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Fragility spinal fractures among cirrhotic liver transplant candidates in Croatia

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ABSTRACT

Introduction: Existing data on fragility spinal fractures prevalence in liver transplant candidates are scarce and inconsistent. This may be due to other comorbidities, besides hepatic osteodystrophy (HO), that contribute to bone loss and fragility fracture prevalence in chronic liver disease (CLD).

Objectives: The aim of this study was to investigate the prevalence of spinal thoracic and lumbar fragility fractures among cirrhotic, non-chronic kidney disease (CKD), non-diabetic liver transplant candidates and to explore their relationship with clinical characteristics, laboratory markers and dual-energy x-ray absorptiometry (DXA) results.

Material and methods: This cross-sectional observational study was conducted at Merkur University Hospital, Croatia, between February 2019 and May 2023. Adult patients with liver cirrhosis referred for liver transplantation were included. Patients with acute infection, CKD, diabetes mellitus, malignancies, inflammatory bone diseases and those on corticosteroid or antiresorptive therapy were excluded. Clinical, laboratory and radiological assessment was carried out and patients were accordingly allocated into non-fractured and fractured group for the purpose of statistical analysis.

Results: A total of 90 patients were included in the study. There was 123 fractures, 87 (70.7 %) in the thoracic and 36 (29.3 %) in the lumbar region. Eighty-nine (72.4 %) fractures were grade 1, 31 (25.2 %) were grade 2 and 3 (2.4 %) were grade 3. Patients in the fractured group were significantly older ($p < 0.001$). No significant differences between fractured and non-fractured group according to laboratory and DXA parameters were noted. Subgroup with lumbar fractures had significantly lower bone mineral density values at L1-L4 region. Statistically significant negative correlation between bone specific alkaline phosphatase (BALP) and hip total BMD (rho = -0.414, $p < 0.001$) and spine total BMD (rho = -0.258, $p = 0.014$) values was found.

Conclusion: Present study confirmed detrimental impact of CLD and HO on bone strength. DXA measurement correlated with the presence of lumbar fragility fractures. A combination of standard X-ray imaging and DXA is needed for adequate bone evaluation in pretransplant period and BALP could be useful for detecting HO in CLD. Searching for other risk factors and implementing bone turnover markers and additional imaging techniques for bone loss evaluation in liver transplant candidates is needed.

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Introduction

Hepatic osteodystrophy (HO) represents alteration of bone-mineral metabolism in chronic liver disease (CLD). Although this term was originally coined for the description of frequently associated combination of osteomalacia and osteoporosis [1] in CLD, nowadays it mostly refers to more prevalent osteopenia or osteoporosis [2]. Different risk factors for the development of HO have been described so far, including dietary deficiencies, alcohol consumption, alteration in vitamin D metabolism, effects of medication usage, iron and copper accumulation and hyperbilirubinemia [3]. These metabolic changes are especially expressed in patients with end stage liver disease (ESLD) and those awaiting liver transplantation (LT) [4–7]. However, little improvement in nutritional, as well as bone mineral density (BMD) status in those patients has been seen over the years [4]. The major feature of HO is BMD reduction and trabecular bone structure deterioration, which undoubtedly increases probability of spinal thoracic and lumbar fragility fractures [2]. Only a few studies so far have assessed fragility spinal fractures exclusively in liver transplant candidates [4,5,8–11], with a reported prevalence of up to 56 %. However, this high prevalence could also be a result of other frequent comorbidities in CLD, such as chronic kidney disease (CKD) [12] or diabetes [13–16]. Distinguishing those conditions may better reflect the real consequences of CLD itself.

The aim of this study was to investigate the prevalence of spinal thoracic and lumbar fragility fractures among cirrhotic, non-CKD, non-diabetic liver transplant candidates in Croatia and to explore their relationship with clinical characteristic, bone-related laboratory markers and dual-energy x-ray absorptiometry (DXA).

