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Association of Lipoprotein(a) with Coronary Artery Calcification and Bone Mineral Density in Elderly Individuals

İleri Yaştaki Bireylerde Lipoprotein(a)'nın Koroner Arter Kalsifikasyonu ve Kemik Mineral Yoğunluğu ile İlişkisi

ABSTRACT

Objective: Coronary artery calcification (CAC) and osteoporosis are common age-related conditions that may share underlying mechanisms such as inflammation and lipid dysregulation. Lipoprotein(a) [Lp(a)] has been suggested as a potential contributor to both processes. This study aims to investigate the relationship between CAC, bone mineral density (BMD), and Lp(a) levels in a statin-naive elderly population.

Method: This retrospective study included 310 patients aged ≥ 55 years who underwent coronary computed tomography angiography and Lp(a) measurement. CAC was assessed visually, and BMD was measured using vertebral Hounsfield units. Patients were stratified into three groups according to Lp(a) levels: ≤ 30, 30–49, and ≥ 50 mg/dL. Propensity score matching was performed for age and sex.

Results: Patients with CAC had higher Lp(a) levels [36.4 ± 33.2 vs. 21.7 ± 27.8 mg/dL, P < 0.001], lower high-density lipoprotein cholesterol (HDL-C) [52.6 ± 14.6 vs. 57.5 ± 17.9 mg/dL, P = 0.010], and lower BMD [152.9 ± 50.2 vs. 169.1 ± 51.0 HU, P = 0.009]. In multivariate analysis, both Lp(a) and HDL-C were independent predictors of CAC. Low BMD and CAC prevalence increased stepwise across Lp(a) strata: in patients with Lp(a) ≤ 30 mg/dL, low BMD was present in 28.9% and CAC in 52.6%; in those with Lp(a) 30–49 mg/dL, 37.2% and 66.7%; and in those with Lp(a) ≥ 50 mg/dL, 58.6% and 80.3%, respectively (P = 0.002 and P = 0.001).

Conclusion: Elevated Lp(a) is associated with both CAC and low BMD. Lp(a) ≥ 50 mg/dL may serve as a shared biomarker to identify individuals at risk for concurrent vascular and skeletal deterioration.

Keywords: Atherosclerosis, bone mineral density, coronary artery calcification, lipoprotein(a), osteoporosis

ÖZET

Amaç: Koroner arter kalsifikasyonu (KAK) ve osteoporoz, yaşa bağlı gelişen, inflamasyon ve lipid düzensizliği gibi ortak mekanizmalara sahip, birbiriyle ilişkili patolojilerdir. Lipoprotein(a) [Lp(a)], her iki sürece de katkıda bulunabilecek potansiyel bir faktör olarak önerilmiştir. Bu çalışmanın amacı, statin kullanmamış ileri yaştaki bireylerde KAK, kemik mineral yoğunluğu (KMY) ve Lp(a) düzeyleri arasındaki ilişkiyi araştırmaktır.

Yöntem: Bu retrospektif çalışmaya, bilgisayarlı tomografik koroner anjiyografisi ve Lp(a) ölçümü yapılmış, ≥ 55 yaş olan 310 hasta dahil edildi. KAK görsel olarak değerlendirildi, KMY ise vertebral Hounsfield birimleri kullanılarak ölçüldü. Hastalar Lp(a) düzeylerine göre, ≤ 30, 30–49 ve ≥ 50 mg/dL olarak üç gruba ayrıldı. Yaş ve cinsiyet için eğilim skoru eşleştirmesi yapıldı.

Bulgular: KAK bulunan hastalarda Lp(a) düzeyleri daha yüksek [36,4 ± 33,2 vs. 21,7 ± 27,8 mg/dL, P < 0,001], HDL-K düzeyleri daha düşük [52,6 ± 14,6 vs. 57,5 ± 17,9 mg/dL, P = 0,010] ve KMY daha düşük [152,9 ± 50,2 vs. 169,1 ± 51,0 HU, P = 0,009] idi. Çok değişkenli analizde hem Lp(a) hem de HDL-K, KAK'ın bağımsız belirleyicileri olarak bulundu. Düşük KMY ve KAK prevalansının, Lp(a) gruplarına göre kademeli olarak arttığı izlendi; Lp(a) ≤ 30 mg/dL olanlarda düşük KMY %28,9 ve KAK %52,6; Lp(a) 30–49 mg/dL olanlarda %37,2 ve %66,7; Lp(a) ≥ 50 mg/dL olanlarda %58,6 ve %80,3 (P = 0,002 ve P = 0,001) olarak saptandı.

