoperative complications.
Conclusions: Livers from elderly donors show similar early postoperative function, similar incidence of complications and similar long-term outcomes when compared to younger liver grafts provided that CIT are kept short.

POS328 POST-TRANSPLANT DIABETES PREDICTS SOLID EXTRA-HEPATIC NON-SKIN CANCER IN LIVER TRANSPLANT RECIPIENTS: A LONG-TERM FOLLOW-UP STUDY

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Background: Transplant recipients show a higher risk of malignancy in comparison with general population due to immunosuppressive therapies, mostly non-melanoma skin cancers, lymphoproliferative disorders and solid-organ tumors. Our main aim was to detect the independent predictors of post-LT extra-hepatic solid non-skin cancer (ESNSC) and to analyze the impact of ESNSC on patient survival.
Methods: Data from five Italian transplant outpatient clinics of patients that underwent liver transplant between 2000 and 2005 were pooled to study long term survival and incidence of ESNSC. Multivariate analysis for searching the independent predictors of ESNSC and overall mortality were performed by stepwise Cox logistic regression. Furthermore, we conducted a case-control (1:2) substudy to analyze the impact of ESNSC on the long-term survival.
Results: 367 patients were included in the study. At univariate analysis, post-LT DM and de novo NAFLD, emerged as potential predictors of post-LT ESNSC (as reported in the Table 4). At multivariate test, only post-LT Diabetes Mellitus (DM) resulted as independently associated with ESNSC, conferring a two-fold higher risk of developing ESNSC. 47 patients developed ESNSC and were randomly compared to 94 matched controls. Controls showed a higher overall survival in comparison with cases (the 5- and 10-year survival probabilities were 76.6% and 68.1% for controls; 60.1% and 46.8% for cases; $p = 0.051$ and 0.023, respectively).
Conclusions: We firstly reported that post-LT DM leads to an increased risk of cancer and we confirm that de novo cancer itself strongly impair 10-year patient survival. The present study offers important information that should be used in developing new surveillance strategies for metabolic disorders.

POS329 DIABETES MELLITUS AND PRE-DIABETES IN PRE-LIVER TRANSPLANT PATIENTS: PREVALENCE AND CHARACTERISTICS

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Background: Glucose metabolism alterations may have negative impact on the outcome of liver transplantation (LT). However, inconsistent information is available on the prevalence and characteristics of diabetes mellitus (DM) and pre-diabetes (PD, impaired fasting glycemia-IFG and/or impaired glucose tolerance-IGT) in pre-liver transplant (PLT) patients.
Methods: We studied 1010 PLT patients [(age: 55 ± 8 yrs, M/F: 758/252, BMI: 25.2 ± 3.5 Kg/m^2, family history of diabetes: 358 (35%), fasting plasma glucose (FPG): 113 ± 36 mg/dl, HbA1c: 35 ± 12 mmol/mol)] who were waitlisted for LT at our institution from January 2012 to May 2019.
Results: Based on the clinical history, FPG and/or oral glucose tolerance test (OGTT), 331 patients (33%) were affected by DM (age: 56 ± 7 yrs, M/F: 260/71, BMI: 25.7 ± 3.5 Kg/m^2); 234 (23%) had PD (age: 56 ± 8 yrs, M/F: 190/44, BMI: 24.5 ± 3.5 Kg/m^2), and 445 (44%) were non-diabetic (ND) (age: 53 ± 9 yrs, M/F: 308/137, BMI: 24.7 ± 3.5 Kg/m^2). FPG (mg/dl) and HbA1c (mmol/mol) values were respectively: 144 ± 47 and 44 ± 15 in DM; 111 ± 10 and 32 ± 6 in PD; 90 ± 7 and 29 ± 6 in ND. DM patients were older than ND ($p < 0.01$) and had a higher rate of family history of diabetes ($p < 0.01$) than ND. In the previously diagnosed DM patients ($n = 243$), 27% were on diet alone, 23% on oral agents, and 50% on insulin.
Conclusions: This study provides information on the prevalence of DM and PD (over 50%) in patients waitlisted for LT. The observation that 23% of patients were on oral agents despite liver failure should prompt to develop guidelines for the therapy of diabetes in these patients. The impact of the metabolic alterations on graft function and patient survival after transplantation is being studied.

POS330 TACROLIMUS BLOOD-BILE RATIO FOR THE EARLY DETECTION OF THE REJECTION GRAFT INJURY AFTER LIVER TRANSPLANTATION

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Background: The importance of immunosuppressant blood dosage in a transplant patient is widely recognized for detecting the immunosuppressive capacity. In case of Tacrolimus in liver recipients, the drug excretion is carried out by the transplanted graft itself. The aim of the "Tacrolimus in Bile"(TUBE) Trial is the creation of a laboratory parameter for the early detection of hepatic injury after liver transplant
Methods: TUBE is a single-blind prospective monocentric trial, in which liver recipients who had Kehr's tube inserted into the biliary tract were enrolled. In the first 10 post-operative days (POD), a bile sample was collected together with a blood sample. The blood and biliary values of Tacrolimus were correlated to create the "blood-bile ratio of Tacrolimus"(BBRT). The primary outcome was the assessment of the predictive ability of BBRT in the evaluation of liver rejection injury, diagnosed through laboratory or pathological analysis. The relationship between BBRT and liver injury was examined through a Wilcoxon-Mann-Whitney test. A ROC curve was developed to estimate the BBRT threshold with the best sensitivity/specificity ratio
Results: Among the 35 patients enrolled, 12 (34%) presented with acute rejection liver injury, diagnosed by standard methods between the 5thand 7thPOD. Transaminases, total bilirubin and blood tacrolimus levels did not differ significantly in the two study patient groups, unlike eosinophils within the rejection period. The mean BBRT value presented a significant difference between the two study groups already in the 4thPOD ($p = 0.026$)(Figure 1). The ROC curve confirmed the statistical significance of BBRT ($p = 0.018$). The sensitivity and specificity achieved with a BBRT cut-off value of 4.1 was 75% and 74%, respectively
Conclusions: The early diagnosis of acute rejection liver injury allows an improvement in the overall transplant outcome. The TUBE trial is the first study evaluating the relationship between blood and biliary concentrations of a marker with hepatic excretion in liver transplant patients. This research field can be deepened by considering other aspects, such as liver enzyme polymorphism or blood flow alterations to the graft. To date, BBRT can be considered an additional laboratory marker for detecting liver rejection damage after liver transplantation

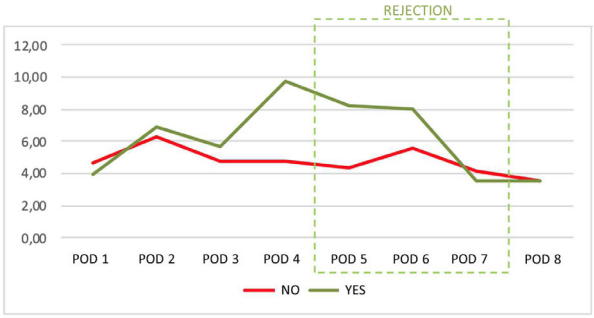

Figure 1. Comparison of mean BBRT values in population with (green line) and without (red line) liver rejection injury

POS331 IN-HOSPITAL GLYCEMIC CONTROL AFTER LIVER TRANSPLANTATION: CIRCADIAN HYPERGLYCEMIC DERANGEMENTS.

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[1]University Medical Center Groningen, Anesthesiology, Groningen, Netherlands; [2]University Medical Center Groningen, Hepatology, Groningen, Netherlands; [3]University Medical Center Groningen, Surgery, Groningen, Netherlands; [4]University Medical Center Groningen, Intensive Care, Groningen, Netherlands

Background: Glycemic derangements are common after liver transplantation (LT), and are associated with surgical stress and use of high-dose

glucocorticosteroids. Hyperglycemia early post-LT is associated with a higher infection rate and increased risk to develop post-transplant diabetes mellitus. Current intensive care unit (ICU) guidelines advise to maintain glucose <8.0 mmol/L after major abdominal surgery. We describe the incidence of post-LT glycemic derangements in the ICU (continuous control) and subsequently at the general ward (interval control).
Methods: Retrospective cohort study of consecutive adult LT recipients (2005–2020). Glucose levels for the first 30 days post-LT or hospital discharge were analyzed. In the ICU, insulin was dosed by a validated computerized algorithm (continuous control). At the ward, glucose measurements were obtained multiple times per day (interval control). All recipients received 1.5 mg/kg dexamethasone during LT and started post-LT with 20 mg/d prednisone maintenance therapy at 7:00 AM.
Results: For 628 LT recipients, 52,116 glucose measurements were analyzed. Between day 1–30 the proportion of measurements between 3.5–8.0 mmol/L was 68% at the ICU, and 51% at the ward ($p < 0.001$). Severe hypoglycemia (<2.8 mmol/L) was very uncommon in the ICU (0.02%) and somewhat higher at the ward (0.20%; $p < 0.001$). Median insulin administration during ICU admission was 60 (IQR 18–101) IU/d over the first 4 days. At the ward glucose levels showed more daily fluctuation than during ICU admission, with maximal glucoses observed between 12:00 and 18:00 ($p < 0.001$).
Conclusion: After LT hyperglycemic derangements were common, but seen more frequently at the ward than during ICU stay. A circadian pattern was observed at the ward with peak glucose levels in the afternoon, possibly associated with prednisone maintenance therapy in the morning. Tighter glycemic control, based on predicted fluctuations, may be advocated to decrease the incidence of glycemic derangements at the ward.

POS332 HETEROGENEOUS INDICATIONS AND THE NEED FOR VIABILITY ASSESSMENT: RESULTS OF AN INTERNATIONAL SURVEY ON MACHINE PERFUSION IN LIVER TRANSPLANTATION

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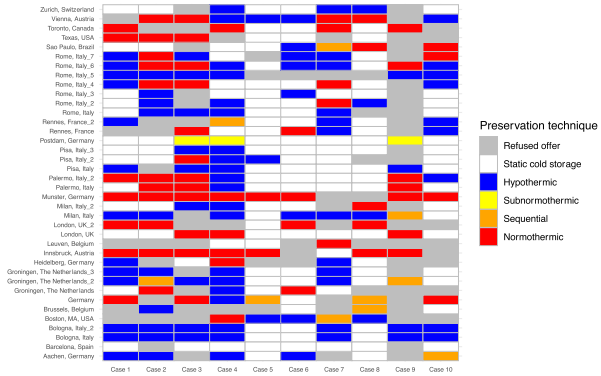
Background: Although machine perfusion (MP) is being increasingly adopted in liver transplantation (LT), indications, timing and technique are debated. To investigate practices in MP a web-based Google Forms® survey (link: https://forms.gle/2DLK3kK1EMCWewbz6) was launched in January 2021.
Methods: Target of the survey were 127 experts in the field, identified among first and corresponding Authors of relevant literature in the last 10 years. 10 real-life cases of donor-recipient matching were presented, asking whether the liver would be accepted (Q1), whether MP would be used (Q2) and, if so, by which technique (Q3) and at what timing during preservation (Q4). Respondents could also comment on each case. Agreement was evaluated using Krippendorff's alpha coefficient.
Results: 38 (29.9%) experts responded. Results of the survey are summarized in table and figure. Acceptance and MP indications varied widely across centres. Hypothermic MP was preferred more frequently by respondents from centres without an established MP program. Agreement was generally poor (Q1, α=0.09; Q2, α=0.11; Q3, α=0.12) except for Q4 (α=0.63). In all but 3 cases, at least a comment was about the necessity to assess liver viability before implantation.
Conclusions: MP indications and practice are highly variable, stressing the need to identify scenarios of utilization for each technique. Viability assessment emerges as a fundamental aspect of MP among experts in the field.

Table 1. Results

	Overall	Machine perfusion program		p*
		No	Yes	
n	38	6	32	
Continent:				0.66
Europe	34 (89.5)	6 (100.0)	28 (87.5)	
North America	3 (7.9)	0 (0.0)	3 (9.4)	
South America	1 (2.6)	0 (0.0)	1 (3.1)	
Centre volume:				0.17
>200	2 (5.3)	0 (0.0)	2 (6.2)	
150–200	1 (2.6)	0 (0.0)	1 (3.1)	
100–150	7 (18.4)	1 (16.7)	6 (18.8)	
50–100	18 (47.4)	1 (16.7)	17 (53.1)	
0–50	10 (26.3)	4 (66.7)	6 (18.8)	
Number of techniques considered:				0.63
0	1 (2.6)	0 (0.0)	1 (3.1)	
1	17 (44.7)	2 (33.3)	15 (46.9)	
2	17 (44.7)	4 (66.7)	13 (40.6)	
3	3 (7.9)	0 (0.0)	3 (9.4)	
Technique:				<0.01
Hypothermic	92 (54.8)	15 (65.2)	77 (53.1)	
Subnormothermic	3 (1.8)	3 (13.0)	0 (0.0)	
Sequential approach	10 (6.0)	2 (8.7)	8 (5.5)	
Normothermic	63 (37.5)	3 (13.0)	60 (41.4)	

Data are presented as number (%). *Chi square test

Figure 1. Machine perfusion technique and indication.



POS333 2,4-DINITROPHENOL TREATMENT DURING NORMOTHERMIC MACHINE PERFUSION OF STEATOTIC HUMAN LIVERS; PHARMACOLOGICAL CONSIDERATIONS IN PERFUSION

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Background: Steatosis is the commonest reason for decline of liver transplants worldwide. Reluctance to use these grafts stems for their sensitivity to ischaemia reperfusion injury. 2,4-Dinitrophenol (DNP) increases metabolism and has been shown to reduce hepatic steatosis in vivo. Separate from these defatting effects, DNP abrogates ischaemia reperfusion injury. We aimed to assess the toxicity, pharmacokinetics and effects of DNP delivery during normothermic machine perfusion (NMP).
Methods: We performed 25 hours of pressure guided NMP on human livers (n = 6) using a standard red blood cell perfusate. All livers were declined for transplant due to steatosis and accepted via the NHS Blood and Transplant research scheme (RINTAG).
Results: Three livers received DNP 15 mg/kg (2 DBD, cold time=1092 ± 396 mins, liver weight=2.4 ± 0.4 kg) with three controls (2 DBD, cold time=879 ± 279, weight=2.7 ± 0.2 kg). Following delivery of DNP at 1 hour there were no toxic effects on flow parameters, lactate clearance, transaminase or lactate dehydrogenase release or histology. Pharmacokinetic studies revealed elimination with first order kinetics and a half-life of 7.7 hrs (95% CI=5.1–15.9; Figure 1). As expected, DNP caused a significant increase in oxygen consumption (Figure 1; p = 0.023). The increase in oxygen consumption was closely correlated with perfusate DNP concentration (r^2=0.975; p = 0.002). Liver temperature was significantly higher in the DNP group, although remained within physiological limits in all livers. Oxidative stress, measured by MDA level, was numerically lower in the DNP group (p = 0.193). The level of steatosis did not change over 25 hours of perfusion in either group.
Conclusions: DNP can be safely delivered during NMP, but is quickly eliminated by the liver. Oxygen consumption is successfully increased whilst perfusate DNP levels remain high. Drug pharmacokinetics should be assessed for any therapeutic intervention during NMP.

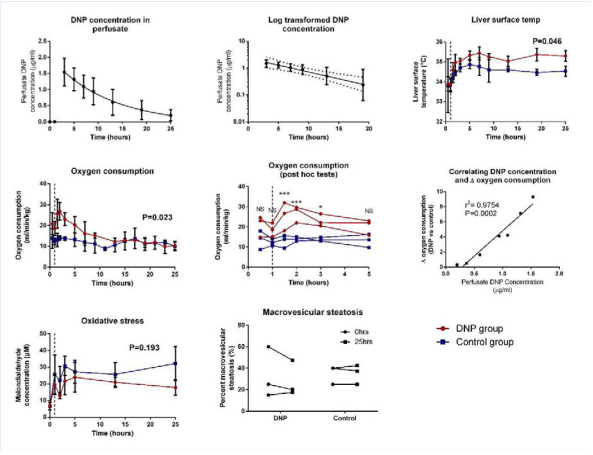

Figure 1. Pharmacokinetics and pharmacodynamics.

POS334 A MATCHED COMPARISON OF HYPOTHERMIC OXYGENATED MACHINE PERFUSION VS. COLD STORAGE IN LIVER TRANSPLANTATION

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Background: Several studies have shown an improved allograft function of donation after circulatory death (DCD) livers after machine perfusion. The aim of this study was to investigate graft function and a potential decrease of biliary complications after transplantation of donation after brain death (DBD) livers subjected to hypothermic oxygenated machine perfusion (HOPE).
Methods: HOPE (Liver Assist device) has been routinely used at the Medical University of Vienna since May 2018. Patients who received a perfused organ between 2018–2019 were 1:2 propensity score matched to a control group whose grafts were stored using static cold storage (SCS). MRCPs were routinely performed 3 months after LT in the perfusion group.
Results: In total, 50 patients who received a perfused organ were compared to 100 controls. 1-year graft and patient survival were 88% and 90% in the HOPE group compared to the control group with 76% and 80% respectively (p = 0.035 and p = 0.05). Early allograft dysfunction occurred in 24 (48%) patients in the perfusion group vs. 56 (56%) in the control group (p = 0.301). ICU stay was shortened to 2 days (IQR 5.25) in the HOPE group compared to 6 days (IQR 9) in the control group (p = 0.008). Lactate levels after LT peaked at 2.5 mmol/l (IQR 2 mmol/l) in the perfusion group vs. 3.9 mmol/l (IQR 3.6 mmol/l) in the control group (p = 0.01). Overall biliary complications after transplantation were similar between the two groups with 16/50 (32%) – 12 leaks and 4 strictures – in the perfusion group and 38/100 (38%) – 14 leaks, 20 strictures and 4 both – in the control group. Biliary strictures were therefore significantly reduced in the HOPE group vs. control group (8% vs 20%, p = 0.025).
Conclusions: HOPE treatment of liver grafts leads to a significantly improved graft and patient survival. Furthermore, it is associated with lower incidence of biliary strictures and decreased post-transplant length of ICU stay compared to static cold storage.

POS335 HYPOTHERMIC OXYGENATED PERFUSION OF LIVER GRAFTS: A COST ANALYSIS

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Background: Ex-situ liver machine perfusion (MP) is widely accepted as a safe and effective strategy for organ preservation, reconditioning and functional assessment prior to transplantation. Procedural extra-costs represent a hindrance to the implementation of MP programs, but preliminary cost-effectiveness analyses suggest that the clinical benefit may translate into a financial benefit. We aimed to analyze the actual cost of the system used for hypothermic oxygenated perfusion (HOPE) of liver grafts in the setting of our MP program.
Methods: We calculated the average actual cost (year 2020 values) of the system we customized for end-ischemic pressure-controlled dual HOPE of liver grafts (figure 1).
Results: The procedure is performed in a facility where liver transplant surgery and cardiothoracic surgery coexist. So, it could be arranged that conventional cardiac surgery equipment, including the heart lung machine (Quantum Perfusion System, Spectrum Medical) and the heater-cooler unit (HCU 40, Getinge), would be lent to the MP program. Consequently, cardiac surgery machines do not represent additional costs, and the average actual cost of the system used for a single HOPE run is the cumulative cost of disposable supplies, which totals 1346.05 euros (table 1).
Conclusions: In the setting of our transplant program, efficient logistics allowed to customize a cost-effective, high-quality system for HOPE of liver grafts. We showed the feasibility of a model whose implementation might lead to both better clinical outcomes and more savings.

Figure 1

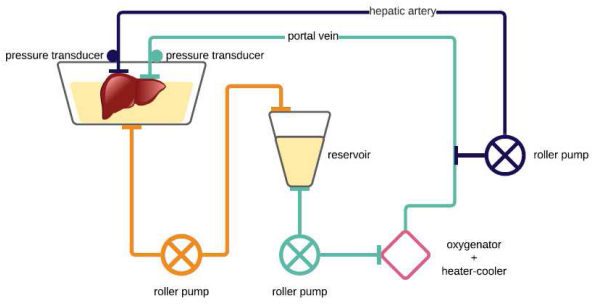

Table 1

Disposable supply	N	Single cost of the specific supply (euros)	Cumulative cost for the specific supply (euros)
Tubing system + Oxygenator with heat exchange performance (Quadrox-i, Getinge), paired with venous hardshell cardiotomy reservoir (VHK, Getinge)	1	578.32	578.32
Medex LogiCal® Pressure Transducer	2	14.64	29.28
Portal cannula: EOPA 3D® (Medtronic)	1	75.00	75.00
Arterial cannula: EOPA 3D® or DLP® Pediatric Arterial Cannula (Medtronic)	1	75.00 or 26.90	75.00 or 26.90
Belzer MPS® UW Machine Perfusion Solution (1 L)	3 or 4	175.00	525.00 or 700.00
Average actual cost of the supplies for a single HOPE run (euros)			**1346.05**

POS336 ROLE OF D-HOPE RECONDITIONING OF LIVER GRAFTS FROM EXTENDED CRITERIA DBD DONORS

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Background: Shortage of organs has increased extended criteria donors (ECD) utilization in order to reduce mortality and drop-out on transplant waiting list. Macrovescicular steatosis more than 30% and cold ischemia time (CIT) longer than 8 hours are commonly associated with increased graft loss. On the other hans, use of Machine Perfusion (MP) in this setting seems to improve short-term outcomes. We present results of a single center Italian experience with MP and grafts from extended criteria brain-dead (DBD) donors.
Methods: From October 2019 to February 2021, 11 liver transplants (LT) were performed at our Institution using MP reconditioned grafts from ECD DBDs. Marginality was defined by percentage of macrovescicular steatosis > 30% and/or prolonged CIT > 8 hrs. All grafts underwent Dual-Hypothermic Oxygenated Machine Perfusion (D-HOPE) after backtable surgery. Short term outcomes and incidence of early allograft disfunction (EAD) were studied.
Results: EAD occurred in 4 cases (36.3%) with no other consequences and no re-transplant needed. One patient developed an acute kidney injury (AKI) after LT, with no renal replacement therapy needed. No biliary or vascular complications were registered. Finally, 1 patient developed Primary Non Function (PNF) and eventually died due to multi-organ failure on POD 8. Median post-LT ICU stay was 2 days (range 1–8), while median in-hospital stay after LT was 9 days.
Conclusions: Our results confirmed that extended criteria donations from brain dead donors had higher rate of early disfunction than regular DBDs, however, incidence of EAD in our experience had lower percentage than moderate-to-severe steatosic non-reconditioned grafts reported in literature. MP has numerous advantages compared to conventional cold storage, some of which include the preservation and reconditioning of borderline transplantable organs, although assessment of high-risk donor allografts quality and viability needs further implementation.

POS337 COMPARISON OF THERMAL VARIATIONS IN POST-RETRIEVAL GRAFT CONDITIONING ON RAT LIVERS

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Background: Machine perfusion was found an effective tool to recover organ grafts from ischemic insults during preservation. It could be observed that organ integrity is significantly affected by abrupt temperature shifts during hypothermic storage and implantation periods. Studies showed that a gentle and controlled rise of the temperature during oxygenated machine perfusion prior to implantation can protect the tissue from reperfusion injury. Now, the possible role of temperature kinetics upon retrieval of the graft and prior to later cold storage should be investigated.
Methods: Rat livers were retrieved after cardiac arrest and subjected to a brief ex situ machine perfusion with either hypothermic resuscitation (HR) at 8°C, near-normothermic resuscitation (NR) at 30°C or progressive resuscitation with lowering the temperature in a controlled fashion from 30°C to 8°C (PR). After cold storage (CS), liver functional parameters were evaluated by an established ex vivo reperfusion system.
Results: NR and PR resulted in significantly lower release of hepatic enzymes and less production of TNF upon reperfusion compared to CS while HR had a far less protective effect. An increase in bile production was only observed in the PR group, which also significantly increased the recovery of tissue ATP, the amount of which was, however, nearly paralleled by the NR protocol.
Conclusions: Given the rather limited amount of benefit provided by the progressive cooling down protocol as compared with the simple normothermic machine perfusion even in a model of pre-damaged liver grafts, it does not seem likely, that the putative effect would play a major role in retrieval of healthy liver grafts. Within the limitations of this primary in vitro model, some evidence has been accumulated that normothermic recirculation appears to be a superior approach for the restitution of warm-ischemically injured liver grafts than immediate hypothermic machine perfusion.

POS338 ASSESSMENT OF MITOCHONDRIAL FUNCTION DURING PROLONGED EX VIVO LIVER NORMOTHERMIC MACHINE PERFUSION

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Background: Extracorporeal regeneration of injured livers may help to overcome organ shortage, but requires a deep knowledge of cellular mechanisms occurring during normothermic machine perfusion (NMP). Mitochondria are key players in tissue bioenergetics, thus, we aimed for an in-depth assessment of mitochondrial respiration during NMP.
Methods: Seven human livers declined for transplantation were perfused under normothermic conditions for up to 5 days. Liver quality was monitored by analyzing the perfusate lactate every 6 h. Mitochondrial respiration was assessed in tissue biopsies by high-resolution respirometry every 12 h. The succinate-linked coupling control states: oxidative phosphorylation (OXPHOS), resting respiration (LEAK), and electron transfer (ET) capacity were determined, the respective coupling control ratios (OCE) were calculated. Cell viability and tissue integrity were assessed in biopsies using real-time confocal microscopy (RTCM) and scored semiquantitatively.
Results: Livers could be perfused for at least 48 h with close to physiological perfusate lactate levels (23.5 ± 27.6 mg/dL), whereas bioenergetics seem to remain stable in tissue biopsies until 60 h of perfusion. Still, OXPHOS capacity halved, but coupling control ratios did not change for further 12 h, indicating shift of quantity of the mitochondria, but not of quality. This observation was confirmed by a significant increase of the RTCM score (pre 0 ± 0, 60 h 1.14 ± 0.69). However, the energy production of the viable mitochondria seem sufficient to maintain cellular homeostasis, since the OCE did not decrease significantly ($p = 0.8830$). Thus, suggesting that the loss of mitochondrial function is not the early limiting factor in the perfusion system. However, after 60 h, the proportion of LEAK respiration doubled due to oxidative damage to the mitochondria, which is also indicated by an exponential increase in lactate levels (119.4 ± 204.4 mg/dL). In line with this, the integrity of the outer mitochondrial membrane deteriorated, resulting in significantly elevated cytochrome c control factor ($p = 0.0001$) and ET excess capacity halved ($p = 0.0006$) as a result of damage to the ET machinery.
Conclusion: Coupling control analysis in mitochondria may serve as a reliable marker for testing of the bioenergetic function during liver NMP.

POS341 MEDICATION NON-ADHERENCE PREVALENCE AND DETERMINANTS IN CHILDREN AND ADOLESCENTS WITH CHRONIC LIVER DISEASES

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Background: Pre-operational behaviors can affect both operation success and graft rejection in the following years. Medication non-adherence is one of these influential factors which is associated with higher rates of morbidity and mortality and increased health care costs in the transplant setting. Surprisingly medication non-adherence before liver transplantation is quite common, and previous studies have estimated it up to 70%. Given that medication adherence is modifiable and has a significant role in transplantation success, it is crucial to recognize the predictors of non-adherence in patients in different settings.
Methods: One hundred sixty children and adolescents with chronic liver disease enrolled in this study through convenience sampling from the outpatient pediatric clinics in shiraz university hospitals. Medication adherence was assessed by using the 8-item Morisky Medication Adherence Scale (MMAS-8) via face-to-face interviews. Scores were classified in three groups (score <6 = low adherence, scores 6–8 = medium adherence, and > 8 = high adherence). Descriptive statistics, Chi-square, ANOVA, Fisher exact test, Kruskal-Wallis, and Multivariate ordinal regression were used to analyze the data.
Results: Of 160 patients, 84 (52.5%) were female, and their mean age was 11.2 ± 4.4 years old; 56 (35%) participants were high-adherers, and 66 (41.25%) were low-adherers. The most common reason for low adherence was forgetfulness in 37 patients (23.13%) and low access to medication in 21 individuals (13.13%). Parental education, higher family income, being closer to the clinic was significantly associated with medication adherence. Based on multivariate logistic regression analysis increase in age would lead to lower adherence in the pediatric setting.
Conclusions: Medication non-adherence prevalence is relatively high, and almost half of children with liver cirrhosis demonstrate low medication adherence in this study, Considering the importance of this issue, management programs should be implanted based on the age group and excuses to improve medication adherence and, as a result, transplantation success in this vulnerable population.

POS342 ARTERIAL AND BILIARY COMPLICATIONS AFTER LIVER TRANSPLANTATION – A SINGLE CENTER STUDY

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Background and Aims: Liver transplantation (LT) is the treatment of choice for patients with end-stage liver disease. It's long-term success may be impaired by a variety of postoperative complications. Among the most clinically significant and frequent complications are hepatic artery and biliary disorders. The aim of the study is to review the incidence, diagnostic methods and management of these complications in the first 46 transplant recipients in our clinic, the second LT center in Romania.
Methods: We analyzed 46 deceased donor LT recipients, from 2014 to 2020, for biliary and arterial complications. Data on the type of complication (biliary fistula or stenosis, hepatic artery thrombosis, stenosis or pseudoaneurysm, early vs late onset), diagnostic and therapeutic modalities and patient outcome were registered.
Results: The median follow-up period for the 46 patients was 49 months. Thirteen biliary complications occurred during this time: 11 biliary stenosis and 2 biliary fistulas. Arterial complications were encountered in 9 cases: 4 hepatic artery thrombosis, 3 hepatic artery stenosis and 2 pseudoaneurysms. Out of a total of 22 complications, 9 appeared early. Biliary stenosis were managed by endoscopic retrograde cholangiopancreatograhy (3 cases) or, when this was not technically feasible, by external biliary drainage (2 cases) or surgery (2 cases). Biliary fistulas required surgical management, with successful outcome. For hepatic artery thrombosis, revascularization was obtained through interventional radiology in 2 patients, while open surgery was performed in one case. Currently, one patient with a history of early hepatic artery thrombosis and multiple biliary stenosis and cholangitic episodes is waiting for retransplantation.
Conclusions: Vascular and biliary complications were recognized early and were managed using diverse therapeutic modalities, from minimally invasive to surgical interventions. Future efforts should be directed toward reducing the incidence of post-transplant complications.

POS343 INFLUENCE OF COVID19 PANDEMIC ON RECENTLY OPENED LIVER TRANSPLANTATION PROGRAMME IN GDAŃSK

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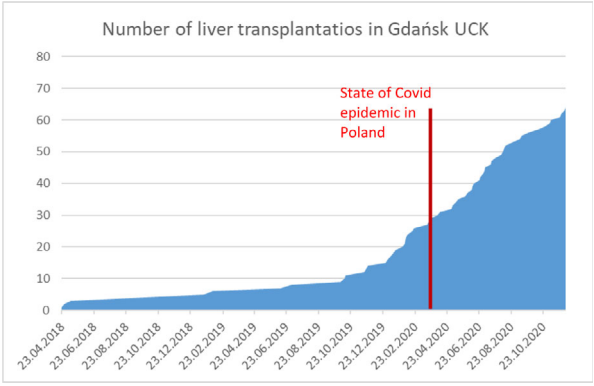
Background: Since December 2019 pandemic of a novel severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) has caused an international health crisis. Consequences of pandemic have left an imprint on whole the health care system, including transplantology. Number of liver transplantation significantly decreased worldwide. The aim of this study is to analyse the influence COVID19 pandemic had on recently created liver transplantation unit in Gdańsk.
Methods: Number of liver transplantations, indications, MELD and Child-Pugh score, length of hospitalisation, post transplantation follow-up frequency, waiting time on active transplant list, were analysed in pandemic period and confronted with a preceding year. T-student and Mann-Whitney tests were used as statistical tools in GraphPad Prism with level of significance $p < 0.05$.
Results: Despite the increasing number of COVID 19 infections in Poland number of performed transplantations was significantly higher than in the first year of liver transplantation programme ($p < 0.05$). As a sign of rising experience length of hospitalisation was significantly shorter ($p = 0.02$). Qualification process and post transplantation care remain at constant high level - main indications, MELD and Child-Pugh score, follow-up visits frequency and waiting time on active transplant list did not change significantly ($p > 0.05$). No intra-hospital transmission of COVID 19 in our recipients was noticed. In three cases transplantation was postponed due to positive SARS CoV 2 PCR test till recovery, two other patients on the waiting list died because of COVID 19 before transplantation. In post-transplantation care five patients tested positive for SARS CoV 2, with no fatalities.



Conclusions: Newly opened liver transplantation programme is prone to be theoretically more vulnerable to health care system crisises, even more so for a worldwide one like pandemic. On basis of our experiences it is possible to constantly develop transplant programme safely even in such an unfavourable situation like SARS-CoV2 pandemic.

POS345 IS THERE A ROLE FOR INTENSIVE CARE IN LIVER TRANSPLANT ASSESSMENT?

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Background: Liver transplant assessment (LTA) is managed by a multi-disciplinary team (MDT). The aims of the LTA process include confirmation of the diagnosis and LT as the most suitable therapeutic option, evaluation of co-morbidities, and optimisation of treatment. Almost all patients require intensive care (ICU) admission post-operatively. ICU trajectory is

determined by recipient pre-operative physiological status, donor graft, and intra-operative course. Prolonged ICU admission is associated with physical and psychological morbidity that affects long-term recovery. A survey of the 7 UK LT centres showed that 5 centres had ICU involvement in the LTA process.
Methods: Single-centre cross-sectional survey of all members of the LTA MDT and ICU consultants based at Addenbrookes Hospital, Cambridge. We asked participants for their job title, whether they would value ICU input on all patients or selected patients only, and to give reasons for their answer. Results were analysed qualitatively using a thematic approach.
Results: We received 29 responses in total. 10/29 (34%) participants valued ICU input on all patients, 19/29 (66%) preferred input for selected patients only. Three major themes emerged: (1) patients benefitting from ICU input; (2) patients not requiring ICU input; (3) benefits of ICU involvement.
Discussion: ICU input would be valued for complex, multimorbid patients with high perioperative risk rather than for younger lower risk patients. ICU involvement would be beneficial for post-operative risk stratification, advice on the impact of medical and surgical issues on ICU survival, and pre-admission planning and management of acute issues. Following this our centre has developed specific triggers to prompt an ICU referral to ensure pre-operative input and optimal use of scarce resources (Table 1).

Table 1

Age > 60 years
BMI > 40
ASA > 2 (excluding liver disease)
Poor functional status
Inpatient liver transplant assessments
Repeat liver transplantation

POS346 IMPACT OF COVID-19 PANDEMIC ON REFERRAL OF PATIENTS WITH LIVER DISEASE TO A LIVER TRANSPLANT CENTER

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Background: Access to liver transplantation (LT) can be affected by several barriers resulting in delayed referral and increased mortality. Hub-and-spoke networks have been implemented to manage patients with liver disease. The COVID-19 pandemic may have significantly changed this scenario, as most of medical resources have been allocated for the care of patients with SARS-CoV-2 infection. This study aimed to assess the influence of COVID-19 pandemic on referrals of patients with liver disease to LT Center.
Methods: An integrated referral program was developed since 10.2017 at Multivisceral Transplant Unit, Padova University Hospital. All consecutive adult patients with liver disease referred for the first time using this referral program from 10.2017 to 10.2020 were prospectively collected. Clinical characteristics were analysed overall and according to era of referral (pre-COVID-19 era: 10.2017-02.2020; COVID-19 era: 03.2020-12.2020).
Results: 231 patients were referred over the study period (men 61%, mean±SD age: 54 ± 10 years). End-stage liver disease was the most common underlying condition (78.3%), followed by acute liver injury (17.3%). During COVID-19 pandemic, the rate of referred patients showed a stable trend, if compared with the previous period (5.1 patients/month vs. 6.1 patients/month), also when only in-patient referrals were considered (pre-COVID-19 vs. COVID-19 era: 2.9 vs. 3.2 patients/month). Considering 181 patients with cirrhosis, underlying aetiology ($p = 0.22$), severity of liver disease (MELD score: 21 ± 7 vs. 20 ± 8; $p = 0.44$), and inpatient referrals (42% vs. 51%; $p = 0.34$) did not differ between pre-COVID-19 and COVID-19 eras. There was a decreasing rate of ICU admission for cirrhosis-related complications during COVID-19 pandemic (22% vs. 34%), with an increased in-hospital transplant-free mortality (41% vs. 30%).
Conclusions: Our results did not show a significant decrease in the number of referrals and type of indications during the COVID-19 pandemic; however, the in-hospital transplant free mortality showed an increasing trend, which could be the consequence of a decreasing rate of ICU admissions. These factors confirmed the importance of a referral network for patients with liver disease, and how the COVID-19 pandemic may influence the short-term outcome.

POS347 TREATMENT OF HEPATIC ARTERY OBSTRUCTION: THE LESSONS LEARNED IN A SERIES OF 2,478 LIVER TRANSPLANTS

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Background: Hepatic artery obstruction (HAO) is one of the most ominous complications after liver transplantation (LT), but treatment options are varied and have evolved over years. The present study was aimed at assessing the efficacy results of initial treatment strategies for HAO at a single center from January 1996 to December 2020.
Methods: This was a retrospective analysis of a prospectively collected database on adult (≥ 18 years) recipients undergoing deceased donor LT. HAO were divided in hepatic artery stenosis (HAS), thrombosis (HAT), and pseudoaneurysm (HAPA) (Table 1). Initial treatment was classified into medical (anticoagulation, fibrinolysis), radiological (balloon dilatation, stent placement), surgical (revascularization), and re-transplantation (re-LT). Efficacy failure was expressed as graft loss. Survival analysis was intent-to-treat (ITT, Kaplan-Meier). Data were censored at latest follow-up, graft loss or wait listing for further transplant.
Results: Out of 2,478 LT procedures, 57 HAO (2.3%) were identified: 33 HAS (1.3%), 15 HAT (0.6%), and 9 HAPA (0.4%). Nineteen HAS (57.6%) were treated by interventional radiology, whilst medical treatment was used in 11 (33.3%), and surgery in 3 (9.1%) (Table 1). Nine HAT (60%) underwent re-transplantation, 2 (13.3%) surgery, 3 (20%) were medically treated, and one (6.7%) underwent interventional radiology (Table 1). All HAPA (100.0%) were treated with radiologic stent placement (Table 1). Efficacy failures were 4 (7.0%): namely, 1 radiologic treatment for HAT, one medical treatment for HAS, and 2 surgical attempts at HAT revascularization (Table 1). The 5-year patient survival rates according to type of procedure are reported in Table 1 and were higher for re-transplantation (88.9%).
Conclusions: HAS were the most common arterial complications after LT; radiology was the most frequent treatment attempted, and efficacy failure of initial treatment was 7%. Re-transplantation is the treatment of choice for HAT, while surgical revascularization procedures are sporadically adopted and associated with inferior outcome.

Table 1: Type of treatment and 5-year patient survival according to category of hepatic artery obstruction and type of treatment as per intent-to-treat.

Treatment	HAS (#33)	HAT (#15)	HAPA (#9)	Overall (#57)
Radiology, total	**19 (57.6%)**	**1 (6.7%)**	**9 (100%)**	**29 (50.9%)**
Failed*	0	1 (100%)	0	1 (3.4%)
5-year patient survival	74.6%	0.0%	68.6%	68.8%
Medical, total	**11 (33.3%)**	**3 (20%)**	**0**	**14 (24.6%)**
Failed	1 (9.1%)	0	-	1 (7.1%)
5-year patient survival	70.0%	66.7%	-	68.2%
Surgery, total	**3 (9.1%)**	**2 (13.3%)**	**0**	**5 (8.8%)**
Failed	0	2 (100.0%)	-	2 (40.0%)
5-year patient survival	66.7%	50.0%	-	60.0%
Re-LT, total	**0**	**9 (60.0%)**	**0**	**9 (15.7%)**
Failed	-	0	-	0
5-year patient survival	-	88.9%	-	88.9%

*efficacy failure was defined as graft loss or need for re-transplant

POS348 EARLY POST-OPERATIVE ANALGESIA FOLLOWING LIVER TRANSPLANT

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Background: Liver transplantation (LT) is the only effective treatment for end-stage liver disease. Advances in peri-operative care have led to the

development of enhanced recovery after surgery (ERAS) protocols to facilitate patient flow through intensive care with the aim of allowing safe expansion of activity and improving individual patient outcomes. Those protocols that advocate early extubation rely on optimal post-operative analgesia to facilitate mobilisation and minimise the risk of developing pulmonary complications. Ahead of introducing an ERAS protocol at our centre we examined current analgesic requirements, quality of pain control, and complications related to analgesia in LT patients.
Methods: Retrospective analysis of all consecutive adult liver-only transplants from 1st January 2018 to 31st December 2019 at Addenbrooke's Hospital, Cambridge. We reviewed analgesic requirements in extubated patients for the first 72 h following graft reperfusion. Pain scores were patient-reported on a of scale 0 to 10. Median opioid requirements were calculated and converted to morphine equivalents using standardised methodology.
Results: 192 patients (120 males, 72 females) were included with a median age 56 years and a UKELD score 55. All patients were initially commenced on patient-controlled analgesia (PCA) following extubation. Median opioid requirements were 50 mg at 24 h, 87.5 mg at 48 h and 75 mg at 72 h with median pain scores of 0, 0 and 1.5 respectively. Multi-modal analgesia was uncommon with Paracetamol (Acetaminophen) being the most frequently used adjunct (60/192) within the first 72 hours. 30/192 had a history of chronic pain and this was associated with a higher median pain score of 2.5 at 72 h. Only 1 /192 required naloxone administered for management of opiate toxicity.
Conclusions: LT was not associated with severe post-operative pain. Opioid PCA is a safe and effective analgesic strategy in this cohort..

POS349 IS EARLY EXTUBATION AFTER LIVER TRANSPLANTATION FEASIBLE?

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Introduction: iver transplantation (LT) is the only effective treatment for end-stage liver disease. Enhanced recovery after surgery (ERAS) protocols can facilitate the expansion of clinical activity within current infrastructures to meet the rising demand for LT. ERAS protocols advocate early extubation. Currently, there are no widely accepted criteria for successful early extubation, but most published ERAS protocols focus on evidence of graft function, the intra-operative course and recipient physiology.
Aims:
1. To identify the proportion of patients suitable for early extubation using established criteria from the literature.
2. To identify barriers to early extubation.

Methods: Retrospective analysis of all consecutive adult liver-only transplants from 1st January 2018 to 31st December 2019 at Addenbrooke's Hospital, Cambridge, UK. Suitability for early extubation was defined as meeting set criteria within 4 h of ICU admission post-LT.
Results: 205 patients (128 males, 77 females) were included with a median age 56 years and UKELD score 55. The median duration of post-operative intubation was 18.1h (interquartile range 12–32.2h). 126/205 patients were identified as being suitable for early extubation. 51/205 patients had a metabolic acidosis requiring sodium bicarbonate infusion or renal replacement therapy, precluding early extubation. In 16/205 extubation was delayed due to large volume intra-operative blood loss or planned return to theatre. The majority (188/205) of extubations occurred between 0800 and 2000. 3/205 patients required re-intubation for failed extubation.
Conclusions: A policy of early extubation would be feasible and safe in the majority of patients undergoing LT at our centre.

POS350 IS ULTRASOUND AN UNNECESSARY BARRIER TO EARLY EXTUBATION AFTER LIVER TRANSPLANTATION?

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Background: Enhanced recovery after surgery (ERAS) protocols are designed to improve patient outcomes by minimising post-operative recovery time and reducing hospital stay. ERAS programmes are being developed to facilitate the expansion of liver transplant (LT) activity within the constraints of current infrastructure.
Doppler ultrasound of the liver following transplantation (USLiD) is routinely performed early in the post-operative period to confirm vascular patency. In this study, we test the hypothesis that the USLiD performed on the first post-operative day in our unit causes unnecessary delays to extubation, prolonging intensive care (ICU) stay and does not change patient management.
Method: Retrospective analysis of all consecutive adult liver-only transplants from 1st January 2018 to 31st December 2019 at Addenbrooke's Hospital, Cambridge, UK.
Results: 209 (136 DBD, 73 DCD) adult liver only transplants with median age 56 years and UKELD score 55 were included in this study. Of these, 3 died on their index ICU admission and were excluded from further analysis regarding extubation. Median time from ICU arrival to extubation was 18.1 hours. 158/206 (76.7%) patients were extubated following USLiD. All patients underwent USLiD post-transplantation with 197/206 (95.6%) performed within 24 hours of ICU admission at a median time 11.4 hours post-arrival. 95/206 (46.1%) had further imaging within 48 hours (16/95 CT, 79/95 USLiD) with 66/96 (68.8%) due to concerns about visualisation of the arterial tree on initial USLiD (typically reported as high resistance waveforms), in these the median time to normalisation of the arterial waveform was 44.6 hours. Only 1/207 USLiD directly led to a return to theatre within 72 hours.
Conclusions: USLiD should not be used as a reason to delay extubation as in isolation it is unlikely to result in return to theatre. Delaying the initial post-operative USLiD may remove a barrier to patient flow and reduce the overall burden of re-imaging

POS351 PROXIMAL SPLENIC ARTERY EMBOLIZATION FOR REFRACTORY ASCITES AND HYDROTHORAX AFTER LIVER TRANSPLANT: A SINGLE CENTER EXPERIENCE

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Background: Refractory ascites (RA) and refractory hydrothorax (RH) are major complications after liver transplantation (LT). Proximal splenic artery embolization (pSAE) has been advocated as a valuable tool to treat both RA and RH.
Methods: A retrospective analysis of consecutive patients who underwent pSAE for RA and or RH after LT between January 2007 and December 2017 was conducted at our transplant center. In this study, we assessed the safety and efficacy of proximal SAE for the treatment of RA, RH or both. We analyzed demographic data, pre- and post-pSAE graft hemodynamic and outcomes to identify predictors of RA/RH response to pSAE. Furthermore, a subgroup analysis of patient with early or late resolution (> 3 months) was made.

Table: Outcomes

RA and/or RH Resolution			**N (%)**	
Clinical resolution post pSAE			30 (100)	
Need of chronic diuretic therapy to control RA/RII			1(3.3)	
Timing			**M±SD; Median (IQR)**	
Time from SAE to clinical resolution , days			59 ± 136; 26 (27)	
Time from SAE to diuretics discontinuation , days			283 ± 582; 48 (167)	
Post pSAE complications			**N (%)**	
Splenic Infarct			2 (6.6)	
Post splenic embolization syndrome			1 (3.3)	
Hepatic artery thrombosis			1 (3.3)	
Portal vein thrombosis			1 (3.3)	
		Early (n=24)	**Delayed (n=6)**	
Pre-transplant parameters		**M±SD**	**M±SD**	**P value**
Splenic/hepatic artery ratio		1.9 ± 0.4	1.6 ± 0.1	**0.04**
Spleen/liver volume ratio		0.98 ± 0.3	0.7 ± 0.2	**0.016**
Spleen volume (cm^3)		1337 ± 413	953 ± 287	**0.04**
Intraoperative data				
Intraoperative PV flow (ml/min/100gr)		139 ± 49	102 ± 13	**0.004**
Percentage of HA augmentation		102 ± 87	32 ± 30	**<0.001**
Pre-SAE				
Pre SAE PV velocity (cm/sec)		80 ± 26	57 ± 4.5	**< 0.001**
eGFR (ml/min/1.73m2)				
Pre SAE eGFR		77 ± 48	43 ± 26	**0.03**
Post pSAE eGFR	1 month	86 ± 40	60 ± 15	**0.02**
	3 months	83 ± 34	62 ± 24	0.06
	6 months	84 ± 28	61 ± 28	0.11

Results: A total of 30 patients underwent pSAE for RA ($n = 19$), RH ($n = 1$), or RA and RH ($n = 10$). Of these, 24 (80%) patients responded to pSAE while 6 (20%) required additional long-term treatment. During the first 6 months after pSAE, all patients experienced: continuous weight loss, a decrease in diuretics dose, an increase in mean eGFR, and a significant improvement in liver ultrasound parameters. Complications after pSAE were limited to 2 (6.6%) cases of splenic infarcts, one case of post splenic embolization syndrome (3.3%), no sepsis or splenic abscess were reported. A lower preoperative spleen-liver volume ratio ($p < 0.05$), intraoperative portal vein (PV) flow ($p < 0.05$), pre-pSAE PV velocity ($p < 0.001$) and a higher percentage of hepatic artery augmentation ($p < 0.001$) are associated with an early RA and/or RH resolution.
Conclusions: pSAE is safe and effective in reversing portal hyper-perfusion and treating RA and RH after LT, with low rate of morbidity and mortality. A meticulous selection of suitable candidates is mandatory to grant pSAE success.

POS352 LIVER TRANSPLANTATION FOR COVID-19-ASSOCIATED CHOLANGIOPATHY

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Background: The hallmark viral pneumonia of COVID-19 is often accompanied by important extra-pulmonary manifestations. Liver dysfunction, assumed to have negligible clinical impact, occurs in up to 45% of COVID-19 patients, mainly as moderate transaminitis whereas a cholestatic pattern is rare. We report 4 patients who developed cholestatic liver dysfunction that progressed towards a destructive cholangiopathy requiring liver transplantation in 2 patients.
Methods: All COVID-19 patients admitted between March and June 2020 to the intensive care unit (ICU) of a tertiary care university centre were retrospectively reviewed for proven cholestatic injury. Additionally, patients referred to our liver transplant unit with a history of COVID-19 were also considered.
Results: Three out of 114 critically ill COVID-19 patients and one externally referred patient were identified. All patients were male (median age 67 [range 48–68]) with median BMI 30 kg/m² (29–31), and needed mechanical ventilation (66 days [54–91]), proning and extracorporeal membrane oxygenation (56 days [20–71]). All developed moderate to severe cholestatic liver injury after resolution of acute respiratory distress syndrome (Figure 1). The clinical presentation, cholangiogram, and histology were typical of the critical care-associated condition 'secondary sclerosing cholangitis in critically ill patients' (SSC-CIP). One patient suffered a fatal hepatic haemorrhage, in the second patient cholestasis improved after discharge and the two other patients received a liver transplantation for refractory cholangitis. Both had an uneventful early postoperative course with rapid normalisation of liver tests. One patient is currently doing well, the other patient suffered a fatal multi-resistant pneumonia 6 weeks post-transplantation.
Conclusion: The high incidence of SSC-CIP suggests that patients surviving severe COVID-19 are at increased risk of developing this rare cholangiopathy. We believe several disease- and treatment-specific features predispose to biliary ischemia and damage, while a direct pathogenic role of SARS-CoV-2 via cholangiocyte angiotensin-converting-enzyme-2 receptors is under investigation. Early diagnosis and timely consideration of liver transplantation as a therapeutic option is therefore warranted.

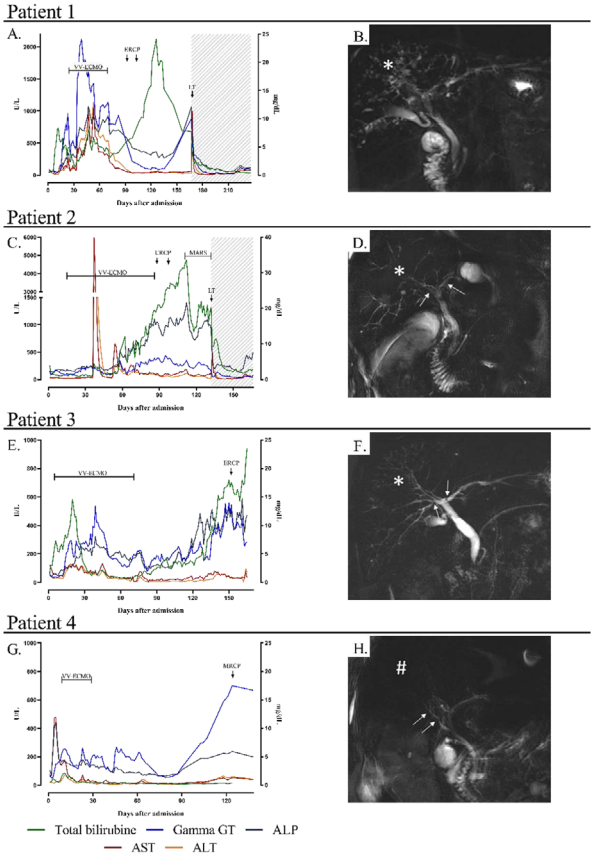

Figure 1. Shown are the temporal evolution of liver enzymes along with critical diagnostic/treatment events (left), a representative MRCP image (right) for each of the 4 patients (rows).

Left: Levels of gamma-glutamyltransferase (Gamma GT), alkaline phosphatase (ALP), aspartate transaminase (AST) and alanine transaminase (ALT) are projected on the left vertical axis and expressed as U/L, total bilirubin is projected on the right vertical axis and is expressed as mg/dl. VV-ECMO: veno-venous extracorporeal membrane oxygenation, ERCP: endoscopic retrograde cholangiopancreatography, MARS: Molecular Absorbent Recirculating System, LT: liver transplantation.

Right: MRCP shows in patient 1, diffuse beading of the intrahepatic biliary system (*); in patient 2 and 3, diffuse beading of the intrahepatic biliary ducts (*) and focal strictures on the left and right hepatic ducts (arrows) (); in patient 4, focal strictures on the right hepatic duct (arrows) and diminished arborisation of the intrahepatic biliary tree (#).

POS353 LDLT DURING COVID -19 PANDEMIC IN A SINGLE ROMANIAN TERTIARY REFERRAL CENTRE

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Background: The SARS-CoV-2 (COVID-19) pandemic has affected national healthcare systems and it may have heavily impacted patients with severe end stage liver disease and liver cancer. We performed LDLT only for very sick young patients with high MELD score or hepatocellular carcinoma following the general rules of COVID 19 infection.
There is a concern that immunocompromised patients may have a higher morbidity and mortality due to COVID-19 infection, and also there is a risk of donor to recipient transmission of COVID-19, both from living and deceased donors. The risk of donor-derived infection depends upon multiple factors.
Methods: Eight LDLT were performed In Fundeni Clinical Institute between April 2020 and February 2021 using the new rules. Our experience includes a case of both donor and recipient patients being infected with SARS-CoV-2 within 60 days prior to LDLT.

They were completely evaluated for living related liver transplantation and all of them signed the informed consent with our general rules related to COVID-19 pandemic.
Results: The average age was 44 years old, 5 male and 3 female patients. In seven cases the indication was severe end stage liver cirrhosis and one patient was diagnosed with hepatocellular carcinoma. The etiology was VHB+VHD infection in four patients, alcoholic liver disease in three patients and one with autoimmune cirrhosis. All the patients received right hepatic lobe. The median MELD score was 26. Seven patients recovered and 1 patient died no COVID 19 infection related. The patients and the donors had a median hospitalization of 14 days, respectively 6 days, according to the standard medical protocol. 3 patients have had fever, cough and breathing difficulty and we performed reevaluation for COVID 19 (re) infection with negative PCR. None of the patients got COVID-19 infection in follow – up period.
We used standard immunosuppression followed in the post-transplant period with very good results.
Conclusions: Our experience during the pandemic period shows that LDLT should be performed with good results. The recipients with high MELD score should have prority.
The outcome in our cases was similar to that before the COVID 19 pandemic.

POS354 VISCERAL AND THORACIC VASCULAR REMODELLING IN POST-LIVER TRANSPLANT PORTAL VEIN THROMBOSIS

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Background: The development of post-liver transplant (LT) portal vein thrombosis (PVT) was associated to different factors and the stigmata of portal hypertension (PH) could play a role. Indeed, PH leads to systemic hyperflow and vascular remodelling that could persist post-LT, even though small data are published. The aim of our study is to evaluate the modifications in systemic circulation in patients with post-LT PVT
Methods: A retrospective study was carried on including all first LT that developed post-LT PVT between 01/2016 and 12/2019 with at least 1 year of follow-up ($n = 17$). Patients with post-LT PVT (pPVT) due to technical problems were excluded. These patients were match 1:2 with cases with similar characteristics without post-LT PVT (wPVT). Chest and abdominal contrast enhanced CT were evaluated to asses vascular remodelling according to Patrono et al. (abdomen) and Daffrè et al. (chest).
Results: Among the study population, 53% of pPVT and 51% of wPVT had pre-LT PVT. The pPVT had higher Child ($p = 0.047$) and a trend toward higher MELD ($p = 0.091$) compared to w-PVT. Pre-LT diameter of gastroduodenal artery (GDA) and gastroepiploic arcade (GEA) were higher in pPVT ($p < 0.001$), while there were no differences in chest vascular diameters. After LT, the diameter of GDA and GEA remained higher in pPVT, while pulmonary artery diameter (PAD) ($p = 0.022$) and its ratio with aorta (PAD/AA) ($p = 0.030$) were higher in pPVT. Interestingly, in wPVT, PAD and PAD/AA decreased after LT ($p = 0.037$), while in pPVT did not ($p = 0.328$). A correlation between PAD/AA and Child was showed (R=0.537; $p = 0.004$). One year survival was 80% in pPVT and 91% in wPVT ($p = 0.482$). All patients were successfully treated with anticoagulants.
Conclusions: Visceral and chest vascular remodelling could partially explain post-LT PVT development and depict a persistent hyperdynamic circulation. PAD and PAD/AA could be identified as markers of hyperdynamic flow, even if these data must be validated with further analyses.

POS355 OUTCOMES AND RISK FACTORS FOR RECURRENCE OF DISEASE IN ADULT LIVER TRANSPLANTATION DUE TO PRIMARY SCLEROSING CHOLANGITIS: A SINGLE-CENTRE EXPERIENCE.

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Background and Aims: Primary sclerosing cholangitis (PSC) is a mysterious cholestatic liver disease often leading to liver failure and liver transplantation (LT). The risk factors associated with recurrent PSC (recPSC) remain controversial. To describe a cohort of PSC-patients undergoing LT we analysed the factors associated with recPSC and its influence on graft and patient survival.
Methods: We conducted a retrospective chart review of patients with PSC undergoing LT at Policlinico S. Orsola-Malpighi (Bologna, Italy) between January 1987 and November 2019. Risk factors for recPSC and graft failure were analyzed.
Results: Among 65 patients transplanted, 12 were excluded from the final analysis: 2 aged <18 years, 1 had no follow-up after surgery, 4 had post-LT survival period <6 months, 5 re-grafted within the first month. Finally, 53 patients were enrolled. Median follow-up was 63 (11–292) months. Patient survival was 98% at 1-year, 94.6% at 3-years, 79.3% at 5-years.
RecPSC was diagnosed in 13 (24.5%) patients, at a median 63 (15–120) months after LT. Among these, 6 developed graft failure secondary to the recurrent disease: 4 were re-grafted and 2 died for liver failure. The cumulative incidence rate of recPSC was 5.5% at 3- and 25% at 5-years. Patient and graft survival rates between the recPSC and no-recPSC groups were similar at 1-, 3-, and 5-years. Patients with recPSC were younger, with lower BMI and shorter cold ischemia time (CIT) than those without rec-PSC ($p < 0.05$). Risk factors for recPSC on univariate analysis were recipient age ≤30 years, BMI ≤22 and CIT <400 minutes ($p < 0.05$). BMI was confirmed at multivariate analysis.
Conclusions: Searching for risk factors for recPSC remains a challenge. Patients with low BMI, young age at the time of LT, and shorter CIT are at increased risk of recurrence. However, recPSC does not reduce survival to 5 years.

POS356 LIVER TRANSPLANTATION AND THE SEVENTH DAY SYNDROME: A SYSTEMATIC REVIEW OF THE LITERATURE AND CASE SERIES.

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Background: Spontaneous failure of a previously functioning liver allograft in the early post-operative period was described two decades ago as Seventh-Day Syndrome (7DS), characterized by patent vasculature and extensive hepatocyte necrosis with minimal immune cell infiltrate. The purpose of this study was to perform a systematic review of the literature reporting 7DS and further describe the cases that have occurred at our institution.
Methods: A systematic literature search was conducted according to PRISMA guidelines. A retrospective review of adult patients that underwent deceased donor liver transplantation at our institution between January 2010 and April 2020 was performed to identify patients that developed 7DS. Relevant variables and histology findings were obtained from medical records. Existing cases in the literature were combined with cases at our institution to determine pooled incidence, retransplantation and mortality rates.
Results: The literature search identified four case series describing a total of 24 patients with 7DS. Cases occurred following living (11/24, 46%) and deceased (13/24, 54%) donor transplantation. Our series identified 6 additional patients. The overall incidence of 7DS was low (pooled incidence 1.1%, 95% CI: 0.2–2.5%) but associated with a high mortality (pooled rate 71.1%, 95% CI: 34.2–98.1%) (Table 1). Retransplantation was performed in 14/30 (47%) patients and 10/14 (71%) survived. Deterioration occurred between post-operative day 4 and 12 with significant elevation in transaminases and fever (Figure 1). Extensive hepatocyte necrosis with minimal immune infiltration was the consistent histological finding.
Conclusion: 7DS is a rare occurrence following liver transplantation with a high mortality, under-reporting may account for such low incidence. Although associated with marked rise in liver enzymes and necrosis, without vascular complications or immune rejection, the causative mechanism remains undefined.

Table 1 Pooled incidence, retransplantation rate and perioperative mortality rate of seventh-day syndrome

	Incidence	Retransplanted	90-Day Mortality
	n/N (%)	n/N (%)	n/N (%)
Memon et al. 2001	10/594 (1.7)	8/10 (80.0)	3/10 (30.0)
Hwang et al. 2006	3/580 (0.5)	0/3 (0.0)	3/3 (100.0)
Zhongwei et al. 2012	8/244 (3.3)	0/8 (0.0)	7/8 (87.5)
Pereira et al. 2015	3/NR (N/A)	2/3 (66.7)	3/3 (100.0)
Birmingham 2020	6/1907 (0.3)	4/6 (66.7)	2/6 (33.3)
Meta-analysis rate (95%CI)	1.1% (0.2%-2.5%)	37.2% (1.4%-82.7%)	71.1% (34.2% -98.1%)
I²	85.9%	80.2%	68.0%

Figure 1: Graphical demonstration of post-operative liver function of institutional case series at the

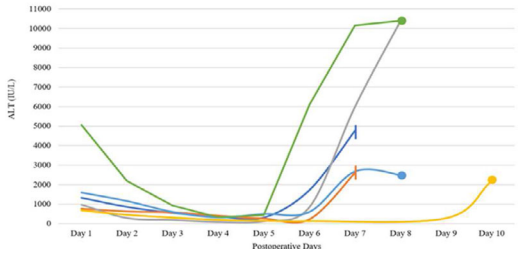

Figure 1. Graphical demonstration of post-operative liver function of institutional case series at the Liver Unit, Birmingham. Legend: ALT: Alanine aminotransferase.

POS357 AN ITALIAN SURVEY ON THE USE OF T-TUBE IN LIVER TRANSPLANTATION

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Background: There is enough clinical evidence that a T-tube use in biliary reconstruction at adult liver transplantation (LT) does not significantly modify the risk of biliary stricture/leak, and it may even sustain infective and metabolic complications. Thus, the policy on T-tube use has been globally changing, with progressive application of more restrictive selection criteria. However, there are no currently standardized indications in such change, and many LT Centers rely only on own experience and routine.
Methods: A nation-wide survey was conducted among all the 20 Italian adult LT centers to investigate the current policy on T-tube use.
Results: It was found that 20% of Centers completely discontinued the T-tube use, while 25% Centers used it routinely in all LT cases. The remaining 55% of Centers applied a selective policy, based on criteria of technical complexity of biliary reconstruction (72.7%), followed by low quality graft (63.6%) and high-risk recipient (36.4%). A T-tube use >50% of annual caseload was not associated with high-volume Center status (>70 LT per year), an active pediatric or living-donor transplant program, or use of DCD grafts. Only 10/20 (50%) Centers identified T-tube as a potential risk factor for complications other than biliary stricture/leak. In these cases, the suspected pathogenic mechanism comprised bacterial colonization (70%), malabsorption (70%), interruption of the entero-hepatic bile acid cycle (50%), biliary inflammation due to an indwelling catheter (40%) and gut microbiota changes (40%).
Conclusions: The prevalence of T-tube use among the Italian LT Centers is still relatively high, compared to the European trend (33%), and the potential detrimental effect of T-tube, beyond biliary stricture/leak, is largely underestimated.

POS358 DUCT-TO-DUCT VS. HEPATICOJEJUNOSTOMY FOR BILIARY RECONSTRUCTION IN ADULT RIGHT LOBE LIVING DONOR LIVER TRANSPLANTATION: A RANDOMIZED CONTROLLED TRIAL

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Background and aims: The best method for biliary reconstruction after adult right lobe living donor liver transplantation (LDLT) remains unknown. We hypothesized hepaticojejunostomy (HJ) had a lower incidence of biliary complication than duct-to-duct anastomosis (DD).
Method: This was a single center randomized controlled trial. The primary endpoint for this study was biliary complication free survival. Only grafts that had suitable anatomy and feasible for both DD and HJ were randomized.
Results: All right lobe LDLT recipients (n = 165) from May 2012 to December 2018 were assessed, 96 were excluded (refusal n = 21, not fit for consent n = 28, donor anatomical issue n = 27, re-transplant n = 4, ABO incompatible n = 4, disease mandated HJ n = 9 and others n = 4). 69 patients were randomized. 34 patients had HJ and 35 had DD.
Pretransplant characteristics were comparable. 94.1% in the HJ group and 94.3% in DD group had right lobe with middle hepatic vein inclusion. Most patients had single graft hepatic artery and portal vein. 30 (88.2%) in the HJ group and 30 (85.7%) in the DD group had type 1 biliary anatomy.
Biliary complication free survival rates were superior in the DD group. (figure 1) The incidence of early (defined as within 3 months from LDLT) biliary complication was [5/34 (14.7%) in HJ group and 3/35 (8.6%) in DD group, p = 0.426] and delayed (defined as >3 months after LDLT) was [8/34 (23.5%) in HJ group vs. 5/35 (14.3%), p = 0.326]. The number of admission required for management of biliary complication was similar (4.5 vs. 4, p = 0971] and extra hospital stay for biliary complication (36.5 vs. 21 days, p = 0.943). In those who developed biliary complication, most patients in HJ arm required re-operation as definitive management (75% vs. 11.1%, p = 0.004). There was no difference in hospital and 90 day mortality between the 2 groups.
Conclusion: DD biliary reconstruction was associated with less biliary complication in adult right lobe LDLT.

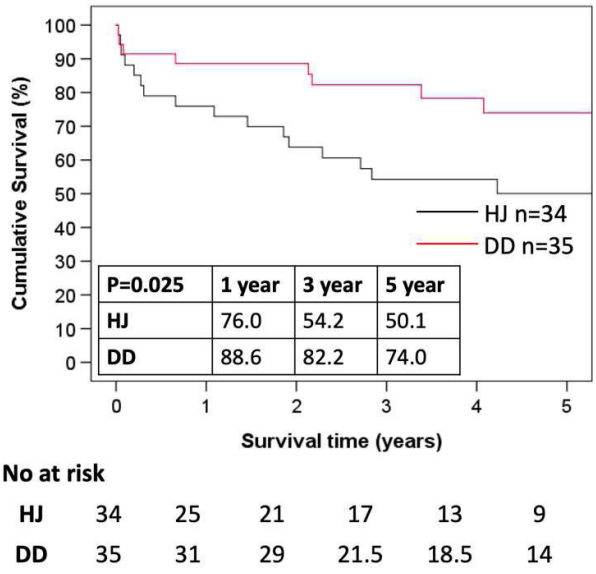

Figure 1. Biliary complication free survival of HJ and DD groups.

POS359 THE EFFECT OF PORTAL HYPERTENSION IN INTRAOPERATIVE BLEEDING DURING LIVER TRANSPLANTATION

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Background: More than a half of patients undergoing liver transplantation (LT) receive intraoperative transfusion. Portal hypertension has been implicated as a contributor to perioperative blood loss during LT though this association has not been well addressed (1). We aimed to assess the relationship between preoperative values of HVPG and intraoperative transfusion requirements in a cohort of adult patients undergoing LT.
Methods: Patients undergoing LT between 2009 and 2019 at our hospital with an HVPG measurement up to 12 months before transplantation were included. Surgical technique was piggyback with portocaval shunt (PCS). The association of HVPG and other baseline variables with transfusion requirements (transfusion yes/no, number of RBC transfused) and with blood loss was studied.
Results: 230 patients were identified. At univariate analysis blood loss (ml/kg) had a positive correlation with MELD, Child and re-transplant while it was negatively correlated with BMI, hemoglobin, prothrombin and fibrinogen; at multivariable analysis remained associated BMI, MELD, hemoglobin and fibrinogen (table 1). Regarding the need and magnitude of RBC transfusion only MELD, hemoglobin and the use of cell saver were associated to it. HVPG was neither correlated with blood loss nor RBC transfusion. A stratified analysis according to surgical stages (hepatectomy, anhepatic, neohepatic) showed the strongest correlation between HVPG and RBC transfusion during hepatectomy only at univariable analysis but not at MV analysis. A detailed study of HVPG at different cut-offs did not identify any significant value associated with RBC transfusion.
Conclusions: The severity of portal hypertension seems to play a minor role in intraoperative bleeding during LT in a contemporary cohort with systematic PCS and a fluid restriction policy. Strategies to improve preoperative hemoglobin level may be the main challenge to reduce intraoperative transfusion in LT.

1. Semin Thromb Hemost 2020; 46 (06): 751–756

POS360 THE INFLUENCE OF SELECTED CRITERIA ON THE BILIARY COMPLICATIONS OCCURENCE

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Background: The aim of this analysis is determining the predisposing factors for biliary complications after orthotopic liver transplantations.
Methods: In the period April 2018 - February 2021, 74 orthotopic liver transplantations (oltx) were performed, including 2 retransplantations. In 66 cases a duct-to-duct and in 7 cases a hepatico-jejunal anastomosis has been made. No case has been excluded from the study.
F/M 29/45, age: 20–67 (avg = 52.89, sd=10.27)
We have compared the donor's and recipient's sex and age, pre-reperfusion liver wash out fluid potassium level , cold ischemia time, sutures diameter used and stitching technique and vena cava inferior anastomosis technique (piggy-back versus classical) using tests in Statistica such as: Fisher's test, ANOVA, U-Mann-Whitney test, Spearman's correlations.
Results: Biliary complications occurred in 13 out of 74 OLTx (17.57%)– it included 8 early complications (62% of all complications, 11% of all cases) and 5 late complications (38% of all complications, 7% of all cases). The age of patients who developed biliary complications: 42–67, avg 54.86.
Most of the selected criteria weren't statistically significant: F/M 6 (46%, 8% total)/7 (54%, 9% total) $p = .39$. Age $p = .77$. Donor age $p = .66$. Potassium level $p = .53$. Suture: 5/0 vs 6/0 – $p = .57$. Suture: interrupted vs continuous $p = .18$. Piggy-back vs classical $p = .20$.
The only chosen criteria with a statistically significant predisposition to biliary complications was the cold ischemia time $p = .048$, with no difference between early and late complications $p = .34$.
Conclusions: There is no set of factors predisposing to biliary anastomosis complications. However, amongst the chosen criteria the cold ischemia time was the only statistically significant variable affecting the possibility of biliary complications ($p = .048$). Despite the fact that the comparison of interrupted and continuous suture wasn't statistically significant ($p = .18$), there is a visible predisposition to the biliary anastomosis leakage while using a interrupted suture and a predisposition to its stenosis while using a continuous suture.

POS361 PORTAL VEIN THROMBOSIS AND LIVER TRANSPLANTATION: RESULTS OF THE ITALIAN SOCIETY OF ORGAN TRANSPLANTATION NATIONAL SURVEY

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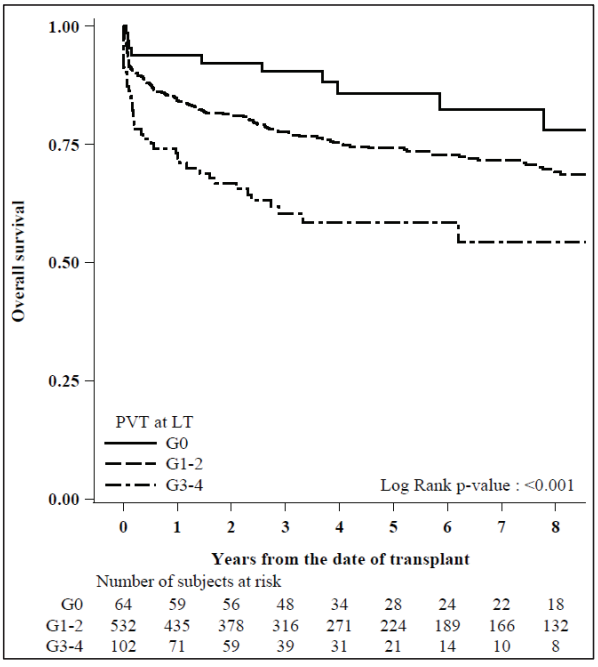
Background: Portal vein thrombosis (PVT) has a significant impact on liver transplant (LT) recipients and poses critical challenges in the intra-operative management to restore an adequate inflow toward the liver. Predictors of outcomes capable to improve organ allocation and LT timing are yet to be defined. We decided to perform an italian survey to have a snapshot of the results achieved so far on a nationwide basis.
Methods: Fourteen Italian liver transplant centers joined the study. Patients who underwent LT in Italy between January 2000 and February 2020 were considered eligible for inclusion in this study. Pediatric LT, combined transplants, and patients without evidence of PVT were excluded. Primary

endpoint was to define overall survival (OS) according to PVT degree and graft survival.
Results: 714 patients were screened, 16 cases not meeting the inclusion criteria were excluded from the analysis and 698 were ultimately included. Median age was 57 (21–71), with a prevalence of male patients (73.2%). 49.3% of patients received anticoagulation and only 25.6% of patients with PVT had a successful downstaging of the thrombosis before LT. Table 1 summarizes the major outcomes by PVT stage according to Yerdel classification at LT (grade 0, grade 1–2. grade 3–4). Figure 1 shows the stratification of OS according to PVT stage at transplant. Notably, 30-days mortality seems to be significantly associated to PVT stage at LT ($p = 0.003$), cavo-portal transposition (0.003), and center volume ($p = 0.007$), while successful downstaging and other technical solutions for portal inflow reconstruction had no significant correlations.
Conclusions: Although post-operative complications and 30-days mortality are significantly increased in patients affected by PVT grade 3–4, 5-years OS exceed 50% even in these complex scenarios. Allocation policies should be carefully balanced to guarantee to these patients an optimal timing to maximize the benefit of LT.