Material and methods

Patient's selection

This cross-sectional observational study was conducted at Merkur University Hospital, Croatia, between February 2019 and May 2023. The study was approved by the Institutional Ethics Committee and Ethical Committee of the School of Medicine, University of Zagreb. Adult patients (age $\geq$ 18 years) with liver cirrhosis referred for LT at the Merkur University Hospital were eligible for the study. The diagnosis of liver cirrhosis was made either by pathohistological analysis of liver biopsy, or according to the typical clinical picture of advanced chronic parenchymal disease with developed portal hypertension, laboratory findings (anaemia, thrombocytopenia, decreased prothrombin time, increased bilirubin value, decreased albumin level) and morphological methods (abdominal ultrasound, computed tomography of the abdomen, magnetic resonance of the liver). Patients with acute infection (febrile patients, antibiotic treatment), CKD (estimated glomerular filtration rate (eGFR)<60 ml/min/m2), diabetes mellitus (antidiabetic drug treatment and/or fasting blood glucose concentration>7mmol/L), other diseases affecting bone-mineral metabolism (ankylosing spondylitis, rheumatoid arthritis, sarcoidosis, haemophilia, and malignancies), and those on corticosteroid or antiresorptive therapy were excluded from the study.

Clinical evaluation

After providing informed consent, relevant anamnestic and clinical data including age, sex, height, weight, body mass index (BMI), menopausal status, history of fragility fractures, family history of hip fractures in a parent, current osteoporosis prevention therapy, current smoking, presence of ascites and encephalopathy, presence of back pain, as well as time spent on liver transplant waiting list have been recorded.

Radiology assessment

DXA

The spine and hip DXA examination have been carried out at a single location (Zagreb University Hospital Centre, Division of Densitometry) using the same device (Hologic Discovery-W Bone Densitometer) and analysed by an experienced endocrinologist. The World Health Organisation criteria were used for the interpretation of DXA results [17].

X-ray

Fragility spinal fractures were assessed using X-ray imaging. Thoracic and lumbar spine series comprising of standard anteroposterior (AP) or posteroanterior (PA) and lateral views were used. AP or PA views were chosen depending on patient history. The central ray was positioned over the L3 vertebral body for the lumbar spine and over the T6 vertebral body for the thoracic spine. On the lateral view of the lumbar spine, all lumbar vertebral bodies were visible, with T11/T12 superiorly and the sacrum inferiorly. On the lateral view of the thoracic spine, all 12 thoracic vertebral bodies were visible. The images were then analysed by two radiologists with different levels of experience in musculoskeletal imaging blinded for patient's data. The vertebral fracture severity was assessed and scored using Genant's visual semi-quantitative grading system where the degree of vertebral height reduction and morphologic change is visually determined [18]. In the case of different fracture scoring, consensus was achieved by a mutual agreement. Upon the visually apparent deformity, each vertebra received a severity grade. A decrease in height of <20 % is considered normal (grade 0), a decrease of 20-25 % is considered mild (grade 1), a decrease of 25-40 % is moderate (grade 2) and a decrease of >40 % is considered as severe (grade 3) fracture [18] (Fig. 1). Other vertebral body deformities, unrelated to fracture, such as Schmorl's hernia and severe osteoarthritis were excluded from the analysis.

Assessment of fragility fracture risk

Fracture risk assessment tool (FRAX) was used to evaluate the risk of a 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture [19,20].

Laboratory tests

Venous blood for laboratory testing was sampled in the morning, after an overnight fast. All laboratory tests were done in Department of Medical Biochemistry and Laboratory Medicine, Merkur University Hospital accredited according to ISO 15189:2012 Medical laboratories – Requirements for quality and competence. Concentrations of serum total calcium (Ca), albumin (Alb), creatinine, total bilirubin (BIL), inorganic phosphate (P), alkaline phosphatase (ALP) were determined in sera by using an automated biochemistry platform (AU680, Beckman Coulter, USA). Plasma INR derived from prothrombin time was measured by an automated coagulation analyser (Sysmex CS 2500, Siemens Healthineers, Germany). After clotting, the sera were immediately separated by centrifugation and stored at - 25°C until the analysis of 25-hydroxyvitamin D (25-OH D) and bone specific alkaline phosphatase (BALP). Concentration of 25-OH D in serum was determined by the LC-MS/MS

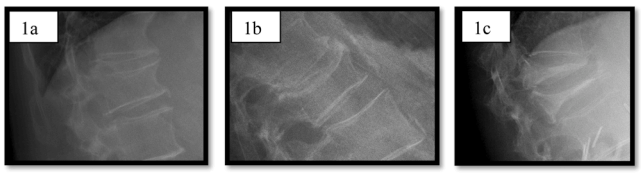

Fig. 1. Lateral x–ray series of the thoracic and lumbar spine from different patients. 1a- Wedge fracture Grade 1 (20-25 %), 1b-Biconcave fracture Grade 2 (25-40 %), 1c-Wedge fracture Grade 3 (>40 %).