Sonuç: Yüksek Lp(a) düzeyleri hem KAK hem de düşük KMY ile ilişkilidir. Lp(a) ≥ 50 mg/dL, hem damar hem kemik yapısında eş zamanlı bozulma riski taşıyan bireyleri belirlemede ortak bir biyobelirteç olarak kullanılabilir.

Anahtar Kelimeler: Ateroskleroz, kemik mineral yoğunluğu, koroner arter kalsifikasyonu, lipoprotein a, osteoporoz

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Arterial calcification, a process closely associated with atherosclerosis, results from the accumulation of hydroxyapatite crystals within the arterial extracellular matrix.[1] It represents an active, cell-controlled process resembling bone formation, involving vascular smooth muscle cell transdifferentiation and extracellular matrix remodeling.[2] While medial calcification predominantly affects peripheral arteries and is commonly related to diabetes and chronic kidney disease, intimal calcification in coronary arteries is primarily related to atherosclerosis and reflects an inflammatory process.[3] Advancement of coronary artery calcification (CAC) is closely related to an increased risk of cardiovascular events and is therefore considered a clinically relevant marker for risk stratification in asymptomatic individuals.[3] Recent guidelines recommend incorporating coronary calcium scoring alongside traditional cardiovascular risk factors to improve risk prediction accuracy.[3] Arterial calcification advances with aging, and osteoporosis frequently coexists as a common age-related comorbidity.

Osteoporosis, caused by low bone mineral density (BMD) leading to an increased risk of fractures, shares multiple pathophysiological mechanisms with vascular calcification, including chronic inflammation, oxidative stress, and dysregulated mineral metabolism.[4,5] This interaction is often referred to as the "bone–vascular axis."[4] Given this overlap, recent studies have emphasized the value of opportunistic screening for osteoporosis using coronary computed tomography (CT) scans. In patients undergoing CT for CAC scoring, vertebral bone attenuation can be simultaneously assessed, providing a cost-effective strategy to identify those at risk for low BMD.[6] The shared mechanisms between osteoporosis and arterial calcification have raised the possibility of common biomarkers related to the presence of both conditions.

Increased Lp(a) concentration has been consistently linked to a higher cardiovascular risk, and its clinical significance has become more widely recognized in recent years.[7] Lp(a) also promotes vascular calcification by enhancing inflammation, increasing the burden of oxidized phospholipids, and stimulating osteogenic differentiation of vascular smooth muscle cells.[8] While several studies have demonstrated an association between Lp(a) and the presence or progression of coronary artery calcification, some studies have failed to replicate this relationship, highlighting the need for further investigation.[9,10] Due to its possible interaction with bone metabolism, Lp(a) has also been investigated as a potential link between atherosclerosis and osteoporosis.[11] Although some studies have reported a negative correlation between Lp(a) levels and BMD or fracture risk, some large prospective cohort studies have not confirmed this association.[12,13] Despite these inconsistent findings, the possible role of Lp(a) in both vascular calcification and bone loss remains a subject of scientific interest due to shared underlying mechanisms.

In light of these conflicting findings, we aimed to investigate the relationships between coronary artery calcification, Lp(a) levels, and bone mineral density in a single cohort of patients who had coronary computed tomography angiography (CCTA). Understanding these associations may help raise awareness for considering screening for osteoporosis or coronary calcification in the presence of high Lp(a) levels and may enable earlier risk identification and clinical intervention.

ABBREVIATIONS

AHA	the American Heart Association
BMD	Bone mineral density
BMI	Body mass index
CAC	Coronary artery calcification
CCTA	Coronary computed tomography angiography
CT	Computed tomography
CVD	Cardiovascular disease
ECG	Electrocardiogram
eGFR	Estimated glomerular filtration rate
HDL-C	High-density lipoprotein cholesterol
hs-CRP	High-sensitivity C-reactive protein
LDL-C	Low-density lipoprotein cholesterol
Lp(a)	Lipoprotein(a)
MDRD	The Modification of Diet in Renal Disease
ROI	Region of interest

Materials and Methods

This retrospective study, which received approval from the Ethics Committee of Koç University School of Medicine (Approval Number: 2025.222.IRB2.102, Date: 15.05.2025), was undertaken in compliance with the Declaration of Helsinki. The study included patients aged 55 years or older who underwent Lp(a) measurement and CCTA at our university hospital between January 2018 and January 2023. Participants signed written informed consent.

