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Association of body mass index and sarcopenia with osteoporosis: a predictive nomogram model for risk assessment

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Abstract

Objective: Body mass index (BMI) and sarcopenia are linked to osteoporosis, but the extent to which BMI influences osteoporosis through sarcopenia remains unclear. This study aims to assess the associations between BMI, sarcopenia, and osteoporosis, and to explore the predictive value of their combined biochemical markers for osteoporosis.

Methods: We retrospectively collected clinical data from 813 inpatients in the endocrinology department to explore the relationships between serum markers and skeletal muscle mass or BMI, and to evaluate the predictive value of BMI and sarcopenia for osteoporosis. Mediation analysis was employed to examine the associations among BMI, sarcopenia, and osteoporosis. Participants were randomly divided into training ($n = 407$) and testing ($n = 406$) sets (5:5). Independent risk factors were identified using least absolute shrinkage and selection operator and logistic regression, leading to the development of a nomogram model. Model evaluation was conducted through receiver operating characteristic curves, confusion matrices, calibration curves, decision curve analysis (DCA), and clinical impact curves (CIC).

Results: BMI and skeletal muscle mass were negatively correlated with serum 25-hydroxyvitamin D and calcium levels. The "BMI < 28 and Non-Sarcopenia" emerged as a protective factor against osteoporosis. Sarcopenia significantly mediated the association between BMI and osteoporosis (46.88%). Gender, age, high-density lipoprotein, alkaline phosphatase, BMI, and sarcopenia emerged as independent predictors of osteoporosis. The area under the curve (AUC) for the training and testing sets was 0.859 and 0.866, respectively, with calibration curves indicating good consistency. DCA and CIC demonstrated clinical net benefits at risk thresholds of 0.02–0.82 and 0.02–0.67. Sankey diagrams and partial AUCs (1.00–0.75 sensitivity and specificity) illustrate the significant negative predictive value of BMI and sarcopenia.

Conclusion: Lower BMI and non-sarcopenia are negatively associated with the risk of osteoporosis. In addition, the nomogram demonstrates good predictive value, with a greater negative predictive value of the BMI and sarcopenia.

Keywords: body mass index, osteoporosis, predictive model, sarcopenia

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Introduction

Osteoporosis is a progressive, systemic skeletal disorder characterized by decreased bone mineral density (BMD) and deterioration of bone microarchitecture, leading to increased bone fragility and susceptibility to fractures.[1] This condition is associated with various adverse health outcomes, notably fragility fractures, which significantly impair quality of life and life expectancy while imposing substantial economic burdens.[2] As a multifactorial disease, understanding the modifiable lifestyle factors associated with osteoporosis is essential for its prevention and treatment. Previous studies have established a link between

sarcopenia and osteoporosis in the elderly.[3,4] Both bone and skeletal muscle are metabolically active tissues, and a balanced interaction between them is crucial for maintaining bone density and muscle mass. Skeletal muscle releases various endocrine molecules that influence bone health, including insulin-like growth factor-1, osteoglycin, irisin, and osteonectin.[5] Consequently, the deterioration of muscle mass and function may contribute to a decrease in BMD. Moreover, patients with both osteoporosis and sarcopenia face an increased risk of hospitalization, falls, and fractures compared to those with sarcopenia alone.[6]

In addition to age-related bone loss, metabolic disorders such as obesity and type 2 diabetes can accelerate detrimental changes in bone homeostasis, leading to the early onset of osteoporosis.[7] Additionally, corticosteroid administration is a risk factor contributing to osteoporosis development.[8] However, some studies suggest that obesity may serve as a protective factor against osteoporosis, with obese individuals exhibiting a lower risk of developing the condition compared to their non-obese counterparts, thereby giving rise to the so-called obesity paradox.[9] At the same time, obesity can lead to insulin resistance in skeletal muscle, causing metabolic disorder, inducing intracellular lipotoxicity and low-grade inflammation, which leads to increased oxidative stress and cell apoptosis. In addition, under the influence of cytokine paracrine signaling, muscle progenitor cells differentiate into adipocyte-like phenotypes, resulting in reduced muscle regeneration, and increased fat infiltration, and thus promoting or exacerbating the development of sarcopenia.[10] Previous studies have established a connection between obesity, sarcopenia, and osteoporosis, a triad known as "osteosarcopenic obesity" (OSO), which can lead to impaired function and systemic metabolic dysregulation.[11] Fortunately, OSO is less prevalent than osteoporosis alone. Moreover, unlike osteoporosis, both obesity and sarcopenia are relatively more amenable to lifestyle modifications, offering potential avenues for intervention.[12] This study aims to assess the effects of obesity and sarcopenia on osteoporosis while investigating the predictive value of their combined biochemical markers for osteoporosis. The goal is to identify potential intervention strategies for preventing the onset and progression of the condition. Furthermore, this research complies with the "Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis" (TRIPOD) guidelines, with Supplemental Materials available for detailed information.

Methods

Patients

This retrospective study selected patients from the endocrinology department of our hospital between June 2020 and June 2024. Inclusion criteria required patients to undergo dual-energy X-ray absorptiometry (DXA; Osteosys Dexxum-T; Osteosys; Korea). Exclusion criteria included: (1) physical activity limitations; (2) coexisting malignancies or infectious diseases; (3) endocrine disorders such as hyperthyroidism, hypothyroidism, Cushing's syndrome, adrenal insufficiency, acromegaly, growth hormone deficiency, and anterior pituitary insufficiency; (4) history of vitamin D, calcium supplements, corticosteroids, weight loss medications, thyroid hormones, or growth hormone use; (5) incomplete clinical data; and (6) severe cardiovascular or other congenital diseases. This study was approved by the ethics committee of our institution (Approval No. 2024-02-03).

Clinical characteristics

General characteristics: Gender, age, body mass index (BMI), smoking, diabetes, systolic blood pressure, and diastolic blood pressure; Biochemical Markers: Serum albumin (ALB), aspartate aminotransferase, alkaline phosphatase (ALP), triglycerides, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein, fasting blood glucose (FBG), glycosylated hemoglobin (HbA1c), uric acid, serum creatinine, blood urea nitrogen (BUN), fasting insulin (FINS), 25-hydroxyvitamin D (25(OH)D), calcium (Ca), platelets (PLT), neutrophils (NEU), lymphocytes (LYM), and monocytes (MON).