Table 1. Outcomes by PVT according to Yerdel stage at transplant

Variable	Level	PVT at LT			P-value
		G0 (N=64)	G1-2 (N=532)	G3-4 (N=102)	
Estimated blood loss (mL)		2000 (250-7750)	1250 (0-20000)	1120 (0-27800)	0.097
Missing		38	191	43	
ICU days		3 (0-60)	4 (0-87)	4 (0-73)	0.22
Missing		0	28	5	
Clavien morbidity	0	3 (5)	75 (14)	11 (11)	<0.001
	1-2	47 (75)	255 (49)	33 (33)	
	>2	13 (21)	194 (37)	56 (56)	
	Missing	1	8	2	
30-days mortality	No	63 (98)	498 (94)	89 (87)	0.017
	Yes	1 (2)	34 (6)	13 (13)	
Re-thrombosis	No	57 (89)	482 (91)	94 (92)	0.81
	Yes	7 (11)	48 (9)	8 (8)	
	Missing	0	2	0	
Re-transplant	No	60 (94)	493 (93)	97 (95)	0.73
	Yes	4 (6)	39 (7)	5 (5)	



PVT at LT	Deaths	1-y OS (95% CI)	2-y OS (95% CI)	3-y OS (95% CI)	5-y OS (95% CI)
G0	11 / 64 (17.2%)	93.8 (84.2-97.6)	92.2 (82.2-96.7)	90.4 (79.7-95.6)	85.7 (73.0-92.7)
G1-2	153 / 532 (28.8%)	84.3 (80.9-87.1)	81.3 (77.7-84.4)	77.7 (73.8-81.1)	74.2 (70.0-77.9)
G3-4	41 / 102 (40.2%)	73.1 (63.2-80.7)	66.7 (56.5-75.1)	60.3 (49.5-69.4)	58.5 (47.6-68.0)

POS362 A PILOT STUDY OF A NON-INVASIVE REAL-TIME OPTICAL BACKSCATTER PROBE IN LIVER TRANSPLANTATION

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Background: Transplantation of severely steatotic donor livers is associated with early allograft dysfunction and poorer graft survival. Histology remains the gold standard diagnostic of donor steatosis despite the lack of consensus definition and its subjective nature.
In this prospective observational study of liver transplant patients, we aimed to demonstrate the feasibility of using a handheld optical backscatter probe to assess the degree of hepatic steatosis and correlate the backscatter readings with clinical outcomes.
Methods: Prospective observational study of patients receiving a whole liver only transplantation performed Cambridge. The probe is placed on the surface of the liver and emits red and near infrared light from the tip of the device and measures the amount of backscatter of light from liver tissue via two photodiodes.
Results: Measurement of optical backscatter (Mantel Cox $p < 0.0001$) and histopathological scoring of macrovesicular steatosis (Mantel Cox $p = 0.046$), was predictive of 5-year graft survival. Recipients with early allograft dysfunction defined according to both Olthoff ($p = 0.0067$) and MEAF score ($p = 0.0097$) had significantly higher backscatter levels in the donor organ. Backscatter levels were predictive of graft loss (AUC 0.75, $p = 0.0045$).
Conclusion: This study demonstrates the feasibility of real-time measurement of optical backscatter in donor livers. Early results indicate readings correlate with steatosis and may give insight to graft outcomes such as early allograft dysfunction and graft loss.

POS363 PURE LAPAROSCOPIC VERSUS OPEN DONOR HEPATECTOMY FOR ADULT LIVING DONOR LIVER TRANSPLANTATION - A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Pure laparoscopic donor hepatectomy (PLDH) for adult living donor liver transplantation (LDLT) remains controversial. The aim of this study was to undertake a systematic review and meta-analysis of donor outcomes following PLDH for adult LDLT.
Methods: Systematic review in line with the Meta-analysis of Observational Studies in Epidemiology guidelines. An electronic search of Medline (1946-present), EMBASE (1974-), PubMed, Cochrane Library (1995-), CINAHL (1937-) and Google scholar was conducted to identify studies evaluating peri-operative results of PLDH in adult LDLT. The random effects, the DerSimonian-Laird method was used for the meta-analysis of outcomes.
Results: Eight studies were included in the systematic review and six in the meta-analysis. A total of 575 donors underwent PLDH for adult LDLT. Mean donor age was 32.8 years with a BMI of 23.4 kg/m^2 and graft weight of 675 g. Mean operative time was 353 min and the conversion rate was 2.8% ($n = 16$). Overall morbidity was 10.8% with 1.6% major complications (Clavien-Dindo grade 3b), zero mortality and 9.0 days length of stay (LOS). The meta-analysis demonstrated that the operative time was significantly longer for the Open Donor Hepatectomy (ODH) group [mean difference 29.15 mins; $p = 0.006$] and the LOS was shorter for the PLDH group [mean difference −0.73 days; $p = 0.02$], with a trend towards lesser estimated blood loss in PLDH group. However, no difference between the two groups was noted in terms of overall morbidity or major complications.
Conclusions: Perioperative outcomes of PLDH are similar to the standard open approach in highly specialised centers with trend towards lesser blood loss and overall shorter hospital stay. Careful donor selection and standardisation of the technique are imperative for the successful implementation and adoption of the procedure worldwide.

POS364 THE CHALLENGING MANAGEMENT OF VASCULAR RECONSTRUCTION IN LIVING DONOR LIVER TRANSPLANTATION THROUGH THE RECENT EXPERIENCE OF THE MODENA UNIVERSITY

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Background: Living Donor Liver Transplantation (LDLT) is still considered a challenging procedure, although several reports have strongly demonstrated its safety and feasibility. Three key points hide the technical complexity of this operation: correct indication for donor and recipient, residual liver volumes and functionality evaluation, vascular and biliary reconstruction. The aim of this study was to report the new program experience from Modena University about the vascular reconstructions in LDLT.
Methods: On July 2020, University of Modena gave life at a new LDLT program for adult patients. Previous program was closed on 2002. Indications for donor and recipients were confirmed after multidisciplinary staff, taking into account donor condition and safety, benefit for recipients, and procedure feasibility. Pre-operative vascular assessment was evaluated by a CT-Angiography and MR-Angiography. Donor's liver 3D reconstruction for volumes and vessels assessment were obtained by MEVIS. Vascular anastomosis were performed using non-absorbable polypropylene and surgeons worn 3.5x loupes.
Results: Four LDLT with right lobe procurement were performed. Donors were 1 male and 3 females. Recipients were 1 female and 3 males. All the donors and recipients are alive, healthy and safe. Right hepatic vein was reconstructed in all the cases; V8 in three; V5 in one; posterior short veins in two. Portal vein anastomoses were end-to-end with the graft right portal vein in 3 cases; one case needed an interposition graft of recipient portal vein bifurcation due to the donor type IV portal vein. Arterial anastomosis was end-to-end between the right hepatic branches of the donors and recipients. None case of vascular complication occurred post-operatively.
Conclusion: The modern approach to LDLT needs to rest on solid pillars to guarantee optimal results for both donor and recipient. The 3D preoperative assessment for volumes and vessels, the multidisciplinary consensus for donor selection and recipient's indications, the extremely accuracy of vessels procurement and reconstruction are unavoidable pillars on which base the LDLT safety and success. The expansion of oncological indications for liver transplant will increase the needing of LDLT, therefore more programs and more cases are demanded.

POS365 LIVER TRANSPLANT EXPERIENCES FOR THE BUDD-CHIARI SYNDROME AT BASKENT UNIVERSITY TRANSPLANT CENTERS

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Background: Budd Chiari syndrome (BCS) is a disease, presented with occlusion of hepatic vein in any localization and can progress to chronic liver failure. The last step treatment of this disease is liver transplantation. We evaluated clinical results of liver transplants performed on patients diagnosed with BCS.
Material and Methods: Between December 1988 and December 2020, 144 patients were diagnosed with BCS and we performed 16 Liver transplant (LT) in 12 patients. Transplantation age, sex, CHILD-PUGH score, model for end-stage liver disease score, histopathologic findings, interventional treatments, graft type, hepatic vein anastomosis, post-transplant complications and mortality were recorded.
Results: We performed 16 LT in 12 patients due to BCS. Six of 12 recipient were female. Mean age of patient was 26.9 (range 9–50). We had liver transplantation once for 9 patients, twice for 2 patients and three times in 1 patient with BCS diagnosis. The median follow-up was 83 months (range, 9–126). The survival rates at 1, 5 and 10 years were 90%, 80% and 30% respectively. Only two patients died postoperatively after second LT.
Conclusion: LT can be performed safely in patients with BCS where chronic liver failure develops and other treatment methods fail.

POS366 CLINICAL OUTCOMES OF LIVER TRANSPLANTATION FOR PATIENTS OVER 60 YEARS OLD; A SINGLE CENTER EXPERIENCE

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Background: Advanced age is not considered an absolute contraindication for liver transplant but transplant in the elderly patient with comorbid diseases still is a subject of debate because of the high risk of surgery. The aim of this study is to describe our experience in the recipient evaluation process, and the outcomes of elderly patients with liver transplant.
Materials and Methods: Since 1988, we have performed 683 (472 living donor and 211 deceased donor) liver transplant at our hospital. 365 of the patients were adult recipients. 276 adult patient's data which were available were included in the study. Patients were divided into two groups according to their ages (Group 1: $\leq$ 59 years old, Group 2: $\geq$ 60 years old). In group 1, there were 247 recipients, and in group 2, 29 recipients.
Results: We evaluated 276 transplant patients' data. The mean age of the patients was 40 $\pm$ 12.3 years in group 1 and 63 $\pm$ 2.3 years in group 2. In group 1, 177 of the patients were male and 22 patient were male in group 2. 97 of the transplants were DD and 150 of them were LDLT in group 1. In group 2, most of the transplants were living related transplant (n = 19). In both group; the most common indication for liver transplant was Hepatitis B (n = 125). One hundred and forty three patients died during the follow-up periods. 132 of them were in group 1, and 11 of them were in group 2. There was no statistically significant difference between the two groups in terms of mortality rates. Overall mean survival time was 10.4 $\pm$ 0.6 years and 1 year, 5, 10 and 15 years patient survival rates were 67%, 54%, 48.4%, 40.4% respectively. In group 1; mean survival time was 10.2 $\pm$ 0.6 years , and 1 year, 5, 10 and 15 years patient survival rates were 65.5%, 53%, 46.3%, 40% respectively. In group 2; mean survival time was 10.6 $\pm$ 1.3 years, and 1 year, 5, 10 and 15 years patient survival rates were 75.9%, 68.6%, 61%, 48.8% respectively. There was no statistically significant difference in survival rates between the two groups.
Conclusion: In this study, LT recipients older than 60 years, had survival rates, acute rejection rates and, complications, equivalent to those of younger recipients. Liver transplant should not be with - held from older recipients on the basis of age alone.

POS367 CAVOPORTAL HEMITRANSPOSITION ASSOCIATED TO PORTOPORTAL ANASTOMOSIS FOR LIVER TRANSPLANT IN PORTOMESENTERIC THROMBOSIS: HOW WE DO IT

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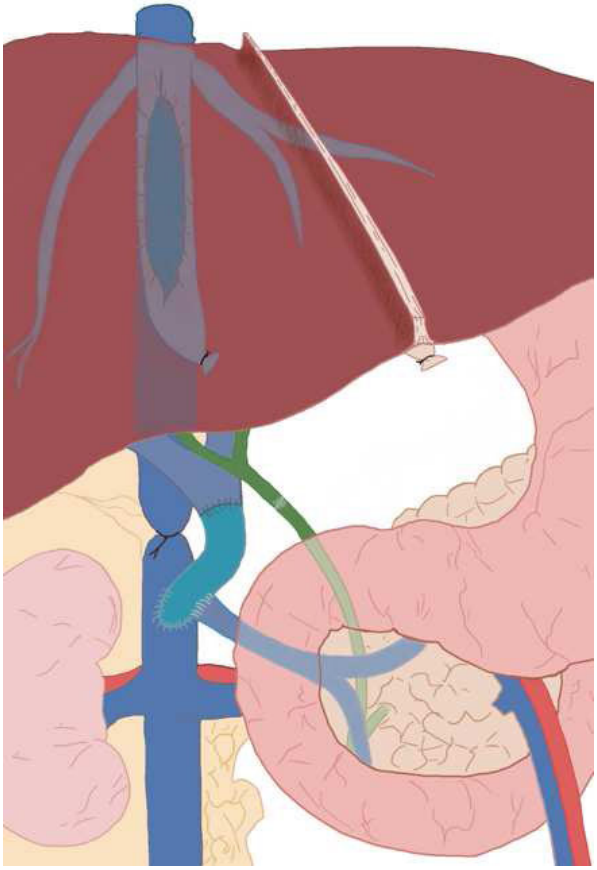
Background: Intraoperative management of portal vein thrombosis (PVT) is one of the challenges of liver transplantation (LT). In presence of complete spleno-mesenteric thrombosis (SMT) or residual but inadequate portal flow (PF) after ineffective thromboendovenectomy (TEV), we implemented thoughts to maintain a more physiologic and efficient splanchnic venous drainage after cavoportal hemitransposition (CPH). An option to rescue the PF and to reduce splanchnic hypertension (SH) is associating to the classical CPH an end-to-side anastomosis (C/PPA) from a major portal collateral (in presence of cavernoma) or from the recipient portal vein (in case of residual but inadequate PF) improving the drainage of splanchnic venous bed into the liver graft (Fig. 1).
Methods: Patients transplanted with CPH between 2010 and 2020 at a single center were retrospectively analyzed. PVT was classified according to the Yerdel classification. CPH was attempted only after failure of TEV.
Results: Between 2010 and 2020, 903 LT were performed. 15 patients underwent CPH (1.7%). 2 were re-LT. 9 (60%) patients had PVT Yerdel grade 4, 3 (20%) grade 3, and 3 (20%) grade 2. Modified CPH with PPA (C/PPA) was utilized in 9 (60%) cases. An interposition iliac graft was used in 4 (44.4%) cases. All but one patient had at least a spontaneous portosystemic shunt according to Azoulay classification. Splenorenal shunts (SRS) were present in 5 (83.3%) of standard CPH compared to 4 (44.4%) of C/PPA. The rate of portal hypertension related complications was similar between the two groups (standard CPH 50% vs. C/PPA 56.6%). Intra-abdominal bleeding was never observed in our series. In-hospital mortality rate was 33.3% and 44.4% in standard and C/PPA respectively. Long lasting hemodialysis treatment is needed in 1 out of 8 living patients. 5-year OS after C/PPA compared to standard technique was 55.6% vs. 50%.

Conclusions: In our experience, C/PPA is a viable alternative to standard surgical approach, in case of residual PF after TEV and fewer spontaneous portosystemic shunts. C/PPA is not particularly demanding from a technical point of view but, as far this gross analysis concerned, C/PPA is not superior to standard CPH. Better analysis, in particular with focus on patients' portal pressure and flow, is needed.



POS368 LAPAROSCOPIC VS. LAPAROTOMIC LEFT LATERAL SECTIONECTOMY IN PEDIATRIC LIVING DONOR LIVER TRANSPLANTATION

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Background : Laparoscopic left lateral sectionectomy (L-LLS) is growing practice in pediatric living donor liver transplantation (pLDLT) demonstrating comparable results to the laparotomic approach. We report a series of L-LLS compared to conventional open approach (O-LLS) for pLDLT performed by a single surgeon (MS).
Method : From 2002 to 2020, 41 consecutive LLS for pLDLT were performed, including 12 O-LLS, 23 L-LLS and 6 hybrid approach (H-LLS). One combined simultaneous liver and kidney open retrieval was excluded from the analysis. We conducted a retrospective comparative analysis of donor and recipient outcomes.
Results : Donor median age was 34.7 years; median BMI was 23 kg/m^2. Median operating time was similar in the three groups: 481, 492 and 610 minutes for O-LLS, L-LLS and I-LLS, respectively ($p = 0.12$). Only one donor in the L-LLS group required blood transfusion, while blood losses were comparable (median 125, 50 and 250 mL; $p = 0.47$). Six patients (26%) were electively converted to open procedure. Median hospital stay was 6 days in all groups. All donors survived the procedure. Overall postoperative complication rate was 17%, 0% and 33%, respectively ($p = 0.07$). L-LLS procedures required less postoperative analgesia compared to other groups ($p = 0.0008$).
Recipient median age and weight were 24 months and 12 kg. Main indication to pLDLT was biliary atresia (51%). One recipient died in open group for multi organ failure, while graft survival was 95% in the O-LLS group and 100% in the other two groups. Postoperative complication rates were 47%, 41% and 16.6%, respectively ($p = 0.23$).
Conclusion: L-LLS is a safe procedure with results comparable to the other approaches in terms of donor and recipient outcome. Advantages on the L-LLS approach include better pain control and cosmesis. Our results suggest that the laparoscopic approach can be considered standard practice when performed by a transplant team with strong laparoscopic background.

POS369 PRESERVATION OF THE REVASCULARIZED UMBELICAL VEIN DURING LIVER TRANSPLANTATION IN PATIENTS AFFECTED BY PORTAL HYPERTENSION

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Background: Spontaneous porto-systemic shunts unable modulation of portal flow in patients affected by portal hypertension (PH). PH deeply affect post-liver transplant (LT) results with possible life-threatening intraoperative complications due to variceal or portal bleeding. The aim of our study is to describe the results obtained thorough the intraoperative preservation of revascularized umbelical vein (rUV) during LT in patients affected by PH.
Methods: During hepatectomy and after laparotomy the rUV was preserved through the dissection of the rUV from the adipose tissue of the round ligament. The rUV was interrupted before portal vein clamp and hepatic vein section. LT were performed with a latero-lateral caval anastomosis. These patients were compared with those affected by PH treated with TIPSS ($n = 10$) and that underwent rUV ligation at laparotomy.
Results: The rUV was preserved in 6 patients until the scheduled intraoperative phase. The hepatectomy time was 211 (175–250) min in rUV and 174 (125–165) min in TIPSS ($p = 0.047$). In rUV 1 (0–3) red blood packed cells were transfused, while 2 (0–7) in TIPSS ($p = 0.103$). Portal and rUV pressure were 18 (15–19) mmHg and 16 (13–17) mmHg before section and rised 24 (20–27) mmHg after rUV section. Conversely, portal pressure in TIPSS group was 17 (13–18) mmHg ($p = 0.394$ compared to rUV before section). In rUV group, the 20% of the LT procedure was carried on by a senior surgeon, while in 70% of TIPSS group ($p = 0.067$). Three-months graft and patient survival were 100%–100% in rUV vs 90%–100% in TIPSS.
Conclusions: rUV preservation during LT is feasible in PH patients. It allows a reduction of the portal vein pressure comparable to TIPSS and enables a possible reduction of intraoperative difficulties linked to PH. This technique must be validated in a prospective study comparing rUV preservation with cases with rUV section in patients with PH.

POS370 TECHNICAL REFINEMENTS TO THE RAPID TECHNIQUE: A POTENTIAL BREAKTHROUGH IN TRANSPLANT ONCOLOGY

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Background: ColoRectal Liver Metastases have an important epidemiological pressure. Approximately the 50% of CRC develop liver metastases, which are the major cause of death. The best therapeutic option is represented by liver resection, but only the 20% of metastatic disease is resectable. For the i-CRLM the gold standard treatment is systemic chemotherapy, with an OS of 20%. The SECA-II trial showed that liver transplantation could be the best treatment for i-CRLM with a 5-years OS of 83%. The RAPID technique was recently introduced as alternative to whole LT. In this context, left lateral living donor LT could be use due to the low donor morbidity and mortality rate, which rebalance the donor equipoise.
Methods: We embraced this new technique that enables left lateral segment grafts to be adopted to transplant adult patients, overcoming the small-for-size syndrome and considerably expanding the donor pool. Moreover, we added three technical refinements to the classic procedure. In particular: Microwave Thermal Ablation along future transection plan to improve oncological radicality and to favor a near-bloodless parenchymal resection, autologous saphenous vein ring graft application on the left supra-hepatic vein to optimize graft outflow and avoid LSV kinking and minimally invasive laparoscopic second stage hepatectomy to speed up the post-operative recovery. We performed our first case in December 2018.
Results: The surgery went well. No major complications were observed. At POM5 metastases occurred in liver and lungs; the liver ones were treated with multiple MWA and adjuvant chemotherapy was administrated. Almost

27 months after surgery, the patient is alive, in good general condition, although the recurrence.
Conclusions: Our proof of concept has potentially underlined the feasibility of this cutting-edge surgery, suggesting wild room for donor, graft and recipient safety. Our technical refinements have hopefully opened the way to a partial conversion of this extremely aggressive procedure into a minimally invasive setting. All these preliminary findings need to be widely confirmed in a pilot study, which is actually ongoing in our center, and subsequently in a prospective study. In times of organ paucity, LD-RAPID procedure might represent a potential breakthrough in the management of i-CRLM.

POS371 IMPACT OF PNPLA3 (RS738409-G) POLYMORPHISM ON POST-TRANSPLANT OUTCOMES AFTER LIVER TRANSPLANTATION FOR ALCOHOL-RELATED LIVER DISEASE

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Background: We aimed to evaluate the association between PNPLA3 polymorphism and post-liver transplantation (LT) outcomes related to alcohol relapse (AR).
Methods: We retrospectively analyzed data from patients receiving LT for alcoholic liver disease (ALD) from 04/2014 to 12/2017. Liver-related clinical outcomes were assessed by the gamma-glutamyltransferase (GGT) level and alcohol-related liver failure (ARLF). Genotyping was performed using prospectively collected DNA samples in both donors and recipients.
Results: A total of 83 recipients were enrolled. Post-LT AR occurred in 31 patients (37.3%). Thirty-one patients (14 AR, 9 abstainers) showed elevated GGT levels, and 3 AR patients experienced ARLF. In the multivariate analysis, rs738409 G allele carrier and heavy drinking (HRAR score≥4) were independent risk factors for elevated GGT levels (odds ratio [OR]=8.69, $p < 0.01$; OR=13.07, $p = 0.01$) and ARLF (OR=4.52, $p = 0.04$; OR=19.62, $p = 0.03$). Among 15 heavy AR patients, being an rs738409 G allele carrier was related to GGT elevation ($p = 0.03$) and ARLF ($p = 0.04$), but it was not to GGT elevation in mild drinkers ($n = 16$) or abstainers ($n = 52$).
Conclusions: PNPLA3 polymorphism of the recipient genotype can independently affect the post-LT prognosis of LT patients for ALD, especially in heavy AR patients. Therefore, strong abstinence education is recommended in patients with this single nucleotide polymorphism.

POS372 IMPROVED PERFORMANCE OF TRAIN SCORE IN PREDICTING HEPATOCELLULAR CANCER RECURRENCE AFTER LIVER TRANSPLANTATION: THE ROLE OF PIVKA-II

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Background: Protein Induced by Vitamin-K Absence-II (PIVKA-II) has been linked to a poor outcome of hepatocellular cancer (HCC) patients after liver transplantation (LT). The Time on waiting list-Radiological response-Alpha-fetoprotein (AFP)-INflammatory marker (or TRAIN) Score has been proposed to select HCC patients with low-risk post-LT recurrence. The present study aims to recalibrate the TRAIN Score in an international cohort by integrating the PIVKA II value.
Methods: We reported an observational retrospective study of data of the international East-West collaborative HCC-LT registry. Between 2000 and 2019, 639 HCC recipients belonging to five collaborative centers (Kyoto, Japan = 230; UCL-Brussels, Belgium=178; Fukuoka, Japan=161; Ancona, Italy=60; Rome Sapienza, Italy=10) were enrolled PIVKA II was integrated into the existing TRAIN score to evaluate the prognostic value of the TRAIN-PIVKA-II score.
Results: Median follow-up was 4.6 years (interquartile ranges=1.8–9.5). The recurrence rate was 12.8% (82 patients). The results of the Fine-Grey competing-risk analysis for the risk of post-LT recurrence are reported in **Fig.1**. According to these results, the TRAIN-PIVKA-II score was created according to the equation: 1.102*(if m-RECIST progressive disease) + 0.668*(log10AFP) + 0.523*(log10PIVKA-II). C-statistics revealed that the TRAIN-PIVKA-II score had the best area under the curve (AUC) (0.79; P-value<0.001) when compared to other scores (e.g., Milan Criteria AUC was 0.70, the AFP-French Model=0.74, and the Metroticket 2.0=0.75).
Conclusions: The reported results suggest that integrating an elevated PIVKA-II level into the previously reported TRAIN Score improves the ability to predict the risk for post-LT HCC recurrence. This new score represents a new tool further to finetune the selection process of HCC patients for LT.

Variable	Beta	SE	Z	SHR	Lower	Upper	P-value
Progressive Disease	1.102	0.243	4.528	3.009	1.568	3.999	<0.001
Log10AFP ng/mL	0.668	0.151	4.417	1.950	1.595	2.757	<0.001
Log10PIVKA-II mAU/mL	0.523	0.119	4.390	1.687	1.378	2.174	<0.001
Age years	-0.024	0.013	-1.869	0.976	0.953	1.002	0.062
Asian	-0.763	0.437	-1.746	0.466	0.205	1.072	0.081
Waiting list duration months	-0.045	0.041	-1.089	0.956	0.878	1.028	0.280
Male sex	0.302	0.284	1.065	1.353	0.714	2.083	0.290
Period of LT (1999-2009)	-0.168	0.384	-.436	0.846	0.406	1.819	0.660

POS373 POSTOPERATIVE TRENDS AND PROGNOSTIC VALUES OF INFLAMMATORY AND NUTRITIONAL BIOMARKERS AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Background. Preoperative inflammatory strongly predict the outcome in surgically treated patients with hepatocellular carcinoma (HCC), while nutritional biomarkers show an analogue prognostic value in hepatic resection but not in liver transplant (LT) cases. The post-LT trends of these biomarkers might explain such discrepancy, but these data are not currently available.
Methods. Retrospective study on a bi-center cohort of 324 HCC patients treated with LT between 2006–2018. Indication to LT was limited to UCSF criteria, defined by preoperative imaging. The investigated inflammatory biomarkers were the Platelet-to-Lymphocyte Ratio (PLR) and the Neutrophil-to-Lymphocyte Ratio (NLR), while the nutritional biomarkers were the Controlling Nutritional Status (CONUT) score and the Prognostic Nutritional Index (PNI). The analyzed time points after LT were postoperative day (POD) 1, 3, 5, 7 and postoperative month (POM) 3, 6, 12.
Results: Inflammatory biomarkers peaked on POD 1, subsequently decreased and at POM 3 leveled off at values similar (NLR) or higher (PLR) than pre-LT ones. CONUT and PNI worsened in the early post-LT period, but at POM 3 they stabilized at significantly better values than pre-LT. In LT recipients with an overall survival >1 year and no evidence of early HCC recurrence, 1 year post-LT NLR and PNI independently predicted patient overall survival, while 1 year post-LT PLR independently predicted late tumor recurrence.
Conclusions: In conclusion, at 1 year post-LT, the nutritional status of liver-transplanted HCC patients significantly improved while their inflammatory state tended to persist. Consequently, post-LT PLR and NLR maintained a prognostic value for LT outcome while post-LT CONUT and PNI acquired it.

POS374 MELDING LOCOREGIONAL TREATMENT OF HEPATOCELLULAR CARCINOMA (HCC) INTO LIVER TRANSPLANTATION PROGRAMME AT NEWLY FOUNDED CENTRE.

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Background: The surgical unit in Gdańsk had vast experience locoregional treatment of HCC by means of radio-frequency ablation (RFA) and transarterial chemoembolization (TACE). Since April 2018 our department became second largest OLTx unit with 52 procedures in 2020 despite COVID-19 pandemic. We look at three years history to evaluate influence of our previous experiences.

Methods: In this retrospective study 74 OLTx from single department were divided into HCC ($n = 14$) and non-HCC ($n = 60$). Urgent transplantations were excluded. In the HCC group 3 cases were diagnosed post-operatively. Initial radiological assessment of hepatic lesions followed CT/MRI LI-RADS protocol. This was confronted with Milano Criteria, University of San Francisco Criteria (USFC) and MetroTicket 2.0. Patients qualifying for locoregional treatment underwent either RFA or TACE with follow-up assessment. The HCC group perioperative course was compared with non-HCC with respect to qualification, demographics, locoregional treatment, surgical procedure and complications (Clavien-Dindo >2). T-student test was performed with GraphPAD Prism, level of significance was set at $p < 0.05$.
Results: All of the post-operative HCC diagnoses would have qualified for OLTx. Among the remaining 11 cases 6 patients did not initially qualify for OLTx but after RFA/TACE sufficient downgrading was observed and patients underwent OLTx. This increased HCC transplantations by 55% ($p < 0.05$). Patients in the HCC group were in better condition based on MELD and Child-Pugh scoring system (11 vs. 16 and 6 vs. 8 respectively, both $p < 0.05$). No significant differences in perioperative course and no HCC recurrencies were detected.

Qualification of HCC patients, observed increase $p < 0.05$

Case	Metro Ticket 2.0	Milano	UCSF	Downnstaging	Prior qualification	Later qualification
1	69.70%	NonQ -> Q	Q	Yes	No	YES
2	86.10%	Q	Q	NA	YES	YES
3	90.80%	Q	Q	NA	YES	YES
4	89.80%	NonQ -> Q	Q	Yes	No	YES
5	67.80%	NonQ -> Q	Q	Yes	No	YES
6	91.60%	Q	Q	NA	YES	YES
7	83.20%	NonQ	NonQ -> Q	Yes	No	YES
8	81.20%	NonQ	Q	NA	YES	YES
9	89.80%	NonQ -> Q	Q	Yes	No	YES
10	84.00%	Q	Q	NA	YES	YES
11	84.00%	NonQ -> Q	NonQ -> Q	Yes	No	YES

Conclusions: Combining three scoring systems and locoregional HCC treatment proved effective and safe method for liver transplantation. This also substantially increased the recipient group.

POS375 MODIFYING THE RETREAT SCORE TO PREDICT RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

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Introduction: A reliable prediction model for hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) could help in developing a surveillance strategy and early detection and treatment of HCC recurrence prolonging the survival after recurrence. Recently, the RETREAT score, based on tumor load, microvascular invasion and alpha-fetoprotein (AFP) was created and externally validated. We aimed to investigate whether the addition of new biomarkers or tumor differentiation grade improves the predictive value of the RETREAT score and studied the relationship between standard immunosuppression and its impact on HCC recurrence.
Methods: Retrospective single center cohort study including all patients transplanted for HCC between 1989 and 2020. Biomarkers such as AFP and protein induced by vitamin K deficiency or antagonist-II (PIVKA-II) were determined. Data on tumor differentiation grade and tacrolimus trough level were retrieved from patients records.
Results: The study cohort consisted of 206 patients, of whom 129 patients were included in the biomarker analyses, 157 in the tumor differentiation grade analyses and 174 in the analysis of tacrolimus trough levels. 80.1% were male, 36% had viral hepatitis as underlying liver disease and 20.4% exceeded Milan Criteria (MC) based on the explant. HCC recurred in 27 patients (13.1%). Median AFP was 7.0 ng/mL (4.6-20.2) and PIVKA-II 72.5 mAU/mL (41.0–211.8). In patients with a lower recurrence risk, i.e. AFP < 8 ng/mL, or within MC, a low PIVKA-II (<90 mAU/mL) was associated with a better recurrence free survival (RFS) ($p = 0.008$ and $p = 0.035$). A poorly differentiated tumor was associated with a worse RFS ($p = 0.002$) compared to well or moderately differentiated tumors. Patients with HCC recurrence tended to have a higher tacrolimus trough level.
Conclusion: PIVKA-II can help in predicting the HCC recurrence risk. PIVKA-II and tumor differentiation grade might be useful to further stratify patients with a high RETREAT score. The level of tacrolimus might influence HCC recurrence and therefore we should aim for the lowest tacrolimus level possible.

POS376 ADVANCED DONOR AGE DOES NOT INCREASE THE RISK OF HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: The impact of donor age on the recurrence of hepatocellular carcinoma (HCC) after liver transplantation is still debated
Methods: Between 2002 and 2014, all patients transplanted for HCC in 2 European liver transplantation tertiary centers, were retrospectively reviewed. Risks factors for HCC recurrence were assessed using competing risk analysis and the impact of donor age $<$ or $\geq$ 65 years and $<$ or $\geq$ 80 years was specifically evaluated after propensity score matching.
Results: 728 patients transplanted with a median follow-up of 86 months were analysed. In competing risk analysis, the 1, 3, and 5-year recurrence rates were 4.9%, 10.7% and 13.9% respectively. In multivariate analysis, recipient age (HR: 0.96 [0.93 ; 0.98], $p = 0.003$), the number of lesions (HR: 1.05 [1.04 ; 1.06], $p < 0.001$), the maximum size of the lesions (HR: 1.37 [1.27 ; 1.48], $p < 0.001$), the presence of a cholangiocarcinoma component (HR: 6.47 [2.91; 14.38], $p < 0.001$) and microvascular invasion (HR: 3.48 [2.42; 5.02], $p < 0.001$) were significantly associated with HCC recurrence. Donor age was not found to be significantly associated with HCC recurrence. After propensity score matching, neither donor age $\geq$ 65 nor donor age $\geq$ 80 years increased the risk of HCC recurrence.
Conclusions: Donor age was not found to be a risk factor for HCC recurrence. Patients listed for HCC can safely receive a graft from an elderly donor.

POS377 COMPLETE RESPONSE AFTER BIOLOGICAL DOWNSTAGING IN HEPATOCELLULAR CARCINOMA: XXL-LIKE PRIORITIZATION FOR TRANSPLANTATION OR "WAITING AND SEE" STRATEGY?

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Background and aims: Although some methodological and ethical issues, the recently published XXL trial represents the first prospective validation of "biological downstaging" in liver transplantation for hepatocellular carcinoma (i.e., selecting tumors with a good biology irrespective of morphological criteria).
The aim of this study is to compare our downstaging protocol with the XXL protocol in terms of downstaging failure rates and patient outcome.
Methods: A total of 191 patients undergoing surgical downstaging and potentially eligible for transplantation from 2012 to 2018 at our Center, were selected according to the XXL trial enrolment criteria.
Differently from the XXL trial we used an aggressive surgical downstaging protocol, and patients with a complete response to downstaging did not receive any prioritization to transplant.
Downstaging failure was defined as progressive disease or post treatment mortality. The statistical method "matching-adjusted indirect comparison" was used to match the study group to the XXL population and to compare the proportion of downstaging failures. The software Engauge digitizer was used to allow a statistical comparison between Kaplan Meier survival curves.

Results: Downstaging failure rate was significantly lower in our cohort than in the XXL trial (12% vs. 39%). Patients with partial response to downstaging had much greater probability of being included in the waiting list than patients with a complete response (OR 20.4, 95% CI 6.9–69.9, $p = 0.0001$). Although patients with complete response were not prioritized to transplant, the survival curves of our cohort overlapped with that of the XXL protocol ($p > 0.05$). Survival curves of non-transplant candidates with a complete response to downstaging were similar to that of transplanted patients ($p > 0.05$).
Conclusions: Our study represents a validation of the current Italian policy of denying any prioritization to patients with complete response to downstaging. Such a policy seems to spare organs without worsening patient outcome.

POS378 DE NOVO MALIGNANCY FOLLOWING LIVING DONOR LIVER TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Background and aims: With the increase in the number of long-term survivors after a living donor liver transplantation (LDLT), there is a need for research on the detection and treatment of de novo malignancies after transplantation. The prognosis of de novo malignancies after transplantation is known to be extremely poor; however, the relationship between transplantation and the development of malignancy has not been clarified. The aim of this study was to elucidate the risk factors for de novo malignancy after LDLT.
Methods: A total of 56 adult (age > 18 years) patients who underwent LDLT at Niigata University Hospital and survived > 3 years were retrospectively analysed. Clinicopathological factors of patients with de novo malignancy ($n = 6$) and those without ($n = 51$) were compared using Pearson's chi-square test or Fisher's exact test. Survival curves were constructed using the Kaplan-Meier method, and the differences in survival were evaluated with the log-rank test.
Results: Of the 56 patients, 6 (10.7%) developed de novo malignancy after transplantation. The de novo malignancy cohort comprised 4 males and 2 females, with a median age of 66 (56–71 years). Types of de novo malignancies were four lung cancers, two malignant lymphomas. Two out of six patients experienced multiple malignancies. The median period from LDLT to the diagnosis of the malignancy was 127 (47–244 months), and the median survival time after diagnosis of malignancy was 2 (2–37 months). Patients with de novo malignancy had a higher rate of preoperative smoking ($p = 0.049$) and poor survival after LDLT ($p = 0.017$) than those without de novo malignancy. There were no differences in the tacrolimus dose, tacrolimus trough level, and steroid use between the two groups in the first year after transplantation.
Conclusions: Preoperative smoking may play a role in the development of de novo malignancies after LDLT. The impact of other factors, including immunosuppressive therapy, on the development of de novo malignancy was not clear. As the prognosis of de novo malignancy after transplantation is extremely poor, a new strategy of cancer screening for patients should be developed.

POS379 ROBOTIC LIVER RESECTION FOR HCC AS A BRIDGE TO TRANSPLANTATION

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Background: Minimally invasive approach to the liver reduces the risks of intraoperative complications and is linked to lower incidence of post-hepatectomy liver failure (PHLF), compared to the traditional open approach. We report our experience with patients affected by hepatocellular carcinoma (HCC) treated at our Institution with robotic liver resection (RLR) before liver transplantation.
Methods: 189 RLR were performed at University of Modena and Reggio Emilia between May 2014 and February 2021. Clinical data of patients underwent RLR for HCC were prospectively collected
Results: 100 patients underwent RLR for HCC in the study period and, 20 underwent LT. Median MELD score at RLR was 8.5 (range 8–14) and 40% of the patients had a clinically significant portal hypertension (CSPH), by the mean of a hepatic venous pressure gradient HVPG) higher than 10 mmHg or presence of esophageal varices. Median in-hospital stay was 4 days (range 2–12 days), without any 30-days readmission, 0% 30-days mortality, no PHLF. Median tumor size was 31 mm (range 12–85 mm), and median resection margin was 10 mm (range 1–20 mm). Median interval between RLR and LT was 9 months (range 1–34 months). All patients are alive and only one developed pulmonary HCC recurrence after LT, and is currently alive under Sorafenib treatment 16 months after LT.
Conclusions: Robotic liver resection is a safe alternative for cirrhotic patients affected by HCC, both for those who need a bridging strategy before LT and as a downstaging tool. Also, patients with CSPH can be safely resected while waiting for LT.

POS380 LONG-TERM OUTCOMES OF DE NOVO MALIGNANCY AFTER LIVER TRANSPLANTATION FOR ALCOHOLIC CIRRHOSIS

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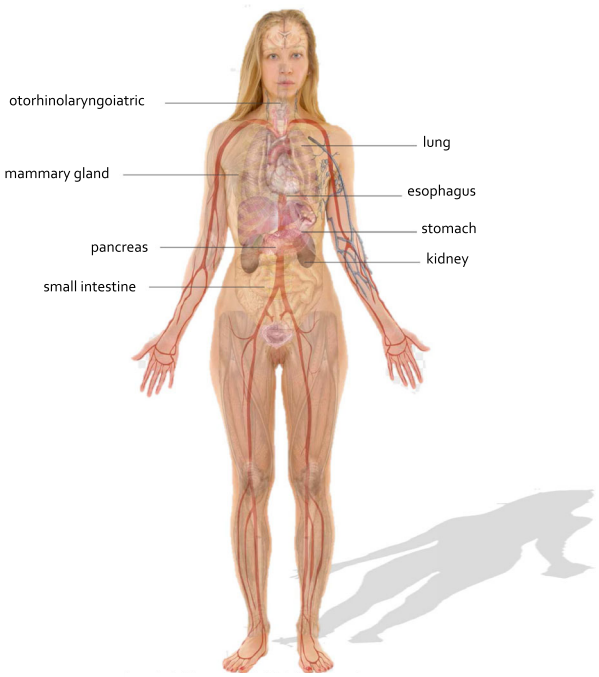
Purpose: De novo malignancy, frequent liver transplant (LT) complication, is one of the long-term major causes of mortality. Risk factors are related to immunosuppressive status, oncogenic virus activation, alcohol abuse. We want to investigate oncogenic action of alcohol after liver transplant in patients without post-transplant alcohol abuse.
Methods: All liver recipients transplanted in our Centre from 1988 to 2018 were included. The latency period of neoplastic pathology onset, the type of tumor, the survival period and the treatment protocol carried out were analyzed.
Results: We enrolled 593 patients undergone liver transplant. We found a de novo malignancy in 45 (8.7%) patients: 5 of hematological origin; 40 with a solid organ onset. In the former population, 35 (87.5%) were male and 5 (12.5%) were female; mean age was 53 ± 9 years. Mean time between transplant and neoplastic diagnosis was 84 ± 63 months. Cirrhosis etiology was alcoholic in 26 (65%) patients (group 1) and non-alcoholic in 14 (35%) patients (group 2). Population of two groups were homogeneous for pre- and post-transplant characteristics (age, sex, BMI, "Model for End Stage Disease" score, graft characteristic, immunosuppressive therapy). Latency time in neoplastic onset was early in group 1. Malignancies typologies encountered were: otolaryngologic; pulmonary; esophageal; gastric; renal; pancreatic; intestinal; mammary (Figure 1). There was a high prevalence of the neoplasm of the upper aerodigestive tract in group 1 (17vs5; $p < 0.05$):



Origin of de novo malignancies

Treatment: surgical (60%); medical (40%). The mean mortality from the diagnosis was, respectively, at 19 months in group 1 and 60 months in group 2 ($p < 0.05$).
Conclusions: Patients undergone LT for alcoholic cirrhosis have a higher risk of de novo malignancies, mainly in the upper aerodigestive tract. Early diagnosis and treatment result in improved prognosis and survival. Adequate management of immunosuppressive therapy and regular transplant and cancer screening are mandatory.

POS381 IMMUNE CHECKPOINT AND IMMUNE CELL EXPRESSION IN THE TUMOR MICROENVIROMENT OF RESECTED HCC

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Background: Understanding the interaction of tumor cells (TC) with host immune cells (IC) in the tumor microenvironment (TME) is essential to develop future immunotherapies.
Aim: Analyze the expression of immune checkpoints (ICP) and immune cells (IC) in the TME of resected hepatocellular carcinoma (HCC) specimens
Methods: The expression of ICP (PD-1, PD-L1), and IC (CD4+, CD8+, NK-CD56, FoxP3-Treg) was assessed by immunohistochemistry in 129 surgically resected HCC specimens, 90 peritumoral, and 20 controls. The biomarkers expression was graded as G0:<5%, G1: 5–25%, G2: 26–50%, G3:>50%. The expression was compared using linear mixed-effects models and Spearman's correlations were calculated.
Results: The mean expression grades of the biomarkers in control, peritumoral, and tumoral samples showed significantly different expression of CD4+, FoxP3-Treg, CD56-NK, and IC-PD-L1. There was not significant difference of PD-1 or CD8+. The pairwise comparisons between control and peritumoral samples did not show significant differences in any markers. However, the comparisons between control and tumoral revealed higher mean expression of FoxP3-Treg in tumoral tissues compared to controls. The comparisons between tumoral and peritumoral showed significantly higher expression of CD4+, FoxP3-Treg, and IC-PD-L1 in tumoral compared with peritumoral samples. In contrast, NK-CD56 expression was higher in peritumoral than in tumoral samples. The correlation between biomarkers showed that each biomarker was significantly correlated pairwise with all other biomarkers, except CD56-NK with PD-L1. The strongest correlation was between CD8+ and CD4+, FoxP3-Treg and IC-PD-L1, and IC-PD-1 with IC-PD-L1 and FoxP3-Treg.
Conclusions: CD4+, FoxP3-Treg, and IC-PD-L1 showed significantly higher expression in tumoral HCC than in peritumoral samples. In contrast, NK-CD56 expression was higher in the peritumoral tissues. The strongest correlation between biomarkers was CD8+ and CD4, and FoxP3-Treg and IC-PD-L1.

ICP and IC Mean Expression

	Tumoral	Peritumoral	Control	Overall	Control v. Peritumoral	Control v. Tumoral	Peritumoral v. Tumoral
	N129	N=90	N=20				
Immune Markers	Mean Grade (SE)	Mean Grade (SE)	Mean Grade (SE)	*p*-value	Pairwise comparisons (*p*)		
CD8+	1.64 (0.06)	1.58 (0.07)	1.95 (0.15)	0.105	-	-	-
CD4+	1.62 (0.06)	1.29 (0.07)	1.45 (0.15)	<0.001	0.621	0.55	<0.001
FoxP3-Treg	0.82 (0.05)	0.40 (0.07)	0.35 (0.15)	<0.001	0.948	0.008	<0.001
CD56-NK	0.91 (0.05)	1.12 (0.06)	0.85 (0.13)	0.014	0.145	0.909	0.018
IC-PD-1	0.80 (0.07)	0.95 (0.08)	0.85 (0.17)	0.299	-	-	-
IC-PD-L1	0.61 (0.06)	0.38 (0.07)	0.35 (0.15)	0.021	0.983	0.249	0.028
TC-PD-L1	0.13 (0.06)	0.00 (0.00)	0.00 (0.00)	-	-	-	-

ICP and IC Correlations

	CD4+		FoxP3-Treg		CD56-NK		IC-PD-1		TC-PD-L1		IC-PD-L1	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
CD8+	0.65	<0.0001	0.43	<0.0001	0.24	0.0063	0.39	<0.0001	0.23	0.01	0.44	<0.0001
CD4+			0.46	<0.0001	0.25	0.004	0.36	<0.0001	0.2	0.0204	0.46	<0.0001
FoxP3-Treg					0.2	0.0209	0.55	<0.0001	0.37	<0.0001	0.62	<0.0001
CD56-NK							0.24	0.0059	0.11	0.2145	0.15	0.0806
IC-PD-1									0.24	0.0068	0.57	<0.0001
TC-PD-L1											0.39	<0.0001

POS382 LIVER TRANSPLANTATION AFTER SUPERDOWNSTAGING USING RADIOEMBOLIZATION IN PATIENTS WITH HEPATOCELLULAR CARCINOMA AND PORTAL VEIN TUMORAL THROMBOSIS

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Background and aims: Portal vein tumoral thrombosis (PVTT) is generally recognized as a contraindication to liver transplantation (LT) for hepatocellular carcinoma (HCC). However, encouraging results in terms of long-term survival have been reported in selected patients submitted to trans-arterial radioembolization (TARE). In this prospective study, according to the intention-to-treat (ITT) principle, we evaluated the effect of TARE in downstaging HCC patients with PVTT to meet criteria for LT.
Methods: Between May 2013 and November 2016, patients aged 18–65 years with diagnosis of HCC and PVTT were evaluated to be enrolled into our "Superdownstaging" protocol. Patients received TARE with yttrium-90 resin microspheres and LT was performed in case of complete and sustained radiological response of PVTT. PVTT was classified according to the classification of the Liver Cancer Study Group of Japan: patients with tumor thrombus in the main trunk and/or in the contralateral portal vein branch (Vp4) were excluded from the present study. Analyses were by ITT.
Results: Seventeen patients were enrolled. Median age at the time of TARE was 53 years (range 50–56). The PVTT was classified as follows: Vp1 ($n = 3$), Vp2 ($n = 5$) and Vp3 ($n = 9$). Six out of 17 patients (35.3%) were successfully downstaged but only 5 (29.4%) underwent LT. Five-year overall survival was significantly higher in patients who underwent LT compared to those who did not (60% vs. 0%, $p = 0.028$). Three out of 5 patients developed recurrence within 1 year after LT.
Conclusions: TARE was effective in downstaging roughly 30% of patients with PVTT. Median survival in LT group was significantly higher compared to those who were not transplanted. However, recurrence of disease after LT was high. Careful selection before LT must be advised.

POS384 LIVER TRANSPLANTATION FOR METASTATIC NEUROENDOCRINE TUMORS: TIME TO EXTEND CRITERIA?

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Background: Liver transplant (LT) might be considered in patients with liver-only neuroendocrine metastases (NELM), representing a potential chance of cure when strict selection criteria are applied, despite the high rate of tumor recurrence. However, due to the lack of randomized trials, controversy continues surrounding patient selection and timing for LT, also considered that such stringent criteria might deny LT to many patients who might benefit from it. The aim of the present study was to analyze prognostic factors for OS in a cohort of LT patients and to assess whether there might be a chance to consider an extension in selection criteria.
Methods: Data for all consecutive patients who underwent LT for NELM at our center between 1991 and 2019 were collected and retrospectively analyzed. A univariate Cox regression analysis was performed to identify prognostic factors for OS.
Results: 53 patients were included in the study. All patients were Milan-IN at pre-LT staging, but 23 (43%) were found to be Milan-OUT at histology after LT (9 H3, 4 G3, 13 N+ at liver hilum). Milan-IN status was associated with better OS, HR 0.27 (CI 0.07–0.96, p 0.044), but the only significant prognostic factor for worsened OS was the presence of a positive lymph node at the liver hilum at LT, HR 8.2 (CI 1.77–37.5, p 0.007). H3 liver involvement, G3 and age > 50 at LT were not associated with worsened OS. Recurrence, analysed as a time-dependent covariate, was not associated with OS (HR 1, CI 0.99–1.01, $p = 0.901$), regardless of site.

Conclusion: Our results show an outstanding long-term OS after LT and tumor recurrence, although common, does not seem to impact survival. Locoregional nodal status seems to have more prognostic relevance than H3 liver involvement, elder age and advanced grade, thus suggesting that an extension in the criteria for LT in NELM might be considered, although further studies are needed to confirm these preliminary observations.

POS385 DOWN-STAGING TREATMENT IMPROVEMENTS CHANGED THE PARADIGM OF LIVER TRANSPLANTATION FOR HCC

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Background: Hepatocellular carcinoma (HCC) is rising as the most common indication for liver transplantation (LT) in Italy. HCCs outside the Milan Criteria (MC) undergo downstaging treatments (DS) and subsequent LT with an increased risk of HCC recurrence (rHCC).
Methods: HCC patients included in the waiting list (WL) between 2012 and 2018 were retrospectively analyzed. Patients were divided in two groups, DS and non-DS. Rates of LT, drop-out (DO) and rHCC were estimated by a competing risk analysis. A logistic regression was performed to identify risk factors associated with rHCC.
Results: On a sample of 329 HCCs, 244 (74%) LT and 85 (26%) DO occurred. Among the 124 (33%) patients enlisted after successful DS, 90 (73%) underwent LT, while 34 (27%) dropped out of the WL. Upon competing risk analysis, patients who underwent DS did not have an increased probability either of DO or LT. Pre-LT MELD was higher in patients that did not undergo DS (10 vs. 12, $p < 0.001$), while waiting time before transplant (WT) did not differ (13.5 vs. 11.8 months, p = n.s.). We observed 24 recurrences (9.6%) in the whole group of patients who underwent LT, 12 rHCC were observed in the non-DS group (12 of 154, 7.8%) and 12 (12 of 90, 13.3%) in the DS group ($p = 0.161$). Tumor features such as number of lesions, diameter and presence of microvascular invasion (mVI) did not differ between DS and non-DS groups. Disease-free survival after LT between groups did not differ significantly. Upon univariable logistic regression, DS, differentiation grade of HCC, and WT were not significantly correlated with rHCC. In contrast, number of lesions, diameter and mVI were associated with rHCC ($p < 0.001$).
Conclusions: Recent improvements in the downstaging strategies allow comparable results among DS and non-DS HCC; tumor biology remains the only relevant variable related to recurrence and outcome.

POS386 LIVER TRANSPLANTATION FOR HCC IN HIV PATIENTS: SINGLE CENTER EXPERIENCE

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Background: Hepatocellular carcinoma (HCC) is the leading cause of death among patients with liver cirrhosis and is the fifth most frequent malignant tumor worldwide. Liver transplantation (LT) is considered the best curative treatment for early HCC, but its role in HIV infected patients is still debated since several studies report a more aggressive tumor behavior in these patients.
Patients and Methods: This is a single Center prospective study on LT for HIV-infected patients presenting with HCC on cirrhosis. Inclusion criteria were: unresectable HCC within Milan Criteria (MC), CD4+ count > 200/mm3, HIV-RNA undetectable, absence of AIDS. The present study compares the long-term outcomes of HIV-infected patients to that of non infected patients who underwent LT for HCC during the same period.
Results: Between January 2009 and December 2020 27 HIV and 245 non-HIV patients underwent LT for HCC within MC. HIV patients were younger (median age 52 Vs 59 respectively p.005), more frequently HCV positive (92.6% Vs 52.4% respectively p .0001), and more frequently had an HBV-HCV coinfection (14.8% Vs 3.3% respectively p .005). Liver function, median AFP and radiological presentation of HCC were similar between the two cohorts both at listing and at the last staging before LT. At histology, HCC was beyond MC in 30.8% vs. 28.2% of HIV vs. non-HIV patients ($p = .75$). After a median follow-up of 62 months (0.5–143), 5-year overall survival (OS) was similar in HIV vs. non-HIV patients (80.7% vs. 82.0% respectively, $p = 0.282$), while 5-year recurrence-free survival (RFS) was significantly lower in HIV patients vs. non-HIV (78.2% vs. 89.3%, $p = 0.018$). 5-year RFS was similar between the two cohorts with HCC within MC at pathology, while it was 62.5% vs. 81.2% in HIV vs. non-HIV patients beyond MC ($p = .009$).
Conclusion: Long-term survival after LT for HCC within MC is similar in HIV and non-HIV patients, but HIV infected patients present a higher risk of HCC recurrence, particularly for tumors beyond MC. These data suggest that LT for HCC in HIV patients should preferably be performed within conventional MC.

POS387 A RETROSPECTIVE SINGLE-CENTER ANALYSIS OF THE ONCOLOGICAL IMPACT OF LI-RADS CLASSIFICATION APPLIED TO METROTICKET 2.0 CALCULATOR: EVERY NODULE MATTERS

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Background: Hepatocellular carcinoma (HCC) represents a leading indication for liver transplantation (LT) in western countries. Several models have been developed in order to predict post-transplant outcomes, all of which include number and size of HCC nodules as major determinants for recurrence-free and overall survival.
The diagnostic value of Li-RADS classification is well recognized in clinical practice, though there is currently little evidence concerning its role in LT setting.
Study aim was to evaluate the prognostic impact of Li-RADS classification applied to Metroticket 2.0 calculator in a single-center cohort of transplanted HCCs.
Methods: Preoperative imaging of patients undergoing LT for HCC between 2005 and 2015 was reviewed, classifying all nodules according to Li-RADS protocol; Metroticket 2.0 accuracy was tested considering different Li-RADS subclasses.
Patients with old or unavailable imaging, missing a-FP, or lacking HCC diagnosis on pathology were excluded.
Results: We identified 245 patients presenting 567 nodules.
Median follow-up lasted 56 months, with 9% cumulative 5-year incidence of HCC-related death.
Incorporation of all vital HCCs identified during multidisciplinary meetings attended before Li-RADS classification resulted in a Metroticket 2.0 c-index of 0.72.
Metroticket 2.0 c-index dropped to 0.60 when Li-RADS-5 and Li-RADS-TR-V ($p = 0.0089$) or Li-RADS-5, Li-RADS-4 and Li-RADS-TR-V ($p = 0.0068$) nodules were entered in the calculator.
Conversely, addition of Li-RADS-3 HCCs raised the Metroticket 2.0 c-index to 0.62, resulting in a not statistically significant diversion from the original performance (0.72 vs. 0.62; $p = 0.08$).
Conclusions: The role of Li-RADS classification in preoperative risk stratification of HCC transplant candidates is still unexplored.
Considering their low probability for harbouring a HCC, Li-RADS-1/3 or Li-RADS-4 nodules are currently managed as non-neoplastic or pre-neoplastic lesions; despite that, exclusion of these nodules from the Metroticket 2.0 calculator resulted in a significant drop in its accuracy.
Every nodule, regardless of its Li-RADS class, seems to contribute to tumor burden and influence oncological results of LT for HCC, and should be entered in the Metroticket 2.0 calculator in order to grant appropriate performance.

POS388 A SHORTER WAITING TIME BEFORE LIVER TRANPLANTATION AFTER TACE FOR HCC IS RELATED TO AN INCREASED RISK OF ARTERIAL POST TRANSPLANT COMPLICATIONS

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Background: It has been shown that transarterial chemoembolization (TACE) before liver transplantation (LT) increases the risk of arterial complications [Transpl Int 2018]. At the same time, locoregional therapy before LT in patients with HCC, even those meeting the Milan criteria, improves long-term survival outcomes [Liver Transpl 2019]. The aim of this study was to evaluate the impact of TACE and waiting time before LT procedure on the incidence of post liver transplant complications.
Methods: A retrospective analysis was performed for 105 consecutive patients undergoing LT for HCC from 2008 to 2019; 53 (51%) of which were treated with TACE before LT. Median waiting time before LT after TACE was 77 days [35; 105].
Results: Arterial complications developed in 8 out of 53 (15%) patients after LT and were represented by: stenosis (4 cases), thrombosis (3 cases) and hepatic artery occlusion (1 case). Arterial complications group was characterized by shorter waiting time 29 [13; 50] vs 89 [47; 129], days ($p = 0.02$); more frequent ITBL development (50% vs 6.7%; $p = 0.007$); higher 90-d mortality rate (25% vs 2.2%; $p = 0.05$). 8 of the 53 patients (15%) developed recurrent HCC after LT. When analyzing the entire cohort of patients who underwent LT in the center ($n = 690$; 2008–2019), it was found that TACE is associated with a higher risk of arterial thrombosis (5.7% versus 1.6%; $p = 0.03$) and ITBL (13.2% versus 3, 9%; $p = 0.002$). The overall one-year and five-year survival rates for HCC patients who underwent TACE before LT were 92% and 80% and were higher than in patients without TACE - 84% and 57%, respectively.
Conclusions: TACE is a risk factor for the development of arterial and, as a consequence, biliary complications after liver transplantation, and a shorter waiting time before LT for HCC is associated with an increased risk of these complications. Nevertheless, this fact did not have a negative impact on overall survival in this group of patients.

POS389 NEW STRATEGIES FOR THE MANAGEMENT OF PATIENTS WITH HEPATOCELLULAR CARCINOMA AFTER COVID-19 PANDEMIC: A PROPOSAL FOR A NEW READY TO USE APP

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Background: After COVID-19 pandemic, telemedicine is a new strategy to reduce patient's mobility. The wide availability of technology, in particular the use of smartphone, can help to facilitate the treatment strategy of patients, away from hub centers. Hepatocellular carcinoma (HCC) has a complex treatment strategy with multiple options. The number of score and treatment algorithm available in the literature is large, but often difficult to analyze during the single outpatient visit.
Aim of the study: Elaborate an App that can facilitate the management of patients with HCC utilizing verified and approved scores and treatment algorithm.
Methods: After the revision of literature on HCC, BCLC and ITA.LI.CA staging systems have been chosen as main output, for the prognostic accuracy, and their treatment algorithms. Useful ancillary scores in the setting of liver transplantation (LT) are BMI, MELD, MELD-Sodium, Milan, UCSF, TTV-AFP, Metroticket 2.0.
For the computation of these scores, 26 variables have been identified, in 3 main categories: clinical assessment (age, gender, height, weight, HCV infection, ascites, encephalopathy, varices status at last EGDS, ECOG PST); laboratory (platelets count, INR, total bilirubin, sodium, creatinine, albumin, AFP); radiology (splenomegaly, ascites, viable HCC, number of nodules, diameter of each nodule, diameter of major nodule, largest cut section of the liver, major vascular invasion intrahepatic, major vascular invasion extrahepatic, extrahepatic disease).
Results: The application will be able to compute automatically the scores from the given variable. The appropriate treatment algorithm according to BCLC and ITA.LI.CA stages will be showed.
Conclusions: The proposed App can help to improve the delivery of HCC care and to reach the goal of leveling the standard of care in patients away from hub centers.

POS390 THE IMPACT OF IMAGING AND PRE-TRANSPLANT TREATMENTS ON LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Background: Liver transplant (LT) results in hepatocellular carcinoma (HCC) patients are affected by pre-LT tumor stage. Neoadjuvant treatments can be applied pre-LT to control HCC staging and HCC response could be achieve through different imaging techniques. The aim of our study is to evaluate the relation between HCC staging through imaging, treatments and post-LT results.
Methods: We retrospectively analyzed the LT performed from 01/2012 to 06/2018 with 18 months follow-up. In our Center, patients Milan-out received downstaging and bridging treatments to achieve Milan-in pre-LT. Imaging findings were compared with the ones derived from pathological report. The patients were grouped according to the concordance (Co) or not (nCo) between imaging and histology.
Results: A total of 134 patients were included: 32 (24%) Co and 102 (76%) nCo. The total number of nodules (Co 2 (1-4) vs nCo 2 (1-29), $p = 0.004$), the number of vital HCC (Co 2 (1-3) vs nCo 2 (1-22), $p = 0.019$) and the total diameter (Co 35 (8-61) vs nCo 59 (8-271) cm, $p = 0.001$) were higher in nCo. The nCo patients received more frequently ≥3 downstaging treatments (Co 33% vs nCo 65%, $p = 0.014$). Concordance did not impact disease and overall survival ($p = 0.945$ and $p = 0.454$, respectively), while a higher number of pre-LT treatment led to a reduced disease free survival ($p = 0.019$). The patients with HCC microvascular invasion had higher levels of alfa-feto protein ($p = 0.005$), but it had no impact on survival. Milan-in patients had a worst disease-free survival compared to Milan-out ($p = 0.023$). However, if Milan-in patients with less than 3 pre-LT treatments were separately evaluated, they showed a better disease-free survival compared to the multi-treated Milan-in patients ($p = 0.015$).
Conclusion: In conclusion, imaging techniques showed poor prediction of HCC staging at LT. Multiple pre-LT treatments could affect post-LT results more than HCC staging. HCC history should be dynamically evaluated before LT to obtain reliable predictors of post-LT results.

POS391 DOES NASH JEOPARDIZE LIVER TRANSPLANT SURVIVAL IN HCC PATIENTS? THE NIGUARDA EXPERIENCE

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Background: The availability of effective therapy for HCV infection is transforming the population demanding for Liver Transplant (LT). In this scenario non-alcoholic steatohepatitis (NASH), a disease associated with many comorbidities, seems to be rapidly gaining room as indication for LT. Considering the burden of these comorbidities, transplanting patients affected by Hepatocellular Carcinoma (HCC) and NASH may jeopardize the transplant survival results. We retrospectively reviewed a monocentric series of 2171 liver transplant aiming to: to evaluate if NASH is gaining room as transplant indication; to evaluate if patients transplanted for HCC and NASH have worst survival results than patient transplanted for HCC without NASH.
Methods: The analysis was conducted on patients transplanted for HCC, NASH or both from 2000 to 2020. To address the first aim the percentage of LTs performed for NASH (with or without HCC) year by year. The second aim was addressed by survival comparison (Kaplan-meier) after case (HCC+NASH+ patients) control (HCC+NASH- patients) matching. Matching was performed on: MELD (+/-4) , number of HCC nodules (+/- 1), maximum size of nodules (+/- 5 mm), AFP (identical range 0–10; 10–50; 50–100; 100–200; 200–500; >500).
Results: From 2000 to 2020 739 patients underwent LT for HCC (688), NASH (22) or both (29). The first NASH LT was performed in 2012. The percentage changed from 2012 to 2020 as follow: 1.13; 1.21; 1.16; 2.43; 4.62; 8.13; 12.82; 9.6; 3.41. Matching 1:1 was possible in 26 cases. Before matching survival was similar in HCC+NASH+ and HCC+NASH- patients (79% and 83% respectively at 3 years, $p > 0.05$). After matching survival remains similar (cases 82% control 74% at 3 years, $p > 0.05$).
Conclusions: The presented results show that NASH is gaining room as indication in LT. Although NASH is generally accompanied by many comorbidities it doesn't seem to jeopardize HCC LT survival outcomes.

POS392 TRANSPLANT BENEFIT AND URGENCY IN LUNG TRANSPLANTATION

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Background: The lung transplant program in Italy suffers greatly from the scarcity of donations and draws a limited benefit from the extension of the donor evaluation criteria such as increasing age and the presence of relative contraindications to donation. Because of the high mortality on the waiting list (WL), it is necessary to optimize the use of available lungs
Methods: In the period 2016–2019 we calculated the satisfaction rate and mortality of patients on the WL, classified on the basis of clinical severity for patients on standard list, in urgency and for urgent listing exceptions. We also compared the available follow-up data of transplanted patients
Results: The patients on the WL were 1228, of which 117 (9.5%) in a priority condition (94, equal to 80.3% for urgencies and 23, equal to 19.7%, for urgent listing exceptions). Total transplanted patients were 588 (47.9%), out of which 60 (63.8%) were urgent patients and 15 (65.2%) were exceptions. Total deaths on the WL totted up to 179 (14.6%), 29 (30.8%) for patients in urgency, 6 (26%) for urgent listing exceptions. The 1-year survival of the elective transplant patients was 77.3%, 44% in urgency, 72.7% for urgent listing exceptions
Conclusions: The already high mortality on the WL increases in case of patients in urgency or waitlisted in urgency as exceptions and their survival is lower. Therefore, proper adjustments to the allocation algorithm are advisable, that would limit the progressive deterioration of the clinical conditions of patients awaiting a lung transplant. The so far adopted centre-based model has been used in the allocation of surplus lungs (organs not allocated in the donor's hospital region because of a lack of transplant centres or recipients), based on the geographical criteria in selecting the Transplant Centre. The LAS, on the other hand, is used locally or in macro-regions. Considering the improvement of organ preservation techniques, also using perfusion machines, we are developing an allocation scheme for surplus lungs based on a national algorithm that takes into account patient's clinical status in terms of severity determined through LAS, in order to curb pathological evolution, to optimize transplant timing and prevent the inclusion in urgency, being aware of the high ethical value that the adoption of such model would entail

POS393 EXTRA-CORPOREAL MEMBRANE OXYGENATION (ECMO) SYSTEM EXCHANGES IN SARS-COV-2 PATIENTS AWAITING LUNG TRANSPLANT: LARGEST CASE SERIES FROM INDIA.

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Background: Severe lung fibrosis from SARS COV2 results in respiratory failure despite mechanical ventilation and may require ECMO support. Coronavirus disease (COVID-19) is recognised as a procoagulant state with many centres recommending maintaining higher level of anti-coagulation on ECMO in these patients. We assessed the frequency, reasons for circuit changes and its associated complications in these patients whilst awaiting lung transplant.
Methods: Single centre retrospective study of post COVID-19 patients requiring ECMO between September 2020 to February 2021. Anticoagulation was maintained with heparin with target activated Partial Thromboplastin Time more than 50 seconds. After confirmation of irreversibility and failure to wean they were evaluated and listed for lung transplant. The need for ECMO system changes were decided based on post oxygenator gases, circuit inspections and lab parameters. We looked at incidence, reason for circuit changes and the need for renal support and mortality.
Results: Veno-venous (VV) ECMO was initiated on 13 severe post COVID-19 fibrosis patients with respiratory failure. 7 (54%) patients required ECMO system exchanges with a mean of 13.5 days from the date of initiation. Commonest reason for it being clotting ($n = 3$) and poor gas exchange ($n = 2$). Bleeding, change of ECMO configuration and haemolysis were the other causes necessitating system exchanges. The total mean duration of ECMO support was 33.15days. Renal Replacement Therapy usage was significantly higher (43%) in patients who had system exchanges. Among the patients who successfully underwent lung transplant, 7 (78%) were alive at the end of our study period.
Conclusions: COVID-19 patients on VV ECMO awaiting lung transplant have high incidence of thrombotic events entailing due diligence in management of these patients.

POS394 LUNG TRANSPLANTATION WITH GRAFTS FROM DONATION AFTER CIRCULATORY DEATH DONORS AND PROLONGED ISCHEMIA TIMES: SINGLE CENTRE EXPERIENCE

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Background: Donor's shortage is one of the main factors limiting lung transplantation (LT), and lung procurement from donation after circulatory death (DCD) donors could represent a valuable resource. We present our centre's experience with grafts procured from DCD donors, and compare the outcomes with those of recipients receiving lungs from donation after brain death (DBD) donors. Our previously described non-rapid normothermic open-lung technique, consisting of recruitment manoeuvres, protective ventilation, and CPAP without topical cooling, was employed for procurement.
Methods: We evaluated patients undergoing bilateral LT at our centre from November 2014 to July 2019; exclusion criteria were as follows: recipients ≤14 years, re-LT, donors ≥65 years, DCD category I and IV. We prospectively recorded variables of interest; respiratory functional parameters throughout the first year after LT were also registered. We compared the outcomes of patients in the DCD Group and DBD Group.
Results: During the study period, we performed 143 LT; 22 cases were excluded, the other 121 were enrolled: 11 recipients with lungs from DCD donors (5 DCD Maastricht category II, 6 category III). Clinical features were homogeneous in the two groups. Cystic fibrosis was the most common indication (72.7% and 61.9% in the DCD and DBD Group respectively). DCD donors had a higher BMI ($p = 0.022$). Machine perfusion was employed in 15.5% of DBD grafts for evaluation. Cold ischemia and preservation time were significantly longer in the DCD Group ($p < 0.001$). Patients in the DCD Group required more days of post-LT mechanical ventilation (DCD Group=2 days; DBD Group=1 day, $p = 0.011$); grade 3 primary graft dysfunction occurred in 27.3% cases in the DCD Group and 18.2% in the DBD Group (0= 0.742). Airway complications were more frequent in the DCD Group (18.2% vs 6.4% in the DBD Group). No patients in the DCD Group experienced chronic rejection or died during the study period. With regard to pulmonary function, mean FEV1 was significantly higher in the DBD Group 6 months (83.5% vs 78.5%), but not 1 year (86.0% vs 81.7%) after LT.
Conclusions: Despite the small population, the results of our experience are encouraging, showing the feasibility of LT with grafts from DCD donors despite prolonged ischemia times, with adequate grafts function and survival.

POS395 TOLERANCE OF ANTI-CMV PROPHYLAXIS WITH VALGANCICLOVIR ONE-YEAR TREATMENT IN D+/R- LUNG TRANSPLANT PATIENTS. A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Management of neutropenia, the main side effect of Valganciclovir, may affect final transplant results. The main objective of this study is to evaluate the safety of Valganciclovir in D+/R- patients. The secondary objectives are to assess the impact of neutropenia and Mycophenolate Mofetil (MMF) daily dosage modification on the outcomes of the transplant.

Methods: We performed a single-center retrospective study from 01/01/2010 to 12/31/2018 including 531 consecutive lung transplant patients.
Results: 59 of the 108 D+/R- patients (55%) experienced at least one episode of neutropenia during the first posttransplant year leading to its premature withdrawal for 31 patients (29%). Among D+/R- patients, subgroup of premature vGCV withdrawal experienced significantly more neutropenia and reduction of MMF in comparison with complete vGCV treatment subgroup (87% vs 42%, p <0.0001; 90% vs 44%, $p = 0.001$). Premature vGCV withdrawal subgroup patients are also more likely to develop late onset CMV event (74% vs 43%, $p = 0.05$). In comparison with non D+/R- patients, D+/R- are significantly more concerned by neutropenia as well as MMF dosage reduction (55% vs 27% and 48% vs 20%, p <0.0001). In multivariate analysis, concerning the transplant population, neither the neutropenia event nor the reduction of MMF or the occurrence of CMV event are associated with increased alloimmunization, chronic lung allograft dysfunction (CLAD) or graft loss. However, in the D+/R- subgroup, neutropenia is a protective factor for CLAD in multivariate analysis (HR 0.12 [0.03–0.49], p <0.001) while longer length of Valganciclovir exposure or reduction of MMF dosage events are identified as independent risk factors (HR 1.31 [1.01–1.70], $p = 0.04$; HR 7.82 [2.02–30.27], p <0.001).
Conclusions: Considering adverse effects associated with Valganciclovir one-year treatment may have a negative impact on the outcomes of the transplant, an alternative should be proposed.

POS396 A RANDOMIZED, MULTICENTER, BLINDED STUDY ASSESSING THE EFFECTS OF GASEOUS NITRIC OXIDE IN AN EX VIVO SYSTEM OF HUMAN LUNGS

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Background: We assessed whether the use of gaseous nitric oxide (gNO) in discarded human lungs improved lung health during ex-vivo lung perfusion (EVLP).
Methods: This randomized, blinded, parallel, 2-arm, study compared gNO delivered via the membrane oxygenator on the XVIVO Perfusion System (XPS) (gNO + perfusate [P]) versus P alone. An additional group of lungs were administered inhaled NO (iNO) via the ventilator circuit (V) in open-label fashion (iNO V + P). Lungs were procured from brain-dead donors that were not suitable for transplantation. Primary endpoints included a novel grading system for assessing the health of EVLP lungs and total time on EVLP. Secondary/exploratory endpoints included clinical assessment of lung suitability for transplantation, left atrium partial pressure of oxygen, change in lung weight, and relevant biomarkers.
Results: A total of 20 bilateral donor lungs (blinded study, $n = 16$; open-label study, $n = 4$) from 3 study centers were enrolled. Overall, lung mean and median grading system scores were generally the same or higher (indicating a better lung health) in the gNO + P group (median score range [min, max], 0–3.5 [0, 7]) versus the P alone group (median score range [min, max], 0–2.0 [0, 5]; $p > 0.12$ for all between-group comparisons). In the open-label study, median scores were generally lower in the lungs in the iNO V + P group compared with the gNO + P group. Median (min, max) EVLP time was longer for lungs in the gNO + P group compared with the P alone group (12.4 [8.6, 12.6] vs 10.6 [6.0, 12.4] hours, respectively; $p = 0.01$). In the open-label study, median (min, max) EVLP perfusion time was 12.4 (8.7, 13.0) hours in the iNO V + P group versus 12.4 (8.6, 12.6) hours in the gNO + P group ($p = 0.81$).
Conclusions: Among lungs deemed unacceptable for transplantation, the addition of gNO to the perfusate was associated with longer stability during EVLP on the XPS system. Our results support further investigation of gNO use during EVLP.

