Original Article

DOI: 10.4274/haseki.galenos.2025.29484
Med Bull Haseki 2025;63(5):252-257

Impact of the Severity of Steatosis due to Non-alcoholic Fatty Liver Disease on Bone Mineral Density in Patients with Osteoporosis

Aylin Ayyildiz*, Selda Ciftci Inceoglu**, Canan Alkim***, Banu Kuran**

*University of Health Sciences Türkiye, Basaksehir Cam ve Sakura City Hospital, Clinic of Physical Medicine and Rehabilitation, Istanbul, Türkiye

**University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Istanbul, Türkiye

***University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital, Clinic of Gastroenterology, Istanbul, Türkiye

Abstract

Aim: Osteoporosis can occur in individuals with liver disease, and its development is thought to be influenced by the activity of the underlying hepatic disorder, as noted in previous studies. This study aimed to investigate the influence of the degree of liver steatosis, an important indicator of non-alcoholic fatty liver disease (NAFLD) severity, on bone mineral density (BMD).

Methods: Between August 2022 and July 2023, this cross-sectional study enrolled patients aged 50 to 90 years who were followed at an osteoporosis clinic and had a diagnosis of NAFLD confirmed by ultrasonography (US). Based on abdominal ultrasound findings, patients were classified into four groups reflecting the degree of liver steatosis. The groups were compared with respect to T-scores and BMD at the total spine, femur, and femoral neck, measured by dual-energy X-ray absorptiometry.

Results: Of the 792 patients assessed for eligibility, 248 met the inclusion criteria. The participants had a mean age of 65.1±11.2 years, and 97.6% (n=242) were female. The mean body mass index was 27.31±4.58 kg/m^2. Significant between-group differences were detected for lumbar total T-scores. A significant difference was identified in the lumbar spine T-score evaluation between the grade 3 and grade 0 groups in abdominal US imaging.

Conclusion: Because NAFLD and osteoporosis share several risk factors and involve chronic inflammation, NAFLD is considered a potential risk factor for bone loss. The findings of our study demonstrate that the risk of low BMD in the lumbar spine is elevated, particularly in advanced stages of liver steatosis.

Keywords: Bone mineral density, liver steatosis, non-alcoholic fatty liver disease, osteoporosis

Introduction

Non-alcoholic fatty liver disease (NAFLD) represents a continuum of chronic liver disorders encompassing simple steatosis, non-alcoholic steatohepatitis, fibrosis, cirrhosis, and ultimately hepatocellular carcinoma (HCC) (1). Non-alcoholic fatty liver disease, a metabolic disorder of the liver, is increasingly prevalent and is estimated to affect approximately 25% of the global population. It is estimated that 3.5 million new cases are diagnosed annually (2). Non-alcoholic fatty liver disease is the most common chronic liver condition globally and imposes a significant health and economic burden (3). Recently, the terminology has been updated to metabolic dysfunction-associated fatty liver disease and subsequently to metabolic dysfunction-

Corresponding Author: Aylin Ayyildiz, MD, University of Health Sciences Türkiye, Basaksehir Cam ve Sakura City Hospital, Clinic of Physical Medicine and Rehabilitation, Istanbul, Türkiye
E-mail: aylin.mrt93@gmail.com **ORCID:** orcid.org/0000-0002-7163-8234
Received: 21.04.2025 **Accepted:** 28.10.2025 **Publication Date:** 28.11.2025

Cite this article as: Ayyildiz A, Ciftci Inceoglu S, Alkim C, Kuran B. Impact of the severity of steatosis due to non-alcoholic fatty liver disease on bone mineral density in patients with osteoporosis. Med Bull Haseki. 2025;63(5):252-257

associated steatotic liver disease (MASLD), following the Delphi consensus statement. This revision reflects recognition that metabolic disorders—including abdominal obesity, type 2 diabetes, dyslipidemia, insulin resistance, and cardiovascular disease—are commonly associated with NAFLD (4).