(UPLC NEXERA X2-LCMS-8050, Shimadzu) accredited according to ISO 15189:2012 and BALP with a dedicated chemiluminescence immunoassay (Access Ostase assay, Beckman Coulter, USA).

Estimation of liver disease

Cirrhosis severity has been estimated by using Child-Pugh score for cirrhosis mortality and original Model for End-Stage Liver Disease [21, 22].

Statistical analysis

In this study, JASP 0.17.1 statistical software was utilized to perform statistical analyses on the dataset, identifying significant differences and correlations. Custom scripts were written in Python 3.8 for preprocessing and data cleaning, as well as the creation of figures. Normality of data was tested using Shapiro-Wilk test. For the analytic purposes patients were divided into two main groups, those with and without fracture, after which subdivision on thoracic and lumbar fractured subgroup was carried out. Accordingly, parametric, and nonparametric t-tests were used for comparisons between the groups. Statistical significance was set at a p-value of less than 0.05.

Results

Out of 114 participants enrolled in the study, 90 (79.6 %) finished all necessary investigations, and their results were eligible for statistical analysis. Anamnestic, clinical, laboratory and radiological data of all patients are listed in Table 1. Most of patients were men (66.7 %). For both sexes, there was dominance of alcoholic liver cirrhosis, 64.4 % for male, and 46.7 % for women, respectively. Among women, 29 (96.7 %) were postmenopausal. Only 7 (7.8 %) patients were previously diagnosed with HO and just 9 (10 %) received osteoporosis prevention therapy (including Vitamin D or Calcium (Ca) supplementation). Most of the patients (88 %) had 25-OH D insufficiency. DXA signs of HO were present in 50 (55.6 %) patients. X-ray imaging revealed a high proportion of fragility spinal fractures: 48.9 %. Only 10 out of 44 (22.7 %) patients with fracture had present back pain. Overall number of recorded fractures was 123, out of which 87 (70.7 %) were in thoracic and 36 (29.3 %) in lumbar region. The distribution and severity of fractures across the spine is depicted in Fig. 2. Most of the fractures, 89 (72.4 %), were grade 1, there were 31 (25.2 %) grade 2 fractures and 3 (2.4 %) grade 3 fractures. The frequency of fractures per individual patient is presented in Table 2. After dividing patients into groups according to the prevalent facture, those in the fractured group were significantly older ($p < 0.001$). Also, the ten-year probability of major fracture was significantly increased in the fractured group according to the FRAX questionnaire. There were no other significant differences between two groups according to clinical and laboratory parameters, including BALP and 25-OH D (Table 3). No significant differences according to DXA parameters were also detected between the groups (Fig. 3). Twenty-six (59.1 %) out of 44 patients with spinal fragility fractures had DXA signs of HO. However, subgroup of patients with lumbar fractures had significantly lower BMD and T-score values at L1-L4 region (Fig. 4). Statistically significant negative correlation between BALP and hip total BMD (rho = -0.414, $p < 0.001$) and spine total BMD (rho = -0.258, $p = 0.014$) values was found.

Discussion

We determined high prevalence of spinal fragility thoracic and lumbar fractures (48.9 %) in liver transplant candidates. Several other studies that investigated prevalence of fragility fractures exclusively in ESLD and those awaiting LT reported wide range of results, from 3 to 56 % [4,5,9,10]. This might be due to the different inclusion criteria according to the CLD type and the patient's comorbidities, particularly CKD [16] and diabetes mellitus [15], which may contribute to the development of bone loss and fragility fractures independently of the liver disease. Therefore, we opted to exclude patients with CKD and possible renal osteodystrophy, those diagnosed with diabetes or taking antidiabetic medication, and patients with malignancies, so the presented patients in vast majority outline the consequences of bone loss due to the CLD itself [23]. Another possible reason is that in some studies mild (Genant I) spinal fragility fractures were not considered clinically relevant and thus remained underreported [9,24–26]. Indeed, most of the fractures (72.4 %) recorded in the present study were classified as Genant I. However, recognition of even these mild fractures is of utmost importance, as it was previously clearly shown that patients who suffered fragility fracture are at imminent risk of experiencing subsequent fracture within the next 2 years [26–28]. Clinicians should also be aware that approximately 25 % of spinal fragility fractures can be asymptomatic [29]. This was again confirmed in our study, as only 22.7 % of patients with fracture had some degree of back pain. Contrary to the previously reported study of Krol et al. [9] in which most of the fractures were in the lumbar region, in our series, majority (70.7 %) were in the thoracic spine, with thoracic vertebrae 6-9 accounting for more than half (60.9 %) of overall thoracic fractures. Although no statistically significant differences according to the fracture severity have been found between the thoracic and the lumbar spine, it appears that more serious fractures could be expected in lower thoracic and upper lumbar vertebrae (Fig. 2). Thus, specific attention should be directed to these regions.