POS397 LUNG BIOMOLECULAR PROFILE AND FUNCTION COMPARING GRAFT FROM MARGINAL BRAIN-DEAD DONORS AND DONORS AFTER CARDIAC DEATH

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Background: Donation after cardio-circulatory death (DCD) might address the limited availability of grafts for lung transplantation (LuTx). We explored graft function, metabolism, inflammasome, endothelial function, and glycocalyx shedding during Ex-Vivo Lung Perfusion (EVLP) in lungs grafts from DCD compared to marginal brain-dead donors (DBD) and correlate it to post-LuTx outcomes.
Methods: From January 2018 to February 2020 all grafts treated with EVLP and subsequently transplanted were studied. Donors' data, harvesting procedure timings, recipient outcomes and graft function up to 1 year post LuTx were collected. Perfusate samples were obtained hourly during the EVLP to quantify graft function, metabolism, inflammatory molecules, glycocalyx breakdown products, coagulation and endothelial activation markers.
Results: 8 DBD and 7 DCD grafts were enrolled. DCD's warm ischemia time in-situ was 201 [185; 247] min. Duration of mechanical ventilation was longer in the DBD group. Recipient's populations did not differ for neither preoperative status nor intraoperative management. No difference was found in lung function during EVLP. Recipients' outcomes are shown in Table. During EVLP at reperfusion a wash-out phenomenon of both inflammatory cells and microthrombi is observed more in the DCD grafts. In all grafts the perfusate molecular profile showed marked endothelial activation, resulting in the release of inflammatory mediators and glycocalyx breakdown products.
Conclusions: Lungs from marginal DBD and DCD are qualitatively comparable. Even in cases of prolonged warm ischemia, DCD lungs, if properly preserved and evaluated, represent a viable resource for donation.

	DBD ($n = 8$)	DCD ($n = 7$)	p-value
ICU Admission			
PaO_2/FiO_2, mmHg*	242 [168; 333]	228 [183; 260]	0.638
PEEP, cmH_2O	10 [10; 13]	11 [10; 12]	0.694
Compliance, ml/cmH_2O	42 [37; 43]	37 [30; 57]	0.955
ICU Discharge			
28-days ventilator free, days	27 [22; 28]	26 [25; 28]	0.779
ICU LOS, days	3 [1; 8.5]	3 [2; 10]	0.613
ICU survival, n (%)	8 (100)	6 (86)	0.467
Hospital Discharge			
Hospital LOS	27 [22; 35]	20 [17; 25]	0.035
Resting SpO_2, %	98 [97; 98]	97 [96; 98]	0.229
FEV_1 , %	60 [51; 74]	57 [37; 65]	0.295
6MWT, m	370 [309; 482]	400 [335; 459]	0.846
12-months post LuTx			
Survival, n (%)	6 (75)	6 (86)	1
Resting SpO_2, %	99 [99; 100]	99 [99, 100]	0.563
FEV_1, %	88 [79; 94]	79 [64; 94]	0.682

POS398 FEMALE RATS PRESENT HIGHER LUNG INFLAMMATION AFTER BRAIN DEATH FOLLOWED BY EX VIVO PERFUSION

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Background: Ex vivo lung perfusion (EVLP) has surged as means to assess and treat marginal lungs. Since organ viability is affected by brain death (BD) repercussions and sex differences could affect lung transplants

success, we investigated sex differences in lung inflammation of rats submitted to BD followed by EVLP.
Methods: Male (M) and female (F) Wistar rats were submitted to BD and maintained for 4 h. As control, Sham-operated animals were used. Heart-lung blocks were procured and preserved in cold Perfadex (1 h). Normothermic EVLP (4 h) was carried on with tidal volume of 7 ml/kg body weight, PEEP on 5 cmH2O, frequency 60/minute and FiO2 of 21%. Perfadex solution with albumin and augmentin (home-made STEEN solution) was infused with a maximal of 12 mmHg pulmonary arterial pressure. Ventilation parameters and lung oxygenation capacity were recorded. Perfusate were sampled over time and lungs were analyzed on cellular infiltrate, myeloperoxidase staining, IL-1β qPCR and culture (explant).
Results: Oxygenation capacity decreased in BD groups with time. Female showed less compliance, despite BD ($p < 0.05$). Perfusate analysis showed greater accumulation of lactate ($p < 0.05$) and IL-1β in BD female ($p < 0.05$) in comparison to BD male. IL-1β gene expression ($p = 0.095$) and 24 h concentration in lung culture ($p = 0.078$) also indicate higher IL-1β in BD female group. Lung infiltrate was significantly increased in BD female compared to BD male ($p < 0.05$), with a tendency of higher number of MPO marked cells ($p = 0.072$), indicating neutrophil infiltration.
Conclusions: Female lungs showed worse inflammatory parameters then male, after BD and EVLP. Indicating that EVLP alone may not improve the lung condition of female donors. Therefore, new studies should focus on EVLP associated therapy in order to improve organ quality.
This study was financed grant 2016/03692-9 and 2018/07289-0, São Paulo Research Foundation (FAPESP)

POS399 DONATION AFTER CARDIAC DEATH: A PERSPECTIVE FOR PEDIATRIC LUNG TRANSPLANTATION

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Background: In children respiratory diseases such as Cystic Fibrosis can lead to end-stage respiratory failure. Lung transplantation represents the only perspective of improving the prognosis. For the year 2020 the data from the Italian Paediatric Programme confirm the inferiority of the lungs available for transplant compared to the patients on the waiting list. International experience of lung procurement by pediatric donor after circulatory death (pDCD) shows how the establishment of these pathways expand the donor pool with excellent results of short and long term follow-up. Currently there is no pDCD programme in Italy but the impact of this procurement can be significant even as demonstrated by the experience adult DCD programmes: no-touch time of 20 min can be bypassed with strict pathway timing and the optimisation of in-situ and ex-situ organ perfusion.
Method: The aim of this work is apply in Meyer Children Hospital a timeline of lung pDCD pathway at potential uncontrolled–controlled pDCD after unexpected – expected cardiac arrest. Refractoriness to cardiopulmonary resuscitation manoeuvres (CPR) and ineligibility for the therapeutic pathway indicate the shift to the donor pathway. Inclusion criteria: CA witnessed; age>1 month; absent medical unsuitability/primary-secondary pulmonary pathology. Lung pDCD timeline:
*CA-CPR<15'
*Low flow < 1 h
*In situ post-mortem lung preservation: two methods in according to the most suitable timing: (1) In situ cooling: warm ischaemia (CA-thoracic drains) < 2 h- Cold ischaemia (thoracic drains-explant) < 4 h; (2) protective ventilation: if chest drains are not placed on time warm ischaemia (CA-explant) < 4 h.
Results: The retrospective analysis of deaths 2013–2020 shows that the donor pool comes from the category DBD 13% and DCD 87%, 7% of thus are eligible pDCD. It is possible to stratify the quota of eligible DCD patients according to the Maastricht Categories: Maastricht II A 36%; Maastricht III 36%; Maastricht IIB 28%. We estimated the expected share of 4 lung with an expected increase of up to 36% of those used.
Conclusion: The identification of these potential donors could contribute to increase the number of organs available with a impact on reduction of waiting lists. The development of a pDCD lung programme make it possible to exploit a donor potential actually not used.

POS400 EFFECTS OF AZITHROMYCIN IN LUNG TRANSPLANT RECIPIENTS

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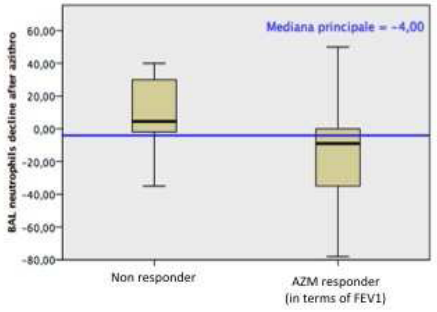
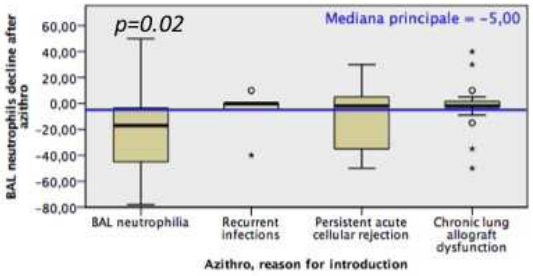
Background: Current evidence for azithromycin (AZM) after lung transplantation (LuTx) covers both prophylactic use to prevent BOS and treatment after the occurrence of CLAD. We hereby report the effects of AZM in our cohort of LuTx patients.
Methods: This was a retrospective study including all adult patients who underwent LuTx from January 2004 to June 2019 and received long term AZM (250/500 mg p.o. 3 times a week) at any time after LuTx. Effects of AZM were evaluated with BAL analysis and pulmonary function tests. Patients were considered "responders" in case of a FEV1 increase > 10% after 3 and 6 months of treatment.
Results: 116 patients (out of 322 LuTx) received long term AZM after LuTx for five main reasons: 56 (48.3%) for BAL neutrophilia; 12 (10.3%) for recurrent respiratory infections; 16 (13.8%) for persistent mild acute rejection; 31 (26.7%) for CLAD onset and 1 (0.9%) as a prokinetic medication. Median FEV1 improvement in the first 3 months of treatment was 20 (−36; +80) mL/month in the whole cohort; AZM responders (85 individuals) showed a 23 (13; 86) mL/month FEV1 increase, while non responders experienced a FEV1 decline of 15 (−33; −8) mL/month. Results regarding BAL neutrophilia and survival can be found respectively in Figure 1 and 2. AZM was discontinued in 9 patients for adverse events: 4 gastrointestinal intolerance; 2 NTM isolated on sputum; 2 asymptomatic QTc lengthening; 1 malaise.
Conclusion: Azithromycin seems to be effective in improving lung graft function, especially in those who were administered it for BAL neutrophilia and frequent respiratory infections. In these subjects, CLAD free survival was also increased. Neutrophils count on BAL was decreased in all the cohort.

Figure 1 – BAL neutrophilia



BAL neutrophils decreased by 4.5% after 6 months in general population; AZM responders, in particular, showed a decline of 9% (p = 0.046).

BAL neutrophils decline (%)	General population	Non responders	AZM Responders	p
	-4.50 (-35.00; 0.00)	4.50 (-10.25; +32.50)	-9.00 (-36.50; 0.00)	0,046



Indication for AZM introduction	BAL neutrophils decline after 6 months (%)
General population	-4.5 (-35; 0)
BAL neutrophilia	-17 (-45; -3.25)
Recurrent respiratory infections	0 (-13.75; 2.5)
Persistent acute rejection	-2 (-37.5; 7)
CLAD onset	-2 (-3.5; 2.25)

POS401 SARS-COV-2 POSITIVE DONORS FROM NON-SUITABILITY TO THE USE FOR ORGAN TRANSPLANTATION

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Italian National Institute of Health, Italian National Transplant Centre, Rome, Italy

Background: During the Sars-CoV-2 pandemic that suddenly broke out in Italy, the Italian National Transplant Center (CNT) constantly monitored and supported donation and transplantation activities, thanks to the dissemination of guidelines, which allowed for their safe performance. The collaboration between transplant network's members and the National Infectious Disease Reference person allowed to use apparently unavailable resources. The study aims at describing how the use of Sars-CoV-2 positive donors (COVID+D) is changing.
Methods: Our study period goes from January 2020 to February 2021, during which the main safety protocols were adopted. During the first phase (January-August 2020) using donors with a negative anamnesis for close contacts and/or negative swab sample was recommended. During the second phase (September-November 2020) COVID+D were considered as suitable for donation but only for Sars-CoV-2 positive recipients (COVID+R), for whom an acute organ failure due to infection was reported. In the third phase (December-February 2021) COVID+D were considered for donation also for COVID+R or recipients with protective antibodies due to a previous infection and waitlisted for a life-saving organ transplant. The data were collected by CNT's Allocation Office who manages 24/7 donation and organ allocation activities.
Results: During the study period, 33 potential COVID+D were procured. Out of these, 6 (18.2%) didn't match the criteria of the first phase and were excluded from donation, 6 (18.2%) matched the criteria set in the second phase but were not used due to the absence of suitable recipients. Out of 21 potential COVID+D procured during the third phase, 11 (52%) didn't match the criteria of suitability for donation and 10 (47.6%) were used: 1 left liver transplant and 9 whole liver transplants were performed, including one national emergency with ongoing SARS-CoV-2 infection. To date, considering a 55-days mean follow-up from transplantation, no transmission of infection or other complications were reported.
Conclusions: The safe use of donors, who were initially considered unsuitable, was possible due to the close monitoring of the pandemic evolution in the donation and transplantation field. More data gathered from recipients' follow-up will be an interesting subject for further studies.

POS402 UNINTERRUPTED AND SUCCESSFUL DECEASED DONATION PROGRAMME DURING THE COVID-19 CRISIS IN SLOVENIA: EXAMPLE OF GOOD PRACTICE

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Background: Despite durable covid-19 healthcare crisis in 2020, Slovenian deceased donation programme (DDP) resulted in higher numbers compared to 2019. With brisk and appropriate measures, epidemics did not impact the quality and effectiveness of DDP. From the start, great attention was put on ethical responsibility and prevention of discharge of procured organs. In Eurotransplant (ET) during the first wave of epidemics too many organs were not transplanted due to no capacity.
Methods: In 2020 Slovenija-transplant has been systematically collecting data in relation to covid-19 in DDP (number of infected deceased donors (DD), family refusals due covid-19, the number of unused procured organs, etc.). The aim was to cope with and respond to the possible negative effect of Sars-CoV-2 on DDP and to assure the usage of organs for patients in need for transplantation.
Results: In 2020, 47 actual deceased donors (44 in 2019) were realized. Average DD's age was 59 years. 139 organs were procured (132 in 2019) and exchanged within ET region. With 76% consent rate to donation remained high (78% in 2019). Out of 17 refusals, at least 4 were related to covid-19. No transmission of Sars-Co-2 from donor to recipient occurred. Slovenia was among successful ET countries that managed DDP with better results compared to 2019.
Conclusions: Success was achieved by highly engaged, cohesive and motivated professionals, timely introduction of preventive measures, continuous updates guidelines, and smooth communication on national and international level. Frequent (daily or weekly) video-conferences among key professionals in Slovenian donation centres and between experts in ET region enabled brisk responsiveness to ever changing protocols. Great efforts were put to assure continuous running of the DDP with limited facilities and reduced human resources in order to cover as much as possible the patients on the waiting lists and decrease the number of unused organs due to no capacity.

POS403 INNATE INFLAMMATORY GENE EXPRESSION PROFILING IN POTENTIAL BRAIN-DEAD DONORS: DETAILED INVESTIGATION OF THE EFFECT OFCOMMON CORTICOSTEROID THERAPY

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Background: Our study aimed to assess the influence of common methylprednisolone therapy on innate inflammatory factors in potential brain-dead organ donors (BDDs).
Methods: The study groups consisted of 50 potential BDDs who received 15 mg/kg/d methylprednisolone and 25 live organ donors (LDs) as control group. Innate immunity gene expression profiling was performed by RT-PCR array. Soluble serum cytokines and chemokines, complement components, heat shock protein 70 (HSP70) and high mobility group box-1 (HMGB1) were measured by ELISA. Surface expression of TLR2 and TLR4 were determined using flow cytometry.
Results: Gene expression profiling revealed up-regulation of TLRs 1, 2, 4, 5, 6, 7 and 8, MYD88, NF-kB, NF-kB1A, IRAK1, STAT3, JAK2, TNF-a, IL-1b, CD86 and CD14 in the BDD group. Remarkably, the serum levels of C-reactive protein and HSP70 were considerably higher in the BDD group. In addition, serum amounts of IL-1b, IL-6, TNF-a, HMGB1, HSP70, C3a and C5a, but not IL-8, sCD86 or monocyte chemoattractant protein-1, were significantly increased in the BDD group. Significant differences were observed in flow cytometry analysis of TLR2 and TLR4 between the two groups.
Conclusions: In summary, common methylprednisolone therapy in BDDs did not adequately reduce systemic inflammation, which could be due to inadequate doses or inefficient impact on other inflammatory-inducing pathways, for example oxidative stress or production of damage-associated molecules.

POS404 NATIONAL DATASET ON DONATION AFTER CIRCULATORY DEATH AND BRAIN DEATH UNDER EXTRA-CORPOREAL SUPPORT: 3-YEAR ACTIVITY AND CRITICAL POINTS

Francesca Vespasiano[1], Francesco Procaccio[1], Francesca Puoti[1], Lucia Masiero[1], Ilaria Lombardi[1], Andrea Ricci[1], Letizia Lombardini[1], Massimo Cardillo[1], Italian Dcd Working Group[2]
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Background: DCD donation is taking hold in Italy despite 20-min no-touch period. National data have been collected to share procedures, results and critical points within the transplant network. Aim of this study is to analyze the preliminary Dataset output.
Methods: A National web-based Dataset has been implemented in 2017 to collect data regarding: (1) DCD donors, in situ (nRP) & ex situ perfusion (MP); (2) DBD donors under ECMO (DBD-ECS). A six-month report is shared with professionals, Regional Transplant Centers and Health Institutions.
Results: Uncontrolled (u) and/or controlled (c) DCD programs have been implemented in 7 out of 20 regions (42 centers) and DBD-under-ECMO in 20 hospitals. Data input has reached a completeness of 96%. 254 potential DCD donors were referred in 2017-2019 (130 uDCD, 122 cDCD, 2 DCD IV) leading to 346 transplanted organs out of 480 recovered - Kidney (K) 288; Liver (Li) 124; Lung (Lu) 68. NRP was used in 82% uDCD, 97% cDCD and 100% DCD IV actual donors, resulting in 95% of total utilized donors. MP followed nRP in 91% of transplanted K and 81% Li. 89 DBD-ECS donors led to 190 recovered organs: 91% of K and Li and 75% of Lu were transplanted, 54% after MP. One year graft survival has been obtained, so far, for 80% of total transplants.
Conclusions: Regional models regarding uDCD and/or cDCD programs are variable and system governance is rarely structured. Clinical procedures aimed to organ function preservation as well as criteria of organ suitability still remain variable among centers.
In conclusion, this national Dataset can be a strategic tool for sharing data among professionals and regional governments; detecting critical points; harmonizing language, definitions and methodology; supporting HTA studies and resources sustainability; defining targets and evaluating results. Moreover, systematic auditing of DCD and DBD-under-ECMO potentiality and results could be fulfilled by quality criteria and validated indicators.

POS405 PROTOCOL FOR ORGAN OFFERS FROM ABROAD DURING THE COVID-19 PANDEMIC

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Background: During the Covid-19 pandemic, the Allocation Office of Italian National Transplant Centre **(CNTO)** has been progressively modifying adopted protocols for donor assessment in relation to the national and European epidemiological situation and to the updated knowledge of the virus
The aim of this work is to evaluate whether the measures adopted by CNTO have been effective in terms of workload and safety standards.
Methods: The period we took in consideration has been divided in 3 phases on the basis of the exams needed to evaluate the infectious risk of the donor: during the first phase (March 3–27 2020), a negative result from a swab or bronchial wash sample was requested; during the second one (March 28- April 23 2020) a negative result on bronchial wash sample or on a deep lung secretions sample was requested; during the third one (April 24- September 3 2020), a negative result on swab sample and a negative medical history for suspicious symptoms and/or absence of close contacts was requested. During these 3 phases we analyzed the number of donors which have been offered us from abroad, eventually accepted and transplanted. A comparison with the pre-pandemic period was also performed
Results: During the considered period, CNTO received 62 offers (VS 50.24% more than in 2019): 11 donors during the first phase, 9 donors during the second one and 42 donors during the third phase.
During the first phase 1 donor (9%) was excluded due to failed testing of swab or bronchial wash sample for Sars-CoV 2; during the second one, 7 (78%) donors were excluded due to failed testing for Sars-CoV 2 on bronchial wash sample; during the third one, 3 (7%) donors were excluded due to the absence of swab sample and/or specific medical history, 8 (21%) donors were considered as suitable but offered only to recipients in serious clinical conditions During the whole period, 3 kidneys and 1 liver have been transplanted (with no virus transmission) while in 2019 4 livers were transplanted
Conclusions: The progression of the epidemiological curve in some European countries involved a suspension or reduction of the transplantation activity, which led to an increase in offers to Italy. The changes that have been made to the protocol, thanks to the support of the National Infectious Disease Second Opinion, have contributed to the safe transplantation of the accepted organs

POS406 A SINGLE CENTRE REVIEW OF THE DECEASED DONOR POPULATION IN A CARDIOTHORACIC INTENSIVE CARE OVER A 5 YEAR PERIOD

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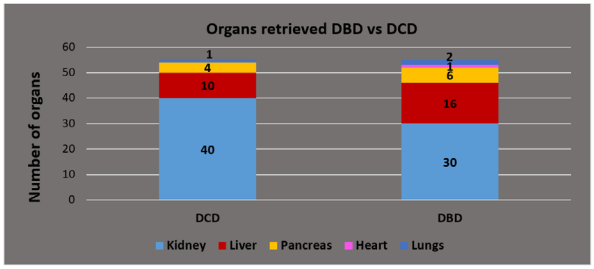
Background: Organ donation and transplantation medicine faces an ongoing complex challenge and rising demand of securing organs for transplant. There are a number of ever increasing barriers and therefore as a result of this, it is important that no donor opportunities are missed in order to maximise the number of organs available for transplant. The aim of this study was to assess the number of deceased organ donors and organs donated within our trust over a five-year period.
Methods: Data were retrospectively collected on all deceased donors in the Royal Brompton and Harefield Hospital over a five-year period from Jan 1st 2016 to Jan 1st 2021. This included age, sex, cause of death, type of donor: Donation after Brain death (DBD) or Donation after circulatory death (DCD) and solid organs donated for transplant.
Results: 40 deceased donors were reviewed in this study, 21 DCD donors and 19 DBD donors. The donor median age was 52 years of age. 77% ($n = 31$) of the donors were male compared to 23% ($n = 9$) female donors. The most common cause of death was a hypoxic brain injury post cardiac arrest ($n = 23$, 57%) followed by Cardiovascular disease ($n = 8$, 20%), Respiratory failure ($n = 5$, 13%) and Intracranial haemorrhage ($n = 4$, 10%). A significant number of patients were supported with Extra corporeal membrane oxygenation ($n = 11$, 28%) and left ventricular assisted devices ($n = 2$, 5%) at the time of donation. 70 kidneys were retrieved from this cohort of organ donors (DCD $n = 40$, DBD $n = 30$), 26 livers (DCD $n = 10$, DBD $n = 16$), 10 pancreas (DCD $n = 4$, DBD $n = 6$), 1 Heart (DCD $n = 0$, DBD $n = 1$) and 3 bilateral lungs (DCD $n = 1$, DBD $n = 2$).
Conclusions: Our retrospective study highlights that organ donors in a cardiovascular intensive care unit are more likely to donate abdominal organs only. Our study demonstrates a remarkably higher percentage of male donors compared to females.

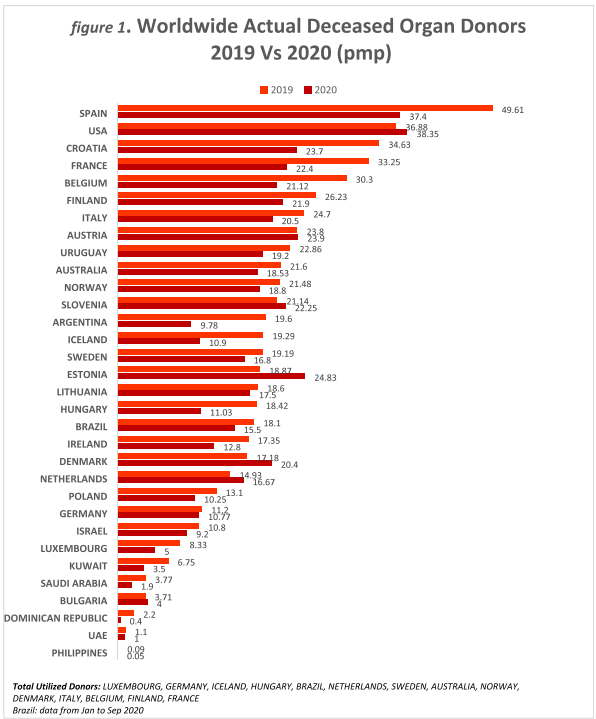
It is important to note that the number of organ donors in our trust decreased significantly during 2020 Covid 19 pandemic. Next steps include conducting a study to further assess the characteristics of organ donors supported with ECMO and LVADs prior to donation. Despite the clinical instability of patients suffering with cardiovascular and respiratory failure, our data demonstrate positive donation outcomes leading to life changing transplants.



POS407 INTERNATIONAL REGISTRY IN ORGAN DONATION AND TRANSPLANTATION (IRODAT) 2019 VS 2020 WORLDWIDE DATA OVERVIEW

Marián Irazábal[1], Maria Gomez[1], Chloe Balleste[1], Entela Kondi[1], Ricard Valero[1,2], Estephan Arredondo[1], Martí Manyalich[1,2]
[1]DTI Foundation, Barcelona, Spain; [2]Hospital Clínic de Barcelona, Barcelona, Spain

Background: IRODaT is a worldwide registry in organ donation and transplantation (D&T). Out of the 111 countries with organ D&T activity, 86 reporters have submitted data to IRODaT since 1998. Our goal is to provide a global overview in D&T.
Methods: Each country is represented by a national reporter, who retrospectively registers the activity on the website. All data are validated prior to be published. IRODaT follows "The Critical Pathway of Deceased Donation" definition, ensuring uniformity and correct interpretation.
Results: 80 countries submitted data from 2019 at the IRODaT registry. Contrarily in 2020, the organ D&T rates mostly dropped due to the emergency of COVID-19 worldwide. As expected, some fluctuations were recorded regarding the deceased donation (DD) activity. Nevertheless in 2020 we have collected data from 32 countries so far. In the EU the most affected countries were: Spain, Croatia, France, Belgium and Italy. Although in South America measures were taken to minimize the impact of COVID-19 observed in the European and Asian continents; Uruguay, Argentina and Brazil reported a downward trend in DD. Similarly, in the Middle East countries occurred the same scenario. Unlikely, the US, Austria, Slovenia, Estonia, Denmark, Netherlands and Bulgaria, reported an increase in DD despite the adverse effects related to the pandemic (figure 1).
The number of living donation (LD) performed was affected significantly since many programs were deferred. As a result, out of 79 countries that reported in 2019, only 18 countries have submitted data in 2020 with a decrease in LD activity between 18 and 67% compared to the previous year, except for Israel, Belgium, Ireland, Estonia and Slovenia.
Regarding the Donation After Circulatory Death (DCD) program, only 6 countries reported DCD activity in 2020 with Spain, Belgium and the US at the top, followed by Austria, Ireland and Israel.
Conclusions: In 2020, the challenges hospitals faced, including restrictions, flight reductions and border closures affected national programs worldwide as reflected above. Nevertheless, coordination and transplant teams have minimised the impacts of the pandemic and while health resources were globally disproportionally affected, certain countries managed to increased D&T rates.



POS408 ORGAN DONATION INNOVATIVE STRATEGIES FOR SOUTHEAST ASIA: ODISSEA

Maria Gomez[1], Patricia Peralta Lasso[1], Elisa Vera[1], Ricard Valero[2], Martí Manyalich[3], Marco Zanello[4], Mirela Busic[5], Melania Istrate[1]
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Background: ODISSeA - Organ Donation Innovative Strategies for Southeast Asia is an Erasmus+ project funded by the European Commission. An academic postgraduate programme on organ donation (OD) in 8 Southeast Asian (SeA) universities from Malaysia, Myanmar, Philippines and Thailand and 3 European universities have been developed.
Methods: Training programmes and OD self-assessment (SA) evaluation of clinical knowledge (A/n21) and of non-clinical competencies (B/n18). SeA universities targeted 3 groups: university personnel, faculty members and potential postgraduate trainees. Train the Trainers (TxT) blended programme for SeA trainers healthcare professionals (HCPs). Pre and post course evaluation results were compared. Multilevel blended Postgraduate Programme in Organ Donation (PPOD) targeting HCPs combining academic training with bedside projects. Pre course evaluation results were compared among the SeA partner countries.
Results: Comparing SA results among trainers and trainees in group A 37% vs 54% scored poor to average while 30% vs 20% scored very good to excellent. The overall average score was 2.91 $\pm$ 0.39 SD vs 2.49 $\pm$ 0.31 SD respectively.
In group B 19% vs 35% scored poor to average while 49% vs 25% scored very good to excellent. The overall average score was 3.43 $\pm$ 0.67 SD vs 2.83 $\pm$ 0.48 SD respectively.
HCPs trained in TxT (n41) pre and post testing shows knowledge increase of 15.14% with an overall average score of 6.67 $\pm$ 0.96 SD in pre-test vs 7.68 $\pm$ 0.66 in post-test.
PPOD pre-test overall average score was 4.59 $\pm$ 1.56 SD with Malaysia achieving the highest results (5.28 $\pm$ 1.32 SD) and Myanmar the lowest (4.38 $\pm$ 1.32 SD).
Conclusion: The innovative approach of ODISSeA as a multilevel educational intervention revealed different results between trainers vs trainees on perception and attitude, clinical knowledge vs non-clinical competencies. Significant knowledge increase was reported upon completion of TxT.

POS409 FIRST ITALIAN EXPERIENCE OF MOBILE ECMO TEAMS FOR CONTROLLED DONATION AFTER CIRCULATORY DEATH

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Background: Although there is a constant increase in the access to transplant facilities, this is still far from accomplishing the request. In Italy

Donation after Circulatory Death (DCD) has been previously considered unadvisable, anyway, the feasibility of a DCD program in Italy has been initiated by the Centro Nazionale Trapianti in 2005 and different Centers in Treviso, Pisa, Cagliari and Pavia started successful DCD programs. Nevertheless, since organ reperfusion may improve organ viability after warm ischemia, DCD can be practiced in Italy without a previous shortening of the no-touch period. Controlled DCD is still a relatively uncharted terrain. We explored the feasibility of a mobile ECMO team for controlled DCD in a Hospital without in loco ECMO facility.
Methods: In the period 2018–2019 we enrolled potential cDCD donors, for whom a planned withdrawal of life sustaining therapies was programmed, with nor opposition or contraindications for organ donation. Interview with the family and a briefing session with the personnel involved with the donation were planned. After WLST and death declaration, NRP was instituted by the external ECMO team in the ICU. We measured WIT, fWIT, NRP duration. Blood Gas Analysis were performed at WLST start, at NRP start and hourly during NRP. Hourly assessment of lactate, liver and renal function, complete blood count and coagulation were assessed. Outcome of the transplanted organ was assessed at 1 week and 3 months.
Results: We enrolled 3 potential cDCD donors and successfully carried out harvesting and transplantation of 4 kidneys and 2 livers. The median fWIT was 57.39 minutes and NRP initiation 70.03 minutes, NRP median duration 3.5 hours, lactate decline was evident after 2 hours from NRP institution. Subsequent MP was applied to liver and kidney grafts.
Conclusion: The application of a mobile ECMO team for NRP application in cDCD is feasible for Hospitals without in loco ECMO facilities. Further experience is needed.

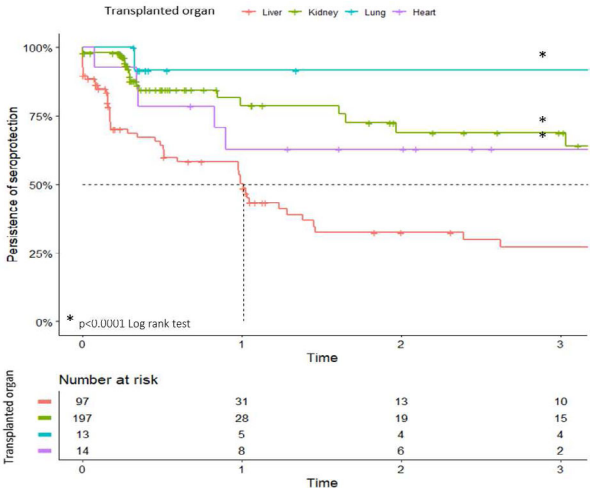

Figure: Loss of seroprotection after SOT by transplanted organ.

POS410 LOSS OF SEROPROTECTION IN PATIENTS TRANSPLANTED FROM SOLID ORGANS PREVIOUSLY VACCINATED AGAINST HEPATITIS B

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Chu Grenoble Alpes, La Tronche, France

Background: Following Solid Organ Transplantation (SOT), immunosuppressive treatments have an impact on anti-infectious host defences. Despite the recommendation for post-transplantation hepatitis B virus (HBV) immunization monitoring, the longevity of this protection is poorly characterized in SOT patients.
Methods: We performed a retrospective study of SOT patients, transplanted at Grenoble University Hospital between 2009 and 2019, including kidney, liver, heart, and lung recipients. We focused on patients negative for both HBs antigen and anti-HBc antibody, with a pre-transplant anti-HBs antibody (HBsAb) level >10 IU/L (reflecting hepatitis B virus vaccination). We explored the post-transplantation persistence of protective anti-HBs antibodies, and the factors associated with the loss of seroprotection.
Results: We included 321 SOT patients, with a median follow-up of 104 days (interquartile range 92–381)). Loss of HBV seroprotection (HBsAbs <10UI/L) was observed in 90/321 (28.0%) patients. In univariate analysis, liver transplantation, age above 50 years, body mass index (BMI) below 18 or above 30 kg/m^2 at time of transplantation, pre-transplantation HBs levels under 100UI/L, induction therapy with tacrolimus or corticosteroids, and maintenance immunosuppression without corticosteroids or mycophenolate mofetil were associated with loss of seroprotection. In multivariate analysis, kidney (HR 0.20 [CI95% 0.12; 0.34]), lung (HR 0.15 [CI95% 0.04; 0.50]) and heart (HR 0.33 [CI95% 0.13; 0.83]) transplantations were associated with delayed loss of seroprotection compared to liver transplantation ($p < 0.001$). Similarly, the risk of loss of seroprotection was lower for patients with pre-transplantation HBsAb levels between 100 and 300 IU/L (HR 0.32 [CI95% 0.18–0.60]) or above 300 IU/L (HR 0.10 [CI95% 0.05–0.21]) ($p < 0.001$) compared to levels under 100 IU/L and higher for patients with a BMI under 18 kg/m^2 (HR 3.28 [CI95% 1.42–7.61], $p = 0.01$) versus 18–30 kg/m^2.
Conclusions: HBV immunization is significantly impacted by SOT, especially with a low pre-transplantation anti-HBs titer. A booster HBV vaccination might improve HBV immunization, especially in liver transplant recipients and / or a BMI < 18 kg/m2.

POS411 INVERTED DIRECT ALLORECOGNITION TRIGGERS EARLY DONOR SPECIFIC ANTIBODY RESPONSE AFTER TRANSPLANTATION

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Background: The generation of antibodies against donor-specific MHC antigens (i.e. Donor Specific Antibodies, DSA) requires that recipient's allospecific B cells receive help from T cells. The current dogma holds that this help is exclusively provided by recipient's CD4+ T cells that recognise the complexes made of recipient's MHC-II molecules and peptides derived from donor-specific MHC proteins: i.e. indirect allorecognition.
Methods and results: In this translational work, we demonstrate that despite being devoid of T cells, CD3εKO mice develop a rapid but transient wave of switched DSA after transplantation with an allogeneic heart graft.
CD4+ T cells can be isolated from the heart of CBA mice and are efficiently depleted by anti-CD3 or anti-CD4 monoclonal antibodies. T cell depletion in the donor abrogates DSA generation in CD3εKO recipient mice.
Interaction between donor's (CBA) T cells and recipient's (C57BL6) B cells were evidenced in vitro, allowing demonstrating that donor CD4+ T cells recognise intact recipient's MHC-II molecules expressed by BCR-activated allospecific B cells.
This "inverted" direct pathway is also operant in transplanted patients. Donor CD4+ T cells are indeed present in the perfusion liquids of human renal grafts and acquire B cell-help functions upon in vitro stimulation. Furthermore, T follicular helper cells, specialised in helping B cells, are present in large number in Mucosal Associated Lymphoid Tissue of lung and intestinal grafts.

In the latter, higher content in passenger T cells correlates with the detection of donor T cells in recipient's circulation, which in turn is associated with an early transient DSA response and a worse graft survival.
Conclusions: Our work demonstrates that donor CD4+ T cells transplanted with the graft can provide help to allospecific B cells through a previously overlooked « inverted direct » pathway, and lead to the production of pathogenic early DSA.

POS412 THE BLACK BOX OF IMMUNOSUPPRESSION AFTER SOLID ORGAN TRANSPLANTATION

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Background: Adequate immunosuppression is essential after solid organ transplantation to prevent acute and chronic rejection. However, a precise balance should be achieved to not over suppress the immune system. Our goal was to assess the effects of immunosuppressive treatment, with a standard dose, in wildtype C57BL/6 mice.
Methods: C57BL/6 mice were assigned in two groups (n = 4/group) receiving daily subcutaneous immunosuppression with 10 mg/kg cyclosporine A (CsA, Sandimmun, Novartis) and 1.6 mg/kg methylprednisolone (SoluMedrol, Pfizer) or the same amount of saline (control) for 3 weeks. Weight was monitored daily. Every two days, blood was drawn and analyzed for differential cell count (Advia 2120i, Siemens). At sacrifice, lungs, spleen and blood were harvested for flow cytometry (LSR Fortessa, BD Biosciences) for standard immune markers (CD3, CD19, CD8, CD4, CD25 and Foxp3) and CsA serum levels were monitored.
Results: Mean serum CsA levels were 610 (±185.9) μg/L at sacrifice. Weight decreased non-significantly over time in immunosuppressed mice. No differences were observed in total differential blood cell count over time. %CD19+ B cells and %CD3+ T cells did not differ between groups in all tissues. %CD8+ cytotoxic T cell increased in immunosuppressed mice compared to controls in spleen, blood and lung ($p = 0.0002$; $p = 0.002$; $p = 0.0016$). %CD4+ helper T cells and %CD25+ Foxp3+ T cells within the CD3+ T cell population were significantly decreased in the immunosuppressed group compared to controls in spleen, blood and lung ($p < 0.0001$, $p = 0.0008$, $p = 0.0014$; $p = 0.018$, $p = 0.0014$, $p = 0.027$).
Conclusion: The combination of methylprednisolone and CsA did not suppress circulating white blood cells, myeloid or lymphoid cells. However, an increase in CD8+ T cells and a decrease in CD4+ T cells and regulatory T cells was observed. These results demonstrate why overimmunosuppression should be avoided and indicate that a balance must be found between cytotoxic and regulatory cells.

POS413 DRUG TRANSPORTERS EXPRESSION IS ASSOCIATED WITH TACROLIMUS INTRACELLULAR CONCENTRATION

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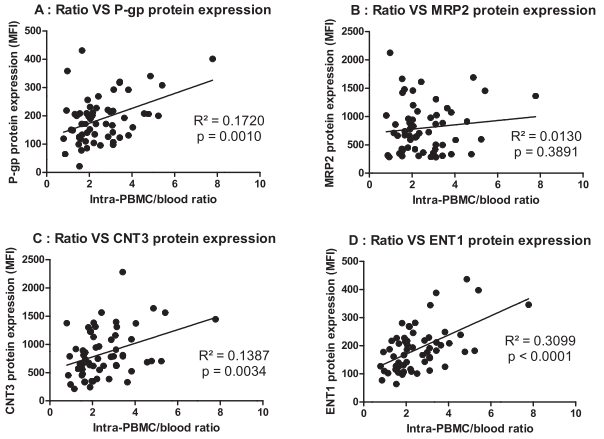
Background: Given the existence of a concentration-effect relationship for tacrolimus (TAC), measuring its blood concentrations (C_{min}) is mandatory in liver and kidney transplant recipients (LTR and KTR). However, while having adequate C_{min}, some patients still experience rejection/adverse events, highlighting the limitation of such monitoring. As TAC exerts its effect inside T-cells, monitoring intracellular instead of whole blood concentrations is an appealing strategy. Drug transporters expressed at the cells membrane could be major factors of TAC diffusion into peripheral blood mononuclear cells (PBMC). The aim of the study was to explore the relationship between TAC diffusion into PBMC and cell membrane expression of 4 drug transporters (P-glycoprotein (P-gp), Multidrug resistance-associated protein 2 (MRP-2), Concentrative nucleoside transporter 3 (CNT-3) and Equilibrative nucleoside transporter 1 (ENT-1)).
Methods: Sixty stable LTR and KTR were included in the study. TAC Blood and PBMC concentrations were determined by liquid chromatography coupled with tandem mass spectrometry. P-gp, MRP-2, CNT-3 and ENT-1 expression at the PBMC surface was evaluated with fluorophore-coupled antibodies using flux cytometry. Correlation between TAC PBMC/blood ratios and transporters expressions were explored using correlation tests (Pearson).
Results: TAC PBMC/blood ratios were not different between LTR and KTR and the results were then pooled. P-gp, CNT-3 and ENT-1 expressions show positive correlation with TAC PBMC/blood ratio. Correlation was stronger for ENT-1 (R^2=0.31, $p < 0.0001$) than for P-gp and CNT-3 (R^2=0.17, $p = 0.001$ and R^2=0.14, $p = 0.003$, respectively). MRP-2 expression were not correlated with PBMC/blood ratio (figure 1).
Conclusions: In this study, TAC diffusion into PBMC increased as a function of membrane expression of ENT-1, CNT-3 and P-gp. ENT-1 expression seems to be the strongest driver of TAC diffusion, which is consistent with its influx transporter role. Findings for P-gp might be explained by an induction of its expression when intracellular TAC concentration increases. ENT-1 and CNT-3 influx effects on TAC diffusion would then outweigh the P-gp efflux effect. TAC intracellular concentration measurement may offer new insight helping in difficult clinical situations.



POS414 SMALL MOLECULE BCL6 INHIBITORS: A NEW DRUG CLASS OF IMMUNOSUPPRESSION FOR TRANSPLANTATION?

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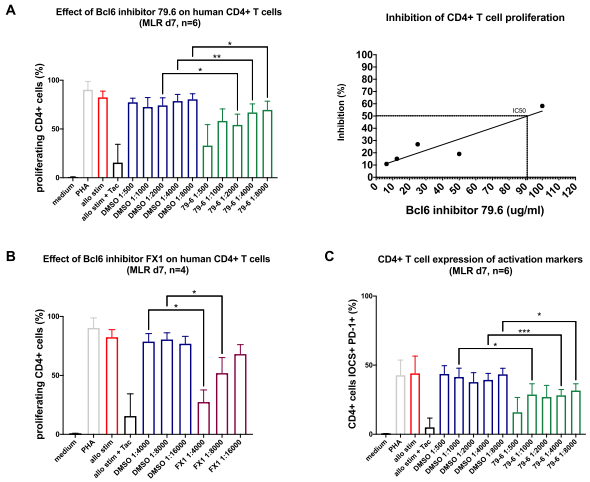
Aims: The transcription factor Bcl6 is critical for humoral immunity and the generation of long-term memory CD4 T cells in mice. To assess the potential of novel Bcl6 inhibitors as immunosuppressive agents, we tested the effects of Bcl6 inhibitors on allogeneic activation of human CD4 T cells.
Methods: We performed mixed lymphocyte reactions (MLR) using allogeneic healthy donor PBMC *in vitro* in the presence of Bcl6 inhibitors 79.6 and FX1 or the vehicle/solvent DMSO as control. Briefly, CFSE-labeled healthy donor responder PBMC, pure CD4+CD45RO- (naive) or CD4+CD45RO+ (memory) and PBMC depleted for CD4+CD45RO+ or CD4+CD45RO- cells were cocultured with irradiated HLA-mismatched stimulator PBMC (1:1). After 7 days, CD4 T cell proliferative response and expression of activation markers ICOS and PD-1 was measured. To determine effects of Bcl6 inhibitor on cytokine responses, we additionally performed IFN-g ELISPOT after donor antigen stimulation of PBMC from KTx recipients.
Results: CD4 T cell proliferation was inhibited by Bcl6 inhibitor 79.6 in a dose-dependent manner with an IC_{50} of 91.5 μg/ml (Fig. 1A). FX1, a different Bcl6 inhibitor, showed similar results (Fig. 1B). The percentage of CD4+ICOS+PD-1+ cells was also significantly reduced after exposure to Bcl6 inhibitors (Fig. 1C). Autologous antigen-presenting cells (APC) were not necessary for activation of naive or memory CD4 T cells in this MLR

setting. Bcl6 inhibitor acted directly on isolated naive and memory CD4 T cells, which were significantly inhibited in their proliferative response by 26 ± 19% (naive cells) and 39 ± 21% (memory cells). Using ELISPOT analysis, we found that addition of Bcl6 inhibitor 79.6 reduced the frequency of allogeneic, donor-specific IFN-g producing cells in patient material.
Conclusion: Novel small molecule Bcl-6 inhibitors may hold potential as immunosuppressive agents in solid organ transplantation due to their inhibition of activation of alloantigen activated naive and memory CD4 cells.



POS415 LACK OF INFORMATION IN RANDOMIZED CONTROLLED TRIALS TO GUIDE TRANSLATION OF MEDICATION ADHERENCE INTERVENTIONS TO CLINICAL PRACTICE: SYSTEMATIC REVIEW

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Background: A lack of translation of efficacious medication adherence interventions into daily clinical practice is observed. Successful implementation of interventions builds on strong evidence and on implementation relevant information. We reviewed published RCTs of adherence-enhancing interventions in adult transplant populations for implementation-relevant information.
Methods: We included RCTs testing interventions to improve any phase of medication adherence in solid organ or allogeneic stem cell transplantation, published between 01/2015 and 11/2020 in MEDLINE, Cochrane, Embase, CINAHL and Web of Science. Study protocols without results, conference abstracts and studies with an exclusive pediatric focus were excluded. Implementation-relevant information was abstracted guided by the adapted 10 Peter's criteria: description of 1) healthcare/organizational and 2) social/economic/policy context; 3) patients/family and 4) other stakeholder involvement; 5) real-world-sample; 6) real-world-setting; 7) feasibility study; 8) implementation strategies; 9) process evaluation and 10) implementation outcomes. Findings were graded using a color-rating system and summarized in a table.
Results: We screened 17'004 titles/abstracts, resulting in 23 RCTs including 2'339 patients (n = 19–209/study). All studies focused on the implementation phase of medication adherence. Limited implementation-relevant information was reported (Table 1): description of the healthcare/organizational and social/economic/policy context (8.7% and 0% resp.), patient (9%) and stakeholder (4%) involvement, implementation strategies (4.3%), absence of process evaluation (4.3%).
Conclusions: There is a lack of implementation-relevant information in the medication adherence literature in transplantation. Early inclusion of implementation science principles in studies testing medication adherence interventions has the potential to fuel the speed of translation of interventions in daily clinical practice.

Table 1. Implementation research components reported in the medication adherence intervention studies in transplantation published between 2015 and 2020

		Garcia et al. 2015	Yang et al. 2015	Bessa et al. 2016	Breu-Dejean et al. 2016	DeVito Dabbs et al. 2016	Henriksson et al. 2016	Cukor et al. 2017	Dobbels et al. 2017	Harrison et al. 2017	Reese et al. 2017	Schmid et al. 2017	Foster et al. 2018	Cote et al. 2019	Grady et al. 2019	Han et al. 2019	Levine et al. 2019	Low et al. 2019	Paterson et al. 2019	Guldager et al. 2020	Jiang et al. 2020	McGillicuddy et al. 2020	Russel et al. 2020	Taber et al. 2020
1	Did the investigators describe the health care and organizational context?	-	-	?	-	?	-	?	-	?		+	?	-	+	-	-	?	-	?		?	-	-
2	Did the investigators describe the social, economic and policy context?	-	-	-	-	-	-	?	?	?	?	?	?	-	?	?	-	-	-	-		?	-	?
3	Were patients and/or family members involved in designing or evaluating the study?	-	-	-	-	+	-	+	-	?	-	-	-	-	-	-	-	?	-	?		?	?	
4	Were other stakeholders, besides patients, involved in designing or evaluating the study?	-	-	-	?	?	-	+	-	?	-	?	-	-	?	-	-	?	-	?		?	-	-
5	Was the included sample representative for the studied population?	?	-	?	?	+	+	?	-	?	?	+	+	-	?	?	-	?	?	?		-	?	
6	Was the research conducted in a real-world setting?	?	?	?	?	+	-	?	?	+	-	?	?	?	+	-	-	?	?	+	?	?	?	?
7	Was a feasibility or pilot study conducted before the evaluation study?	-	-	-	-	+	-	+	-	+	+	-	-	+	+	-	-	+	-	?		+	+	+
8	Was an implementation strategy reported?	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-
9	Was a process evaluation conducted parallel to the outcome evaluation?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-
10	Were implementation outcomes such as adoption and costs measured?	-	?	-	-	+	?		-	?	?	+	?	+	?	?	-	?	?	?	?	+	?	

Green + = component clearly addressed, yellow ? = component mentioned but not clearly addressed, red - = component not addressed

Green + = component clearly addressed, yellow ? = component mentioned but not clearly addressed, red - = component not addressed

POS416 OUTCOMES OF SARS-COV-2 INFECTION IN PATIENTS UNDER PHARMACOLOGICAL IMMUNOSUPPRESSION: IS THERE ANY ADDITIONAL RISK? A SWISS COHORT STUDY.

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Background: Pharmacological immunosuppression (IS) may be associated with more severe Covid-19. In this study we evaluated outcomes of hospitalized patients on IS, focusing on those with chronic liver disease (CLD).
Methods: Patients admitted at our institution with SARS-CoV-2 infection during the first pandemic wave (n = 442) were prospectively included and their data collected and analysed.
Results: Thirty-five patients (7.9%, 65.7% male, median age 70.6 years) were found to be under IS at the time of hospital admission, of whom 19 (54.3%) for autoimmune diseases, 4 (11.4%) being solid organ transplant recipients, 4 (11.4%) for malignancy, 4 (11.4%) for COPD and 4 (11.4%) for other chronic conditions. Steroids (n = 30, 85.7%) were the most commonly used immunosuppressive medication. Patients under IS showed higher rates of comorbidities including diabetes (n = 14 / 35, 40% p = 0.01). Compared with patients without IS, immunosuppressed patients showed higher mortality (n = 16 / 35, 45.7% vs n = 95 / 407, 23.3% p = 0.003) and longer hospital stay (median = 15.5 days vs median = 11, p = 0.0144). Moreover, in the univariate and multivariable logistic regression, IS was independently associated with mortality (OR = 2.76 (1.37–5.59) and 2.66 (1.19–5.94)) and in the linear regression with length of stay (coefficient = 6.14, p = 0.005 and 5.98, p = 0.007). Treatment with immunosuppressants in patients with concomitant CLD (n = 8 / 35, 22.9%), mostly NASH (n = 6 / 8, 75%) and mild disease (1 with cirrhosis), was not associated with worse outcomes (cave: sample size very small). The distribution of IS in this subgroup of patients

was similar to the whole group of patients under IS, being the majority (6 / 8, 75%) under steroids, with one patient under methotrexate and one patient under tacrolimus because of previous liver transplantation.
Conclusions: Patients under IS were significantly at higher risk of severe and prolonged COVID-19 disease, with higher mortality and longer hospital stay. However, the presence of CLD was not associated with worse outcomes in immunosuppressed patients.

POS417 PHARMACOKINETIC ASSESSMENT OF TACROLIMUS EXPOSURE BEFORE AND AFTER A SWITCH FROM IMMEDIATE-RELEASE (IR) TO LCP-TACROLIMUS: THE ENVARSWITCH STUDY

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Background and Aims: LCP-tacrolimus displays an enhanced oral bioavailability compared to IR-tacrolimus. The ENVARSWITCH study aimed to compare tacrolimus $AUC_{0\text{-}24h}$ in transplant recipients on IR- followed by LCP-tacrolimus, so as to re-evaluate the dose ratio recommended in the context of a switch and the efficiency of individual dose adjustment after the switch.
Methods: Adult stable kidney or liver transplant patients in whom a switch from IR- to LCP-tacrolimus was planned (with a 0.7 dose conversion factor) were recruited. Tacrolimus $AUC_{0\text{-}24h}$ was calculated by Bayesian estimation based on a limited number of concentrations measured in dried blood spots (DBS) before (V2) and after the switch (V3). LCP-tacrolimus dose was then adjusted in order to target the pre-switch $AUC_{0\text{-}24h}$, followed by an $AUC_{0\text{-}24h}$ verification (V4). $AUC_{0\text{-}24h}$ estimates and distributions were compared using the bioequivalence rule for narrow therapeutic range drugs (AUC 90%CI within the 0.90–1.10 acceptance interval).
Results: Fifty-six kidney and 51 liver transplant patients were included. The subgroups were comparable except for a later post-transplantation period (164 ± 86 vs. 116 ± 89 months, $p = 0.005$), better renal function (eGFR=69.7 ± 22.4 vs. 50.3 ± 14.3 ml/min, $p < 0.001$) and lower tacrolimus C_0 at V2 (7.51 ± 2.21 vs. 8.59 ± 1.65 µg/L, $p = 0.001$) in liver transplant recipients. $AUC_{0\text{-}24h}$ "bioequivalence" was met in the entire population between V2 and V3 (ratio: 1.01, 90%CI=[0.97–1.05]) and between V2 and V4 (ratio: 0.99, 90%CI=[0.95–1.02]). $AUC_{0\text{-}24h}$ "bioequivalence" was met in the each transplant subgroup, except between V3 and V2 in liver transplant patients (ratio = 0.95, 90%CI=[0.89–1.01]).
Conclusions: The 1:0.7 dose ratio applied for the switch from IR- to LCP-tacrolimus seems adapted for kidney but may be improved for liver transplant recipients. The combination of DBS and Bayesian estimation for tacrolimus dose adjustment in the context of a switch is easy, efficient and helps reaching rapidly appropriate exposure to tacrolimus after the switch.

POS418 FINGERPRICK SAMPLES FOR TACROLIMUS LEVELS DURING THE COVID-19 PANDEMIC: SINGLE CENTRE EXPERIENCE WITH HEART AND LUNG TRANSPLANT RECIPIENTS

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Background: Regular monitoring of tacrolimus levels is an essential part of the post-transplant follow-up in heart and/or lung transplant recipients receiving this drug. In response to the COVID-19 pandemic use of fingerprick capillary blood samples were trialled and then implemented using BD Microtainer tubes; the patients posted these to the centre for analysis using HPLC-MS.
Methods: From March-May 2020, paired venous and capillary samples were collected from 30 patients to validate tacrolimus measurement in capillary blood, and assess feasibility of collecting adequate sample volume by this method (lab method requires 150µL EDTA blood). From June 2020, heart and/or lung transplant patients were offered the option for postal tacrolimus monitoring, rather than attendance at the hospital, being provided with kits containing lancets, blood tubes and appropriate postage materials to return their samples to our laboratory. Patient advice leaflets were generated to optimise the sample collection procedure.
Results: From the initial 30 patients, paired data from 16 venous and capillary tacrolimus samples were compared and a strong correlation (R^2=0.9115) was found. Samples that could not be analysed were due to insufficient sample volume (9) or sample clotting (5). From June 2020 to February 2021, 243 capillary samples were received from 55 patients, 176 (72.4%) samples had adequate volume for analysis and 67 (27.6%) were unable to be analysed due to clot (45), insufficient sample (20), other (2).
Conclusions Remote collection of fingerprick capillary samples posted to the laboratory for Tacrolimus monitoring can be a suitable option for long-term follow-up, reducing the frequency of patient attendance. Improvement in patient education in the collection process improves success rates.

POS419 INCIDENCE OF STREPTOCOCCUS PNEUMONIAE AND HEMOPHILUS INFLUENZAE INFECTIONS IN ADULT SOLID ORGAN TRANSPLANT RECIPIENTS

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Background: Solid organ transplant (SOT) recipients receive life-long immunosuppression and therefore remain susceptible to infections that, in turn, lead to increased morbidity and mortality. The aim of this study was to determine the incidence of *Streptococcus pneumoniae* (*S. pneumoniae*) and *Hemophilus influenzae* (*H. influenzae*) infections (invasive and non-

invasive), the related hospitalization, and 30- and 180-days all-cause mortality in adult SOT recipients.
Methods: We included 1182 SOT recipients, between 2011 and 2017. Clinical characteristics and microbiology data were obtained from the Centre of Excellence for Personalized Medicine of Infectious Complications in Immune Deficiency (PERSIMUNE) data warehouse. Data from several clinical databases and national registries, such as the national Danish Microbiology Database (MiBa), are combined in the PERSIMUNE data repository. MiBa contains all microbiological data in Denmark from both hospitals and general practice since 2010. We calculated 95% confidence intervals (CI) of incidence rate (IR) using Byar's approximation to the Poisson distribution.
Results: The overall IR (95% CI) of *S. pneumoniae* and *H. influenzae* were 1086 (796–1448) and 1293 (974–1687) per 100,000 person-years of follow-up (PYFU), respectively. The IR of invasive infections were 76 (21–202) and 25 (2.3–118) per 100,000 PYFU, respectively (Table 1). Hospital admission was required in >50%, 30-days mortality was 0, and 180-days mortality was 8.8% and 4.5% after *S. pneumoniae* and *H. influenzae* infections, respectively.
Conclusions: The IR of invasive *S. pneumoniae* and *H. influenzae* infections in SOT recipients were higher than reports from the general population (10 and 1.3 per 100,000 PYFU, respectively) in Denmark. Furthermore, a large proportion of infected SOT recipients were hospitalized. These findings highlight the need for further studies to assess uptake and immunogenicity of vaccines against *S. pneumoniae* and *H. influenzae* in SOT recipients.

Table 1: Incidence rates of *S. pneumoniae* and *H. Influenzae* infections in adult solid organ transplant recipients.

Category (N= population size)	Time interval post-transplantation	Incidence rate (95% CI) of *S. pneumoniae* per 100,000 PYFU	Incidence rate (95% CI) of *H. Influenzae* per 100,000 PYFU
Overall (invasive and non-invasive infections) N= 1182	5 years	1086 (796-1448)	1293 (974-1687)
	First year	1235 (707-2017)	1059 (578-1794)
	First six months	873 (331-1914)	1049 (436-2163)
	First month	1000 (91-4662)	1002 (91-4672)
Only invasive infection N=1182	5 years	76 (21-202)	25 (2-118)
	First year	88 (8-411)	88 (8-411)
Heart transplant recipients N=84	5 years	1682 (638-3688)	33 (3-156)
Lung transplant recipients N=210	5 years	996 (414-2053)	1517 (749-2770)
Liver transplant recipients N=293	5 years	1410 (790-2343)	1091 (560-1935)
	Only invasive infection, 5 years	217 (43-695)	109 (10-509)
Kidney transplant recipients N=577	5 years	903 (562-1381)	1477 (1023-2069)
	Only invasive infection, 5 years	48 (4-221)	-*
Simultaneous pancreas and kidney transplant recipients N=18	5 years	-*	-*

* No infection was reported in this group.

POS420 EARLY DETECTION OF EPSTEIN-BARR VIRUS (EBV) IN SOLID ORGAN TRANSPLANT RECIPIENTS. COMPARISON OF PCR FOR EBV DNA IN THREE DIFFERENT BLOOD COMPARTMENTS

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Background: EBV is associated with the development of a wide range of cancers including posttransplant lymphoproliferative disease (PTLD) in transplant recipients. As part of a preventive approach against PTLD, several transplantation units monitor the occurrence of EBV DNAaemia after transplantation. However, there is little evidence to guide this strategy; nor is there consensus concerning the best specimen (whole blood or plasma) to use for EBV analysis.
We aimed to compare WHO-standardised quantitative polymerase chain reaction (qPCR) analysis for EBV DNA performed on plasma, whole blood and a combination of plasma and peripheral mononuclear cells (PBMCs) in solid organ transplant (SOT) recipients.
Methods: We included all blood samples for qPCR for EBV DNA in the study, which were sent to the Department of Clinical Microbiology at Aarhus University Hospital from November 1st 2017 to March 1st 2019. We performed qPCR for EBV DNA on plasma according to routine practice in the laboratory. Furthermore, we created a mix of plasma and PBMCs, and we aliquoted whole blood, if possible, from samples that had not been centrifugated before we received them. Both types of specimens were tested with qPCR for EBV DNA according to the WHO-standard.
Results: Three hundred and twenty-nine SOT recipients had an EBV DNA test performed at least once during the study. A total of 837 blood tests for EBV DNA were collected in EDTA gel tubes. In plasma, 43 patients were positive for EBV DNA in 107 samples (13%). In 784 samples analysed for EBV DNA in the mix of plasma and PBMCs, we detected EBV DNA in 342 samples (44%). Whole blood could be obtained from 274 specimens from 136 patients, in which EBV DNA was found in 108 samples (39%). Only 2 of 329 patients developed PTLD during follow-up.
Conclusions: EBV DNA was frequently detected in both plasma, whole blood and in the combination of plasma and PBMCs. More knowledge on monitorering strategy and risk assessment for PTLD is needed.

POS421 THE CLINICAL OUTCOMES OF COVID-19 DISEASE IN PATIENTS WITH SOLID ORGAN TRANSPLANTATION

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Background: Solid organ transplantation (SOT) patients are at high risk for SARS-COV-2 infection as well as other infection agents.
We aimed to investigate risk factors and clinical outcomes for Covid-19 Disease in SOT patients. We reviewed 818 SOT patients (n: 238 liver, 580 renal, M/F: 543/275 and mean± SD age 31± 18 years) who underwent SOT between February 2011-December 2020 at Baskent University.
Materials and Methods: We present the cases of 23 SOT patients (18M/5F, 4 liver, 19 renal) hospitalized for Covid-19 Disease in our center. Post transplantation time, smoking history, received immune suppressive drugs, comorbidities, duration of hospitalization, and need for intensive care for Covid-19 Disease were prospectively recorded. All patients were received a standard treatment regimen according to the recommendations of National Ministry of Health Covid-19 Science Board which based on disease severity.
Results: The treatment for Covid-19 Disease was generally well-tolerated by patients. Age and sex were main risk factors for Covid-19 Disease ($p < 0.05$). Mechanical ventilation (8 patients 34%), high flow nasal oxygen (2 patients 9%), and intensive care unit (10 patients 43%) were required in our patients. Nine of the patients received pulse therapy with methylprednisolone (250 mg/day for three consecutive days) and one patient received IV immunoglobulin 20 g/day. A prolonged RT-PCR positivity was detected in 3 patients (up to 75 days). Among 23 patients, a secondary infection was diagnosed in 7 patients (26%). Seventeen (74%) of the patients were (74%) totally cured while six patients (26%) died due to secondary infections. One patient had *Aspergillus fumigatus* growth in bronchoalveolar lavage fluid, 1 patient had *Acinetobacter baumannii* growth in tracheal aspirate, 2 patients had multiple drug resistant *Klebsiella pneumoniae* growth in deep tracheal aspirate, and 2 patients had *Escherichia coli* growth in urine.
Conclusions: A successful response was achieved in the treatment of Covid-19 Disease in our SOT patients. Even we had a successful response in the treatment of Covid-19 Disease, secondary infections increased mortality in our patients. We believe that preventive strategies to reduce secondary infections will be beneficial in SOT patients with Covid-19 Disease.

POS422 EVALUATION OF TRANSPLANTS PERFORMED IN ITALY WITH DONOR ORGANS WITH INFECTIOUS AND NEOPLASTIC RISK

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Background: The guidelines (GL) used by the Italian National Transplant Center (CNT) for evaluating the suitability of solid organ donors ascribe a risk level to each procured donor, so as to minimize disease transmission. GL, introduced in 2003, are subject to continuous update over the years. The current version was introduced in February 2017, mainly on the basis of the outcomes of kidney, liver and heart transplants (Tx) from Non Standard Donors (NSD) with single transmissible disease (HCV, HBsAg, HBcAb, Meningitis, Bacteremia or Neoplasia) compared to Standard Donors (SD), performed during the period 2006–2012. A further analysis of the complications occurred in the post transplant follow-up (FUP) was conducted for all Tx in the same period. We present updated data with transplants performed until 2016.
Methods: A mandatory data collection on donors, transplant patients and FUP through the CNT Information Transplantation System (SIT) started in 2002; the collection function of donor suitability data was implemented in the SIT in 2006. The multivariable graft survival analysis on first non-emergency, non combined Tx from SD or NSD, performed in the period 2006 to 2012, are updated to 2016.
Results: In the period 2006–2016, 14.168 kidney, 7.095 liver and 1.870 heart Tx were performed in Italy. The overall average follow-up time was 5.8 years (IQ_1=3 and IQ_3= 9). The results obtained in the period 2006–2012 did not show statistically significant (ns) differences in graft survival in the comparison of organ recipients from SD and NSD: the Hazard Ratios, adjusted for the considered recipient characteristics, are ns and about 1 for the analyzed pathologies.
Conclusions: The results show no difference in the incidence of infectious complications either related to hepatotropic viruses or neoplastic ones in transplant recipients, who received organs from SD compared to recipients of organs from NSD.

POS423 UNCOVERING THE GEOGRAPHICAL DISPARITIES IN ORGAN DONATION AND TRANSPLANTATION IN BRAZIL DURING THE COVID-19 PANDEMIC

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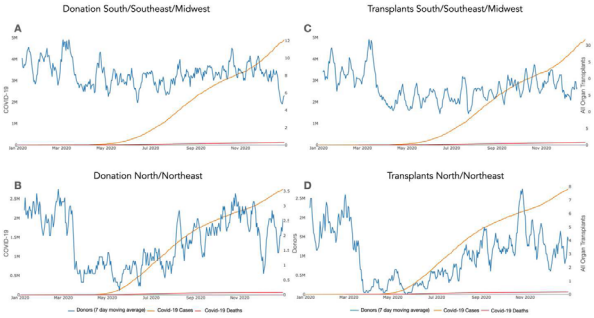
Background and Aims: Brazil is one of the leading countries in organ transplantation. In 2019 there were 9,187 solid organ transplants. Although the national program is funded by the Brazilian universal public health system, geographical disparities still exist, resulting in limited access and inferior outcomes in lower-income macro-regions. The first case of COVID-19 in Brazil was confirmed on February 26th, 2020, and, since then, Brazil is one of the most affected countries worldwide. As experienced by other countries, the burden of the COVID-19 pandemic in the Brazilian health-care system has been considerable and extended to organ donation and transplantation activities.
Methods: We analyzed nationwide data from the Brazilian Organ Transplantation Association and Health Ministry on COVID-19 cases, organ donations, and solid organ transplants performed from January 1st to December 31st 2020. We used a 7-day moving average to compare the impact of COVID-19 pandemic on Brazilian wealthiest (South, Southeast, and Midwest) with lowest-income (North and Northeast) macro-regions.
Results: After three months of the first confirmed case, Brazil was on the outbreak peak and had suffered a decrease of 19% and 30% in organ donation and transplantation, respectively. When analyzed by macro-region, a discrepancy was found. South, Southeast, and Midwest states had decreased by 13% and 24% in organ donation and transplantation since the outbreak started in Brazil. Otherwise, North and Northeast states had reduced by 40% and 53% in organ donation and transplantation, respectively.
Conclusions: In Brazil, the pandemic exacerbated geographical disparities, and most centers have reduced or stopped activities. In order to keep the transplant soul alive in Brazil, special attention should be focused on regions with less economic resources, with rescue measures being taken, both for the time of the pandemic and for the long-term consequences for the national health system.



POS424 IMPACT OF SARS-COV-2 INFECTION IN SOLID ORGAN TRANSPLANT RECIPIENTS: THE REPORTING DATA AT THE END OF A DIFFICULT YEAR IN ITALY.

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Background: the year 2020 will be remembered around the world as the year of the COVID pandemic. To date (February 15, 2021), Italy is the fifth European country for total confirmed cases (2,721,879) and the second for reported deaths (93,577). Solid organ transplant recipients (SOTRs) were shown to be more exposed to infection but even more those on the waiting list. Consequently, the transplant activity continued throughout the year, as life-saving, reduced by only 10% compared to the previous year. Our study aimed at quantifying the impact the SARS-CoV-2 infection had on SOTRs at the end of this year and before the start of the vaccination campaign in Italy.
Methods: we cross-referenced the data of Italian National Institute of Health-integrated surveillance system with those inside the Information Transplantation System in order to assess the cumulative incidence (CI) and the outcome of SARS-COV-2 infection in SOTRs, providing data also relating to the two peak periods that occurred. The outcome of solid organ transplants (SOTs) carried out throughout the year were described too.
Results: The CI of SARS-CoV-2 infection in SOTRs was 4.96%, higher than in COVID+ Non-SOTRs [CI 3.63%, $p < 0.001$]. The CI by kind of organ transplant was confirmed to be lower for liver [CI 3.76%; Incidence Rate Ratio 0.68, 95%Confidence Interval [Conf.Int.(0.61–0.74), $p < 0.001$] while no differences were observed among the others. The CI of SARS-CoV-2 infection in SOTRs who underwent SOT during the year (6.4% of the total SOTs performed in 2020) was higher compared to the long-lasting ones (CI 6.37%, $p < 0.001$) but only 18% became infected less than 45 days after transplantation (CI 1.20%). The SOTRs lethality rate was much more higher than Non-SOTRs (CI 12.63% vs 3.63%, $p < 0.001$) but no more risk was observed for SOTRs transplanted in the year (9.04%, $p = 0.11$). The lowest lethality rate was observed in liver recipients (8.33%) with an Odds Ratio of 0.41 [95% Conf.Int. (0.30–0.57)] with reference to kidney.
Conclusions: SARS-CoV-2 infection had a greater impact on SOTRs compared to Non-SOTRs but the different CI observed during the first peak period faded at the end of the year. The lethality rate showed that this category is actually more fragile but no additional risk was observed for SOTs performed during the pandemic confirming their safe continuing.

POS425 THE IMPACT OF TRANSPLANT TYPE, AGE AND IMMUNOSUPPRESSION ON POST COVID-19 INFECTION SURVIVAL: A SINGLE CENTER UNITED STATES PROSPECTIVE COHORT STUDY.

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Background: COVID-19 was declared a pandemic in March 2020 and has taken the globe by storm since. The effect of transplant status on post COVID-19 outcomes has been conflicting. Aim of the study was to assess the effect of transplant status and organ, demographics and treatments on COVID-19 survival.
Methods: Study period 2.2020- 2.18.2021. UAMS Medical Center is the only transplant center for the State of Arkansas (AR). After obtaining institutional IRB approval, a prospectively populated de-identified RedCap database was developed, recording variables including demographics, comorbidities, immunosuppression, patient hospitalized status and treatment modalities; the latter evolving to include treatments such as monoclonal antibodies and convalescent plasma. The cohort was split into survivors and fatalities and further stratified for transplant type [kidney (KT) vs. liver (LT)], and age groups. The cohorts were studied for the effect of transplant type, age group and other recorded covariates on COVID-19 specific fatality. The subcohorts were compared to the AR and US COVID-19 fatality rates.
Results: (n = 103; 76 KT; 27 LT) Compared to the general (US) population, KT status had a 6.98 RR (95%CI 3.8–12.9). LT status effect was insignificant (p = 0.452). Comparison to the local (AR) population reflected the same. Overall case-fatality rate was 9.7%: 11.8% KT vs. 3.7% LT; RR 2.8 (95%CI 0.42–18,465) vs. 0.8 (95%CI 0.63–1.02, p = 0.22). Age >60 RR was 12.17 (95%CI 2.4–61.49; p = 0.000). Covid-19 specific death rate on transplant recipients >60 years was 26.7% (LT, 12.5%; KT, 38.9%).
Lymphocyte depletion was not associated with increased mortality. Tacrolimus was protective (RR 0.2; 95%CI 0.05–0.83, p = 0.016), contrary to cyclosporine (RR 7.54; 95%CI 1.49–38.31, p = 0.006) and belatacept (RR 7.5; 95%CI 1.09–51.67, p = 0.019).
Conclusions: Even though not probably powered enough to show significant effect on the relative death risk between the KT & LT recipients within our cohort, our study showed that the KT status was associated with a 6-fold COVID-19 related relative death risk in relation to the local and general US population. LT status did not trigger this effect. Age>60 was associated with 12-fold relative death risk. In our patient population, tacrolimus was associated with decreased RR of fatal COVID-19 infection.

POS426 NEGATIVE PRESSURE TREATMENT OF WOUND AND ABDOMINAL INFECTIONS AFTER SOLID ORGAN TRASPLANTATION: BOLOGNA TRANSPLANT CENTER EXPERIENCE.

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Background: Solid Organ Transplantation (SOT) recipients are at high risk of severe abdominal and wound infections. In particular they are more likely to be affected by multi drug resistant bacteria (MDR) infections which are associated with more elevated morbidity and mortality. The relatively newer techniques like Negative Pressure Wound Therapy (NPWT) using the Vacuum Assisted Closure (VAC) are very promising in the management of wound and abdominal infections.
Methods: We performed a retrospective observational study that included all SOT recipients who required the use of NPWT after transplant or elected surgery in our center, between January 2010 and December 2019.
Results: NPWT was applied to 46 SOT recipients, divided as follows: liver transplant (n = 32), kidney transplant (n = 5), combined liver-kidney transplant (n = 3), bowel transplant (n = 1) and multi-visceral transplant (n = 3). NPWT was placed after surgery for hemoperitoneum (n = 3), biliary fistula (n = 8), intestinal obstruction (n = 4), acute pancreatitis (n = 2), intestinal perforation (n = 9), peritonitis (n = 10), wound and wall infection (n = 8) or other causes (n = 10). In 10 cases a suprafascial NPWT was placed, while in 36 cases the NPWT was used for open abdomen; of the latter, 77.8% (n = 28) of patients had an abdominal infection, with positive tests for MDR bacteria in 72.5% of cases (n = 26). The median *Comprehensive Complication Index* (*CCI*) was 69.8 and 90-day mortality was 21.7% (n = 10), of which 86% (n = 12) for sepsis. There were no complications related to the placement of the NPWT. The median duration of NPWT was 34 days (iQR 17–49). A small group of patients (15.25%) required a skin graft, prosthesis or skin suture; and 15.2% continued NPWT after hospital discharge.
Conclusions: NPWT is a valid and safe treatment option in the management of SOT recipients affected by surgical wound infections and abdominal infections.