Patients with a history of cardiovascular disease (CVD) were excluded from the study. CVD was defined as a history of myocardial infarction, unstable angina, ≥ 50% stenosis in the epicardial coronary arteries confirmed by prior computed tomography or conventional invasive angiography, ischemia detected on stress imaging, or previous coronary revascularization. Patients receiving statin therapy were also excluded. In addition, individuals with significant arrhythmias, valvular heart disease, cardiomyopathy, or pulmonary heart disease were not included.

In addition, individuals with chronic liver disease, chronic kidney disease with estimated glomerular filtration rate (eGFR) < 45 mL/min/1.73m^2, active cancer or a history of cancer, and women on hormone replacement therapy were not eligible. Considering the effect of Lp(a) on inflammation, patients with signs of acute infection or inflammation [high-sensitivity C-reactive protein (hs-CRP) > 10 mg/L, leukocytosis (white blood cell count > 11 × 10^9 cells/L), fever > 38°C, or antibiotic use] were also excluded.

Data on age, sex, smoking status, the presence of hypertension and diabetes, body mass index (BMI), and laboratory findings including fasting glucose, HbA1c, creatinine, estimated glomerular filtration rate, total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides, high-density lipoprotein cholesterol (HDL-C), and Lp(a) levels were collected. The Modification of Diet in Renal Disease (MDRD) formula was used to calculate eGFR.[5] Hypertension was considered present if

Table 1. Baseline characteristics of study population

Variables	CAC (-) (n = 124)	CAC (+) (n = 186)	P
Age (mean ± SD)	66.96 ± 7.09	68.26 ± 6.78	0.106
Sex (female), n (%)	75 (60.5)	96 (51.6)	0.131
BMI, kg/m^2 (mean ± SD)	28.29 ± 5.54	29.55 ± 5.35	0.068
Smokers, n (%)	40 (32.2)	65 (34.9)	0.627
Hypertension, n (%)	63 (50.8)	121 (65.05)	**0.012**
Diabetes, n (%)	33 (26.6)	66 (35.5)	0.101
eGFR, mL/min/1.73 m^2 (mean ± SD)	83.67 ± 19.95	80.83 ± 20.23	0.232
Glucose, mg/dL (mean ± SD)	112.97 ± 30.95	119.05 ± 40.06	0.165
HbA1C, % (mean ± SD)	6.08 ± 0.81	6.86 ± 5.01	0.211
Total cholesterol, mg/dL (mean ± SD)	201.06 ± 52.78	201.95 ± 55.02	0.887
HDL-C, mg/dL (median, Q1-Q3)*	58 (45-66.5)	51 (42.75-60.25)	**0.041**
LDL-C, mg/dL, mean ± SD	128.88 ± 48.73	130.81 ± 50.43	0.738
Triglycerides, mg/dL (median, Q1-Q3)*	121 (84-175.5)	140 (106-184)	0.118
hsCRP, mg/L (median, Q1-Q3)*	1.9 (1-3.7)	2.1 (1.15-4.8)	0.916
Lp(a), mg/dL (median, Q1-Q3)*	14 (5.25-25.75)	27 (10-52)	**<0.001**
Bone mineral density (mean ± SD)	169.12 ± 51.03	152.86 ± 50.20	**0.009**
Coronary stenosis > 50%	31 (25.00)	77 (41.39)	**0.004**

BMI, Body mass index; CAC, Coronary artery calcification; eGFR, Estimated glomerular filtration rate; HDL-C, High-density lipoprotein cholesterol; hsCRP, High-sensitivity c-reactive protein; LDL-C, Low-density lipoprotein cholesterol; Lp(a), Lipoprotein (a). *Nonparametric analyses were performed due to the absence of a normal distribution.

previously diagnosed or if repeated office blood pressure readings were consistently over 140/90 mmHg. Diabetes was identified based on a prior diagnosis or laboratory findings of fasting glucose ≥ 126 mg/dL or HbA1c ≥ 6.5%. Lp(a) levels were determined by an immunoturbidimetric method using the Roche Cobas Tina-quant Lipoprotein(a) Gen 2 kit in the institution's laboratory.