Osteoporosis is a common systemic condition characterized by decreased bone mass and deterioration of bone microarchitecture. According to the World Health Organization, it affects approximately 6.3% of men aged 50 years or older and 21.2% of women aged 50 years or older worldwide. Additionally, it is estimated that approximately 37 million fragility fractures occur annually among individuals older than 55 years, corresponding to approximately 70 fractures per minute globally (5). A substantial body of research has highlighted the causal relationship between NAFLD and osteoporosis (1). These two diseases share similar risk factors, including older age, obesity, type 2 diabetes mellitus, and a sedentary lifestyle (6). The prevalence of osteoporosis is higher in patients with chronic liver disease than in people without liver disease, with figures ranging from 10% to 40% (7). Studies have shown that the prevalence of osteoporotic fractures is 2.5 times as high in individuals with NAFLD as in those without the condition (8). Substantial evidence from the literature substantiates the presence of osteoporosis in individuals with chronic liver disease. Nevertheless, no study has yet evaluated the impact of disease severity on osteoporosis.

In our study, we hypothesized that bone mineral density (BMD) would be lower in patients with a high degree of hepatic steatosis. The purpose of this study was to evaluate how different levels of liver steatosis affect BMD in patients with NAFLD. Consequently, this study will facilitate the incorporation of liver stenosis as a risk factor into osteoporosis clinical practice.

Materials and Methods

Compliance with Ethical Standards

The study received approval from the Ethics Committee of the University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital, (approval number: 4061, date: 29.08.2023). Informed consent was obtained from all participants during their initial outpatient visit. The research was conducted in accordance with the Declaration of Helsinki and adhered to the Strengthening the Reporting of Observational Studies in Epidemiolog guidelines for observational studies.

Study Design

Patients followed at the osteoporosis outpatient clinic of our hospital between August 2022 and July 2023 were screened in this cross-sectional study. Throughout the study period, 792 patients followed at our osteoporosis clinic were assessed for eligibility. Inclusion criteria required that participants be aged 50-90 years, be either men or postmenopausal women, and have undergone abdominal ultrasonography (US) within six months of their dual-energy X-ray absorptiometry (DXA) assessments. Furthermore, they were required to have US-defined NAFLD and a diagnosis of NAFLD by a gastroenterologist at our hospital. Individuals with any disease that would impair liver function (e.g., hemochromatosis, HCC, cirrhosis), a history of malignancy, or a history of surgery and biopsy of the liver, bile ducts, or intestines were excluded from this study.

Patients meeting the inclusion criteria underwent abdominal US to assess the degree of hepatic steatosis, on the basis of which they were assigned to one of four groups. The grading of steatosis was as follows: Grade 0 (absent)—normal liver echotexture; Grade 1 (mild)—slight, diffuse increase in echogenicity with clear visualization of the diaphragm and portal vein walls; Grade 2 (moderate)—moderate echogenicity elevation with partial blurring of the diaphragm and portal vein walls; and Grade 3 (severe)—pronounced echogenicity increase, with poor or absent visualization of the diaphragm, portal vein wall, and posterior right hepatic lobe (9). Demographic and clinical data, including age, sex, height, weight, body mass index (BMI), and comorbid conditions, were retrieved from the hospital records. Laboratory assessments included albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase, alkaline phosphatase, phosphorus, calcium, 25-hydroxyvitamin D, and international normalized ratio. Bone mineral density and T-scores for the lumbar spine (L1-L4 and L2-L4), femoral neck, and total femur were determined using DXA.

Statistical Analysis

Descriptive statistics included the mean, standard deviation, median, minimum, maximum, frequencies, and proportions. The Kolmogorov–Smirnov test was employed to assess the distribution of variables. The homogeneity of variances was evaluated using the Bartlett's test; since the variances were homogeneous, the Analysis of Variance F-test p-value was used. Subsequent between-group comparisons were conducted using the Bonferroni correction for post-hoc analyses. Statistical analyses were conducted using Jamovi (The Jamovi Project, 2024; Version 2.5) (Computer software), retrieved from https://www.jamovi.org, Sydney, Australia.

Results

Of 792 patients screened according to the study criteria, 248 were included in the study (Figure 1). Participants had a mean age of 65.1±11.2 years, and 242 (97.6%) were female. Their mean BMI was 27.31±4.58 kg/m². The remaining demographic and clinical features are provided in Table 1.