POS427 INTEREST IN AND EXPOSURE TO TRANSPLANT SURGERY AMONG MEDICAL STUDENTS AND TRAINEE DOCTORS

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Background: There is an increasing need for more transplant surgeons as the number of patients requiring transplantation continues to rise and the specialty continues to expand. The aim of this survey was to determine the level of interest in and exposure to abdominal transplant surgery among medical students and trainee doctors.
Methods: A 10-question online survey was sent to all medical students, foundation doctors and general surgery trainees in one Scottish deanery. Responses were anonymised and analysed in two groups; group 1 included medical students and foundation doctors and group 2 included general surgery trainees.
Results: There were a total of 40 respondents (31 in group 1, 9 in group 2). Overall, 3 (7.7%) respondents were interested in a career in transplant surgery. The most common reason against choosing a transplant surgery career in group 1 was little or no previous exposure to the specialty, while in group 2 it was seen as too competitive (Figure 1). The most common reason for interest in the specialty in both groups was the life saving surgery. All of the respondents in group 1 and 44.4% in group 2 did not know the UK training pathway for transplant surgery. The majority of respondents had never had a placement in transplant surgery (93.6% in group 1; 55.6% in group 2), however most respondents believed that a placement would be beneficial (92.6% in group 1; 71.4% in group 2), the reasons for which are shown in Table 1.
Conclusion: Exposure to transplant surgery at medical school and in the early years of medical training is poor and seen as the main reason for not considering it as a career. There is poor knowledge about the transplant training pathway. Most trainees believe they would benefit from a placement in transplant surgery regardless of their chosen career. Greater exposure at an early stage may lead to improved interest in the specialty.

Figure 1: Reasons against choosing a career in transplant surgery

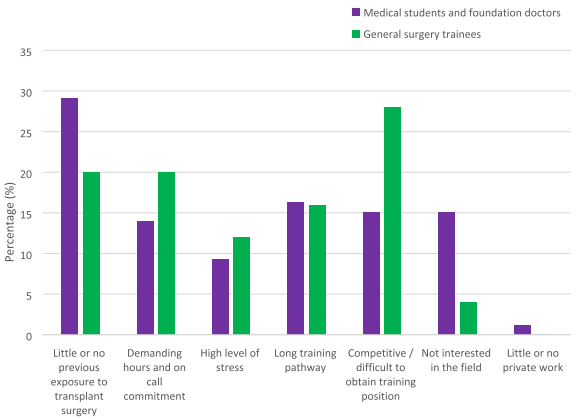

Table 1

Do you think a placement in transplant surgery would be beneficial to you? Please specify why. *(Free text responses were collated into themes)*	All respondents	Medical students and foundation doctors	General surgery trainees
Yes	30 (88.2%)	25 (92.6%)	5 (71.4%)
Interesting	3	3	0
To understand what transplant patients go through	3	3	0
To help decide about a career in transplant	6	6	0
To get exposure to the specialty	14	13	1
Likely to encounter transplant patients in other specialties	7	5	2
Transferable skills to other specialties	7	4	3
No	4 (11.8%)	2 (7.4%)	2 (28.6%)
Too niche	1	1	0
Will not be caring for transplant patients	2	1	1
Can gain insight into the specialty through reading	1	0	1

POS428 AN OVERVIEW OF EHEALTH DELIVERED INTERVENTIONS FOR PATIENTS AFTER SOLID ORGAN AND STEM CELL TRANSPLANTATION: A SCOPING REVIEW.

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Background and aims: EHealth delivered interventions are increasingly considered as part of follow-up of solid organ transplant (SOT) and stem cell transplant (SCT) patients. We aimed to provide an overview and description of eHealth delivered interventions used in SOT and SCT applied in trial or real world settings.
Methods: A scoping review was used. The search strategy included PubMed, EMBASE, Cochrane Library, Web of Science Core Collection and CINAHL databases until January 2020. Data abstraction included eHealth type, purpose, platform, user interface, setting, age group and type of transplantation. Descriptive statistics were applied.
Results: 12.774 references were screened, 371 full-text papers identified resulting in 99 papers meeting the eligibility criteria. This corresponded to 81 unique eHealth delivered interventions. 61 interventions (75.3%) corresponded to telehealth and 20 to interactive health technology (24.7%). The interventions were mainly used for behaviour counselling (n = 56), self-monitoring (n = 35) and/or education purposes (n = 25). MHealth was the most common platform, more specifically a patient monitoring device (n = 37), website (n = 17) the most common user interface. Most interventions were used in the trial world setting (n = 53; 65.4%). Most interventions were for adults (n = 45; 55.6%), 27 aimed at a mixed or undefined population (33.3%) and 9 reserved for pediatrics (11.1%). Interventions in SOT (n = 66; 81.5%) were more common compared to SCT (n = 15; 18.5%) (Table 1).
Conclusion: Around 70 000 papers have been published concerning eHealth since 1995, with the majority of articles published in the past 10 years, showing the growing interest in eHealth. Our scoping review has identified that many of these refer to transplantation follow-up. Future research on subsequent research questions such as effectiveness, implementability, usability, acceptability and feasibility of the interventions is definitely warranted.

		Interventions aimed at Adult Transplantation recipients (N = 45; 55.6%)	Interventions aimed at Pediatric Transplantation recipients (N = 9; 11.1%)	Interventions aimed at mixed/undefined age Transplantation populations (N = 27; 33.3%)
eHealth type				
	Telehealth	N = 35 (77.8%)	N = 6 (66.7%)	N = 20 (74.1%)
	Interactive health technology	N = 10 (22.2%)	N = 3 (33.3%)	N = 7 (25.9%)
Purpose*				
	Behaviour counselling	N = 34	N = 5	N = 17
	Self-monitoring	N = 22	N = 3	N = 10
	Clinical-decision aid	N = 2	N = 1	N = 0
	Reminder	N = 6	N = 1	N = 7
	Educational	N = 13	N = 3	N = 9
Platform*				
	mHealth	N = 53	N = 9	N = 31
	Computer	N = 19	N = 2	N = 11
User interface*				
	Application	N = 8	N = 3	N = 5
	Website	N = 8	N = 3	N = 6
	Text-message	N = 6	N = 1	N = 7
	Videocounselling	N = 10	N = 2	N = 4
	Audio-call	N = 8	N = 0	N = 2
	Diagnostic imaging	N = 2	N = 1	N = 1
	Electronic health record	N = 2	N = 0	N = 4
	E-mail	N = 4	N = 0	N = 1
	Social media	N = 0	N = 0	N = 1
Setting				
	Trial world	N = 33 (73.3%)	N = 2 (22.2%)	N = 18 (66.7%)
	Real world	N = 9 (20%)	N = 7 (77.8%)	N = 8 (29.6%)
	Mixed	N = 3 (6.7%)	N = 0	N = 1 (3.7%)
Type of transplantation				
	Solid organ transplantation	N =36 (80%)	N = 5 (55.6%)	N = 25 (92.6%)
	Stem cell transplantation	N = 9 (20%)	N = 4 (44.4%)	N = 2 (7.4%)

*One single eHealth delivered intervention could be classified in several categories, so the total does not equal 100%.

POS429 FRAMEWORK FOR SOLID ORGAN TRANSPLANTATION IN EUROPE DURING COVID-19 PANDEMIC

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Background: Since the effect of COVID-19 pandemic on solid organ transplantation is unclear, an online survey on the specific framework of leading European transplant centers (n = 155) in 31 European countries was distributed between April 24 - May 15, 2020.
Methods: A questionnaire was designed to collect information on (i) restrictions in solid organ transplantation, (ii) protective measures, (iii) (non-) governmental information politics, and (iv) personal opinion on how to deal with solid organ transplantation during COVID-19 pandemic.
Results: The response rate was 37.4% (58/155). (i) Overall, in 84.5% an effect of COVID-19 pandemic on solid organ transplantation in Europe was reported. In 49% of these centers, an actual limited capacity was stated, in 51% the reason for restricted resources was strategic preparedness. As a result, solid organ transplantation was totally or partially suspended for several weeks. (ii) 93.1% of centers implemented protective measures against COVID-19. (iii) (Non-) governmental information politics was felt to be adequate in 90%. (iv) A continuation of transplant activities was demanded by 97% of centers.
Conclusion: Results of this survey highly suggest the desperate need of intensive care unit -capacity during COVID-19 pandemic in most countries to guarantee adequate and timely treatment of other patient cohorts.

POS430 EUROPEAN INITIATIVES IN LIVING ORGAN DONATION PROGRAMS

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Background: Living organ donation (LD) provide 40% of all kidneys and almost 20% of all livers transplanted in Europe. The majority of the European countries consider LD as complementary to the deceased donation meanwhile LD is the only source for organ for transplantation for more other countries. Despite this diversity here is a common understanding, complying also the directive of the EU council, to provide protection and safety for the living donors and to perform high quality in LD procedure. To unify the quality and safety standards, several European initiatives have gathered EU countries to perform actions to reach such consensus.
Methods: Several consortiums have been created and worked together in the identification of the following field of inters in LD (fig 1)
-Legal aspects
-Ethical aspects
-Living donors' safety and protection at medical and psychosocial level
-Registration practice
-Identification of recommendation for high quality practice in LD
Assessment questionnaires, evaluation of current practice in LD, an up- to 16 years post donation follow-up of the living donors, and the design of a

registry database model; have been the means of the projects development.
Results: To assure the safety and the protection of the living donors, common European recommendation on the legal and ethical aspects have been developed. The data registry model has been created and used to monitor the living donors. Up to day, follow-ups data at psychological aspects have been registered for approximately 800 European living donors; meanwhile follow-up data for the medical outcome have been collected for more than 30.000 European living donors.
Conclusions: There is a need for common quality and safety standards for the LD at European level. Joining efforts form EU countries is the needed methodology to reach such consensus. A European registry is the needed tool to monitor the follow-up of the living donors giving transparency of the procedures.

POS431 PERCEPTIONS ON THE COVID-19 VACCINE: A PILOT STUDY

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Background: The COVID-19 pandemic has resulted in over 120,000 deaths in the UK, and severely impacting and suspending the Renal Transplant Programme at the Royal Free Hospital (RFH). The successful roll out of the vaccination programme enabled end-stage renal patients to enter into the 1st phase of delivery. It was noted that uptake was variable amongst dialysis units. The implication of not vaccinating but proceeding to transplantation remains unclear. Pilot data from a staff opinion survey from the RFH renal unit on vaccination and transplantation are reported. We examine the perceived reasons and implications on declining the vaccine.
Methods: A short survey was emailed to all the staff in the Renal Department.
Results: A total of 362 recipients were sent a survey, with a response rate of 13.3% ($n = 48$) consisting of 43 individuals who work with patients and 5 which included scientist and administrative personnel. Ethnicity consisted of white ($n = 21$), BAME ($n = 17$) and other ($n = 10$). In our department 93.75% of individuals received the vaccine, with 6.25% declining it. Twenty-five of the 48 responders were clinicians, including renal physicians and renal transplant surgeons of all grades. Amongst the clinicians, there was a general consensus that the entire transplant waiting list should be OFFERED the vaccine ($n = 25$). However, there was a relative mixed response, but slight inclination towards disagreeing for the vaccination being a REQUIREMENT in order to be active in the waiting list (agreeing $n = 8$ vs disagree $n = 13$). Furthermore, declining the vaccine was not viewed as a need to be removed from the waiting list (agree $n = 5$ vs disagree $n = 16$). Clinicians felt that this should be highlighted in the medical records (agree $n = 18$ vs disagree $n = 4$)
Conclusion: The pandemic has caused immense pressure on our Renal Service. The vaccine has been viewed as an way out of lockdown, and with it the return of societal/healthcare norms. We have demonstrated varied opinions within our renal healthcare professionals. It is clear that a reasoned risk benefit discussion of vaccine uptake with patients should happen. Further work with patient groups is the next logical step prior to improving vaccine delivery.

POS432 ORGAN DONATION AND TRANSPLANTATION DURING COVID-19 IN THE UK: CHALLENGES, LESSONS AND OPPORTUNITIES FOR FUTURE

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Background and Aims: COVID-19 has impacted organ donation and transplantation (ODT) around the world. In this research, we considered the views of professionals involved with ODT activity in the UK in relation to the countrywide response during the first surge of COVID cases in spring 2020.
Methods: A 22 item survey was developed and distributed electronically over a 2 week period in May/June. Items required mainly single tick responses with two free text items. A broad range of networks were used to gain input from staff with a range of job roles related to ODT. Items were structured into 5 sections exploring respondent demographics, impact of COVID-19 on ODT programmes, equitable access to healthcare resources during the pandemic, absolute conditions under which transplant activity should resume, and the transplant community response. Statistical analyses (version 26) were performed in SPSS and qualitaive comments analysed thematically in Nvivo (version 12).
Results: Three hundred and fourteen people accessed the survey and engaged with at least 50% of items (85% completed all items). Collectively, respondents covered all ODT regions across the UK. The majority of respondents were employed as nurses (30%) and transplant physicians (24.2%). The immediacy of impact of the pandemic on ODT activity was evident in all but one region. There were mixed views as to whether resource allocation for ODT had been equitable. Qualitative findings highlighted that disparity was related to perspectives on how principles of maximisation are realised with equity of opportunity of all patients. Notable strengths of the countrywide response were identified, particularly the donation and transplant community acting responsibly and proportionately (51.6%) and providing access to up to date information and data (43.9%).
Conclusions: The impact of the pandemic on non COVID related care should inform recovery plans that retain trust in the enterprise of transplantation as a whole. There is an opportunity to think collaboratively about how we further embed ethical values as we develop new pathways of care that take account of and respond to the additional risks that COVID-19 brings to particular age groups and communities.

POS433 EVALUATING THE IMPACT OF CLINICAL LEADS FOR UTILISATION IN THE UNITED KINGDOM IN ADDRESSING NATIONAL AND LOCAL BARRIERS TO ORGAN TRANSPLANTATION

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Background: There are many challenges to maximising the potential for transplantation in the United Kingdom. The introduction of opt-out legislation in the UK is expected to lead to over 700 additional organs each year. This, combined with COVID-19 and changing donor demographics, led to a need to review/ improve utilisation practices.
Methods: NHS Blood and Transplant invited all UK Transplant Centres to appoint a CLU for a 4-month period, to:
- Assess barriers to utilisation
- Share lessons learned during COVID-19
- Evaluate the effectiveness/ benefits of national utilisation initiatives
- Link with local organ donation leads
- Develop and implement interventions at both local and national levels
- Participate in online meetings to share information and best practice
- Complete two online surveys, outlining progress and evaluating the CLU scheme.

Results: There was a 98% uptake to the invitation, with 46 CLUs appointed within 5 weeks, covering all organs and adult and paediatric units. There was excellent engagement with both the surveys and online meetings. Table 1 summarises the barriers identified.

Table 1. Summary of barriers to local organ utilisation

Categories	Total
Resources	61
Culture	29
Staffing	23
Process	21
Knowledge	16
Imaging	7
Communications	5
Other	5
Technology	4
Data	1
Total	172

All CLUs submitted at least 3 local action plans. The high level of engagement has improved collaboration across all transplant units. National multicentre improvement activity is underway, with a focus on identifying and sharing best practice. Initial responses to the second survey suggest a positive reception for the scheme and that it could have further value if implemented in the long term.

Describe the impact…	1 - Strongly negative	2 - Somewhat negative	3 - Neutral	4 - Somewhat positive	5 - Strongly positive
On Local Utilisation	0	1	0	5	0
On Understanding of Local Issues	0	0	2	2	2
On understanding of National Issues	0	0	1	2	3
On relationships within hospital	0	0	0	6	0
On relationships with other hospitals	1	0	2	1	2
Of a potential long term implementation of the scheme on utilisation in your unit?	0	0	0	4	2
Rate the project organisation	0	0	0	1	5

Conclusions: The CLU appointments have demonstrated that placing local leads in transplant centres can lead to rapid development and innovation. In only 4 months, the CLU scheme has instigated multiple initiatives to maximise the UK's transplant potential and is already providing national and local benefits, particularly in improving collaboration within and between units and sharing best practice.

POS434 SURVEY ON REGIONAL INITIATIVES SUPPORTING FOLLOWUP OF TRANSPLANTED PATIENTS DURING SARS-COV-2 PANDEMIC

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Background: The health emergency linked to the new Coronavirus pandemic has led, also in the transplant field, to a reorganization of hospital and territorial structures with the aim of ensuring healthcare continuity and reducing patient waiting times, thus minimizing the exposure of immunosuppressed subjects to Sars-Cov-2 contagion.
Methods: Thanks to the collaboration of the Regional Transplant Centers, Transplant Centers have been asked to report the initiatives, launched during the Sars-CoV -2 pandemic, to support patients in post-transplant follow-up. In particular, the following aspects were analyzed: 1) new protocols for access to hospital daily outpatient visits in the post-transplant phase; 2) definition of dedicated pathways for chronic patients; 3) promoting the use of telemedicine; 4) development of partnerships with local medicine; 5) changes in staff organization; 6) definition of training courses for the management of the immunosuppressed patient.
Results: Out of a total of 78 centers, we received feedback from 73 of them (93.6%) with the following results: in 90.4% of cases, new access protocols were put in place for follow-up visits, mainly for critically ill or recently transplanted patients (less than a year), and dedicated paths have been defined for chronic patients, postponing visits for the more stable ones; the use of telemedicine systems increased in 80.8% of the centers, in 76.7% collaborations with local medicine were fostered, in 38.3% changes were made in health personnel organization, while in 53.4% tailored training courses were organized.
Conclusions: The situation linked to the pandemic has led to an adjustment of the access routes to hospital outpatient visits for transplant patients, giving priority to the most serious cases and to more recently transplanted patients. Follow-ups in the presence of chronic patients, if in stable conditions, are often delayed, but offset against the use of telematic systems for carrying out remote controls. Collaboration with local doctors was also encouraged, while the availability of adequately trained health personnel should be enhanced.

POS435 PILOT OBSERVATIONAL STUDY TO OBTAIN FEEDBACK ON MEDICATION COUNSELLING POST HEART & LUNG TRANSPLANT DURING THE COVID -19 PANDEMIC

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Background: Increasing patients' knowledge on their medicines is crucial in ensuring the effectiveness of treatment in heart and lung transplant patients. Pharmacist delivered medication counselling can help improve adherence to treatment.
Methods: All patients receive 3 comprehensive education sessions regarding their medications A pilot observational study was undertaken, patients were sent a short questionnaire to gain insight into their experience managing medications after discharge from hospital.
Results: 34 participants (23 male) at a median of 8.4 (IQR: 6–11.9) months post-heart (15) and lung (19) transplant were recruited between the 15th–21st February. 55% (19) patients responded to the survey.
95% patients felt confident about taking their medications at the point of discharge.
Results are summarized in the table below

Question	Strongly disagree n (%)	Disagree n (%)	Neither agree nor disagree n (%)	Agree n (%)	Strongly agree n (%)
I understand why I'm taking all these medications and what each one is for	0 (0)	0 (0)	1 (5)	7 (37)	11 (58)
I knew what to do if I forgot to take my anti-rejection medication	0 (0)	0 (0)	1 (5)	5 (26)	13 (69)
I received appropriate advice and support regarding the side-effects of my newly initiated medications	0 (0)	2 (11)	1 (5)	5 (26)	11 (58)
I was given time to ask any follow-up questions that I had prior to leaving hospital	0 (0)	1 (5)	1 (5)	2 (11)	15 (79)
I felt supported by a follow-up review in clinic with a pharmacist	0 (0)	0 (0)	0 (0)	6 (32)	13 (68)
I was sign-posted to various online resources to go back to for more information	0 (0)	3 (16)	7 (37)	6 (32)	3 (16)
I was given time to ask any follow-up questions that I had in clinic	0 (0)	1 (5)	0 (0)	7 (37)	11 (58)
I felt like my family/ next of kin were included in the discussions post- transplant	2 (11)	5 (26)	2 (11)	7 (37)	3 (16)

Table. Continued.

Question	Strongly disagree n (%)	Disagree n (%)	Neither agree nor disagree n (%)	Agree n (%)	Strongly agree n (%)
I felt I was provided with sufficient information regarding my medications post-transplant	0 (0)	0 (0)	0 (0)	7 (37)	12 (63)

94% of patients stated that they would find it useful to use an app to record their medication list and observations such as blood pressure and temperature.

Conclusions:
Current practice is popular with patients however, there is scope for delivering this in other ways. This has helped identify the potential for an IT tool to support patients' knowledge of their medicines post-transplantation.

POS436 SOLID ORGAN TRANSPLANT RECIPIENTS' RISK PERCEPTIONS, SHIELDING BEHAVIOUR AND PUBLIC TRUST DURING THE COVID-19 PANDEMIC

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Introduction: Solid organ transplant (SOT) recipients are particularly impacted by the COVID-19 pandemic. In order to provide effective communication to SOT recipients, it is important to understand their perceptions of risks relating to COVID-19, preventive behaviour and concerns. Our aim was to assess these perceptions and concerns in the SOT recipient population.

Methods: All adult SOT recipients at a regional transplant centre were invited to complete a secure online survey, between 3rd–31st July 2020. The survey included demographic, transplant, shielding and health items. In addition, a modified version of the World Health Organisation COVID-19 survey tool was used.

Results: 826/3839 recipients completed the survey. The demographic and health characteristics are displayed in Table 1. Shielding advice was followed by 96% (n = 793). The probability of contracting COVID-19 was perceived as extremely or somewhat likely in 26.9%, and a high level of knowledge regarding how to protect themselves from COVID-19 was reported on a visual analogue scale (94/100, 0=Don't know at all, 100=know very well). The median perceived susceptibility to infection was 78/100 (0=not at all susceptible, 100=very susceptible) and respondents believed they would be severely unwell with COVID-19 (91/100, 0=not severely unwell, 100=severely unwell) (Table 2). 201 (24.4%) responders reported their access to healthcare had been compromised during shielding, putting them at potential risk. Compared to local health care facilities and government, SOT recipients had the greatest trust in their transplant centre to manage COVID-19 well (95/100, 80-100).

Conclusion: Perceived susceptibility to severe COVID-19 may contribute to higher shielding adherence, which consequentially reduces their perception of risk. High confidence in the professionals at the transplant centre was reported. Transplant centres should play an important role communicating evidence-based information to this patient group and preserving access to healthcare.

Table 1

	Survey responders (n=826)
Age, median (IQR)	60 (50-67)
Female	355 (43%)
Type of transplant	
Liver	595 (72.2%)
Lung	23 (2.8%)
Heart	66 (8.0%)
Kidney	161 (19.5%)
Pancreas	2 (0.1%)
Time since transplant	
<6 months	13 (1.6%)
6 months-1 year	45 (5.5%)
1-2 years	74 (9.0%)
2-5 years	188 (22.8%)
>5 years	503 (61.0%)
Shielded during pandemic	791/824 (96.0%)
Diabetic	140 (17.0%)
Obese	267 (32.0%)
Dialysis	6 (0.7%)
Heart disease	74 (9.0%)
Chronic lung disease	65 (7.9%)
Current smoker	38 (4.6%)

Table 2. Solid organ transplant perceptions of risk, knowledge and confidence.

	Responders (n=826)
Do you know people in your immediate social environment who are or have been infected with COVID 19?*	
Yes, tested and the result was positive	47 (5.7%)
Yes, suspected but not confirmed by a test	43 (5.2%)
No, tested and the result was negative	29 (3.5%)
No	655 (79.5%)
Don't know	50 (6.1%)
What do you consider to be your own probability of getting infected with COVID-19?*	
Extremely likely	77 (9.3%)
Somewhat likely	145 (17.6%)
Neither likely nor unlikely	228 (27.7%)
Somewhat unlikely	251 (30.5%)
Extremely unlikely	123 (14.9%)
How susceptible do you consider yourself to be to an infection with COVID-19?* *0-100 Scale, 0= Not at all susceptible 100=Very susceptible* (IQR)	78 (50-95)
How severe do you think contracting COVID-19 would be for you (in other words how seriously ill do you think you would become)?* *0-100 Scale, 0= Not severely unwell 100=Very unwell* (IQR)	91 (80-100)
Do you know how to protect yourself from COVID-19?* *0-100 Scale, 0= Don't know at all 100=Know very well* (IQR)	94 (83-100)
For me avoiding an infection with COVID-19 in the current situation is? *0-100 Scale, 0= Extremely difficult 100=Extremely easy* (IQR)	75 (50-88)
How much confidence do you have in the below individuals and organisations that they can handle COVID-19 well?* *0-100 Scale, 0= No confidence 100=Very confident* (IQR)	
The specialist doctors and nurses of the transplant unit	95 (80-100)
Your own family doctor/GP	75 (50-90)
Your local hospital	75 (50-90)
Department of Health	51.5 (41-80)
The Government	50 (22-72)
Has your access to healthcare been compromised due to shielding, putting you at potential risk?	
Yes	201 (24.4%)
No	623 (75.6%)

* Questions adapted from the World Health Organisations (WHO) tool for behavioural insights on COVID-19 to assess risk perceptions, behaviours, trust and knowledge.

POS437 T REGULATORY CELLS IN PATHOGENESIS OF CORNEAL GRAFT REJECTION

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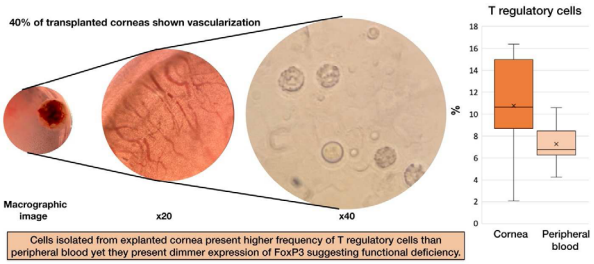
Background: Cornea is the most frequently and successfully transplanted tissue worldwide. Even though cornea is an immune privileged tissue, rejection rates are as high as 30%, and cause significant clinical burden. Immunosuppressive environment of the eye is supported by avascularity of the cornea, expression of immunomodulatory cytokines and molecules, and induction of antigen-specific regulatory T cells (Tregs). The long-term survival of grafts is mediated by allo-specific T regulatory cells, and recent studies indicate Tregs dysfunction in corneal graft rejection models. We aimed to evaluate Tregs in human corneas from patients qualified for retransplantation.
Methods: In the study we analyzed cells isolated from rejected corneal grafts from patients qualified for retransplantation as well as peripheral blood mononuclear cells ($n = 14$). The samples were analyzed by flow cytometry for lineage markers, additionally, for peripheral blood, extended phenotype of Tregs, memory, migration and apoptosis antigens were evaluated. Peripheral blood from healthy volunteers served as controls.
Results: In rejected grafts infiltrating cells consisted predominantly of effector T cells. We observed an increased frequency of T regulatory cells in the site of rejection (mean=10.8%) compared to peripheral blood (mean=6.7%). Tregs from the cornea presented decreased Foxp3 and Helios expression. Compared to healthy controls, in peripheral blood of graft rejectors lower frequency of Foxp3high Tregs was found, while overall peripheral Tregs had higher expression of suppressive markers CTLA-4 and TIGIT. Additionally, conventional B cells and follicular Tregs were increased.
Conclusions: Tregs in rejected human corneas are increased in frequency however their phenotype indicates impaired suppressive function. Elevated expression of CTLA-4 and TIGIT on peripheral Tregs, as well as the presence of follicular Tregs seems to be insufficient to limit the alloimmune response to grafted cornea.



POS438 PANCREAS TRANSPLANTATION IN BLACK, ASIAN AND ETHNIC MINORITIES-A SINGLE CENTRE EXPERIENCE IN THE UK

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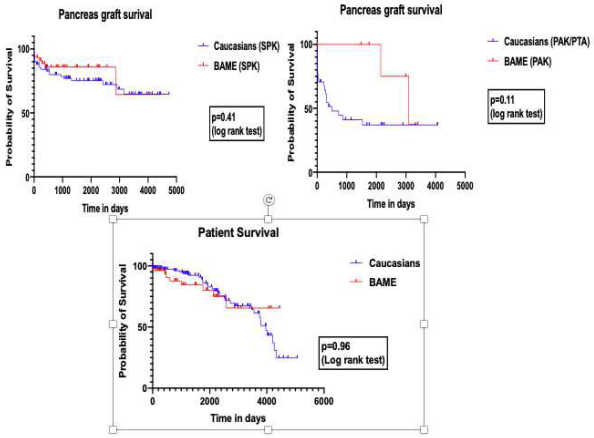
Background & Aims: It is reported that ethnic disparities in the outcomes after SPK transplantation still exist. The influence of ethnicity on the outcomes of pancreas transplantation in the UK has not been studied. We therefore investigated the influence of ethnicity in patients undergoing pancreas transplantation at our center.
Methods: A retrospective analysis of 171 pancreas transplant (SPK/PAK/PTA/ Re-transplants) recipients (Caucasians=118/ Black Asian Ethnic Minorities, BAME=53) from 2006 to 2020 was done. The median follow-up was 80 months. Patient & graft survival, rejection rate, steroid free maintenance rate, HbA1C, weight gain & the incidence of secondary complications of diabetes post-transplant were compared between the groups. After Holm-Sidak correction for multiple comparisons, p <0.003 = significant. Immunosuppression consisted of alemtuzumab induction and steroid free maintenance with tacrolimus and MMF.
Results: There was no difference between the groups in terms of donor age, donor BMI, proportion of DCD donors, proportion of sensitized recipients (CRF>5%), HLA mismatches, recipient age and proportion of PAK/PTA. Caucasians had all re-transplants ($n = 11$) & BAME had no PTA. We noted equivalent pancreas graft & patient survival in BAME (Fig 1). BAME had more % of type-2 DM pre-transplant (BAME=30.19% vs. Caucasians=0.85%, $p < 0.0001$), and had similar access to transplantation once waitlisted (Median waiting time, Caucasians=232 days vs. BAME=217 days, $p = 0.96$), although, Caucasians had a higher % of pre-emptive SPK transplantation (Caucasians=78.5% vs. BAME=0.85%, $p < 0.0001$). Despite equivalent rejections & steroid usage, BAME gained more weight (Median % weight gain, BAME=7.7% vs. Caucasians=1.8%, $p = 0.001$) but had similar HbA1C (functioning grafts) at 3, 12, 36 & 60-months post-transplant. Caucasians had a higher incidence of secondary complications of diabetes (Caucasians=33.8% vs. BAME=13.5%, p = ns).
Conclusions: BAME & Caucasians had comparable overall patient and pancreas graft survival. BAME had a higher proportion of pre-transplant type 2 DM and had similar access to transplantation once waitlisted, although there was a higher proportion of pre-emptive SPK transplantation in the Caucasians. Despite equivalent rejections & steroid usage, BAME gained more weight



POS439 PLASMA CONCENTRATION OF SELECTED INFLAMMATORY MARKERS IN TYPE 1 DIABETIC KIDNEY OR PANCREAS-KIDNEY RECIPIENTS

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Background: In patients with type 1 diabetes (T1D) injury of cardiovascular system is related to increased inflammatory status. Since patients after simultaneous pancreas-kidney transplantation (SPK) present slower progression of atherosclerosis, lower cardiovascular complications rate, and reduced mortality, decreased inflammatory status should be observed in them compared to T1D patients after kidney transplantation (KTx).
The aim of the study was the analysis of plasma concentration of selected inflammatory markers in patients with T1D after SPK or KTx.
Methods: The study included 21 patients with end-stage renal disease in the course of T1D after SPK and 18 patients after KTx. The control group consisted of 15 non-diabetic kidney recipients. In all patients clinical parameters, blood glycated hemoglobin (HbA1c), serum creatinine, and selected plasma inflammatory markers were assessed.
Results: SPK and KTx groups did not differ as regards gender, age at the time of transplantation (Tx) and the study, duration of T1D and dialysis therapy prior Tx, follow-up after Tx, BMI, and serum creatinine. Blood HbA1c was lower in SPK group [5.27% (5.14–5.66)] compared to KTx [7.20% (6.31–7.72); $p < 0.001$]. Plasma concentration of interleukin-1β (IL-1β),

matrix metalloproteinase-8 (MMP-8), resistin, tumour necrosis factor-α (TNF-α), and YKL40 was lower in SPK group than in KTx (table). The concentration of all the markers in KTx group was higher than in control, whereas in SPK group IL-1β, MMP-8, and TNF-α was comparable to it.
Conclusions: Patients after SPK present lower inflammatory status compared to T1D patients after KTx, often similar to non-diabetic kidney recipients.

Table. Comparison of plasma concentration of inflammatory markers between the groups of patients with T1D after SPK or KTx, and control group (mean ± SD or median and IQR).

	SPK	KTx	Control	p SPK vs. KTx	p SPK vs. Control	p KTx vs. Control
IL-1β [pg/mL]	1.54 (1.12–1.88)	2.24 (1.63–3.07)	1.58 (1.05–1.88)	<0.01	0.97	<0.01
MMP-8 [ng/mL]	12.19 ± 1.71	15.45 ± 3.02	11.53 ± 3.09	<0.01	0.77	<0.001
Resistin [ng/mL]	7.97 ± 2.16	10.31 ± 2.63	6.10 ± 0.53	<0.05	<0.01	<0.001
TNF-α [pg/mL]	10.96 ± 2.27	13.78 ± 1.22	10.11 ± 1.87	<0.001	0.44	<0.001
YKL40 [pg/mL]	40.50 (36.10–45.20)	53.25 (49.80α60.30)	33.20 (28.70–38.70)	<0.001	<0.01	<0.001

POS440 WEIGHT GAIN FOLLOWING PANCREAS TRANSPLANTATION IN TYPE 1 DIABETES IS ASSOCIATED WITH A WORSEN GLYCEMIC PROFILE: A RETROSPECTIVE COHORT STUDY

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Background: Information regarding weight changes after pancreas transplantation (PT) in type 1 diabetes (T1D) is scarce. We assessed the weight trajectories post-PT and their relationships with pancreas graft outcomes.
Methods: In this retrospective cohort study, T1D individuals who underwent PT were recruited (T1D-PT; $n = 194$) and divided into three groups according to transplantation data: 1999–2004 ($n = 57$), 2005–2009 ($n = 79$), 2010–2015 ($n = 58$). For weight comparisons, a random sample of T1D without end-stage kidney disease were also recruited during 2015 ($n = 61$; T1D-control). Univariate and multivariate relationships between weight trajectories and graft function were studied.
Results: The median follow-up for the T1D-PT group was 11.2 (6.7–15.3) years. Although at 6 months there was a significant weight loss (65.7 ± 12.4 vs. 64.1 ± 11.4 Kg; $p < 0.001$), a steep increase was seen thereafter (weight at 60 months: 68.0 ± 14.0 Kg; $p < 0.001$). Participants from the last period (2010–2015) showed higher weight gain ($p < 0.001$), outweighing the observed in the T1D-control group (at 60 months: 4.69 ± 8.49 vs. −0.97 ± 4.59 Kg; $p = 0.003$). Weight gain between 6–36 months was independently associated with fasting glucose and HbA1c at 36 months, but also with HbA1c at 60 and decline in c-peptide between 36–60 months ($p < 0.05$). However, in Cox-regression models adjusted by age, sex, cardiovascular disease, pre-transplant body mass index or diabetes duration, the third tertile of weight gain between 6–36 months showed a non-significant increase in the graft failure/dysfunction (HR 1.65 [0.58–4.68]).
Conclusions: In T1D population, weight gain is common post-PT, especially in the last years. This finding associated biochemical markers of graft dysfunction, which need confirmation in further studies.

POS441 THERE IS NO 'WEEKEND' EFFECT IN PANCREAS TRANSPLANTATION

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Background: The weekend effect describes an association of adverse outcomes amongst patients hospitalised during the weekend. The aim of this study was to determine whether pancreas transplants performed during the weekend had inferior outcomes to those performed during weekdays.
Methods: Data were collected from a prospectively maintained database for consecutive pancreas transplant recipients in a single centre. The outcomes measured were patient survival, graft survival, rates of acute rejection, and length of hospital stay.
Results: A total of 159 pancreas transplants were performed (SPK $n = 108$, PAK $n = 33$, PTA $n = 18$) over a 13-year period (Dec 2004-Nov 2017), of which 62 were performed during the weekend (Friday-Sunday) and 97 performed during weekdays (Monday-Thursday).
Recipient and donor demographics (gender, age, BMI), HLA mismatch, Cold Ischaemia Time were similar and statistically non-significant between both 'weekend' and 'weekday' groups.
One-year patient survival was 99% and 97% for 'weekday' and 'weekend' groups respectively (log rank p-value of 0.215). One-year graft survival was 93% and 82% for 'weekday' and 'weekend' groups respectively (log rank p-value of 0.351).
Length of stay was a median of 15 and 17 days for 'weekday' and 'weekend' groups respectively ($p = 0.963$).
Forty-six (29%) patients experienced at least one episode of biopsy proven acute rejection, excluding those with borderline changes. Of these, 29 (30%) and 17 (27%) were in 'weekday' and 'weekend' groups respectively ($p = 0737$).
Conclusion: This study showed that pancreas transplants performed during the weekend do not have any inferior outcomes compared with those performed during weekdays. The absence of the weekend effect on outcomes following pancreas transplantation is reassuring for prospective transplant recipients.

POS442 PATIENT EXPERIENCE IN PANCREAS TRANSPLANTATION – A METHODOLOGICAL APPROACH TOWARDS INNOVATION IN AN ESTABLISHED PROGRAM

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Background: Pancreas transplantation is an established treatment alternative to patients with advanced kidney disease and diabetes mellitus, resulting in a significant improvement in patient's quality of life (QoL). These evaluations have, nonetheless, been based on standardized questionnaires following transplantation, with little focus on individual patient experience.
Methods: We applied a systematic methodology aiming at evaluating whole Patients Journey for Pancreas Transplantation (PT). During a period of 6 months 12 patients and a Multi-disciplinary Team of 13 health care workers (including physicians, nurses, administrative staff, nutritionist, and social worker) participated in the co-creation and review of materials. At the end we describe a quality process comprising various phases:
1. Understand: the professional perspective (clinical practice, literature review) and patient's perspective (own experience, suggestions)
2. Explore: check to what extent insights and suggestions are generalizable
3. Experiment: improve clinical care according to patient experiences
4. Evaluate: define indicators of QoL that matter to patients and defined Patient Reported Experience Measurements (PREM)

Results: During the first and second phases there were three major layers of unmet needs identified and re-evaluated by patients' focus group in a feedback loop:
a Clinical: necessity to establish referral to certain professionals - nutritionist, smoking cessation, psychology.

b Logistics: optimization of circuits – management of patients' time and displacements; improve communication with referral centers;
c Information: Four key periods were identified as critical regarding the type of information required by the patient, and 9 different documents (both clinical and logistical) needed to be developed to fill this gap.
To evaluate the impact of the actions taken and before the introduction of novel material/circuits, a questionnaire will be sent to patients prior to and after the new documents/circuits are established.
Conclusions: We describe a methodology aiming at exploring and improving holistic recipients experience in PT, using a feedback loop between patients' and health care professionals.

POS443 HEMOGLOBIN A1C AFTER PANCREAS-KIDNEY TRANSPLANTATION AS A PREDICTIVEMARKER FOR ENDOCRINE FUNCTION FAILURE IN PANCREATIC GRAFTS.

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Background: Pancreas transplantation is the only treatment that establishes normal glucose levels and normalizes glycosylated hemoglobin levels in type 1 diabetic patient. Survival of the pancreatic grafts exceed in the fifth year post-transplant 60%. The aim or our study was evaluate clinical, biochemical and immunological variables of the donor and recipient in order to discover a biomarker of pancreatic graft disfunction.
Methods: The study used information regarding 30 patients (29 simultaneous kidney pancreas transplantation and 1 pancreas retransplant; 8 with pancreatic disfunction, 22 without). Overall, 35 features were evaluated and features were scored according to Relief method, resulting in the usage of 27 features. In this work, 2 machine learning algorithms were used: Tree and Random Forest. Tree is a simple algorithm that splits the data into nodes by class purity. It's a precursor to Random Forest that is an ensemble learning method used for classification and regression. The resampling method used in both methods as the LOOCV validation. Due to the low number of dysfunctional patients, the distance between the transplant and the dysfunction wasn't considered.
Results: As presented in Fig.1A the AUC and classification accuracies were 0.78, 0.88 and 0.87, 0.83 for Tree and Random Forest models, respectively. In the case of the Tree model resulted in the misclassification of 4 patients. In the Decision Tree Diagram presented in Fig.1B, the HbA1c at 6 months post-transplant >5.6 combine with hospital readmission rate >4 allows the correct classification of 95% of non-dysfunction patients. In conclusion, despite the very preliminary nature of this pilot study, these models point to a new category of patients that are more likely to have early loss of endocrine function and recurrence of diabetes *mellitus*. In this group of patient's surveillances should be tighter and immunosuppression assess more closely. These models should be further validated in a larger cohort of patients.

Model	AUC	CA	F1	Precision	Recall
Tree	0,78	0,87	0,86	0,86	0,87
Random Forest	0,88	0,83	0,80	0,86	0,83

Confusion matrix for Tree (showing number of instances)

Actual \ Predicted	NO	YES	∑
NO	21	1	22
YES	3	5	8
∑	24	6	30

FIG 1A

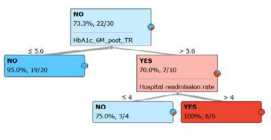

FIG 1B

POS444 ENTERIC CONVERSION AFTER BLADDER-DRAINED KIDNEY-PANCREAS TRANSPLANTATION

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Background: In simultaneous kidney-pancreas transplantation (SPK), bladder (BD) and enteric (ED) are both options for pancreaticoduodenal exocrine drainage. While BD provides good early and long term SPK survival, it is associated with metabolic, urological and pancreatic complications leading to need for enteric conversion (EC). We report our single center experience in SPK patients (pts) who underwent EC after initial BD.
Methods: Between 1990 and 2019, we performed 541 SPK, of which 474 were BD and 67 were ED. We retrospectively studied pts who underwent EC. Indications for EC, time from SPK to EC, resolution of symptoms, complications and pancreas graft survival were analyzed.
Results: 56/474 pts underwent EC (11.8%). The mean time to EC was 4.5 years (yrs) (median 2.58 yrs) with intervals <1 yr = 19 (33.9%), 1–5 yrs =20 (35.7%), 5–10yrs=7 (12.5%), 10–20 yrs =10 (17.8%) . The main indication for EC was dehydration followed by recurrent urinary tract infections (UTI). 4/11 (36.4%) pts who had EC due to UTI had persistent UTI, 7/11 (63.6%) had resolution of UTI; the rest of the pts had complete resolution of the primary indication. 6 (10.7%) pts had surgical complications post EC and 4 required re-exploration with ileoduodenostomy (bailout) operation for duodenal leak. Graft rejection was observed in 3 pts (5.3%) after EC and all were done 6–12 months post-transplant. The mean follow-up after EC was 5.7 yrs (median 4.25 yrs). Overall pancreas graft loss (GL) occurred in 7 pts (12.5%) after EC, including 2 pancreatectomies: 1 for duodenal fistula and 1 for gastrointestinal bleed. The mean interval between EC and GL was 4.1 yrs.

Indications	Total: 56 N (%)	Time to EC from Transplant Mean (yrs)	Pancreas GL N (%) 7/56 (12.5%)
Pelvic Congestion syndrome	3 (5.3%)	15.1	0
Recurrent UTI	11 (19.6%)	4.3	0
Hematuria	6 (10.7%)	8.56	1/6 (16.6%)
Pancreatitis	9 (16%)	4.29	1/9 (11%)
Dehydration	14 (25%)	2	4/14 (28.5%)
Acidosis	7 (12.5%)	2.6	0
Leak	3 (5.3%)	0.33	1/3 (33.3%)
Other	3 (5.3%)	17.3	0

Conclusion: In this single center review of SPK pts with initial BD, the rate of EC was low at 11.8%. Persistent UTI post EC may be due to diabetes-related bladder dysfunction and in isolation should not lead to EC. BD may still be considered as primary drainage in SPK if indicated with the caveat of possible reoperation for EC.

POS445 ENTERIC LEAK IN PANCREAS TRANSPLANTATION: COMPARING HAND-SEWN VS STAPLED ENTERIC ANASTOMOSES

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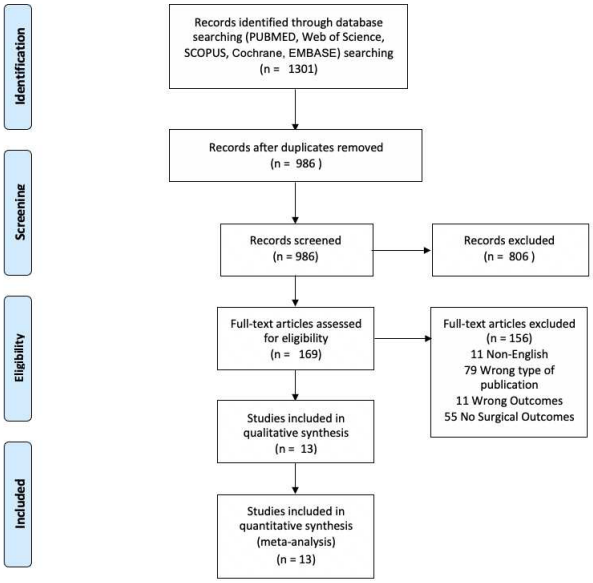
Background: Early pancreatic graft failure in the immediate post-transplant period is often attributed to complications related to surgical technique. Enteric leak (EL) remains a serious complication following pancreas transplantation (PT) with enteric drainage (ED). The aim of our study was to investigate the impact of different surgical techniques (hand-sewn or using a stapling device) on the overall incidence of EL following PT.
Methods: The electronic databases MEDLINE via PubMed, Cochrane, EMBASE, Web of Science and Scopus were interrogated for articles published up to 30/1/2021 reporting data on surgical outcomes in PT with ED in adults; and specific details of the surgical technique used for the enteric anastomosis. The exclusion of studies was in line with PRISMA guidelines. 2 independent authors extracted data on cohort demographics, surgical technique, and complications.
Results: Out of 986 studies screened (after removal of duplicates), 13 studies met the inclusion criteria, 4 of which reported stapled anastomosis and 10 reported hand-sewn anastomoses (1 study reported both). These studies included 1079 recipients with 883 hand-sewn and 196 stapled anastomoses. 928 were part of a simultaneous pancreas and kidney (SPK) transplantation, 79 were PT after kidney (PAK) transplantation and 72 were solitary PT (SPT), of which 35 were re-transplants. 2/13 studies did not report the arrangement of their enteric anastomosis, with most centres

preferring side-to-side (94%; $n = 948/1008$). EL was reported in 2.55% ($n = 5$) and 3.51% ($n = 31$) of recipients with stapled and sutured anastomosis respectively (OR 1.39, 95% CI: 0.568–3.341; $p = .660$).
Conclusions: EL following PT is an uncommon complication affecting 3.45% of pancreas recipients. Current evidence does not favour a surgical technique between stapled vs hand-sewn anastomosis in PT with ED to prevent EL. Future studies reporting outcomes relevant to PT should include detailed methodology on surgical techniques used.



POS446 SURGICAL COMPLICATIONS AFTER PANCREAS TRANSPLANTATION – SINGLE CENTRE EXPERIENCE

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Background: Pancreas transplantation is a well established method of treatment for patients with complicated type 1 diabetes. Because of severe complications of diabetes, the number of pancreas transplant recipients with type 2 disease grows steadily. Pancreas transplant procedure is associated with a high risk of surgical complications that affect graft and recipient survival.
Methods: The transplant team of our institution implemented a new protocol of pancreas transplantation in January 2016. Despite high accuracy and repeatability some complications have appeared. All complications were dealt with by the same team and recorded in a prospective manner.
Results: Three recipients lost their grafts because of severe complications during first year (7.9%). Thirty-five (92.1%) insulin-free recipients are still followed (mean follow-up: 35.17 months). No deaths were recorded. Nine (23.7%) patients needed laparotomies because of grade III/IV Clavien-Dindo Classification complications. Two patients suffered pancreas thrombosis and early graft loss. These cases were followed by prompt graftectomies. During longer follow-up a pancreas transplant alone recipient had her graft removed for pancreatitis and rejection after multiple episodes of abdominal pain and inconclusive surgical explorations. One profuse bleeding was challenged. Two patients developed lower limb vascular complications that needed amputation. Another two patients suffer from diabetic foot. One recipient was diagnosed repetitively with retroperitoneal abscess and several attempts to solve it were performed. Eight cases needed following eventration repair or therapy against wound infection. These patients were treated by vacuum-assisted closure and extended antibiotic therapy without graft function deterioration.
Conclusions: Excellent early results of surgery and meticulous recipient management could not prevent surgical complications following pancreas transplantation. Clavien-Dindo grade III/IV complications occur in nearly a quarter of patients during 2 months of follow-up.

POS447 FROM A HOSPITAL-BASED OPO TO THE FIRST INDEPENDENT PROVINCIAL OPO IN CHINA: SHANXI EXPERIENCE

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Background: While the reform of Organ transplantation in China achived a great success, the organ procurment model remains on its exploring period. Starting from a hospital-based organ procurment organization (OPO) in Shanxi Province, we expanded the infrastructure, following by establishing the first independent non-profit regional OPO (Shanxi OPO) in the country, with a donation service area of 37.29 million pupolation. This study compares results reagarding the quantity, quality and efficiency of the Organ donation and tranplantation (OD & OT) service in Shanxi Province before and after the establishment of Shanxi OPO, aiming at exploring the best practice and procurment managment model in China.
Methods: Based on the data collected from 2015 to 2020, we analyzes the data regarding the organizational structure, personnel composition, equipment management, core quality indicators and compare the results before and after the establishment of the regional OPO.
Results: In the past two years, a professional team with 57 employess has been bulit and the organziaton was equited with advanced facilities for managing donation activities. A council, ethics committee and scientific committee have been set up to supervise and guide the work. By analyzing the quality control indicators, the number of OD increased from 35 cases (PMP: 0.9) in 2015 to 94 cases (PMP: 2.5) in 2020, with an increase of 168%. The incresing trend remains for our region even under the COVID-19 pandanic, whlie the annual numuber of the country deceased in 2020. Since 2018, the number of organs recovered per donor and the organ utilization rate of Shanxi OPO has increased year by year, reaching 2.86 and 99% respectively in 2020. These results indicate that quality of our service in organ viability assessment, donor maintenance, organ recovery and corrodination are gradually improved, even under the impact of COVID-19 pandanic.
Conclusions: Efficiency and the quality of our medical service has been improved in the past two years due to the establishment of an independ OPO for the region. This also provides a solution , of which guilds a clear direction in the standardization of organ procurment model in China.

POS449 YOUNG ADULTS TRANSPLANTED IN ADULT CARE REQUIRE INCREASED SUPPORT OVER TRANSITIONING PAEDIATRIC TRANSPLANTED TEENAGERS

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Background: Young adult transplant recipients (aged 16–29) have an increased risk of non-engagement, non-adherence, late acute rejection and transplant loss
Methods: A youth worker implemented a 4-point risk assessment scale in our transition and young adult transplant clinic (2015–20): Level 1 High risk of non-adherence supported by 1:1 support; Level 2 Non-critical personalised regular youth worker support; Level 3 Low risk-general support in young adult clinic through to Level 4: Very Low Risk-independent but part of young adult community group. We assessed the initial and latest risk categorisation of 81 young adult transplant recipients presenting from both paediatric transition and through direct adult care.
Results: 81 kidney transplant recipients: 37 (46%) transitioned from paediatrics median age 17 (16–20) 24 m: 13f; 44 (54%) presented direct to adult care median age 26 (18–30) 30m :14f. 23 (54%) of adult presentation and 7 (19%) [$p < 0.003$] of transition patients were initially in Level 1; with 21 (46%) and 25 (54%) in Level 2 respectively. At latest follow-up for both groups initially in Level 1; now 0% in Level 1, 6 (20%) in Level 2, 14 (47%) in Level 3 and 10 (33%) at very low risk in Level 4.
Conclusions: A much higher risk of non-engagement and non-adherence requiring customised youth worker support is present amongst teenagers and young adults transplanted in adult units, contrary to published literature

which focuses on transition patients alone as at highest risk. This calls for new strategies in adult units to focus on teenage and young adult patients presenting directly to adult care to improve outcomes.

POS450 DETECTING TISSUE DONORS IN A HOSPITAL EMERGENCY DEPARTMENT DURING COVID-19 PANDEMIC

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Background: Some studies describe the importance of specific units or wards, in determining the size of the possible donor pool.
The aim of this study was to evaluate a hospital emergency department´s potential to identify and provide tissue donors.
Methods: It is a 12-month retrospective and descriptive study of patients who died in Hospital Emergency department between 1rst January and 31th December 2020.
Patients were classified as potential tissue donors if they met specific age criteria and had an absence of contraindications based on a preset checklist.
Results: There were 56.173 emergencies attended of whom 0, 2% died in A&E (101) during the study period.
Within 101 deaths occurred, 27.72% (28) were evaluated, and 39.29% (11) were identified as possible tissue donors .
When the family was approach, 100% of them accepted tissue donation. Due to the human scarcity of resources, only 3 of the 11 possible donors families where approach.
The miss opportunity, that means, patients without medical contraindication were 36, 63% (37) of patients that were not identified as potential for the professional in charge. The total amount of non-evaluated patients is 72, 28% (73).
Conclusions: Emergency Department will provide an important place for future interventions to improve the rate of tissue donation.
More human resources with specific training for tissue detection are needed to evaluate all patients and improve this rate.

POS451 APPROACHING FAMILIES FOR ORGAN DONATION AUTHORISATION: HOW DO WE ASSESS A SOCIAL PROCESS?

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Background: An increasing demand for transplantations has motivated many countries worldwide to move their policies towards opt-out consent systems. In 2010, Chile changed to a soft opt-out system to increase its organ donation rates. However, the outcomes are fluctuant, and little research analysed the change and policy implementation. This paper presents doctoral research findings examining approaching families as a social process.
Methods: Qualitative study included seventy-one participants, healthcare professionals ($n = 51$) and bereaved families ($n = 20$). Participant observations across two large public hospitals in Chile, documents ($n = 80$), interviews ($n = 27$) and focus groups ($n = 14$) were collected and analysed following Charmaz' constructivist grounded theory approach (Charmaz, 2014).
Results: Approaching families of potential organ donors is carried out by small teams of nurse organ donor coordinators in Chile, who led the organ donation process within health institutions as an isolated policy. Organ donation remained conflictive among professionals due to the lack of training in bad news communication, emotion management, organ donation and end-of-life care. Despite these complexities, the organ donation policy is assessed almost exclusively by organ donation rates, tensioning professional-family relationships and organ donor coordinators' role.
Conclusion: The study shows in-depth data of approaching families as a social process, and its complexity is partially assessed with the current quantitative quality indicators. It draws attention to review more complex and multifactorial ways to assess organ donation policy implementation within health institutions. The findings inform clinicians, educators and policymakers and suggest further research to design a mixed-method approach that can better evaluate a multidisciplinary and integrated process.

POS452 EXPERIENCE OF WELL-BEING AND MENTAL HEALTH AMONG TRANSPLANTED PATIENTS -A SYSTEMATIC LITERATURE REVIEW

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Background: Patients waiting for an organ transplantation as well as transplanted patients have a long and close contact with nurses and transplant coordinators. Waiting for an organ can be very strenuous. After transplantation waits a life-long follow-up and medication. Most studies show that patients get a better quality of life after the transplantation but what affects their well-being is poorly investigated.
Aim: The aim of this literature review was to investigate what is written about how transplanted patients experience well-being and mental health.
Method: A systematic literature study has been conducted including 12 studies. The database search was carried out in PubMed, Cinahl and Psych Info. The articles were reviewed and analysed through a protocol from SBU Swedish Agency for Health Technology Assessment and Assessment of Social Service (2017).
Result: The different subcategories from the studies were analysed and ten new subthemes; body/physic, medication and side effects, fear of rejection, psychological condition, thoughts about the donor, philosophical life of view, family, social relations, work and coping. Four new themes were built: health of the body, mental experience, relations and ordinary day life. Finally, the synthesis of all studies resulted in "Adaption for well-being after transplantation". It is obvious for the recipients that there is a transition in before-and-after-transplantation. Many of the recipients did not experience the well-being and mental health as they had hoped for.
Conclusions: One of the goals in today's care of transplanted patients should be to improve the possibilities for the patients´ health literacy and support them in their adaption to life with a new organ.

POS453 IMPROVING IMMUNOSUPPRESSIVE MEDICATION ADHERENCE USING THE MARS-INTERVENTION: CASE STUDY ON ACHIEVING ENGAGEMENT AND ADHERENCE

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Background: Immunosuppressive medication (IM) nonadherence after kidney transplantation is common. However, not taking IM at all is exceptional. This abstract reports a case study of a young kidney transplant recipient, who intentionally did not take IM for two years post-transplant and was therefore enrolled in the pilot-study of the MARS-intervention.
Methods: The MARS-intervention integrated principles of (multi) systemic therapy and was outreaching. During the intervention, the social network was involved. By identifying determinants, specific evidence-based strategies and techniques for changing behavior were employed. Duration and frequency of the intervention were, just like the strategies and techniques, tailored to the patients' needs.
Results: Although at first the patient was very ambivalent about taking IM, he was curious about participating in the intervention because of the possible positive effects on the lifespan of his kidney. The possibility to discuss other self-management issues further motivated the patient to participate. Awareness concerning the risks of not taking medication was raised and discrepancies between current behavior and personal goals were addressed. Simultaneously beliefs about medication were explored and reframed when the patient was in (pre-contemplation phase of behavior change. Strategies to increase adherence and self-efficacy were addressed when patient shifted to the phases of preparation and action which resulted in initiation of medication taking. The principles from (multi) systemic therapy and the outreaching component of the intervention facilitated the effects of the intervention. During a follow-up consultation in the hospital, lab results showed the patient was still taking his medication up to two years after termination of the intervention.
Conclusions: Findings from this case study suggest that the behavior change techniques and strategies employed have the potential to improve IM adherence.

POS454 FIRST BILATERAL ARM TRANSPLANTATION INCLUDING SHOULDER RECONSTRUCTION

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We report for the first time a double arm transplantation including left shoulder reconstruction.
The recipient was a 48-years old liver transplant patient with bilateral amputation at proximal arm level on both sides since 1998 after he was electrocuted on a power line. The donor was a 35-year-old man and they shared the same blood group and 7 HLA mismatches. Continuous Veno-Venous hemodialysis was performed during the surgical procedure to reduce reperfusion-induced ischemic and metabolic disorders after revascularization.
The surgical procedure consisted in a total arm transplantation on the left side with reconstruction of the gleno-humeral joint. On the right side, the humerus of the donor was fixed on the remaining proximal 9 cm humerus which was reinforced with an intra medullary fibula from the donor. The arterial connections were axillary on both sides. The venous connections were axillary on the right side and subclavian on the left, added with a retro clavicular bypass in between the axillar and medial jugular veins. The nerve repair was at the proximal nerve level on the right side and the secondary trunk level on the left. Both deltoid muscles were transplanted, non-innervated on the right side and used as the skin blood supply provider, innervated on the left side. Ischemic times were 1h50 on the right side and 2h20 on the left.
Immunosuppression included tacrolimus, mycophenolate mofetil, prednisone and Thymoglobulin for 5 days.
Patient was extubated on day 1 after surgery and eligible for ICU discharge on day 2 after surgery.
Post-operative complications included: left and right humeral infection due to propionibacterium acnes; partial venous thrombosis of the left internal jugular vein; a left pectoralis hematoma and finally one episode of grade 2 acute skin rejection treated by 3 methylprednisolone boluses.
One month after the procedure, the patient is doing well and in a stable condition.
Conclusion: Bilateral arm and shoulder transplantation is feasible and restores body image in bilateral arm amputees. Functional recovery is not assessable at one-month post transplantation

POS455 MULTIFACETED APPROACH FOR DESENSITIZATION OF A HYPERIMMUNE HEART TRANSPLANTATION RECIPIENT

Denise Galbiati[1], Cristiano Amarelli[2], Lucrezia Palmieri[1], Irene Mattucci[1], Vittorio Palmieri[1], Maria Mottola[3], Emanuele Durante Mangoni[4], Roberto Andini[4], Bruno Zuccarelli[3], Claudio Napoli[5], Marisa De Feo[1], Ciro Maiello[1]
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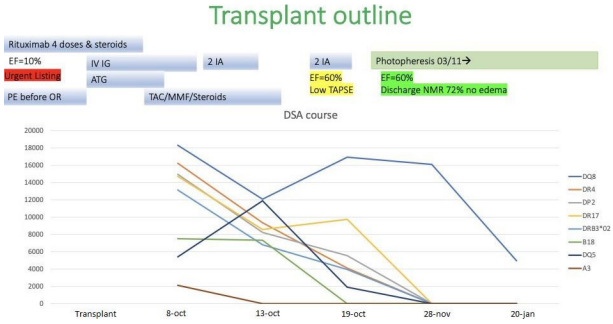
We describe the case of a 36 years old woman affected by familiar hypertrophic cardiomyopathy, with class II PRA (Panel Reactive Antibodies) 91% and DSA (Donor-Specific Antibodies). The patient was already listed for heart transplantation and was urgently hospitalized for biventricular heart failure with initial signs of liver failure. She was treated with intravenous inotropic drugs (enoximone 2-2.5 mcg/kg/min), improving clinical status and, after 8 days, entered in macro-area urgency (level 2) due to the difficulty of allocation due to elevated class II PRA.
Due to the sliding on inotropic support state, the patient underwent immunoadsorption (IA) (five sessions) and started rituximab (4 doses in two weeks), resulting in a 5% reduction of PRA. During the rituximab cycle, due to the onset of supraventricular tachycardia and loss of pulse, treated with antiarrhythmic and inotropic drugs, she was nevertheless placed in level 1 urgency. For the onset of sepsis, the patient was suspended from the emergency program for 6 days, showing an antibodies rebound. After a plasma exchange (PE) session and after a negative virtual cross-match, as previously decided by the Heart Transplantation Team, she was transplanted.
After cardiac transplantation she was treated with standard immunosuppressive therapy and required multiple apheretic treatments (PE and IA) and rituximab. Moreover in the post-operative period she presented a TIA, without neurological sequences, DSA increase and prolonged Troponin release and pro-BNP wash-out. The patient underwent EMB (Endomyocardial Biopsy), which tested negative; ECO-TT (TransThoracic Echocardiography), which showed good biventricular function; cardio-MR, which showed mild myocardial edema of the left ventricle. Pre-discharge extracorporeal photopheresis (ECP) has been started; she was discharged at home in good clinical conditions and is now in follow-up from 3 months. Intriguingly, after ECP the Donor-Specific Antibody titer abruptly decreased.



POS456 A CASE OF CARDIAC TRANSPLANT COVID-19 - ASSOCIATED ACUTE MYOCARDITIS

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Objectives: In the spring of 2020, the first cases of myocarditis in COVID-19 patients were reported; myocarditis was recognized as the cause of death in some COVID-19 patients. Here is the report of a case of 2019-nCoV pneumonia with the associated acute myocardial injury in a heart transplant recipient.
Methods: A 44-year-old patient with hypertrophic cardiomyopathy underwent the heart transplantation in August 2018. Immunosuppressive regimens included an induction therapy (Basiliximab) and supportive immunosuppressive regimen of tacrolimus and Mycophenolate mofetil.
The patient developed fever, chills, nonproductive cough and anosmia on April 29th, 2020. A SARS-CoV-2 test was positive. Laboratory results revealed elevated C - reactive protein (CRP, 121 mg/L), D – dimer (550 ng/ml), fibrinogen (6.07 g/l) and NT-proBNP (32054 ng/L). Screening tests excluded co-infection (including CMV, pneumocystis and fungal infections). Echocardiogram demonstrated left and right ventricular systolic dysfunction. The chest CT scan showed ground-glass opacities mainly in the upper right lobe with right-sided parenchyma seal.
Results: We reduced immunosuppressive therapy and started empirically therapy COVID – 19. Antibacterial treatment was started as bacterial superinfection was revealed. We also started heart failure therapy; the patient needed inotropic support. Endomyocardial biopsy (EMB) was performed for the differential diagnosis of myocarditis and acute cells or antibody-mediated rejection

(AMR). After the treatment, the next two tests SARS-CoV-2 were negative, but transplant function did not recover. After 14-day VA-ECMO support patient died before the planned transplantation.
Conclusion: Here is the description of the first case of acute COVID-19 - related myocardial injury in a heart transplant recipient. EMB demonstrated a low-grade myocardial inflammation and absence of myocyte necrosis. This case demonstrates the complexity of COVID-19 treatment in cardiac recipients.

POS457 BARIATRIC SURGERY AFTER INTESTINAL TRANSPLANTATION IS SAFE AND EFFECTIVE

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Obesity post-transplantation (Tx) is seen in 30% of recipients at 3 years. Contributing factors are suboptimal diet, reduced activity, medications, and endocrine changes. Obesity limits long-term outcome, as it is an independent risk factor for graft loss, delayed graft function and decreased patient survival. Bariatric surgery is currently the most effective long-term treatment for morbid obesity. Bariatric surgery for obesity after liver-, kidney-, pancreas- and heartTx is safe and renders good results on the long-term. Currently, no reports of bariatric surgery after intestinalTx (ITx) have been published.
A 46-year-old female, previously overweight with body mass index (BMI) of 29 kg/m^2, underwent combined liver-ITx in 2011 for short bowel syndrome following mesenteric ischemia. At the time of ITx, she weighed 58 kg (BMI: 19 kg/m^2). Within 1-year post-ITx, she regained her premorbid weight (90 kg; BMI: 29 kg/m^2) and developed arterial hypertension, for which she was treated with amlodipine. At 3 years post-ITx, she gained more weight, with a BMI of 35 kg/m^2. Lifestyle changes, diet and exercise did not result in significant weight loss. Nine years post-ITx, still at BMI 35 kg/m^2, a laparoscopic sleeve gastrectomy was performed after careful multidisciplinary consideration. The procedure was uneventful and at 6 months follow-up, her weight decreased to 87 kg (BMI: 29 kg/m^2). The procedure had no effect on liver and intestinal graft function, nor on absorption of immunosuppressive drugs. There was a temporary decline in renal function due to reduced oral intake, which fully recovered.
To the best of our knowledge, this is the first report of a patient undergoing sleeve gastrectomy for obesity after ITx. We conclude that this procedure is effective and safe as no effects were observed on absorption of immunosuppressive drugs. Bariatric surgery after ITx should be limited to experienced centers with a multidisciplinary intestinal failure team and obesity clinic.

POS458 NATIVE JEJUNAL CONDUIT FOR URINARY DIVERSION IN EN-BLOC LIVER-INTESTINE-KIDNEY TRANSPLANTATION

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Background: Recipients requiring kidney-enbloc visceral allograft often face challenges during transplantation. We report a case with a unique technique of urinary diversion in en-bloc liver-intestine-kidney transplantation for irradiation enteritis and cystitis.
Clinical case: A 65-year-old male presented to our institution with intestinal failure due to short bowel syndrome, complicated with intestinal failure-associated liver disease (IFALD) and kidney failure.
His past medical history included a proctocolectomy due to complicated inflammatory bowel disease and abdominoperineal resection for anal adenocarcinoma, followed by adjuvant chemo- and radiotherapy. He developed actinic cystitis, complicated by urinary incontinence and frequent urinary tract infections that led to kidney failure, and actinic enteritis complicated by bowel obstructions with the need of further bowel resections in a setting of frozen abdomen.
He was listed for combined liver-intestine-kidney transplantation and received en-bloc allograft from a 35-year-old male dead-brain donor.
During evisceration of native organs, a subtotal enterectomy leaving 30 cm of jejunum was performed. Urinary bladder was not suitable for allograft ureter implantation. Arterial inflow was established with an aortic conduit between the native and allograft infra-renal aorta. The native jejunum was transected at 10 cm from treitz ligament and the proximal segment was connected to the allograft jejunum to establish the continuity of alimentary tracts. The distal 20 cm of native jejunum was anastomosed to the allograft ureter for urinary diversion.
Postoperative course was unremarkable with adequate urinary output and allograft functions. The patient was well rehabilitated in hospital due to lack of safe rehabilitative facilities during COVID pandemic and was discharged home on post-operative day 47.
Conclusions: Combined kidney and visceral transplantation in the setting of irradiated bladder requires pre-operative planning of urinary reconstruction with several options. When native intestine is available and not damaged from the primitive disease, urinary diversion using the native jejunum is a safe option among others including cystoplasty and urinary diversion using allograft ileum.

POS459 RENAL TRANSPLANTATION IN GIGANTISM-A CASE REPORT AND REVIEW OF THE LITERATURE

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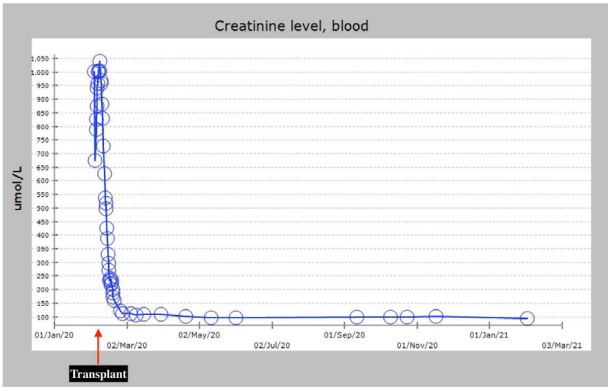
Background: Gigantism, characterized by excessive growth and height is due to increased secretion of growth hormone, most commonly from a pituitary adenoma. In addition to the surgical and anesthetic complexity, the extreme stature of these patients presents a unique challenge for kidney transplantation in deciding whether to proceed with a single or dual kidney transplantation. The lack of relevant literature further adds to the dilemma.
Case Summary: A 45-years-old patient with untreated gigantism and end stage renal failure due to IgA nephropathy with secondary focal segmental glomerular sclerosis, on renal replacement therapy was waitlisted for a deceased donor dual kidney transplantation (after discussion in our MDT & approval by the NHS Blood and Transplant's Kidney Advisory Group) due to the extreme physical stature (Height-247 cms, weight-200 kgs, body mass index-33 kg/m^2, and body surface area with the DuBois formula-3.7 m^2, which was twice than the normal upper limit). He was offered 2 kidneys from a 1-0-1 HLA mismatched 24-year-old DCD donor (Height-179 cms and weight-75 kgs), and was planned for a bilateral retroperitoneal implantation into the recipient external iliac vessels. The immunosuppression consisted of alemtuzumab induction (5 0 mgs) and steroid-free maintenance with tacrolimus. The donor's right kidney was uneventfully implanted extra-peritoneally into the right external iliac vessels. On contralateral exposure, the left common and external iliac arteries were ectatic and frail. A complex vascular reconstruction was not preferred in order to preserve the arterial supply to the left lower limb, to minimise the cold ischemia time and prevent additional warm ischemic insult to the second kidney. Hence, it was decided not to proceed with dual transplantation. Amidst concerns of nephron mass insufficiency, the graft function was remarkable with a serum creatinine of 120 μmol/L within a month from transplantation and 94 μmol/L at 1-year post transplantation, and without proteinuria.
Conclusion: To our knowledge, this is the first case report on kidney transplantation in gigantism. Although it is believed that dual kidney transplantation is ideal, a single kidney transplantation from an appropriately selected donor can provide sufficient functioning nephron mass in patients with gigantism.



POS460 LIVING-RELATED KIDNEY TRANSPLANTATION IN A PATIENT WITH JUVENILE NEPHRONOPHTHISIS

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University hospital Martin and Jessenius Faculty of Medicine Comenius University, Martin, Slovakia

Background: Nephronophthisis (NPHP) is an autosomal recessive disease manifesting as tubulointerstitial nephritis uniformly progressing to end stage renal disease in childhood. Living kidney donation is contraindicated in potential donor with diseases of autosomal dominant mode of inheritance potentially leading to kidney failure in future. On the other hand, autosomal recessive genetic kidney diseases, such as NPHP, are not usually contraindication to living kidney donation.
Method: We are reporting related living kidney transplantation (KT) with a family history of NPHP form 46-year-old mother to 17-year-old daughter with.
Results: A 17-year-old girl presented to the Transplantation Center in Martin with chronic kidney disease (CKD) KDIGO stage 5 on peritoneal dialysis. A genetic examination confirmed diagnosis of NPHP type, the patient is homozygote for deletion of NPHP1 gene (2q13 in exon 1-20). Parents, who were in consanguineous marriage (they are third cousins) are both transmitter of NPHP type 1, according to complementary genetic diagnosis. Potential candidate for living donor KTx was one of the parents. The patients' mother, 46 year old, has been treated for arterial hypertension (perindopril/indapamide) with optimal blood pressure control and estimated glomerular filtration rate (eGFR) was 1.68 mL/s. She had undergone complete diagnostic algorithm for potential living kidney donor according to KDIGO guidelines. Genetically, she was diagnosed as a heterozygote for type 1 NPHP. Because of direct relation between donor and recipient, we put in consideration whether mother is an appropriate living kidney donor with regard to the risk of developing CKD even though she was heterozygote for type 1 NPHP, but in rare cases, ESRD can also occur later during adulthood. We compared risk versus benefit of living kidney donation from mother and considered her as a suitable donor. Nephrectomy procedure was performed without any complication. Basic parameters monitored after nephrectomy are shown in table 1.
Conclusion: According to KDIGO guidelines for living donor, genetic kidney diseases are an important consideration when evaluating potential living donor candidates, especially when they are genetically related to an intended recipient.

Table 1. Basic parameters monitored after nephrectomy

	Before nephrectomy	1 month	6 months	12 months
Systolic BP, mm Hg	125	120	132	146
Diastolic BP, mm Hg	86	87	95	98
Weight, kg	90.0	93.0	86.5	81.0
BMI, kg/m^2	30.1	31.1	28.9	27.1
eGFR, mL/s	1.68	0.99	1.04	1.00
Proteinuria, g/day	0.120	0.207	0.118	0.160
Total cholesterol, mmol/L	5.01	5.47	5.93	5.34
TAG, mmol/L	1.27	1.32	1.29	1.25
HDL – cholesterol, mmol/L	1.27	1.31	1.35	1.54
LDL – cholesterol, mmol/L	3.16	3.60	2.97	3.49

BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TAG, triacylglycerides.