Bone loss in pretransplant period was another important predictive factor for future fracture, especially in the first six months after LT [30]. It is therefore recommended that due to the high prevalence of bone loss in ESLD, routine evaluation of bone status using DXA should be

Table 1
Patient characteristics.

Number of patients	90
Anamnestic and clinical data	
Gender M/W N (%)	60/30 (66.7/33.3)
Age (years) median (IQR)	59 (54.3-65)
BMI median (IQR)	29.3 (25.8-32.8)
Current Smoker N (%)	27 (30)
Ascites N (%)	36 (40)
Encephalopathy N (%)	23 (25.6)
Aetiology of cirrhosis N (%)	
Alcohol/Viral/NAFLD/Wilson disease/ Cholestatic	58(64.4)/3(3.3)/16(17.8)/4 (4.4)/9(10)
HO in medical history N (%)	7 (7.8)
Osteoporosis prevention therapy N (%)	9 (10)
DXA results	
Normal BMD N (%)	40 (44.4)
Osteopenia N (%)	31 (34.4)
Osteoporosis N (%)	19 (21.1)
Laboratory tests	
Total calcium (Ca) (mmol/L) mean (SD)	2.26 (0.12)
Inorganic phosphate (P) (mmol/L) mean (SD)	1.11 (0.17)
Alkaline phosphatase (ALP) (IU/L) median (IQR)	112.5 (88.5-138)
Bone specific alkaline phosphatase (BALP) (μg/L) median (IQR)	14.2 (10.7-18.5)
25-hydroxyvitamin D (25-OH D) (nmol/L) mean (SD)	45.9 (20.9)
Estimation of liver disease	
MELD score median (IQR)	11 (9-15.8)
Fragility fracture risk evaluation	
FRAX with BMD The ten-year probability of fracture (%)	
Major fracture median (IQR)	4.4 (2.7-7)
Hip fracture median (IQR)	0.7 (0.3-1.7)

Abbreviations: N-number, M-men, W-women, IQR-interquartile range, SD-standard deviation, BMI-bone mass index, NAFLD- non-alcoholic fatty liver disease, HO-hepatic osteodystrophy, DXA-dual-energy x-ray absorptiometry, BMD-bone marrow density, FRAX-fracture risk assessment tool, MELD-model for end stage liver disease.

