Am J Transl Res 2024;16(1):163-178
www.ajtr.org /ISSN:1943-8141/AJTR0152228

Original Article

TC and LDL-C are negatively correlated with bone mineral density in patients with osteoporosis

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Received July 15, 2023; Accepted December 10, 2023; Epub January 15, 2024; Published January 30, 2024

Abstract: Objective: To investigate the relationships of multiple lipid metabolism indicators and bone turnover markers (BTMs) with bone mineral density (BMD) and osteoporosis, in order to identify high-risk populations. Methods: A total of 380 patients were recruited and their general information was collected. Linear and logistic regression models were used to analyze the correlation of these indicators with BMD and osteoporosis. Results: Lipid metabolism indices and BTMs exhibited varying degrees of positive or negative correlation with BMD. Elevated levels of triglycerides ($r = -0.204$, $P = 0.004$), total cholesterol (TC) ($r = -0.244$, $P < 0.001$), low-density lipoprotein cholesterol (LDL-C) ($r = -0.256$, $P < 0.001$), apoprotein B ($r = -0.292$, $P < 0.001$) and lipoprotein-associated phospholipase A2 (Lp-PLA2) ($r = -0.221$, $P = 0.002$) in women were associated with a reduction in BMD. This relationship persisted even after adjusting for confounding factors and in the subgroup analysis of elderly women. In males, TC ($r = 0.159$, $P = 0.033$), LDL-C ($r = 0.187$, $P = 0.012$), apoprotein B ($r = 0.157$, $P = 0.035$), and Lp-PLA2 ($r = 0.168$, $P = 0.024$) exhibited a positive correlation with BMD, while free fatty acid (FFA) ($r = -0.153$, $P = 0.041$) was negatively correlated with BMD. However, after adjusting for confounding factors, only FFA remained negatively correlated with BMD, which was not observed in the age subgroup analysis. Furthermore, elevated levels of TC and LDL-C in elderly women were positively associated with the risk of osteoporosis or low bone mass. Conclusion: Elevated levels of TC and LDL-C not only indicate a decrease in BMD in females but also positively correlate with the occurrence of osteoporosis and low bone mass in elderly females.

Keywords: Bone mineral density, osteoporosis, low bone mass, lipid metabolism indicators, lipid, dyslipidemia, bone turnover markers

Introduction

Bone is a complex organ that serves multiple functions, including structural support, movement, hematopoiesis, and calcium storage [1]. It is a dynamic tissue that undergoes continuous remodeling through the coordinated actions of osteoblasts and osteoclasts [2, 3], and the balance between bone formation and resorption is critical for maintaining bone microarchitecture and stability [4]. However, when the body is subjected to physiological or pathological changes, this balance is disrupted, and bone mass is gradually lost, leading to osteoporosis and increased risk of fractures [5].

Osteoporosis is a multifactorial disease, and dyslipidemia resulting from lipid metabolism disorders may represent a risk factor for its development. Because an increasing number of studies have shown that osteoporosis is closely related to the occurrence of cardiovascular disease [6, 7], the common feature of these patients is concomitant dyslipidemia, especially hyperlipidemia, which is associated with lower bone mass and a high incidence of fractures [8-10]. This may be due to the mutual restriction effects of osteoblasts and adipocytes, with elevated blood lipid levels leading to a suppression of osteoblast differentiation and proliferation, resulting in a decline in bone formation and mass, and ultimately leading to osteoporosis [11-13].

https://doi.org/10.62347/DTXZ3175

Lipid metabolism indices have exhibited varying effects in diverse clinical investigations. Studies evaluating the relationship between lipid metabolism indices and BMD in health adults and those with metabolic syndrome have shown that they are associated with a low bone mass [14, 15], but there is great inconsistency among the reported findings [16-19]. Most previous research regarding the relationships between the lipid metabolism indices and the BMD has small samples, and focused mainly on postmenopausal women with regard to a few confounding factors [20]. Therefore, further elucidation of the relationships between them is warranted.

Osteoporosis brings economic losses and painful experiences to patients because of its serious complications. Unfortunately, a considerable proportion of individuals remain unaware of their disease status, and most patients receive a diagnosis of osteoporosis only after experiencing a fracture [21, 22]. Currently, osteoporosis is commonly diagnosed through clinical assessment of BMD using dual energy X-ray absorptiometry (DXA) or quantitative CT (QCT) scans of the lumbar spine, hip, femoral neck, and other sites [23]. Although imaging is popular due to its convenience and accurate results [24], it only reflects the result of many factors acting on the bone and cannot promptly indicate metabolic changes of bone cells, posing certain limitations. In contrast, bone turnover markers (BTMs) exhibit rapid responsiveness to physiological changes of bone and offer superior accuracy in reflecting alterations in bone cell metabolism. They serve as reliable predictors of bone loss and fracture risk, and contribute significantly to the diagnosis of osteoporosis [25, 26]. Therefore, combining BMD and BTMs [27] to evaluate bone status by integrating the advantages of both is a promising method for predicting the risk of osteoporosis and fractures.

In this study, we conducted a comprehensive analysis of various indicators, including triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apolipoproteins A (Apo A), apolipoprotein B (Apo B), Apo A/B, lipoprotein a (LP(a)), lipoprotein-associated phospholipase A2 (Lp-PLA2), free fatty acid (FFA), as well as commonly used BTMs such as procollagen type I N-propylene (PINP), osteocalcin (OC), C-terminal telephony of type I collagen (β-CTX), parathyroid hormone (PTH), and 25-hydroxyvitamin D (25(OH)D). The aim of this study was to investigate the relationship of these indicators with BMD and to explore the most effective indicators for predicting BMD levels and the occurrence of osteoporosis. The findings may facilitate the precise evaluation of fracture risk and early intervention for bone metabolic disorders.

Materials and methods

Participants

This is an observational cross-sectional study of inpatients undergoing spine surgery at the Provincial Hospital Affiliated to Shandong First Medical University (Shandong Provincial Hospital) from September 2019 to December 2022. The following inclusion and exclusion criteria were applied to ensure the accuracy and reliability of the study results. Inclusion criteria: (1) patients were over 30 years of age; (2) patients had complete medical data; (3) patients were not accompanied by infectious, gastrointestinal, dermatological or endocrine disorders. Exclusion criteria: (1) patients diagnosed with malignant tumor, or liver or kidney dysfunction; (2) patients received lipid-lowering drugs, anti-osteoporosis drugs or hormone replacement therapy; (3) women with premature menopausal (menopausal age < 40 years old); (4) patients with missing data. In the end, a total of 380 subjects (180 males and 200 females) were included in the study, as seen in **Figure 1**. The personal history and past medical history of each participant was obtained through an individual questionnaire, and all the subjects signed an informed consent before enrollment. This study was approved by the Ethics Committee of Shandong Provincial Hospital (Ethics approval number: No. 2019-213).