POS461 ISOLATED SUPERIOR MESENTERIC ARTERY DISSECTION IN A LIVING KIDNEY DONOR: SAFE TO DONATE OR NOT? AN ETHICAL CASE DILEMMA AND REVIEW OF THE LITERATURE

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Background: A true isolated superior mesenteric artery dissection (ISMAD) is considered a rare occurrence. To our knowledge, ISMAD has never been reported in a living kidney donor (LD). We discuss the ethical dilemma of allowing or denying donation to a patient with this type of risk factor.
Case report: Among 367 consecutive adult potential LD who underwent investigation at our institution from January 2005 to December 2020, one patient (0.3 %) demonstrated a communicating ISMAD type I according to Sakamoto's classification initiating 3 cm from the root of the SMA and ending 57 mm distally. Patient characteristics were the following: 65 years old ABO compatible father donating to his son on CRF secondary to Henoch-Schonlein vasculitis. Donor comorbidities were mild hypertension, well controlled with two drugs, and psoriasis on treatment with retinoic acid. The diagnosis of ISMAD was made incidentally by contrast CT done as part of the LD study. The donor denied any possibly related symptom and the remaining cardiovascular and renal diagnostic work-up was normal.
Discussion: Given the life-threatening potential of ISMAD we discussed in the context of our multidisciplinary group whether or not it was ethical to candidate such a patient to LD nephrectomy. After the initial decision to exclude donation, due to the insistence of the donor who firmly reiterated his willingness to absolutely go ahead against all risks, we decided to discuss the case again, also by confronting with colleagues from other LD transplant centres. We received different opinions, however, based on the reported very low mortality of 1% associated with asymptomatic ISMAD, the majority suggested potential donor acceptance.
Conclusion: Non-ideal LDs are becoming increasingly common and their acceptance frequently poses ethical dilemmas: ISMAD is a rare but potentially life-threatening condition, nevertheless, given the very low mortality of its asymptomatic form and the life-saving role of kidney transplantation in the long term, donation should not be excluded by default in the presence of ISMAD but considered on a case-by-case basis.

POS462 RENAL TRANSPLANTATION FROM A LIVING DONOR WITH RENAL ARTERY FIBROMUSCULAR DYSPLASIA

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Background and Aims: Renal transplantation is considered the most effective and less costly modality of renal replacement therapy. The disparity between allografts and recipients has led to a global effort to increase the pool of donors. Accordingly, fibromuscular dysplasia (FMD) is no longer considered an absolute contraindication for kidney donation.
This is a case of a living kidney donor with no history of hypertension, diabetes, proteinuria or elevated serum creatinine, whose intra-arterial digital subtraction angiography revealed FMD lesions in the left renal artery.
Results: A 54-year-old Caucasian female with medical history of hypothyroidism took the decision to offer her kidney to her 37-year-old son who was diagnosed with end-stage renal disease five years ago secondary to diabetes mellitus type I. Her vital signs, urinalysis, biochemical profile and serological evaluations were all within normal ranges. The abdominal ultrasound and renogram with Tc-99m DTPA showed no remarkable findings. On intra-arterial digital subtraction angiography an abnormal succession of dilatations and multifocal stenoses of the left renal artery, characteristic of medial FMD, was found.
Apart from a dysfunctional permanent left femoral catheter, the patient had no other vascular access for hemodialysis.
Taking all of these into consideration, the patient was offered renal transplantation. A left open donor nephrectomy was performed; the renal artery was divided distal to the stenotic dysplastic area. Post-operatively, the recipient had a delayed graft function lasted 13 days. On renal artery Doppler in the allograft we found increased resistance index (RI) that gradually normalized without any intervention. An immunosuppressive regiment of tacrolimus, mycophenolate and prednisone was administered according to our center protocol. At discharge serum creatinine was 1.7 mg/dL (eGFR: 50 ml/min/1.73 m^2).

Conclusion: Allografts harvested from carefully selected donors with renal arterial FMD can be successfully used. Detailed pre-transplantation imaging of donor's renal arteries, selection of the appropriate screening method, as well as close monitoring of both donor and recipient for early interventions after transplantation is of paramount importance.

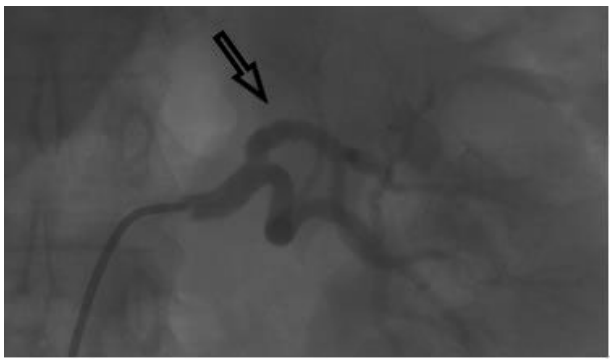

Figure 1. lesion characteristic of medial FMD

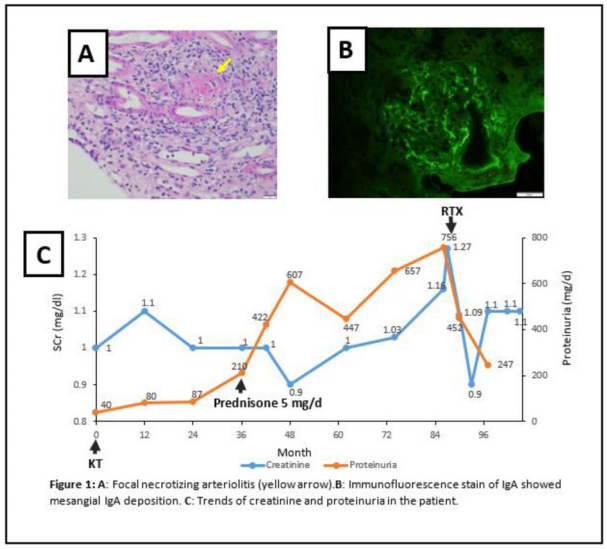

Figure 1: A: Focal necrotizing arteriolitis (yellow arrow).**B**: Immunofluorescence stain of IgA showed mesangial IgA deposition. **C**: Trends of creatinine and proteinuria in the patient.

POS463 RITUXIMAB IS EFFECTIVE IN TREATING KIDNEY ALLOGRAFT RECURRENT IGA NEPHROPATHY WITH NECROTIZING ARTERIOLITIS: A CASE REPORT

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Recurrence of IgA nephropathy (IgAN) in allograft is common and associated with an increased risk of graft loss. Effective therapy of recurrent IgAN, especially those with vasculopathy, is unknown. A 40-year-old female with kidney failure secondary to IgAN, initially diagnosed at the age of 29. She underwent a preemptive, HLA identical living donor kidney transplant (KT) at 3 years post diagnosis. She received basiliximab induction and maintained with tacrolimus and mycophenolate mofetil. Early post KT course was unremarkable with serum creatinine (SCr) of 0.9-1.0 mg/dl. At four months post KT, protocol biopsy (Bx) showed evidence of recurrent IgAN with mild mesangial IgA deposition on immunofluorescence, but no mesangial proliferation. Subsequent protocol Bx demonstrated progression with increasing mesangial proliferation at 1 and 2 year post KT, but SCr remained stable. Prednisone 5 mg/d and lisinopril were added at year 3 for IgAN due to increasing proteinuria. At 5 years post KT, Bx showed focal endocapillary proliferation and fibrinoid necrosis. SCr was stable with stable proteinuria. Conservative management was continued. At 7 years, protocol Bx showed severe arteriolar hyalinosis and focal necrotizing arteriolitis at the corticomedullary junction accompanied by increased SCr and proteinuria (Fig. 1). ANCA serology was negative. She was treated with methylprednisolone 1 g and rituximab (RTX) 1 g $\times$ 1 dose. CD19+ B-cell was adequately suppressed after RTX. SCr improved to 1.1 mg/dl at 3 months post treatment and proteinuria improved. Repeated kidney Bx 3 months post RTX revealed evidence of mild mesangial proliferative IgAN but no arteriolitis or fibrinoid necrosis. Recurrent IgAN with active vasculitis in allograft pose a therapeutical challenge. This entity may respond to RTX, but more studies are needed to confirm its role in this population.

POS464 SUCCESSFUL REUSE OF A KIDNEY GRAFT SEVERAL MONTHS AFTER EARLY RECURRENCE OF RESISTANT PRIMARY FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS

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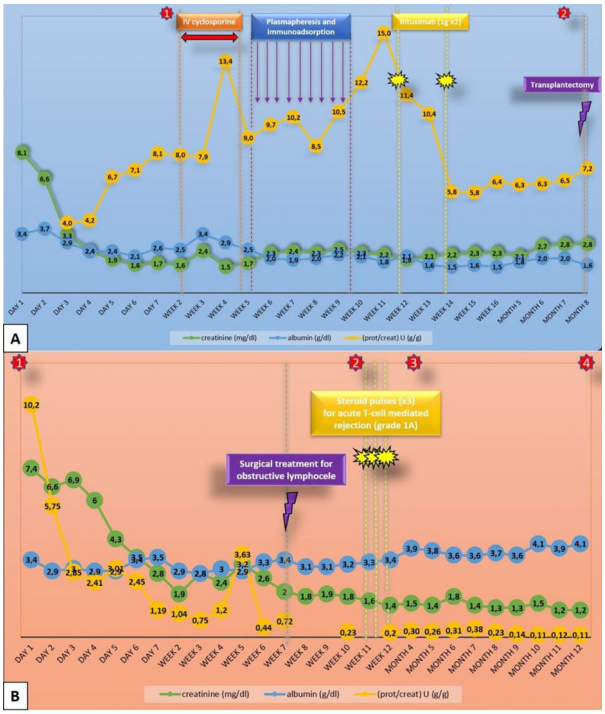
Introduction: Primary focal and segmental glomerulosclerosis (pFSGS) frequently recurs after transplantation (30-40% of cases) and is associated with poor prognosis. Due to the lack of any effective therapy, the question of transplantectomy may arise in this situation. To date, only 2 cases described the reuse of a detransplanted graft for a second recipient very shortly after transplantation (within a month). We describe hereafter the successful reuse of a kidney graft in an adult recipient eight months after early pFSGS recurrence resistant to all available therapeutics.
The case: The patient #1, a 23-year-old man, followed for end-stage kidney disease secondary to pFSGS, was first transplanted in 2018 with a cadaveric donor graft. We observed an immediate recurrence of biopsy-proven pFSGS (within the first week). After four lines of treatment including intravenous cyclosporin, plasma exchanges, immunoadsorption and 2 injections of 1g-rituximab, the patient remained heavily nephrotic (proteinuria 7 g/24 h, albuminemia 1.6 g/dL). Serum creatinine levels were respectively at 1.9 and 2.8 mg/dL, three and eight months after transplantation (Figure, panel A).
Eight months after transplantation, with the approval of both Biomedicine Agency and patient #1, the graft was detransplanted and reimplanted in patient #2, a 78-year-old, isogroup, non-immunized, and anephric recipient (binephrectomy 2 years before for bilateral renal carcinoma). We observed an immediate kidney function and a progressive decrease in proteinuria: creatinine serum level at 1.2 mg/dL and proteinuria at 0.11 g/24 h one year after transplantation (Figure, panel B). Biopsies performed after surgery showed persistent FSGS lesions with a decrease in overall foot process effacement.
Conclusion: To our knowledge, this is the first reported case demonstrating that kidney graft transfer may still be a viable option for refractory pFSGS several months after initial transplantation.



POS465 ERTANACEPT-INDUCED LUPUS NEPHRITIS IN A KIDNEY TRANSPLANT RECIPIENT

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Introduction: Certain drugs can cause immune responses that generate autoantibodies and clinical autoimmune disease including immune complex-mediated or pauci-immune glomerulonephritis. Etanercept is a soluble TNF-alpha receptor that is known to rarely cause drug-induced lupus nephritis. Here we present a case of etanercept-induced lupus nephritis in a kidney transplant recipient.
Case report: We present a 42 -year old male patient who underwent kidney transplantation ten years ago. Native kidney disease was secondary amyloidosis, as a complication of ankylosing spondylitis. Prior to kidney transplantation ankylosing spondylitis was treated with corticosteroids and adalimumab and with etanercept after transplantation. On a regular outpatient visit worsening kidney function and proteinuria were noted. Kidney ultrasound findings were normal, so biopsy was performed. The pathohistological results showed signs of chronic immune complex-mediated glomerulonephritis (full-house" immune pattern). Additional immunological assessment showed raised anti- double-stranded DNA antibody titers, positive ANA and a decrease in complement C3 levels. Lupus nephritis was diagnosed. Immunosuppression was modified with a higher dose of mycophenolate and etanercept was discontinued. His renal function did not improve upon cessation of the offending drug, and he required additional immunosuppressive therapy. High-dose corticosteroids where given (500 mg of methylprednisolone daily through three days). Follow up biopsy showed no histological signs of lupus nephritis, and levels of anti dsDNA titers, complement levels and ANA normalized. The patient had stable kidney function at his last outpatient visit.
Conclusion: Etanercept is a rare cause of drug-induced lupus nephritis and can also affect transplanted kidneys. Discontinuation of the drug may lead to full recovery, but sometimes additional immunosuppressive therapy may be needed.

POS466 AB0 INCOMPATIBLE TRANSPLANTATION IN A PATIENT WITH COMPLEMENT DYSREGULATION: A DELICATE MATTER

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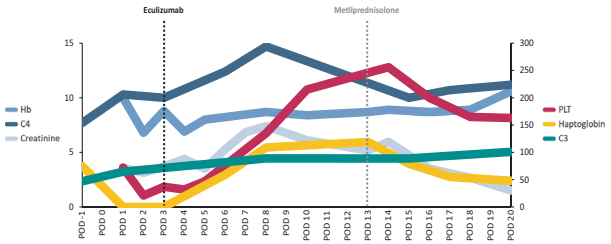
A 32-year-old Caucasic female was admitted to our center to receive a living donor AB0 incompatible (A to B) transplant. She was on dialysis treatment for renal failure whose etiology was not histologically established. Chronic C3 hypocomplementemia and complement factor H antibodies (Ab-CFH) suggested a complement-mediated hemolytic uremic syndrome (HUS), but their pathogenic role was considered uncertain given a not relevant titer.
Our desensitization protocol started 6 weeks before (mycophenolate mofetil, steroid, tacrolimus plus 15 plasmapheresis sessions and 2 Rituximab doses) until anti-A antibodies 1:128 titer lowered to 1:1. Basiliximab and intravenous (IV) immunoglobulin as induction therapy at transplantation. No complications during or right after surgery.
On day 1 post operation (POD) an abrupt onset of thrombocytopenia and anemia occurred, worsening progressively (PLT 72000 → 27000 10^9; Hb 10 → 8 g/dL). Few schistocytes were detected in peripheral blood smears, no other abnormalities. Anemia and thrombocytopenia persisted, leading to constant transfusional support. Soon, further alterations appeared: C-reactive protein and lactate dehydrogenase rose, while haptoglobin, serum C3 and C4 dropped. Graft function was stable until POD 3, then it started to rapidly decline. Urinary sediment showed isomorphic red blood cells and rare CD68+ elements.
Given patient's immunological history and data suggesting thrombotic microangiopathy, we started eculizumab immediately, 900 mg weekly. Blood parameters normalized quickly while serum creatinine (sCr) peaked at POD 8 (sCr 7.4 mg/dL). Graft biopsy performed on POD 12 revealed thrombotic microangiopathy paired with acute antibody-mediated rejection. No rebound of anti-A antibodies was present. Negative anti-HLA antibodies. Anti-rejection therapy was started with methylprednisolone (500 mg iv, 5 pulses) on POD 10, promptly improving graft function. Patient was tested again for complement-mediated HUS: ADAMTS13, Von Willebrand Factors products and both complement pathways were normal. Even Ab-CHF was negative despite previous medical records.
Patient was dismissed on POD 20 with normal graft function and blood count. She is regularly monitored in our outpatient clinic and 6 months after transplantation she is still on eculizumab.



POS467 DRUG INDUCED PURE RED CELL APLASIA IN RENAL TRANSPLANT RECIPIENT: CASE REPORT AND REVIEW OF LITERATURE

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Background: Severe anemia requiring multiple blood transfusions in post-transplant period triggers rejection. The evaluation of anemia among transplant recipients is a challenging task. Tacrolimus needs to be kept in the suspect box in the management of pure red cell aplasia (PRCA), but further evidence is needed to prove whether Tacrolimus is a real cause in post-transplant anemia.
Methods: Renal transplant recipient with severe anaemia that was fully investigated to show the aetiology of such anaemia. After exclusion of common causes, we found that it could be drug-induced PRCA.
Preliminary Results: A 66-year-old male diabetic nephropathy underwent preemptive live renal transplant on 13.9.2018. He had a past history of CABG and TAVI 3 years' prior transplantation. Initially, he was maintained on prednisolone, mycophenolate-mofetil and tacrolimus, after basileximab

induction. One month later he started to complain low cardiac output symptoms. CBC showed normocytic normochromic anemia (with hemoglobin dropped from 112 down to 69 g/l) with reticulocytopenia necessitated regular blood transfusion. He has normal iron profile, serum folate and vitamin B12, as negative hemolytic and autoimmune screen. Bone marrow biopsy was revealed acquired PRCA most likely drug induced as viral profile were negative for Parvovirus B19, CMV, and EBV. Patient was managed by discontinuing mycofenolate-mofitel, and steroid dose was increased up of 20 mg/day but without improvement. Considering tacrolimus as a cause, three weeks later, cyclosporine was replacing tacrolimus, CBC follow up showed improvement without any need for further blood transfusion. After one month of Cyclosporine maintenance, Mycophenolate-mofetil was resumed with steady increase of hemoglobin up to 150 g/l, and serum creatinine of 122 μmol/l.
Conclusions: PRCA is rare disorder among renal transplant recipients which could be induced by the maintenance Tacrolimus.

POS468 SYNTHETIC ADRENOCORTICOTROPIC HORMONE A TREATMENT OPTION FOR POST RENAL TRANSPLANT RECURRENT RESISTANT PRIMARY FOCAL SEGMENTAL GLOMERULOSCLEROSIS

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Introduction: Recurrence of primary FSGS after renal transplantation is estimated to occur in 30%-50% of cases. Treatment of recurrent FSGS is challenging because specific pathogenic targets are unknown and available therapeutic options have limited efficacy. Commonly used therapies are Plasmapharesis(PEX), IVIg and Rituximab (RTX), used with varying success. We report a case report of resistant recurrent FSGS managed with synthetic ACTH. ACTH is available as synthetic and gel preparations
Case Report: A fifty-year old male patient with biopsy-proven FSGS, resistant to Prednisolone, Cyclosporine and Tacrolimus had a pre-emptive live unrelated renal transplant in June 2014. He was induced with basiliximab and maintained with Prednisolone, MMF and Tacrolimus. He presented with nephrotic range proteinuria and pedal oedema nine months post transplant. Biopsy confirmed recurrent FSGS. Due to his occupation, PEX was not possible, as he could not have a vascular catheter inserted. He was treated with a RTX and IVIg. The patient was then started on synthetic depot formulation of intramuscular ACTH at a dose of 1 microgram twice weekly. The patient had a remarkable response, where the UPCR treated over seven months.

Figure 1. Time scale with graph showing the UPCR response to various treatment including ACTH
Subsequently in view of the response, when the intramuscular ACTH dose was reduced to once a week, UPCR had increased, suggesting an ACTH dependant response.

Discussion: ACTH may induce a potent anti-inflammatory effect and also have a direct, podocyte-sparing effect. There are two approved formulations of ACTH used for treatment of nephrotic syndrome in adults, ACTH gel formulation in USA and a synthetic formulation used in Europe. ACTH gel (HP ACTHar gel; Cost 39,000 USD per 5 ml) is a natural form of ACTH whereas the synthetic derivative of ACTH which is called as Cosyntropin or tetracosactide (Cost – 38 GBP per 1 ml of synthetic ACTH). In view of the high cost of ACTH gel but similar efficacy, the synthetic ACTH is the formulation that is available in UK. We conclude that ACTH should be considered as potential therapeutic options for resistant post transplant recurrence of FSGS and further randomised controlled trials are required.

POS469 BELATACEPT AS MAINTENANCE THERAPEUTIC: AN ANSWER FOR DE NOVO THROMBOTIC MICROANGIOPATHY WITH ACUTE ANTIBODY-MEDIATED REJECTION

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Introduction: De novo thrombotic microangiopathy (TMA) is a serious, but rare, complication of kidney transplantation (KT). Calcineurin inhibitors contribute to the appearing and worsening of the disease. The elimination of these drugs promotes the resolution but carries a high risk of rejection. We believe Belatacept can play an important role in these situations.
Clinical Case: Male, 55 years old, medical history of arterial hypertension and chronic kidney disease of undetermined etiology, submitted to deceased donor KT after six years on hemodialysis. He had 3/6 HLA mismatches and donor-specific antibodies (DSA) anti-DQ7 [mean fluorescence intensity (MFI) 2053].
Induction therapy included thymoglobulin, mycophenolate mofetil, prednisolone and tacrolimus.
The lowest serum creatinine (sCr) after immediate transplant was 2.4 mg/dL, maintaining DSA Anti-DQ7 (MFI < 1088), without active urinary sediment or proteinuria. A graft biopsy was performed on the 23rd day after KT, which revealed acute antibody-mediated rejection (AAMR) with glomerulitis (g3), peritubular capillaritis (c2) and C4d in the region of peri-tubular capillaries (C4d1). Plasmapheresis, immunoglobulin, methylprednisolone, and rituximab were performed with improvement of kidney function (KF).
Concomitantly, there was worsening of anemia and thrombocytopenia with increased lactate dehydrogenase (LDH) and low haptoglobin, with rare schistocytes. Thrombotic thrombocytopenic purpura was excluded. No complement levels or genetic changes were found.
After 1 month, in spite of adequate tacrolimus levels, worsening of KF (sCr 3.2 mg/dL) and proteinuria (1.2 g/24 h) was noticed, maintaining anemia and thrombocytopenia.
A new biopsy was performed, still revealing signs of AAMR (g3 ptc2 C4d1), along with thrombotic microangiopathy.
Thus, tacrolimus was discontinued and belatacept (10 mg/kg) was started with reversal of thrombotic microangiopathy and improvement of kidney function.
Discussion: The reported case is particularly challenging because it deals with a patient who develops a TMA, probably secondary to tacrolimus, simultaneously with AAMR. Belatacept seems to be an effective and safe option, contributing to better renal graft survival.

POS470 THE FIRST REPORT OF HIV-POSITIVE KIDNEY TRANSPLANTATION IN THAILAND: PROVIDING THE OPPORTUNITY AND ACCESSIBILITY TO TRANSPLANTATION

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The prevalence of human immunodeficiency virus (HIV) infection is high in Southeast Asia (SEA). Indonesia, Thailand, and Myanmar are the top three high-burden countries, and have cumulative of 1.4 million HIV patients. The estimation of ESRD in HIV patients in SEA is around 7,000 cases and is giving pressure on the dialysis system. HIV infection has been an exclusion criteria of kidney transplantation in Thailand and other developing countries in SEA. In this article, we reported the first successful kidney transplantation in HIV-positive recipient in Thailand. Our aim is to encourage kidney transplantation in ESRD patients with well-control HIV infection, especially in the countries where the prevalence of HIV infection is high and the accessibility to transplantation is still limited.
Case Presentation: A 33-year-old male with HIV infection received kidney transplantation from his sister. The patient had HIV infection for 13 years and developed ESRD which was suspected from tenofovir disoproxil fumarate (TDF), which he received peritoneal dialysis for 1 year. Pretransplantation ART was abacavir 300 mg/day, lamivudine 150 mg/day, and nevirapine 200 mg/day, which could control his HIV viral load to <20 copies/mL and CD4+ T lymphocyte 604 cells/μL. Anti-thymocyte globulin (ATG) was given as an induction therapy. CD4+ and lymphocyte counts were closely monitored in the first week after transplantation, and the total dose of ATG was adjusted to 2.5 mg/kg. The maintenance regimen included tacrolimus, mycophenolate mofetil, and prednisolone. His posttransplant clinical course is shown in Table 1. Posttransplantation complications were experienced, including perinephric collection which was treated conservatively, and CMV

viremia that needed 1-month course of ganciclovir. The patient is doing well and has stable graft function after 6 months posttransplantation. This case represents the importance of multidisciplinary team approach in conducting the high-risk transplantation and breaking the barrier that prevent patients from standard of care.

Table 1. Posttransplant clinical course

Parameters	D0	D1	D7	D15	D30	D45	D120
Cr (mg/dL)	16.7	3.5	1.0	1.3	1.1	1.3	1.5
Proteinuria (mg/day)	-	833	55	<30	<30	<30	<30
TAC (C0, ng/mL)	-	12.8	6.7	7.6	5.1	7.0	9.2
CD4+ (cells/μL)	604	-	10	46	-	217	237
HIV VL (copies/mL)	<20	-	<20	-	<20	-	<20

POS471 DISSEMINATED RHINOCLADIELLA MACKENZIEI INFECTION IN A KIDNEY TRANSPLANT RECIPIENT: CASE REPORT AND LITERATURE REVIEW

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Rhinocladiella mackenziei is a rare fungal pathogen which belongs to a large group of pigmented fungi named phaeohyphomycosis. *R. mackenziei* primarily infects the brain and leads to a high mortality rates among both immune competent and immune compromised individuals. Among transplant recipients, the infection may disseminate to extra-neuronal sites, necessitating comprehensive radiologic imaging. In this paper, we describe a new case of *Rhinocladiella mackenziei* infection in a renal transplant patient involving the brain and kidney. She received amphotericin B and voriconazole but with no surgical intervention. Ultimately, the patient died 2 months after admission. A review of all infected transplant patients with *R. mackenziei* is also presented.

POS472 SUCCESSFUL LIVE RELATED KIDNEY TRANSPLANT AFTER RECOVERY OF COVID-19 PNEUMONIA: CASE REPORT AND REVIEW OF LITERATURE

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Introduction: We do not have specific information on whether COVID-19 infection will be more severe in transplant recipients compared to healthy people.
The case report: We report a successful kidney transplant in 36-year-old female Kuwaiti lady who had ESRD due to Ig A nephropathy, she started regular hemodialysis on 17/8/2020 through right internal Jugular vein permcath. She has hypertension and past history of preeclampsia occurred during her 4 pregnancies that were terminated by caesarian sections. She has tertiary hyperparathyroidism on cinacalcet. She had COVID-19 pneumonia on 2/8/2020 necessitate admission to isolation hospital followed by full clinical recovery, negative NP swab(twice) for COVID-19 PCR and mild residual ground glass infiltrates by high-resolution CT chest 1 month before transplant. She underwent live related (bother) right iliac renal allo-transplant on 20/10/2020 with mm 1:0:0 and negative CXM with negative DSA. She received basiliximab as induction, and she was maintained on prednisolone, mycophenolate sodium and cyclosporine. The donated kidney was left kidney with single vessels anastomosed end to side to the external iliac vessels, she had immediate graft function, with early recovery and was discharged from the hospital 7 days after surgery. Before discharge NP swab was repeated and came negative for the third time and the COVID-19 IgG antibody test came positive. Patient was followed up for three months in the OPD and renal function is improved to a nadir of 92 μmol/l and the last immunosuppressant doses were prednisolone 7.5 mg plus Myfortic 540 mg BD and Neoral 75 mg BD achieving a level around 100 ng/ml.
Conclusion: Renal transplantation can successfully be carried out cautiously among ESRD patients who got infected by COVID-19 during the current pandemic specially among low-risk patients.

POS473 NEW ONSET HYPERCALCEMIA AFTER RENAL TRANSPLANTATION: AN INFECTIOUS ETIOLOGY BEYOND PERSISTENT HYPERPARATHYROIDISM

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Pneumocystis jirovecii pneumonia (PJP) is an opportunistic infection which may present with hypercalcemia. A kidney transplant recipient with hypercalcemia secondary to PJP is presented.
A 59 years-old man who underwent kidney transplantation 2 years ago. He developed hypercalcemia secondary to hyperparathyroidism and was treated with cinacalcet for six months. After discontinuation of cinacalcet, calcium level was normal.
On admission, he had cough and dyspnea. Physical examination was normal except for fever. Laboratory findings are presented on the table. HRCT revealed bilateral extensive ground-glass opacities distributed predominantly at the perihilar regions and apices (Figure). Bronchoalveolar lavage (BAL) fluid demonstrated *P. jirovecii* cysts with Gram-Weigert stain. BAL fluid PCR for CMV was positive. Intravenous TMP-SMX, methylprednisolone and gancyclovir were initiated. Patient required two sessions of hemodialysis for hypercalcemia. Calcium began to decrease by sixth day of TMP-SMX. Patient was treated with TMP-SMX for 21 and gancyclovir for 14 days. TMP-SMX prophylaxis was given for three months.
Hypercalcemia is almost always secondary to persistent hyperparathyroidism after kidney transplantation. Recently, two case series of kidney transplant recipients with PJP reported hypercalcemia in nearly 35% of patients. Extrarenal production of 1,25-dihydroxyvitamin D secondary to granulomatous inflammation against *P. jirovecii* may be the underlying mechanism. However, granulomatous inflammation was detected in 5% of lung biopsies among patients with AIDS and PJP. Incidence of granulomatous inflammation during PJP is unknown in kidney transplant recipients. In our case, suppression of PTH at diagnosis and normalization of calcium and increase in PTH to baseline level after treatment suggest extrarenal production of 1,25-dihydroxyvitamin D secondary to PJP.
In conclusion, PJP should be considered as one of the underlying etiologies among kidney transplant recipients in the presence of hypercalcemia.

Laboratory findings	Normal	2 months prior to PJP	On admission	At discharge	6 months after PJP
Creatinine (mg/dL)	0.7-1.13	1.98	2.23	1.65	2.52
Total calcium (mg/dL)	8.6-10.2	10.1	13.8	10.2	10.1
25 hydroxyvitamin D (ng/mL)	20-50	-	29	-	-
Parathormone (ng/L)	15-65	484.5	100.5	-	560.9

POS474 KIDNEY TRANSPLANTATION FROM COVID-19 POSITIVE DECEASED DONOR

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In recent months, with the spread of COVID 19, the number of kidney transplants from deceased donors has declined significantly in most countries. Determining the risk of transmission of COVID 19 with a donor organ is very important for developing a kidney transplantation policy during a pandemic.
We present cases of kidney transplantation from COVID 19 positive deceased donor to two dialysis patients in single center.

Deceased donor: a 45 years old man with diabetes, who had a major hemorrhagic stroke resulting in brain death. For a few hours after organ harvesting, the donor was diagnosed COVID 19 (retrospective nasopharyngeal swab rRT-PCR which was confirmed by morphological examination).
Recipient 1: a 49 years old man with polycystic kidney disease had been on hemodialysis for 28 months. Recipient 2: a 45 years old man with polycystic kidney disease on continuous ambulatory peritoneal dialysis (CAPD).
Both patients received only basic immunosuppression, including tacrolimus, methylprednisolone and a mycophenolic acid. In first case cold ischemia time was 22 hours. The recipient had delayed graft function with increasing of urine output on day 8 post-transplant. No other deviations from the usual course were seen during hospital stay. The patient was discharged from hospital with serum creatinine level 122 mkmol/L. The cold ischemia time was 21 hours in another patient. Graft function was immediate with a decrease serum creatinine to 92.5 mkmol/L at discharge.
Both patients had no febrile and no other symptoms of acute respiratory disease. No abnormalities on chest X-ray were seen. No serum anti-SARS-CoV-2 IgM and IgG were detected before and during 6 weeks after surgery. Repeated nasopharyngeal swabs rRT-PCR were negative. Both recipients were discharged for 5 weeks after.
Today we have no evidence of the possibility of transmission of COVID-19 from a SARS-Cov-2 positive donor to a kidney recipient.

POS475 FOSCARNET INDUCED GENITAL LESIONS IN A KIDNEY TRANSPLANT RECIPIENT: A CASE REPORT

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Foscarnet(FOS), antiviral pyrophosphate analogue, is labelled as a second-line treatment for drug-resistant Cytomegalovirus(CMV)infection in immunocompromised patients. FOS is associated to adverse systemic reaction, sometimes severe(i.e. nephrotoxicity, electrolyte alteration)but minimizable by a careful monitoring. Among severe complications, genital ulcerations are reported in10% of treated patients. It is supposed to be due to drug local irritation as it is almost exclusively renal excreted, and it is usually described as a local dermatitis. Management is based on prevention with a careful hygiene, especially in uncircumcised patient. No specific therapy has so far been reported in literature even if it is usually reported a wound healing after FOS discontinuation.
A 31 years old kidney transplant recipient presented genital lesions during treatment of drug resistant-CMV primary infection with iv Foscarnet BID. According to dermatological evaluation lesions were treated at first with local Zinc-Oxide ointment and Phytostimulines15% medicated gauzes without any improvement. Serological screening excluded active infection by HIV,HSV type 1-2 and Syphilis. A biopsy of the ulcerated lesions documented keratinocytes with enlarged and bizarre nuclei with some HSV2+ cells at immunohistochemistry. Despite these histologic finding, consultant dermatologist suspected a drug-induced lesion and recommended a topical ointment with steroid and antifungal associated, as supportive therapy, with a careful local skin hygiene. Lesions improved a little but complete resolution only occurred at FOS suspension.
FOS is the empiric choice to treat a Ganciclovir resistant CMV infection in immunocompromised patients, allowing recovery with both graft and patients survival. Penile ulcerations are reported as an important cause of therapy discontinuation and clinicians should be aware of the problem in order to get an early recognition, ruling out of alternative diagnoses and a correct management.

POS476 PULMONARY MUCORMYCOSIS IN A KIDNEY TRANSPLANT RECIPIENT

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Mucormycosis (formerly zygomycosis) is a serious infectious disease with various forms of manifestation caused by group of molds called Mucorales. We present a case of a patient after a kidney transplant with a fatal course of the lung form.
We describe the case of a 60-year-old patient with IgA nephropathy and hypertension, without other serious comorbidities. The patient was after the 2nd cadaveric transplantation of a kidney in 2014 (first transplant 1994 – 2013 – failed for chronic humoral rejection). The patient was admitted to the internal clinic of the University Hospital Ostrava in the summer of 2018 for several weeks of diarrhoea, weight loss and weakness.
Initially, oral candidiasis, pancytopenia and function deterioration of the transplanted kidney was found with creatinine level 454 μmol/l (last value 394 μmol/l and eGF 0.22 ml/). The patient was hydrated, treated for oral candidiasis and cytomegalovirus infection (as the cause of pancytopenia). After a week of hospitalization, shortness of breath and cough had developed. Chest X-ray showed pleural effusion on the right and a laboratory-significant increase in inflammatory parameters (CRP 226 mg/l). The origin could not be identified despite extensive testing. Anti-Infectives were changed repeatedly, pleural evacuation and drainage were performed, as well as thoracoscopic revision. As part of the expansion of diagnostics, mucormycosis (Rhizopus microsporus) was finally identified as the causative agent. Despite targeted therapy with amphotericin, the condition had become complicated by other nosocomial infections and the patient dies due to MODS. An autopsy showed extensive, bilateral pulmonary infliction, and mucormycetes were detected microscopically.
Fungi of the order mucorales occur naturally in soil and other places of decomposition of organic substances (e.g., mouldy bread). Patients after solid organ transplantation belong to one of the risk groups (further corticotherapy, diabetes, malnutrition, oncological diseases). We distinguish several forms of the disease (the most common rhino-cerebral, then pulmonary, cutaneous, gastrointestinal and disseminated). The basis of therapy is antifungals (the first choice is amphotericin) and surgical (even repeated) removal of the affected tissue.

POS477 SUCCESSFUL TREATMENT OF TYPICAL HEMOLYTIC UREMIC SYNDROME IN A KIDNEY TRANSPLANT RECIPIENT USING ECULIZUMAB AND HAEMOADSORPTION DEVICES

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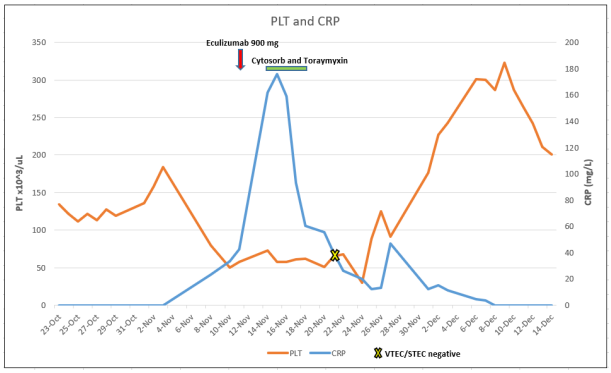
Typical hemolytic uremic syndrome (STEC-HUS) is a rare and potentially fatal disease caused by Shiga toxin-producing E. Coli (VTEC/STEC), that can lead to thrombotic microangiopathy with multi-organ involvement. A 35-year-old male, who underwent kidney transplantation at the age of 26 years due to IgA nephropathy (immunosuppressive therapy: cyclosporine and mycophenolic acid), was hospitalized for nephrotic syndrome and worsening of renal function. The patient received steroid therapy for allograft IgA nephropathy. Hemodialysis treatment was also needed. During hospitalization, bloody diarrhea was observed, and stools tested positive for a high virulence VTEC/STEC strain (stx2+, eae+). Blood tests showed: thrombocytopenia (80×10^3/ul), Hb 11.4 g/dL, leukocytosis, haptoglobin 1.86 g/L, LDH 311 U/L, bilirubin within the limits, reduction of C3, schistocytes at peripheral blood smear. STEC-HUS was diagnosed, fluid therapy and plasma-exchange were started, and immunosuppressive therapy was suspended. Eculizumab 900 mg was administered after the sudden onset of generalized tonic-clonic seizures associated with a state of impaired consciousness and taking into account the role of complement in the pathogenesis of STEC-HUS. Because of critical clinical conditions and septic shock, the patient was transferred to intensive care unit where invasive mechanical ventilation and continuous renal replacement therapy (CRRT), were performed. To reduce severe inflammation, 2 hemoadsorption devices, Toraymyxin® and Cytosorb®, were consecutively added to the CRRT. A second administration of Eculizumab was contraindicated because of the presence of K. pneumoniae and S.marcescens in bronchoalveolar lavage and coexisting immunosuppressive condition. The immediate reduction in endotoxin levels and inflammatory markers, normalization of platelet count and VTEC negativization on stools were associated with clinical improvement. The patient was discharged with an indication for chronic dialysis treatment. This case supports the validity of the combined use of Eculizumab along with Toraymyxin (a powerful endotoxin adsorber) and CytoSorb (with documented efficacy in the removal of Shiga-like toxin) in minimizing the multi-organ damage during STEC-HUS and in determining a rapid clinical improvement.



POS478 STRONGYLOIDES STERCORALIS HYPERINFECTION SYNDROME IN A PATIENT UNDERGOING KIDNEY TRANSPLANT

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Introduction: Strongyloidiasis is endemic in tropical and subtropical belts. Strongyloides stercoralis infection in transplant recipients can evolve into a fatal hyperinfection syndrome. The infection, in addition to deriving from a new contact, can be transmitted by the donor or secondary to the reactivation of a quiescent infection.
Methodology: 54-year-old patient from the DOMINICAN REPUBLIC in good general condition, subjected to kidney transplantation from a deceased donor of Italian origin in January 2020, showed inappetence, fever, diarrhea, skin rash and epigastralgia 3 months after the transplant. Blood chemistry tests showed marked eosinophilia (30%) and preserved renal function. Nasopharyngeal swab for SARS-COV-2, urine and blood cultures were negative. The EGDS showed severe duodenitis and the histological examination revealed the presence of Strongyloides stercoralis larvae, confirmed by the parasitological examination of the faeces. Chest x-ray and chest CT performed in suspicion of systemic infestation were negative.
Results: On infectious disease indication, therapy with Albendazole 400 mg/day was started for seven days. In the absence of respiratory symptoms, BAL was not performed. Discharge after improvement of the clinical picture and negativization of three parasitological tests of the faeces. One month after hospitalization for septic shock and hyperinfection syndrome with detection of S.stercoralis in BAL after orotracheal intubation. Ivermectin therapy with resolution of the infectious disease picture.
Conclusions: Patients from tropical and subtropical areas should be screened for S. Stercoralis as they are potential healthy carriers of the parasite. In the event of a diagnosis of post-transplant infection, it is essential to investigate the presence of systemic dissemination by adapting the therapy to the patient's immunosuppression picture.

POS479 COVID-19 EARLY AFTER RENAL TRANSPLANTATION: LIMITATIONS AND HAZARDS OF UNPROVEN THERAPIES

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Background: The interactions of immunosuppressants with antivirals against SARS-Cov2 are largely unknown. We present a case of COVID-19 contracted in the early postoperative period after kidney transplantation.
Methods: A 64-year-old man underwent kidney transplantation from a 75-year-old donor who died of a hemorrhagic stroke. The donor risk profile index was 1.25 and the renal biopsy had a score of 5/12. Bronchoalveolar lavage was negative for SARS-Cov2. Basiliximab was used for induction, for the maintenance tacrolimus, mycophenolic acid and steroids were administered.
Results: On the asymptomatic recipient, during the hospitalization, a protocol nasopharyngeal swab was performed and resulted positive for SARS-CoV2. For the onset of respiratory symptoms, leukopenia and pulmonary consolidations, mycophenolic acid was suspended and therapy with darunavir/ritonavir and hydroxychloroquine was introduced. Blood levels of tacrolimus immediately increased (28.7 ng/dl) and was promptly withdrawn. For clinical worsening, the patient was intubated, and the therapy was enhanced with steroids, tocilizumab and azithromycin. The elevated levels of tacrolimus persisted despite discontinuation and sessions of erythropheresis. The patient died in the thirty-fourth day post-transplant.
Conclusions: Considering the high risk of overexposure to tacrolimus and data from a recent randomized study, which did not show clear benefits of lopinavir/ritonavir in SARS-CoV2 infection, the systematic use of protease inhibitors in transplant recipients with COVID-19 should be considered cautiously

POS480 KINETICS OF LYMPHOCYTE SUBSETS IN A RENAL RECIPIENT WITH CMV DISEASE TREATED WITH GANCYCLOVIR AND ANTI-CMV HYPERIMMUNE INTRAVENOUS IMMUNOGLOBULIN

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CMV disease is a severe infectious complication after kidney transplantation. Very few studies have evaluated the cellular immune response to CMV disease during therapy. We prospectively evaluated functionally distinct lymphocyte subsets in a kidney recipient who developed difficult to control CMV disease after transplantation and who received combined therapy with gancyclovir and anti-CMV hyperimmune intravenous immunoglobulin (CMV-IVIG).
A prospective follow-up evaluation of a 44 year old men with high-risk second renal transplantation (donor CMV seropositive, receptor CMV seronegative). 200 days prophylaxis with valgancyclovir was used. By day 235 CMV primoinfection (CMV viral load 87681 IU/mL) was detected and IV gancyclovir therapy was started. Despite antiviral therapy viral load increased to 196700 IU/mL. At this time 5% CMV-IVIG (containing at least 100 Paul Ehrlich Institute Units/mL of specific anti-CMV antibodies) was added to antiviral therapy at a dose of 100 ml/week. A total of 4 doses of CMV-IVIG were used. Lymphocyte subsets were evaluated by eight-colour flow cytometry at the time of diagnose of CMV disease (gastrointestinal compromise + positive CMV viral load), at the time of the last dose of CMV-IVIG (when CMV viremia became negative, <150 IU/mL) and at 2 months after virus was controlled.
During follow-up of combined therapy with gancyclovir and CMV-IVIG a decrease of activated T lymphocyte subsets was observed as follows: CD4+CD38+DR+ 42.10% to 8.15% and 7.31%, CD8+DR+ 82.17% to 28.66% and 30.66%, CD8+CD38+DR+ 79.78% to 20.18% and 23.29%. A increase of naïve B cells CD19+CD27-IgM+IgD+ from 56.38% to 78.57% and 92.65% was also observed. A decrease of MFI of anti-HLA Class I and negativization of anti-HLA Class II DSA was demonstrated (12 months DSA assessment vs day 90, time of de novo appearance of DSA).
Conclusion: During combined therapy with antivirals and CMV-IVIG we observed an immune modulation of activated T-cells and of naïve B-cells in a renal recipient with difficult to control CMV disease.

POS481 HERPES SIMPLEX VÍRUS-2 HEPATITIS FOLLOWING KIDNEY TRANSPLANT: TAKE A SECOND LOOK

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A 50-year-old male received a kidney transplant (KT) from a deceased donor. Immunosuppression included basiliximab, tacrolimus (TAC), mycophenolate mofetil and prednisolone. Both donor and recipient were seropositive for cytomegalovirus and negative for HIV, hepatitis B and C. The recipient also was seropositive for herpes simplex virus (HSV) type 1 and 2 as well for varicella zoster virus, with positive IgG and negative IgM. The first postoperative days were unremarkable. By day 7 posttransplant, labs showed an hepatocellular pattern of injury with serum aminotransferases about 20 times the upper limit of normal (aspartate greater than alanine transaminase), gamma-glutamyl transferase mildly increased, normal alkaline phosphatase, bilirubin levels and prothrombin time. Potential hepatotoxic drugs were suspended (cotrimoxazole) or adjusted (TAC was reduced due to toxic blood levels) without analytic improvement. Abdominal ultrasound was normal. Blood viral screening was notable for positive HSV-2 assessed by polymerase chain reaction (PCR), and negative for hepatitis A, B, C and E. Repeated serological study showed positive HSV-2 IgG and negative IgM antibodies. Although he referred past recurrent ulcerative genital lesions, his physical examination was inconspicuous with no mucocutaneous lesions. Abdominal magnetic resonance showed homogeneous hepatomegaly and peri-portal edema, suggestive of viral hepatitis. HSV-2 hepatitis diagnosis was assumed and treated with intravenous acyclovir (10 mg/kg, 8/8 h). Blood HSV-2 PCR became negative and hepatic labs parameters normalized after 14 days of therapy, allowing hospital discharge on oral acyclovir. Acute hepatitis is a rare complication of HSV-2 infection. It is mostly seen on the first weeks after transplant, may be donor derived and frequently causes a rapid fulminant hepatic failure and multiorgan collapse. With this case, we highlight the importance of including HSV-2 infection on the differential diagnosis of an anicteric hepatitis, for early diagnosis and timely start of proper treatment to improve prognosis.

POS482 ALTERNARIA ALTERNATA PHAEOHYPHOMYCOSIS POST RENAL TRANSPLANT MASQUERADING AS CUTANEOUS TUMOUR

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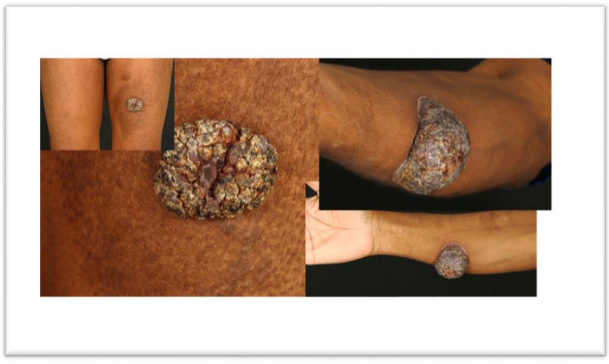
Introduction: *Alternaria alternata* is a common saprophyte found in nature, rarely affecting immunocompetent humans but may cause opportunistic cutaneous infection in immunosuppressed hosts. We present a patient with tumorous lesions rarely seen with this fungal infection.
Case presentation: A 61-year-old man from Nigeria, presented 3-months post deceased donor kidney transplantation. Induction was with interleukin-2 antagonist and immunosuppression included tacrolimus, mycophenolate and prednisolone. He had a 5-month history of slowly growing, tender, verrucous nodules on the left thigh and right forearm with bleeding and purulent discharge. Initially treatment was with flucloxacillin for presumed bacterial abscesses. Possible skin malignancy was considered, and an MRI demonstrated features of possible inflammatory or neoplastic aetiologies. The thigh lesion was excised, and the arm was biopsied and cultured (fungal and atypical mycobacterial). Both lesions revealed extensive mixed suppurative and non-necrotising granulomatous inflammation. Multinucleate giant cells containing intracytoplasmic spherical organisms with relatively thick refractile walls highlighted by Grocott's and PAS stains as round to oval yeast-like forms. A number of septate hyphae were also identified. Mycology culture was positive after 5 days incubation and A alternata was identified by 18S PCR, confirmed by the Mycology Reference Laboratory.



After multidisciplinary meeting (dermatology, microbiology, histopathology, plastic surgery and transplantation), the patient was started on Itraconazole 400 mg twice daily, then reduced to 200 mg BD with target levels 1-4 mg/L. After 3 months treatment the lesion on the thigh healed and arm lesion was flatter. Itraconazole was well tolerated but required significant reduction of tacrolimus dose. The graft function remained stable throughout (median creatinine serum 121 μmol/L).
Discussion: *A. alternata* infection can be challenging to diagnose and can masquerade as malignancy. Skin biopsy for histopathology and culture for accurate fungal identification is essential. Antifungal agents are the mainstay of treatment with careful monitoring of the immunosuppression. Treatment of this opportunistic infection is prolonged and requires a multidisciplinary approach.

POS483 MALAKOPLAKIA: A RARE CAUSE OF KIDNEY GRAFT DYSFUNCTION

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We report a 75-year-old woman with an end-stage kidney disease who received a kidney transplant from a deceased donor on May 2016, achieving a serum creatinine of 1.6 mg/dL.
In May 2019, she was admitted to the Intensive Care Unit due to a urinary septic shock and acute renal failure with requirement of renal replacement therapy. Blood cultures were positive for multisensitive *Escherichia coli* and urine culture was not assessable (contamination). Despite targeted therapy and resolution of the infectious condition she did not recover the renal function and remained on hemodialysis. Thus an allograft biopsy was performed.
There were different possible diagnoses that we considered in this setting. The suspicion of acute rejection was very low; although the antimetabolite was withdrawn, the patient was under steroids and tacrolimus with adequate trough levels. Other diagnoses considered were acute tubulo-interstitial nephritis due to drugs, post-infectious glomerulonephritis or severe acute tubular necrosis in the context of the septicemia.
The renal biopsy was diagnostic of malakoplakia and the antibiotic treatment was definitively switched to ciprofloxacin due to its better intracellular activity.
She experienced a favourable evolution after prolonged antibiotic therapy (12 weeks), with recovery of diuresis, discontinuation of renal replacement therapy and progressive improvement of the renal function.
Malakoplakia is a chronic granulomatous disease originally described in the urinary bladder, but it can virtually affect any organ. The mechanism involved in the pathogenesis is a defect in the bacterial phagocytic system that prevents lysosomes from digesting bacteria. Histologically, the Michaelis-Gutmann bodies are pathognomonic of the disease.
Immunosuppressive states are an important risk factor for malakoplakia. There are only 50 published cases with malakoplakia affecting kidney recipients. Its prognosis has dramatically improved with the use of antibiotics with greater intracellular penetration, and also the decrease of the immunosuppressive load.
Although malakoplakia is an unusual cause of graft dysfunction, it should be considered among the differential diagnosis in recipients presenting with an unexplained dysfunction with a history of recurrent urinary tract infection.

POS484 THROMBOTIC MICROANGIOPATHY SECONDARY TO COVID-19 IN A RECENT ABO-INCOMPATIBLE KIDNEY TRANSPLANT RECIPIENT

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We present a 35-year-old woman with end-stage kidney disease secondary to a Schoenlein-Henoch purpura, who preemptively received an ABO-incompatible kidney transplant from her father. She required ten immunoadsorption sessions and Rituximab before transplantation. She had a favorable evolution achieving a serum creatinine of 1.55 mg/dl at discharge. A week later she was readmitted with fever due to SARS-CoV-2 infection, that rapidly evolved to acute respiratory failure with bilateral interstitial pneumonia requiring orotracheal intubation. The antimetabolite was withdrawn, the dose of tacrolimus was reduced , and dexamethasone was initiated. Laboratory tests showed anemization with schistocytes, thrombocytopenia, elevated LDH and indetectable haptoglobin levels with a negative Coombs test. She also presented acute renal failure. The determination of isoagglutinins and donor-specific HLA antibodies (DSA) were negative, and the determination of complement and ADAMTS-13 levels were normal. Serological tests for HIV, HVC, HVB, parvovirus B19; and PCR for CMV and EBV were negative.

Given the absence of DSA or isoagglutinins, the diagnosis of antibody-mediated rejection was reasonably ruled out, and main diagnostic orientation was thrombotic microangiopathy (TMA) secondary to SARS-CoV-2 infection. At that point, treatment with eculizumab was started. Because of the need for invasive ventilation, the allograft biopsy was differed.
Finally, kidney biopsy was performed, which showed findings compatible with TMA (Figure 1). The immunohistochemistry technique for SARS-Cov2 was negative.
After receiving eculizumab she started to improve, with normalization of the parameters of hemolysis, and improvement of both renal and respiratory functions. The complement molecular and genetic assessments did not show any pathogenic variations.
Thrombotic microangiopathy is a severe complication of kidney transplantation that can lead to graft loss. Viral infections are known to trigger TMA, and TMA has already been described in the setting of COVID-19. SARS-CoV-2 infection can trigger endothelial damage and activation of the complement system, favoring a procoagulant state with generation of microthrombi and systemic inflammation.

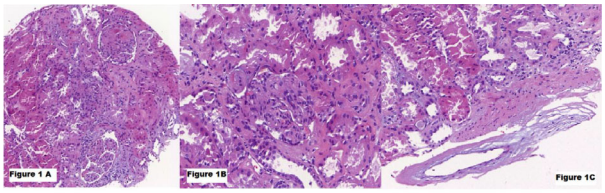

Figure 1. A y B. Glomeruli with signs of mesangiolysis with hematic extravasation and arteriolar myointimal hyperplasia. C. Intimal fibrous thickening with arterial mucoid edema, interstitial edema, and acute tubular damage, consistent with TMA.

POS485 IS THERE ANY ROOM FOR A CONSERVATIVE APPROACH FOR A GRAFT ARTERY ANEURISM?

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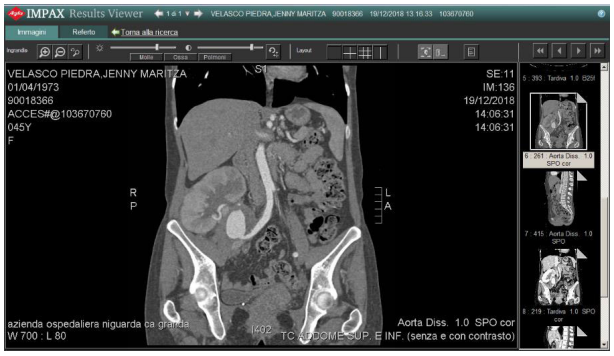
Allograft artery mycotic aneurysm (MA) is a life-threatening Kidney Transplantation (Ktx) complication mostly attributable to Candida or Aspergillus transmitted by donors or contaminated allografts. Graftectomy is the safest option for ruptures, but elective treatment is controversial. Prolonged antifungal administration is anecdotal. Endovascular procedures long-term results seem disappointing, yet carefully selected cases can offer excellent outcomes.
A 45-year Ecuadorian woman in haemodialysis due to unknown kidney disease underwent a donor deceased-KTx.
3 months later a saccular aneurysm (45 × 43 mm) was diagnosed in the graft arteria during a routine ultrasound. TC scan confirmed US findings. Since no clinical, laboratory, microbiological or radiological findings suggested localized or systemic infection, we opted for endovascular procedure by placing two endoprosthesis excluding the aneurysm. Normal post-operative course, stable allograft function. Beta glucan slightly increased (10.4, cut off: 11) so Caspofungin administered for 21 days.
Patient was discharged on hospitalization day 19 and then monitored in our outpatient clinic. Conditions were good, normal graft function, aneurysm gradually reduced.
Patient was admitted again 8 months post transplantation due to abrupt fever and diarrhea, worsening renal function and high inflammatory indicators (CRP 4 mg/dL). Beta glucan rose to 10,9. Blood cultures were positive for yeast. Caspofungin was started immediately.
TC scan showed focal hypodense points under graft cortex middle third, adjacent renal lobe edema, corresponding arteriole thrombosis. Excluded aneurysm was further reduced (23 × 25 mm) with no perfusion sign.
Thereafter, Beta glucan levels increased to 164. Amfotericin B was started without sepsis resolution. Graft function quickly deteriorated until haemodialysis' need.
Graft was explanted 9 months post-transplant.
Histological samples detected Aspergillus hyphaes in blood vessels walls. Graft artery was thrombosed. A segmental vessel wall was desiccated. Coagulative necrosis with small septic emboli was visible in large graft areas.
Despite absence of any clue, graft artery lesions are invariably related to mycotic infection and, even if carefully considered, a conservative approach is doomed to fail.



POS486 REVERSIBLE ISCHEMIC NEPHROPATHY IN CADAVERIC RENAL TRANSPLANT RECIPIENT

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Background: Atherosclerotic renal artery stenosis is one of the risk factors for cardiovascular death. It can lead to the ischemic nephropathy. We aimed to report a case of successful management of ischemic nephropathy that develops in kidney transplant recipient with graft artery stenosis.
Methods: We present 52-year-old-male diabetic, hypertensive, non-smoker patient with hypothyroidism on replacement therapy. He had a history of recurrent urinary tract infection -due to vesico-ureteric reflux- before starting hemodialysis on July, 2009. He received his cadaveric renal allo-graft in 11.3.2020 with slow graft function. He received thymoglobulin as induction and steroid, tacrolimus, and mycophenolate mofetil as maintenance. He was discharged with nadir creatinine around 130 μmol/L. His diabetes was controlled by intensive insulin regimen.
Preliminary Results: Later, he developed graft dysfunction with partially controlled hypertension and suspected r graft artery stenosis by Doppler ultrasound but no evidence of obstruction. His tacrolimus level was adequate and his echocardiography was unremarkable. He received empirical pulse steroid, and his graft biopsy showed severe acute tubular necrosis, suspicious T cell-mediated rejection, negative C4d, and positive SV40 stain suggesting BK nephropathy. Both BK viremia and viruria was improving on immunosuppression minimization but without positive impact on graft function (dialysis-dependent). Because of flattening of systolic wave (by Doppler US), computed tomographic angiography revealed diffusely attenuated graft arteries. So, satisfactory graft artery angioplasty was carried out in addition to stenting of the two arteries. Fortunately, the patient started to make urine in the same day with good systolic wave by doppler. His graft function started to improve and he was discharged with stable graft function. Later, his immunosuppressive regimen was tailored to steroid and low dose tacrolimus.
Conclusions: Ischemic nephropathy is reversible if properly managed even in presence of other comorbidities.

POS487 TREATMENT OF PSUEDOANEURISM OF EXTERNAL ILIAC ARTERY IN PATIENT UNDERGOING KIDNEY TRANSPLANT

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Introduction: There are several causes of kidney transplant dysfunction. The most common vascular complications are thrombosis and stenosis of the main vessels, while the formation of pseudoaneurysms is rarer. The role of the EcoColorDoppler is fundamental in the early and differential diagnosis of these complications.
Methodology: 66-year-old patient with IPA and end-stage IRC secondary to ADPKD underwent in January 2020 FID kidney transplant from a marginal deceased donor. The graft presented one renal and one inferior polar arteries that were anastomosed with a single aortic patch. Four months later, there was a worsening of renal function and turbulent flow ecocolor-doppler with aliasing at the iliac-renal anastomosis of the graft. The

AngioTC showed the presence of two pseudoaneurismatic dilations with bilobed morphology and post ostial stenosis of the inferior polar artery. Subsequent selective angiography with placement of open mesh stents in the External Iliac Artery to cover the emergence of the two renal neo arteries, release of embolizing spirals within the pseudoaneurysms and PTA of the lower polar artery.
Results: The patient performed monthly EcoColorDoppler and 3-month MRI angiography showing patency of the stent pseudoaneurysm thrombosis. Renal function remained stable. The double anti-aggregation was maintained for 3 months to obtain a slow occlusion of the aneurysmal sacs, reducing the risk of embolization in the neo renal artery.
Conclusions: The follow up of kidney transplantation includes the use of ECD and the participation of a multidisciplinary team consisting of the transplant surgeon, the vascular surgeon and the interventional radiologist in order to achieve excellent management of complications.

POS488 TIGECYCLINE-INDUCED ACUTE PANCREATITIS IN RENAL TRANSPLANT RECIPIENT: CASE REPORT AND REVIEW OF LITERATURE

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Introduction: Tigecycline is a broad-spectrum antibacterial drug structurally related to minocycline. Pancreatitis has been associated with the tetracycline class of antibiotics and concerns about tigecycline-induced acute pancreatitis have recently been raised.
Aim: To report kidney transplant recipient with tigecycline induced acute pancreatitis.
Case report: We describe a 34-year-old female who had a history of ANCA associated vasculitis reached end stage kidney disease (ESKD) and was maintained on regular hemodialysis for 2 years till she has a deceased donor kidney transplant on 14.11.2020. Her serum creatinine dropped to a nadir of 160 μmol/L. She received meropenem and tigecycline for treatment of a complicated perianal abscess for 5 days when she started to complain of severe agonizing epigastric pain necessitating omeprazole infusion, intravenous fluid plus keeping the patient fasting after 2 days' patient start to have high blood sugar needed multiple corrective insulin doses. Her serum amylase and lipase started to rise with leukocytosis and renal allograft dysfunction (serum creatinine rose up to 252 μmol/L) suggesting acute pancreatitis. Abdominal ultrasound was done and revealed bulky pancreas with intra-abdominal free fluid. Perianal tissue cultures grew *Pseudomonas aeruginosa* sensitive to ciprofloxacin so, tigecycline was replaced by ciprofloxacin. After 2 days of stopping the tigecycline serum amylase start to decrease and blood sugar also controlled without insulin need together with improvement of her leucocytic count and serum creatinine then the abdominal pain improved after 4 days of its discontinuation.
Conclusion: Acute pancreatitis is rare disorder among renal transplant recipients which could be induced by tigecycline. So, we recommend monitor kidney recipients for signs and symptoms of pancreatitis, during treatment with tigecycline.

POS489 TRANSIENT HYPERPHOSPHATASEMIA IN AN ADOLESCENT AND AN ADULT RENAL TRANSPLANT PATIENT

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Background: In renal transplant patients receiving immunosuppression, a significant increase in alkaline phosphatase (ALP) might be indicative of liver or bone diseases caused by many factors including infections, medication toxicity and rarely tumors. In infancy and early childhood, a transient and therefore benign increase in ALP has been often described, usually during a course of infectious disease. Rarely, transient hyperphosphatasemia occurs in adults. We herein present two cases of transient hyperphosphatasemia in an adolescent and an adult, renal transplant recipient, respectively.
Clinical Cases – patients' relevant data and investigations performed: In the first case, a 17 year old adolescent, one month after uneventful kidney transplantation, presented with an ALP value up to 2451 U/l, reporting no symptoms. Diagnostic workout included biochemical markers of liver function, viral serology, abdomen ultrasound, bone scanning, ALP electrophoresis and measurement of bone-specific isoform of ALP. In the second case, a 56 year old female with a second well-functioning kidney transplant presented with an ALP value up to 1532 U/l, without symptoms. A history of osteoporosis under treatment was recorded and, therefore, a bone density test was performed as well as osteoblast and osteoclast activity markers (total PINP and CTx respectively).
Final diagnosis: In both cases biochemical profile and ultrasound study were negative for liver disease while no viral or other type of infection was detected. Bone scanning was within normal range and parathyroid hormone was also normal. However, bone ALP was measured 8.9 and 11.9 times, respectively, above reference values. In the second case, the additional tests pended did not reveal any further abnormality. ALP electrophoresis had a characteristic pattern with involvement of both liver and bone-specific isoforms. About six weeks after their peak, ALP values gradually returned to normal range.
Discussion points: Benign transient hyperphosphatasemia, although rare should be considered in the differential diagnosis of isolated ALP increase, even in adult patients with kidney transplant. Electrophoresis of ALP could narrow the diagnostic procedure in cases when neither liver nor bone disease is clinically apparent.

POS490 A SUCCESSFUL KIDNEY AUTOTRANSPLANTATION IN A PATIENT WITH MULTIPLE RENAL ARTERY ANEURYSMS

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Background: Literature has shown that kidney artery aneurysms are a rare, with an incidence of about 1%. The aneurysm location can be classified as extraparenchymal or intraparenchymal. They can be fusiform or saccular in appearance and are extraparenchymal in 90% of cases.
Methods: We report on a 37-year-old woman who was symptomatic since 2001 suffered from arterial hypertension (max BP 180/90 mmHg). 10/26/2020 computed tomography angiography showed changes in right kidney artery: 2 extraparenchymal saccular aneurysms (aneurism №1 – 8 mm and №2 – 9 mm) and one intraparenchymal high rupture risk fusiform aneurism (№3 – 8 mm), proximal stenosis of artery 80%. Renal scintigraphy: the right kidney is omitted, the size is reduced. Separate glomerular filtration in the right kidney it is reduced by 51%. In December 2020 was performed CT angiography, there was the growth of aneurysm № 1 to +0.2 mm, aneurysm № 2 + 0.1 mm and increase proximal stenosis up to 90%.
Results: The operation was performed in February 2021 right-sided nephrectomy, extracorporeal renal artery reconstruction and a heterotopic kidney autotransplantation. Ex vivo kidney preservation by Custodiol solution was performed, the aneurysms №1 and №2 were resected completely and a suture for aneurism №3 (intraparenchymal) by polypropylene 8/0 was done. The right kidney was repositioned into the left pelvic region. The renal artery was anastomosed to the iliac artery and the left renal vein to the left common iliac vein. Total ischemic time was 75 min. The autograft was reperfused homogenously and urine production started immediately. Postoperatively, mean arterial blood pressures remained to the normal range. Blood samples were in the normal range. Histopathological findings: fibromuscular dysplasia, thrombosis of aneurysm №2.
Conclusion: The patient suffered from renovascular hypertension as a result of fibromuscular hyperplasia of the renal artery with the formation of aneurysms, one of which was located at the hilum of the kidney (intraparenchymal). The performed extracorporeal artery reconstruction with kidney autotransplantation achieved normalization of the renal hemodynamic and a blood pressure.

POS491 EN-BLOC KIDNEY TRANSPLANT USING AN AORTIC EXTENSION FROM A PAEDIATRIC MULTI-VISCERAL DONOR TO A PAEDIATRIC RECIPIENT

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Background: Renal transplantation is the gold standard treatment for end stage kidney disease (ESKD) in children. EBKT from small paediatric donors under five years of age and weighing less than 20 kg can be a good option for selected paediatric renal transplant recipients. EBKT refers to transplantation of both kidneys from the same donor into a single recipient.The utilisation of these organs has a higher risk of vascular thrombosis, stenosis and ureteral leak in children.
Methods: Case presentation and literature review. This is the first case using an aortic extension on the proximal segment of an EBKT.
Results: We present the case of a successful EBKT, which was performed with an aortic extension using a segment of the aortic arch since the donor operation included multivisceral donation requiring the patch of the Superior Mesenteric Artery (SMA). This is the first description of utilising the thoracic aorta as an extension graft for EBKT in paediatric multivisceral donor for a paediatric recipient. The aorta was reconstructed and the en-bloc kidneys were successfully implanted into the left iliac fossa onto the iliac vessels.

POS492 IS PREGNANCY SAFE IN THE EN BLOC RENAL RECIPIENTS FROM INFANT DONORS? A CASE REPORT

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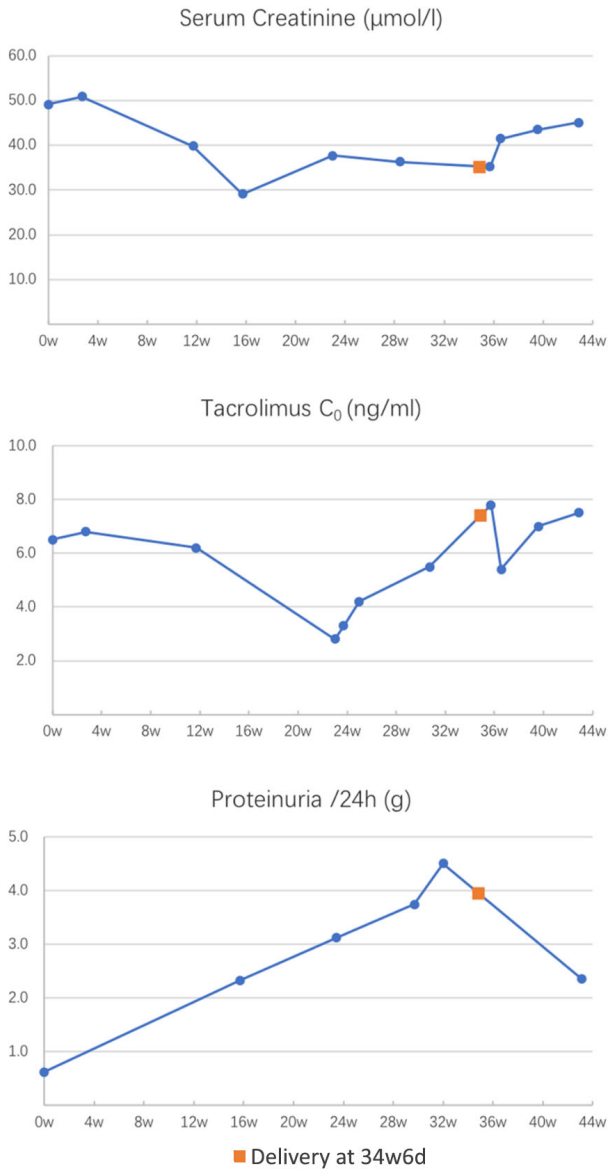
Background: Very low bodyweight pediatric donor kidneys are underutilized for transplantation into adult recipients. Therefore, pregnancy in the en bloc renal recipients from infants were rarely reported. Except for the common risks like maternal and fetal complications in all renal graft recipients, worries also include compression of the medial graft, and worsening hyperfiltration injury. We reported one case focusing on the complications.
Methods: One 24-year-old female received en bloc renal grafts from one infant weighing 3.7 kg after cardiac death about 3 years ago. Clinical characteristics of donor and recipient were shown in Table 1. Induction immunosuppression consisted of thymoglobulin+methylprednisolone, and the recipient was maintained with tacrolimus (TAC)+mycophenolate mofetil (MMF)+prednisone. MMF dosage was tapered and subsequently transferred to Azathioprine 6 months before planned pregnancy. Low molecular weight heparin (4000 u, s.c., qd) was started at 23rd week of gestation, and tapered at 1 week after delivery.
Results: During pregnancy, there was a remarkable drop down of whole blood TAC trough concentration and serum creatinine (Figure 1). Moreover, urinary protein excretion increased substantially (Figure 1). The recipient had a scheduled Caesarean section at 34 weeks 6 days of pregnancy because of progressive aggravated hypertension and proteinuria (Figure 1). A healthy female baby weighing 2.5 kg was born. Repetitive prenatal renal grafts ultrasound showed normal perfusion and absence of hydronephrosis.
Conclusions: Although the outcome of this case is favorable, the recipient did have preeclampsia, especially remarkable aggravating proteinuria which lead to preterm delivery. Considering of the potential preexisting higher risk of glomerular hyperfiltration injury of en bloc grafts due to the huge size disparity between pediatric donors and adult recipients, pregnancy of these recipients needs serious consideration. Future expanded studies are warranted.

Table 1. Donor and Recipient Characteristics

Donor Wt (kg)	3.7
Donor Age (day)	33
Recipient Wt (kg)	46
Recipient Age (year)	24
Recipient/Donor Wt Ratio	12.4
Recipient gestational age	34w6d

Figure 1. Perinatal serum creatinine, Tac C0, urinary protein/24 h



POS493 WEST NILE ENCEPHALITIS IN AN ADOLESCENT KIDNEY TRANSPLANT RECIPIENT

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Background: West Nile Virus (WNV) infection is mainly asymptomatic and only 20% of infected patients present viral symptoms. The disease can become severe in immunocompromised patients, with a high risk of central nervous system (CNS) manifestations, including meningitis, encephalitis and acute loose paralysis. We describe a case of an adolescent kidney transplant recipient, who developed acute encephalitis due to WNV infection.
Clinical case: A 19-year-old kidney transplant recipient with fever and headache for five days presented sudden confusion, right hemiparesis and hemianopsia. Brain magnetic resonance imaging was normal and

cerebrospinal fluid (CSF) cytology revealed 270 cells with predominance of lymphocytes, which was in favor of encephalitis. The patient initially received antibacterial (ceftriaxone, linezolid, ampicillin/sulbactam) combined with antiviral (acyclovir, valganciclovir) treatment, while immunosuppressive therapy was reduced. Multiplex PCR for CNS viruses and bacteria and PCR for EBV, CMV, JCV, BKV, toxoplasma and mycobacterium tuberculosis in CSF were negative. CSF culture for bacteria and fungi was negative. Anti-WNV IgM antibodies were ultimately detected in initial blood serum and anti-WNV IgM titers increased 5 days later, setting the diagnosis of WNV infection. The patient presented remission of neurological symptoms and fever within the first 48 hours of encephalitis onset and antimicrobial treatment was gradually discontinued.
Conclusions: WNV infection should be included in the differential diagnosis of encephalitis in kidney transplant recipients. Immediate reduction of immunosuppressive therapy is important to avoid further complications.

POS494 ACQUIRED FACTOR VII DEFICIENCY POST RENAL TRANSPLANTATION

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52-year-old male, a case of Living Unrelated Renal Transplantation in 2005 but no records were provided about his operation. He is on cyclosporine, prednisolone and mycophenolate. Hypertension, Post-transplant DM with Stable allograft function with creatinine of 100-130 micromole/L.
In late 2020 he had recent increase in creatinine and got admitted for kidney biopsy. His coagulation profile showed prolonged PT more than 120 seconds and normal PTT with INR of 10. He had no history of prolonged bleeding, No family history of bleeding disorders. He does not recall any bleeding post his renal transplantation, he did not require blood transfusion and his wound healing was excellent. His creatinine improved back to baseline and biopsy was declined at that time. Mixing studies showed mildly elevated PT, but further workup showed decreased factor VII coagulant activity. Other coagulation factors including factor II, factor IX and factor X were normal. Qualitative FVII inhibitor screening assay shows no evidence of a specific inhibitor of coagulation factor VII. Hematology team recommended No treatment needed but in case of surgery or any invasive procedure Factor VII 30-40 units per kg need to be considered preoperatively. The diagnosis of acquired factor VII deficiency post organ transplantation is rare and documented in case reports of patients who underwent stem cell transplantation. Some patients were reported with veno-occlusive disease.