CCTA images of eligible patients were retrospectively analyzed. Scans were acquired using 64-slice and 128-slice scanners (Somatom Definition AS, Siemens Healthineers) with retrospective electrocardiogram (ECG) gating to synchronize image acquisition with the cardiac cycle. A 70–90 mL dose of intravenous contrast (iopromide) was injected at 4–5 mL/s, then flushed with 40 mL of saline. Bolus tracking was used with a threshold of 100 HU in the ascending aorta. Image reconstruction was performed with a medium-soft tissue kernel, an interval of 0.5 mm, and a slice thickness of 0.75 mm.

CAC was visually assessed based on 18 coronary artery segments, following the American Heart Association (AHA) classification. All scans were independently reviewed by an experienced cardiologist and an experienced radiologist, both blinded to clinical data. Any discrepancies between the readers were resolved by consensus.

Thoracic vertebral bone density was measured on axial bone window images with a slice thickness of 1.5 mm, along with sagittal reformatted images. The seventh thoracic vertebra (T7) was used for the assessment due to its consistent visualization across scans and acceptable distance from the aortic calcification zone. A circular region of interest (ROI) was manually placed in the anterior trabecular part of the vertebral body, avoiding cortical bone and vascular structures.

Statistical analyses were carried out using SPSS version 28.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism 10.5.0 (GraphPad Software, San Diego, USA). Propensity score matching was performed to eliminate age and sex differences between the CAC groups. After excluding 56 cases, the analysis continued with a total of 310 age- and sex-matched patients, of whom 124 did not have CAC and 186 had CAC.

The Kolmogorov-Smirnov test was used to evaluate the distribution of continuous variables. If the continuous data were normally distributed, they were presented as mean ± standard deviation (SD); if the distribution was not normal, continuous data were presented as median with interquartile range (IQR). Categorical variables were reported as counts and percentages. Categorical data were compared using the Chi-square test, continuous data with a normal distribution were compared using the Student's t-test, and data without a normal distribution were compared using the Mann–Whitney U test. To identify independent predictors, logistic regression analyses, including both univariate and multivariate, were conducted. Statistical significance was defined as a two-tailed p-value of less than 0.05.

Although bone mineral density was primarily analyzed as a continuous variable, it was also categorized into two groups, low and high BMD, using the cohort mean value of 173 as the cutoff, to allow for analyses requiring categorical variables. Similarly, although Lp(a) was mainly treated as a continuous variable, to evaluate the potential effects of commonly used Lp(a) thresholds recommended by the European Atherosclerosis Society on BMD and arterial calcification, the cohort was further classified into three groups according to Lp(a) levels: ≤ 30 mg/dL, > 30 and < 50 mg/dL, and ≥ 50 mg/dL.[14]

Table 2. Independent predictors of coronary artery calcification (CAC)

Variables	OR	95% CI	P
Model 1			
Hypertension	1.461	0.858–2.489	0.163
HDL-C	0.976	0.960–0.993	0.004
Lp(a)	1.017	1.007–1.028	<0.001
Bone mineral density	0.996	0.991–1.001	0.149
Model 2			
Hypertension	1.49	0.863–2.574	0.152
HDL-C	0.983	0.966–0.999	0.043
Lp(a)	1.013	1.003–1.024	0.012
Bone mineral density	0.996	0.991–1.001	0.141
Coronary stenosis > 50%	3.537	1.765–7.088	<0.001

OR, Odd ratios; CI, Confidence interval; HDL-C, High-density lipoprotein cholesterol; Lp(a), Lipoprotein (a).

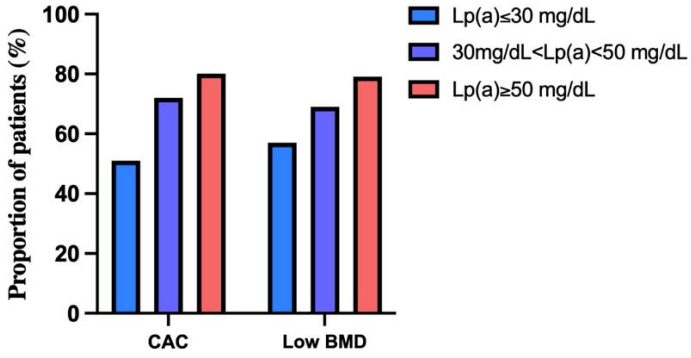

Figure 1. Proportions of patients with coronary artery calcification (CAC) and low bone mineral density (BMD) across Lp(a) categories. Patients were stratified into three groups based on guideline-recommended Lp(a) thresholds: ≤ 30 mg/dL, 30–49 mg/dL, and ≥ 50 mg/dL. The prevalence of CAC and low BMD increased with higher Lp(a) levels.