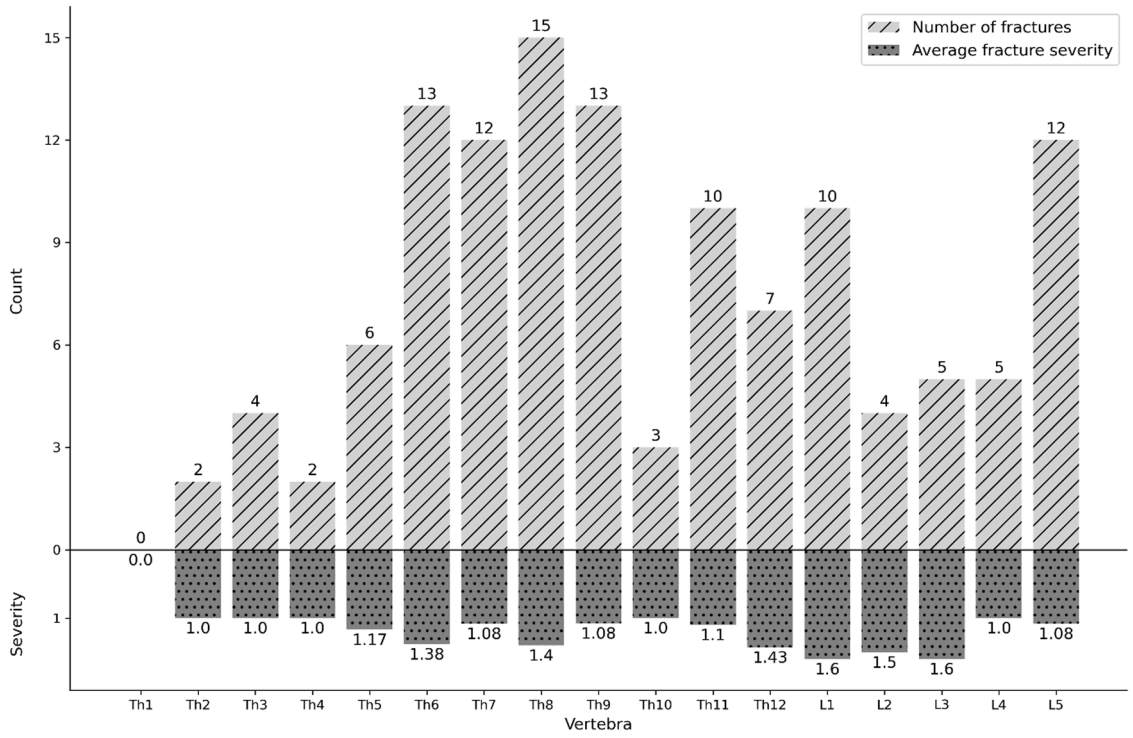

Fig. 2. The distribution and severity of fractures across spine.

Table 2
Overall number of spine fragility fractures per patient.

Number of fractures	1	2	3	4	5	6	7
Number of patients	10	13	7	7	5	1	1

mandatory before LT [31]. Interestingly, no significant differences neither in hip nor spine BMD or T-scores have been found in our study between the fractured and non-fractured groups. At the same time, 40.9 % of patients with spinal fragility fracture had normal DXA values. However, considering fragility fractures as an ultimate sign of osteoporosis [29], it appears that the overall prevalence of HO in the present study was 75.6 %. After division of fractured group into lumbar and thoracic subgroups, patients with lumbar fracture had statistically significantly lower BMD and T-score across all lumbar regions (Fig. 4.). These results are in line to those of Monegal et al. [4], whereas Wibaux et al. [5] additionally found a connection of spinal fragility fractures with lower total hip BMD and lower total hip and femoral neck T-scores. Contrary, Krol et al. reported no significant relationship between any DXA values and fragility fracture prevalence [9]. It is of note that DXA lumbar values should be interpreted with caution, while the presence of over 4 L of ascites may give a falsely lower BMD result [32], which could make eventually an even bigger discrepancy regarding the X-ray assessment. On the other hand, various artifacts or local structural changes, especially spinal degenerative changes will spuriously elevate BMD values [33]. As known, BMD determined by using DXA represents only a quantitative determinant of bone strength, without the qualitative status, that is, bone geometry, microarchitecture, and composition [34,35]. Some authors therefore proposed additional imaging techniques such as DXA-derived trabecular bone score (TBS) and vertebral fracture assessment (VFA) that could serve in better prediction of fragility fracture [36]. High resolution peripheral quantitative computerized tomography (HR-pQCT) allows for the evaluation of microarchitecture and 3D imaging of cross sections of the central and axial skeleton [36]. However, studies in CKD and cirrhotic patients showed no advantages of this method in terms of fracture prediction over conventional DXA [36,37].