Abdominal US scores were used to divide patients into four groups, which were then compared with total lumbar spine, femoral neck, and total femur T-scores. A Statistically significant difference was identified between the groups for lumbar total T-scores (p=0.027). Nevertheless, no significant differences were observed between the groups for femoral neck and total femur T-scores (p=0.073 and p=0.088, respectively) (Table 2). To ascertain the stages at which this statistically significant difference occurred, a post-hoc comparison was conducted using the Bonferroni correction. Consequently, it was determined that the notable difference was between Grade 0 and Grade 3 (p=0.46). There was no significant difference among the remaining groups (p=0.995, p=0.436) (Table 3).

All patients were evaluated, without grouping, for potential correlations between AST, ALT, and CRP levels and T-scores of the total lumbar spine, femoral neck, and total femur, as well as BMD values. Nevertheless, no statistically significant correlation was identified (p>0.05).

Discussion

The findings of our investigation demonstrated that the presence of advanced liver steatosis is associated with a reduction in BMD in the lumbar spine in patients diagnosed with NAFLD. Chen et al. (10) reported that individuals with moderate-to-severe NAFLD had an increased risk of osteoporosis, whereas no significant association was observed in patients with mild NAFLD. In a cohort study by Shen et al. (11), patients with NAFLD had an increased risk of both osteoporosis and osteopenia. Additionally, a correlation was identified between the increase in fibrosis markers and the decrease in BMD. In a cross-sectional study of postmenopausal women, Lee et al. (12) found that NAFLD patients had reduced BMD, particularly at the lumbar spine and femoral neck, whereas no significant decrease was observed in the total femur. According to Moon et al. (13), postmenopausal women diagnosed with NAFLD exhibited reduced BMD at the lower lumbar spine, whereas this association was not observed among premenopausal women. In the current study, both male and postmenopausal female participants were assessed. The analysis revealed that lumbar spine BMD varied with the degree of hepatic steatosis. In contrast, BMD values at the total femur and femoral neck showed no statistically significant differences. Xie et al. (14) demonstrated a positive association between BMD and the presence of advanced fibrosis or cirrhosis. Furthermore, an independent negative correlation between NAFLD and BMD was observed in individuals aged 20-59 years.