Results

Following propensity score matching, the baseline characteristics of patients with and without CAC were compared (Table 1). Among the age- and sex-matched cohort, patients with CAC had a higher prevalence of hypertension (65.1% vs. 50.8%, P = 0.012), coronary stenosis > 50% (41.4% vs. 25.0%, P = 0.004) compared to those without CAC. Additionally, HDL-C levels were significantly lower [51 mg/dL (Q1-Q3: 42.75–60.25) vs. 58 mg/dL (Q1-Q3: 41–64), P = 0.041], and median Lp(a) levels were significantly elevated in patients with CAC [27 mg/dL (Q1-Q3: 10–52) vs. 14 mg/dL (Q1-Q3: 5.25–25.75) P < 0.001]. Furthermore, BMD was significantly lower in the CAC group compared to the non-CAC group (152.86 ± 50.20 vs. 169.12 ± 51.03, P = 0.009).

Independent predictors of CAC were identified using multivariate logistic regression analysis across two models (Table 2). In the first model, variables that were statistically significant in the univariate analysis, excluding coronary stenosis > 50%, were included. Higher Lp(a) levels (odds ratio [OR]: 1.017; 95% confidence interval [CI]: 1.007–1.028; P < 0.001) and lower HDL-C levels (OR: 0.976; 95% CI: 0.960–0.993; P = 0.004) were independently associated with CAC. In contrast, hypertension and BMD were not independently associated with CAC in this model. In the second model, coronary stenosis > 50% was added to the regression analysis. Lp(a) levels (OR: 1.013; 95% CI: 1.003–1.024; P = 0.012), lower HDL-C levels (OR: 0.983; 95% CI: 0.966–0.999; P = 0.043), and the presence of significant coronary stenosis (OR: 3.537; 95% CI: 1.765–7.088; P < 0.001) continued to show an independent association with CAC. Similar to the first model, hypertension and BMD did not show significant associations. Correlation analysis was performed between BMD and lipoprotein levels. BMD was not significantly correlated with LDL-C, HDL-C, triglycerides, or total cholesterol. However, a weak but statistically significant negative correlation was observed between BMD and Lp(a) levels (r = -0.136, P = 0.020). Patients were stratified into two groups based on the mean BMD of the cohort (173 HFU). While total cholesterol, HDL-C, LDL-C, and triglyceride levels did not differ significantly between the groups, Lp(a) levels were significantly higher in the low BMD group [24.00 (8.00–48.00) vs. 14.00 (6.00–34.50) mg/dL, p = 0.006]. A comparison of other characteristics is presented in Appendix 1. In addition, Lp(a) level was identified as an independent predictor of low BMD after adjustment for age and sex (OR: 1.010; 95% CI: 1.001–1.019).

When patients were classified based on guideline-recommended Lp(a) cut-off levels, the highest proportions of CAC (80.3%) and low BMD (79.3%) were in the group with Lp(a) ≥ 50 mg/dL. This was followed by the group with Lp(a) between 30 and 50 mg/dL, in which 72% had CAC and 69% had low BMD. The lowest proportions were seen in patients with Lp(a) ≤ 30 mg/dL, where 51% had CAC and 57.8% had low BMD (Figure 1). Mean BMD was highest in patients with Lp(a) ≤ 30 mg/dL (167.0 HFU), and significantly lower in those with Lp(a) between 30–49 mg/dL (144.5 HFU, P = 0.015) and Lp(a) ≥ 50 mg/dL (140.3 HFU, P = 0.001) (Figure 2). BMD was not significantly different between the 30–49 mg/dL and ≥ 50 mg/dL groups (P = 0.902).