Study showed that female gender, advanced age, lower BMI, malnutrition, alcohol and tobacco consumption are the most important factors contributing with the development of bone loss [11]. However, risk factors associated with the fragility fractures in ESLD frequently differ from those commonly related to bone loss as measured by DXA. Wibaux et al. [5] reported that patients awaiting LT with radiographic spinal fractures had lower body weight, less often history of alcohol abuse and lower level of 1,25-(OH)2D [5]. The only patient characteristic significantly associated to higher prevalence of vertebral fractures in the study of Krol et al. [9] was male gender, which was independent of age, underlying disease pathology, or severity of liver disease. Similar results were also revealed by Carey et al., where significantly higher fragility fracture rate, especially for spinal fractures, was found only in males. In our study only older age was significantly associated with higher prevalence of spinal fragility fractures, with median age in fractured group being 62.5 years, as opposed to 57 years in non-fractured group. It is known however, that older age is responsible for an increased risk of fracture regardless of BMD in elderly population [38], so the effects of aging on bone health in those suffering from liver cirrhosis seems to be pronounced at an earlier stage of life. Additionally, we found that only lumbar fractured subgroup had significantly lower body weight and height, but no association to BMI has been detected. As known, Vitamin D metabolism in CLD is usually highly impaired due to the combination of malnutrition, low exposure to sunlight and low intestinal absorption [39]. Hepatic hydroxylation of vitamin D that is necessary for the incorporation of calcium into the bone, is also blocked. Indeed, we found 25-OH D insufficiency or deficiency in almost 88 % of our patients, with only small amount of them (10 %) using osteoporosis prevention therapy. However, no significant difference in circulating 25-OH D level was noted between the fractured and nonfractured group. Such data suggest that factors other than those commonly associated with bone loss detected by DXA are involved in the evolution of fragility fractures [40] in ESLD. One possibility may lie in the fibroblast growth factor 23 (FGF23), which appears to be elevated in a majority of ESLD patients, independently of CKD [41]. Interestingly, in CKD patients and

Table 3
Differences between non-fractured and fractured group of patients.

	Non-fractured group (N 46)	Fractured group (N 44)	p-value
Anamnestic and clinical data			
Gender M/W N (%)	32/14 (70/30)	28/16 (63.7/36.3)	0.556
Age (years) median (IQR)	57 (49.3-61.8)	62.5 (56-67.3)	**< 0.001**
Time on liver transplant list (months) median (IQR)	10.5 (10.5-23.8)	5 (3-26)	0.811
BMI median (IQR)	29.3 (25.2-31.5)	29.3 (25.8-33.5)	0.425
Current Smoker N (%)	16 (34.8)	11 (25)	0.311
Ascites N (%)	19 (41.3)	17 (38.6)	0.796
Encephalopathy N (%)	13 (28.3)	10 (22.7)	0.547
Aetiology of cirrhosis N (%)	32 (69.6)/1 (2.2)/5 (10.9)/	26 (59.1)/2 (4.5)/11 (25)/	
(Alcohol/Viral/NAFLD/Wilson disease/Cholestatic)	3 (6.5)/5 (10.9)	1 (2.3)/4 (9)	0.370
HO in medical history N (%)	3 (6.5)	4 (9.1)	0.649
Osteoporosis prevention therapy N (%)	5 (10.9)	4 (9.1)	0.779
MELD-score median (IQR)	11 (9-15)	11 (9-16)	0.685
Laboratory tests			
Total calcium (Ca) (mmol/L) mean (SD)	2.25 (0.12)	2.26 (0.12)	0.706
Inorganic phosphate (P) (mmol/L) mean (SD)	1.12 (0.17)	1.10 (0.18)	0.571
Alkaline phosphatase (ALP) (IU/L) median (IQR)	112 (91.3-137.5)	116 (84.5-141.8)	0.790
Bone specific alkaline phosphatase (BALP) (μg/L) median (IQR)	14.1 (10.9-16.8)	14.6 (10.3-19)	0.509
25-hydroxyvitamin D (25-OH D) (nmol/L) mean (SD)	47.1 (20.8)	44.8 (21.5)	0.609
Estimation of liver disease			
MELD score median (IQR)	11 (9-15)	11 (9-16)	0.685
CP score median (IQR)	7 (6-8)	7 (5.5-8)	0.618
Fragility fracture risk evaluation			
FRAX with BMD			
The ten-year probability of fracture (%)			
Major fracture median (IQR)	3.3 (2.3-5)	0.5 (0.2-1.1)	**< 0.001**
Hip fracture median (IQR)	5.5 (4-8)	0.8 (0.4-2.4)	0.062

Abbreviations: N-number, M-men, W-women, IQR-interquartile range, SD-standard deviation, BMI-bone mass index, NAFLD- non-alcoholic fatty liver disease, HO-hepatic osteodystrophy, DXA-dual-energy x-ray absorptiometry, BMD-bone marrow density, MELD-Model for end stage liver disease, CP-Child-Pugh, FRAX-Fracture risk assessment tool.

those awaiting kidney transplantation, elevated FGF23 levels were an independent risk factor of fragility fracture, but not an indicator of decreased BMD [42]. However, no studies observed this connection specifically in ESLD and those awaiting LT [43,44].