Osteoporosis and sarcopenia

BMD and muscle mass were assessed using DXA. A lumbar spine T-score of < -2.5 indicates osteoporosis. Sarcopenia was defined according to the guidelines established by the Foundation for the National Institutes of Health, using the ratio

of appendicular lean mass (ALM) to BMI. Specifically, values $<0.512\,kg/m^2$ for women and $<0.789\,kg/m^2$ for men indicate sarcopenia.[13,14]

Combined assessment of BMI and sarcopenia

Participants were categorized into two groups based on BMI: <28 and $\geqslant 28\,kg/m^2$. Sarcopenia was also classified into two groups: presence (Yes) and absence (No). Based on the combined assessment of BMI and sarcopenia, patients were classified into four categories: "BMI $\geqslant$ 28 and Sarcopenia," "BMI $\geqslant$ 28 and Non-Sarcopenia," "BMI $<$ 28 and Sarcopenia," and "BMI $<$ 28 and Non-Sarcopenia."

Systemic inflammatory markers

Systemic inflammatory markers include the systemic immune-inflammation index (SII) and the systemic inflammation response index (SIRI). SII is defined as the product of peripheral blood PLT and NEU divided by the LYM count, calculated as SII = (NEU $\times$ PLT)/LYM. SIRI is defined as the product of NEU and MON divided by the LYM count, calculated as SIRI = (NEU $\times$ MON)/LYM.[15]

Statistical analysis

All statistical analyses were performed using R Studio software (v4.2.3, http://www.rproject.org/). The "plotRCS" package was employed to create restricted cubic spline plots, examining the dose-response relationships among serum calcium, 25(OH)D, muscle lean mass, and BMI. Logistic regression, both adjusted and unadjusted, was conducted using the "rms" package to determine the assessment value of the BMI and sarcopenia for osteoporosis. Mediation analysis (1000 bootstrap) was employed to explore the direct and indirect associations between BMI, sarcopenia, and osteoporosis. The "glmnet" package was employed for least absolute shrinkage and selection operator (LASSO) regression and multifactorial logistic regression to identify predictors of osteoporosis. Nomograms were generated using the "nomogramFormula" package. Receiver operating characteristic (ROC) curves and partial ROC (pROC) curves were plotted using the "pROC" package. Model performance was evaluated with confusion matrices from the "epiR" package. Calibration curves and goodness-of-fit tests (Hosmer–Lemeshow) were conducted using the "rms" package. Decision curve analysis (DCA) and clinical impact curves (CIC) were created using the "rmda" package. $p < 0.05$ was considered statistically significant. Detailed information is provided in Information S1.

Results

General results

Based on the inclusion and exclusion criteria, a total of 813 patients were included in the study, comprising 327 males and 486 females, with an age range of 47–94 years and a mean age of 59.57 ± 14.74 years (comparative data on osteoporosis and non-osteoporosis patients can be found in Table S1). Among these patients, 104 were diagnosed with osteoporosis, resulting in a prevalence rate of 12.79%.

Relationship between ALM, BMI, and parameters related to osteoporosis

BMI exhibits a negative linear correlation with serum 25(OH)D ($p < 0.001$, $P_{nonlinear} = 0.154$) and a negative nonlinear correlation with serum Ca ($p < 0.001$, $P_{nonlinear} = 0.007$). In addition, ALM shows a negative linear correlation with serum 25(OH)D and Ca ($p < 0.001$ and 0.147, $P_{nonlinear} = 0.156$ and 0.778; Figure S1). Figure 1 indicates that "BMI $<$ 28 and Sarcopenia" and "BMI $<$ 28 and Non-Sarcopenia" serve as protective factors against osteoporosis compared to "BMI $\geqslant$ 28 and Sarcopenia." Figure 2 demonstrates that sarcopenia mediates the relationship between BMI and osteoporosis with mediation proportions of 814.81% ($p < 0.001$) and 46.88% ($p < 0.001$) in unadjusted and adjusted analyses, respectively. No significant mediating effect of BMI was observed between sarcopenia and osteoporosis ($p = 0.284$ and 0.096).

Development of the nomogram model

Random sampling was conducted using the createDataPartition function from the R "caret" package, dividing the collected cases into training ($n = 407$) and testing ($n = 406$) sets in a 5:5 ratio, with all features exhibiting $p > 0.05$ (Table 1, Information S2, Table S2, and Figure S2). To prevent overfitting, each feature required a minimum of 10–15 patients for model development.[16,17] Consequently, with 407 patients in the

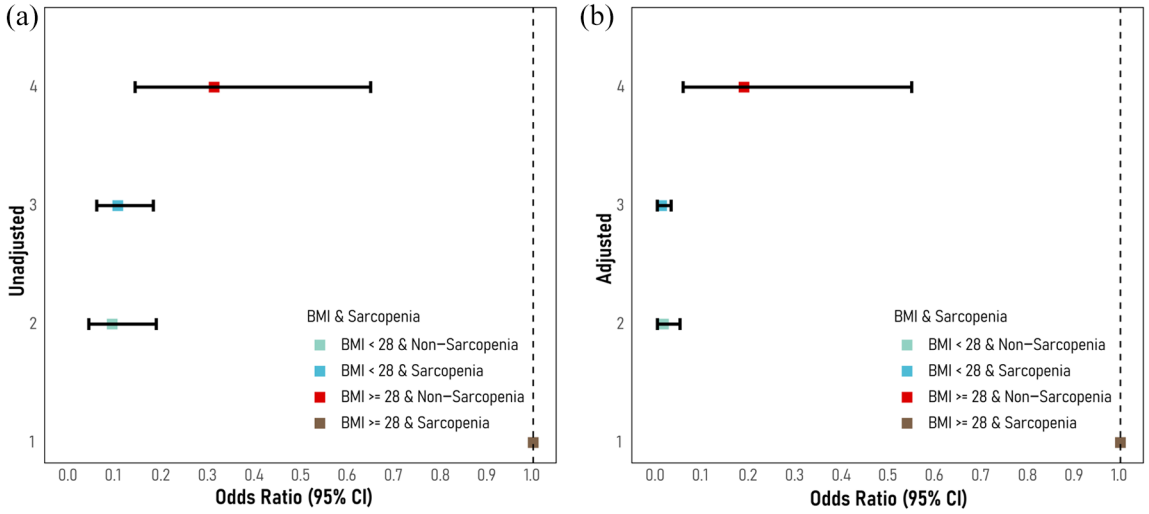

Figure 1. BMI and sarcopenia in the combined assessment for osteoporosis: adjusted and unadjusted logistic regression forest plots. (a) Unadjusted logistic regression results of the combined assessment of BMI and sarcopenia. (b) Adjusted logistic regression results of the combined assessment of BMI and sarcopenia after adjustment for SBP, DBP, ALB, AST, ALP, TG, TC, HDL, LDL, FBG, HbA1c, UA, Scr, BUN, FINS, Ca, SII, SIRI.
ALB, albumin; ALP, alkaline phosphatase; AST, asparagine aminotransferase; BUN, blood urea nitrogen; Ca, calcium; DBP, diastolic blood pressure; FBG, fasting blood glucose; FINS, fasting insulin; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; Scr, serum creatinine; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; TC, total cholesterol; TG, triglyceride; UA, uric acid.