Clinical data collection and inspection

Upon admission, one to two medical professionals collected relevant medical history and personal information, including demographic characteristics (height, weight, etc.), smoking and alcohol consumption status, medication history, clinical history, and other essential clinical data. The body mass index (BMI) was calculated as the weight (kg) divided by the square of the height (m^2). Smoking and drinking status

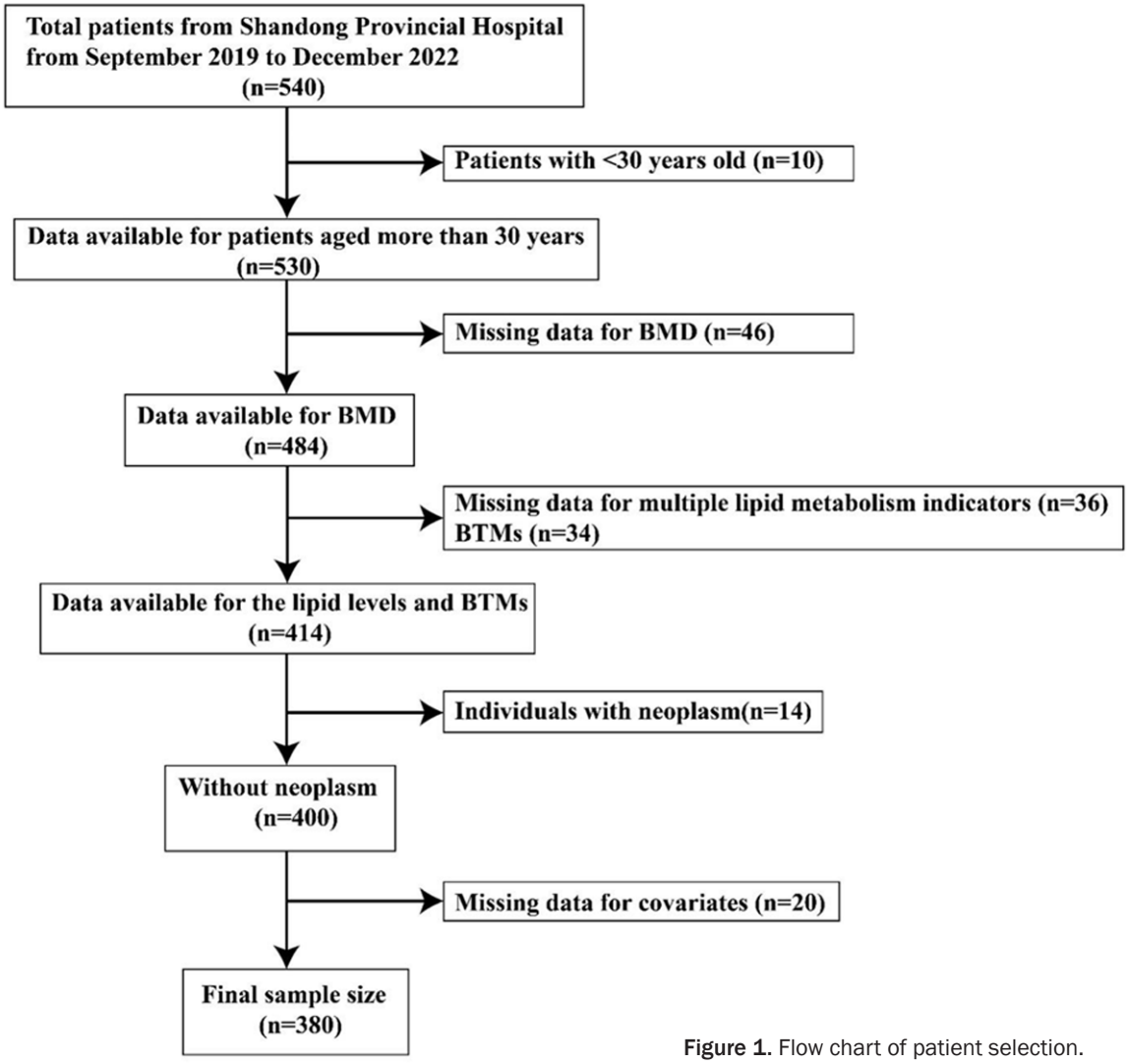

Figure 1. Flow chart of patient selection.

were defined as smoking at least one cigarette per day and consuming at least 100 grams of alcohol per week on average in the past year. After adequate rest and a minimum of 8 hours of fasting, patients provided fasting blood and urine samples in the morning, which were analyzed using standard experimental techniques. Lipid metabolism markers, including TG, TC, HDL-C, LDL-C, Apo (A), Apo (B), Apo A/B, LP(a), Lp-PLA2, and FFA, were measured. Bone metabolism markers, including PINP, OC, β-CTX, PTH, and 25(OH)D, were also measured. Additionally, other blood indicators that may affect BMD, such as blood type, glucose, phosphorus, and iron, were also analyzed. All participants in the study underwent BMD measurement using QCT, and all measurements were analyzed using Mindways QCT software for lumbar spine scans. The average value was used as the BMD result, and the patients were divided into two groups based on the 2018 Chinese guidelines for the diagnosis and treatment of osteoporosis in the elderly [28]: BMD > 120 mg/cm^3 for a normal bone mass group and BMD < 120 mg/cm^3 for an osteoporotic and low bone mass group.

The main outcome of this study included correlation analysis of lipid metabolism with BMD, the influence of lipid metabolism on BMD, and the association of lipids level with the risk of osteoporosis in elderly women. The secondary ones included basic characteristics of patients, the relationship between lipid metabolism indexes and BTMs, and correlation analysis of BTMs with BMD.

Table 1. Baseline patient characteristics

Variable	Men (n = 180)	Women (n = 200)	*P*
Age	57.19±11.28	59.37±10.19	0.048
Blood group (%)			0.037
A	46 (25.6)	63 (31.5)	
B	75 (41.71)	57 (28.5)	
AB	14 (7.8)	26 (13.0)	
O	45 (25.0)	54 (27.0)	
Total	180 (100)	200 (100)	
CHD (%)	18 (10.0)	15 (7.5)	0.388
CVD (%)	10 (5.6)	11 (5.5)	0.981
Hypertension (%)	50 (27.8)	71 (35.5)	0.107
Diabetes (%)	24 (13.3)	28 (14.0)	0.850
Smoking (%)	67 (37.2)	4 (2.0)	< 0.001
Drinking (%)	67 (37.2)	18 (9.0)	< 0.001
Height (cm)	170.31±5.62	159.26±5.26	< 0.001
Weight (kg)	74.46±10.18	65.96±10.15	< 0.001
BMI (kg/m^2)	25.68±3.34	25.99±3.70	0.392
BMD (mg/cm^3)	121.76±34.65	108.05±42.34	0.001
GLU (mmol/l)	5.05 (4.70, 5.89)	5.12 (4.70, 5.80)	0.852
P (mmol/l)	1.23±0.18	1.32±0.18	< 0.001
Fe (umol/l)	19.16±6.57	16.78±5.97	< 0.001
TG (mmol/l)	1.48 (0.97, 1.99)	1.33 (1.01, 1.85)	0.404
TC (mmol/l)	4.68±1.01	5.07±1.03	< 0.001
HDL-C (mmol/l)	1.22±0.28	1.38±0.33	< 0.001
LDL-C (mmol/l)	3.01±0.81	3.21±0.83	0.019
Apo A (g/l)	1.08±0.18	1.18±0.19	< 0.001
Apo B (g/l)	0.91±0.26	0.96±0.30	0.117
Apo A/B	1.16 (1.00, 1.47)	1.22 (1.02, 1.62)	0.197
Lp(a) (g/l)	0.12 (0.07, 0.23)	0.14 (0.08, 0.28)	0.133
Lp-PLA2 (IU/l)	540.24±121.33	503.81±116.68	0.003
FFA (mmol/l)	0.41±0.21	0.45±0.20	0.056
PTH (pg/ml)	32.35±10.49	37.56±13.25	< 0.001
β-CTX (ng/ml)	0.62±0.24	0.69±0.33	0.023
PINP (ng/ml)	44.24±22.79	51.48±27.13	0.005
25(OH)D (ng/ml)	30.04±10.54	22.61±6.79	< 0.001
OC (ng/ml)	16.55±6.43	19.39±8.43	< 0.001