Table of blood tests

PT	* >120.0	* >120.0		* (c) 68.6 sec(s	* (c) 68.4 sec(s
INR	* >10.0	* >10.0		* 5.6	* 5.6
APTT	* 31.8 sec(s)	* 33.1 sec(s)		* 33.7 sec(s)	* 32.6 sec(s)
Fibrinogen Lvl	4.34 g/L	4.04 g/L		4.11 g/L	4.03 g/L
Factor II	* 106.0 %				
Factor VII	* <2.5 %		* <2.5 %		
Factor IX	* 151.0 %				
Factor X	* 108.0 %				
Path Review Coag	Path Review Coag				
Anticoagulant?	None, None, None, None, None	None	None	None	None
D-Dimer Auto	* 0.49 mcg/mL	* 0.53 mcg/ml		* 0.58 mcg/ml	* 0.63 mcg/ml
PT-Mix 50:50 Incub	* 15.9 sec(s)				
PT-Mix 50:50 No Incub	16.1 sec(s)				15.1 sec(s)

POS495 KIDNEY TRANSPLANTATION AS A TREATMENT OF CHOICE FOR AA AMYLOIDOSIS DUE TO PERIODIC FEVER SYNDROME

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Background: Renal AA amyloidosis is the most serious complication of periodic fever syndrome which leads to nephrotic syndrome and renal failure.
Method: We present cases of two patients after deceased donor kidney transplantation, who have been diagnosed with adult periodic fever syndrome.
Results: First case report: A 24-year-old man was referred by an immunologist for end-stage CKD based on AA amyloidosis. A clinical diagnosis of familial Mediterranean fever was, Colchicine treatment was initiated in combination with the IL-1 inhibitor (canakinumab). Hemodialysis (HD) therapy was initiated and after 6 months the patient underwent a successful primary deceased donor kidney transplantation. The patient undergoes regular outpatient checks graft function is adequate, treatment with colchicine and canakinumab continues, with CRP and IL-6 within the physiological range, with serum amyloid A only slightly elevated (Fig 1). Second case report: A 50-year-old male patient with terminal stage of CKD based on histologically confirmed amyloidosis with mesangioproliferative glomerulonephritis in the regular HD program (since July 2018) underwent a primary deceased donor kidney transplantation in June 2019. Six months after kidney transplantation, the patient began to recur at a regular 3-day interval with fever responding to paracetamol with increasing CRP and muscle pain, but showed no signs of localized infection. This condition did not respond adequately to any antibiotic treatment. Based on the presence of a recurrent inflammatory reaction with polyserositis, without a proven infectious and autoimmune source, the patient was reported to a clinical immunologist. Hereditary form of autoinflammatory disease was suspected by a clinical and laboratory evaluation. Using the EuroFEVER scoring system and the IL inhibitor (anakinra) therapeutic assay, CAPS (periodic cryopyrin-related syndromes) is the most likely diagnosis. Genetic testing is currently in progress.
Conclusion: Adequate targeted treatment against IL-1 or TNF is important and appears to be safe during the post-transplant period, with regular monitoring of renal function.

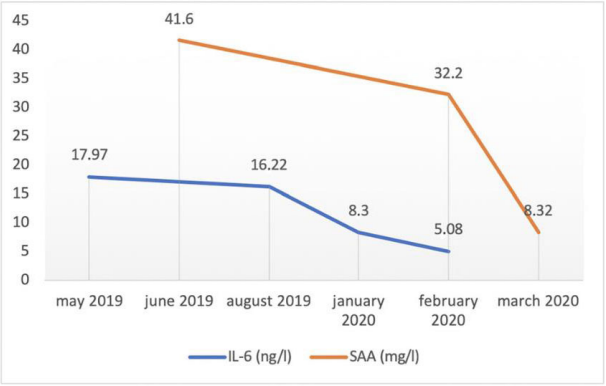

Figure 1. Development of IL-6 and SAA levels during treatment of FMF. IL, interleukin; SAA, serum amyloid A; FMF, familial Mediterranean fever

POS496 50TH ANNIVERSARY OF THE FIRST KIDNEY TRANSPLANT IN BELARUS:SUCCESS PROGRAM HIGHLIGHTS AND CURRENT RESULTS

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Background: The first kidney transplant in Belarus was performed on September 11th, 1970.The experience of the last decade shows that the successful transplant program was created in Belarus.
Methods: Several key highlights can be determined as the main methods that helped us to reach the objective.
November 2006 – First LRD Transplants were performed in Minsk.
January 2007 – The updated Transplant Legislation was released. The Presume Consent Law was established followed by the first OPO created in Minsk.
April 2009 – First LRD pediatric kidney transplantation was performed.
June 2009 – First SPKT was performed in Minsk.
April 2010 – The National Transplant Center was created.
November 2011 – First regional transplant Center in Brest was launched followed by the annual launches of the regional transplant program in each district. The whole country kidney transplant network was finalized in 2018.
December 2012 – The international collaboration started: Minsk Transplant Team performed the first LRD pediatric kidney transplant in Astana (Kazakhstan), followed by first pediatric and adult LRD in Bishkek (Kyrgyzstan), followed by ongoing hands on support for the kidney transplant centers in Shymkent (Kazakhstan) and Tbilisi (Georgia).
Results: there were 3886 kidney transplants performed. During the last decades 2889 KTx were done: including 182 (6.3%) LRD, 178 pediatric KTx and 29 multiorgan transplantation (23 SPKT, 5 kidney-liver and 1 kidney-heart).
Delayed graft function was found in 537/2889 (18.6%) cases. 713 kidney graft biopsies were performed. The analysis showed acute cellular rejections in 143/713(20.76%), acute humoral rejection in 140/713 cases (19.6%), recurrent kidney diseases in 69/713 (9.7%) and IFTA in 122/713 (17.1) cases.

Median serum creatinine level at year 1-, 3-, 5- and 8 are: 114.5 (96.9-140.8) μmol/l, 114 (88.6-142), 109.7 (86-144) μmol/l, 106.1 (80-137.9) μmol/l. The 10 years transplant survival rate is 84%.
Conclusions: According to the IRODAT Registry over the last 5 years Belarus keeps stable place in the top 15 countries with the most developed kidney transplant program. It allows us to postulate that fortunately everyone who needs the kidney transplant has got it without any limitation except his/her own health condition.

POS497 RENAL LYMPHANGIECTASIA: A CHALLENGING DIAGNOSTIC APPROACH FOR A RARE COMPLICATION AFTER KIDNEY TRANSPLANTATION

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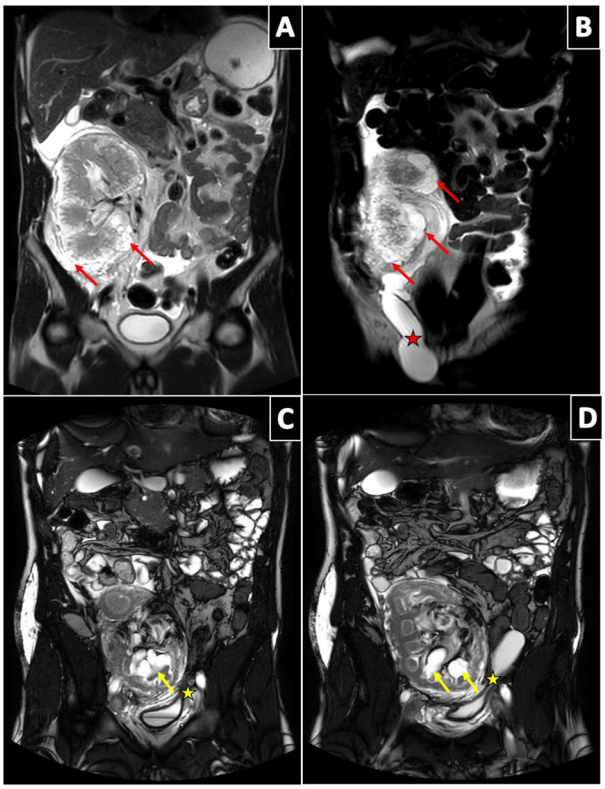
Introduction: Lymphatic complications are very frequent after kidney transplantation, the most common being lymphocele which can affect up to 40% of patients. Among the lymphatic disorders, renal lymphangiectasia is an extremely rare complication of unknown pathophysiology, making its diagnosis and management particularly challenging.
Case findings: We present here two cases of renal lymphangiectasia occurring after kidney transplantation, both revealed by atypical ascites, nephromegaly and local mechanical complications: inguinoscrotal hydrocele (patient #1, panel B, red star) and bladder compression (patient #2, panels C-D, yellow stars). This pathology was characterized by late occurrence after kidney transplantation (between 8 and 10 years), in young patients, with preserved graft function despite a history of acute rejection. These two cases illustrate different anatomical presentation patterns, from cortical (patient #1, panels A-B, red arrows) to peri-hilar involvements (patient #2, panels C-D, yellow arrows). In both cases, making a definitive diagnosis was very complex, with serial misdiagnosis and the multiplication of additional and invasive examinations. Therapeutically, a similar development was interestingly noticed in both patients with mTOR inhibitors: better control of ascites, at the expense of increased nephromegaly.
Conclusion: The diagnosis of kidney graft lymphangiectasia should be suspected in case of multiple perirenal and/or peripelvic cysts, responsible for progressive nephromegaly and atypical ascites after kidney transplantation. This remains an exclusion diagnosis which relies on the combined findings of sequential imaging examinations (ultrasound, CT scan, and MRI). The prognosis is mostly driven by local mechanical complications and alteration of quality of life. There is no specific treatment and transplantectomy may unfortunately be justified in case of poor outcome. The evolution presently described after mTOR inhibitors introduction brings new insights on pathophysiology of kidney graft lymphangiectasia. These observations however confirm the challenging diagnostic process for this very rare complication after kidney transplantation and the value of a multidisciplinary approach.



POS498 THROW THE HEART OVER THE FENCE: SUCCESSFUL LIVING DONOR KIDNEY TRANSPLANT IN YOUNG MALE WITH SEVERE DISABILITY

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Preterm 21 years old patient born by caesarian section for maternal pregnancy-induced hypertension. Intrauterine growth restriction, low birthweight, postnatal respiratory illness and cardiac dysfunction, blindness, hearing loss, severe mental retardation, lack of autonomy, only haptic communication and renal failure from birth caused by prematurity. In the last year progressive loss of kidney function required renal replacement therapy. Dialysis treatment was not possible to perform for his fear of needles and medical patches. This condition induced his father to propose himself as potential kidney donor. Despite the limits imposed by the Sars-CoV-2 disease emergency, the transplantation team (anesthesiologists, nephrologists, transplant surgeons) decided to accept this challenge.
After performing all the necessary tests and evaluating the feasibility of surgery, the patient underwent a pre-emptive living donor kidney transplant. Immunosuppressive therapy: induction with Steroids and Basiliximab, maintenance with Steroids and Cyclosporine administered intravenously because of the difficulty of taking oral medications. In the immediate post-operative period, curarization and light sedation with Dexmedetomidine were required and the recipient was observed in an Intensive Care Unit. Early graft function. In postoperative day four chest CT was performed due to deteriorating of gas exchanges. The CT showed bilateral atelectasias and opacities. Antibiotic therapy and pronation cycles were started with clinical improvement. In sixth postoperative day the patient was ready to wean from mechanical ventilation by conducting a spontaneous breathing. Finally, he was transferred to the Urology Unit, with transition from intravenous to oral immunosuppressive therapies with the use of Cyclosporine (oral solution) and Everolimus (orodispersible). The patient was then discharged home and started the clinical follow-up at Nephrology Division. After three months from transplant, stability of graft function was observed (serum creatinine 0.8 mg/dl).
In conclusion, a multidisciplinary approach involving nephrologists, transplant surgeons and anesthesiologists makes it possible to perform a successful kidney transplant as a real therapeutic strategy also in patients with a severe disability.

POS499 THE RELEVANCE OF NATURALLY OCCURRING NON-HLA ANTIBODY TO ANTIBODY-MEDIATED REJECTION IN PATIENTS WITHOUT ANTI-HLA ANTIBODIES

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Background: Very few papers describe the association between non-HLA antibodies and the incidence of antibody-mediated rejection (AMR) in kidney recipients. We investigated the incidence rate of AMR in recipients with or without non-HLA antibody and anti-HLA antibodies (DSA).

Methods: The sample serum was collected from 130 recipients before kidney transplantation. Basically, all patients with DSA detected by Luminex received desensitized protocol including low-dose rituximab and plasmapheresis to remove DSA prior to transplantation. In contrast, except for patients with DSA, none received desensitization protocol. The frequencies of AMR due to non-HLA antibodies were examined.
Results: Totally 130 recipients were divided into 4 groups according to the presence of HLA antibodies (DSA) and non-HLA antibodies as follows; G1: DSA+/non-HLA Ab+ $N = 21$; G2: DSA+/non-HLA Ab- $N = 3$; G3: DSA-/non-HLA Ab+ $N = 76$; G4: DSA-/non-HLA Ab- $N = 30$. In G1, 5 of 21 (5/21, 24%) showed active and chronic AMR, each one did BK viral infection, TMR and IFTA. In G2, 1 of 3 showed AMR. In G3, 5 (5/76, 7%) recipients showed AMR. Two showed TMA. Totally, 7 of 76 (7/76, 9%) in G3 showed AMR and suspicious AMR. These 7 recipients with AMR, probably due to the presence of non-HLA antibodies, were completely rescued by postoperative desensitized treatments including rituximab administration and plasmapheresis. The remaining 30 recipients in G4 without DSA as well as non-HLA antibodies showed no AMR after kidney transplantation.
Conclusions: Immediately after kidney transplantation, non-HLA antibody seems to be capable of causing AMR, however, followed by complete recovery from AMR by the antibody removal treatment postoperatively. In recipients with non-HLA antibodies, the incidence rate of AMR is not so high and its intensity is not so severe, compared to HLA antibodies (DSA), although further examination is needed for understanding long-term influence of non-HLA antibodies after kidney transplantation.

POS500 RENAL ARTERY STENOSIS AFTER KIDNEY TRANSPLAN: ANGIOPLASTY NOT ALWAYS THE FIRST CHOICE

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Background and Aims: Post kidney transplant (KT) renal artery stenosis (RAS) occurs in 1-23% patients. It might be the result of artery trauma, subtle intimal ap or sub-intimal dissection with ultimately narrowing of lumen. Classically endovascular management is the rst line of treatment. However restenosis rate is around 40%. Surgical revascularization is exceptionally used in patients unt for angioplasty or stent placement.
Materials & Methods: A 61 year old female recipient with suboptimal renal function (creatinine 3.0 mg/dl) after KT presented a dopplerUS study with peak systolic velocity (PSV) >500 cm/s, suggestive of RAS. Diagnosis was confirmed by angio-CT and angiography. Percutaneous angioplasty was performed with partial improvement of doppler-US pattern (PSV 270 cm/s) and suboptimal creatinine levels (>2 mg/dl). Surgical revascularization was decided.
Results: Resection of the stenotic segment and resolution of an associated kinking were followed by an end-to-side anastomosys to the distal external iliac artery. In situ reperfusion of the graft was performed with 4°C Ringer-lactate prior to revascularization. Excellent reperfusion took place and was confirmed with a contrast-enhanced ultrasound study in the post-operative period. Doppler-US showed normalization of PSV (120 cm/s) and creatinine decreased to 1.3 mg/dl. Surgical details are showed.
Conclusions: RAS should be suspected in KT with immediate suboptimal function specially in recipients with kidneys from expanded criteria donors. Although angioplasty is the usual treatment, in selected cases (early, long stenosis and kinking) surgical revascularization may be considered the rst choice of treatment.

POS501 NEVER FORGET YOUR TRANSPLANT SURGERY – IT COULD BE A LATE CAUSE OF ALLOGRAFT DYSFUNCTION

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Iliac artery dissection (IAD) is a rare vascular complication of kidney transplant (KT) surgery. Few cases were reported, most of them had occurred intra-operatively or in the early postoperative period.

We present a case of a 47-years-old man with end-stage renal disease due to IgA nephropathy who received a living-donor kidney graft in 2016. He was on maintenance immunosuppression with prednisolone, tacrolimus, and mycophenolate mofetil, with normal kidney function (KF) and no previous complications. Four years after KT he presented in the emergency department complaining of intense pain located at right iliac fossa (RIF) and lumbar region that started 24 h earlier after lifting some heavy boxes, associated with low urinary output. Vital signs were normal except for hypertension. Physical examination was unremarkable not for RIF pain. Blood tests revealed acute kidney injury (AKI), with serum creatinine (sCr) of 5.24 mg/dL and urea of 81 mg/dL. Computed tomography showed a small dissection of the right external iliac artery (EIA), extending to the common iliac artery (CIA), but stated that the transplant renal artery (TRA) was permeable and graft properly perfused. Considering the AKI, endovascular stenting of the right CIA and EIA was performed. Kidney function had worsened on the first days after surgery (maximum sCr 12 mg/dL) prompting the need for hemodialysis. Kidney function had slowly recovery, and the patient was discharged after 19 days on dual antiplatelet therapy. Follow-up at 9 months revealed sCr of 2.22 mg/dL. Genetic testing for collagen diseases found a variant of undetermined significance in the COL1A1 gene.
The IAD in this setting is presumably related to traumatic vascular procedures during KT surgery years before. Although the TRA was permeable, allograft dysfunction occurred most likely due to hemodynamic changes of flux leading to acute tubular necrosis. This case is unique, with no similar reports, for its timing of presentation 4 years after KT surgery.

POS502 URETERIC TRAUMA FOLLOWING STENT REMOVAL IN KIDNEY TRANSPLANT RECIPIENT: A UNIQUE CASE OF PROLONGED MORBIDITY

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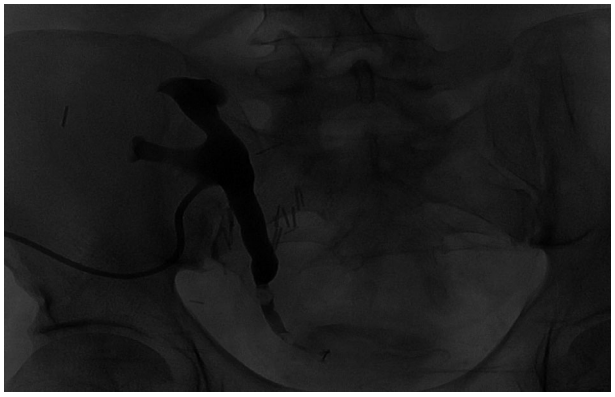
Background: In most transplant centers it is routine practice to use ureteric stents for ureter to bladder anastomosis during kidney transplant and it is removed after 3 to 4 weeks with flexible cystoscopy. The stent removal procedure is essentially a non-traumatic procedure. We report a case of ureteric stent removal which resulted in significant morbidity.
Methods: Data was collected for a 52 year old African-American patient who underwent an uncomplicated deceased donor kidney transplant procedure. The post-procedure complications, interventions and course were recorded.
Results: The routinely placed ureteric stent was removed with flexible cystoscopy on post-opt day (POD) 26. Patient was re-admitted with anuria and abdominal pain 24 hours later. An urgent ultrasound and non-contrast CT scan showed grade 4 hydronephrosis. Interventional radiology placed a percutaneous nephrostomy for urinary diversion. A large ureteric hematoma was identified and evacuated which was filling the lumen of the mid to distal (Figure 1). Follow-up nephrostogram POD 45 revealed a distal stricture and persistent well-formed mid-ureter filling defect. A repeat nephrostogram performed at POD 43 resulted in stricture dilatation, internalization of stents and removal of percutaneous nephrostomy tube. Patient was maintained on antibiotics for UTI prophylaxis.
Conclusions: Ureter stent removal is safe procedure. However most likely the stent migrated and kinked. During removal resulted in internal laceration of the ureter causing large hematoma and anuria. Though considered a safe procedure, in our case it resulted in significant morbidity and required several procedures by interventional radiology.

Figure 1.



POS503 NOVEL MINIMALLY INVASIVE HYBRID APPROACH FOR TRANSPLANT URETERIC STENT EXCHANGES IN THE CONTEXT OF DIFFICULTY ACCESSING THEATRE DURING PANDEMIC

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In patients in which open repair and re-anastomosis is not an option, transplant ureteric strictures are often managed with interval stent changes. The position of the transplant ureterovesical anastomosis, however, creates difficulties with direct cystoscopic access and complicates the retrograde approach. There are reports in the literature of minimally invasive retrograde techniques which involve passing the guidewire alongside the in situ ureteric stent at cystoscopy, however this is technically challenging with variable success rates.
In this report we describe a hybrid technique using flexible cystoscopy and fluoroscopic guidance. Pre-procedure prophylactic antibiotics are administered. The flexible cystoscope is inserted and the tip of the ureteric stent identified. The stent is then gently withdrawn until the tip of stent is visible at the urethral orifice. A guidewire (75 cm Amplatz) is fed through the stent, under fluoroscopic guidance, into the renal pelvis. Once position confirmed, the old stent is then removed. The new stent (typically 8Fr 14 cm Bard) is replaced over the guidewire into the renal pelvis using the 'pusher', until the top end is in position, and the stent can be deployed.
To date we have used this technique on three patients. Use was prompted by service limitations during the COVID-19 pandemic. In two patients (both female), we performed this procedure in interventional radiology suite without sedation: One patient required long term interval stent changes, the other had reimplantation surgery delayed. In a third, male patient, we performed this technique under general anaesthetic while he was operated on for a concurrent condition. His scheduled stent exchange had been delayed by four months by that point. This technique worked well without complications with no post-procedure urinary tract infections.
The advantages of this approach are technical simplicity (particularly in females) and avoidance of general anaesthesia. The disadvantages are that in male patients, a longer stent is required to facilitate future exchange which can be irritative. This technique allowed us to circumvent access to theatre issues during the COVID-19 pandemic and change three complex renal transplant ureteric stents.

POS504 URETERAL REIMPLANTATION FOLLOWING KIDNEY TRANSPLANTATION AND URETERAL OBSTRUCTION DUE TO SEVERE URETERAL STENOSIS: A CASE REPORT

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Aim: To present our technique of ureteral reimplantation in a case of ureteral obstruction due to ureteral stenosis after kidney transplantation.
Material: We present the case of a 49-year-old male, who presented deterioration of renal function in May 2019, three months after kidney transplantation. The U/S imaging revealed hydronephrosis due to ureteral obstruction. A nephrostomy tube was immediately placed. An antegrade nephrostogram revealed obstruction from the middle ureter up to the ureterovesical anastomosis. Two months later and since his renal function was restored, we proceeded with reconstruction of the ureter.
Methods: The nephrostomy tube was replaced by an angiography sheath under C-Arm guidance. A guide- wire was placed through it up to the prestenotic ureter. A Pfannenstiel incision with right lateral extension was used. Bladder dome was dissected from its peritoneal attachment and urachus was divided in order to facilitate bladder mobilization to the right. The plane of dissection was developed between the bladder and the lower pole of the graft. Spermatic cord was dissected and divided. Ureter recognition was facilitated with the use of methylene blue solution and the pre-stenting guide wire, through the nephrostomy-angiography sheath. Ureter was transected in its stenotic part and then it was carefully dissected from the surrounding scar tissues taking care not to impair its vasculature. The stenotic part was then divided. After the mobilization of the right anterolateral bladder wall, the site of previous obstructive ureterovesical anastomosis was recognized and transected. It was then rejuvenated and fixed at the psoas muscle, using the psoas hitch technique, to reduce tension to the new anastomosis. Ureter was spatulated accordingly and a direct wide anastomosis over a 7 Fr. ureteral double J-J stent was carried out. The angiographic sheath was replaced by a nephrostomy tube and drainage was placed.
Results: The patient presented no post-operative complications . The nephrostomy tube was closed 10 days post-operatively and was removed four days later. The patient was discharged from hospital 15 days post-operatively, with the JJ stent and a urethral catheter. A month later both the catheter and the stent were removed. His renal function remains normal, 20 months following surgery.

POS505 SYMPTOMATIC INCISIONAL HERNIA REPAIR POST KIDNEY TRANSPLANT: A SINGLE CENTRE EXPERIENCE

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Introduction: Incisional hernia is a common postoperative complications in general surgery. In kidney transplant recipients, this is associated with increasing morbidity and mortality.
Methods: A retrospective review of all transplant patients who had undergone an elective repair of large symptomatic incisional hernias between 2015 and 2020.
Results: A total of 18 patients were identified (14 male (78%), mean age 56.6 years [range 41-71], 22% diabetic, 27% on PD at the time of transplant. A significant proportion of these patients had polycystic kidney disease (28%). The median eGFR was 40 ml/min [range 8-79], the median BMI was 27 [range 21.5-35.8]. All patients underwent CT scanning pre operatively. The repair was performed at a median 544 days [range 84-3349] after transplant and the median length of in-hospital stay is 4 days [range 1-24]. In 7 patients (39%) hernia was repaired with prolene mash, in 5 (27%) patients pedicled vastus lateralis flap was used (27%), in 4 (22%) patients strattice mash (22%) and 2 (12%) had anatomical repair. Complication rate was 39%, 2 patients required re-intervention due to bleeding from a venous branch within rectus femoris muscle, and due to abdominal compartment syndrome, 1 developed seroma needing drainage and 1 developed haematoma. Infection rate was 10% and the 30-day mortality rate was 5%. One of the patient with pedicles vastus lateralis flap repair developed sepsis from the ischaemic flap and died, due to multiorgan failure, 15 days after the surgery. The recurrence rate was 6% at the latest follow up [range 6 months – 5 years].
Discussion: Complex incisional hernia remain challenging to treat. There a significant rate of complications despite multidisciplinary approach to these repairs and patients must be carefully counselled.

POS506 RETROPERITONEOSCOPIC HAND-ASSISTED RIGHT NEPHRECTOMY IN LIVE DONOR WITH LEFT-SIDED INFERIOR VENA CAVA: CASE REPORT

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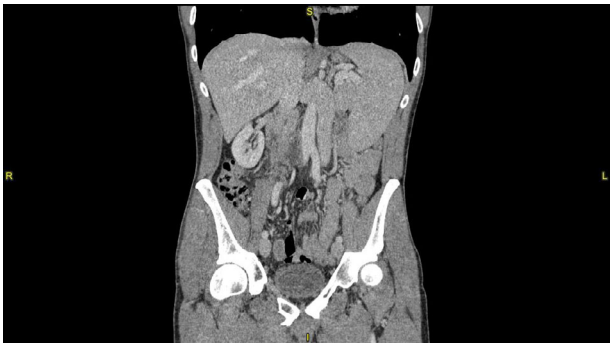
Background: vascular anomalies are a common finding during work-up images of living kidney donors and can sometimes raise doubts about the eligibility of the donor. Left-sided inferior vena cava (LIVC) is a rare anatomic variant with an estimated incidence in the general population between 0.04 and 0.5% and is the second most common anatomical IVC anomaly after IVC duplication. We report a case of kidney living donor with LIVC where a right retroperitoneoscopic hand-assisted live donor nephrectomy (LDN) was performed.
Methods: in a husband to wife living donation the donor was 50 years old with BMI 21.4. Last examination of the donor work-up was a CT Angiogram that showed a LIVC. During work up a severe benign prostatic hyperplasia was also diagnosed.
Results: measurement of renal vessels were as follow: right side vessels length were 25 mm vein and 50 mm artery, on the left side there were 2 veins with an equal length of 20 mm each and the artery was 50 mm long 25 mm and a with caliber 13 mm compared to the left 20 mm long with caliber 15 mm. Renal volumes of right and left kidney were 159cc and 191cc, respectively. After multidisciplinary images a review retroperitoneoscopic hand-assisted right nephrectomy was planned together with a transurethral resection of the prostate. LDN was conducted through 3 port plus a Gelport Laparoscopic System for hand access. Operation time was 210 minutes and 60 minutes respectively. Donor was discharged at 5 postoperative and recipient reached normal function 2 day after transplant.
Conclusions: LIVC is not a contraindication for LDN. The fundamental principle of living donation about preserving the best organ for the donor need to be maintained by ensuring that the nephrectomy is performed safely. A multidisciplinary CT Angio evaluation is mandatory to best evaluate the side choice and to best plan the procedure in order to have optimal results for donor and recipient.



POS507 MALIGNANT LYMPHOMA IN LIVING KIDNEY DONOR AND ITS RECIPIENT: THE DIAGNOSIS AFTER TRANSPLANTATION

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Background: Solid-organ transplantation inherently carries the risk of donor-to-recipient disease transmission, nevertheless, cancer transmission is rare (0.01% -0.05%).
Methods: In 2015, a 30-year-old man underwent a living donor (mother) kidney transplant due to chronic renal failure (on hemodialysis since 2013) due to vesicoureteral reflux. The extensive screening for cancer on the donor, including gastroscopy and contrast-enhanced CT scan, was negative. The immunosuppressive therapy used was: basiliximab, tacrolimus, mycophenolic acid and steroids. The postoperative course was regular for both donor and recipient, with a prompt resumption of the function of the transplanted organ (Cr 2.08 mg/dL at 1 month).
Results: Fifteen days after donation, the donor was diagnosed with diffuse B-cell Hodgkin's lymphoma with predominantly gastric localization. The recipient was also found to have triple hit B-cell lymphoma, stage IVA starting from the graft with skeletal localizations. Both mother and child underwent medical therapy according to the R-CODOX-M scheme, subsequently to the R-IVAC scheme and again to the R-CODOX-M regimen. At 6 years from diagnosis, both are disease-free in the follow-up with good renal function. The recipient maintained normal renal function throughout the five-year period (cr 2.32 mg/dL at 3 months; 1.75 mg/dL at 6 months; 1.43 mg/dL at 1 year; 1.5 mg/dL at 3 years; 1.65 mg/dL at 5 years; 1.68 at 6 years).
Conclusions: Despite the extremely careful assessment of the clinical suitability of living donors, subclinical cancer detection is always challenging. Tumour transmission in solid organ transplantation represents a concrete risk for the recipient, with a low incidence, but cannot be excluded, aggravated by the need to use immunosuppressive drugs.

POS508 POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD): IS THE SECRET HIDDEN IN THE SPLEEN?

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A 55-years-old male underwent kidney transplantation (KT) from a deceased donor after circulatory death. Immunosuppression (IS) consisted in anti-thymocyte globulin, tacrolimus (TAC), mycophenolate mofetil and prednisolone. Regarding serology both donor and recipient were positive for Epstein-Barr Virus (EBV), and for cytomegalovirus (CMV) donor was positive and recipient negative. During valganciclovir prophylaxis, he was diagnosed with CMV gastrointestinal disease from a resistant strain which was successfully treated with high dose ganciclovir, anti-CMV immunoglobulin and IS reduction. The patient evolved with multiple infectious complications and pancytopenia which was attributed to drug-induced myelotoxicity. IS was switched to everolimus and low dose TAC. Eleven months after KT he presented with fever, asthenia and pancytopenia. Labs were unremarkable except for pancytopenia. Endocarditis was excluded and CT scanning showed only splenomegaly. Microbiologic study was negative and bone marrow examination showed no evidence of lymphoproliferative or infectious diseases including leishmania. Positron emission tomography captured only a slight and diffuse activity on the spleen and axial and appendicular skeleton. Despite large spectrum antimicrobial treatment, he evolved unfavorably and a splenectomy with liver biopsy were performed. A diagnosis of a post-transplant EBV negative monomorphic peripheric T-cell lymphoma with associated erythrophagocytosis in liver biopsy was made. Unfortunately, the patient rapidly deteriorated with no conditions to initiate chemotherapy and died.
Posttransplant lymphoproliferative disorder (PTLD) is a serious complication of KT. It is mostly of B-cell origin and EBV is known to play a major role, particularly on early-onset PTLD. As an early-onset T-cell PTLD confined to the spleen, this case is remarkable for its rarity and difficult diagnosis. Due to the immunomodulatory effect of CMV, we also hypothesize that it may have contributed to this rare form of PTLD.

POS509 MERKELL CELL CARCINOMA AFTER KIDNEY TRANSPLANTATION

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Background: Merkel Cell Carcinoma (MCC) is a rare but aggressive neuroendocrine tumor of the skin, associated with high risk of recurrence, metastasis and poor prognosis. MCC typically occurs in elderly white men and in immunosuppressed individuals.
Here, we report a case series of MCC diagnosed in a single-center kidney transplant (KT) population.
Methods: We retrospectively reviewed the data of the KT performed in our center.
All the cases of MCC, confirmed by histology, occurred in KT patients were included and analyzed for incidence, clinical features, therapy and prognosis.
Results: On 2150 KT performed after 1983, we found 4 cases of MCC.
Table shows the main clinical features and the treatments.
Three of the 4 patients died for MCC recurrence occurred after surgery .
Conclusions: The analysis confirms MCC as a rare but aggressive tumor in KT patients.
Routine skin examination is crucial for an early diagnosis.
Multidisciplinary and aggressive treatments can play a decisive role for the prognosis.

Case #	1	2	3	4
Ethnicity	Caucasian	Caucasian	Caucasian	Caucasian
Sex (M:F) - Age at KTx (years)	F - 41	M - 29	M - 66	M - 63
Kidney disease	ESRD	Focal glomerulosclerosis	Hypertensive Nephrosclerosis	Nephroangiosclerosis
KTx (year)	1983	1993	2017	2001
Fitzpatrick skin type (#)	2	3	2	2
Previous skin tumors (type)	No	Squamous cell carcinoma	No	Basal and squamous cell carcinoma
Immunosuppression	AZA- Steroids	CSA-AZA-Steroids	Tacrolimus- MMf- Steroids	CSA-MMF- Steroids
MCC Onset (year)	2015	2017	2018	2019
time laps after KTx (years)	32	24	1	18
Age at MCC onset (years)	73	53	68	81
MCC site	Left leg	Right Pectoral	Left leg	Left thigh
Max MCC dimension	3 cm	6.6 cm	2.5 cm	3 cm
Stadiation	T2N0M0	T4N1bM1	T2N1M0	T2NXM1
Immunosuppression variations	--	--	Switch FK to Everolimus	Switch CSA to Everolimus
Therapy	1-Surgical exeresis 2- ILP (Melphalan)	1-Surgical exeresis	1-Surgical exeresis 2-Limphoadenectomy and ILP (Melphalan) 3-Adjuvant radiotherapy 4-Chemotherapy (Carboplatin + Etoposide)	1- Surgical exeresis 2- Chemotherapy (Carboplatin)
Recurrence (yes/no)	no	yes	yes	yes
Prognosis (deceased/alive)	Alive	Deceased	Deceased	Deceased
MCC Follow-up (months)	62	2	20	11

POS510 GUILLAIN-BARRE SYNDROME CAUSED BY AN ALLOGRAFT RENAL CELL CANCER

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Guillain-Barré syndrome (GBS) is an acute polyneuropathy affecting the peripheral nervous system. Severe phase of ascending and in most cases symmetrical motor dysfunction may lead to patient's disability. GBS has been especially observed in bone marrow transplant recipients but after kidney transplantation is rare. Viruses and immunosuppressive agents are the main causes of GBS in renal transplant recipients. Immunoglobulins or therapeutic plasma exchange are main treatment of GBS.
In this study, we present a case of a 47-year-old male patient twelve years after his second kidney transplantation who developed GBS due to papillary renal cell carcinoma of the graft. Infectious and drug-related origins of GBS were excluded.
Despite TPE procedures were carried out neurological symptoms did not significantly improved and graftectomy was performed, after which complete neurological recovery was achieved.
In kidney transplant recipients, paraneoplastic etiology should be taken under consideration in the differential diagnosis of GBS. Standard therapeutic procedures may have limited effect in the paraneoplastic GBS.

POS512 TAKOTSUBO CARDIOMYOPATHY IN POTENTIAL LIVER TRANSPLANT RECIPIENT

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Introduction: We present a postmenopausal cirrhotic woman which over Takotsubo cardiomyopathy (TCM) and successfully undergo liver transplant.
Case Report: A 70 years old woman with primary biliary cirrhosis was admitted at the Intensive care unit of Clinical Hospital Merkur because of acute dyspnea and chest pain. Chest X-ray showed bilateral pleural effusion with presence of pneumonic infiltrate. Elevated ST segment in V1 to V3 was noticeable on electrocardiogram. Serum troponin I (TnI) level total 19 885.8 ng/L (reference range <15.6). Echocardiogram has showed decreased ejection fraction estimated at 30%, due to ballooning of the lower part of the left ventricle. Due to the patient's clinical state and laboratory findings we didn't perform an urgent coronary angiography. The diagnosis of TCM was based on International Takotsubo Diagnostic Criteria (1). The patient was mechanically ventilated and received conservative therapy. Control echocardiogram on the 5th day revealed recovered systolic function with regular movement of distal third of the left ventricle. The patient was extubated on the 6th day. Three months after experienced TCM, the patient undergo liver transplant without any cardiac complications.
Discussion: Regarding main suggested pathophysiological changes in cirrhosis including autonomic dysfunction, increased cardiac output and a compromised ventricular response to stress, cirrhotic patients may have increased risk of development TCM. There are no strong recommendation on management of TCM, exact period of abstaining from liver transplantation and what are additional risks during liver transplantation. According to our report, for cirrhotic patient who got over TCM with completely restored heart function, TCM does not present an obstacle to liver transplantation surgery.

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POS513 LIVER TRANSPLANTATION AFTER TAVI PREHABILITATION COMPLICATED BY CARDIAC ARREST, PULMONARY EMBOLISM AND STENOSIS OF IVC

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Clinical case: A 64 y old female patient was admitted for orthotopic liver transplantation for decompensated liver cirrhosis, Child-C, MELD-19, due to nonalcoholic steatohepatitis (NASH) and a recent history of TAVI for significant aortic valve stenosis with aortic valve square 1.0 cm^2 and systolic gradient of 40 mmHg. Medical history also included ischemic heart disease, tricuspid valve regurgitation, arterial hypertension, Diabetes mellitus type 2.
The LT procedure was performed with IVC replacement technique and blood loss of 1000 ml. Intraoperative course was complicated by ventricular tachycardia, ventricular fibrillation and cardiac arrest reverted by electropulse therapy. Treatment in ICU lasted for 3 days. On 5 postoperative day she developed the Pulmonary embolism, bilateral hydrothorax and acute kidney injury with increase in urea (25.5 mmol/l) and creatinine (253.4 μmol/l) levels and was readmitted to ICU for thrombolysis. Next day after

thrombolysis she developed a paroxysm of atrial fibrillation, treated by amiodarone.
CT scan on 6 POD showed stenosis and thrombosis of retrohepatic IVC were and marked liver parenchyma perfusion deterioration and infarction and ultrasound showed no signs of DVT.
Cavagraphy confirmed the diagnosis and revealed a 30 mmHg gradient between infrastenotic IVC and right atrium. After predilation a WallStent 24 × 45 was implanted into IVC and post-dilated with a 10 × 40 balloon at 14 atm. This reverted the gradient almost to 0.
Over the next day, there was a gradual improvement in the condition: shortness of breath disappeared, urine output increased to 1450 ml/day. Anticoagulant therapy with calcium nadroparin continued (the level of 0.37-0.38 U/ anti-Xa/ml was reached). On 8 POD the patient was transferred to regular ward, where the dosage of anticoagulants was adjusted and the patient was transferred to antiplatelet therapy (clopidogrel 75 mg/day, aspirin 75 mg/day). There was also a gradual decrease in the level of liver enzymes, urea and creatinine. On 16 POD the patient was discharged for outpatient treatment.
Conclusion: A complicated case of LT was reported to show both the prehabilitation of patient for LT with TAVI as well as successful treatment of intraoperative cardiac arrest due to ventricular tachycardia and postoperative IVC stenosis.

POS514 EMERGENCY ABO-INCOMPATIBLE LIVING DONOR LIVER TRANSPLANTATION USING A MODIFIED DESENSITIZATION PROTOCOL FOR ACUTE LIVER FAILURE

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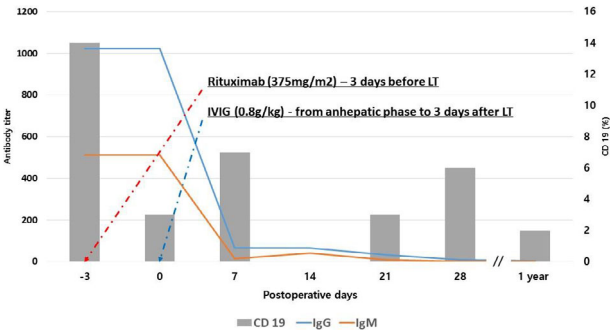
Background: Desensitization protocol for liver transplantation (LT) is usually started 2-3 weeks before transplantation. Therefore, patients with acute liver failure who require urgent LT are usually ineligible for ABO-incompatible (ABOi) LT. There have been several attempts to shorten the desensitization protocol for emergency Case report: ABOi LT. Here we report a 40-year-old female with acute liver failure. Because there was no suitable compatible donor, emergency ABOi LT was planned using a modified desensitization protocol. The preoperative isoagglutinin (IA) titer was 1:1024 and the preoperative T-/B-cell cross-matches were positive. The patient received a single dose of rituximab (375 mg/m^2) and IVIG (0.8 g/kg) was administered to three days after transplantation. The patient's outcomes were optimal with normal graft function at 5-years after LT.
Conclusion: In summary, a modified desensitization protocol consisting of rituximab and IVIG is a feasible strategy for highly sensitized patients with elevated IA titers who require urgent ABOi LT.



POS515 GRAFT VERSUS HOST DISEASE FOLLOWING LIVER TRANSPLANTATION – A CLINICAL CASE

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A 63-year-old male was admitted to the transplant department of our hospital, due to fever, persistent diarrhea and vomiting 4 months after receiving a liver transplantation for cirrhosis from nonalcoholic fatty liver disease (NASH). The deceased donor was ABO identical with the patient and homozygous at the HLA A, DR and DQB and DQA loci (A24, A24, B35, B44, DR11, DR11, DQ7, DQ7, DQA5, DQA5).
Post-transplant immunosuppressive therapy included tacrolimus and mycophenolate mofetil.
Patient's vital signs were stable and clinical examination revealed decreased bowel sounds and an extended maculopapular rash on the back. Laboratory results showed normal liver function , elevated CRP and low white blood cell (1.6 K/μl – lymphocytes :16.6%), Hb (8.9 gr/dL) and PLT (95 K/μl) counts. The patient was treated with broad spectrum antibiotics, antiviral and antifungal treatment. Peripheral blood flow cytometry showed a decreased CD4/CD8 ratio (0.1) , decreased CD19+ cells (0.3%) increased NK cells (9.2%) and increased CD3+HLA-DR+ cells (51.1%).HLA typing revealed donor-derived chimerism in peripheral blood (recipient's HLA A2, A24, B35, B39, B44, Cw*04, Cw*12, Cw*16, DR11, DR16, DQ7, DQ5).
Parasitological stool examination and *CMV PCR studies were negative*.
Even though skin biopsy was negative for Graft versus Host Disease (GvHD) due to the patient's clinical picture corticosteroids were added to the treatment.
Colonoscopy results were normal however Computed Tomography (CT) scans showed findings of colitis with signs of peritonitis and active ileal bleeding. A small bowel resection of the affected part was performed with an end-to-end anastomosis. Small bowel biopsy revealed signs of necrosis. The postoperative period was marked with deterioration of the clinical picture (fever, diarrhea, vomiting) and laboratory findings (elevated γ-glutamyltransferase, bilirubin levels, transaminases), sepsis, multi organ failure and death.
Even though GvHD is not common after liver transplantation it has high mortality rate, >75%. Clinical manifestations include fever, skin rash, diarrhea and pancytopenia .
HLA-homozygous donors have been described as a risk factor especially after living donor transplantation . Physicians should be alerted for signs of GvHD and include it in the differential diagnosis.

POS516 THE HIDDEN ENEMY BEHIND COVID-19 IN A RECENT LIVER TRANSPLANT PATIENT

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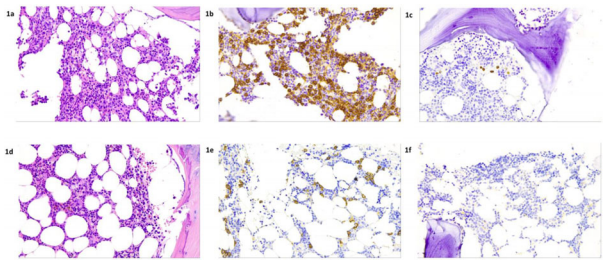
There are few data about management of transplanted patients affected by Sars-Cov-2 pneumonia. We present a challenging differential diagnosis during the pandemic era.
Our patient is a 58 years old man, underwent to liver transplantation on January 2020 for alcoholic cirrhosis complicated by hepatocellular carcinoma. His immunosuppressive therapy consisted by tacrolimus and steroids. 23th march he was admitted to our hospital for SARS-CoV-2 pneumonia. Hydroxychloroquine and lopinavir/ritonavir associated with azithromycin and ceftriaxone were started. Reservoir mask was posed.
At laboratory findings: WBC 15910/mm3; HGB 94 g/L; PLT 10000/mm3; PTC 14.6 ng/ml; D-Dimer 6111 ng/ml; creatinine 3.10 mg/dl; bilirubin 2.7 mg/dl; Albumin 2200 mg/dl. FK was 20.7 ng/ml. Tacrolimus was stopped. Patient become anuric. CMV DNA and EBV DNA were negatives.
Patient conditions worsted, fever was persistent and antibiotic treatment was switched to meropenem and added Daptomycin. A chest CT scan showed a bilateral ground-glass pneumonia that interested 45% of pulmonary parenchyma and multiples mediastinal, mesenteric and pelvic lymph nodes (Figure 1-2). In view of the clinical worsening, patient was transferred to Intensive care unit (ICU). HHV8 was positive: 154900065 cp/ml. On a suspicion of HHV-8 related multicentric Castleman disease (MCD), a lymph-node biopsy was done without success. Patient presented all the clinical and biochemical features for HHV8-MCD, except for histological lymph nodes.
After a multidisciplinary meeting, bone marrow biopsy was performed: cellular infiltrate constituted by >40 % of plasma cells and the presence of HHV-

8 was proven (Fig.1a-1b-1c). Rituximab was started (375 mg/m^2) and he underwent to ultrafiltration.
Immunosuppressive treatment was re-started, switching CNI to mTOR. After two months he returned to the hospital as outpatient, a total body CT showed HHV-8 was negative. A bone marrow biopsy was re-performed: plasma cells were rare and there was no evidence of HHV-8 (Fig. 1d-1e-1f)
Our transplanted patient was immunocompromised and the worsening outcomes could be related to SARS-CoV-2 pneumonia. We want to underline how in a recent liver transplant patient, all causes of infection and rare disease should be excluded, even if "diagnosis" was already done.



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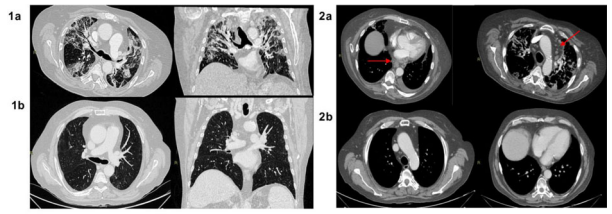

Figure 1: 1a Pulmonary lesions by SARS-CoV-2 pneumonia at admission. 1b Pulmonary parenchima after 2 months from Rituximab treatment

Figure 2: 2a Mediastinal lymph nodes at admission. 2b Mediastinal lymphnodes after 2 months from treatment with Rituximab

POS517 LIVER TRANSPLANTATION IN RECIPIENTS WITH HISTORY OF AIDS-DEFINING CLINICAL CONDITIONS: IS IT POSSIBLE TO EXTEND THE INDICATIONS?

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Background: In Italy, liver transplantation inclusion criteria for patients living with HIV with previous AIDS-related conditions contemplate stable CD4 count >200/μL, non-detectable HIV-RNA blood levels, treatment adherence and absence of non-treatable AIDS-related infections or neoplasm.
Methods: We report the case of a patient with chronic cholangitis and multifactorial hepatic cirrhosis, caused by mycobacterial hepatic infection and macrolides-related damage, with a history of AIDS treated with highly-active antiretroviral therapy (HAART) since 2015 with viral load suppression but suboptimal white blood cells count. The patient also had a history of CMV-related systemic infection, chronic biliocutaneous fistula due to recurrent biliary duct obstruction and previous bowel resection for EBV-related leiomyosarcoma without any sign of relapse after 4 years. The patient was brought to our attention for severe hepatic failure (MELD 28). Despite low WBC count, considering the severity of the disease and the current absence of AIDS-defining infections or neoplasm recurrence, we decided to list the patient for liver transplantation. Surgery was performed with veno-venous bypass due to severe portal hypertension and subsequent massive bleeding during adhesiolysis.
Results: The postoperative course was characterized by severe pancytopenia, improved after splenectomy performed during re-laparotomy. The patient also experienced CMV systemic infection relapse, controlled by specific antiviral therapy, and multiple septic events, controlled with antibiotic therapy. Ten months after surgery the patient presents optimal liver function, without any sign of AIDS or neoplasm recurrence.
Conclusions: An adequate follow-up may allow to evaluate options for the extension of liver transplantation indications in patients with AIDS history and hepatic failure.

POS518 TRANSPLANTATION OF A DISCARDED LIVER AFTER ISCHEMIA-FREE PROCUREMENT

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Background: Ischemia reperfusion injury (IRI) is a harmful event in liver transplantation. Ischemia free liver transplantation is an arising technique but it is complex. We investigated a method linked to ex-vivo liver normothermic machine perfusion (NMP) to avoid cold ischemia time during the procurement only.
Clinical Case: An orphan liver graft from 43-year-old donor was accepted for evaluation and reconditioning through NMP. Discarded reasons were donor's 25 min of cardiocirculatory arrest, full thickness ischemic necrosis of the colon and part of the ileum and hyper-transaminasemia with 25% of macro-steatosis. The recipient was a 66-year-old male affected by alcoholic liver cirrhosis complicated by hepatocellular carcinoma.
The graft was procured and preserved under continuous normothermic machine perfusion according to the ischemia-free technique. It was cannulated in situ without prior cold flushing, firstly portal vein and then the arterial axis. Ex-vivo NMP started immediately after cross-clamping and lasted 3 hours 49 min. Liver perfusion was carried without any variation from the standard internal protocol and no logistic or technical problems occurred. Lactates levels dropped from 8.27 to 0.4 mmol/L within the first hour, total bilirubin remained stable at 1 mg/dL, whereas mean AST, ALT and γGT were 149 ± 43, 73 ± 11 and 29 ± 16 U/L, respectively. Bile production consisted of 14 ml within the first hour and then 6 ml/hour, with a pH above 8 since 15 min of NMP. The perfusate's glucose level was 550 mg/dL at the beginning and 177 mg/dL at the end of NMP, whereas bile glucose was always inferior to 30 mg/dL.
During NMP, the average hepatic artery and portal vein flow was 602 ± 53 and 1996 ± 83 ml/min, whereas mean hepatic artery and portal vein pressure were 58 ± 1 and 5 ± 1 mmHg. Liver weight was 2840 g after procurement and 2805 g after NMP. Cold ischemia time after NMP was 16 min and recipient warm ischemia time was 53 min.
No post-reperfusion syndrome occurred and total operation times was 7 hours 2 min.
Neither PNF nor EAD occurred. The patient was discharged home in post-operative day 8 after an unremarkable course.
Conclusion: Avoiding ischemia during implantation is complicated, whereas eliminating it during procurement represents a simpler method to minimize IRI that can be considered in centers with expertise in NMP.

POS519 ATOVAQUONE INDUCED FULMINANT HEPATIC FAILURE IN LIVER TRANSPLANTATION

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Background: Toxoplasmosis is a rare, but life-threatening complication that may occur after liver transplantation (LT). Different prophylaxis regimens are suggested in literature all based on sulfamethoxazole/trimethoprim (Tr/Sx); the use of Atovaquone (Atv) is suggested as alternative treatment. Here we report a case of a LT patient that suffered a toxic fulminant failure due to Atv and underwent urgent re-LT.
Methods: Since 2013 in our LT Center Tr/Sx based Toxo prophylaxis was successfully adopted in case of Toxoplasma IgG mismatch (1 tab x 3 times/week for six months).
Case report: A 54 year old woman affected by primary biliary cirrhosis with autoimmune hepatitis overlap underwent LT. Comorbidities were Sjogren's syndrome with correlated pulmonary interstitial disease, osteoarthritis complicated by Heberden nodules and relapsing urinary tract infections. Due to Toxoplasma IgG mismatch and Tr/Sx severe allergy, Atv prophylaxis was started in POD 2. On POD 5 she referred abdominal pain and developed persistent fever. Infections were ruled out and antibiotic and antimycotic therapies introduced. However, the patient developed severe lactic acidosis, anasarca and encephalopathy. At the same time, liver function tests progressively deteriorated. Doppler ultrasound, magnetic resonance, computed tomography and angiography were performed without significant alterations.

On POD9, liver biopsy was performed which demonstrated submassive necrosis. Due to the worsening general conditions, liver function and haemodynamic, the patient was listed for re-LT that was performed on POD 11.
At histopathology, the liver parenchyma showed mild lympho-monocytic portal infiltrate, with focal biliary and subendothelial infiltration and focal spill over; diffuse hemorrhagic necrosis was constantly present in the mid-centrilobular regions, with diffuse endothelial damage of the central veins, and minimal inflammatory infiltration; minimal C4d deposits were demonstrated by immunohistochemistry (plasma research was negative).
After re-LT, the patient promptly recovered, was rapidly discharged and is now in good conditions.

POS520 PROLONGED QT DURING ANAESTHESIA FOR PEDIATRIC CADAVERIC LIVER TRANSPLANTATION: A CASE REPORT

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We report a case of a 7-month-old-girl with biliary cirrhosis due to a biliary atresia who developed a long QT (LQT) during general anesthesia for cadaveric liver transplantation (LT).
Pre-LT cardiology evaluation ruled out arrhythmias with QTc 397 msec. The anesthesia was induced with propofol 3 mg/kg, fentanyl 2 mcg/kg and rocuronium 1 mg/kg. The maintenance was performed by sevoflurane, fentanyl and cisatracurium. Fluid intake consisted in 100 ml/kg/h (glucose 10% at 4 ml/kg/h, electrolytic balance solution and albumin 5%). Routinely, in LT, we check hourly acid base equilibrium and serum electrolytes, because, after reperfusion, severe hypokalemia may occurs[1]. During hepatectomy a QT of 560 msec was noted, potassium level was 3.5 mmol/l (Fig. 1). Sevoflurane administration was stopped, and midazolam iv infusion (0.2 mg/kg/h) was started. Potassium and magnesium infusions were supplemented. After 20' the ECG was normalized. After the reperfusion the potassium level fall down at 1.7 mmo/l and supraventricular extrasystoles were noted. The administration of potassium and magnesium was implemented and sinus rhythm was restored. The patient was transferred with deep sedation in PICU, after 12 hours was extubated without any complication. A 12-lead ECG registration the QTc was 460 msec. In our center more than 50% of pediatric LTs are biliary cirrhosis and we routinely use sevoflurane to maintain general anesthesia, but no ECG abnormalities have been detected before[2]. The LQT (>440 msec) is observed in up to 50% of adult cirrhotic patients and is not related to liver cirrhosis etiology, but within 6 months of LT returns to normal[3]. The LQT is associated with liver dysfunction and hyperdynamic circulatory syndrome typical of cirrhotic patients[4]. Therefore, it is necessary to prevent severe ventricular arrhythmias during LT by optimizing electrolyte balance and avoiding drugs that can prolong QT through accurate hourly analysis of ECG and kalemia during LT.

POS521 CONTINUOUS RENAL REPLACEMENT THERAPY IN SMALL PEDIATRIC LIVER TRANSPLANT PATIENTS WITH ACUTE RENAL FAILURE

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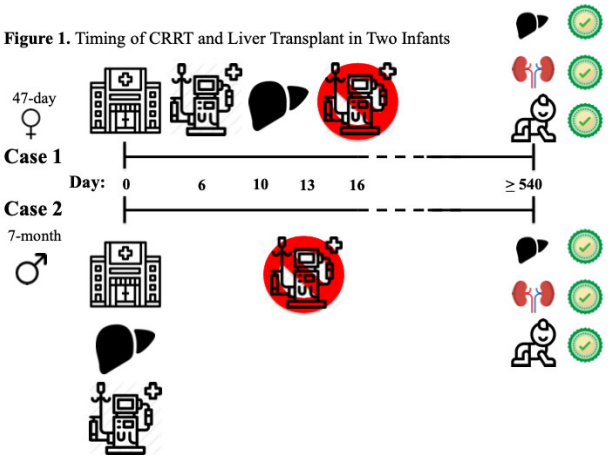
Introduction: Continuous renal replacement therapy (CRRT) is commonly required peri-operatively for adult liver transplant recipients, but reports on this therapy in pediatric liver transplantation are limited. Herein, we present two cases of emergent use of CRRT in infant liver transplant recipients.
Case 1: A 47 day-old female (4.6 kg) presented to our pediatric transplant center with idiopathic acute liver failure. CRRT was initiated on hospital day 6 for hyperammonemia, hypervolemia, and anuric renal failure. 4 days later, she underwent a left lobe liver transplant from a deceased donor. CRRT was successfully weaned 6 days post-transplant. At 42 month follow up, she continues to have good graft function, normal renal function, and meeting developmental milestones.
Case 2: A 7 month-old male (7.5 kg) with biliary atresia status post failed kasai was admitted for planned left lateral segment living donor liver transplant. Intra-operatively, CRRT was initiated emergently for acute oliguric renal failure and refractory hyperkalemia. CRRT was successfully weaned 13 days post-transplant. On 18 month follow up, he remained with good graft function, normal renal function, and was meeting all developmental milestones appropriately.
Conclusion: CRRT can be a life-saving rescue treatment for infant liver transplant recipients and has various indications and uses for these high-risk patients. In our experience, CRRT can be used transiently with good outcomes and without compromising long-term graft or renal function (Figure 1). Additional, multi-center studies are required to better characterize indications, risk factors, and long-term outcomes with CRRT in pediatric liver transplantation.

Figure 1. Timing of CRRT and Liver Transplant in Two Infants



POS522 APPLICATION OF AMPLTZER CARDIAC PLUG FOR FLOW MODULATION IN POST-TRANSPLANT PORTAL-STEAL SYNDROME FROM A SURGICAL LINTON'S SPLENO-RENAL SHUNT

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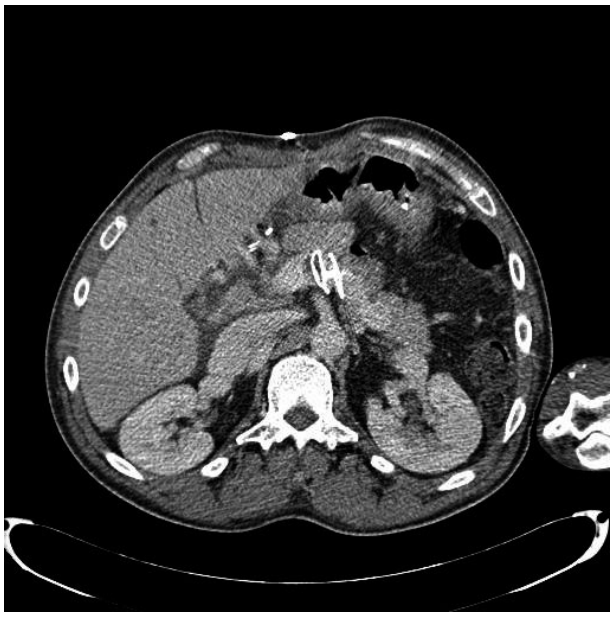
A 34-years old male patient referred to our Center as a candidate to liver transplantation for progressive hepatic failure in the setting of congenital hepatic fibrosis. In pediatric age, the patient underwent splenectomy with proximal Linton's splenorenal surgical shunt for symptomatic portal hypertension with hypersplenism.
Preoperative computed tomography (CT) scan documented the patency of the 58 mm proximal surgical shunt along with a patent portal vein without thrombosis.
The patient received a AB0-compatible 1331 g graft from a 60-year-old brain-dead donor; no liver biopsy was retrieved during procurement. A portal flush test performed after hepatectomy highlighted adequate flow; considering the risks of bleeding, shunt ligation was not attempted.
The patient developed an early allograft dysfunction with encephalopathy; CT scan showed a patent portal vein without any anastomotic stricture, splenic vein dilation up to 25 mm, persistent patency of the 58 mm Linton's surgical shunt and infrahepatic caval distension up to 76 mm; doppler-ultrasound documented reduced 5 cm/sec portal flow.
The diagnosis of portal steal syndrome was advocated, and the case discussed with the interventional radiologists.
Considering shunt size and hemodynamics, we opted for an off-label utilization of a 30 mm Amplatzer cardiac plug (Amplatzer PFO occluder, Abbott) in order to achieve shunt exclusion and portal flow modulation, avoiding the risks of embolization or transjugular intrahepatic portosystemic shunt.
The patient was successfully treated with endovascular placement of the plug at the origin of the splenic vein, with intraoperative evidence of increased portal flow.
After the procedure, transaminase and bilirubin values gradually dropped within the normal range by postoperative day 10; a CT scan performed before discharge documented adequate portal perfusion and proper plug positioning, along with significant reduction of the caval diameter up to 40 mm and initial clot formation on the portal side of the Amplatzer plug

(see figure); doppler-US highlighted a 20 cm/sec hepatopetal portal flow. The patient was discharged on postoperative day 20.
This experience evidenced the need for an accurate peri-operative evaluation and management of porto-systemic shunts and the importance of an endovascular approach.



POS523 A CASE OF LIVER AUTOTRANSPLANTATION FOR GIGANTIC HEMANGIOMA WITH COAGULOPATHY

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Hepatic hemangiomas are the most frequent benign tumor of the liver. Most patients do not report symptoms or require treatment. However, in rare cases they may grow up to giant hemangioma larger than 20 cm in size, can be symptomatic, and can lead to coagulation disorder "Kasabach Merritt's syndrome" (KMS). In those cases, surgical treatment is considered and tumor enucleation or resection is usually selected. When the giant hemangiomas replace over most of the liver, compress vena cava and limit hepatic reserve, it is reported that transplantation can be one of the treatment options.
Here, we experienced 46-year-old patient complaining of abdominal bloating and pain in right upper quadrant. CT showed 25 cm x 25 cm wide in diameter giant hemangioma that completely replaced right and caudate lobe of the liver, surrounded and compressed vena cava, and that cave in to the left lobe of the liver. Accordingly, the giant hemangioma was complicated with consistent abdominal pain and bloating, implicating the risk of rupture, ongoing consumptive coagulopathy suspected of shifting toward KMS, surgical tumor resection was indicated. However, the giant tumor caved in the left hepatic lobe, left medical segment (S4) was compressed by tumor and it is estimated that the residual liver volume is 25 percent when we perform right hepatic trisegmentectomy. In addition, the boundary between the hemangioma and liver parenchyma was indistinct. Therefore, to preserve residual volume of the liver especially in the left medial segment (S4), *Ex-vivo* liver enucleation and auto-transplantation were performed under extracorporeal circulation. Operation time was 13 hour 25 minutes.
The hepatic hemangioma can become gigantic size that limit residual liver volume and compress vena cava . *Ex-vivo* liver enucleation and auto-transplantation were useful in preserving residual liver volume in patient with giant hemangioma with indistinct boundary between hemangioma and normal liver.

Table 1. The list of patients who underwent transplantation for gigantic hepatic hemangioma.

Author	Year	Age	Sex	Clinical Manufestation	Tumor size (cm)	Donor type	Follow-up (month)
Klopmaker	1989	42	F	Hepatomegaly	NA	Living donor	NA
Mora	1995	42	F	Coagulopathy	NA	Cadaver donor	NA
Chui	1996	33	F	Abdominal pain, distention	NA	Cadaver donor	18
		43	F	Abdominal pain, distention	40x35x15	Cadaver donor	14
Russo	1997	43	F	NA	21	Cadaver donor	NA
Longeville	1997	47	M	Massive bleeding after teeth extraction	25	Cadaver donor	12
Keegan	2001	34	M	Abdominal distention, respiratory distress	63x45x51	Cadaver donor	12
Kumashiro	2002	48	F	Abdominal distention	NA	Living donor	NA
Ferraz	2004	25	F	Abdominal distention	46x40x15	Cadaver donor	30
Meguro	2008	45	F	Abdominal distention	15	Living donor	10
Aseni	2010	46	M	Pulmonary thromboembolism	NA	Cadaver donor	25
Vagefi	2011	32	F	Abdominal distention	18x23	Cadaver donor	NA
Unal	2011	56	F	Upper abdominal pain	NA	Cadaver donor	6
Zhong	2014	27	F	Upper abdominal pain, distention	50x40x25	Living donor	17
Yildiz	2014	44	F	Abdominal distention, petechial hemorrhages	22x18x23	Cadaver donor	1
Lange	2015	46	F	Abdominal distention	21.7x23.7x25.5	Cadaver donor	NA
Obana	2020	46	F	Abdominal distention	25x25x15	Autograft	12

POS524 EXTENSIVE OPERATIVE THROMBECTOMY FOR ADVANCED BENIGN PORTAL VEIN THROMBOSIS WITH SUPERIOR MESENTERIC VEIN INVOLVEMENT IN LIVING-DONOR LIVER TRANSPLANT

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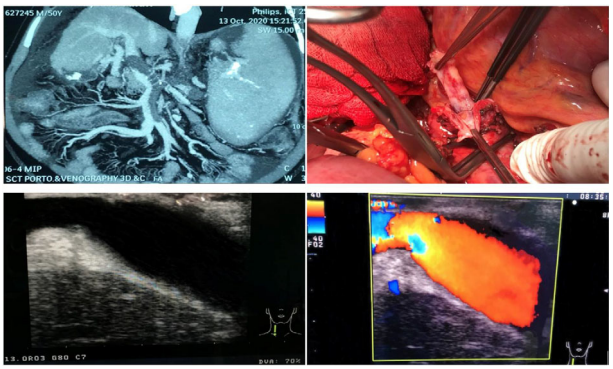
Introduction: Management of advanced benign portal vein thrombosis (PVT) with superior mesenteric vein (SMV) involvement remains a major challenge in living-donor liver transplantation (LDLT).
Case Presentation: A 50-year old male patient with history of hepatosplenic schistosomiasis presented to our Transplant Unit at a tertiary hospital in Giza, Egypt with decompensated cirrhosis. Laboratory workup revealed pancytopenia & negative viral serological markers. The Model for End-stage Liver Disease (MELD) score was 12. Triphasic computed tomography (CT) scan of the abdomen & pelvis with CT portography showed a shrunken cirrhotic liver, moderate splenomegaly, mild ascites, and advanced 'grade 3' PVT [chronic hypodense partially occlusive mural thrombus, extending along the main portal vein (PV), splenic vein & SMV]. Upper gastrointestinal endoscopy revealed grade 2 oesophageal varices for which endoscopic band ligation was carried out. In November 2020, the patient underwent LDLT using a 'right-lobe graft without the middle hepatic vein'. After recipient total hepatectomy, the thrombosed PV was dissected all around down to the upper border of the pancreas. A vascular clamp was then applied to the PV at the most proximal point possible; and an extensive eversion PV thrombectomy was undertaken, where the mural thrombus was exposed, carefully dissected from the vein wall down to the level of the vascular clamp, and then extracted. A blood flush was subsequently performed to remove any residual blood clots & to assess the portal venous flow (PVF). Standard anatomical PV reconstruction (graft PV to recipient main PV) was used for graft implantation. Intra-operative doppler ultrasound scanning showed complete thrombus resolution down to the splenomesenteric confluence, a small residual SMV thrombus & good PVF [pre-anastomotic, anastomotic & post-anastomotic PVF velocities = 40 cm/s, 76 cm/s & 74 cm/s; respectively]. Post-transplant thromboprophylaxis (recombinant Hirudin 15 mg twice daily) was initiated on postoperative day (POD)3. The patient had an uneventful recovery, and was discharged home on POD8.
Conclusion: Advanced 'grade 3' benign PV thrombosis with SMV involvement can be successfully managed by extensive operative eversion thrombectomy, thereby allowing anatomical PV reconstruction in LDLT.



POS525 RESTORATION OF PORTAL INFLOW AFTER CAVOPORTAL HEMITRANSPOSITION IN A LIVER TRANSPLANT RECIPIENT WITH COMPLETE SPLANCHNIC THROMBOSIS

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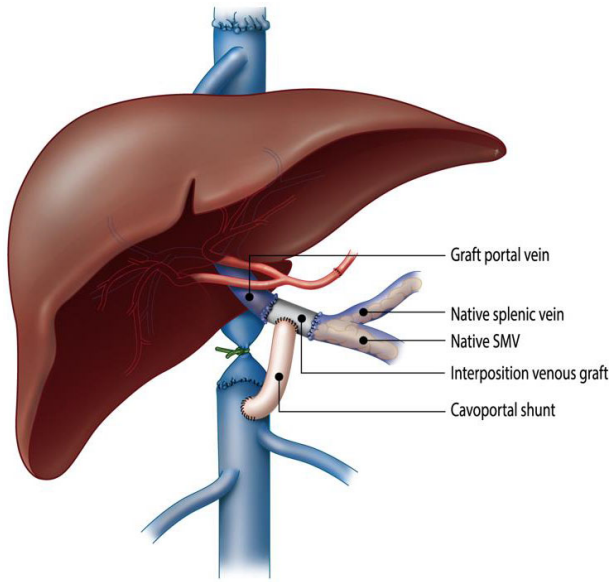
Diffuse splanchnic thrombosis may render standard liver transplantation (LTx) difficult to perform. This is a unique case of a 19-year-old female, who underwent an urgent re-LTx for recurrent portal vein thrombosis (PVT). Initially, she presented with acute liver failure, due to acute-on-chronic Budd-Chiari syndrome, and complete PVT. She was under full anticoagulation therapy, in addition to low dose aspirin. Urgent LTx was performed with thromboendovenectomy and Fogarty-thrombectomies, which gave some portal vein (PV) inflow. Essential thrombocythemia and JAK2-mutation were found post-LTx and treated with hydroxycarbamide and ruxolitinib, respectively. Despite this and multiple re-interventions, PV thrombosis recurred, acute liver failure developed, and she was listed for urgent re-LTx.
At re-LTx, PV inflow remained insufficient. Cavoportal shunt was created with donor aorta between inferior vena cava (IVC) and PV. Initial 30% tapering of the IVC, above the shunt, gave sufficient PV inflow. One day later, PV re-occlusion occurred. As last resort, complete occlusion of the IVC was required to acquire sufficient PV inflow. Liver function normalized, ascites and portal hypertension resolved and no IVC syndrome occurred. Five days later, native portomesenteric axis gradually reopened. Now, 2 years post-LTx, she is well, leading a normal life pattern, with normal liver function, no IVC syndrome or residual portal hypertension, while still being under full anticoagulation. Her liver is now perfused via both physiological and non-physiological route.
Creation of a cavoportal hemitransposition with maintenance of an anatomical porto-portal axis should be considered in patients with (sub)acute diffuse splanchnic thrombosis, when sufficient physiological PV inflow cannot be restored at the time of LTx, but in whom native portomesenteric axis may recanalize later.



POS526 INTRALUMINAL BLEEDING FROM JEJUNAL ANASTOMOSIS STOPPED WITH INTRAOPERATIVE HAND ASSISTED ENTEROSCOPYAFTER ORTHOTROPIC LIVER TRANSPLANTATION

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Background: Around 75% of gastrointestinal bleeding with no identified origin has its source in the small intestine. This is even more of a challenge after orthotropic liver transplantation (OLTx) with biliary drainage via Roux-en-Y intestinal loop. We present a case of successful intraoperative hand assisted enteroscopy used to locate and ligate a source of bleeding in jejuno-jejunal anastomosis.
Methods: A 59 year old female had modified piggy-back method OLTx due to alcoholic liver cirrhosis. Roux-en-Y biliary drainage was performed because of disproportionate biliary ducts. On 13th day post-op drop in haemoglobin was observed (9.5 to 5.8 g/dl) with corresponding blood in stool and tachycardia. Gastroscopy revealed blood in small intestine beyond Treitz ligament, too distal for intervention. Arteriography of mesenteric artery showed small angiodysplasia near jejuno-jejunal anastomosis, due to high estimated risk of ischaemia no embolization was performed. During another gastroscopy a possible site of haemorrhage was localized beyond therapeutic range. Enteroscopy was performed but no active bleeding was observed. Despite blood products transfusions patient showed signs of persistent bleeding.
Results: During a laparotomy on 15th day intraoperative gastroscopy was performed, the endoscope was manually guided towards the anastomosis. Great care was taken regulate the intraluminal pressure – no signs of serosa tearing, ischaemia or mesentery injury were seen. The site of bleeding in the jejuno-jenunal anastomosis was found and illuminated, a single suture was put in that location. No residual bleeding was seen via endoscopy. No clinical or biochemical signs of haemorrhage were observed post-op. The patient suffered TRALI on 3rd day post op and required 4 days of ventilatory support. No further complications were observed, the graft function was optimal and remains such after a year-long follow up with no other issues.
Conclusions: The case demonstrates feasibility of careful intraoperative enteroscopy. Possible complications must be kept in mind and weighed against prolonged diagnostics and less invasive therapeutic attempts.

POS527 LIFE-SAVING LEFT RENAL VEIN LIGATION TO INTERRUPT SPONTANEOUS PORTOSYSTEMIC SHUNT AND RESTORE PORTAL VEIN FLOW AFTER SPLIT LIVER TRANSPLANTATION

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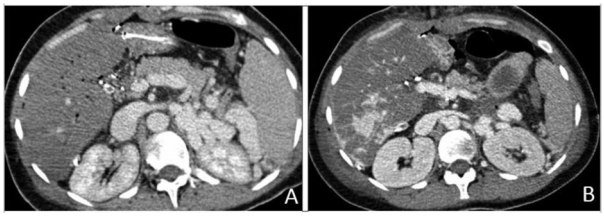
Different strategies to manage the portal vein thrombosis (PVT) and spontaneous portosystemic shunts (SPSSs) have been reported.
A case of a life-saving left renal vein (LRV) ligation performed at our center further corroborates the importance of the shunt interruption to restore portal vein (PV) flow after liver transplantation (LT).
A 31-year-old female with cryptogenic cirrhosis, history of portal hypertension, previous Grade 2 PVT by Yerdel's classification successfully treated with anticoagulants, and with persistent large SPSSs, underwent a extended right graft split-liver transplantation.