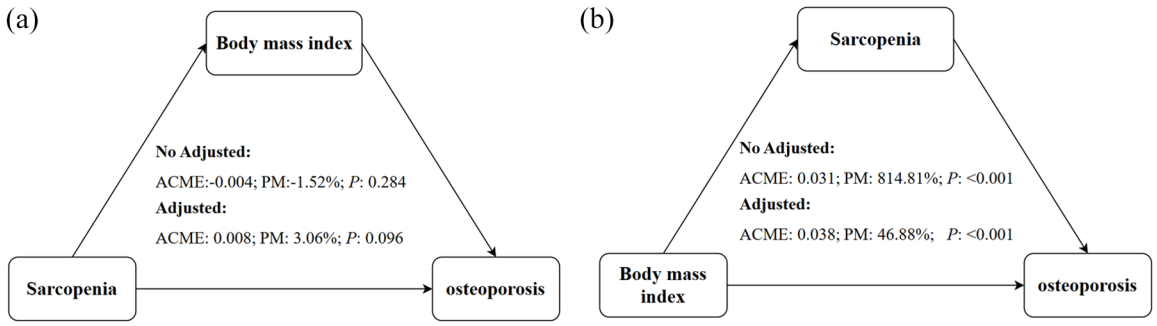

Figure 2. Mediation analysis among BMI, sarcopenia, and osteoporosis. (a) The mediation effect results of BMI between sarcopenia and osteoporosis. (b) The mediation effect results of sarcopenia between BMI and osteoporosis.
BMI, body mass index.

training set, the feature count was limited to 27–40. Variable selection was performed using LASSO regression, achieving optimal performance with 11 predictors at lambda = 0.0104 (Figure 3). These predictors were then incorporated into a logistic regression model, identifying sex, age, HDL, ALP, BMI, and sarcopenia as independent predictors of osteoporosis ($p < 0.05$; Table 2). A nomogram was developed based on these five predictors (Figure 4) and is available at https://sofarnomogram.shinyapps.io/Osteoporosis_Nomapp/. For usage instructions, please refer to Information S3.

Testing of the nomogram model

The area under the curve (AUC) for the training set was 0.859 (95% confidence interval (CI): 0.812–0.905), while the AUC for the testing set was 0.866 (95% CI: 0.815–0.917), with a

Table 1. Comparison of characteristics between the train set and test set.

Characteristic	Training set (*n* = 407)	Testing set (*n* = 406)	*p*
Osteoporosis (yes)	52 (12.78%)	52 (12.81%)	1.000
Age (⩾60)	174 (42.75%)	182 (44.83%)	0.599
Gender (male)	241 (59.21%)	245 (60.34%)	0.797
Smoking (yes)	75 (18.43%)	80 (19.70%)	0.708
Diabetes (yes)	190 (46.68%)	208 (51.23%)	0.220
SBP (mmHg)			0.984
<140	309 (75.92%)	307 (75.62%)	
⩾140	98 (24.08%)	99 (24.38%)	
DBP (mmHg)			0.980
<90	267 (65.60%)	265 (65.27%)	
⩾90	140 (34.40%)	141 (34.73%)	
ALB (g/L)			0.371
<35	4 (0.98%)	1 (0.25%)	
⩾35	403 (99.02%)	405 (99.75%)	
ALP (U/L)[a]			0.913
<130/125	220 (54.05%)	222 (54.68%)	
⩾130/125	187 (45.95%)	184 (45.32%)	
AST (U/L)			0.604
<40	391 (96.07%)	386 (95.07%)	
⩾40	16 (3.93%)	20 (4.93%)	
BUN (mmol/L)			0.501
<7.5	395 (97.05%)	398 (98.03%)	
⩾7.5	12 (2.95%)	8 (1.97%)	
Scr (μmol/L)[a]			1.000
<97/106	399 (98.03%)	398 (98.03%)	
⩾97/106	8 (1.97%)	8 (1.97%)	
Ca (mmol/L)			0.443
<2.25	20 (4.91%)	26 (6.40%)	
⩾2.25	387 (95.09%)	380 (93.60%)	

(Continued)

Table 1. (Continued)

Characteristic	Training set (*n* = 407)	Testing set (*n* = 406)	*p*
25(OH)D (nmol/L)			0.993
<25	24 (5.90%)	25 (6.16%)	
⩾25	383 (94.10%)	381 (93.84%)	
TC (mmol/L)			0.490
<5.72	363 (89.19%)	369 (90.89%)	
⩾5.72	44 (10.81%)	37 (9.11%)	
TG (mmol/L)			1.000
<1.70	324 (79.61%)	324 (79.80%)	
⩾1.70	83 (20.39%)	82 (20.20%)	
UA (μmol/L)[a]			0.194
<360/420	364 (89.43%)	350 (86.21%)	
⩾360/420	43 (10.57%)	56 (13.79%)	
FINS (μU/mL)			0.520
<20	334 (82.06%)	325 (80.05%)	
⩾20	73 (17.94%)	81 (19.95%)	
FBG (mmol/L)			0.752
<7.0	312 (76.66%)	316 (77.83%)	
⩾7.0	95 (23.34%)	90 (22.17)	
HbA1c (%)			0.073
<6.5	236 (57.99%)	209 (51.48%)	
⩾6.5	171 (42.01)	197 (48.52%)	
HDL (mmol/L)			0.485
<1.04	58 (14.25%)	66 (16.26%)	
⩾1.04	349 (85.75%)	340 (83.74%)	
LDL (mmol/L)			0.994
<4.1	388 (95.33%)	386 (95.07%)	
⩾4.1	19 (4.67%)	20 (4.93%)	
SII (cut off)			0.645
<398.43	216 (53.07%)	223 (54.93%)	

(Continued)

Table 1. (Continued)