Note: CHD: coronary heart disease; CVD: cerebovascular disease; BMI: body mass index; BMD: bone mineral density; GLU: glucose; P: phosphorous; Fe: ferrum; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein Cholesterol; LDL-C: low-Density Lipoprotein Cholesterol; Apo-A: apolipoprotein A; Apo B: apolipoprotein B; LP(a): lipoprotein a; Lp-PLA2: lipoprotein-associated phospholipase A2; FFA: free fatty acid; PTH: parathyroid hormone; β-CTX: C-terminal telephony of type I collagen; PINP: procollagen type I N-propylene; 25(OH)D: 25-hydroxyvitamin D; OC: osteocalcin.

Statistical analysis

The study utilized the Kolmogorov-Smirnov test to assess whether continuous variables followed a normal distribution. Mean ± standard deviation and median and quartile (25 and 75% intermediate) were used to describe continuous variables of normal distribution and skewed distribution, respectively. Categorical variables were described using quantity and proportion. The unpaired t-test or Mann-Whitney U test was used to compare differences between two groups, while one-way analysis of variance (ANOVA) or the Kruskal-Wallis-test was used for three or more groups. The chi-square test was used for categorical variables. Pearson or Spearman correlation analysis was used to determine the associations between the independent variable and BMD. Three regression models were established, with Model 1 being unadjusted, Model 2 adjusted for gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, and BMI, and Model 3 further adjusted for GLU, P, and Fe based on Model 2. Unadjusted and multivariable adjusted multiple linear regression analyses were used to calculate the regression coefficient (β) and corresponding 95% confidence intervals (95% CI) for the associations between BMD and the level of lipid metabolism and bone metabolism. Logistic regression equations were used to explore the association between lipid metabolism indexes and the risk of osteopenia or osteoporosis. The study also explored changes in BMD in different age groups, specifically the middle-aged group (45-59 years old) and the elderly group (≥ 60 years old). Statistical analyses were performed using SPSS statistical software 25.0 (IBM SPSS Inc., USA). A two-sided *P*-value < 0.05 was considered significant.

Results

Basic characteristics of research participants

A total of 380 patients were included in this retrospective study, and **Table 1** compares the baseline characteristics of the population stratified by gender. Of the participants, 180 were

Table 2. Correlation between lipid metabolism indices and BTMs

		TG	TC	HDL-C	LDL-C	Apo A	Apo B	Apo A/B	Lp(A)	Lp-PLA2	FFA
Men	PTH	-0.145	-0.182*	-0.026	-0.180*	-0.062	-0.12	0.068	-0.019	-0.058	0.084
	β-CTx	-0.014	0.013	-0.010	0.001	-0.027	0.022	-0.049	0.061	0.048	0.104
	PINP	0.004	-0.052	-0.119	-0.054	-0.091	-0.062	0.012	-0.027	-0.064	-0.068
	25(OH)D	0.041	0.188*	0.172*	0.162*	0.234**	0.122	-0.023	0.035	0.003	-0.187*
	OC	0.081	-0.008	-0.100	-0.013	-0.080	-0.015	-0.039	-0.047	0.035	-0.086
Women	PTH	-0.004	-0.002	0.027	-0.01	-0.026	-0.019	-0.006	-0.029	-0.019	0.147*
	β-CTx	0.074	0.052	0.013	0.047	0.002	0.036	-0.126	0.068	0.062	-0.131
	PINP	0.001	0.020	-0.05	0.048	-0.046	0.035	-0.109	0.009	0.113	-0.162*
	25(OH)D	0.033	0.087	0.025	0.084	0.059	0.108	-0.058	0.029	0.089	-0.057
	OC	0.023	0.106	0.020	0.116	0.020	0.078	-0.106	-0.012	0.077	-0.175*

Note: TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein Cholesterol; LDL-C: low-Density Lipoprotein Cholesterol; Apo-A: apolipoprotein A; Apo B: apolipoprotein B; LP(a): lipoprotein a; Lp-PLA2: lipoprotein-associated phospholipase A2; FFA: free fatty acid; PTH: parathyroid hormone; β-CTX: C-terminal telephony of type I collagen; PINP: procollagen type I N-propylene; 25(OH)D: 25-hydroxyvitamin D; OC: osteocalcin. *P*-values for correlations of lipid metabolism index with bone transformation markers: *P < 0.05; **P < 0.01.

male with a mean age of 57.19±11.28 years, and 200 were female with a mean age of 59.37±10.19 years. As expected, males had a higher prevalence of smoking and alcohol consumption (P < 0.001) and higher height and weight than females (P < 0.001). Moreover, males had significantly higher levels of BMD (P = 0.001), Fe (P < 0.001), Lp-PLA2 (P = 0.003), and 25(OH)D (P < 0.001) than females. Conversely, females had significantly higher levels of P (P < 0.001), TC (P < 0.001), HDL-C (P < 0.001), LDL-C (P = 0.019), Apo A (P < 0.001), PTH (P < 0.001), β-CTX (P = 0.023), PINP (P = 0.005), and OC (P < 0.001) than males.

Relationship between lipid metabolism indexes and BTMs

Table 2 presents the correlation analysis between bone metabolism markers and various lipid indexes. PTH exhibited a negative correlation with male TC (r = -0.182, P = 0.015) and LDL-C (r = -0.180, P = 0.016) levels, and a positive correlation with female FFA (r = 0.147, P = 0.038). Additionally, FFA in females was negatively correlated with P1NP (r = -0.162, P = 0.022) and OC (r = -0.175, P = 0.013). 25(OH)D was found to be positively correlated with male TC (r = 0.188, P = 0.012), HDL-C (r = 0.172, P = 0.021), LDL-C (r = 0.162, P = 0.030), and Apo-A (r = 0.234, P = 0.002) levels, and negatively correlated with FFA (r = -0.187, P = 0.012). No correlation was found between β-CTX and lipids in males and females.