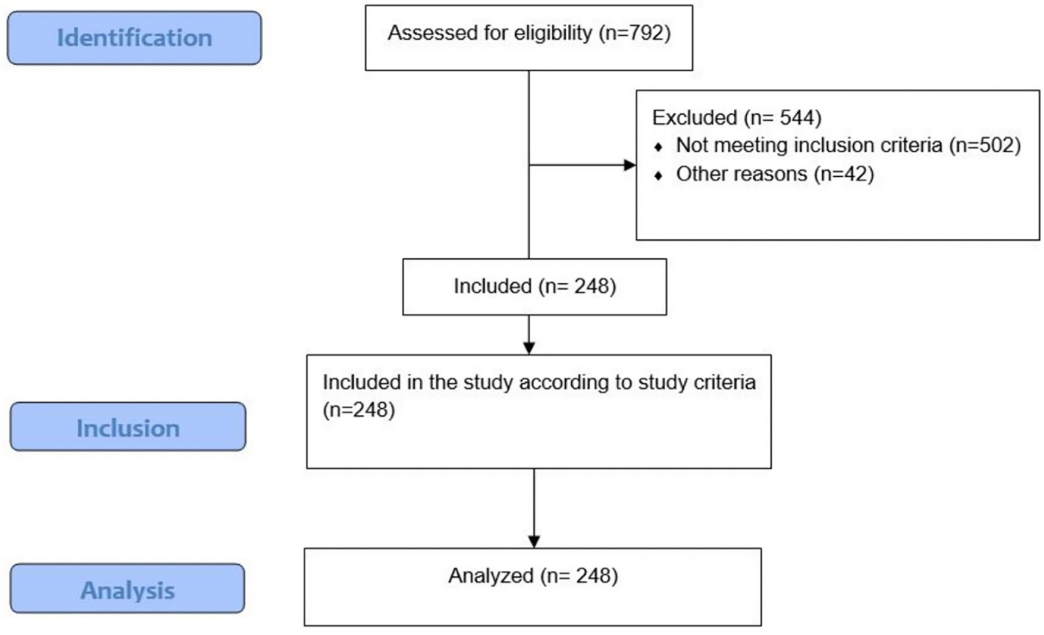

Figure 1. Flow chart of the study

Table 1. Demographic and clinical values of patients		
	Mean/ number	Standard deviation %
Age	65.1	11.2
Sex (number)		
Female	242	97.6
Male	6	2.4
Height (cm)	157.218	7.028
Weight (Kg)	67.375	11.300
Body mass index (kg/m²)	27.313	4.589
L1-L4 BMD	0.911	0.129
L2-L4 BMD	0.927	0.138
L1-L4 total T-score	-2.279	1.050
L2-L4 total T-score	-2.341	1.069
Femur neck BMD	0.745	0.106
Femur total BMD	0.795	0.113
Femur neck T-score	-2.102	0.810
Femur total T-score	-1.655	0.936
Albumin (g/dL)	4.737	3.673
ALP (IU/L)	69.395	25.250
ALT (IU/L)	17.354	12.532
AST (IU/L)	20.493	9.584
Phosphorus (mg/dL)	3.543	0.572
GGT (IU/L)	20.069	16.532
Calcium (mg/dL)	9.54	0.485
25-hidroxy vitamin D (ng/mL)	30.558	12.544
INR	1.050	0.264
APTT	28.031	11.801
PT	13.285	3.678

BMD: Bone mineral density, ALP: Alkaline phosphatase, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma-glutamyl transpeptidase, INR: International normalized ratio, APTT: Activated partial thromboplastin time, PT: Prothrombin time

Table 2. Comparison of lumbar total, femur neck and femur total T-scores according to abdominal USG grading				
Abdominal USG	**N**	**Mean**	**SD**	**p**
L1-L4 T Score				**0.027***
Grade 0	71	-2.55	0.901	
Grade 1	63	-2.10	0.997	
Grade 2	62	-2.35	1.099	
Grade 3	52	-2.05	1.171	
FN T-score				0.073
Grade 0	71	-2.26	0.724	
Grade 1	63	-1.93	0.891	
Grade 2	62	-2.18	0.764	
Grade 3	52	-2.00	0.840	
FT T-score				0.088
Grade 0	71	-1.88	0.955	
Grade 1	63	-1.53	0.869	
Grade 2	62	-1.65	0.932	
Grade 3	52	-1.51	0.960	

*: P≤0.05 means statistically significant, One-Way ANOVA (Fisher's)
USG: Ultrasound, SD: Standard deviation, FN: Femur neck, FT: Femur total

Table 3. Intergroup comparison of lumbar total (L1-L4) T-scores				
Abdominal USG	**Grade 0**	**Grade 1**	**Grade 2**	**Grade 3**
Grade 0				
Mean difference	—	-0.446	-0.201	**-0.4946**
p-value	—	0.064	0.679	**0.046***
Grade 1				
Mean difference		—	0.245	-0.0481
p-value		—	0.549	0.995
Grade 2				
Mean difference			—	-0.2932
p-value			—	0.436
Grade 3				
Mean difference				—
p-value				—

*: P≤0.05 means statistically significant, Tukey Post-hoc test
USG: Ultrasound

Despite numerous supporting studies, the risk of osteoporosis in individuals with NAFLD remains a subject of debate within the scientific community. In their retrospective cohort analysis, Sung et al. (15) found that the presence of NAFLD was not significantly associated with the occurrence of osteoporosis. It is plausible that the observed discrepancy arises from the larger representation of mild NAFLD cases and the comparatively brief observation period of two years. In a meta-analysis conducted by Vachliotis et al. (6), numerous studies reported no association between NAFLD and osteoporosis. Nevertheless, it is imperative to acknowledge that these studies were conducted in heterogeneous groups. Consequently, it is not possible to reach a definitive conclusion. Furthermore, although some studies have not identified a correlation between NAFLD and BMD, elevated serum ALT levels have been linked to reduced BMD (16-18). It has been demonstrated that increases in ALT levels serve as indicators of liver damage in advanced chronic liver disease. This finding provides further evidence to support the hypothesis that a reduction in BMD may occur in the context of advanced steatosis. However, the present study did not identify a correlation between ALT levels and BMD.