Characteristic	Training set ($n = 407$)	Testing set ($n = 406$)	p
⩾398.43	191 (46.93%)	183 (45.07%)	
SIRI (cut off)			0.112
<0.846	246 (60.44%)	222 (54.68%)	
⩾0.846	161 (39.56%)	184 (45.32%)	
BMI and Sarcopenia			0.898
BMI ⩾ 28 and Sarcopenia	40 (9.83%)	44 (10.84%)	
BMI ⩾ 28 and non-Sarcopenia	34 (8.35%)	29 (7.14%)	
BMI < 28 and Sarcopenia	244 (59.95%)	245 (60.34%)	
BMI < 28 and non-Sarcopenia	89 (21.87%)	88 (21.67%)	

[a]Men and women are classified based on ALP levels at 125 and 130 U/L, respectively; Scr levels are classified at 106 μmol/L for men and 97 μmol/L for women; and UA levels are classified at 420 μmol/L for men and 360 μmol/L for women.
ALB, albumin; ALP, alkaline phosphatase; AST, asparagine aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; Ca, calcium; DBP, diastolic blood pressure; FBG, fasting blood glucose; FINS, fasting insulin; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; Scr, serum creatinine; SII, systemic Immune-Inflammation Index; SIRI, Systemic Inflammation Response Index; TC, total cholesterol; TG, triglyceride; UA, uric acid.

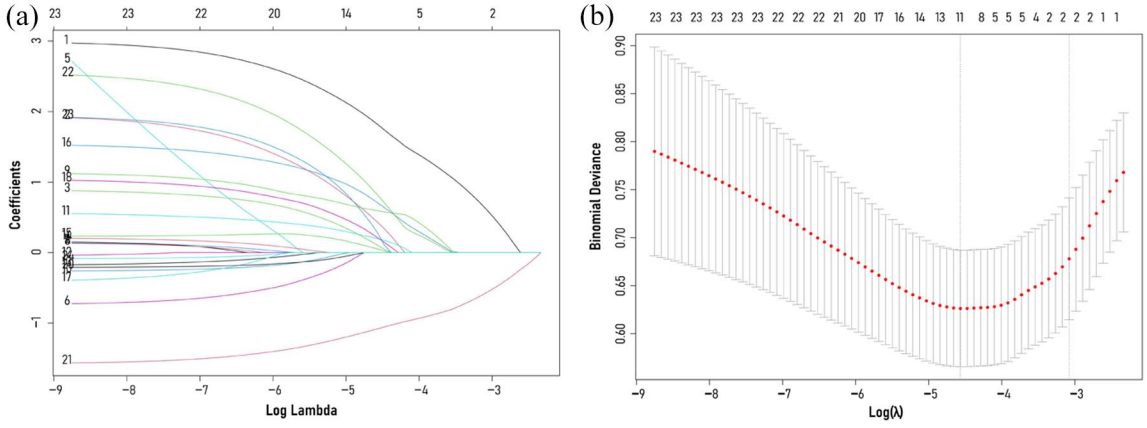

Figure 3. (a) Characterizing the variations of LASSO regression coefficients. (b) LASSO regression selects the optimal parameter lambda through cross-validation. The dashed line on the right represents lambda values with average error within ±1 standard deviation, indicating improved model performance.
LASSO, least absolute shrinkage and selection operator.

DeLong test p-value of 0.835 (Table 3, Figure 5, Figure S3). The Hosmer–Lemeshow goodness-of-fit test yielded $\chi^2 = 3.017$, $p = 0.933$ for the training set and $\chi^2 = 4.788$, $p = 0.780$ for the testing set (Figure 5). Subgroup analyses indicated that the model's performance was unaffected by smoking history, diabetes, FBG, and HbA1c (AUC: 0.844–0.910; $p = 0.091$–0.800). However, in cases of hypocalcemia and low 25(OH)D levels, the model demonstrated superior predictive value (AUC: 0.979–0.993; $p < 0.001$; Table S3).

Clinical utility of the nomogram model

In the DCA curves for the training and testing sets, the model provided the greatest clinical net

Table 2. Logistic regression analysis of risk factors for osteoporosis in the training set patients.

Variable	*B*	SE	*p*	OR	OR 95% CI	
					Lower	Upper
Gender	2.839	0.517	<0.001	17.106	6.737	52.462
Age	2.342	0.779	0.003	10.399	2.550	54.906
HDL	2.067	0.889	0.020	7.898	1.712	62.154
ALP	2.457	0.749	0.001	11.673	3.056	58.705
BMI and Sarcopenia						
BMI ⩾ 28 and Sarcopenia	REF					
BMI ⩾ 28 and Non-Sarcopenia	−1.284	0.690	0.063	0.277	0.066	1.012
BMI < 28 and Sarcopenia	−3.435	0.581	<0.001	0.032	0.009	0.095
BMI < 28 and Non-Sarcopenia	−3.738	0.747	<0.001	0.024	0.005	0.095

ALP, alkaline phosphatase; BMI, body mass index; CI, confidence interval; HDL, high-density lipoprotein; OR, odds ratio; SE, standard error.

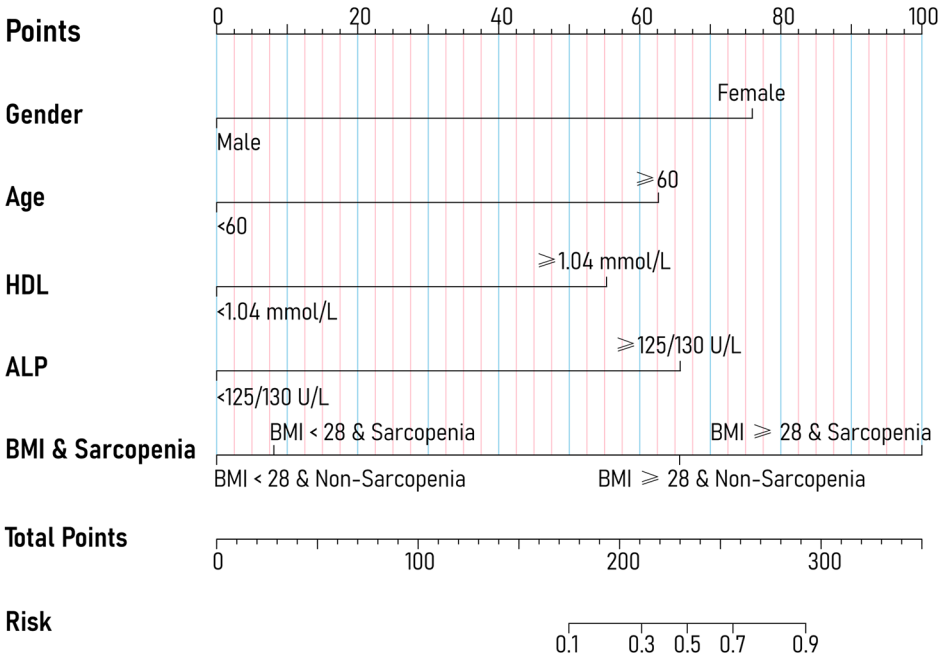

Figure 4. Developed nomogram based on multifactorial logistic regression analysis. Men and women are classified based on ALP levels at 125 and 130 U/L, respectively.
ALP, alkaline phosphatase; BMI, body mass index; HDL, high-density lipoprotein.