Correlation analysis of lipid metabolism and BTMs with BMD

In **Table 3**, correlation analysis was used to explore the relationship between lipid metabolism or bone metabolism indicators and BMD. After discovering the correlation between BMD and gender (r = -0.174, P = 0.001), subgroup analysis was performed. The results showed that age had the highest correlation with BMD (r = -0.611, P < 0.001), and this strong negative correlation still existed in the subgroup analysis, with the correlation being stronger in females than males (males: r = -0.477, P < 0.001; females: r = -0.722, P < 0.001). In males, BMD was positively correlated with BMI (r = 0.198, P = 0.008) and negatively correlated with FFA (r = -0.153, P = 0.041), but no correlation was found in females. In females, TG (r = -0.204, P = 0.009), β-CTX (r = -0.258, P < 0.001), P1NP (r = -0.238, P = 0.001), 25(OH)D (r = -0.194, P = 0.006), and OC (r = -0.151, P = 0.033) were all negatively correlated with BMD, but no correlation was found in males. Interestingly, some indicators showed opposite results in males and females, such as TC (males: r = 0.159, P = 0.033; females: r = -0.244, P < 0.001); LDL-C (males: r = 0.187, P = 0.012; females: r = -0.256, P < 0.001); Apo-B (males: r = 0.157, P = 0.035; females: r = -0.292, P < 0.001); Apo A/B (males: r = -0.200, P = 0.007; females: r = 0.234, P = 0.001); Lp-PLA2 (males: r = 0.168, P = 0.024; females: r = -0.221, P = 0.002). However, HDL-C, Apo A,

Table 3. Correlation of lipid metabolism indices and BTMs with BMD

Variable	Total	Men	Women
Sex	-0.174**	-	-
Age	-0.611***	-0.477***	-0.722***
BMI	0.067	0.198**	-0.005
GLU	-0.133*	-0.128	-0.131
P	0.017	0.117	0.026
Fe	0.096	0.03	0.095
TG	-0.037	0.135	-0.204**
TC	-0.104*	0.159*	-0.244***
HDL-C	-0.047	-0.016	0.005
LDL-C	-0.090	0.187*	-0.256***
Apo-A	-0.093	0.015	-0.099
Apo-B	-0.129*	0.157*	-0.292***
Apo A/B	0.035	-0.200**	0.234**
LP(a)	-0.100	-0.040	-0.131
Lp-PLA2	-0.024	0.168*	-0.221**
FFA	-0.086	-0.153*	-0.01
PTH	-0.087	-0.131	0.01
β-CTX	-0.182***	0.003	-0.258***
PINP	-0.195***	-0.103	-0.238**
25(OH)D	0.011	0.046	-0.194**
OC	-0.131*	-0.014	-0.151*

Note: BMI: body mass index; GLU: glucose; P: phosphorous; Fe: ferrum; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein Cholesterol; LDL-C: low-Density Lipoprotein Cholesterol; Apo-A: apolipoprotein A; Apo B: apolipoprotein B; LP(a): lipoprotein a; Lp-PLA2: lipoprotein-associated phospholipase A2; FFA: free fatty acid; PTH: parathyroid hormone; β-CTX: C-terminal telephony of type I collagen; PINP: procollagen type I N-propylene; 25(OH)D: 25-hydroxyvitamin D; OC: osteocalcin. *P*-values for correlations of different genders with age, BMI and biochemical parameters: *P < 0.05; **P < 0.01; ***P < 0.01.

LP(a), and PTH were not found to be correlated with BMD in both sexes.

Levels of lipid metabolism influence BMD

Table 4 presents the results of linear regression analysis conducted to investigate the relationship between lipid metabolism indexes and BMD. The findings indicate that in female patients, TG, TC, LDL-C, Apo-B, and Lp-PLA2 were negatively associated with BMD in the univariate regression model. Specifically, an increase of 1-SD in these indexes was linked to a decrease of 7.893 mg/cm^3 (P = 0.027, 95% CI = 0.910-14.876), 10.037 mg/cm^3 (P < 0.001, 95% CI = 4.447-15.626), 13.104 mg/cm^3 (P < 0.001, 95% CI = 6.167-20.041), 40.836 mg/cm^3 (P < 0.001, 95% CI = 22.059-59.614), and 0.080 mg/cm^3 (P = 0.002, 95% CI = 0.031-0.130) in BMD, respectively. Conversely, Apo A/B was positively associated with BMD, with an increase of 1-SD leading to an increase of 17.625 mg/cm^3 (P = 0.004, 95% CI = 5.606-29.643) in BMD. In males, TC, LDL-C, Apo-B, and Lp-PLA2 were positively correlated with BMD in the univariate analysis, with an increase of 1-SD associated with an increase of 5.448 mg/cm^3 (P = 0.033, 95% CI = 0.456-10.439), 8.069 mg/cm^3 (P = 0.012, 95% CI = 1.815-14.322), 20.821 mg/cm^3 (P = 0.035, 95% CI = 1.442-40.200), and 0.048 mg/cm^3 (P = 0.024, 95% CI = 0.006-0.090) in BMD, respectively. Only FFA was found to be negatively correlated with male BMD, with an increase of 1-SD leading to a decrease of 25.709 mg/cm^3 (P = 0.041, 95% CI = 1.091-50.328) in BMD. After multivariable adjustment, FFA remained significantly negatively associated with BMD in men, with an increase of 1-SD in FFA leading to BMD decreases of 23.440 mg/cm^3 (P = 0.045, 95% CI = 0.521-47.359) and 24.143 mg/cm^3 (P = 0.046, 95% CI = 0.481-47.805) in Model 2 and Model 3, respectively. An increase of 1-SD in TC, LDL-C, Apo-B, and Lp-PLA2 in females was associated with decreases of 4.725 mg/cm^3 (P = 0.028, 95% CI = 0.518-8.932), 6.493 mg/cm^3 (P = 0.016, 95% CI = 1.236-11.751), 18.860 mg/cm^3 (P = 0.011, 95% CI = 4.381-33.338), and 0.038 mg/cm^3 (P = 0.046, 95% CI = 0.001-0.075) in BMD, respectively.

To account for the impact of age on BMD, we stratified the study population by gender and age group, as shown in **Tables 5** and **6**. In elderly female patients, after adjusting for multiple factors, TC, LDL-C, Apo-B, and Lp-PLA2 remained negatively associated with BMD, with an increase of 1-SD leading to a decrease of 5.819 mg/cm^3 (P = 0.045, 95% CI = 0.133-11.505), 7.544 mg/cm^3 (P = 0.037, 95% CI = 0.474-14.614), 21.269 mg/cm^3 (P = 0.026, 95% CI = 2.558-39.979), and 0.066 mg/cm^3 (P = 0.012, 95% CI = 0.015-0.117) in BMD, respectively. For males, only HDL-C was significantly positively correlated with BMD in the Model 2 of the middle-aged group, with an increase of 1-SD leading to an increase of 26.677 mg/cm^3 (P = 0.029, 95% CI = 2.806-50.548) in BMD.