Discussion

In this study of statin-naive individuals aged 55 years and older, patients with CAC were found to have lower HDL-C levels and higher Lp(a) levels. Both low HDL-C and elevated Lp(a) remained independent predictors of CAC, even after adjusting for coronary stenosis > 50%. We also demonstrated that low BMD was associated with elevated Lp(a) in our cohort. Furthermore, patients with Lp(a) ≥ 50 mg/dL had the highest prevalence of CAC and the lowest mean BMD, suggesting a potential shared mechanism linking Lp(a) with both vascular and skeletal pathology.

To minimize the influence of potential confounders, we restricted our analysis to individuals aged ≥ 55 years, an age group in which both osteoporosis and vascular calcification become more common. Furthermore, Lp(a) levels are known to rise following menopause in women, which may have contributed to the associations observed.[15] Statin users were excluded from the study, as statins may accelerate CAC independent of their lipid-lowering effect, potentially biasing the assessment of calcification severity.[16]

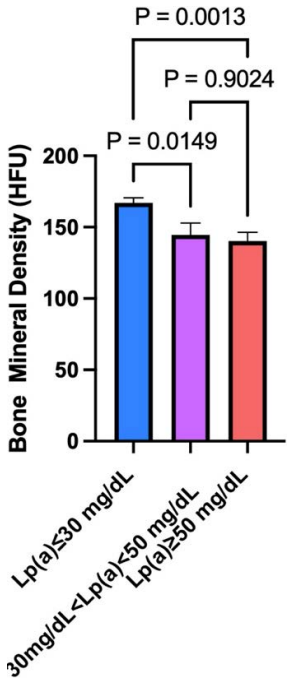

Figure 2. Mean bone mineral density (BMD) across Lp(a) categories. Patients were stratified into three groups based on Lp(a) levels: ≤ 30 mg/dL, 30–49 mg/dL, and ≥ 50 mg/dL. A trend toward lower BMD was observed with increasing Lp(a) levels.

CAC is associated with advanced atherosclerosis and increased cardiovascular risk; therefore, identifying factors related to CAC is crucial for developing effective prevention strategies. The role of Lp(a) in atherosclerosis and degenerative aortic stenosis is well established, and numerous observational studies and meta-analyses support the contribution of Lp(a) to the progression of CAC.[9,14,17] Consistent with these findings, our study demonstrated that Lp(a) levels were significantly higher in patients with CAC, and Lp(a) was found to be independently associated with CAC. In contrast, a recent prospective study did not find a significant relationship between Lp(a) and CAC.[10] While the prospective design is valuable for exploring causal relationships, certain limitations, particularly the relatively young mean age of participants (around 40 years) and the short follow-up period (3–5 years), may have hindered the ability to capture the long-term effects of Lp(a) on vascular calcification. Further longitudinal studies involving older populations and longer follow-up durations are needed to definitively assess the contribution of Lp(a) to CAC. We also demonstrated that HDL-C levels were lower in the CAC group and that low HDL-C was an independent predictor of CAC. This finding aligns with the well-established role of low HDL-C as a cardiovascular risk enhancer. Numerous studies have investigated the relationship between lipid parameters and CAC. While some have reported an association between low HDL-C levels and increased CAC, others have failed to confirm this relationship or have suggested a U-shaped association instead.[18–20] These discrepancies may be attributed to differences in HDL-C subfractions and the functional properties of HDL particles.[21]

Osteoporosis and vascular calcification are increasingly recognized as interrelated conditions that share common pathophysiological mechanisms. These mechanisms may promote both osteoclast-mediated bone resorption and vascular smooth muscle cells' osteogenic differentiation, thereby contributing to bone loss and vascular calcification.[4] In line with this concept, the impact of atherogenic risk factors associated with vascular calcification on bone density and osteoporosis, particularly the influence of lipid parameters, has been investigated in numerous studies. In agreement with our findings, Pliatsika et al.[12] reported a relationship between high Lp(a) levels and low BMD. However, a UK Biobank study did not demonstrate a consistent association between Lp(a) levels and osteoporotic fractures; instead, it identified Lp(a) as a potential risk enhancer for osteoporosis only during the one-year follow-up period.[22] Similarly, Haring et al.[13] reported no significant difference in BMD prevalence across Lp(a) quintiles in postmenopausal women. In contrast, our study demonstrated that in women aged ≥ 55 years, the prevalence of low BMD increased progressively across Lp(a) strata (26.7%, 30.3%, and 52.3%, respectively; P = 0.010). The discrepancies among these studies may be attributed to differences in cohort characteristics, genetic backgrounds, and the Lp(a) cut-off values used for classification. Nevertheless, the stepwise increase in both CAC and low BMD prevalence across ascending Lp(a) strata in our cohort further supports the potential value of Lp(a) as a shared biomarker. Notably, patients with Lp(a) ≥ 50 mg/dL, a threshold recommended by the European Atherosclerosis Society for enhanced cardiovascular risk, had both the highest CAC prevalence and the lowest BMD, suggesting that Lp(a) elevation may serve as a useful marker to prompt further cardiovascular and osteoporosis screening. Furthermore, despite the clear association between CAC and lower BMD in univariate analysis, BMD was not identified as an independent predictor of CAC in multivariate models. This may be due to the confounding influence of Lp(a), a shared risk factor included in the model.