benefit within risk thresholds of 0.02–0.82 and 0.02–0.67, respectively, demonstrating a significant net gain in predicting osteoporosis risk (Figure 5). Risk stratification using the CIC for 1000 predicted cases indicated that, within these probability thresholds, the predicted number of osteoporosis cases exceeded the actual cases. In the training and testing sets, the nomogram's

Table 3. Diagnostic performance of nomogram model in the training and testing sets.

	AUC (95% CI)	Accuracy	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Training set	0.859 (0.812, 0.905)	0.720	0.904 (0.790, 0.968)	0.693 (0.642, 0.741)	0.301 (0.231, 0.380)	0.980 (0.954, 0.994)
Testing set	0.866 (0.815, 0.917)	0.815	0.788 (0.653, 0.889)	0.819 (0.775, 0.858)	0.390 (0.297, 0.491)	0.963 (0.936, 0.982)

AUC, area under the receiver operating characteristic curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

partial AUC for 1.00–0.75 specificity ($pAUC_{SP}$) and 1.00–0.75 sensitivity ($pAUC_{SE}$) yielded DeLong p values of 0.033 and 0.640, respectively (5000–bootstrap; Figure S4). For BMI and sarcopenia, these values were 0.032 and <0.001 (Figure 6). Sankey diagrams also indicated that "BMI <28 and Non-Sarcopenia" provided superior negative diagnostic value over "BMI $\geqslant 28$ and Sarcopenia" (Figures S5 and S6).

Discussion

In this study, we observed a negative correlation between BMI, ALM, and serum levels of 25(OH)D and Ca. In addition, "BMI <28 and Non-Sarcopenia" is associated with a lower osteoporosis risk than "BMI $\geqslant 28$ and Sarcopenia." Mediation analysis indicated that sarcopenia significantly mediated the association between BMI and osteoporosis (46.88%). When splitting the data 5:5 into training and testing sets, the combined assessment of "BMI and Sarcopenia" had the greatest impact on the osteoporosis nomogram compared to other factors. In the training set, the confusion matrix for the nomogram showed sensitivity (0.904) exceeding specificity (0.693), while in the testing set, specificity (0.819) surpassed sensitivity (0.789). To further clarify the nomogram's predictive value, pROC analyses for 1–0.75 sensitivity and specificity were conducted for both the training and testing sets. No significant difference was found in the testing set ($p>0.05$). However, the combined "BMI and Sarcopenia" assessment had a significantly lower 1–0.75 sensitivity than specificity in both the training (0.064 vs 0.095) and testing sets (0.048 vs 0.110), supported by Sankey diagram results. To evaluate the applicability of the nomogram, we conducted a subgroup analysis. Results indicated that the model's performance was unaffected by smoking, diabetes, FBG, and HbA1c levels (AUC: 0.844–0.910; $p=0.091$–0.800). However, in cases of hypocalcemia and low 25(OH)D, the model demonstrated significantly enhanced predictive value (AUC: 0.979–0.993; $p<0.001$).

Osteoporosis is a skeletal disorder characterized by bone loss and disrupted bone microarchitecture. As key components of the musculoskeletal system, bone and skeletal muscle are functionally and structurally interconnected. Muscle contraction not only provides support and movement for bones but also promotes bone metabolism and helps maintain bone density through mechanical loading.[18,19] Studies indicate a close association between reduced skeletal muscle mass and function and the development of osteoporosis, a relationship termed "muscle-bone interaction."[19–21] When sarcopenia and osteoporosis co-occur, this condition is referred to as "osteosarcopenia."[21] A cross-sectional study of 26,855 Korean adults found that osteoporosis prevalence was higher in the low muscle strength (LMS) group (15.6%) than in the normal muscle strength group (4.2%). After adjusting for confounders, LMS remained significantly more prevalent among individuals with osteoporosis than those without.[22] Chiapparelli et al.[23] also demonstrated a positive correlation between paraspinal muscle cross-sectional area and vertebral BMD, especially in women, underscoring the critical role of muscle in bone health. Comprehensive musculoskeletal management approaches, including resistance training and nutritional interventions, have been shown to significantly improve bone density.[24]

Unlike sarcopenia, the impact of obesity on osteoporosis remains debated. While some studies suggest that women with higher BMIs (25–29.9 kg/m^2)