Table 4. Association between lipid metabolism indices and lumbar bone mineral density (subgroup analysis stratified by sex)

	Male		Female	
	β (95% CI)	P	β (95% CI)	P
Model 1				
TG	4.065 (-2.083, 10.213)	0.194	-7.893 (-14.876, -0.910)	0.027
TC	5.448 (0.456, 10.439)	0.033	-10.037 (-15.626, -4.447)	< 0.001
HDL-C	-1.959 (-20.084, 16.166)	0.831	0.671 (-17.202, 18.544)	0.941
LDL-C	8.069 (1.815, 14.322)	0.012	-13.104 (-20.041, -6.167)	< 0.001
Apo-A	2.882 (-25.208, 30.973)	0.840	-22.272 (-53.625, 9.081)	0.163
Apo-B	20.821 (1.442, 40.200)	0.035	-40.836 (-59.614, -22.059)	< 0.001
Apo A/B	-9.417 (-20.545, 1.710)	0.097	17.625 (5.606, 29.643)	0.004
LP(a)	-7.130 (-31.264, 17.003)	0.561	-12.125 (-39.647, 15.397)	0.386
Lp-PLA2	0.048 (0.006, 0.090)	0.024	-0.080 (-0.130, -0.031)	0.002
FFA	-25.709 (-50.328, -1.091)	0.041	-2.043 (-31.300, 27.213)	0.891
Model 2				
TG	-2.934 (-8.822, 2.955)	0.327	-2.183 (-7.266, 2.899)	0.398
TC	1.861 (-2.822, 6.543)	0.434	-4.078 (-8.234, 0.078)	0.054
HDL-C	9.283 (-8.554, 27.120)	0.306	1.807 (-10.803, 14.417)	0.778
LDL-C	2.572 (-3.312, 8.457)	0.389	-5.806 (-11.003, -0.609)	0.029
Apo-A	3.450 (-23.088, 29.989)	0.798	-5.825 (-28.200, 16.551)	0.608
Apo-B	6.205 (-11.665, 24.075)	0.494	-17.150 (-31.401, -2.899)	0.019
Apo A/B	-2.469 (-12.913, 7.974)	0.641	6.893 (-1.898, 15.683)	0.124
LP(a)	-9.851 (-31.456, 11.753)	0.369	-0.932 (-20.594, 18.729)	0.926
Lp-PLA2	0.016 (-0.022, 0.054)	0.407	-0.032 (-0.068, 0.004)	0.082
FFA	-23.440 (-47.359, -0.521)	0.045	12.547 (-9.520, 34.614)	0.263
Model 3				
TG	-3.832 (-9.797, 2.133)	0.206	-1.610 (-6.905, 3.686)	0.549
TC	1.632 (-3.141, 6.406)	0.500	-4.725 (-8.932, -0.518)	0.028
HDL-C	11.817 (-6.251, 29.884)	0.198	-0.269 (-13.066, 12.527)	0.967
LDL-C	2.239 (-3.777, 8.254)	0.463	-6.493 (-11.751, -1.236)	0.016
Apo-A	4.917 (-22.006, 31.840)	0.719	-9.127 (-31.722, 13.468)	0.427
Apo-B	4.471 (-13.934, 22.876)	0.632	-18.860 (-33.338, -4.381)	0.011
Apo A/B	-1.130 (-11.768, 9.508)	0.834	7.412 (-1.431, 16.256)	0.100
LP(a)	-8.104 (-29.865, 13.657)	0.463	-2.890 (-22.805, 17.024)	0.775
Lp-PLA2	0.012 (-0.028, 0.052)	0.549	-0.038 (-0.075, -0.001)	0.046
FFA	-24.143 (-47.805, -0.481)	0.046	15.396 (-7.738, 38.529)	0.191

Note: Model 1 adjusted for: None. Model 2 adjustede for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, and BMI. Model 3 adjusted for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, BMI, GLU, P, and Fe. TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein Cholesterol; LDL-C: low-Density Lipoprotein Cholesterol; Apo-A: apolipoprotein A; Apo B: apolipoprotein B; LP(a): lipoprotein a; Lp-PLA2: lipoprotein-associated phospholipase A2; FFA: free fatty acid.

Lipid level is associated with the risk of osteoporosis or low bone mass in elderly women

According to the aforementioned grouping, we utilized binary logistic regression to investigate the potential association between lipid metabolism and the risk of osteoporosis or low bone mass events. BMD ≤ 120 mg/cm^3 was defined as osteoporosis or low bone mass, which was considered a positive result, and BMD > 120 mg/cm^3 as normal bone mass, which was considered a negative result. After excluding interfering factors, we found that TC (P = 0.030) and LDL-C (P = 0.041) were positively correlat-

Table 5. Association between lipid metabolism indices and lumbar bone mineral density in females (subgroup analysis stratified by age)

	Middle-aged Female		Elderly female	
	β (95% CI)	P	β (95% CI)	P
Model 1				
TG	-4.399 (-14.078, 5.280)	0.369	-0.481 (-7.244, 6.282)	0.888
TC	-2.749 (-10.636, 5.139)	0.490	-3.871 (-9.600, 1.857)	0.183
HDL-C	7.377 (-14.304, 29.057)	0.501	-3.322 (-22.516, 15.873)	0.732
LDL-C	-4.748 (-14.362, 4.866)	0.329	-5.186 (-12.287, 1.914)	0.150
Apo-A	3.100 (-37.056, 43.257)	0.878	-12.121 (-45.045, 20.802)	0.466
Apo-B	-16.648 (-43.797, 10.502)	0.226	-17.208 (-36.005, 1.589)	0.072
Apo A/B	8.699 (-8.269, 25.668)	0.311	5.160 (-6.756, 17.077)	0.392
LP(a)	18.926 (-25.180, 63.032)	0.396	-9.333 (-34.412, 15.746)	0.462
Lp-PLA2	-0.005 (-0.079, 0.069)	0.893	-0.035 (-0.084, 0.013)	0.152
FFA	4.575 (-36.368, 45.518)	0.825	18.275 (-9.178, 45.728)	0.189
Model 2				
TG	-3.627 (-13.210, 5.955)	0.453	-1.055 (-7.733, 5.624)	0.754
TC	-2.015 (-9.181, 5.150)	0.577	-5.063 (-10.740, 0.614)	0.080
HDL-C	11.751 (-7.667, 31.170)	0.232	-4.349 (-23.583, 14.886)	0.654
LDL-C	-4.777 (-13.472, 3.918)	0.278	-6.663 (-13.752, 0.425)	0.065
Apo-A	12.480 (-23.688, 48.648)	0.494	-14.999 (-47.738, 17.740)	0.365
Apo-B	-16.962 (-41.352, 7.428)	0.170	-19.303 (-38.063, -0.543)	0.044
Apo A/B	11.559 (-3.371, 26.489)	0.127	3.945 (-8.354, 16.244)	0.525
LP(a)	7.415 (-31.527, 46.357)	0.706	-7.713 (-32.718, 17.292)	0.541
Lp-PLA2	-0.037 (-0.104, 0.030)	0.273	-0.042 (-0.091, 0.007)	0.096
FFA	15.517 (-26.264, 57.298)	0.462	13.921 (-14.268, 42.110)	0.329
Model 3				
TG	-2.303 (-12.705, 8.100)	0.661	0.205 (-6.767, 7.176)	0.954
TC	-2.837 (-10.059, 4.386)	0.436	-5.819 (-11.505, -0.133)	0.045
HDL-C	8.190 (-12.031, 28.412)	0.422	-6.820 (-26.097, 12.457)	0.483
LDL-C	-5.616 (-14.495, 3.264)	0.212	-7.544 (-14.614, -0.474)	0.037
Apo-A	7.887 (-28.207, 43.980)	0.665	-19.874 (-52.942, 13.194)	0.235
Apo-B	-18.881 (-43.856, 6.093)	0.136	-21.269 (-39.979, -2.558)	0.026
Apo A/B	11.683 (-3.588, 26.954)	0.132	4.844 (-7.436, 17.124)	0.435
LP(a)	-3.994 (-43.810, 35.822)	0.842	-8.593 (-35.038, 17.852)	0.519
Lp-PLA2	-0.034 (-0.103, 0.035)	0.328	-0.066 (-0.117, -0.015)	0.012
FFA	20.933 (-24.752, 66.619)	0.364	20.833 (-8.296, 49.962)	0.158