The pathophysiology of osteoporosis in chronic liver diseases is complex. The mechanism underlying the

development of NAFLD involves increased osteoclastic activity, modulated via the receptor activator of nuclear factor κB ligand (RANKL)/RANK–osteoprotegerin (OPG) pathway. Receptor activator of nuclear factor κB ligand, via its receptor, RANK, stimulates osteoclastogenesis; in contrast, OPG, a second RANKL receptor that acts as a decoy, restrains osteoclastogenesis and inhibits bone loss by binding RANKL, thereby preventing the RANK-RANKL cascade. In chronic liver diseases, the concentration of soluble RANKL in the extracellular matrix increases, thereby accelerating bone turnover. Despite the increase in OPG production to promote hemostasis and elevate the OPG/RANKL ratio, this increase is not sufficient. Furthermore, chronic liver diseases are characterized by sustained inflammatory processes. Proinflammatory cytokines, including interleukin-1, interleukin-6, and tumor necrosis factor-α (TNF-α) when produced, cause bone resorption in two ways: directly by increasing osteoclast activity and indirectly by increasing RANKL production. Furthermore, TNF-α has been demonstrated to enhance osteoclastogenesis via colony-stimulating factor-1 receptor gene expression, a mechanism that operates independently of the RANKL pathway (19). Furthermore, the synthesis of select hepatokines, including fibroblast growth factor-21 and insulin-like growth factor-binding protein-1, is elevated during the pathogenesis of NAFLD. These can cause bone loss via two distinct mechanisms: first, through the action of RANKL, and second, through binding to integrin-beta. Fibroblast growth factor-21 suppresses the maturation of bone marrow–derived mesenchymal stem cells into osteoblasts through interaction with the peroxisome proliferator-activated receptor-γ (6).

The term "NAFLD" has been modified to reflect its association with metabolic disorders, including obesity. This enabled the establishment of an association between NAFLD and osteoporosis, the most severe metabolic bone disease. Previously, it was postulated that elevated BMI was associated with increased BMD. It was argued that osteocytes are active in response to mechanical loading, particularly in relation to weight, and that bone formation is enhanced as a result (20). Nevertheless, a considerable body of recent research has demonstrated that fracture risk is elevated in individuals with obesity even when BMD is within the normal or high range (21). In particular, low muscle mass in obesity reduces the mechanical load applied to bone, thereby increasing the risk of falls in sarcopenic obesity. Metabolically unhealthy obesity, often accompanied by reduced muscle mass, is an important determinant of osteoporosis and fracture susceptibility. In a comprehensive review, Khanmohammadi and Kuchay (22) reported that individuals with MASLD have an increased risk of low BMD and fractures. Nevertheless, it was underscored that additional research is imperative, particularly for this recently designated disease with evolving diagnostic criteria.

Study Limitations

The main limitation of this research is the relatively small sample size. In the present study, NAFLD diagnosis and grading were performed using US, whereas neither elastography nor liver biopsy was used. The study population included only postmenopausal patients and male patients; premenopausal patients were excluded. Despite these limitations, our study can be considered the first to reveal the effect of liver steatosis on osteoporosis. Further research is required to assess this issue in greater depth.

Conclusion

This study demonstrated that patients with NAFLD showing advanced grades of hepatic steatosis tend to have reduced BMD, particularly at the lumbar spine. These observations imply that increasing steatosis severity may play a role in bone deterioration, underscoring the need to recognize NAFLD as a possible contributing factor in osteoporosis management.

Ethics

Ethics Committee Approval: The study received approval from the Ethics Committee of the University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital, (approval number: 4061, date: 29.08.2023).

Informed Consent: Informed consent was obtained from all participants during their initial outpatient visit.

Footnotes

Authorship Contributions

Concept: A.A., S.C.I., B.K., Design: A.A., S.C.I., C.A., Data Collection or Processing: S.C.I., B.K., Analysis or Interpretation: S.C.I., C.A., Literature Search: A.A., S.C.I., Writing: A.A., B.K.

Conflict of Interest: No conflicts of interest or competing interests have been reported by the authors or any individuals with control over the content of this article.

Financial Disclosure: No financial support was received for this paper or the research that resulted in this paper.