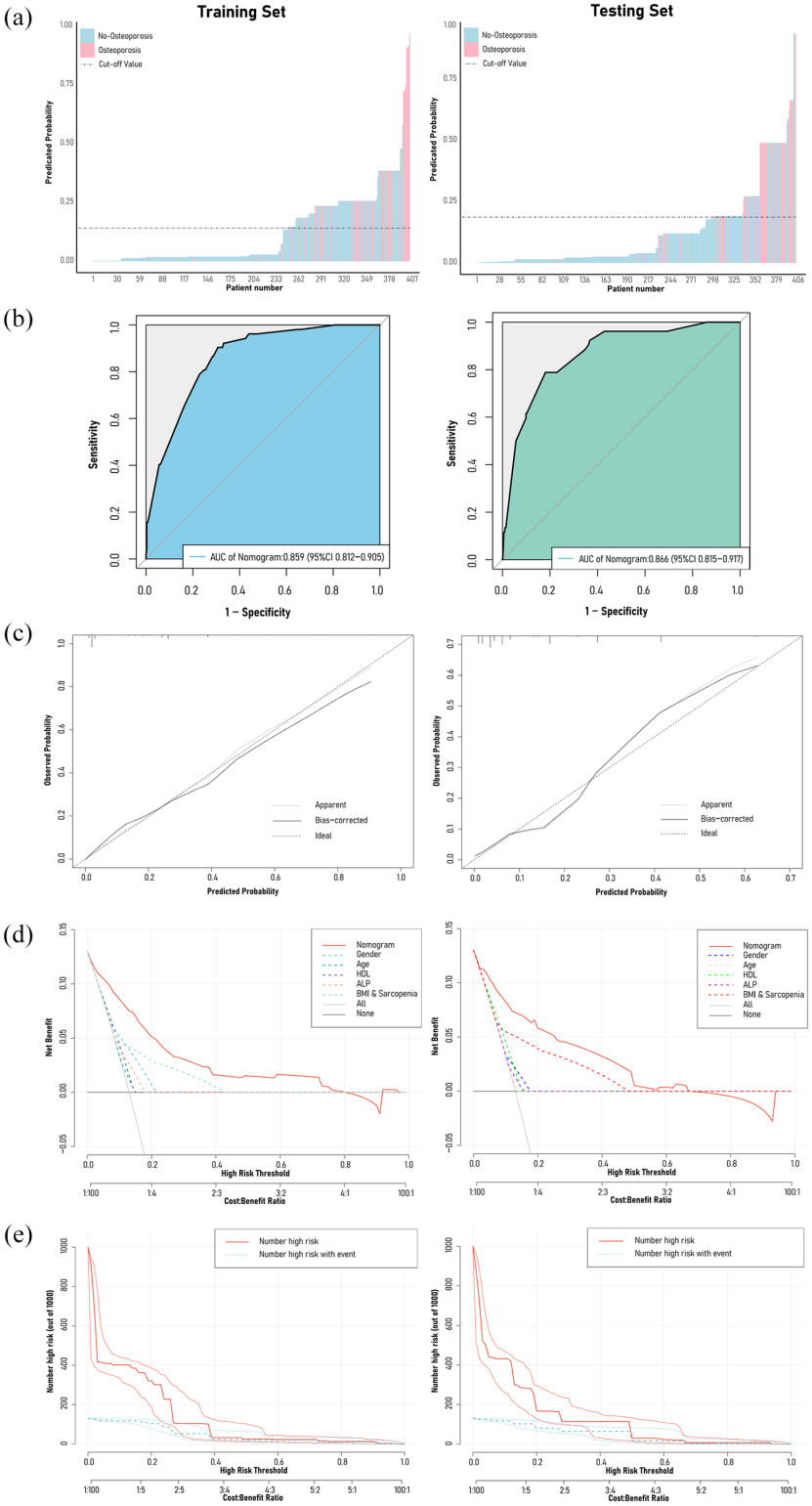

Figure 5. Diagnostic performance of the Nomogram model. (a) Nomogram model predicted the probability of osteoporosis in the training and testing sets, compared with actual diagnoses. The dot-dash line represents the cutoff value. (b) AUC of the ROC curves for the two sets. (c) Calibration curves for the three sets. (d, e) Decision curve analysis and clinical impact curve demonstrate the net benefit in the low-risk population for the training and testing sets.
AUC, area under the curve; ROC, receiver operating characteristic.

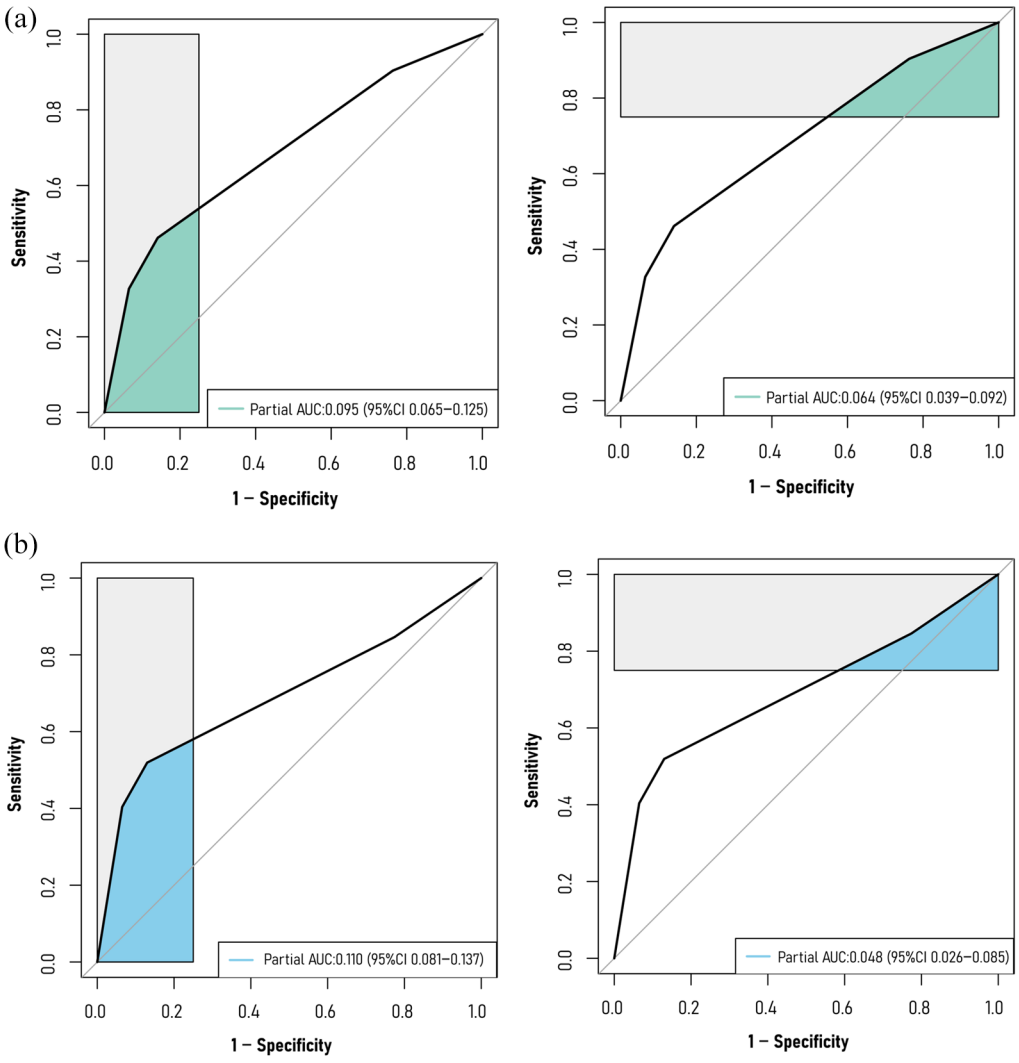

Figure 6. pAUC for combined assessment of BMI and sarcopenia. (a) The combined assessment of BMI and sarcopenia in the training set with specificity and sensitivity (1.00–0.75). (b) The combined assessment of BMI and sarcopenia in the testing set with specificity and sensitivity (1.00–0.75).
AUC, area under the curve; BMI, body mass index; pAUC, partial AUC.