The main goal of the bone turnover markers (BTM) should be an early recognition of bone metabolism changes, as in CLD first sign of HO is usually osteopenia or osteoporosis diagnosed with DXA. Measurements of BTM have been previously used in CLD patients [45–49], with majority of them reporting high bone turnover. For example, study by Jørgensen et al. [50] demonstrated that HO in cirrhotic patients was a result of decreased bone formation (indicated by lower procollagen of type I collagen propeptide (PINP) and increased bone resorption shown by higher level of C-telopeptides of type I collagen (CTX). Although the level of PINP was increased in the

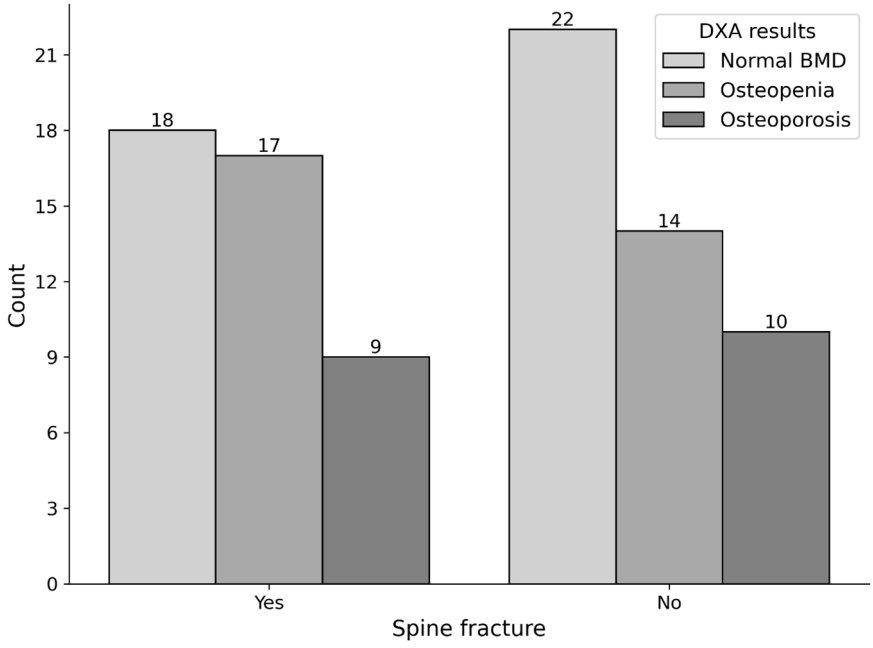

Fig. 3. Prevalence of HO in fractured and non-fractured group.
Abbreviations: HO-hepatic osteodystrophy, DXA- dual-energy x-ray absorptiometry, BMD- bone mineral density.