Note: Model 1 adjusted for: None. Model 2 adjust for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, and BMI. Model 3 adjusted for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, BMI, GLU, P, and Fe. TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein Cholesterol; LDL-C: low-density lipoprotein Cholesterol; Apo-A: apolipoprotein A; Apo B: apolipoprotein B; LP(a): lipoprotein a; Lp-PLA2: lipoprotein-associated phospholipase A2; FFA: free fatty acid.

ed with the risk of osteoporosis and low bone mass in elderly females, as seen in **Table 7**. Specifically, for each unit increase in TC and LDL-C, the probability of a positive result increased by 238.5% (OR = 3.385, 95% CI = 1.123-10.206) and 291.6% (OR = 3.916, 95% CI = 1.059-14.482), respectively. Notably, this positive correlation was only observed in the elderly female group, but not in the middle-aged female and male groups, as shown in **Table 8**.

Discussion

This study investigated the impact of lipid metabolism indices on BMD to identify high-

Table 6. Association between lipid metabolism indices and lumbar bone mineral density in males (subgroup analysis stratified by age)

	Middle-aged male		Elderly male	
	β (95% CI)	P	β (95% CI)	P
Model 1				
TG	-0.158 (-9.118, 8.802)	0.972	1.096 (-8.814, 11.007)	0.826
TC	5.046 (-2.238, 12.330)	0.172	4.009 (-3.251, 11.268)	0.275
HDL-C	5.714 (-17.749, 29.178)	0.629	-7.638 (-36.181, 20.906)	0.596
LDL-C	6.713 (-2.564, 15.991)	0.154	6.770 (-2.331, 15.871)	0.143
Apo-A	5.817 (-28.554, 40.188)	0.737	-2.794 (-52.024, 46.437)	0.910
Apo-B	15.184 (-12.309, 42.676)	0.275	24.438 (-5.464, 54.341)	0.108
Apo A/B	-3.434 (-19.017, 12.148)	0.662	-15.020 (-31.658, 1.617)	0.076
LP(a)	8.642 (-44.971, 62.256)	0.749	-6.724 (-35.969, 22.521)	0.648
Lp-PLA2	0.023 (-0.038, 0.084)	0.451	0.045 (-0.013, 0.103)	0.126
FFA	-13.679 (-51.406, 24.048)	0.472	-19.325 (-53.829, 15.180)	0.268
Model 2				
TG	-0.433 (-9.393, .527)	0.923	-3.456 (-14.071, 7.158)	0.518
TC	4.899 (-2.164, 11.963)	0.171	2.789 (-4.502, 10.079)	0.448
HDL-C	26.677 (2.806, 50.548)	0.029	0.375 (-31.427, 32.176)	0.981
LDL-C	4.003 (-5.362, 13.369)	0.396	4.879 (-4.145, 13.903)	0.284
Apo-A	28.429 (-5.493, 62.352)	0.099	-9.088 (-59.995, 41.818)	0.723
Apo-B	5.802 (-21.507, 33.110)	0.672	16.662 (-12.739, 46.063)	0.262
Apo A/B	7.736 (-8.464, 23.936)	0.343	-11.877 (-28.425, 4.672)	0.157
LP(a)	8.537 (-44.445, 61.519)	0.748	-11.586 (-40.417, 17.244)	0.425
Lp-PLA2	-0.007 (-0.066, 0.053)	0.826	0.039 (-0.018, 0.095)	0.174
FFA	-29.707 (-66.284, 6.870)	0.110	0.639 (-35.891, 37.169)	0.972
Model 3				
TG	1.179 (-8.087, 10.445)	0.800	-3.805 (-14.404, 6.793)	0.476
TC	4.147 (-3.283, 11.576)	0.268	1.683 (-5.678, 9.045)	0.649
HDL-C	23.673 (-1.130, 48.475)	0.061	-0.039 (-31.630, 31.552)	0.998
LDL-C	3.140 (-6.705, 12.985)	0.526	3.999 (-5.100, 13.097)	0.383
Apo-A	28.081 (-6.277, 62.439)	0.107	-12.544 (-63.174, 38.085)	0.622
Apo-B	3.019 (-25.544, 31.582)	0.833	10.971 (-19.329, 41.271)	0.472
Apo A/B	8.374 (-8.243, 244.990)	0.317	-9.751 (-26.540, 7.037)	0.250
LP(a)	9.534 (-43.475, 62.542)	0.720	-7.273 (-36.024, 21.477)	0.615
Lp-PLA2	-0.0011 (-0.065, 0.062)	0.968	0.029 (-0.028, 0.086)	0.308
FFA	-36.081 (-73.536, 1.374)	0.059	-5.695 (-44.418, 33.028)	0.770

Note: Model 1 adjusted for: None. Model 2 adjusted for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, and BMI. Model 3 adjusted for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, BMI, GLU, P, and Fe. TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein Cholesterol; LDL-C: low-Density Lipoprotein Cholesterol; Apo-A: apolipoprotein A; Apo B: apolipoprotein B; LP(a): lipoprotein a; Lp-PLA2: lipoprotein-associated phospholipase A2; FFA: free fatty acid.

risk groups and indicate the risk for osteoporosis or osteoporotic fracture. The study found that age was the strongest negative indicator affecting BMD, particularly in women, where BMD decreased significantly with increasing age. This decline in BMD is attributed to the increase in bone volume rich in trabeculae in women [29], especially postmenopausal women, and the decline in estrogen levels [30], which leads to a greater loss of bone mass in women than in men [31]. This may be a reasonable explanation for our sample results: women are generally lower than men in BMD results.

Another reason for lower BMD in women may be due to differences in lipid metabolism. In the

Table 7. Association between lipid metabolism indices and the risk of osteopenia or osteoporosis in females (subgroup analysis stratified by age)