tend to have higher BMD,[25] growing evidence presents conflicting results, indicating that obesity (BMI >30 kg/m²) may actually compromise bone health.[26] This effect may stem from the association of BMI with muscle mass and strength, which influence bone integrity. Rikkonen et al.[27] found that women with osteoporosis had lower BMIs and a lower proportion of lean muscle mass compared to others, despite similar fat mass. This finding suggests that BMI may not only have a direct impact on bone health but also influence bone strength indirectly by affecting muscle mass. Our findings also indicate that "BMI < 28 and Non-Sarcopenia" consistently act as a protective factor, with BMI showing significant inverse correlations with serum 25(OH)D and calcium levels. The Framingham Heart Study indicates an inverse relationship between obesity and serum 25(OH)D levels,[28] likely due to reduced release of 1-25$(OH)_2$D from subcutaneous fat and increased vitamin D catabolism within adipose tissue.[29,30] In addition, multiple studies have shown a significant negative correlation between BMI and serum calcium.[31,32] Our subgroup analysis also confirmed that this association impacts model performance.

Compared to men, postmenopausal women experience a significant decline in estrogen levels

within their bodies, leading to an exacerbation of bone loss.[33] This is related to the direct effects of estrogen on osteoblast lineage cells, osteocytes, and osteoclasts.[34] The impact of HDL on the risk of developing osteoporosis is also a subject of debate. Research by Xie et al.[35] found that HDL is positively correlated with lumbar spine bone density and exhibits a U-shaped relationship. Conversely, research by Tang et al.[36] also identified a U-shaped relationship between HDL and bone density, but their conclusion was that the two are negatively correlated. The potential mechanisms of this negative correlation are as follows: (1) HDL affects BMD through sex hormones. Research by Jirapinyo et al.[37] found that combined oral estrogen/progestogen can increase BMD in postmenopausal women but decrease HDL levels; (2) HDL activates inflammatory responses affecting BMD. Studies by Mazidi et al.[38] found that HDL-C is positively correlated with inflammatory markers such as C-reactive protein, white blood cells, and fibrinogen. Lastly, serum ALP levels are one of the markers reflecting osteogenic activity in bone turnover, and their increase may suggest accelerated bone turnover, a process that is particularly evident in the elderly.[39] Bone quality is determined by factors such as microarchitecture, bone turnover rate, mineralization, and the accumulation of microdamage.[40] Serum ALP is synthesized during bone matrix maturation and plays a crucial role in the mineralization process.[41] When BMD is low, osteoblasts proliferate reactively, synthesizing bone-specific alkaline phosphatase (B-ALP), which significantly increases total serum ALP.[42]

The limitations of this study are as follows. First, this study is a single-center retrospective study. Therefore, prospective large-scale clinical cohort studies are still needed for validation; second, previous studies have shown that obtaining vertebral bone density through CT can better reflect the body's bone density situation, but since vertebral CT is not a routine examination for patients in this center. In addition, the European Working Group on Sarcopenia in Older People recommends alternative methods for assessing sarcopenia, such as measuring grip strength.[43] Future studies could attempt to use this method for further research; third, we only included six predictive variables, and many other factors were not included, such as seasonal and exercise conditions. Therefore, future studies should address these limitations and further explore the impact of more related factors.

Declarations

Ethics approval and consent to participate

This study adhered to the Declaration of Helsinki. Ethical approval (2024-02-03) was granted by the Clinical Trial Ethics Committee of Huining County People's Hospital, with a waiver for written informed consent. Informed consent was obtained from each patient at diagnosis, permitting further clinical research use of their records.

Consent for publication

Not applicable.

Author contributions

Qingling Liu: Conceptualization; Data curation; Formal analysis; Investigation; Writing – original draft; Writing – review & editing.

Shengquan Pan: Investigation; Resources; Writing – review & editing.

Ming Tang: Investigation; Methodology; Validation; Writing – review & editing.

Shiwu Yin: Resources; Supervision.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Supplemental material

Supplemental material for this article is available online.