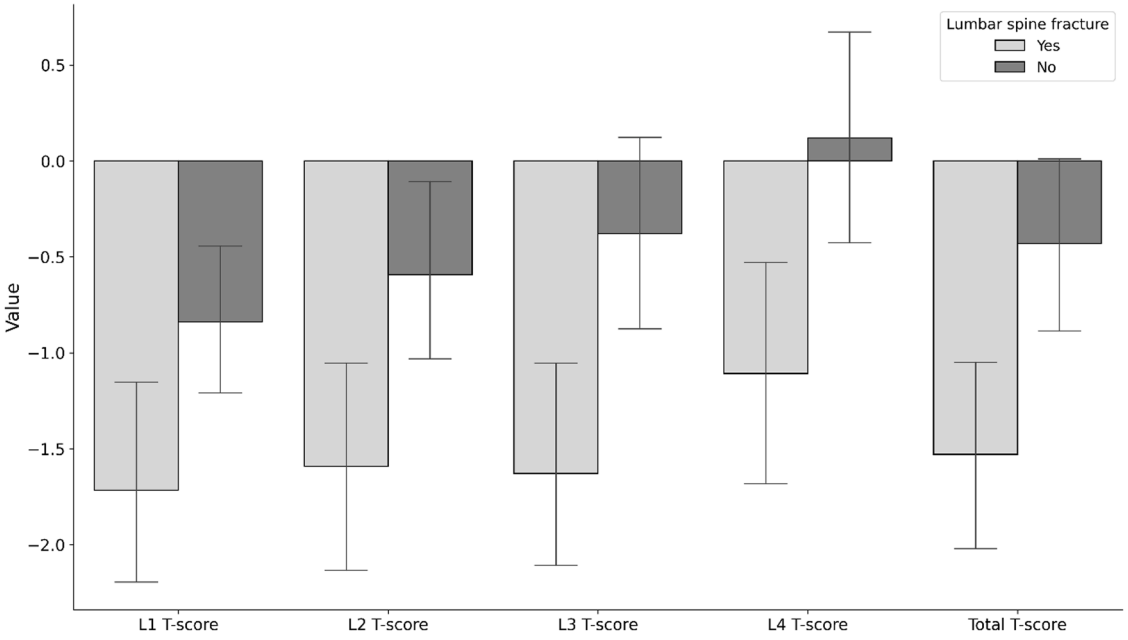

Fig. 4. Relationship between spine T-score values and lumbar spine fractures.

peripheral circulation, these results were due to the reduced BTM elimination by the liver and the kidney. On the other hand, no elevation in serum CTX level was found in postmenopausal women with decreased BMD in the study of Naeem et al. [48]. BALP is another enzyme released by osteoblast that reflects mineralisation phase of bone formation and can be used as marker of bone formation [51]. Schiefke et al. [49] evaluated BTM in non-cirrhotic CLD patients, and found BALP and intact parathyroid hormone (iPTH) to be significantly elevated in more advanced stage of liver fibrosis. Significant inverse correlation of iPTH to BMD at the femoral neck region has been noted. Although elevation of iPTH correlated with BALP increase, no significant relationship between BALP and DXA parameters was found. In the present study, BALP was also used for the assessment of bone turnover. The values were in majority of patients in reference range, with no statistically significant difference between non-fractured and fractured group. However, BALP was in statistically significant correlation with hip and spine BMD and T-score values. This suggests that it could be a useful biomarker for HO monitoring in ESLD, as previously noticed for patients suffering from other illnesses such as diabetes or systemic lupus erythematosus [52, 53].

As expected, we found a statistically significant increase in the probability of major fracture according to the FRAX questionnaire in the fractured group (Table 3). However, since many patients had more than one fracture, the fracture probability in those subjects may be underestimated. Such patients should therefore be under special attention of both, internists, and radiologists, so the continuous monitoring and adequate treatment could be carried out.

Advantages

The main advantage of the present study is the inclusion of a specific group of patients with liver cirrhosis and related complications, free from other common independent causes of bone loss such as CKD, diabetes, and malignancies. So, the study group was designed to evaluate primarily the effects of the liver disease on the bone health. The DXA measurement was obtained in a single centre, using the same device, and interpreted by an experienced endocrinologist. The X-ray images were blindly analysed by two musculoskeletal radiologists to improve overall accuracy in detection and grading of fragility fractures.

Limitations

There are several limitations of our study. The type of cirrhosis was predominantly alcoholic for both sexes, so no relevant analyses between different groups according to cirrhotic type could have been made. There were no healthy controls included in study. Most of female patients were postmenopausal, and no influence of hormonal status was observed. We didn't exclude patients with ascites prior to DXA assessment. Except for BALP, no other commonly used BTM were analysed.

Conclusions

There is a high prevalence of spinal fragility fractures among liver transplant candidates due to cirrhosis in Croatia. Besides the older age, there was no significant relationship between prevalent spinal fragility fractures and clinical and laboratory parameters. 25-OH-D insufficiency was highly prevalent, but with no effect to bone fragility. Regarding noted discrepancy between X-ray and DXA assessment, both methods for evaluation of impaired bone status are warranted in pretransplant period. DXA measurement seems to be more relevant for the prediction of lumbar fragility fractures. Although BALP showed significant association with hip and lumbar BMD and T-score, its usefulness in detecting HO and fracture prediction in ESLD needs to be further investigated. Searching for new predictive biomarkers and risk factors as well as implementing additional imaging techniques for the better assessment of bone loss in liver transplant candidates is needed, since timely recognition of fragility fractures could decrease patient's morbidity in peritransplant period.

Declaration of Competing Interest

None.

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