	Middle-aged Female		Elderly female	
	OR (95% CI)	P	OR (95% CI)	P
Model 1				
TG	1.381 (0.804, 2.373)	0.242	1.628 (0.558, 4.750)	0.372
TC	1.211 (0.780, 1.881)	0.394	1.674 (0.848, 3.303)	0.137
HDL-C	0.886 (0.267, 2.936)	0.843	2.152 (0.238, 19.464)	0.495
LDL-C	1.294 (0.756, 2.216)	0.348	1.856 (0.787, 4.377)	0.158
Apo-A	1.556 (0.171, 14.130)	0.694	11.285 (0.242, 526.393)	0.216
Apo-B	2.620 (0.543, 12.630)	0.230	5.184 (0.415, 64.740)	0.201
Apo A/B	0.791 (0.307, 2.036)	0.627	0.833 (0.255, 2.718)	0.762
LP(a)	0.762 (0.066, 8.799)	0.828	0.271 (0.031, 2.411)	0.242
Lp-PLA2	0.999 (0.995, 1.003)	0.698	1.003 (0.997, 1.008)	0.326
FFA	2.157 (0.226, 20.615)	0.505	0.236 (0.013, 4.168)	0.324
Model 2				
TG	1.718 (0.787, 3.750)	0.174	2.076 (0.523, 8.245)	0.299
TC	1.185 (0.680, 2.064)	0.550	2.494 (1.001, 6.213)	0.050
HDL-C	0.466 (0.100, 2.168)	0.330	3.116 (0.218, 44.468)	0.402
LDL-C	1.381 (0.702, 2.718)	0.350	3.039 (0.945, 9.766)	0.062
Apo-A	0.763 (0.045, 13.087)	0.852	34.663 (0.333, 3613.680)	0.135
Apo-B	3.437 (0.484, 24.384)	0.217	16.614 (0.565, 488.858)	0.103
Apo A/B	0.603 (0.194, 1.875)	0.382	0.661 (0.157, 2.792)	0.573
LP(a)	1.808 (0.101, 32.365)	0.688	0.199 (0.011, 3.446)	0.267
Lp-PLA2	1.001 (0.995, 1.006)	0.790	1.005 (0.999, 1.011)	0.121
FFA	1.708 (0.083, 35.173)	0.729	0.070 (0.002, 2.824)	0.159
Model 3				
TG	1.742 (0.744, 4.082)	0.201	2.306 (0.556, 9.562)	0.249
TC	1.225 (0.697, 2.152)	0.481	3.385 (1.123, 10.206)	0.030
HDL-C	0.394 (0.072, 2.165)	0.284	5.021 (0.277, 90.996)	0.275
LDL-C	1.465 (0.728, 2.946)	0.284	3.916 (1.059, 14.482)	0.041
Apo-A	0.672 (0.032, 14.311)	0.799	133.513 (0.868, 20534.052)	0.057
Apo-B	3.904 (0.503, 30.307)	0.193	42.876 (0.848, 2168.635)	0.060
Apo A/B	0.537 (0.162, 1.779)	0.309	0.537 (0.117, 2.476)	0.426
LP(a)	2.067 (0.103, 41.487)	0.635	0.283 (0.013, 6.047)	0.419
Lp-PLA2	1.000 (0.995, 1.006)	0.922	1.007 (1.000, 1.014)	0.051
FFA	1.792 (0.056, 56.842)	0.741	0.063 (0.001, 3.045)	0.162

Note: Model 1 adjusted for: None. Model 2 adjusted for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, and BMI. Model 3 adjusted for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, BMI, GLU, P, and Fe. TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein Cholesterol; LDL-C: low-density lipoprotein Cholesterol; Apo-A: apolipoprotein A; Apo B: apolipoprotein B; LP(a): lipoprotein a; Lp-PLA2: lipoprotein-associated phospholipase A2; FFA: free fatty acid.

study, women had higher levels of lipid metabolism, and these lipids were correlated with BMD. A positive correlation was observed only for Apo-A/B in women, while TG, TC, LDL-C, Apo-B, and Lp-PLA2 were all negatively correlated with BMD. In contrast, more positive correlations with BMD were observed in men, such as TC, LDL-C, Apo-B, and Lp-PLA. Therefore, lipids have a strong negative impact on BMD in women, causing a significant decrease in BMD compared to men. Although many studies have investigated the relationship between lipids and BMD, no consensus has been reached, and the results are still subject to debate. For

Table 8. Association between lipid metabolism indices and the risk of osteopenia or osteoporosis in males (subgroup analysis stratified by age)

	Middle-aged male		Elderly male	
	OR (95% CI)	P	OR (95% CI)	P
Model 1				
TG	0.881 (0.490, 1.583)	0.672	1.262 (0.659, 2.415)	0.482
TC	0.705 (0.427, 1.162)	0.171	0.758 (0.476, 1.207)	0.243
HDL-C	1.236 (0.287, 5.314)	0.776	0.807 (0.135, 4.821)	0.814
LDL-C	0.602 (0.324, 1.121)	0.110	0.709 (0.393, 1.277)	0.252
Apo-A	0.845 (0.093, 7.685)	0.881	0.498 (0.023, 10.628)	0.655
Apo-B	0.419 (0.071, 2.492)	0.419	0.234 (0.033, 1.669)	0.147
Apo A/B	1.912 (0.727, 5.034)	0.189	1.760 (0.553, 5.597)	0.338
LP(a)	0.138 (0.003, 6.270)	0.309	1.517 (0.214, 10.744)	0.677
Lp-PLA2	0.998 (0.994, 1.002)	0.383	0.999 (0.995, 1.003)	0.635
FFA	1.291 (0.122, 13.717)	0.832	3.063 (0.299, 31.336)	0.345
Model 2				
TG	1.077 (0.554, 2.096)	0.826	1.886 (0.773, 4.599)	0.163
TC	0.674 (0.380, 1.195)	0.177	0.819 (0.467, 1.437)	0.487
HDL-C	0.168 (0.019, 1.518)	0.112	0.588 (0.046, 7.533)	0.684
LDL-C	0.667 (0.308, 1.444)	0.305	0.800 (0.400, 1.600)	0.528
Apo-A	0.065 (0.002, 1.852)	0.110	1.050 (0.019, 57.155)	0.981
Apo-B	0.661 (0.076, 5.792)	0.709	0.344 (0.036, 3.326)	0.357
Apo A/B	0.862 (0.222, 3.352)	0.830	1.545 (0.428, 5.575)	0.506
LP(a)	0.070 (0.001, 8.885)	0.282	5.018 (0.452, 55.747)	0.189
Lp-PLA2	1.000 (0.995, 1.004)	0.851	0.999 (0.994, 1.004)	0.665
FFA	9.313 (0.494, 175.456)	0.136	0.875 (0.049, 15.512)	0.927
Model 3				
TG	0.991 (0.487, 2.017)	0.980	2.618 (0.857, 7.998)	0.091
TC	0.708 (0.393, 1.277)	0.252	0.898 (0.496, 1.626)	0.722
HDL-C	0.191 (0.018, 2.003)	0.167	0.340 (0.022, 5.178)	0.437
LDL-C	0.708 (0.318, 1.575)	0.397	0.902 (0.436, 1.866)	0.780
Apo-A	0.062 (0.001, 2.626)	0.146	0.740 (0.010, 57.126)	0.892
Apo-B	0.793 (0.079, 7.964)	0.844	0.664 (0.060, 7.306)	0.738
Apo A/B	0.825 (0.189, 3.595)	0.798	1.002 (0.259, 3.882)	0.998
LP(a)	0.098 (0.001, 11.587)	0.340	3.720 (0.320, 43.186)	0.294
Lp-PLA2	0.999 (0.994, 1.005)	0.835	1.001 (0.996, 1.006)	0.806
FFA	16.958 (0.686, 418.952)	0.084	8.788 (0.178, 434.275)	0.275

Note: Model 1 adjusted for: None. Model 2 adjusted for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, and BMI. Model 3 adjusted for: gender, age, blood group, cardiovascular disease, hypertension, diabetes, smoking and alcohol history, BMI, GLU, P, and Fe. TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein Cholesterol; LDL-C: low-density lipoprotein Cholesterol; Apo-A: apolipoprotein A; Apo B: apolipoprotein B; LP(a): lipoprotein a; Lp-PLA2: lipoprotein-associated phospholipase A2; FFA: free fatty acid.

instance, TC and LDL were negatively correlated with lumbar spine and whole-body BMD in postmenopausal women [32] and were also found to be negatively correlated in middle-aged men and women [33, 34]. However, in a study in Chinese women, the relationship between TC, LDL-C levels, and lumbar spine BMD was found to be nonlinear, with a negative correlation on the left side of the inflection point and an increase in BMD with an increase in TC and LDL-C on the right side [35]. Zhu et al. [36] observed a significant negative correlation between Apo-B concentrations in men and lumbar spine bone density; namely, an increase in

Apo-B concentrations elevated the risk of osteoporosis or bone loss.