References

1. Gregson CL, Armstrong DJ, Bowden J, et al. UK clinical guideline for the prevention and treatment of osteoporosis. *Arch Osteoporos* 2022; 17(1): 58.
2. Melton LR, Achenbach SJ, Atkinson EJ, et al. Long-term mortality following fractures at different skeletal sites: a population-based cohort study. *Osteoporos Int* 2013; 24(5): 1689–1696.
3. Ontan MS, Dokuzlar O, Ates BE, et al. The relationship between osteoporosis and sarcopenia, according to EWGSOP-2 criteria, in outpatient elderly. *J Bone Miner Metab* 2021; 39(4): 684–692.
4. Reiss J, Iglseder B, Alzner R, et al. Sarcopenia and osteoporosis are interrelated in geriatric inpatients. *Z Gerontol Geriatr* 2019; 52(7): 688–693.
5. Tagliaferri C, Wittrant Y, Davicco MJ, et al. Muscle and bone, two interconnected tissues. *Ageing Res Rev* 2015; 21: 55–70.
6. Hassan EB and Duque G. Osteosarcopenia: a new geriatric syndrome. *Aust Fam Physician* 2017; 46(11): 849–853.
7. Ali D, Tencerova M, Figeac F, et al. The pathophysiology of osteoporosis in obesity and type 2 diabetes in aging women and men: the mechanisms and roles of increased bone marrow adiposity. *Front Endocrinol (Lausanne)* 2022; 13: 981487.
8. Wang CY and Lai CC. The association between inhaled corticosteroid and osteoporosis and fracture. *Eur Respir J* 2021; 57(6): 2100216.
9. Qiao D, Li Y, Liu X, et al. Association of obesity with bone mineral density and osteoporosis in adults: a systematic review and meta-analysis. *Public Health* 2020; 180: 22–28.
10. Kob R, Bollheimer LC, Bertsch T, et al. Sarcopenic obesity: molecular clues to a better understanding of its pathogenesis? *Biogerontology* 2015; 16(1): 15–29.
11. Kelly OJ, Gilman JC, Boschiero D, et al. Osteosarcopenic obesity: current knowledge, revised identification criteria and treatment principles. *Nutrients* 2019; 11(4): 747.
12. Migliaccio S, Greco EA, Aversa A, et al. Age-associated (cardio)metabolic diseases and cross-talk between adipose tissue and skeleton: endocrine aspects. *Horm Mol Biol Clin Investig* 2014; 20(1): 25–38.
13. Studenski SA, Peters KW, Alley DE, et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. *J Gerontol A Biol Sci Med Sci* 2014; 69(5): 547–558.
14. Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol* 1998; 147(8): 755–763.
15. Qi Q, Zhuang L, Shen Y, et al. A novel Systemic Inflammation Response Index (SIRI) for predicting the survival of patients with pancreatic cancer after chemotherapy. *Cancer* 2016; 122(14): 2158–2167.
16. Peduzzi P, Concato J, Kemper E, et al. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996; 49(12): 1373–1379.
17. Schober P, Boer C and Schwarte LA. Correlation coefficients: appropriate use and interpretation. *Anesth Analg* 2018; 126(5): 1763–1768.
18. Herrmann M, Engelke K, Ebert R, et al. Interactions between muscle and bone—where physics meets biology. *Biomolecules* 2020; 10(3): 432.
19. Villa P, Cipolla C, Amar I, et al. Bone mineral density and body mass composition measurements in premenopausal anorexic patients: the impact of lean body mass. *J Bone Miner Metab* 2024; 42(1): 134–141.
20. Clynes MA, Gregson CL, Bruyere O, et al. Osteosarcopenia: where osteoporosis and sarcopenia collide. *Rheumatology (Oxford)* 2021; 60(2): 529–537.
21. Kirk B, Zanker J and Duque G. Osteosarcopenia: epidemiology, diagnosis, and treatment—facts and numbers. *J Cachexia Sarcopenia Muscle* 2020; 11(3): 609–618.
22. Choi JY and Yang YM. Analysis of the association between osteoporosis and muscle strength in Korean adults: a national cross-sectional study. *J Health Popul Nutr* 2023; 42(1): 97.
23. Chiapparelli E, Okano I, Adl AD, et al. The association between lumbar paraspinal muscle functional cross-sectional area on MRI and regional volumetric bone mineral density measured by quantitative computed tomography. *Osteoporos Int* 2022; 33(12): 2537–2545.

24. Watson SL, Weeks BK, Weis LJ, et al. High-intensity resistance and impact training improves bone mineral density and physical function in postmenopausal women with osteopenia and osteoporosis: the LIFTMOR randomized controlled trial. *J Bone Miner Res* 2018; 33(2): 211–220.

25. Albala C, Yanez M, Devoto E, et al. Obesity as a protective factor for postmenopausal osteoporosis. *Int J Obes Relat Metab Disord* 1996; 20(11): 1027–1032.

26. Zhao LJ, Jiang H, Papasian CJ, et al. Correlation of obesity and osteoporosis: effect of fat mass on the determination of osteoporosis. *J Bone Miner Res* 2008; 23(1): 17–29.

27. Rikkonen T, Sirola J, Salovaara K, et al. Muscle strength and body composition are clinical indicators of osteoporosis. *Calcif Tissue Int* 2012; 91(2): 131–138.

28. Cheng S, Massaro JM, Fox CS, et al. Adiposity, cardiometabolic risk, and vitamin D status: the Framingham Heart Study. *Diabetes* 2010; 59(1): 242–248.

29. Pramono A, Jocken J, Goossens GH, et al. Vitamin D release across abdominal adipose tissue in lean and obese men: the effect of β-adrenergic stimulation. *Physiol Rep* 2019; 7(24): e14308.

30. Perna S. The enigma of vitamin D supplementation in aging with obesity. *Minerva Gastroenterol (Torino)* 2022; 68(4): 459–462.

31. Jafari-Giv Z, Avan A, Hamidi F, et al. Association of body mass index with serum calcium and phosphate levels. *Diabetes Metab Syndr* 2019; 13(2): 975–980.

32. Yang J, Wang P, Liu C, et al. Relationship of ionized calcium and 25-(OH) D in serum with obesity. *Wei Sheng Yan Jiu* 2013; 42(1): 78–81, 86.

33. Yoo JE, Shin DW, Han K, et al. Association of female reproductive factors with incidence of fracture among postmenopausal women in Korea. *JAMA Netw Open* 2021; 4(1): e2030405.

34. Khosla S, Oursler MJ and Monroe DG. Estrogen and the skeleton. *Trends Endocrinol Metab* 2012; 23(11): 576–581.

35. Xie R, Huang X, Liu Q, et al. Positive association between high-density lipoprotein cholesterol and bone mineral density in U.S. adults: the NHANES 2011–2018. *J Orthop Surg Res* 2022; 17(1):92.

36. Tang Y, Wang S, Yi Q, et al. High-density lipoprotein cholesterol is negatively correlated with bone mineral density and has potential predictive value for bone loss. *Lipids Health Dis* 2021; 20(1): 75.

37. Jirapinyo M, Theppisai U, Manonai J, et al. Effect of combined oral estrogen/progestogen preparation (Kliogest) on bone mineral density, plasma lipids, and postmenopausal symptoms in HRT-naive Thai women. *Acta Obstet Gynecol Scand* 2003; 82(9): 857–866.

38. Mazidi M, Mikhailidis DP and Banach M. Associations between risk of overall mortality, cause-specific mortality, and level of inflammatory factors with extremely low and high high-density lipoprotein cholesterol levels among American adults. *Int J Cardiol* 2019; 276: 242–247.

39. Szulc P, Kaufman JM and Delmas PD. Biochemical assessment of bone turnover and bone fragility in men. *Osteoporos Int* 2007; 18(11): 1451–1461.

40. Jain S and Camacho P. Use of bone turnover markers in the management of osteoporosis. *Curr Opin Endocrinol Diabetes Obes* 2018; 25(6): 366–372.

41. Park SY, Ahn SH, Yoo JI, et al. Clinical application of bone turnover markers in osteoporosis in Korea. *J Bone Metab* 2019; 26(1): 19–24.

42. Westerlind KC and Turner RT. The skeletal effects of spaceflight in growing rats: tissue-specific alterations in mRNA levels for TGF-beta. *J Bone Miner Res* 1995; 10(6): 843–848.

43. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019; 48(1): 16–31.