Following pre-transplant evaluation of PV and collaterals with contrast-enhanced computed tomography (CT) and color doppler ultrasound (CDUS), the decision was taken not to interrupt any major shunt vessels.
During the anhepatic phase, a PV flush demonstrated satisfactory portal flow. No SPSS clamp/unclamp test was performed, being considered time consuming and risky.
A portal reconstruction was performed with an end-to-end portoportal anastomosis, and the SPSSs were left intact. The CDUS of the PV performed intraoperatively showed an adequate waveform and hepatopetal portal flow, as well as an adequate arterial waveform.
A post-operative CDUS performed 6 h after surgery showed complete PVT and hepatic artery thrombosis (HAT), confirmed by subsequent CT (Figure 1A).
Given the worsening of the portal hypertension due to complete PVT, access to and ligation of the large splenorenal shunt was considered too risky.
Ligation of the LRV and a PV thrombectomy was therefore performed, with recovery of adequate portal flow (Figure 1B).
Given the extension of the HAT the patient underwent emergency liver retransplantation 36 h after. The procedure and the post-operative period were uneventful, with no issues related to the portal flow or the vein reconstruction. Renal function was always excellent.
In the case reported, the SPSS was known preoperatively, but we failed intraoperatively to anticipate its potential negative impact on PV hemodynamics.
Although the risk of permanent renal dysfunction remains an open debate, LRV ligation is extremely effective and safe, with no procedure-related complications.

Figure 1. CT executed 6 h after LT documenting complete PVT and HAT (A) and 12 h after ligation of the LRV (B)



POS528 PORTO-CAVAL SHUNT IN SPLIT LIVER TRASPLANTATION: IS THERE ANY TIME LIMIT TO CLOSE IT?

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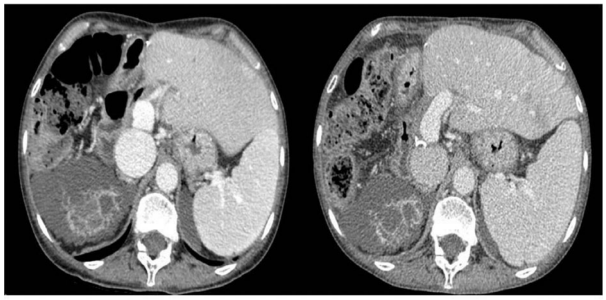
Background: Partial liver transplantation is burdened by the risk of Small For Size Syndrome (SFSS), due to increased portal venous pressure associated to reduced liver volume. SFSS can be prevented through modulation of the graft portal inflow by a porto-caval shunt. However, liver regeneration and increase of intra-parenchymal vascular resistances can determine flow inversion through the shunt (so called "steal phenomenon"), which requires its closure.
Methods: We report the case of a patient who required porto-caval shunt closure eight years after liver transplantation.
Results: In 2011 a 51-year-old patient underwent combined split-left liver lobe (segments II-III) and kidney transplantation for hepatorenal polycystosis, and a porto-caval shunt was created with an iliac venous graft to reduce the portal vein pressure. The post-operative outcome was uneventful; one year after transplantation the patient developed a biliary anastomosis stricture, successfully treated by endoscopic stent placement.
After eight years, the patient presented with worsening encephalopathy and hyperammonaemia (191 μmol/L). Abdominal CT demonstrated a shrunken portal venous system, and Doppler ultrasonography showed portal flow inversion through the shunt. Therefore, the patient underwent surgical shunt ligation with immediate re-expansion of the portal vein and normalization of blood ammonia levels (25 μmol/L).
Conclusions: The right timing for porto-caval shunt closure can be variable (even many years). During follow-up, the decision to close or modulate a shunt should be taken considering portal inflow (measured by Doppler ultrasonography), shunt size and blood ammonia levels.



POS529 PURE ROBOTIC RIGHT HEPATECTOMY FOR A LIVING LIVER DONOR

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Background and Aims: It is common step forward, open right hepatectomy, pure laparoscopic right hepatectomy, then pure robotic right hepatectomy for a liver donor. Pure robotic Right hepatectomy for a liver donor is a challenging procedure and only a few cases have been reported in a few institutions so far. It is well known even if this does not mention its benefits of minimally invasive surgery. Here, although there is no experience of pure laparoscopic right hepatectomy for a liver donor, we briefly introduce the experience of pure robotic right hepatectomy compared to that of open right hepatectomy for a liver donor.
Methods: Between Jan 2020 and Jan 2021, 13 patients received open surgery (group 1), and 6 patients underwent robotic living donor right hepatectomy (group 2) in our institute.
Results: The age, Body mass index, graft volume, operation time and hospital stay in group 1 and 2 were 35.7 $\pm$ 14.8 and 34.0 $\pm$ 10.4, 24.4 $\pm$ 2.7 and 25.2 $\pm$ 2.8, 747.6 $\pm$ 128.5 and 616.6 $\pm$ 71.7, 289.6 $\pm$ 34 and 425 $\pm$ 58.4, 14.9 $\pm$ 7 and 9.1 $\pm$ 3.1, respectively. Graft volume and operation time had statistical significance ($p < 0.05$). In this series, no conversion was conducted for robotic donor right hepatectomy. There was no transfusion during operation in two groups. Unfortunately, there were no significant complications in group 2, but 2 significant complications occurred in group 1.
Conclusions: Although small cases of pure robotic right hepatectomy without any experience of pure laparoscopic right hepatectomy for a liver donor, the robotic surgery would be a big step in achieving minimally invasive surgery for a liver donor.

POS530 A CASE OF SUCCESSFUL LIVER TRANSPLANTATION FROM DECEASED DONOR WITH BRAIN DEATH IN A PATIENT WITH RANDU-OSLER-WEBER DISEASE

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Introduction: Rendu-Osler-Weber disease (or hereditary hemorrhagic teleangiectasia; ROW) is a rare autosomal dominant vascular abnormality, which frequency in general population is 1-2:100,000. It is characterized by the presence of arteriovenous malformations of different localizations (skin, mucous, gastrointestinal tract, brain, lungs etc.). A liver localization is observed in 8%-30% of patients with ROW disease and often becomes a cause of life-threatening complications. There are 106 cases of liver localization of ROW disease, which have been described in the literature, 30 cases from which were asymptomatic and 76 had symptoms.
Objective: To demonstrate a case of successful treatment of a patient suffering from ROW disease with diffuse liver injury in the form of multiple arteriovenous malformations (type I) by means of liver transplantation (LT) from deceased donor with brain death.
Case: A 53 y.o. woman. In 2017 on elective US-examination of abdominal cavity was identified the presence of multiple formations in liver, which kind was initially identified as benign. The course of the disease was uneventful and asymptomatic to the end of 2019, when it manifested for the first time with gradually increasing pain in the back, jaundice with high body temperature of 38°C in the evening, swelling of the lower extremities, which was refractory to diuretic therapy, and dyspnea. Based on the computer tomography data, the differential diagnostics was performed between angiosarcoma, hemangiomatosis and liver form of ROW disease. Because of the presence in the liver parenchyma of multiple arteriovenous fistulas, which was filled with contrast in both venous and arterial phases, had a diffuse character of localization, the diagnosis was defined as liver form of ROW

disease and the patient was included in the LT Wait List. The operation of LT was performed on 18 April 2020, a postoperative period was complicated by anastomotic biliary stricture, on 27 April 2020 balloon dilatation and stricture stenting were performed. The patient was discharged from the transplantation department on 22th postoperative day in a good stay.
Conclusions: LT is a method of choice in patients with severe liver form of ROW disease, which is accompanied by portal hypertension, cholangitis and jaundice.

POS531 LIVER TRANSPLANTATION FOR INTRAHEPATIC MASS-FORMING CHOLANGIOCARCINOMA FOLLOWING NEOADJUVANT CHEMOTHERAPY AND TRANS-HEPATIC RADIOEMBOLIZATION

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We present the case of a 59-year old female patient that, in July 2017, was diagnosed with a 10 cm central liver lesion. At CT, the lesion extended into segments 4, 7 and 8, encased the right and middle hepatic veins and was in close proximity to the retrohepatic inferior vena cava, with no infiltration of the hepatic hilum, but presence of periportal, inter-cortical and paraaortic lymphadenopathies. The preoperative liver biopsy suggested a diagnosis of cholangiocarcinoma (CCC), while the PET showed uptake in the liver lesion only. The patient underwent staging laparotomy in August 2017, during which the lesion was deemed unresectable due to its infiltration of the hepatic axis and the biliary carrefour; the lesion was biopsied, with a histological diagnosis of intrahepatic mass-forming CCC.
After multidisciplinary assessment, the treatment plan was defined as neoadjuvant chemotherapy and trans-hepatic radioembolization with Y90 (Y90-TARE), followed by orthotopic liver transplantation (OLT).
Between August and September 2017, the patient underwent neoadjuvant chemotherapy with 4 cycles of Cisplatin + Gemcitabine, with a subsequent minimal reduction of the hepatic lesion at follow up CT. In December 2017, the patient underwent Y90-TARE. Figure 1 shows the CT appearance of the lesions at diagnosis (A) and after neoadjuvant chemotherapy and Y90-TARE (B).
In May 2018, the patient underwent OLT. The postoperative course was uneventful, and the patient was discharged on postoperative day 12. The histopathological examination of the lesion was of a ypT2 ypN0 CCC.
In June 2018, the patient underwent adjuvant chemotherapy with 4 cycles of m-FOLFOX-6.
After 31 months since OLT, the patient remains disease-free and in good health.

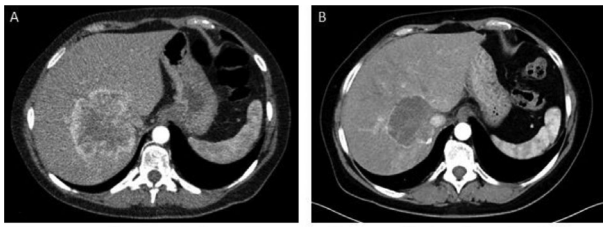

Figure 1. CT imaging A) At diagnosis B) After chemotherapy and transhepatic radioembolization

POS532 THE EFFECT OF PRE-TRANSPLANT LIPID PROFILE ON POST-TRANSPLANT HCC RECURRENCE

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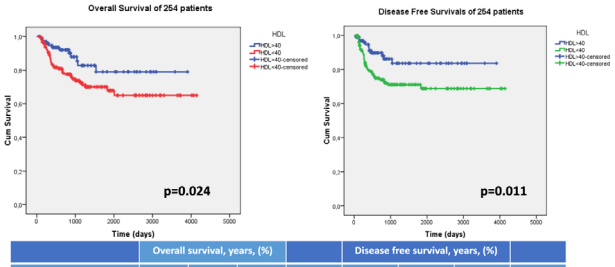
Background: We aimed to analyse the pre-transplant lipid profile, in terms of post-transplant tumor recurrence in patients with HCC, and to search is there any relationship between the pre-transplant lipid profile with MTD, number of nodules, differentiation, vascular invasion and GGT.
Methods: The patients with HCC who undergone LT between 2006 and 2021 (n = 438) were analysed retrospectively. Exclusion criteria: Patients whose data of the lipid profile before Tx date is not available (n = 136), and Patients with post-Tx follow up period <90 days (n = 48).
Inclusion criteria: Patients with post-Tx follow-up period >90 days (n = 254 were included).
Results: Only the HDL cholesterol was significantly associated with post-Tx recurrence (38 vs 29.5, $p < 0.001$, Table 1).
In terms of venous invasion only the HDL cholesterol was significantly associated with recurrence (39 vs 30.4, $p < 0.021$, Table 2). There was no significant association with recurrence, in terms of differentiation. HDL cholesterol was also significantly associated with Overall and disease-free survivals ($p = 0.024$ and $p = 0.011$, Figure)
Conclusion: HDL cholesterol is worth to investigate as a predictor of post-Tx HCC recurrence. Because we found that there is significant association between pre-Tx HDL cholesterol and post-Tx recurrence, venous invasion and survivals.

Table 1. Lipid profile and post-Tx recurrence

All Cohort (n=254)	Recurrence Negative (n=214)			Recurrence Positive (n=40)			p
Pre-Tx Lipid Profile	Median	Minimum	Maximum	Median	Minimum	Maximum	
Triglyceride, mg/dl (0-150)	84,5	17,0	376,0	76,5	51,0	243,0	0,330
Cholesterol, mg/dl (0-199)	136,0	12,0	250,0	134,0	41,0	372,0	0,852
HDL cholesterol, mg/dL (40-60)	**38,90**	3,90	84,00	**29,00**	5,00	59,08	**<0,001**
LDL cholesterol, mg/dl (30-130)	79,8	5,9	185,6	83,0	15,2	304,0	0,176
VLDL cholesterol, mg/dL (10-40)	16,9	3,4	115,6	15,3	10,2	49,0	0,393

Table 2. Lipid profile and venous invasion

All Cohort (n=254)	Venous Invasion									
	None (n=144)			Microscopic (n=86)			Macroscopic (n=24)			
	Median	Minimum	Maximum	Median	Minimum	Maximum	Median	Minimum	Maximum	p
Triglyceride, mg/dL (0-150)	82,0	39,0	376,0	86,0	17,0	290,0	75,5	36,0	173,0	0,494
Cholesterol, mg/dL (0-199)	135,5	18,0	250,0	136,5	12,0	288,0	141,0	70,0	372,0	0,755
HDL cholesterol, mg/dL (40-60)	**39,00[a]**	3,90	70,80	**36,25[a]**	3,90	84,00	**30,40[b]**	5,00	61,30	**0,021**
LDL cholesterol, mg/dL (30-130)	80,3	5,9	179,0	79,9	7,3	197,6	93,2	35,0	304,0	0,265
VLDL cholesterol, mg/dL (10-40)	16,7	7,8	115,6	16,9	3,4	58,0	15,1	7,2	43,2	0,590



	Overall survival, years, (%)				Disease free survival, years, (%)			
All cohort (n=254)	1	3	5	p	1	3	5	p
HDL≥40 mg/dL	94.7	82.7	79	0.024*	94.7	83.6	83.6	0.011*
HDL<40 mg/dL	84.6	73.7	70.1		80.3	71.2	71.2	

Figure. Survivals according to HDL ≥ 40 mg/dL vs HDL < 40 mg/dL

POS533 LUNG TRANSPLANTATION AFTER COVID-19: FIRST ITALIAN EXPERIENCE

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Background: Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) typically targets the respiratory system, particularly the lung. The infection can exhibits a broad spectrum of severity, from asymptomatic up to acute respiratory distress syndrome (ARDS) requiring an urgent admission to the intensive care unit (ICU). Lung transplantation (LT) is an established therapy for end-stage chronic respiratory diseases. Its use in an acute setting, however, brings about some uncertainty do to the lack of experience, donor shortage, and the complexity of potential recipient assessment. We report our first two cases of LT for ARDS after SARS-CoV-2 infection.
Methods: We retrospectively collect data on the first two cases of bilateral LT for ARDS after COVID-19. We recorded data on pre-LT clinical course, transplantation management and outcomes.
Results: The COVID-19 clinical course was similar in the two patients. In both cases, transplantation was successful. The first patient is alive and in good condition 9 months after transplantation (last FEV1 = 73%); the clinical course of the second patient was complicated by septic shock, and he died 62 days after surgery.
Conclusion: Our experience demonstrates the feasibility of LT for COVID-19. A dedicated protocol is mandatory to ensure the safety of healthcare professionals involved. Nonetheless, our second unsuccessful case raises some concerns: we recommend to reserve lung transplantation to highly selected patient, after thorough clinical, infective and psychiatric evaluation. In these circumstances, the ethical aspects must also be taken in consideration, with regard to the centre's mortality rate on waiting list. Since LT has a potential role in acute, sub-acute and chronic settings, it is vital to keep transplantation centre active during pandemic and to share knowledge on possible therapies for COVID-19.

POS534 STENTING OF PULMONARY VEIN STENOSIS AFTER LOBAR LUNG TRANSPLANTATION: MINIMAL INVASIVE INTERVENTION TO AVOID GRAFT LOSS

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Introduction: Pulmonary vein stenosis (PVS) represents a rare surgical complication after lung transplantation (LTx) with an incidence of 1.4% and a mortality rate of 45% [1]. Therapeutic options are limited, often resulting in re-thoracotomy and potentially graft loss. We present a case of successful endovascular stenting of PVS 131 days after LTx.
Case report: A 60-year-old woman with chronic obstructive pulmonary disease underwent sequential single lobar-LTx (right lower/middle lobe; left lower lobe).
The postoperative course was complicated by prolonged mechanical ventilation requiring tracheostomy, residual pleural effusion and hindered rehabilitation. A trans-esophageal cardiac ultrasound and computed tomography (CT)-angiography revealed a high grade left PVS (diameter: 3.7 mm) at postoperative day (POD) 72. Ventilation/perfusion (V/Q) scintigraphy showed a left lung distribution of 39%/11.9%, respectively.
To avoid the risk of graft loss by surgical reintervention, endovascular treatment was performed on POD 131. Via femoral vein access and trans-atrial puncture, the solitary left pulmonary vein (LPV) was reached. After 12 mm balloon dilatation (Powerflex 440-1204X), a 26 mm stent (Intrastent LDMAX S18-26) was implanted.
Seven days later, mechanical ventilation was weaned. The patient was discharged from ICU on POD 152 and from hospital on POD 176. Follow-up CT and V/Q scan 65 days post stenting confirmed success of the treatment: CT-measured LPV diameter was 7.5 mm and V/Q scintigraphy showed a left lung distribution of 40/41%, respectively.
Conclusion: Endovascular approach for PVS after lobar LTx is an effective yet undervalued treatment option that should be considered in the surgical LTx armamentarium to tackle this challenging complication.
[1] Kumar N et al. Pulmonary cuff dysfunction after lung transplant surgery: A systematic review of the evidence and analysis of its clinical implications. J Heart Lung Transplant 2019; 38:530-44.

POS535 DONOR-DERIVED TUBERCULOSIS IN LUNG TRANSPLANT RECIPIENT: THE NEED OF DONOR SCREENING

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Introduction: Tuberculosis (TB) is a rare complication of solid-organ transplant with an increased risk of graft loss and death. Donor-derived (DD) TB transmission risk is often undervalued. We report a case of DD pulmonary and extra-pulmonary TB in a lung transplant recipient.
Clinical case: A 39 years-old woman, recipient of lung transplantation from 2011 due to pulmonary hypertension, was admitted for chronic graft dysfunction requiring new transplant. Pre-transplant screening was performed including interferon-gamma release assays and mycobacterial culture of bronchoalveolar lavage (BAL), both resulting negative. The patient underwent lung re-transplantation in July 2020. At the end of September the patient developed a progressive respiratory failure. Chest CT scan showed pulmonary consolidation with ground glass to the left upper lobe. Bronchial whitish lesions were observed at fibrobronchoscopies. BAL culture showed *Pseudomonas aeruginosa* growth. The patient did not improve and pleural effusion occurred. Biopsies of bronchial lesions, BAL culture and thoracentesis with pleural biopsies were performed, mycobacterial culture and molecular test (Xpert MTB/RIF Ultra) for *Mycobacterium tuberculosis* were requested on all samples. The latter test was positive on bronchial lesions, BAL and pleural biopsies. Therapy with rifampicin, isoniazid, ethambutol and pyrazinamide was started. After 3 weeks, rifampicin was replaced by rifabutin due to interactions with tacrolimus. When cultures confirmed *M. tuberculosis* growth with susceptibility to all first-line antitubercular drugs, ethambutol was stopped. A slow but gradual clinical and radiological improvement was observed. Currently the patient stopped pyrazinamide continuing a maintenance regimen with rifabutin and isoniazid. At time of TB diagnosis, donor history, BAL cultures and radiological findings were revised. Calcified pulmonary lesions were found, which had not been evaluated for TB etiology due to the donor low-risk profile.
Discussion: Donor-derived TB is an uncommon event, especially in low TB incidence countries, where screenings are mainly focused on recipients. However, our case suggests that screening of latent more than active TB in donors is highly recommended, to guide TB preventive strategy after transplantation.

POS536 A CHALLENGING CASE SOLVED AT AUTOPSY. PRIMARY TOXOPLASMA GONDII INFECTION IN A LUNG TRANSPLANT RECIPIENT

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Toxoplasmosis in the immunocompromised host can be lethal if not diagnosed and treated. Postmortem examination was decisive to find out the cause of death. A 29-year old woman underwent bilateral lung transplant in 2012. Serological matches of donor and recipient were as follow: CMV +/+, EBV +/+, Toxoplasmosis -/-, HSV 1 +/+, HSV 2 -/-, VZV +/+, HHV8 -/-. In 2015 the patient was admitted for fever, pneumonia and eyesight impairment. Blood tests showed pancytopenia and elevated inflammatory markers. The ophthalmologist diagnosed diabetic retinopathy. Her eyesight gradually deteriorated, she started confabulating and vomiting. Brain CT and MRI showed a pre-existing subcortical ischemic area. CMV, JCV, HHV8, HHV6, BKV viraemia, bacterial and fungal cultures, test for mycobacteria and galactomannan were negative on blood, bronchoalveolar lavage and cerebrospinal fluid (CSF). Serology for *Toxoplasma gondii* (IgM and IgG) was negative. EBV-DNA was 260 cp/ml on CSF and 6900 cp/ml on blood. The patient died after 4 weeks of hospitalization, due to cardiovascular collapse. Challenges of this case were: the mistaken interpretation of the fundus oculi examination, that could have oriented the diagnosis, negative *Toxoplasma* serology, probably influenced by the severe status of immunosuppression and Real Time PCR for *Toxoplasma* not available at our institute. The autopsy revealed a disseminated *Toxoplasma gondii* infection with prevalent encephalic and cardiopulmonary involvement. With the aim of reducing the risk of primary infection in negative SOT recipients, we implemented a systematic counseling and written recommendation to reduce the risk of acquiring toxoplasmosis from food and environment. Additionally *Toxoplasma gondii* PCR testing was implemented at our Laboratory. Autopsy could be considered as a "final consultation" before closing a patient file. Unexpected autoptical findings could provide life-long learning opportunities.

POS537 NEPHROTIC SYNDROME DUE TO NODULAR GLOMERULOSCLEROSIS IN A NON-DIABETIC LUNG TRANSPLANT RECIPIENT WITH CYSTIC FIBROSIS

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Kidney disease is a severe complication of a lung transplantation (LT), commonly attributed to calcineurin inhibitor use, but other renal disorders related to end stage lung disease have also been implicated. Cystic fibrosis (CF) is a common indication for LT and it can result in a large spectrum of post-transplant kidney diseases. We here report a case of nephrotic syndrome in a non-diabetic CF lung transplant recipient with severe nodular glomerulosclerosis
A 34-year-old Caucasian woman with a history of CF end-stage lung disease underwent LT in 2013. Maintenance immunosuppression consisted of tacrolimus, mycophenolic acid and prednisone. The post-transplant course was complicated by acute renal failure episodes associated with infections. At the end of 2018, her serum creatinine was 115 μmol/l and proteinuria (1 g/l) was apparent. Following a respiratory tract infection in March 2019, she presented with edema. Her blood pressure was 146-88 mmHg and laboratory results indicated a serum albumin level of 26 g/l, proteinuria of >5 g/l, urine protein/creatinine ratio of 0.606 g/mmol and serum creatinine of 154 μmol/l. A kidney biopsy revealed features consistent with nodular glomerulosclerosis which is very similar to diabetic glomerulosclerosis. HbA1c level and fasting and oral glucose tolerance tests were normal and screening for diabetic retinopathy was negative.
LT improves survival outcomes in CF patients and CF-related comorbidities will increase after transplantation. However, among the many renal manifestations associated with CF, nephrotic syndrome is uncommon and is usually related to secondary amyloidosis or diabetic nephropathy. Nodular glomerulopathy without diabetes has rarely been described in CF patients. Our current case did not show blood glucose regulation abnormalities although the patient was at increased risk of diabetes (CF-related pancreatic dysfunction and impaired glucose tolerance induced by corticosteroid and tacrolimus).
Given the high risk of a rapid kidney function decline in CF LT recipients, a better understanding of the early mechanisms leading to nodular glomerulosclerosis in CF patients without overt diabetes could help to improve renal outcomes following LT.

POS538 NORMOTHERMIC EX-VIVO LUNG PERFUSION (EVLP) WITH PULMONARY ARTERY (PA) RECONSTRUCTION AFTER ITS MAIN TRUNK ACCIDENTAL DIVISION DURING HARVESTING

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Normothermic ex-vivo lung perfusion (EVLP) is an established strategy to increase donor pool, improving graft quality assessment, facilitating self-repair mechanisms, providing a platform for active drug treatments and safely prolonging the preservation time.
We report a case of a successful EVLP after retrieval in a 29-years-old donor deceased for car accident with associated chest trauma. Despite bilateral infiltrates on CT-scan, P/F was 440 mmHg at beginning of procedure; during evaluation P/F dropped to 280 mmHg, with lungs maintaining optimal compliance except for the right lower lobe showing some degree of contusion.
We decided to proceed with retrieval planning further evaluation of lungs on EVLP.
During harvesting with cardiac surgeons, the main PA trunk was accidentally divided leaving right and left branches disconnected, posing a crucial issue for EVLP cannulation.
Once back to our hospital we evaluated the damage and in order to connect the graft to the PA cuff of the EVLP system, we planned main PA reconstruction using donors aortic arch with supra-aortic trunks. Before starting the EVLP process a right lower lobectomy was required due to massive contusion of this area.
EVLP was performed according to Toronto protocol, after 4 hours of EVLP lungs were considered suitable for transplant (P/F 430 mmHg, left atrial and PA both stable during procedure, bronchoscopy negative and no signs of congestion on X-rays).
Lung transplant was carried out on a 48-years-old recipient affected by primary pulmonary hypertension, performed through a clamshell incision with central VA ECMO support.
Postoperative period was uneventful, characterized by slow recovery; patient was discharged on 51st postoperative day.
EVLP is a well standardized technique but requires intact vessels and airways. Precise levels of division of main PA trunk and left atrial cuff during harvesting are critical maneuvers which may incidentally result in PA injury or short vein stumps.
Additional care should be taken when the EVLP process is planned.
This article highlights successful EVLP reconditioning and lung transplantation, despite PA division during retrieval, reporting a technical detail to restore an adequate arterial length in order to overcome lack of tissue when connecting PA to the cannula.

POS539 A LUNG TRANSPLANT PROGRAM SNAPSHOT AT THE TIME OF COVID-19: STILL EMERGENCY CASES FEASIBLE?

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Background: Although lung transplant is a well-defined procedure in terms of technique and clinical follow-up, recruiting donors has been challenging during the COVID-19 pandemic period. In our Centre, on the 27th of October 2020, two patients were transplanted simultaneously. We present our experience in the management of two potential demanding emergencies.
Methods: A 45-year-old man (PTS1), affected by MDA5 amyopathic dermatomyositis with rapidly progressive interstitial lung disease, arrived at our Pneumology unit for acute respiratory failure. Medical rescue therapy with a high dose of methylprednisolone was not sufficient, and he was transferred to ICU to start V-V ECMO support as a bridge to transplant. Protective ventilation tracheostomy performed. During sixteen days of ECMO support the pre-transplant screening was completed. The second patient (PTS2) was a 60-year-old woman affected by a severely compromised idiopathic interstitial fibrosis. After a first unsuccessful call for transplantation for a sub-clinical COVID-19 infection, another compatible organ was identified the same night as PTS1. Two different teams were alerted to ensure both patients a safe procedure with acceptable ischemic time. The organs were explanted almost simultaneously in two hospitals in North of Italy.
Results: Both patients were prepared for intra-operative A-V ECMO, and the two recipients underwent a double-lung transplant at the same time. The post-operative course was characterized by early weaning from ECMO (3 days PTS1, 2 days PTS2). Respiratory decannulation was possible at 35 days post-surgery for PTS1 and discharged 63 days post-transplant for a severe bed rest syndrome and a slow functional recovery. PTS2 underwent percutaneous tracheostomy on day 10 after surgery due to difficult respiratory weaning. PTS2 was complicated by mild anastomotic stenosis treated with serial balloon dilatation obtaining satisfactory results. So far, the two patients are on strict outpatient follow-up and have a good respiratory function. Both patients recovered, and PTS2 has no sign of obstruction at recent spirometry.
Conclusions: Emergency lung transplant cases are feasible to be managed even simultaneously by intraoperative ECMO and close-knit teamwork, leading two patients safely through the COVID-19 pandemia.

POS540 LUNG TRANSPLANT FOLLOWING COVID-19 INFECTION AFTER 6 MONTHS ON ECMO SUPPORT DEVELOPED SEVERE AMR POST TRANSPLANTATION

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62-year-old man with diabetes mellitus, myocardial infarction 2002, with percutaneous coronary intervention towards right coronary artery. Presented with 7 days of dyspnoea and fever. He was positive for COVID-19 at the time of admission. Within 4 days he deteriorated and was transferred to the intensive care unit (ICU) and was intubated.
On hospital day 17 he required veno-venous-extracorporeal membrane oxygenation (VV ECMO). Despite aggressive supportive care his condition progressed to end-stage lung disease (Figure 1A).
During 6 months of VV ECMO support the patient suffered numerous complications including cerebral haemorrhage, cor pulmonale, and blood stream infections.
Given the relative contra indications for lung transplantation (LTx) the decision to LTx was mainly based on the ethics with a neurological intact, awake, mobilized patient in combination with the lack of experience on LTx outcome in COVID-19 cases.

The patient was taken to the operating room after suitable donor lungs were allocated. With on-going ECMO support, the patient underwent median sternotomy. No major signs of adherences between chest wall and lung were seen why central cannulation and conversion to cardiopulmonary bypass (CPB) was done. Hilar dissection was completed, and the lungs were explanted. Donor lungs were then implanted in sequential standard fashion. The patient was separated from CPB, without the need of ECMO support. Explanted lungs are shown in Figure 1B.
The patient received standard immunosuppressive therapy. He was extubated 3 days later. Post-transplant he suffered a long post-operative course at the ICU with heart failure, infectious diseases, and kidney insufficiency. He was treated with Levosimendan, hemodialysis and a diverse of antibiotics.
3 months post transplantation, without significant prior signs, the patient shocked down at the hospital ward with acute hypoxia and acute respiratory distress and was intubated acute at the ward and brought back to ICU. Chest imaging showed suspect acute rejection (Figure 1C). De novo DQ8-DSA, mean fluorescence intensity (MFI) 5000 was found. He was successfully treated with high dose of corticosteroids, and plasmaphereses with good response and was extubated 4 days later. 5 months post transplantation he is being planned for transition to a rehabilitation center.

Figure 1A

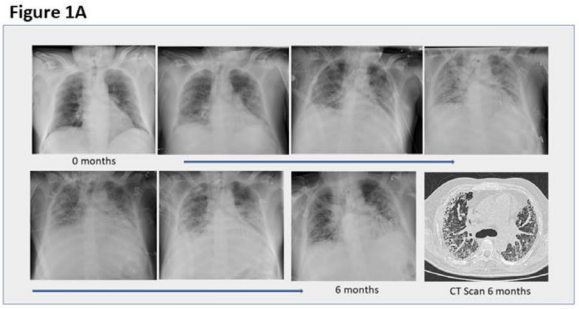


Figure 1B

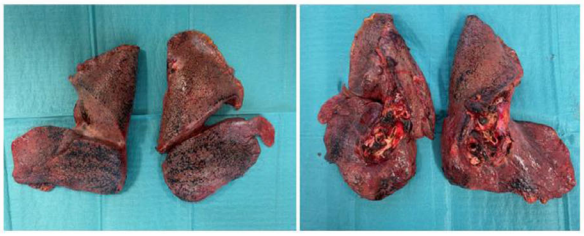
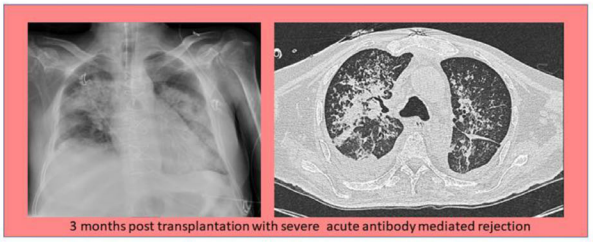


Figure 1C



POS541 A RARE CASE EVEROLIMUS-ASSOCIATED ALVEOLAR HEMORRAGE IN A KIDNEY TRANSPLANT RECIPIENT

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Introduction: Pulmonary toxicity of Everolimus is a rare side effect that consists of diverse entities such as interstitial pneumonitis, lymphocytic alveolitis, bronchiolitis obliterans with organizing pneumonia and, very rarely, diffuse alveolar hemorrhage.
Case report: A 51-year-old male affected by end-stage renal disease related to diabetic nephropathy underwent single kidney transplantation (KTx) from a standard DBD donor.
Two months after KTx patient shown haemoptysis and shortness of breath; auscultation revealed diffuse inspiratory crackles and expiratory wheezing over both lungs. HRCT shown bilateral multiple "ground-glass"-like areas and infiltrated consistent with alveolar hemorrage. Rhinopharyingeal swab for Sars-CoV-2 was negative. Empiric antibiotic therapy with pipiracillin/tazobactam was started with no response and blood tests shown severe anemization. Everolimus therapy was suspended and patient was hospitalized for severe respiratory failure, requiring high flux O_2 therapy, and blood transfusion.
BAL shown progressively more bloody samples, typical of diffuse alveolar hemorrhage, whose analysis was negative for bacterial, viral and fungal culture while the cytological evaluation detected several hemosiderin-laden macrophages (>20%).
ANCA and Ab antiGBM were negative; blood and respiratory cultures were negative. Respiratory clinical picture progressively improved after everolimus discontinuation, patient was discharged after 9 days and follow-up HRCT shown global improvement.
Ten days after patient was re-admitted due to a relapse of the haemoptysis and respiratory symptoms. A new HRCT shown a re-worsening of pulmonary inflammatory infiltrates and ground glass areas requiring high dosage intravenous pulse steroids to achive complete resolution of symptoms and radiological picture.
Conclusion: Pulmonary toxicity related to everolimus is a rare complication that must be always considered as differential diagnosis in patients complaining respiratory symptoms. Prompt recognition, managing and treatment of this class-related side effect is crucial to guarantee good outcomes of these patients.

POS542 SYSTEMIZING GUIDELINES, MEMORANDAS AND ROUTINES WITH ADDITIONAL CASE MEETINGS –A TRANSPLANT COORDINATOR´S ON CALL BOOK AND A COORDINATOR´S CLUB

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A Qualitative Improvement project.
Background: The complexity in coordinating a donation processes is well-known among those in involved. The process is regulated by laws, constitutions, medical assessments, allocation rules/ethics. Memoranda, routines and systems for registration and documentation are constantly revised to correspond to latest regulation from the authorities and societies.
When complicated cases occur, they are later discussed and analyzed in the Coordinator´s club so all aspects and experiences can be highlighted.
Aim: The aim of the project was to systemize guidelines, memoranda and routines in an on-call book for the Transplant Unit coordinators. To share experience and gain knowledge a Coordinators club was established.
Method: To facilitate the coordination - donation process according to given memoranda, guidelines and routines a former on-call book was reorganized in content and in form. We identified 17 categories. New documents were written. The on-call book exists in digital form and is available to everyone working in the Transplant Unit. The on-call book covers 196 documents.
The Coordinator´s club is scheduled once a month. Each meeting has a theme based on a complicated case. Presentation of a case with a specified problem -virology, diagnostics etc., followed with a briefing. According to the case an additional article is discussed.
Result: With the on-call book with current guidelines, memoranda and routines the transplant coordinators can work safely. The project has resulted in a quality improvement for coordinating a donation process.
In the Coordinator´s club cases with a special topic is highlighted and learned from. This increase competence and ability to handle new complicated cases.
Conclusion: The quality improvement project and the Coordinator's club are resulting in safe coordinating and increasing competence among the coordinators at the transplant unit.

POS543 SALVAGING GRAFT PANCREAS IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT RECIPIENT WITH SPLENIC ARTERY THROMBOSIS AND STENTING OF Y ARTERIAL GRAFT STENOSIS

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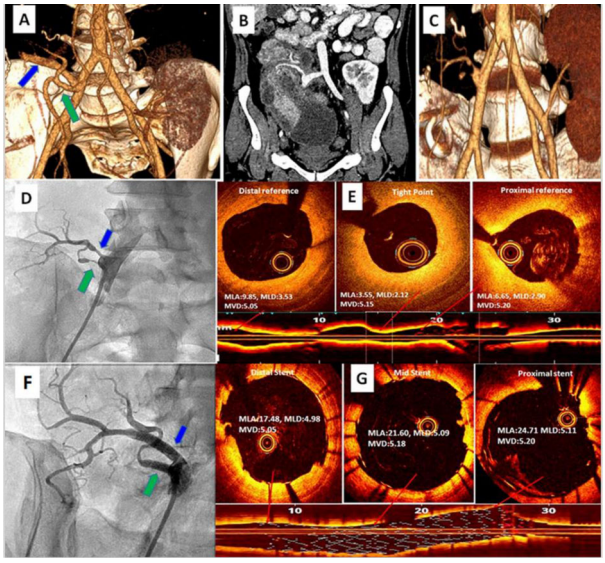
Background: Unlike other solid organ transplantation, the pancreatic allograft is more prone to thrombosis in the early period following transplantation due to its inherently slow microcirculatory flow. Factors leading to this typical non-immunological alarming event fall under a wide range of donor and recipient-related factors like procurement injury, longer ischemia time, allograft pancreatitis, infections, and graft rejection. Allograft thrombosis is the leading cause of graft loss in the early postoperative period; even with effective anticoagulation strategies, allograft salvage following this event is rare.
Clinical Case: The present case describes salvage of pancreatic allograft in a simultaneous pancreas-kidney transplant recipient following an unrecognized isolated splenic artery thrombosis leading to early acute graft pancreatitis(E-AGP), walled-off pancreatic necrosis (WOPN) of graft pancreas tail at two months post-transplant with subsequent transplant pancreatic artery stenosis (TPAS) of both limbs of Y arterial graft causing allograft dysfunction at six-month post-transplant. A multidisciplinary conservative approach was used for the salvage of pancreatic allograft. The TPAS was managed by Optical Coherence Tomography (OCT) guided drug-eluting stenting of both limbs of Y arterial interposition graft.
Conclusions: Arterial thrombosis in pancreas transplant is catastrophic and leads to graft loss. Salvaging graft complicated by consecutive events using a conservative approach is feasible; however, interventions should always be individualized according to the patient's condition and technical feasibility. Literature documenting the effect of pancreatic artery stenosis on glycemic control is scarce. The present case is the first reported case in English literature where graft salvage was possible following isolated splenic artery thrombosis and the first case to successfully resolve pancreatic allograft dysfunction following percutaneous endovascular stenting of Y arterial interposition graft.



POS544 EFFECTS OF COMPLETE IMMUNOSUPPRESSION SUSPENSION AFTER PANCREATIC GRAFT LOSS

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Background: In the event of loss of function of a pancreatic graft, there are two safe options: suspension of immunosuppressive therapy followed by explantation of the grafted pancreas, or maintenance of reduced doses of mycophenolate without explanting the graft.
Methods: A 73-year-old woman, who had received a pancreas transplant alone in 2001 when she was 54, since 2018 suffered the loss of renal function requiring hemodialysis treatment. In 2019, due to repeated acute rejection episodes, she has lost also the function of the grafted pancreas. First, tacrolimus therapy was suspended then, in March 2020 also mycophenolate was interrupted. In September 2020, the patient has accessed the emergency room for massive hematemesis. A contrast-enhanced computed tomography scan of the abdomen showed infected perigraft hematoma with an anastomotic pseudoaneurysm that fistulized in the graft duodenum.
Results: The patient was immediately stabilized and underwent a radiological interventional procedure for stent placement in the native right common iliac artery, excluding the native right internal iliac artery and the anastomosis with the common branch of the Y artery graft for the transplanted pancreas. Two days later the patient underwent graft removal with ligation and section of the native right common iliac artery at the level of the anastomosis serving the transplanted pancreas. Due to acute ischemia of the right lower limb, 24 hours later a femoro-femoral arterial crossover was constructed using a cryo-preserved graft. Despite the full restoration of arterial vascularization to the ischemic limb, the patient died five days later.
Conclusions: After the loss of a pancreatic graft, if not explanted, it is advisable to maintain immunosuppression at low doses to avoid recurrence of severe acute rejection phenomena with colliquative evolution of the transplanted organ, potentially leading to anastomotic pseudoaneurysms and/or fistulization in the grafted duodenum.

POS545 THE FIRST EXPERIENCE OF RETROPERITONEAL TRANSPLANTATION OF THE DISTAL SEGMENT OF PANCREAS USING A PANCREATICOJEJUNAL ANASTOMOSIS ON A ROUX-EN-Y LOOP

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Numbers of pancreatic transplants remains low. One of the reasons is the shortage of transplantable organs. We offer the technique of retroperitoneal transplantation of the distal segment of the pancreas with pancreaticojejunal anastomosis on Roux-en-Y loop that could be possible to increase the number of transplants from extended criteria donors.
A 40-year-old man was receiving renal replacement therapy with peritoneal dialysis for 6 years. Lifelong insulin therapy was started at 3 years of age. In November 2020 the patient underwent a simultaneous kidney and pancreas transplantation.
At the back table the orifice of the inferior pancreatoduodenal artery fell into a linear mechanical suture during the treatment of the small intestine's mesentery root. Test for adequate collateral blood flow through the splenic artery was positive.
Intraoperatively anastomoses were made between the portal vein of the graft and the inferior vena cava, then between the splenic artery and the common iliac artery. After reperfusion there were noted blood supply to the body and tail. But there was insufficient blood supply to the head and duodenal stump. The pancreatic parenchyma is acutely transected along the surgical neck with mobilization of the distal part of the pancreatic duct.
An antiperistaltic Roux-en-Y anastomosis was applied 80 cm distal to the Treitz ligament. The proximal part of the intestine through the mesentery of the ascending colon is brought out into the retroperitoneal space, where pancreaticojejunal anastomosis was formed using the stent. Kidney transplantation was performed according to the standard technique in the left iliac region.
From the first postoperative day there were registered immediate graft function, euglycemia and normalization of uremia. Revision of the distal segment of the pancreas graft on day 3 demonstrated the consistency of pancreaticojejunal anastomosis.
Transplantation of the distal segment of the pancreas using the proposed surgical method is able to return to modern transplant techniques. This will help avoid transplantectomy with a partially inadequate organ blood supply and increase numbers of transplants performed.

POS546 BEING AHEAD OF THE GAME. ORGAN OPTIMISATION PRIOR TO THE MOBILISATION OF A FULL CARDIOTHORACIC RETRIEVAL TEAM. THE NURSES EXPERIENCE

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Introduction: Last year 350 people died in the UK waiting for a solid organ transplant highlighting the shortage of donor organs and the need to improve organ utilisation. Donor optimisation, 'Scouting' is a way to optimise donor organ function and increase the utilisation of organs deemed marginal

or non-transplantable. Scouts at a leading cardiothoracic centre are nurses. This team of non-medics are mobilised in advance of donor offering commencing and independently attempt to optimise organs. The following case study evidences the benefits of an isolated Scout attendance in ITU and the successful transplantation of heart and lungs by two different cardiothoracic centres.

Case Presentation: Scout attended a 56 yrs female with high inotropic requirements (Norepinephrine >0.2 mcgs/kg/min) and long-standing hypertension taking a single agent. The donor also had a low PaO2/FiO2 ratio (24). These initial details are linked to un-transplantable organs.

A pulmonary artery catheter was inserted by the Scout to assess preload and afterload of the heart. Information gained allowed optimisation to improve cardiac performance. Inotropes were successfully weaned off. Improved cardiac function was confirmed on transoesophageal echocardiography (TOE). Fibre optic Bronchoscopy and lung recruitment were used to successfully optimise lung function.

Results: TOE undertaken demonstrated a left ventricular ejection fraction of 65%. Post optimisation cardiac output studies were; CO 6.4, CI 3.3, PCWP 9, CVP 8, SVR 731 with no inotropic support. Arterial blood gas analysis showed a significant improvement in PaO2/Fio2 ratio from 24 to 38 following optimisation. This improvement in function resulted in a full NORS team being mobilised and successful use of accepted heart and lungs.

Conclusion: Two patients were transplanted with excellent post-transplant allograft function. We recommend that a formalised national scouting programme should be commissioned for in-situ optimisation of marginal donor organs. Advantages, Reduces mobilisation of full organ retrieval team and Increase organ utilisation for Heart and Lung transplantation. We have been recognised at this years British Transplant Society and NHS Blood and Transplant Congress for our "scouting" work and our aim is to roll out a National Scouting Programme.

POS547 NURSING MANAGEMENT IN POST-OPERATIVE PEDIATRIC LIVER TRANSPLANTATION: OUR EXPERIENCE

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The nursing management associated with the intensivist and surgical experience, in the first 24 hours after pediatric liver transplantation carries out a fundamental role for obtaining a good outcome of the graft.

In our center, every year, more than 30 pediatric liver transplantation are performed, about 20% are living donor liver transplantation. In the pediatric population the causes of liver transplantation are different than in the adult population. In children the most frequent cause of liver transplantation is biliary atresia, acute liver failure, liver tumors and metabolic disorders. Our target is to describe to intensive care nursing management in the first postoperative period of pediatric liver transplantation. All patients arrive in pediatric intensive care (PICU) under sedation and mechanical ventilation, with at least two abdominal drainages, central venous line, arterial line, nasogastric tube and urinary catheter. At the admission in PICU we start the infusion to maintain deep sedation, fluid therapy with glucose and electrolytes, inotropic drug if are necessary and we collect blood sample for checking blood sugar level, transaminases, coagulation factors, level of hemoglobin and platelets. In all patients we have to compensate the fluid lost by abdominal drainages as soon as possible, after the admission in PICU using Albumin 5%. This is most important to maintain a target value of central venous pressure at least 10-12 mmHg to preserve the vascular anastomoses. Moreover, during the first 24 hours we use to collect, every 2-4 hours, blood samples for blood gas analysis, lactate, glycemia, electrolytes and hematocrit. Fluid balance is calculated hourly for avoiding fluid overload. Every abnormalities are detected and managed with the physicians. We conclude that the first 24 hours after pediatric liver transplantation is a critical period in which a multidisciplinary approach is fundamental to prevent complications for the graft and the patient.

POS548 MAINTAINING AND DELIVERING A WORLD CLASS EDUCATION SERVICE TO SPECIALIST NURSES IN ORGAN DONATION DURING A PANDEMIC

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NHS Blood and Transplant aim to save and improve the lives of the thousands of individuals in the UK awaiting a life changing organ or tissue transplant. Within the Organ and Tissue Donation and Transplantation Directorate, Nurse Education is researched, designed and delivered by a team of Professional Development Specialists (PDS), all Nurses with a background in Organ Donation as Specialist Nurses (SN) themselves. The PDS team aim to Educate, Develop and Empower our SN's and support overarching aim of saving and improving lives through organ donation.

Our core course delivery includes award-winning bespoke training for new SN's that was standardised across the UK in 2006 to provide a consistent and quality programme to develop nurses ready to embrace their specialist role. Alongside this we offer an annual advanced communication training, mentorship, clinical donor management, collaborate with medical education and utilise novel and innovative teaching techniques such as high fidelity clinical simulation.

March 2020 saw the world that we were used to deliver our training in cease abruptly. Despite redeploying to aid our hospital teams, It was apparent alongside this we would need to meet the challenge of translating what was predominantly face to face training into a virtual world, in order to sustain organisational need and offer support and training to our nurses.

We remodelled our courses, we utilised a flipped learning approach and aimed to reduce screen fatigue and maintain engagement. Reflective models are used as part of the learning process, to encourage critical thinking. Inclusivity of learners was a key consideration in planning – IT access, environment, and consideration of additional learning needs.

Throughout this challenging time, our priority has always been to continue to deliver our core business – what we have achieved, is a refreshed and adapted way to deliver. Looking forward, we plan to continue a blended learning approach with both virtual and face to face elements. This will encompass a significant continued cost saving on delivery (reduction in travel and accommodation costs resulting from national geographical spread of delegates) for the organisation, whilst still recognising the health and wellbeing benefits of face to face contact, networking and connection.

POS549 ALEMTUZUMAB INDUCTION ALLOWS THE EFFECTIVE USE OF CYCLOSPORINE A IN STEROID-FREE REGIMES OF IMMUNOSUPPRESSIVE TREATMENT AFTER KIDNEY TRANSPLANTATION

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There are few comparisons of alemtuzumab induction therapy followed by calcineurin inhibitors (CNI) maintenance therapy based on cyclosporine A allowing early glucocorticoid withdrawal in renal transplant recipients. The purpose of the present study was to compare cyclosporine A based immunosuppressive (IS) therapy with the most commonly used maintenance regimen based on tacrolimus in renal transplantation after alemtuzumab induction.

Methods: In retrospective study we followed the results of kidney transplantation in 32 recipients who received 2 doses of alemtuzumab at day 0 and day 1. Male sex was in 18/32 (56.25%). The median age was 48 (21-65) years old. The main cause of renal failure was chronic glomerulonephritis 24/32 (75%). Hemodialysis before transplantation was received 30/32 (93.75%) patients.

Methylprednisolone was not employed in the IS protocol. All the patients took CNIs and mycophenolate mofetil (MMF). Cyclosporine A was used in 21/32 (66.6%) recipients (main group). Tacrolimus was prescribed to 11/32 (34.37%) (control group). Median dose of MMF was 1250 (1000-1500) mg per day and it was similar in both groups.

Results: Delayed kidney graft function was seen in 8/32 (25%) recipients. There was no significant difference in the rate between groups in this parameter. In one month after kidney transplantation in the main and control group level of serum creatinine was 138 (110-204) mcmol/l vs 124 (104-230) mcmol/l ($p = 0.619$) respectively and estimated glomerular filtration rate (eGFR) were 62.5 (53.5-68.5) ml/min vs 58 (30-99) ml/min ($p = 0.791$) respectively.

During follow up period (more than 8 years) 8/32 (18.75%) patients came back to dialysis. There were 5/21 (23.8%) in the main group and in the control group – 3/11 (23.8%) patients (log-rank test, $p = 0.72$). Oncological complications developed in 2/32 (6.25%) patients by one in each group. Infection complications were diagnosed in 8/32 (25%) patients in the post-transplant period. There was no difference in rate of infection disease between groups.

Conclusion: Cyclosporine A based two-component immunosuppressive protocol without steroid is as effective and safe as immunosuppressive protocol with tacrolimus in case of alemtuzumab induction therapy using.

POS730 THE STATE OF INTERSTITIAL GLUCOSE METABOLISM IN DECEASED DONOR LIVER DURING STATIC COLD STORAGE MAY PREDICT ORGAN VIABILITY AND INITIAL GRAFT FUNCTION

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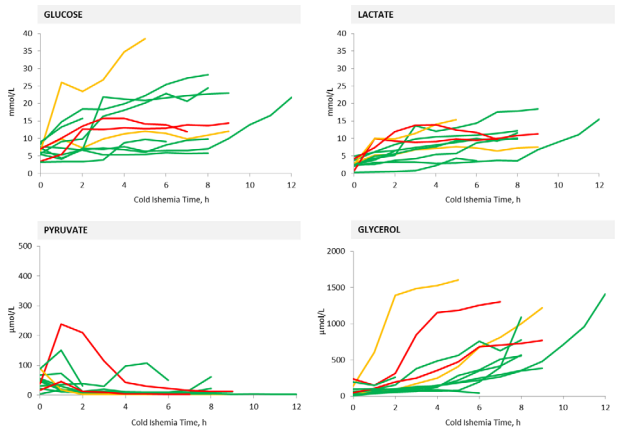
Burnasyan State Research Center, Surgery and Transplantation Center, Moscow, Russian Federation

Background and Aims: The assessment of donor liver viability and prediction of its initial function after transplantation are of crucial importance for avoiding primary non-function (PNF) and early life-threatening complications. One of the main disadvantages of traditional static cold storage (SCS) is the lack of objective data on the state of the donor organ during preservation. Measurement of interstitial glucose, lactate, pyruvate and glycerol concentrations during SCS may be considered as useful diagnostic and/or prognostic tool.
Methods: After laparotomy in 12 brain-dead standard criteria donors, the microdialysis catheters were inserted into the liver. In each case, the first sample of interstitial fluid was obtain prior to flushing with histidine-tryptophan ketoglutarate solution. The second and subsequent probes were collected hourly until start of back-table preparation in the transplant center. Liver interstitial glucose (GLU), lactate (LAC), pyruvate (PYR) and glycerol (GLYC) levels were measured retrospectively.
Results: All transplants were elective. The recipient's lab MELD-Na scores varied from 10 to 19. Cold ischemia time (CIT) ranged from 3.5 h to 12.5 h (median – 8.5 h). There were no PNFs. However, there were 2 cases of early allograft dysfunction with AST/ALT levels more than 2000 IU at 24 h after transplant. During the SCS in all cases, there were an increase in median values of GLU (6.4 -> 19.8 mmol/L), LAC (2.6 -> 11.6 mmol/L) and GLYC (30 -> 775 μmol/L) levels (Figure 1), while the level of PYR after 1 h and until the end of SCS was close to the 0 μmol/L.
Figure 1. Interstitial GLU, LAC, PYR and GLYC concentrations during deceased liver SCS. 24-h post-transplant AST/ALT < 1000 U/L – green, between 1000 U/L and 2000 U/L – yellow, more than 2000 U/L – red.



Conclusions: These findings show that the parameters of interstitial glucose metabolism depend not only on SCS duration; therefore, they can probably be used to assess the quality of the donor organ before transplantation.
This study was supported by the Russian Science Foundation (grant number: 19-75-10040).

POS731 AFFECTS OF COLD ISCHEMIA ON AMPK REGULATION IN A FATTY LIVER MODEL

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Background: When fatty livers are transplanted, they function much later, or primary dysfunction and rejection are observed more frequently. AMPK has organ protective functions during ischemia. Metformin had been used for the activation of AMPK in hepatocytes. In this study, we will examine the alteration of AMPK proteins in fatty and normal livers with or without metformin at varying times of ischemia.
Methods: Seven-week C7BL56 mice (n = 110) were randomly divided into four groups; fatty and not-fat without metformin, fatty and non-fat with metformin. A diet model was administered for ten weeks for achieving fatty liver. 0.2 m/kg of metformin was administered by oral gavage for the last four weeks. After performing total hepatectomy, the tissues were kept for 0-6-12-24 hour ischemia periods with UW solutions. Histopathological examinations were performed to calculate scores of macrosteatosis, fibrosis, inflammation, vacuolar changes, necrosis. Western blot method used for p-AMPK and AMPK protein expressions. Descriptive statistics performed.
Preliminary Results: When comparing fatty mice with metformin and fatty mice without metformin, metformin had a statistically significant reducing effect on the fat percentage. (median 75%,45–88 vs. 55%, 25–65 p = 0.007)
There was no difference between the groups in the median of vacuolar change (reversible ischemic change) (p = 0.263) On contrary, moderate and severe necrosis (irreversible ischemic change) was not observed in the both metformin (+) groups and overall necrosis was statistically less observed (p = 0.001) (Table 1)
The preliminary results showed that AMPK was regulated in both fatty and non-fat without metformin mice group was at 12 hours, while the amount of regulated AMPK was significantly higher at non-fat mice without metformin, especially at 12 hours (Figure 1). The AMPK analysis of all mice will be possible with the completion of western protein analysis.

Table 1: Differences according to fat and metformin status

	Fat(+) (met-) (n = 28)	Fat(-) (met-) (n = 28)	Fat(+) (met+) (n = 25)	Fat(-) (met+) (n = 29)
Macrosteatosis (%)	75 (45–88)	0 (0–5)	55 (65–25)	0 (0–5)
Vacuolar change (%)	38 (20–48)	33 (18–45)	25 (15–45)	25 (15–50)
Necrosis (n) (none-mild-moderate-severe)	15 11 1 1	16 8 2 2	24 1 0 0	26 3 0 0

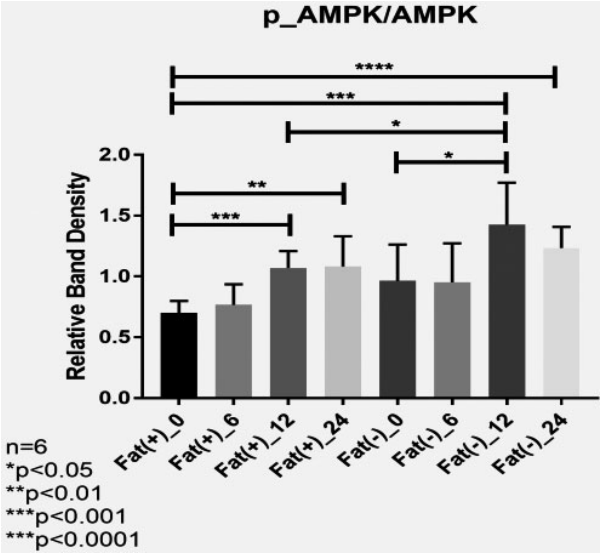

Figure 1: p-AMPK/AMPK ratio according to ischemia hours (Metformin (-))

POS732 THE ROLE OF HLA ANTIGENTS ON COVID-19 INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background and Aims: Kidney transplant recipients appear to be at higher risk of critical COVID-19 disease. However, our clinical experience with patients after the kidney transplantation indicated relatively good course of the COVID-19 disease. The aim of our analysis was to identify risk factors for severe course of the COVID-19 disease and to determine the influence of immunosuppression and certain HLA antigens on the course of the disease.
Method: This is a prospective multicenter analysis, which included patients with confirmed SARS-CoV-2 positivity after the kidney transplantation with a 3-month follow-up after infection. The group of patients was divided in 3 subgroups according to the course of the infection as follows: asymptomatic or oligosymptomatic, medium severe and severe course (hospitalization).
Results: There were 186 patients (men 69.4%) with confirmed SARS-CoV-2 positivity included in this multicentric analysis. Following independent risk factors were identified: age at the time of infection more than 59 years (OR 4.72, $p < 0.0001$), BMI more than 29.9 kg/m2 (OR 8.62, $p < 0.0001$), prednisone dose/day less than 7.5 mg (OR 2.45, $p = 0.0001$); and HLA DQ2 has protective nature (OR 0.02, $p = 0.0033$). The only independent risk factor for the outcome death was age at the time of infection more than 59 years (OR2.76, $p = 0.0104$.
Conclusion: Higher dose of corticoids in standard immunosuppressive regime (more than 7.5 mg/kg) and HLA DQ2 appear to be protective factors in our analysis. However, it shall be supported with further data on larger sample of patients.

POS733 LUMINAL PRESERVATION OF THE SMALL BOWEL IN A PRECLINICAL PORCINE BRAIN DEATH DONOR MODEL

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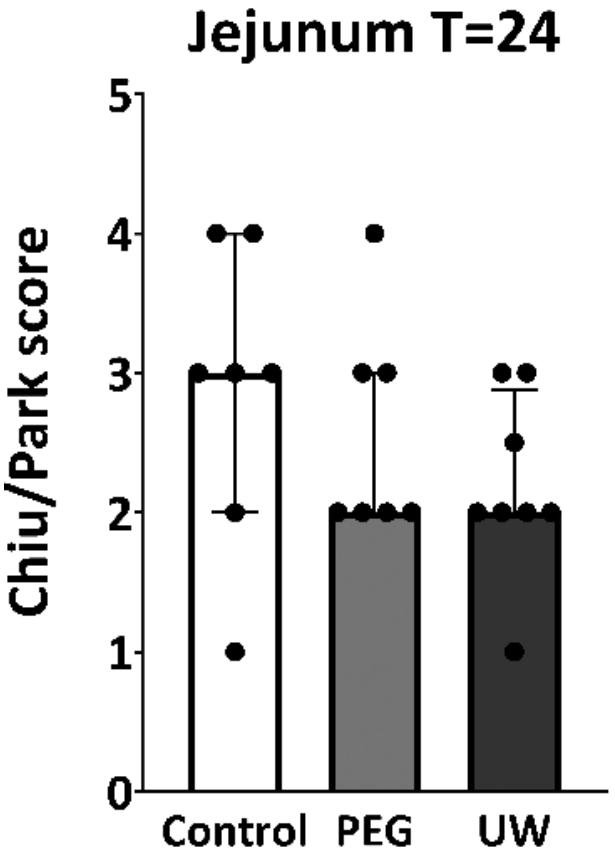
Background and Aims: Small bowel grafts are retrieved from donation after brain death (BD) donors. The negative impact of BD on organ quality has previously been demonstrated, yet the effect of BD is often omitted in experimental preservation injury models. The goal of this study was to develop a brain death donor model resembling clinical practice, and use it to examine the effect of additional luminal preservation (LP) of the small bowel on preservation injury in comparison to standard preservation methods.
Methods: Twenty-two female Danish Landrace pigs (56–86 kg) were included and randomized into a control group ('control', $n = 7$) or an LP group with either a polyethylene glycol-based solution ('PEG', $n = 7$) or University of Wisconsin solution ('UW', $n = 8$). In all animals, BD was induced by inflation of an epidural balloon and defined when the intracranial pressure exceeded the mean arterial pressure. Animals were observed for six hours after BD followed by multi-organ retrieval surgery including *in vivo* vascular perfusion of the abdominal organs with UW. In the LP groups, 2000 ml of LP solution was administered into the small bowel in $\pm$ 2 hrs during surgery. Jejunum and ileum were sampled directly following procurement (T = 0) and after 8, 14 and 24 hrs of cold storage (CS). Intestinal preservation injury was assessed using the histological Chiu/Park score (grade 0–8).
Results: Inflation of the epidural balloon led to an increase in the intracranial pressure exceeding the mean arterial pressure after a median duration of 19 min (range 7–45 min). The following reaction was observed: a rapid increase followed by a decrease in blood pressure and heart rate, increased cardiac output, hypothermia, hypernatremia and diabetes insipidus. Intestinal preservation injury was scored blind in jejunum samples after 24 hrs of CS. Median (min-max) Chiu/Park scores for the control, PEG and UW group were 3 (1–4), 2 (2–4) and 2 (1–3) respectively (see Graph).
Conclusions: We established BD in a porcine model resulting in a physiological response similar to the clinical setting, and used this model to examine the effect of an additional preservation technique for the small bowel on preservation injury. The results suggest that LP with PEG or UW has the potential to decrease the severity of intestinal preservation injury by one point in the jejunum.



POS734 ANALYSING THE FINANCIAL COSTS AND BENEFITS OF UNSPECIFIED KIDNEY DONATION IN THE UK: RESULTS FROM THE BOUND STUDY

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Background: The BOUnD study is a national study conducted in the United Kingdom with the aim of assessing different components of Unspecified Kidney Donation (UKD), including the economic implications. One of the main concerns voiced by the transplant community in relation to UKD are the cost implications of assessing donors who do not go on to proceed, and to what extent this is offset by the financial benefits gained by the National Health Service (NHS) from those who do. The aim of this study was to determine the cost-benefit of the UKD programme in the UK.
Methods: Individuals presenting as potential living kidney donors to each of the 23 UK kidney transplant centres were consented to take part in a longitudinal prospective questionnaire study. The questionnaire comprised questionnaires related to the donation process and physical outcomes (including length of stay, complications and the physical component of the Short-Form 12). The Client Service Receipt Inventory (CSRI; a questionnaire used to collect data on healthcare service use) was distributed at four time points: twice before surgery, and at 3 and 12 months post-operatively.
Preliminary Results: This results of this study will provide the largest dataset to date on the costs of healthcare service use amongst individuals who present as potential Unspecified Kidney Donors (UKDs). Data on UKDs will be compared with those who present as potential Specified Kidney Donors (SKDs; individuals donating to someone they know. 837 patients have been recruited to the study, of which 366 have donated to date (166 UKDs and 200 SKDs). At the time of writing, follow-up data were available for 303 donors (148 UKDs and 155 SKDs) and 89 withdrawn participants. Post-operative data will include hospital stay, complications and data from the CSRI to ascertain the cost-benefit of the UKD programme. Analysis into the extended financial benefits of UKDs participating in the UK Living Kidney Sharing Scheme will also be discussed.

POS735 USABILITY OF AN INTERACTIVE HEALTH TECHNOLOGY FOR KIDNEY LIVING DONORS ASSESSMENT: TOWARDS A STANDARDIZED INFORMED PROCESS

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Background: Providing standardized information about the risks of living kidney donation is crucial. The Finnish web portal Health Village contains the *Kidney hub*, which provides general information about kidney diseases and treatment. In 2019, a personalized *digital care path for kidney living candidates (LD-dcp)* was launched containing information about the donation process and facilitating communication between stakeholders. Our aim was to investigate living donor candidates' experience with the web portal *Kidney hub* and the *LD-dcp*. The secondary aim is to investigate the attitude of living donor candidates to eHealth services.
Methods: A two-part prospective cross-sectional survey study will involve *LDdcp* users. First, surveys will include questions on general demographics, device ownership and purpose of use. Secondly, eHealth literacy will be assessed with the eHeals questionnaire; the platform's ease of use will be assessed with the System Usability Scale; and users´ feedback on the *LD-dcp* will be explored with 6 Likert-scale questions and an open question for qualitative analysis. All users were invited ($N = 117$).
Results: First results show 169,000 *Kidney hub* sessions were initiated, with 146 users/day on average. Mobile devices were the most common method of use (51%) vs desktop users (42%). The *Kidney hub living kidney donation* page was opened 4,212 times. Sixty-one percent of the *LDdcp* users were 40–69 years old (). 94 % of living donor candidates used the *LD-dcp* and 44.4% gave consent to participate. Mean age was 53 YO (range 26–76) and 69 % were women. In all, 88% believed the information was easy to understand; 90% agree on the information being useful, 88% considered they received enough information about the risks on donation, 92% considered the communication with the transplant team was easy. Over 1,900 messages were exchanged. Only 22% considered the LDdcp helped with donation decision making. eHealth literacy was good (eHeals median 30.5; range 18).
Conclusions: We conclude that living donor candidates benefit from the digital care path, received standardized information about the donation process but this digital service did not significantly support decision making.

POS736 LAPDOCTOR: SCORING SYSTEM FOR PREOPERATIVE EVALUATION OF DIFFICULTY OF LAPAROSCOPIC DONOR NEPHRECTOMY. A MULTICENTRE VALIDATION: PRELIMINARY RESULTS

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Background: There are no objective parameters for predicting the difficulty of laparoscopic donor nephrectomy (LDN). We developed LAPDOCTOR, a scoring system that showed accuracy in detecting the preoperative difficulty level of LDN, combing preoperative CT scan parameters with demographic variables. This study has been designed for the prospective multicentre validation of LAPDOCTOR.
Methods: Five Italian transplant centres were involved in this prospective multi-centre national study. The study was started in January 2020, we planned to enroll 120 donors over 12 months. Demographics and CT scan parameters were collected centrally, blinded to the surgical difficulty score to validate the correlation of LAPDOCTOR. We present here the preliminary result of an interim analysis.
Results: Due to the COVID-19 pandemic, the study has suffered delays and 50 donors have been enrolled as of 15 May 2021. Forty-four percent males, mean age 55 $\pm$ 10 yrs, BMI 26 $\pm$ 3 kg/m^2. Ninety-two percent nephrectomy were left, most (42%) hand assisted LDN, no major complications occurred with 100% patient and graft survival. An interim analysis supported a very high correlation between subjective surgical difficulty level and LAPDOCTOR score.
Conclusion: Although during the pandemic, living donor transplant activity was reduced worldwide, impacting study enrollment, our preliminary results support the accuracy of LAPDOCTOR in predicting difficulty of LDN. We have extended donor recruitment in order to reach a powerful sample to statistically validate our score. LAPDOCTOR can be useful in assessing operative risk and possibly reducing LDN morbidity.

POS737 INFLUENCE OF IMMUNOSUPPRESSIVE DRUG TROUGH LEVELS ON NK CELLS IN LIVER TRANSPLANTATION

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Background: Natural killer (NK) cells are enriched in lymphocytes within the liver and are considered to be main regulators of liver transplantation (LT) rejection and tolerance. However, the effects of immunosuppressants on NK cells are not clearly understood. The purpose of this study was to evaluate the impact of trough level conditions in long-term patients on NK cells activation and function.
Methods: Peripheral blood mononuclear cells (PBMC) isolation and flow cytometry : PBMC of LT recipients and healthy individuals (control) were collected by gradient density centrifugation. Flow cytometry was done to analyze the lymphocyte subsets and phenotype of NK cells in vivo.
PBMC culture and flow cytometry:PBMC were exposed to single drugs [Everolimus(EVE), 5ng/ml; Sirolimus(SIR), 5ng/ml; Tacrolimus(TAC), 5ng/ml; Cyclosporine A (CSA), 125ng/ml; Mycophenolate Mofetil (MMF), 15ug/ml; Steroid, 0.5ug/ml], and typical combination drugs [Group 1:TAC, 5ng/ml + MMF, 15ug/ml + Steroid, 0.5ug/ml; Group 2: TAC, 5ng/ml+ SIR, 5ng/ml + Steroid, 0.5ug/ml; Group 3: TAC, 5ng/ml + EVE, 5ng/ml + Steroid, 0.5 ug/ml] for 3 days. Flow cytometry was used for analysis in vitro.
Bulk RNA-Seq of NK cells: NK cells were sorted from PBMC under the same culture conditions, and RNA-Seq was performed analysing genes for transcriptional features of NK cells.
Preliminary Results: This is the first time to use drug plasma concentration simulating the clinical microenvironment in stable liver transplant recipients under in vitro conditions.

1. The function of NK cells was inhibited in calcineurin inhibitors (TAC or CSA) and all combination groups, and calcineurin inhibitors (CSA/TAC) played a major role.
2. Transcriptome sequencing results showed that NK cells were exposed to immunosuppressive agents, their activation decreased, function decreased, proinflammatory activity decreased, and apoptosis increased. The inhibitory effects of the combined drugs were the strongest.
3. Immunosuppressants reduced the number of CD4T, CD8T and NK cells, but did not change the percentage in vivo. For NK cells, the number of CD56dimCD16+/- subgroups were mainly reduced. It was worth noting that NK cells activity increased in LT.

POS738 PRE-TRANSPLANT AFP>25.5 IS ASSOCIATED WITH A HIGHER RISK OF HCC RECURRENCE AFTER LIVER TRANSPLANTATION FOR PATIENTS MEETING MILANO CRITERIA

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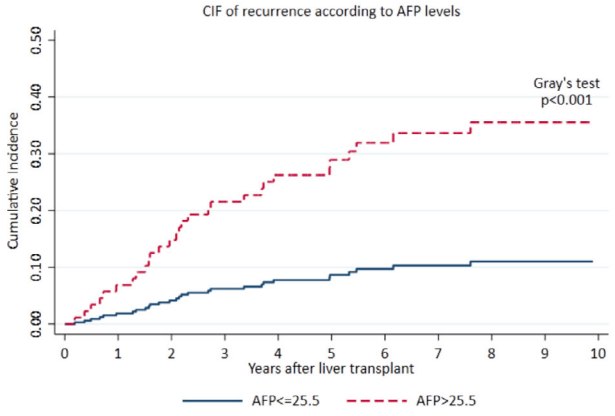
Background and Aims: Hepatocellular carcinoma (HCC) recurrence rates after liver transplantation (LT) range between 8 and 20%. Elevated alpha-fetoprotein (AFP) levels at transplant can predict post-transplant HCC recurrence; however, a clear cut-off value is needed in order to identify patients at higher risk. Our aim was to evaluate possible predictors of HCC recurrence after LT, in a cohort of patients meeting Milano criteria (MC), especially exploring the role of AFP.
Methods: We retrospectively analysed 236 consecutive patients waitlisted for HCC, all meeting Milan criteria, from January 2001 to December 2017 at our liver transplant centre. Twenty-nine patients dropped out while waitlisted, and 207 patients were included in the analysis.
Results were subsequently validated in a cohort of 502 patients also meeting MC who underwent LT at the Cleveland Clinic. All survival analyses included the competing-risk model.
Results: A total of 709 patients participated in the study. Median age was 59.0 (55.0–65.0) years. Eighteen percent were female (n = 130/709). Median MELD at LT was 12 (9–16).
In the development cohort, HCC recurrence rate was 16.4% (n = 34/208), median AFP at LT was 8.4 (3.8, 21.3), 14% (n = 29/207) of patients had MVI (microvascular invasion).
In the validation cohort HCC recurrence was 13.3% (n = 67/502), median AFP at LT was 8.6 (4.2–32.2), 23.4 % (n = 117/502) of patients had MVI. Median AFP levels at transplant were higher in patients with HCC recurrence ($p < 0.001$).
At multivariate analysis AFP value at transplant greater than 25.5 ng/ml (AUC 0.69) was a strong predictor of HCC recurrence after LT [sHR 3.3 (1.6–6.81); $p = 0.001$] and HCC cumulative incidence function (CIF) of recurrence at 10 years from LT was significantly higher in patient with AFP >25.5 ng/ml [34.3% vs. 11.5% ($p = 0.001$)].
Also, microvascular invasion (MVI) was almost significant ($p = 0.063$)
Conclusions: We found that AFP > 25.5 at LT, is a strong predictor of HCC recurrence after LT for patients meeting MC, and we validated it in an international cohort. These data could be used to stratify correctly HCC patients before LT and to improve surveillance after LT, but further studies are needed to validate these results.



*death was considered as competing event

POS739 CAN WE PREDICT INCISIONAL HERNIA AFTER KIDNEY TRANSPLANTATION?