The results of linear regression and correlation analysis in women were consistent; an increase in TC, LDL-C, Apo-B, and Lp-PLA2 levels caused varying degrees of BMD reduction, and this relationship persisted in the subsequent analysis of the elderly female subgroup. The univariate linear regression results in men showed that TC, LDL-C, Apo-B, Lp-PLA2, and FFA were all negatively correlated with BMD. However, after excluding other confounding factors, only FFA continued to have a negative impact on BMD, and this negative correlation was no longer present in the age subgroup analysis. The mechanism of action of FFA on BMD may be achieved by increasing the activity of osteoclasts and reducing the function of osteoblasts. This leads to increased bone resorption and decreased bone formation, resulting in decreased BMD and an elevated risk of lipotoxic-mediated osteoporosis [37].

The increase of TC and LDL-C levels in the elderly women group was related to the increased risk of osteoporosis or low bone mass, which were independent risk factors for osteoporosis or low bone mass, and also reflected the negative correlation with BMD to some extent. Relevant basic research also explains this result. Excessive cholesterol intake and storage in the body can form hypercholesterolemia and damage tissues and organs, which is called “cholesterol toxicity” [38] and is the basis for many metabolic diseases. Animal studies have shown that hypercholesterolemia promotes osteoclast formation in mice [39], and LDL-C increases osteoclast activity by mediating cholesterol transfer. When LDL-C levels decrease, osteoclast activity also decreases [40]. High concentrations of cholesterol not only affect osteoclasts but also inhibit osteoblast proliferation and reduce the expression of osteoblast markers [41]. Intermediate metabolites activate estrogen receptors [42] and liver X receptors [43] to promote osteoclastogenesis and inhibit osteogenesis. In humans, mutations in the LDL receptor-related protein 6 (LRP6) gene are associated with severe osteoporosis concurrent with high serum LDL-C levels [44]. Therefore, high concentrations of LDL-C and TC reduce bone formation and have an adverse effect on patient BMD, inducing the occurrence of osteoporosis. Even after adjusting for age and BMI, a decrease was still found in the bone density of patients with familial hypercholesterolemia [45]. There are many studies on the relationship between osteoporosis and lipid metabolism levels, but no consistent conclusions have been drawn. Demir et al. regarded LDL-C as an important factor for postmenopausal women with osteoporosis [46]. Kim et al. also found a negative correlation between TC and LDL-C and BMD in the general population [17]. However, a meta-analysis [47] in 2018 found no relationship between LDL-C and osteoporosis, and postmenopausal women with osteoporosis had higher serum levels of HDL-C and TC. Another cross-sectional study also showed no relationship with LDL-C, and osteoporosis increased with increasing TC and triglyceride levels [48]. The reasons for these differences may be related to various factors such as age, gender, race, weight, exercise, and lifestyle habits of the study population [49]. In fact, the probability of osteoporosis in women is higher than that in men [50], and osteoporotic fractures in women are more common in clinical practice [51]. Each standard deviation decrease in BMD increases the risk of fracture by 2 times [52]. It is predicted that by 2050, the number of osteoporotic fractures in China will increase to 5.99 million cases, causing an annual cost of 25.43 billion US dollars [53]. Therefore, it is crucial to pay attention to the BMD of women, especially postmenopausal women.

BMD reflects the mineral density of bones, which is the result of long-term accumulation of bone metabolism activities and cannot promptly reflect changes in the bone microenvironment. However, BTMs are blood indicators with biological sensitivity that can theoretically promptly indicate the general condition of bones and predict changes in BMD. Our study results suggest that in women, BTMs such as β-CTX, P1NP, 25(OH)D, and OC are negatively correlated with BMD. Elevated levels of these markers are associated with reduced BMD and an increased risk of high turnover osteoporosis, as they promote bone remodeling [9]. Therefore, we should be vigilant about the decrease in BMD caused by increased bone turnover levels, which may lead to osteoporosis and osteoporotic fractures [54]. However, some other studies had different results than ours.

For instance, Yang et al. found that β-CTX was significantly negatively correlated with BMD in both men and women but was not correlated with P1NP [55]. Lumachi et al. pointed out that no correlation was observed between the bone formation marker P1NP and BMD [56]. Our study also found that the content of BTMs was closely related to the lipid level, and there was no gender difference in this correlation. Therefore, a high or low BMD is not only influenced by independent effects of lipid metabolism or bone metabolism but also by the combined effects of their interactions. This may also explain why the conclusions regarding the predictive effect of lipid and BTMs on BMD differ in different studies.

This study has several strengths. First, regarding the association between some intermediate substances in lipid metabolism and BMD, such as LP(a), Lp-PLA2, and FFA, there is limited research or even a lack of research. Although these substances participate in lipid metabolism and their content is relatively low, they can reflect the level of blood lipids to some extent and may be closely related to bone health. Therefore, our study includes them together, which supplements the research field of lipid spectrum and its association with BMD and osteoporosis. Second, the present study explores the factors that affect BMD from multiple aspects and uses multiple linear regression and logistic regression models to link lipids with the occurrence of BMD and osteoporosis.

However, there are also several limitations in this study. First, this is a cross-sectional study, and the causal relationship between independent and dependent variables is not clear. Prospective studies are expected in the future to investigate the impact of improving lipid metabolism on BMD, BTMs, and osteoporosis. Second, the study sample is limited to inpatients in spinal surgery, which may lead to a population selection bias and affect the research results. Third, some confounding variables, such as estrogen levels, physical activity, dietary habits, and menopausal status, were ignored, which may affect the research results.

In conclusion, based on our study, several factors, such as age, sex, blood lipids, and BTM levels, have an impact on BMD. Among these factors, age has the most significant influence on BMD. Blood lipids have a more pronounced effect on female BMD, with TC, LDL-C, Apo-B, and Lp-PLA2 showing a negative correlation with BMD in elderly women. An increase in TC and LDL-C levels may elevate the risk of osteoporosis or low bone mass. Therefore, their combined effects should be taken into account in the prevention and treatment of osteoporosis. Further research is necessary to investigate the underlying mechanisms and potential interventions.

Acknowledgements

This study was supported by the Natural Science Foundation of Shandong Province (No. ZR2021MH040 and ZR2020QH074), and the Clinical medicine technology innovation program of Jinan (202225048).

Disclosure of conflict of interest

None.

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