References

1. Zhou Y, Ni Y, Wang Z, Prud'homme GJ, Wang Q. Causal effects of non-alcoholic fatty liver disease on osteoporosis: a Mendelian randomization study. Front Endocrinol (Lausanne). 2023;14:1283739
2. Stefan N, Cusi K. A global view of the interplay between non-alcoholic fatty liver disease and diabetes. Lancet Diabetes Endocrinol. 2022;10:284-96.
3. Younossi Z, Anstee QM, Marietti M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol. 2018;15:11-20.
4. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol. 2023;79:1542-56.
5. Tao J, Li H, Wang H, Tan J, Yang X. Metabolic dysfunction-associated fatty liver disease and osteoporosis: the mechanisms and roles of adiposity. Osteoporos Int. 2024;35:2087-98.
6. Vachliotis ID, Anastasilakis AD, Goulas A, Goulis DG, Polyzos SA. Nonalcoholic fatty liver disease and osteoporosis: a potential association with therapeutic implications. Diabetes Obes Metab. 2022;24:1702-20.
7. Guañabens N, Parés A. Osteoporosis in chronic liver disease. Liver Int. 2018;38:776-85.
8. Li M, Xu Y, Xu M, et al. Association between nonalcoholic fatty liver disease (NAFLD) and osteoporotic fracture in middle-aged and elderly Chinese. J Clin Endocrinol Metab. 2012;97:2033-8.
9. Ferraioli G, Soares Monteiro LB. Ultrasound-based techniques for the diagnosis of liver steatosis. World J Gastroenterol. 2019;25:6053-62.
10. Chen DZ, Xu QM, Wu XX, et al. The combined effect of nonalcoholic fatty liver disease and metabolic syndrome on osteoporosis in postmenopausal females in Eastern China. Int J Endocrinol. 2018;2018:2314769.
11. Shen Z, Cen L, Chen X, et al. Increased risk of low bone mineral density in patients with non-alcoholic fatty liver disease: a cohort study. Eur J Endocrinol. 2020;182:157-64.
12. Lee DY, Park JK, Hur KY, Um SH. Association between nonalcoholic fatty liver disease and bone mineral density in postmenopausal women. Climacteric. 2018;21:498-501.
13. Moon SS, Lee YS, Kim SW. Association of nonalcoholic fatty liver disease with low bone mass in postmenopausal women. Endocrine. 2012;42:423-9.
14. Xie R, Liu M. Relationship between non-alcoholic fatty liver disease and degree of hepatic steatosis and bone mineral density. Front Endocrinol (Lausanne). 2022;13:857110.
15. Sung J, Ryu S, Song YM, Cheong HK. Relationship between non-alcoholic fatty liver disease and decreased bone mineral density: a retrospective cohort study in Korea. J Prev Med Public Health. 2020;53:342-52.
16. Umehara T. Nonalcoholic fatty liver disease with elevated alanine aminotransferase levels is negatively associated with bone mineral density: cross-sectional study in U.S. adults. PLoS One. 2018;13:e0197900.
17. Xia MF, Lin HD, Yan HM, et al. The association of liver fat content and serum alanine aminotransferase with bone mineral density in middle-aged and elderly Chinese men and postmenopausal women. J Transl Med. 2016;14:11.
18. Purnak T, Beyazit Y, Ozaslan E, Efe C, Hayretci M. The evaluation of bone mineral density in patients with nonalcoholic fatty liver disease. Wien Klin Wochenschr. 2012;124:526-31.
19. Yang YJ, Kim DJ. An overview of the molecular mechanisms contributing to musculoskeletal disorders in chronic liver disease: osteoporosis, sarcopenia, and osteoporotic sarcopenia. Int J Mol Sci. 2021;22:2604.
20. Walsh JS, Vilaca T. Obesity, type 2 diabetes and bone in adults. Calcif Tissue Int. 201;100:528-35.
21. Sadeghi O, Saneei P, Nasiri M, Larijani B, Esmaillzadeh A. abdominal obesity and risk of hip fracture: a systematic review and meta-analysis of prospective studies. Adv Nutr. 2017;8:728-38.
22. Khanmohammadi S, Kuchay MS. Effects of metabolic dysfunction-associated steatotic liver disease on bone density and fragility fractures: associations and mechanisms. J Obes Metab Syndr. 2024;33:108-20.