Our study has several strengths, including the use of a well-defined cohort with comprehensive imaging and laboratory assessments, and adjustment for potential confounders through propensity score matching. However, it also has limitations. A cross-sectional design prevents establishing causality and the use of a single Lp(a) measurement does not reflect long-term exposure or variability. Additionally, BMD assessment was performed opportunistically from non-dedicated CT scans, which, although practical, may not accurately capture fracture risk.

Conclusion

In conclusion, our study demonstrates that elevated Lp(a) levels are associated with both coronary artery calcification and lower bone mineral density in a Turkish cohort aged ≥ 55 years, suggesting that Lp(a) may play a dual role in promoting both vascular and skeletal deterioration. Further prospective, longitudinal studies will clarify causality and explore whether Lp(a)-lowering interventions may simultaneously reduce cardiovascular and osteoporotic risk.

Ethics Committee Approval: Ethics committee approval was obtained from Ethics Committee of Koç University School of Medicine (Approval Number: 2025.222.IRB2.102, Date: 15.05.2025).

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Appendix 1. Baseline characteristics stratified by bone mineral density groups

Variables	Lower BMD (≤ 173 HFU) (n = 187)	Higher BMD (≤ 173 HFU) (n = 105)	P
Age (mean± SD)	69.34 ± 6.50	65.25 ± 6.82	**<0.001**
Sex (female) n (%)	123 (65.8%)	41 (39.0%)	**<0.001**
BMI,m^2/ kg (mean± SD)	29.33 ± 5.18	28.56 ± 5.46	0.268
Smokers, n (%)	59 (33.1%)	37 (36.6%)	0.556
Hypertension, n (%)	121 (64.7%)	54 (51.4%)	0.026
Diabetes, n (%)	64 (34.2%)	32 (30.5%)	0.513
eGFR ml/min/1.73 m^2 (mean± SD)	80.86 ± 19.10	85.38 ± 20.85	0.066
Glucose mg/dL (mean± SD)	115.44 ± 36.23	119.10 ± 34.79	0.411
HbA1C, % (mean± SD)	6.78 ± 4.97	6.23 ± 0.98	0.417
Total cholesterol, mg/dL(mean± SD)	203.35 ± 56.61	200.29 ± 49.48	0.646
HDL-C mg/dL (median, Q1-Q3)*	52 (43.75-64)	51.00 (43.00-60.50)	0.402
LDL-C, mg/dL (mean± SD)	131.11 ± 45.24	130.04 ± 51.65	0.859
Triglycerides, mg/dL (median, Q1-Q3)*	137.00 (105.00-184.00)	132.00 (92.50-174.50)	0.266
hsCRP mg/L (median, Q1-Q3)*	2.00 (1.00-4.05)	2.1 (1.10-5.00)	0.565
Lp(a), mg/dL (median, Q1-Q3)*	24.00 (8.00-48.00)	14 (6.00-34.50)	**0.006**
Bone mineral density (mean± SD)	127.21 ± 28.02	212.64 ± 34.75	**<0.001**
CAC (%)	127 (70.2%)	54 (51.9%)	**0.002**

BMD, Bone mineral density; BMI, body mass index; CAC, Coronary artery calcification; eGFR, estimated glomerular filtration rate; HDL-C, high density lipoprotein cholesterol; hsCRP, high sensitive C reactive protein; LDL-C,low density lipoprotein cholesterol; Lp(a), lipoprotein (a). * Nonparametric analyses were performed due to the absence of a normal distribution.