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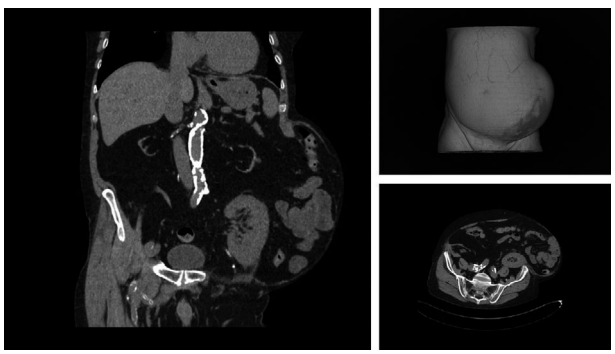
Background: Incisional hernia (IH) after kidney transplantation (KT) affects ca 4–7% of adult patients, Figure. Although IH may cause substantial morbidity, little has been reported on its' risk factors and IH prevention. Recently an app (MobileHernia) for estimating the risk of IH after general abdominal surgery became available (Basta 2019). However, end-stage kidney disease patients are at especially high risk of IH due to uremia and a possibly sarcopenia, neither included as risk factors in the MobileHernia app.
Aim: To create an improved predictive model of IH after KT by combining known risk factors of IH with radiologic analyses of abdominal muscular quality.
Methods: Of 694 adult patients undergoing KT between 2010 and 2017, all 582 recipients receiving a 1st or 2nd kidney transplant only were included. Data on 33 parameters were obtained from the medical records and registries and KDPI/LDKDPI calculated. A logistic regression analysis was conducted and the MobileHernia app used. In a subset of 71 patients, sarcopenia was assessed by preoperative computerized tomography and a case-control subanalysis performed.
Results: IH was diagnosed in 46 patients (7.9%) at a median of 1.6 years after KT. Age at KT (OR 1.56 per 1-SD increase), years in renal replacement therapy before transplantation (RRT) (OR 1.45 per 1-SD increase), female sex (OR 2.0) and deceased donor (OR 3.3) were significant independent factors associated with IH (pseudo R^2 0.15). The sensitivity of this model was higher than that of MobileHernia (13.5% vs 5.8% ($p < 0.001$). When applying a risk threshold of 20%, sensitivity was 15% compared with 0% using MobileHernia. Specificity was 96%, resulting in a number needed to treat of 1:3. In the subanalysis of sarcopenia, patients with IH had significantly lower skeletal muscle mean radiation attenuation (SMRA), median 23.5 HU vs 29.0 HU ($p = 0.02$) implying a higher grade of myosteatosis compared with controls without IH. Skeletal muscle index did not differ between the groups. When SMRA was added to the model in the subanalysis, pseudo R^2 increased to 0.21 and percentage correctly classified increased to 38.5%.
Conclusion: By using a set of clinical predictors including age at KT, time in RRT, gender and SMRA, we believe the risk of IH can be predicted with much higher accuracy than any currently available IH tool.



POS740 PHARMACOKINETIC MODELLING OF DIFFERENT TACROLIMUS FORMULATIONS IN CHILDREN AND ADOLESCENTS

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Background: The Commission on Human Medicines issued advice to healthcare professionals in 2012 that if 'switching a patient to a different brand of oral tacrolimus would be of benefit, the change requires careful supervision and therapeutic monitoring by an appropriate specialist'. The hospital approved the use of Adoport® from April 2019 for paediatric renal transplant recipients. Patients were switched in a planned way.
Methods: Patients taking Prograf® or Modigraf® were identified from planned clinics and contacted by a nurse or pharmacist beforehand to ascertain medicine stocks to minimise waste. Patients were commenced on the same dose of Adoport® and levels were measured between day 2 and 5 (where possible this was organised for their next visit). Data were extracted, retrospectively, from the hospital's electronic health records and uploaded into the digital research environment. Modelling using nlmixr (a R package for population pharmacokinetic/pharmacodynamic modelling (v2.0.4)) was performed to estimate parameters for different formulations.
Results: Seventy-five patients were identified (52 (69%) male; aged 7 - 18 (median 14) years) of whom 48 (64%) and 27 (36%) were taking Prograf® and Modigraf® respectively with 1,025 tacrolimus levels (April 2019 to November 2020) available for modelling. The mean sample time post-dose was 15.5 hour, thus a one compartment first order model was applied with a fixed absorption rate constant (ka 4.5hr^{-1}) taken from the literature. Allometric body weight scaling with fixed exponents of 0.75 for clearance and 1 for volume was applied, and a proportional model used for residual error.

	Number of levels	Parameter estimate	CI Lower	CI Upper	Between subject variability (CV%)
Adoport®	531				
Clearance /F(L hr^{-1})		41.2	40.7	41.7	80.5
Volume /F(L)		500	482	518	33.4
Proportional error		0.140			
Prograf®	328				
Clearance /F (L hr^{-1})		29.4	29.1	29.8	32.4
Volume /F(L)		512	512	513	32.4
Proportional error		0.100			
Modigraf®	166				
Clearance /F(L hr^{-1})		44.4	44.3	44.5	80.5
Volume /F(L)		453	452	454	33.8
Proportional error		0.141			

Conclusions
The estimated values for apparent clearance and volume are similar to those reported elsewhere. The differences in apparent clearance between the formulations, particularly Prograf®, reinforces the need to manage the transition from one formulation to another carefully.

POS741 THE PARADOX EFFECT OF PRE-TRANSPLANT LOCO-REGIONAL THERAPIES ON CANCER-RELATED DEATH AFTER LIVER TRANSPLANTION FOR HCC

Jacopo Lanari[1], Alessandro Vitale[1], Marco Colella[1], Nicola Canitano[1], Chiara DI Renzo[1], Enrico Gringeri[1], Francesco D'amico[1], Domenico Bassi[1], Francesco Enrico D'amico[1], Riccardo Boetto[1], Marina Polacco[1], Alessandra Bertacco[1], Salvatore Piano[2], Martina Gambato[3], Umberto Cillo[1]

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Background: The prognostic impact of loco-regional therapy (LRT) before liver transplantation (LT) on the post-transplant outcome in patients with hepatocellular carcinoma (HCC) remains controversial. We sought to evaluate the relationship between LRT and post-LT competing events at our Center and identify outcome predictors.
Methods: We retrospectively analyzed 325 consecutive patients transplanted for HCC from January 2010 to December 2018 (minimum post-LT follow-up = 24 months) at our liver transplant center. Our center adopts a liberal pre-LT biological selection policy for HCC patients based on aggressive LRT before LT irrespective of morphological criteria. All survival analyses included the competing-risk (CR) model to identify predictors of HCC-related death (competing event: death for other causes).
Results: Median age was 60 years (IQR, 27–72), and 14% of patients were female (n = 45/325). Median MELD at LT was 13 (IQR, 9–18). Median time on waitlist was 6.5 (IQR, 2.7–12.5) months, 238 patients (73.2%) had at least one LRT before LT, 137 (42.2%) more than three LRTs, 174 (54.5%) were Milan out at explant histology, 97 (31.7%) had micro-vascular invasion. HCC recurrence rate was 15.4% (n = 50/325). Median time to HCC-related death was 13.1 (IQR, 8.1–25.5 months). At multivariate cancer-related death CR analysis, LRTs > 3 (HR 2.16, 95% CI 1.09 – 4.29, p = 0.028) and micro-vascular invasion (HR 3.2, 95% CI 1.7–6.0, p = 0.000) were the strongest predictors of HCC-related death after LT (Figure 1a). Conversely, LRTs > 3 vs. LRTs ≤ 3 significantly decreased the risk of post-LT non-HCC-related death (HR 0.87 95% CI 0.76–0.98, p = 0.020) (Figure 1b), while they did not have any impact on overall survival after LT.
Conclusions: Although multiple pre-transplant LRTs may increase the risk of HCC-related death after LT, they have a negligible effect on overall survival after LT. Our results, therefore, strongly support the adoption of aggressive LRT protocols before LT both for HCC downstaging or dropout prevention.

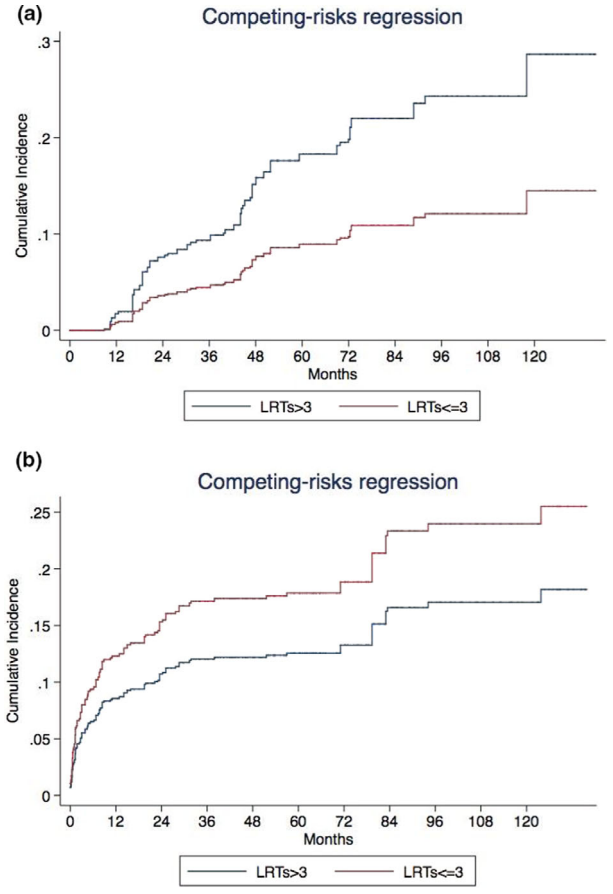

Figure 1: Competing risk post-LT HCC-related (**a**) and non-HCC-related (**b**) death curves comparing patients undergoing LRTs > 3 vs. those undergoing LRTs ≤ 3.

POS742 THE USEFULNESS OF CONTRAST-ENHANCED ULTRASOUND IN PREDICTING THE OUTCOME OF KIDNEY TRANSPLANTS

Giuseppe Ietto[1], Valentina Iori[1], Christian Ossola[2], Mauro Oltolina[1], Federica Masci[1], Caterina Franchi[3], Andrea Vigezzi[1], Natalia Palamara[1], Marta Ripamonti[1], Elisa Ileana Bottazzoli[1], Domenico Iovino[1], Elia Zani[1], Cristiano Parise[1], Aroa Gnesutta[2], Filippo Piacentino[2], Federico Fontana[2], Daniela Dalla Gasperina[4], Matteo Tozzi[5], Giulio Carcano[1]

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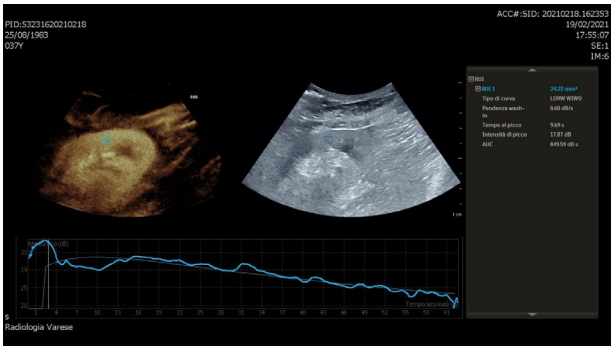
Background and Aims: Renal transplantation is the gold standard treatment for end-stage renal disease. Each transplanted organ has a variable time to resume its function. The delayed graft function (DGF) is an acute kidney injury occurring in the first week after transplantation that requires dialysis, presenting in 20% of the cases. Predicting the outcome of the graft would be the key in optimizing the management of the patients, with tailored immunosuppressive therapies. Our aim was to construct a predictive model of the outcome of the graft using the contrast-enhanced ultrasound (CEUS).
Methods: Conventional two-dimensional and dynamic ultrasound scan was performed with EPIQ ultrasonoscope (Philips Healthcare, Andover, MA) using SonoVue (Bracco Company, Milan, Italy) as contrast agent (a bolus of 1 mL followed by 5 mL of physiologic saline 1 ml) in the immediate post-operative period. The ultrasound dynamic (US) evaluation started at the injection and was conducted for 1 minute. To evaluate renal tissue perfusion, a 10 mm side square region of interest (ROI) was placed on the superior polar renal cortex. QLAB analysis software was used to obtain quantitative analysis of renal tissue perfusion including the time-intensity curve, the slope rate of the ascending curve (A), the time to peak (TTP), the derived peak intensity (DPI) and the area under the curve (AUC).
Results: Thirteen transplanted patients were included in the final analysis. The results revealed that TTP in patients with DGF was significantly later than those with Early Graft Function (EGF). DPI and AUC were lower in the DGF group than EGF group. A patient in whom TTP, DPI and AUC were found to be undetectable, developed primary nonfunction (PNF) and underwent explantation. No correlation between A and the functional recovery of the graft was found.
Conclusions: The CEUS seems to provide an evaluation of the graft's microcirculation, thanks to the micro-bubble diameter of 3–8 μm, allowing to predict its functionality and therefore the outcome.
This preliminary prospective research attempted to explore the application of CEUS on the assessment of transplanted kidney.
With further data, we will obtain a Perfusion Index, that will let us to construct a predictive model of functional recovery, in which stratify transplanted patients to optimize their management.



POS743 A CLINICAL LIFESTYLE DASHBOARD USING ROUTINE CLINICAL CARE DATA TO IMPROVE KIDNEY TRANSPLANTATION CARE

Jip van den Berg[1], Gerjan Navis[1], Simon De Graaff[2], Jan-Stephan Sanders[1], Stefan Berger[1]

[1]UMCG, Kidney transplantation, Groningen, Netherlands; [2]UMCG, Business Intelligence Competence Center, Groningen, Netherlands

Background: Care after kidney transplantation (KT) has broadened its focus on preventing graft rejection with cardiovascular risk management (CVRM). CVRM guidelines combine lifestyle improvement and drug treatment. Systematic monitoring of routine measurements in the electronic health record (EHR) allows for a plan-do-check-act (PDCA) cycle. In the University Medical Center Groningen (NL), a population dashboard (DB) was developed showing lifestyle and CVRM indicators.
Methods: A 6-month CVRM focused PDCA-cycle was started with monthly meetings for feedback, evaluation and discussion of the data, targets and policy along with transparency of individual results. Indicators regarding systolic blood pressure (SBP), LDL cholesterol, HbA1c and body mass index (BMI) were selected by the KT team for this PDCA-cycle. Additionally, medication use, salt intake (SI, <6 g/d) and dietician referral (DR) were included. Indicators are based on KDIGO-guidelines and department policy. The DB shows proportions and numbers per indicator, creates patient reports.
Results: The DB has a dynamic cohort of ± 1700 KT patients. At baseline, SBP, LDL and HbA1c targets were not met for 65%, 56% and 15% of patients, resp. Both under prescription (statins), and unmet lifestyle targets (SI, BMI) contributed. DR for glycaemic control was unexpectedly underutilized (20%). Intermediate process indicators for SBP (130–140 mmHg), SI (>8 g/d) and weight gain (WG>5kg) were added, to better monitor progress towards targets. Follow-up data were virtually unchanged, but compromised by COVID which limited visits and assessments. However, DR for glycaemic control increased to 33%.
Conclusions: PDCA-cycles using the DB will continue, with other indicators and improvement windows per cycle. The next PDCA-cycle will focus on smoking cessation. While providing care, we can unravel care-gaps, explore intervention targets, monitor intervention effectiveness and create practice-based evidence with readily available patient data.

Indicator	Baseline
SBP >140 mmHg	29%
AHT[1]	91%
SI >6/8 g/d	69% / 48%
SBP 130–140 mmHg	36%
AHT	87%
SI >6/8 g/d	75% / 53%
LDL >2.59 mmol/L	56%
Statin	45%
HbA1c >53 mmol/L	15%
BGLD[2]	93%
DR	20%
BMI >30 kg/m^2	25%
Weight gain >5kg	11%

1: Antihypertensive treatment.
2: Blood glucose lowering drugs.
SI: Salt intake; DR: Dietician referral.

POS744 TOWARDS ROUTINE SURVEILLANCE OF KIDNEY ALLOGRAFT REJECTION USING A FULLY AUTOMATED URINARY CXCL9 AND CXCL10 IMMUNOASSAY AND A WEB APPLICATION

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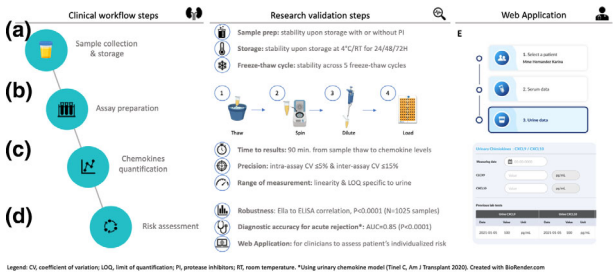
Background: For kidney transplant recipients (KTRs), assessing non-invasively the individualized risk of acute rejection is one of the most unmet need. Urinary chemokines are one of the short-term most promising biomarkers, because of their simple and low-cost analytical method in easily accessible samples, and their high diagnostic performance consistently assessed over the last decade. In this study, we aimed at confronting all practical issues of routine implementation of kidney allograft rejection monitoring using urine CXCL9 and CXCL10 (uCXCL9/10).
Methods: The next-generation immunoassay Ella® (ProteinSimple™) was investigated as feasible quantification platform, from sample collection to render of the results (Figure 1). UCXCL9/10 levels were measured using Ella® microfluidic cartridges, across preanalytical (sample preparation, storage conditions, freeze-thaw cycles) and analytical (linearity, ranges, intra/inter-assay variability) performances studies, and diagnostic accuracy was assessed in comparison with the ELISA reference method, in KTR urine samples from previously published cohorts.
Results: Upon assay preparation, Ella® appeared very efficient with a minimal workflow (urine sample thaw> centrifugation>1:2 dilution>loading) and a time to result of 90 minutes (Fig. 1B). Preanalytical studies showed high stability of uCXCL9/10 levels across various temperatures (4° vs 25°C) and

time (24/48/72H) before storage and over 5 freeze-thaw cycles (Fig. 1A). How complex urine matrix, analytical studies confirmed excellent linearity of dosage, as well as intra-assay (≤5%) and inter-assay precision (≤15%, Fig. 1C). Across 1024 samples, Ella® results were highly correlated with those quantified by ELISA ($p < 0.0001$), and further entered into our previously validated urine chemokine model. 268 out of the 1024 samples were collected at time of acute rejection (26.2%). In this cohort, accuracy was 0.85 for acute rejection diagnosis (Fig. 1D).
Conclusion: Ella® fulfils all prerequisites for clinical implementation of urinary chemokines monitoring. It has proven a robust, easy-to-use platform with unprecedented validation to quantify urine chemokines. A Web Application is made available to clinicians to use uCXCL9/10 for routine surveillance of KTR's acute rejection risk (Fig. 1E).

Figure 1. Assessment of kidney allograft acute rejection risk using Ella quantification or urine chemokines



Legend: CV, coefficient of variation; LOQ, limit of quantification; PI, protease inhibitors; RT, room temperature. *Using urinary chemokine model (Tinel C, Am J Transplant 2020). Created with BioRender.com

POS746 OUTCOMES OF AKI IN RENAL TRANSPLANT RECIPIENTS WITH COVID-19 INFECTION: A TRAINEE-LED, MULTICENTRE, INTERNATIONAL REGISTRY STUDY

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Background & Aims: SARS-CoV-2 (COVID-19) emerged in China in late 2019 and rapidly spread throughout the world. Whilst most patients with COVID-19 infection develop a mild syndrome, a subset progress to multi-organ failure and death. Conflicting data have emerged about the relative risk of complications and mortality in immunosuppressed populations.
We initiated a trainee-led, multicentre, international collaboration to create a granular registry of patients on haemodialysis or with a renal transplant who develop COVID-19 infection, with the aim of identifying clinical and immunological features associated with outcome worldwide
Methods: Laboratory-confirmed cases of COVID-19 infection with a functioning renal transplant or receiving dialysis at diagnosis were prospectively entered into an online database by local teams, commencing May 2020. AKI was identified in transplant recipients with full renal function data available as per the AKIN staging system and grouped as a binary variable for analysis. Transplant recipients with renal function data were compared with patients on haemodialysis (HD) and peritoneal dialysis (PD) with COVID-19 infection for outcomes including mortality during the course of disease and length of stay, if admitted to hospital. Immunosuppression reduction was classed as a reduction or omission of any immunosuppressive medication during the first 14 days of admission.
Results: 509 records were analysed from a total of 21 centres in 8 countries on 4 continents. 133 had a functioning renal transplant and 92 had renal function data available. The demographics of cohorts are shown (Table 1).

Table 1: Cohort demographics	Tx, No AKI (n=58)	Tx, AKI (n=34)	HD (n=287)	PD (n=11)
Male Sex	40 (69)	23 (68)	173 (60)	6 (55)
Median (IQR) Age	56 (45 – 60)*	56 (48 - 65)*	69 (55 – 78)*	54 (42 – 69)*
Caucasian Ethnicity	38 (66)	21 (62)	196 (68)	5 (46)
Median (IQR) years since transplant	7 (2 – 12)	4 (1 – 10)	N/A	N/A
Immunosuppression at diagnosis:				
Calcineurin inhibitor	52 (90)	31 (91)	N/A	N/A
Antimetabolite	51 (88)	26 (77)		
Steroids	42 (72)	26 (77)		
mTOR inhibitor	5 (9)	0		
Median (IQR) baseline creatinine (μmol/L)	140 (102 – 180)	146 (102 – 207)	N/A	N/A
Median (IQR) peak creatinine (μmol/L)	147 (121 – 204)*	403 (195 – 600)*	N/A	N/A
Death	6 (10)*	12 (35)*	69 (24)*	3 (27)*
Any reduction in immunosuppression within 14 days	31 (53)	22 (65)	N/A	N/A
Median (IQR) length of stay in survivors (days)	12 (6 – 30)	16 (8 – 49)	12 (8 – 18)	7 (4 – 17)

* p<0.05 by Mann-Witney, Kruskal-Wallis or chi-squared test

Transplant patients with and without AKI were similar in age, ethnicity, baseline immunosuppression and renal function. 15 (44%) of transplant recipients required renal replacement therapy during the course of their infection.
Transplant AKI was associated with the highest risk of death, despite younger age versus dialysis cohorts. Furthermore, there was a trend towards longest length of stay in transplanted survivors of AKI, longer than dialysis controls ($p = 0.08$).
We conclude that AKI during COVID infection in transplant recipients confers a higher risk of mortality than COVID infection in end-stage renal failure and is associated with a longer length of stay in survivors.

POS747 PREDICTORS OF OUTCOMES IN COVID-19 POSITIVE ABDOMINAL ORGAN TRANSPLANT

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Background: Between March 2020 and February 2021, we identified 108 liver transplant recipients and 123 kidney transplant recipients with PCR confirmed COVID-19. The purpose of this abstract was to review the outcomes of COVID-19 infection and identify the predictors of hospitalization and death.
Methods: Thirty-four patients were treated with anti-COVID mAb therapy (Bamlivimab) and their outcomes were compared to potentially eligible patients (diagnosed >24 hours prior to hospitalization). We then performed Logistic regression analysis to identify patient characteristics associated with hospitalization and death on the patients who did not receive mAb therapy.
Results: 44% of our kidney transplant patients and 33% of our liver transplant patients were hospitalized. 22% for our kidney patients and 10% of our liver patients died. mAB therapy was able to reduce hospitalization from 29% to 9% ($p = 0.01$) and deaths from 13% to 0% $p = 0.04$). Table 1 shows the patient characteristics associated with hospitalization or death. For kidney transplant recipients, Age and DM proved to be important predictors of poor outcomes (OR 3.67 and 2.62). For liver transplant recipients, DM and

renal failure were the most important predictors (OR 2.73 and 2.63). Thymoglobulin induction, obesity, CAD, and recent transplantation did not significantly influence outcomes in this study. Hispanic ethnicity lead to a greater risk of infection (82% of cases vs 58% of patients transplanted) but Hispanic patients trended towards better outcomes when infected.
Conclusions: Early Bamlivimab therapy proved to be effective in preventing poor outcomes. Our study reveals Age, DM, and Renal failure as strong predictors of poor outcomes. Although limited by sample size, thymoglobulin induction, obesity, CAD and recent transplantation did not portend worse outcomes. In the general population of Los Angeles, Hispanic ethnicity was a risk factor for infection, hospitalization, and death. However, in high-risk medical patients with access to care, Hispanic ethnicity was not associated with worse outcomes.

Kidney Transplant Recipients						
		N (%)	Univariable OR (95% CI)	p-value	Multivariable OR (95% CI)	p-value
Age	< 65 ≥ 65	74 (73) 28 (27)	1 3.67 (1.47-9.87)	0.007	1 2.60 (0.96-7.45)	0.07
Ethnicity	Non-Hispanic Hispanic	18 (18) 84 (82)	1 0.73 (0.25-2.02)	0.54		
DM	No Yes	57 (56) 45 (44)	1 2.62(1.18-5.95)	0.019	1 2.18 (0.90-5.35)	0.08
CAD	No Yes	95 (93) 7 (7)	1 2.78 (0.57-0.07)	0.24		
Induction	Thymo Simulect	65 (65) 35 (35)	1 1.66 (0.73-3.84)	0.23	1 1.96 (0.79-5.03)	0.15
BMI	< 30 ≥ 30	77 (75) 25 (25)	1 0.95 (0.38-2.35)	0.91		
Time from transplant	< 1 year ≥ 1 year	21 (21) 81 (79)	1 2.26 (0.85-6.52)	0.11	1 2.30 (0.78-7.43)	0.14
Liver Transplant Recipients (including combined liver/kidney)						
		N (%)	Univariable OR (95% CI)	p-value	Multivariable OR (95% CI)	p-value
Age	< 65 ≥ 65	57 (65) 31 (35)	1 0.96 (0.36-2.49)	0.94		
Ethnicity	Non-Hispanic Hispanic	18 (20) 70 (80)	1 0.43 (0.15-1.29)	0.13	1 0.37 (0.12-1.15)	0.08
DM	No Yes	42 (48) 46 (52)	1 2.73 (1.06-7.54)	0.043	1 3.02 (1.13-8.76)	0.033
CAD	No Yes	85 (97) 3 (3)	1 1.20 (0.05-13.08)	0.88		
BMI	< 30 ≥ 30	52 (59) 36 (41)	1 1.36 (0.53-3.44)	0.52		
Renal Failure (Cr>2.0)	No Yes	80 (91) 8 (9)	1 2.63 (0.58-12.05)	0.20	1 3.25 (0.68-16.03)	0.13
Time from transplant	< 1 year ≥ 1 year	23 (26) 65 (74)	1 0.94 (0.34-2.79)	0.91		

POS748 HEART TRANSPLANTATION FROM CONTROLLED DONATION AFTER THE CIRCULATORY DETERMINATION OF DEATH USING THORACO-ABOMINAL NORMOTHERMIC REGIONAL PERFUSION.

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Background: Heart transplantation is currently the most effective treatment to improve the prognosis of patients with end-stage heart failure. In recent years, donation after circulatory death (cDCD) with regional normothermic thoracoabdominal perfusion (TA-NRP) has been developed in Spain. We present the initial experiences in heart transplantation from cDCD donors with TA-NRP at the Hospital Virgen de la Arrixaca in Murcia.
Methods: cDCD was considered in patients under 55 years of age admitted to the ICU in whom the medical team and legal representatives had made the decision for withdrawal of life support therapy (WLST) and the donation was accepted. The evaluation was performed as usually. Donor heart monitoring was performed using a Swan-Ganz catheter and continuous transesophageal echocardiography (TEE). Brain activity was monitored using the bispectral index. After declaration of death (5 minutes no touch), the 3 aortic arch vessels were clamped to exclude cerebral flow. Simultaneously, the patient was intubated and mechanical ventilation was initiated. The values of troponin I and lactate were monitored during the whole procedure.
Results: Three procedures were performed. In all cases, the heart reverted to sinus rhythm within 1 minute. Dobutamine infusion was started in one of the donors; the left ventricular ejection fraction and the cardiac index at the time of validation was optimal. Three heart transplantation were performed to local recipients with an excellent outcome. None of them required mechanical support after transplantation. All recipients had a short ICU stay and were discharged home with an excellent evolution and optimal cardiac index.
Conclusions: Transplantation from cDCD donors represents an important source of grafts in countries with an adequate legal framework. TA-NRP may become a way to make cDCD donor heart transplantation feasible, reducing the costs of ex situ machine devices by making this procedure economically affordable.

Table 1. Donor characteristics and key features of TA-NRP.

	Donor 1	Donor 2	Donor 3
Age (years)	43	28	55
Gender	M	F	M
FWIT (min)	8	13	11
Knife to skin to onset TA-NRP (min)	3	5	5
Time to restoration of spontaneous sinus rhythm after TA-NRP (min)	1	1	1
TA-NRP duration (min)	99	23	107
TA-NRP > 1L duration (min)	24	13	22
Dobutamine	No	Yes	No
Noradrenaline	No	No	No
Left ventricular EF% at validation	74	60	54
Left ventricular EF% at 60 minutes	70	60	60
CI at validation	3,6	3,4	3,4

F: female; M: male; WLST: withdrawal of life sustainina therapy;FWIT: functional warm ischemic time; TA-NPR: thoraco-abominal normothemic regional perfusion; capillary wedge pressure; EF: eyection fraction; CI: cardiac index

POS749 TRANSFORMING GROWTH FACTOR BETA 1 GENE POLYMORPHISM IN PEDIATRIC LIVER RECIPIENTS

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Background: Transforming growth factor β1 (TGF-β1), a pleiotropic cytokine with profibrogenic and immunosuppressive activities, may have an impact on graft function after liver transplantation (LT). It has been shown that TGF-β1 blood level correlates with hepatic fibrosis severity and tacrolimus dose requirements in pediatric recipients after living donor LT. But the causality of differences in TGF-β1 level is not clear. The aim was to evaluate the impact of three types of TGFB1 gene polymorphism on TGF-β1 blood level and outcome after LT in pediatric recipients.
Materials: 103 pediatric liver recipients (49 boys) aged 3–73 (median - 8) months and 43 healthy liver donors aged 36 ± 12 years (16 men) were included. Single nucleotide polymorphism (SNP) of TGFB1 gene (rs1800469, rs1800470 and rs1800471) was studied by TaqMan SNP genotyping assays. TGF-β1 concentration was measured by ELISA.
Results: The transplanted patients had next frequencies of the investigated alleles: rs1800469 - 22% AA homozygotes, 33% AG heterozygotes, and 45% GG homozygotes; rs1800470 – 77% AA, 15% AG, 8% GG; rs1800471 – 0% GG, 11% GC, 89% CC. The SNPs frequencies in the donors had next profile: rs1800469 - 14% AA, 37% AG and 49% GG; rs1800470 - 94% AA, 5% AG and 0% GG, and rs1800471 – 0% GG, 3% GC, 97% CC. There was deviation from Hardy-Weinberg equilibrium in distribution of SNPs rs1800469 and rs1800470 in pediatric liver recipients. In healthy liver donors, all the investigated SNPs were in Hardy-Weinberg equilibrium. For rs1800470, G allele frequency differed between the recipient`s and the control group (odds ratio = 6.55, C.I. [1.49–28.86], $p = 0.005$). Association study between the TGFB1 polymorphism and TGF-β1 blood level, pre- and post-transplant clinical parameters (gender, PELD score, liver disease etiology, removed liver fibrosis grade, development of rejection, different complications, dysfunction and mortality) revealed the significant association of rs1800470 AG genotype with development of infection complications in the recipients (odds ratio = 4.53, C.I. [0.94–21.908], $p = 0.048$); no other associations were found.
Conclusions: AG genotype rs1800470 in TGFB1 gene may be associated with predisposition to development of infection complications in pediatric liver recipients. More cases should be investigated to prove the finding.

POS750 COMPARING PHYSICAL AND PSYCHOSOCIAL OUTCOMES IN UNSPECIFIED VS. SPECIFIED KIDNEY DONORS AT 3 MONTHS AFTER DONATION: RESULTS FROM THE UK BOUND STUDY

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Background: The BOUnD study is a national study conducted in the UK with the aim of assessing different components of Unspecified Kidney Donation (UKD). This includes a comparison of physical and psychosocial outcomes between Unspecified Kidney Donors (UKDs) and Specified Kidney Donors (SKDs), and between donors and those who do not complete the donation process.
Methods: Individuals presenting as potential living kidney donors to each of the 23 UK kidney transplant centres were consented to take part in a longitudinal prospective questionnaire study. The questionnaire comprised purposefully designed and validated questions specific to the donation process, and well established validated psychosocial outcome measures (including, amongst others, the General Anxiety Disorder-7 and the Perceived Health Questionnaire-9). All participants completed a questionnaire at the beginning of the donation process.
For donors, a second questionnaire was administered 2–4 weeks pre-operatively. Post-operative questionnaires were completed at 3 and 12 months. Physical outcomes were measured with the physical component of the Short-form 12 and clinical data. For those who withdrew or were withdrawn from the process by the clinical team, a questionnaire was completed at the time of withdrawal and at 3 and 12 months.
Preliminary Results: This study is the world's largest study comparing physical and psychosocial outcomes between UKDs and SKDs, incorporating 837 patients. Of these, 366 have donated to date (166 UKDs and 200 SKDs). At the time of writing, follow-up data were available for 303 donors (148 UKDs and 155 SKDs) and 89 withdrawn participants.
We will present comparison data between UKDs and SKDs, including demographics and predictors of donation status. Post-operative outcomes will be compared between UKDs and SKDs, and with those withdrawn from the process to ascertain whether there is a psychosocial sequalae from not proceeding with donation.

POS751 COMPLICATIONS FROM URETER-BLADDER ANASTOMOSES DURING RENAL TRANSPLANTATION MSO-SPACERUN:YES'> IN RENAL TRANSPLANT RECIPIENTS

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Introduction: Urinary tract complications still remain the most common surgical problem following renal transplantation(9%). These include obstruction, urinary leak and reflux, and the outcome is very important for the graft survival.
Aim: Our purpose was to estimate retrospectively, the incidence of ureter and ureter-bladder anastomoses complications in a Renal Transplant Unit of a General Hospital.
Method: This retrospective study includes 225 consecutive renal transplants using the same technique for anastomoses , from January 2011 to December 2020. An anastomotic stent and percutaneous drainage were used in all patients. An ultrasound scan was performed on the first postoperative day, and a baseline nuclear scan was performed 7 days postoperatively, to investigate whether an acute tubular necrosis or rejection was present. We tried to associate complications with the following risk factors: gender, age, virological profile, type of transplantation (live or cadaveric) and donor's characteristics.
Results: Of 225 renal transplant recipients, 15 presented with urinary complications, (6.7%).These included anastomotic stricture (46.7%), obstruction (13.3%), angulation (13.3%) and ureter ischemia in 6.7% of patients. More than half of complications (53.3%) concerned the distal part of the ureter. The majority of patients presented with increased blood creatinine and urea and nephrostomy and pigtail insertion were performed. Nine of 15 underwent surgery with neoureterocystostomy in 8 and a Boari flap in one patient. Two patients (13.3%) died from sepsis.
Conclusion: Although renal transplantation is the only treatment for end stage renal disease, the ureter-bladder anastomosis remains the "Achilles Heel" of this procedure.

POS752 FACTORS INFLUENCING ACCESS TO KIDNEY TRANSPLANTATION (FIAT): FIRST RESULTS OF STAKEHOLDERS' PERSPECTIVE

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Background: Kidney transplantation is considered the optimal form of renal replacement therapy. However, in the Netherlands, roughly sixty percent of patients on dialysis are not considered for transplantation, which is difficult to explain based on basic medical variables only. Various (non-) medical barriers to optimal access to transplantation have been mentioned in literature. Remarkably, no systematic inventory exists on these multiple (non-) medical barriers and the different perspectives on these barriers by these multiple stakeholders' perspectives. The present qualitative study presents the various (non-)medical barriers to optimal access to transplantation.
Methods: Participants are interviewed about their perceptions, opinions and attitudes on access to kidney transplantation nationwide. The topic list for the interviews contains the following domains: clinical, psychological, ethical, social, economic and policy regarding the access to kidney transplantation.
Results: We have interviewed 117 stakeholders from different organizations/sites; patients (21), donors (10), social workers (25), nephrologists (22), surgeons (5), nurses (6), policy employees (24) and insurance representatives (4). In general, the results show that kidney transplantation is not equally accessible for all patients with the following major six underlying factors as arguments:
1. Psychological: There is a small group of patients with strong motivations for staying on dialysis and a small group which fear transplantation.
2. Policy-based: The perceived lack of or unclarity regarding guidelines hampers equal access.
3. Medical: The missing of uniform eligibility criteria for transplantation mostly on age, BMI and/or comorbidity.
4. Social: There is a lack of specific support for patients with language and/or cognitive difficulties.
5. Economical: Various purchasing criteria are used by insurers. The economic incentives are more favorable for dialysis treatment compared to transplantation.

Conclusion: The results indicate room for improvement over different factors for a more equal access to transplantation. Follow-up research is currently being conducted, which is aimed at reporting on solutions for barriers and implementation strategies for facilitating factors.

POS753 OPINIONS ON COVID-19 VACCINATION IN TRANSPLANTATION: RESULTS OF A NATIONAL SURVEY

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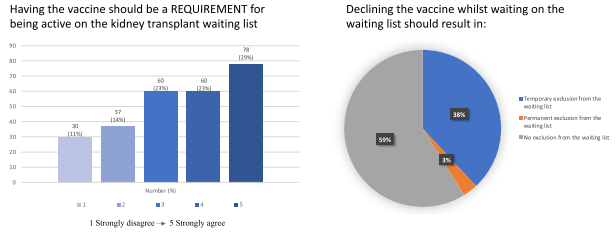
Background: COVID-19 has had a significant impact on renal transplantation activity in the UK, with suspension of programmes in most transplant centres at some point in the pandemic. The UK national vaccination strategy has prioritised elderly and clinically vulnerable patients as well as healthcare staff. Lower vaccination uptake has been observed in some ethnic minority and younger patient groups; however, limited data are available on vaccine hesitancy within professional groups. The aim of this study was to gauge the opinion of transplant professionals on the implications of both staff and transplant candidates' vaccination status.
Methods: We created an online survey, incorporating questions on staff vaccination and management of vaccination in waitlisted patients and access to transplantation. This was approved and circulated by the British Transplant Society as well as via national trainee societies. Data collected

include respondents' professional background, demographics and vaccination status. Views on factors affecting vaccine uptake and implications were assessed by agreement with statements, stratified using a Likert scale.
Results: 265 survey responses were received, with representation from transplant nurses, pharmacists, histocompatibility, physicians and surgeons. 96% of respondents had accepted a vaccination and 88% are affiliated with a transplant centre that had to close temporarily during the pandemic. 29% of respondents strongly agreed that vaccination should be a requirement for waitlisted patients and 38% felt that declining the vaccine should result in temporary exclusion from the waitlist (Figure 1). Sub-group analyses by professional group were performed to delineate differences in opinions on vaccination management and implications.
Conclusion: This study presents the first national assessment of views on vaccination management within the UK transplant community. Professional opinions and behaviours may have an impact on supporting and influencing patients' views. A UK-based ethical framework has been established, supporting patient-tailored solutions for those declining vaccination following a documented risk -benefit discussion with each patient.

Figure 1: Views on implications of patients' vaccination status.



POS754 NEOPLASTIC LESIONS IN TRANSPLANTED PATIENTS: THE CANCER GENESIS

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Background and Aims: The cancer stem cell hypothesis model states that this subset of tumor cells drive tumor initation, progression, and recurrence. Moreover, the clonal evolution model states that a normal cell becomes neoplastic due to an irreversible genetic change or an heritable epigenetic change, giving rise to a neoplastic cell clone. Anyway, tumors originate from a single cell that has acquired multiple mutations and gained unlimited proliferative potential. Information concerning the hierarchy of tumor cells might be derived from data available on tumors developed in transplanted patients, who are chimera subjects. The paternity of tumor in transplanted recipient could be useful to detect the earliest stages of tumorigenesis to prevent the disease and identify new targets therapies.
Methods: We performed a systematic review of literature on topics concerning Circulating Stem Cells (CSCs) and Circulating Tumor Cells (CTCs), to select the most recent markers of CTCs and stemness, with meta-analysis regarding the prognostic value of their detection and title compared with conventional staging. We performed an histopathological re-examination of available surgical specimens and checked the presence of CTCs and CSCs and their parental origin: donor vs recipient.
Results: We analyzed 462 patients who underwent kidney transplantation between 2010 and 2020. Among these, 28, 6%, developed malignancy (20 men and 8 women), with an approximately 3-fold increased risk of developing cancer compared with general population.
Genetic analysis to verify donor-derived forms is still in process. However, one patient developed a highly aggressive, disseminated anaplastic tumor form a few months after surgery. Afterwards, other recipients developed this type of neoplasm.
Conclusions: The rising incidence of malignancies in the transplant population is encouraging the study of the cancer development process. The case we found of disseminated tumor might be useful for the study of the metastatic phenomenon of cancer: it is plausible that the metastatic process is an early event of the carcinogenic process and not a late process. We believe that it could be easier and effortless trace the hierarchical pyramid of carcinogenicity starting from a chimera patient such as the transplanted one.

POS755 NON-HLA ANTIBODY STUDY IN ANTIBODY-MEDIATED REJECTION IN A SPANISH MULTICENTER COHORT

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Background and Aims: Anti-human leukocyte antigen (HLA) antibodies (Abs) explain the majority of antibody-mediated rejection (ABMR), still, poor graft outcomes are reported in the absence of donor-specific anti-HLA Abs (DSA). This suggests that allograft rejection could be produced by another kind of Abs. The non-HLA Abs are acquiring more significance in the role of solid organ rejection but their mechanism remains unclear. We aimed to study the presence of anti-non-HLA Abs prior to transplantation in order to assess its potential involvement in ABMR.
Methods: We evaluated serum samples selected from a multicenter cohort (InmHuForum) of 1,024 kidney transplant recipients. A total of 28 patients developed ABMR without DSA. Another two groups of patients matched by center and follow-up were recruited and divided regarding their sensitization status prior to transplantation (sensitized, $n = 15$; non-sensitized, $n = 13$). A panel of several non-HLA antigens was determined in pre-transplant samples using One lambda LABScreen-autoantibodies following manufacturer instructions and acquihired using Luminex® 200 platform. For results interpretation 95% cut-off was used in HLA Fusion Research 6.3.
Results: The frequency of Abs against Regenerating islet-derived protein 3 alpha (REG3A) was increased in ABMR patients previous to transplantation compared with non-sensitized (51.72% vs 7.69%, $p = 0.007$). Similarly, anti-REG3A Abs were also increased in a sensitized group compared with the non-sensitized (46.67% vs 7.69%, $p = 0.022$).
Conclusions: It has been described that higher serum levels of REG3A have been correlated with compromised renal function and in simultaneous pancreas-kidney transplantation with histological rejection. In this work, we found anti-REG3A Abs in both sensitized and ABMR groups suggesting a potential role of a previous graft in their development. Larger prospective studies should be addressed to confirm the potential role of anti-REG3A in ABMR.

POS756 THE SMALL-MOLECULE BCL6-INHIBITOR 79-6 SUPPRESSES FOLLICULAR T HELPER CELL DIFFERENTIATION AND PLASMA BLAST FORMATION

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Background: Current immunosuppressive treatments insufficiently control humoral B cell-mediated immune responses. The humoral response is dependent on the specialized help function of follicular T helper (TfH) cells that express the transcription factor BCL6 We investigated whether targeting transcription factor BCL6, inhibits B cell responses *in vitro*. Here we tested the effects of 79-6, a small molecule BCL6 inhibitor on T and B cell proliferation and differentiation.
Methods: First, we determined the effect of 79-6 on Tfh cell differentiation. For this, isolated naïve CD4 helper T cells were stimulated with anti-CD3/28 and IL-12 and IL-21. Next, to examine the effects of 79-6 on B cell differentiation, naïve B cells were stimulated with anti-IgM/anti-CD40 and IL-21 in the presence of 79-6. To study its effect on T-B cell crosstalk we co-cultured FACS-sorted CXCR5+ T cells and memory B cells that were stimulated with alloantigen and studied plasmablast formation.
Results: In the mixed lymphocyte reaction, a dose dependent inhibition of T and B cell proliferation was found, in the presence of 100 μg/ml of 79-6 (median inhibition: 53% and 54%, respectively). This dose also suppressed differentiation of naïve T helper cell into "TfH-like" cells under polyclonally stimulated conditions (median inhibition: 57%). In addition, we found that 76-9 significantly affected B cell proliferation, and differentiation i.e., B cell class switching and plasmablast formation (median inhibition: 52%, 22%, and 77%, respectively).
A similar pattern was found under allogeneic stimulation conditions. In the presence of 79-6 the TfH - B cell culture response was significantly inhibited, resulting in a >50% decrease of B cells and formed plasma blasts.

Conclusion: Targeting BCL6 transcription with 79-6 inhibits the differentiation of T and B cells towards TfH cells and plasmablasts, respectively. This compound has promise as a therapeutic agent to control the humoral alloimmune response.

POS757 A SINGLE-CENTRE ANALYSIS OF ELDERLY (≥70 YEARS) DONATION AFTER CIRCULATORY DEATH (DCD) KIDNEY TRANSPLANT OUTCOMES

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Background: The growing demand for organs for kidney transplantation has led to an increase in the use of marginal donors, including from donation after circulatory death (DCD) and elderly donors; however, outcomes are conflicting. We aim to determine the outcomes of utilising DCD kidney donors over the age of 70 years and aim to compare with non-elderly (<70 years) DCD kidneys utilised at a single centre.
Methods: This is a retrospective analysis of kidney transplant recipients who received a DCD kidney from a donor over the age of 70 years between 2012–2020 at a single centre and compared with DCD donors <70 years. Outcomes included 12 and 60 month patient survival, graft survival and transplant survival. Secondary outcomes include graft function and 30-day complications.
Preliminary Results: There were 71 patients who received a graft from a DCD donor over the age of 70 years, with a median donor age of 73 years. The median recipient age was 67 years. There were 38 recipients (53.5%) who received a single DCD kidney, and 33 (46.5%) received dual DCD kidney grafts. The median follow up was 102 months. Patient survival at 12 and 60 months was 95.7% and 79.1%, respectively. Graft survival at 12 and 60 months was 93.9% and 92.3% respectively, and transplant survival (censored for death and graft failure) at 12 and 60 months was 94.3% and 75.1%, respectively. There were two perioperative deaths. Primary non function (PNF) occurred in 1 (1.4%) recipient, 31 (43.7%) had delayed graft function and the median 1 year creatinine was 150uM. One recipient (1.5%) suffered rejection at 90 days. There was no difference in patient or graft survival for those who received a dual or single DCD kidney donors.

POS758 FAMILY BEREAVEMENT AND ORGAN DONATION. A PROSPECTIVE LONGITUDINAL OBSERVATIONAL STUDY

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Background and Aims: The procurement of deceased organs in Spain is governed by a presumed consent model in which the family of the deceased is systematically asked for their authorisation to obtain organs (Caballero & Matesanz, 2015). Decision-making in organ donation is a complex situation that can lead to complex emotional responses in family members and, in some cases, important consequences for their health, both in the short and long term. It is necessary to study the emotional process they go through and how the experience affects their grief. We propose a longitudinal multicentre study to evaluate the experience of the organ donation process and its impact on the bereavement of the families of patients diagnosed as brain dead or candidates for asystole donation.
Methods: Three groups will be established: relatives who authorise procurement (G1), relatives who refuse procurement (G2), relatives who are not offered the option of donation (relatives of patients rejected as candidates for donation) (G3). For this purpose, at least one family member of all critical care patients meeting the inclusion criteria will be recruited. Bereavement characteristics will be specifically assessed with respect to the following indicators: complicated grief (using Complicated Grief Inventory), anxiety (using State-Trait Anxiety Questionnaire), post-traumatic stress (using Revised Stress Impact Scale), depression (using Beck Depression Inventory), resilience (using Connor-Davidson Resilience Scale) and personal growth (using Post-Traumatic Growth Inventory). In addition, the lived experience will be explored through a semi-structured interview with open-ended and closed-ended questions that will be qualitatively assessed.
Preliminary results will be presented in the oral presentation.

POS759 MODELING ACUTE REJECTION USING PRECISION-CUT LUNG SLICES

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Background: Despite great advances made in lung transplantation, patient outcomes are still hampered by high rates of acute lung allograft dysfunction. The complexity of the molecular and cellular mechanisms governing acute cellular rejection (ACR) have meant there is yet much to learn about this significant complication of transplantation. Resultantly, there is great interest in the potential of *ex vivo* models to create a framework in which to study these disease processes. Precision-cut lung slices (PCLS) have historically been employed in toxicological studies and more recently in the research of chronic diseases such as chronic obstructive pulmonary disease (COPD).This tool of culturing lung tissue cut to specific dimensions preserves the architecture of the native lung while maintaining the populations of resident cells, including alveolar type I and II cells. PCLS also allows for the generation of many tissue punches from the lung which enables the study of many parameters and assays within a single individual, eschewing many of the logistical concerns facing *in vivo* work.
Methods: PCLS in this study were generated from lung tissue from healthy pigs (n = 11). Here, we describe the administration of exogenous peripheral blood mononuclear cells (PBMCs) both intravascularly and intrabronchially within PCLS. 10 x10^6 PBMCs were isolated from the recipient itself (control) or from a blood type-matched donor (transplant environment) and then added to 50 mL of agarose to fill the lung. Tissue was also filled with just agarose as a healthy control. Filled tissue was cut using a vibratome generating punches 4mm in diameter with a thickness of 500 um and kept in culture and observed over a period of 10 days.
Results: These experiments aim to recreate the conditions that facilitate acute rejection to note the resulting histopathology. Labelled PBMCs were visible in the punches throughout observation and the tissue was imaged using both confocal microscopy and H&E staining. The lung tissue was noted to be metabolically active at days 1, 2, 5, and 10.
Conclusions: The results suggest that PCLS can be considered for the development of an *ex vivo* model to predict acute rejection and that the technique has potential to be applied to human donor lungs with recipient PBMCs prior to transplantation to predict the occurrence of rejection.

POS760 IMMUNOSUPPRESSION MANAGEMENT OF 25 KIDNEY-TRANSPLANTED PATIENTS AFFECTED BY COVID-19, A MULTICENTRE PROSPECTIVE STUDY.

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Background and Aims: The risk of developing a serious SARS-CoV-2 infection in transplant recipients seems to be higher.
Methods: A prospective multicentre study focusing on the IS management, graft and survival of kidney transplant (KT) recipients affected by COVID-19.
Results: 25 KT recipients enrolled, 3 from living-donor, 17 males (68%), with a median age of 58.5 years (36–76). Median BMI was 26 (17–31) and most patients with systemic hypertension (84%). Median time from transplantation to the molecular diagnosis of COVID-19 was 2 years (0–17).
Induction therapy at transplantation was Simulect (76%), Thymoglobulin (8%) and 4 patients did not receive any induction therapy (16%). As maintenance therapy all patients were treated with calcineurin-inhibitors (CNI), 23 with antimetabolites (ADs) (92%) and 22 with steroids (88%). 13 patients (52%) required hospitalization and 9 of them invasive mechanical ventilation (36%). 9 patients reduced Ads (36%), 6 stopped it (24%), and 5 reduced CNI (20%).
None acute renal injury was observed nor any patients required replacement renal treatment. 7 patients died for SARS-CoV-2 infection (28%), all with a functioning graft. Between dead and alive, no difference was observed in time from transplantation to infection nor in baseline IS (p ns); a significant difference in BMI, 30.7±4.2 vs 25.3± 5.1 respectively (p 0.0203).
Conclusions: In this limited cohort of KT recipients, SARS-CoV-2 infection did not affect graft functioning; however, immunosuppressed patients have higher risk of hospitalization, invasive respiratory support and mortality than general population (52%vs5.3%, 36%vs0.5% and 28% vs 3.4% respectively), still BMI negatively affect patient survival. The management of KT recipient was mainly based on reduction or withdrawal of ADs (80% of

cases). Further studies are needed to clarify the role of kidney transplant and immunosuppressive therapy in defining SARS-CoV-2 infection severity.

POS761 EVEROLIMUS IN HEART RECIPIENTS FOR PROTECTING RENAL FAILURE: A SINGLE-CENTER RUSSIAN EXPERIENCE

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Introduction: In the last decade, everolimus use in immunosuppressive regimens after heart transplantation aimed at the preservation of post-transplant renal function that potentially improves long-term heart transplantation (HTx) outcomes.
Objectives: The study was aimed to compare renal function in HTx recipients receiving everolimus and reduced dose CNIs to compared HTx recipients who continued to take mycophenolate mofetil and therapeutic dose CNIs.
Methods: In a retrospective cohort of 577 HTx recipients, we compared 29 patients who take everolimus and reduced dose CNIs (group 1) with 548 patients who take CNIs and mycophenolate mofetil (group 2) who underwent heart transplantation from January, 2013 to December, 2018. Conversion to everolimus was carried out no earlier than 4–6 weeks after HTx with complete withdrawal of mycophenolate mofetil and reduction of CNI dose.
Results: There were no significant differences of renal function between the groups prior heart transplantation (creatinine level 130.13 ± 68.74 (group 1) vs 138.46 ± 71.32 (group 2), respectively ($p = 0.41$). When we started everolimus, creatinine level in groups was 135.24 ± 56.6 (group 1) vs 101.98 ± 63.02 (group 2) ($p = 0.04$). After a median time of 2 years from initiation everolimus, the renal function was assessed. Creatinine level in HTx recipients for group 1 was 149.67 ± 54.33 vs 138.29 ± 63.15 for group 2, respectively ($p = 0.6$). We did not find differences for the evolution of renal function, but in group 2 renal function was worse.
Conclusions: Our results support the use of everolimus can preserve renal function in HTx recipients who take long-term CNIs. The selection of either a conversion or a CNI minimization protocol should be based on the clinical characteristics of the patients, particularly their rejection risk, immunosuppression, and patient management protocols.

POS762 THE IMPACT OF INTRA-ABDOMINAL HYPERTENSION AFTER LIVER TRANSPLANTATION IN ADULT PATIENTS

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Background: The clinical relevance of the intra-abdominal hypertension (IAH) and the abdominal compartmental syndrome in the patients of the intensive care unit (ICU) and the impacts on morbidity and mortality have come into focus in recent years. The IAH in patients after liver transplant (LT) could compromise vascular flow in the graft with early graft dysfunction (EAD) or primary non function. Aim of this prospective study was to determine the incidence of the IAH in adult patients following LT and to confirm that the IAH in associated to a worsen outcome in terms of patients and grafts' survival and development of multiorgan dysfunction.
Methods: In this prospective study were enrolled all adult patients consecutively subjected to LT in our center from 01/03/2020 to 22/02/2021. Combined organ transplant, LT using living donor or split-liver graft and polycystic recipients were excluded. The intra-abdominal pressure (IAP) was measured immediately before and after the LT and every 8 hours during the permanence of the patient in ICU. The graft and the patients' survival and all complications up to 3 months after the LT were recorded to evaluate the short-term outcome.
Results: In the study, 102 patients were enrolled, 74 males (73.3%) and 27 females (26.7%). Median of labMELD was 15.4. The median of IAP at the end of LT was 10mmHg (IQR 8–12), and 35 (34.1%) patients presented IAH of grade 1–3. A total of 45 (42.9%) patients presented IAH of grade 1–4 during the permanence in ICU. IAH was associated with higher incidence of EAD ($p = 0.003$), acute kidney injury ($p < 0.001$) and patient's death ($p = 0.013$). According to univariate logistic regression, the principal factors associated with IAH were as follows: operative time ($p = 0.022$), graft/patients weight ratio ($p = 0.046$), reperfusion syndrome ($p = 0.001$) and total volume of fluid infused ($p = 0.04$). The presence of ascites before LT was protective from IAH ($p = 0.017$).
Conclusions: Increased IAP is present in a large percentage of the adult patients after the LT. IAH is associated to a worsen post-transplant outcome, even in case of IAH of grade 1 or 2. Presence of ascites protects the patients from the IAH. As for the pediatric LTs, this topic is certainly of great interest even in adult population. Further studies could identify the best strategies to avoid the presence of IAH, improving the outcome of these patients.

POS763 STEATOTIC LIVER ALLOGRAFTS INCREASE THE RISK OF POSTOPERATIVE SEVERE KIDNEY INJURY REQUIRING CONTINUOUS VENO-VENOUS HEMOFILTRATION

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Background: The use of steatotic allograft is increasing to fill the need of graft for liver transplantation. However, there is evidence that the use of steatotic grafts is associated with impaired postoperative renal function and need of continuous veno-venous hemofiltration (CVVH).
Aim of the study: Assess the impact of steatotic grafts (≥ 30%) on postoperative acute kidney injury (AKI).
Methods: Between 2010 and 2018, 657 full graft liver transplants have been performed at liver transplant center of Padova. Donor and recipient characteristics, intraoperative and postoperative outcomes were reviewed. Patients with available biopsy were 416. Of these 32-graft had steatosis ≥ 30%.
Preliminary Results: Postoperative AKI occurred in 230 patients (55.3%). Patients who received a steatotic graft who develop AKI were 17 (53.1%) with no difference with control group. Patients who required CVVH were 16 (3.8%) of which 4 in the steatotic group (12.5%) with significant difference with the control group (3.1% - $p = 0.02$).

POS764 LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS

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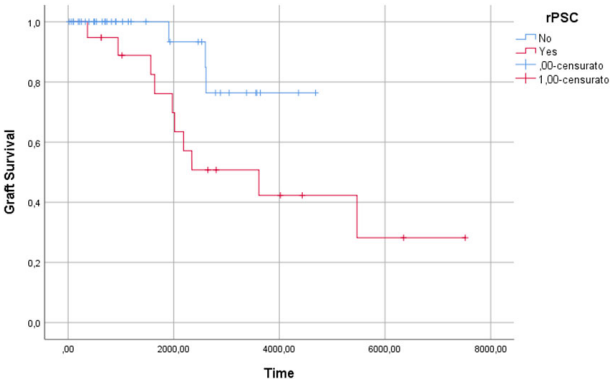
Background and Aims: The outcome of liver transplantation (OLT)in primary sclerosing cholangitis (PSC) has improved significantly over the past decades with many centres reporting 1-y patient and graft survival above 90% and 85% respectively.
However, specific complications in PSC OLT recipients, such as IBD activity, cholangiocarcinoma (CC) and colorectal neoplasia (CRC) development, remain problematical. Our aim was to evaluate the following: a)patient and graft survival; b) IBD activity after OLT; c) incidence of CRC and CC.
Methods: We retrospectively evaluated the clinical data of 33 patients with primary sclerosing cholangitis (PSC) transplanted at our center in the last 20 years. Between 2000 and 2020, 58 adult patients (median age 42 years old, 72% male) receiving transplantation for PSC at Niguarda Hospital (Milan) and Papa Giovanni XXIII Hospital (Bergamo). rPSC was confirmed by magnetic resonance or endoscopic retrograde cholangiopancreatography and liver biopsy.
Results: The features of the study population are showed in Tab.1. rPSC occurred in 19 of 58 (33.3%). In the univariate analysis, younger age at liver transplant ($p < 0.001$), long history of psc (0.041) before LT and higher MELD score at LT (0.014) were associated with rPSC. Moreover, donor age (0.045) and CMV mismatch (0.05) were both associated to an increased risk of rPSC. A total of 32 patients (55%) patients had PSC and



Variables		*Values*
Age at transplant (years)	Median (Range)	42 (18-64)
Male	N (%)	42 (72)
Active smoker	N (%)	10 (17)
Time of disease before transplant (years)	Median (Range)	8 (1-38)
Body Mass Index, N (%)	**<18.5 Kg/ m²**	5 (10)
	18.5-25 Kg/m²	38 (78)
	> 25 Kg/m²	6 (12)
MELD at transplant	Median (Range)	17 (6-40)
Bilirubin at transplant	Median (Range)	11 (1-34)
INR at transplant	Median (Range)	1.27 (1-2)
Tumor at LT	N (%)	6 (10.3)
Type of graft	Whole	52 (91.4)
	Split	4 (5.2)
	Living donor	2 (3.4)
Donor Age	Median (Range)	61 (10-86)
Type of Donor	DCD	4 (5.2)
	DBD	53 (91.4)

Inflammatory bowel disease pre-LT. The presence of IBD pre-transplant was not associated with rPSC after LT (0.35); the occurrence or reactivation of IBD post-transplant was associated with rPSC (0.05). Eight patients experienced occurrence or reactivation of IBD post- LT. The median time between LT to occurrence or recurrence of IBD was 3 years (1–5). In the multivariate analysis, younger age (0.007) at LT and IBD post-LT (0.043) were independently associated with rPSC (Tab. 2). 10 patients were retransplanted during the follow-up period. 9 of them were retransplanted for rPSC, while the other one for late artery thrombosis. Three patients experienced rPSC of the second graft and underwent to a third transplant and they are still alive.
Conclusions: rPSC was associated with a limited graft survival compared to patients without recurrent of primary liver disease ($p = 0.44$), while rPSC does not have any influence on overall patient survival.

POS765 MIXED METHOD STUDY TO COMPARE AN OUTREACHING, MULTI SYSTEMIC INTERVENTION VERSUS CARE AS USUAL TO PROMOTE ADHERENCE AFTER KIDNEY TRANSPLANTATION

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Background: Nonadherence after kidney transplantation undermines optimal health outcomes. Current interventions lack effectiveness, focus solely on patients and are one-size fits all. Combining evidence-based techniques from behavior change theories and principles from multisystemic therapy with the possibility of tailoring has led to the development of the MARS-intervention. The aim was to evaluate this intervention in promoting adherence.
Methods: A single-center, parallel arm RCT was used to compare the MARS-intervention to standard care. Non adherent kidney transplant recipients (≥12 years) were eligible for inclusion. The primary outcome was immunosuppressive medication adherence, assessed with electronic monitoring. Secondary quantitative outcomes regarding to medication adherence are assessed. Data were collected at baseline (T0), after a run-in period (T1), after 6 months (T2) 12 months; follow-up period (T3). Qualitative content analysis was conducted through semi-structured interviews with several stakeholders.
Results: Including non-adherent patients proved difficult and combined with the outbreak of COVID-19, led to an underpowered sample size, making it difficult to quantitatively assess effectiveness. Electronic monitoring showed variable patterns of medication taking and timing. Nonadherent patients were not always aware of their problem, or willing to discuss it during the intervention. Raising awareness was reported to be one of the important factors in changing medication adherence. Although described as effective for improving medication in some patients, there was a substantial group of patients which experienced multiple problems on several areas, making their nonadherence to medication a side issue. Specific elements, holistic nature, therapeutic alliance and the outreaching aspect of the intervention were appreciated. Involvement of the social network was variable.
Conclusions: The intervention was appreciated by all participants and appeared effective in changing nonadherence by some patients. However, including nonadherent patients was difficult and the reluctance to participate underestimated. Furthermore, patients with severe problems on multiple areas in life need more extensive guidance to establish change in medication adherence.

POS766 ABSENCE OF RESUSCITATION DURING NORMOTHERMIC REGIONAL PERFUSION USING A PORTABLE GAMMA-CAMERA SYSTEM

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Background: The aim of the study was to verify that during the donation after circulatory death there is an absence of cerebral blood flow and that this condition is irreversible. In this way, we want to demonstrate that there is no recovery of cerebral flow from the thoracoabdominal collateral circulation through the vertebral artery.

Methods: Experimental study, prospective, one-center. A portable gammagraphy (Sentinella®) is performed to donors after circulatory death (5 minutes delayed for legal reasons) with normothermic regional perfusion (NRP). In abdominal NRP, an intraaortic balloon occludes completely the descending aorta to prevent recovery of brain flow. In case of thoracoabdominal NRP, cardiac surgeon clamps the supraaortics vessels and connects the aortic arch vessels to a collecting bag. A Nuclear physician administrates technetium 99 in return cannula of extracorporeal circulation system at the beginning of NRP. The absence of perfusion in the cerebral hemispheres and brainstem confirms the absence of resuscitation.
Results: Between January and February 2021, 3 donors have been studied. 2 cases were abdominal NRP and 1 of them thoracoabdominal NRP. Average time until cardiac arrest was 12.7 minutes. None of them showed cerebral perfusion using the portable gamma-camera. In addition, there were no modifications with Bispectral Index, remaining at value 0.
Conclusions: Absence of cerebral reperfusion using a portable gamma-camera has shown that cessation of brain circulation is permanent after starting the extracorporeal circulation, using the current protocols.

POS767 GENETIC VARIABILITY IN GLUCOCORTICOID PATHWAY AND NEW-ONSET DIABETES MELLITUS AFTER TRANSPLANTATION

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Background: New-onset diabetes mellitus after transplantation (NODAT) contributes to morbidity and mortality after kidney transplantation. NODAT develops due to nongenetic factors such as obesity, hepatitis C virus infection and drugs like tacrolimus and steroids. Biological effects of glucocorticoids are determined by daily dose of glucocorticoids and patient's sensitivity to them. Individual variation in glucocorticoid sensitivity might be partially determined genetically by functional polymorphisms in the glucocorticoid receptor gene or in the genes in the metabolic pathway of glucocorticoids. We report on interim results of our study which investigated the associations between these polymorphisms and the development of NODAT in kidney transplant patients.
Methods: A total of 290 patients transplanted in 6 consecutive years (2010–2015) were included in the study. All patients were genotyped for polymorphisms in genes coding for glucocorticoid receptor (*NR3C1*), p-glycoprotein (*ABCB1*) and glutathione S-transferase P1 (*GSTP1*) using competitive allele-specific polymerase chain reaction (KASPar). *GSTM1* and *GSTT1* gene deletions were determined using multiplex PCR reaction. For interim analysis, clinical data were obtained from medical records for 79 patients. NODAT was defined as the need for oral antidiabetic drugs or subcutaneous insulin prescription after transplantation. Nonparametric tests and logistic regression were used to assess the associations between the investigated polymorphisms and NODAT.
Results: In a subset of 79 patients (53 men and 26 women) with a median age of 51.9 years of whom 45.6% were receiving methylprednisolone, 22.8% developed NODAT. Two polymorphisms in *GSTP1* gene were associated with an increased risk for NODAT in univariate analysis, both in additive and dominant genetic models (*GSTP1* rs1695 $p = 0.045$ and $p = 0.04$, respectively; *GSTP1* rs1138272 $p = 0.015$ and $p = 0.01$, respectively). These associations remained statistically significant after adjustment for age and concurrent treatment with methylprednisolone in multivariate analysis. *NR3C1*, *GSTM1* and *GSTT1* polymorphisms were not associated with the risk for NODAT.
Conclusions: *GSTP1* rs1695 and rs1138272 polymorphisms are significantly associated with the risk for NODAT in the first posttransplant year.

POS768 DECIPHERING BIOLOGICAL DETERMINANTS OF PREFORMED T AND B-CELL ALLOSENSITIZATION IN KIDNEY TRANSPLANT CANDIDATES

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Background: Preformed T-cell immune sensitization increases the risk of acute T-cell mediated rejection and impacts on kidney transplant (KT) outcome. While HLA-specific humoral sensitization has clear determinants such as previous transfusions, pregnancies and transplantations, risk factors associated with anti-HLA T-cell sensitization are still poorly understood as no accurate means of assessment are available. Also, the relationship between humoral and cellular allosensitization prior to KT is still uncertain.
Methods: In a set of well-characterized waitlisted KT candidates with different HLA sensitization background, we analyzed T-cell sensitization through a Panel of Reactive T-cell ELISPOT assays (PRT, using nine distinct splenocytes lines covering most HLA class I and II antigens as stimulators) as well as donor-reactive T-cell responses. Also, B-cell sensitization both through the calculated Panel Reactive Antibodies (cPRA, based on single antigen beads) and by measuring circulating donor(HLA)-specific memory B cells (mBc).
Results: A total of 67 waitlisted KT candidates were included (17 had No previous history of classical Immunizing Events (NIE), 21 were women with previous pregnancies (PG) and 15 had received a previous KT. Fifty-nine patients (88%) were transplanted during the follow-up time. While the percentage of cPRA was higher within the KT and PG, than NIE patients (mean cPRA: 56.5%, 33.2% and 14.3% respectively, $p < 0.001$), PRT was similar across the three groups (mean PRT: 41.2%, 28.8% and 40.1% respectively, $p = 0.35$). No correlation was found between PRT and PRA ($r = -0.18$, $p = 0.15$). Among patients with subsequent KT, there was a significant correlation between PRT and donor-reactive T-cell response ($r = 0.43$, $p = 0.025$). The frequency of donor-specific mBc was high in most previous KT patients even in patients without DSA, and low in the NIE patients regardless the presence of anti-HLA antibodies.
Conclusion: Preformed T-cell sensitization may be detected in a wide range of KT candidates and does not seem to be exclusively related to previous classical HLA immunizing events nor with cPRA. Assessment of PRT prior to transplantation could help stratifying patients at high-risk of anti-donor T-cell immune responses, which may ultimately challenge successful KT.

POS769 PEDIATRIC – TO – ADULT DOMINO LIVER TRANSPLANTATION FROM MSUD DONORS: A SAFE STRATEGY TO INCREASE THE ORGAN POOL?

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Background: Maple Syrup Urine Disease (MSUD) is a metabolic disease due to deficiency of Branched-Chain- Keto-acid DeHydrogenase enzyme complex (BCKDH), an ubiquitary enzyme, leading to progressive accumulation of branched-chain amino acids with severe ketoacidosis and neurological damage. The liver from MSUD patients, otherwise healthy, has already been used successfully for liver transplantation (LT) with the domino technique.
Methods: All DLT were retrospectively analyzed with a minimum 1-year follow-up. Donor and recipient characteristics, vascular complications, metabolic profile, patient and graft survival were analyzed. All DLT recipient were selected according to size and had low-priority according to national allocation policies.

Results: From December 2013 to October 2016, 5 domino LT (DLT) were performed at Our Center from pediatric MSUD donors to adult recipients. The indication for DLT recipients was hepatocellular carcinoma (HCC) at high risk for drop-out in 80% of patients. Median MSUD donor age was 13.7 years (range 11 to 16), median MSUD recipients age was 57.5 years (range 51 to 67). All but one patient had a GRWR > 0.8. All MSUD recipient was transplanted according to modified piggy-back technique. One patient required supraceliac aorta-hepatic jump-graft, one patient portal vein elongation by interposition of cadaveric venous graft and one other patient required suprahepatic IVC elongation by using a cadaveric venous graft. One patient underwent ligation of the splenic artery during LT in order to avoid the risk of a small-for-size-syndrome. All DLT recipients had an immediate functional recovery of the graft. No vascular complications in the perioperative period occurred. None of DLT recipients presented pathological changes in amino-acid profile in blood samples at postoperative controls. Mortality at 30-day follow-up for both donors and recipients was nil.
Conclusions: Our experience in DLT from MSUD pediatric donors to adult recipients could suggest a systematic application of this technique for recipient with low priority but potentially high transplant benefit. The size match between donors and recipients is an important issue in DLT. A national network of potential small recipients could be created in order to maximize the utilization of this potential source of organs.

POS770 USING THE LASER SPECKLE DOPPLER TO QUANTIFY PERFUSION QUALITY IN KIDNEY AND PANCREAS GRAFTS ON VASCULAR REPERFUSION

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Background: Reperfusion during solid organ transplantation is associated with ischaemia reperfusion injury (IRI), which itself is linked to the quality of organ reperfusion. The adequacy and degree of organ perfusion is critically linked to peri-operative management, therapeutic strategies and graft outcomes. Laser Speckle Doppler (LSD) imaging is a non-invasive imaging technique that can assess vascular flow, and obtain full field, high resolution images of microvascular perfusion of an organ. The aim of the study was to utilise LSD intraoperatively during kidney and simultaneous kidney and pancreas transplantation, as proof of principle to evaluate the parameters of reperfusion that could be obtained.
Methods: The Moor FLPI-2® blood flow imager was used in three patients during re-vascularization: 1) deceased donor kidney transplant 2) living donor kidney transplant; 3) simultaneous pancreas and kidney transplant.
Preliminary results: In an initial review of these 3 patients, there was a disparity between the description of perfusion by the surgeon using vision alone and the perfusion quantified using the laser speckle Doppler. The laser speckle Doppler closely correlated with post-operative MAG3 renogram findings, which were also incongruent with the vision alone assessment by the surgeon. This *may* suggest that LSD provides a more accurate measure of reperfusion, which correlates with the MAG3 renogram, warranting further investigation as a potential tool to guide peri-operative therapeutic interventions.
We are currently collecting data on kidney and pancreas graft function and correlating with microcirculatory measurements obtained with the LSD, developing intra-operative parameters of reperfusion. We would like the opportunity to present these findings at ESOT, believing this represents a valuable tool in quantification of reperfusion and could guide resultant peri-operative therapeutic interventions.

POS771 PROSPECTIVE ASSESSMENT OF GRAFT RECOVERY AFTER KIDNEY TRANSPLANTATION BY MEANS OF DONOR-DERIVED CELL-FREE DNA

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Background and Aims: Ischemia and reperfusion injury (IRI) is unavoidable in renal transplantation and one of most important triggers for delayed-graft function (DGF). Long term, it is also associated with acute rejection and chronic graft dysfunction. The use of Donor derived cell-free DNA (dd-cfDNA) has proved to be of value at surveillance to distinguish acute rejection from normal graft histology and chronicity. Exploring the kinetic of dd-cfDNA soon after kidney transplantation in the recovery phase after IRI remains unknown.
Methods: Prospective observational study to assess the relation of dd-cfDNA with early recovery after kidney transplantation and clinical course afterwards, including per-protocol (3-month) and per-cause biopsies. A total of 60 patients are planned to be enrolled. dd-cfDNA will be tested using AlloSeq cfDNA assay (CareDx) at day 1, 7, 14, 30 and 90 post-transplant.
Results: Up to date, 28 kidney recipient patients have been enrolled, 5 recipients of living donor, 9 recipient of donor after circulatory death type III and 14 recipients of donor after brain death. Median cold ischemia time was 13.1[7.2–18.3]hours and DGF occurred in 8 patients (28.6%). Mean levels of dd-cfDNA at day 1, 7, 14 and 30 were 2.90[1.85–5.87]%, 0.52[0.32–0.86]%, 0.34[0.28–0.51]% and 0.31[0.26–0.47]% respectively, showing a significant ($p < 0.001$) decrease early after transplantation. Values of dd-cfDNA in recipients from cadaveric donors were significantly higher at day 7 ($p = 0.005$). Considering a normal dd-cfDNA cutoff of <1.0%, recipients of a living donor were all below it starting from day 7, while in recipients of a cadaveric donor dd-cfDNA was above limit in 25.0% of cases at day 7 and in 5.3% of cases at day 14. Only one case of ABMR was observed 7 days after kidney transplantation (dd-cfDNA 1.2%) and 3 more cases of borderline rejection were observed at day 14, without significant differences compared with the other cases. In patients with DGF, dd-cfDNA value at day 7 correlated significantly DGF duration (Pearson = 0.891, $p = 0.003$).
Conclusions: During the first month after kidney transplantion, values of dd-cfDNA indicate progressive recovery from IRI and are below normal cut-off starting from day 7 in recipients of a living donor and starting from day 14 in the majority of recipients of a cadaveric donor.