Lipids in Health and Disease

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Non-linear association of the platelet/high-density lipoprotein cholesterol ratio with bone mineral density a cross-sectional study

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Abstract

Background Numerous studies have demonstrated shared risk factors and pathophysiologic mechanisms between osteoporosis and cardiovascular disease. High-density lipoprotein cholesterol (HDL-C) and platelets have long been recognized as crucial factors for cardiovascular health. The platelet to HDL-C ratio (PHR) combines platelet count and high-density lipoprotein cholesterol (HDL-C) level, It is a novel biomarker for metabolic syndrome and cardiovascular disease. The platelet to HDL-C ratio (PHR) possibly reflects the balance between proinflammatory and anti-inflammatory states in the body. Therefore, we hypothesized that changes in PHR ratios may predict a predisposition to pro-inflammatory and increased bone resorption. However, the relationship between the platelet to HDL-C ratio (PHR) and bone mineral density (BMD) remains insufficiently understood. This study aimed to elucidate the relationship between the platelet to HDL-C ratio (PHR) index and bone mineral density (BMD).

Methods Data from the NHANES 2005–2018 were analyzed, excluding adults with missing key variables and specific conditions. Nonlinear relationships were explored by fitting smoothed curves and generalized additive models, with threshold effects employed to calculate inflection points. Additionally, subgroup analyses and interaction tests were conducted.

Results The study included 13,936 individuals with a mean age of 51.19 ± 16.65 years. Fitted smoothed curves and generalized additive models revealed a nonlinear, inverted U-shaped relationship between the two variables. Threshold effect analysis showed a significant negative *association* between PHR and total femur bone mineral density (BMD) beyond the inflection point of platelet to HDL-C ratio (PHR) 33.301. Subgroup analyses showed that a significant interaction between these two variables was observed only in the age and sex subgroups (*P*-interaction < 0.05).

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Conclusions Our study identified a complex, nonlinear, inverted U-shaped relationship between platelet to HDL-C ratio (PHR) and total femur bone mineral density (BMD). These findings underscore the importance of maintaining optimal PHR levels to support bone health, especially in high-risk populations.

Keywords Bone mineral density, Osteoporosis, National health and nutrition examination survey, High-density lipoprotein cholesterol, Platelets

Introduction

Osteoporosis, a common metabolic bone disease, is characterized by a decline in bone microarchitecture and a reduction in bone mineral density (BMD), which leads to increased bone fragility and a higher risk of fractures [1]. BMD measurements are widely used as a gauge of bone health, and it is well-known that low BMD is linked to a higher risk of fracture [2]. In addition, femoral bone mineral density is an extremely effective method of recognizing and diagnosing osteoporosis and has been shown to be very effective [3]. As the world's population ages, osteoporosis poses a heavy and growing socioeconomic and public health burden [4]. However, it is both treatable and preventable [5]. Therefore, the search for new metrics to predict low BMD in osteoporosis is of increasing interest and has become particularly important for exploring osteoporosis prevention and treatment.

In recent years, in addition to genetic factors, a large number of studies have demonstrated that reductions in BMD are not only associated with age, lifestyle, and inflammation [6–8] but also with cardiovascular disease, which shares potentially common risk factors and pathophysiologic mechanisms [9, 10]. Platelets are widely known for their critical role in hemostasis and thrombosis; however, emerging evidence suggests that platelets also contribute to bone and vascular homeostasis. Activated platelets release a range of cytokines and growth factors, including transforming growth factor-β (TGF-β) and platelet-derived growth factor (PDGF), which are essential for osteoblast activity and the proliferation of vascular smooth muscle cells [11, 12]. Additionally, platelets can release proinflammatory cytokines, which exacerbate vascular inflammation and calcification, and affect bone resorption [13, 14]. These effects suggest that platelet function and activity are closely related to bone health. High-density lipoprotein cholesterol (HDL-C), often referred to as the "good cholesterol", has antiplatelet and anti-thrombotic properties [15]. Moreover, HDL-C is involved in anti-inflammatory and antioxidant activities, which are beneficial for bone health [16]. HDL-C plays an important role in the regulation of lipid metabolism and has been implicated in osteoblast and osteoclast function, which affects bone homeostasis [17]. The platelet to HDL-C ratio (PHR) has recently been proposed as a novel biomarker of metabolic syndrome and also of the risk of atherosclerotic thrombosis, possibly reflecting the balance between proinflammatory and anti-inflammatory states in the body [18]. In addition, *research has shown* that metabolic syndrome is associated with an increased risk of low BMD [19]. However, the relationship between PHR and BMD is currently unclear, this study hypothesized that an elevated PHR is associated with a decreased BMD. By studying PHR as a novel biomarker, we hope to deepen our understanding of the cardiovascular factors that influence bone health and identify valuable predictors of BMD.

To investigate the relationship between PHR and femoral BMD in adult Americans, we examined cross-sectional data from the National Health and Nutrition Examination Survey (NHANES).

Methods

Population studies and data sources

An extensive, ongoing cross-sectional survey in the United States, the National Health and Nutrition Examination Survey (NHANES), provided data from 2005 to 2018 for this study's periodic cross-sectional analysis. NHANES aims to offer unbiased statistical data on health-related topics, addressing new public health concerns. To gather data, NHANES uses a sophisticated, multistage probability sampling design that combines in-person interviews, physical examinations, and laboratory testing. The National Center for Health Statistics Institutional Review Board granted ethical approval for the survey, and written informed consent was obtained from each participant. Please visit https://www.cdc.gov/nchs/nhanes/index.htm for additional information. Subjects with missing total femur BMD data (n=45,221), missing HDL-C levels (n=4221), missing platelet counts (n=55), participants under 20 years old (n=5616), and participants lacking data for pertinent covariables (n=1457 for income to poverty ratio, n=695 for alcohol status, n=55 for alkaline phosphatase, n=17 for total calcium, n=4 for phosphorus), along with subjects with tumors or pregnant women (n=1713), were sequentially excluded from the 70,190 participants in the seven cycles. After applying these exclusion criteria, a total of 13,936 participants were included in the study (Fig. 1).

Exposure variable

In this study, PHR was specifically designed as an exposure variable. A transformation was necessary because the values of PHR varied greatly. The platelet count (PC) was divided by the HDL-C level, and the quotient was

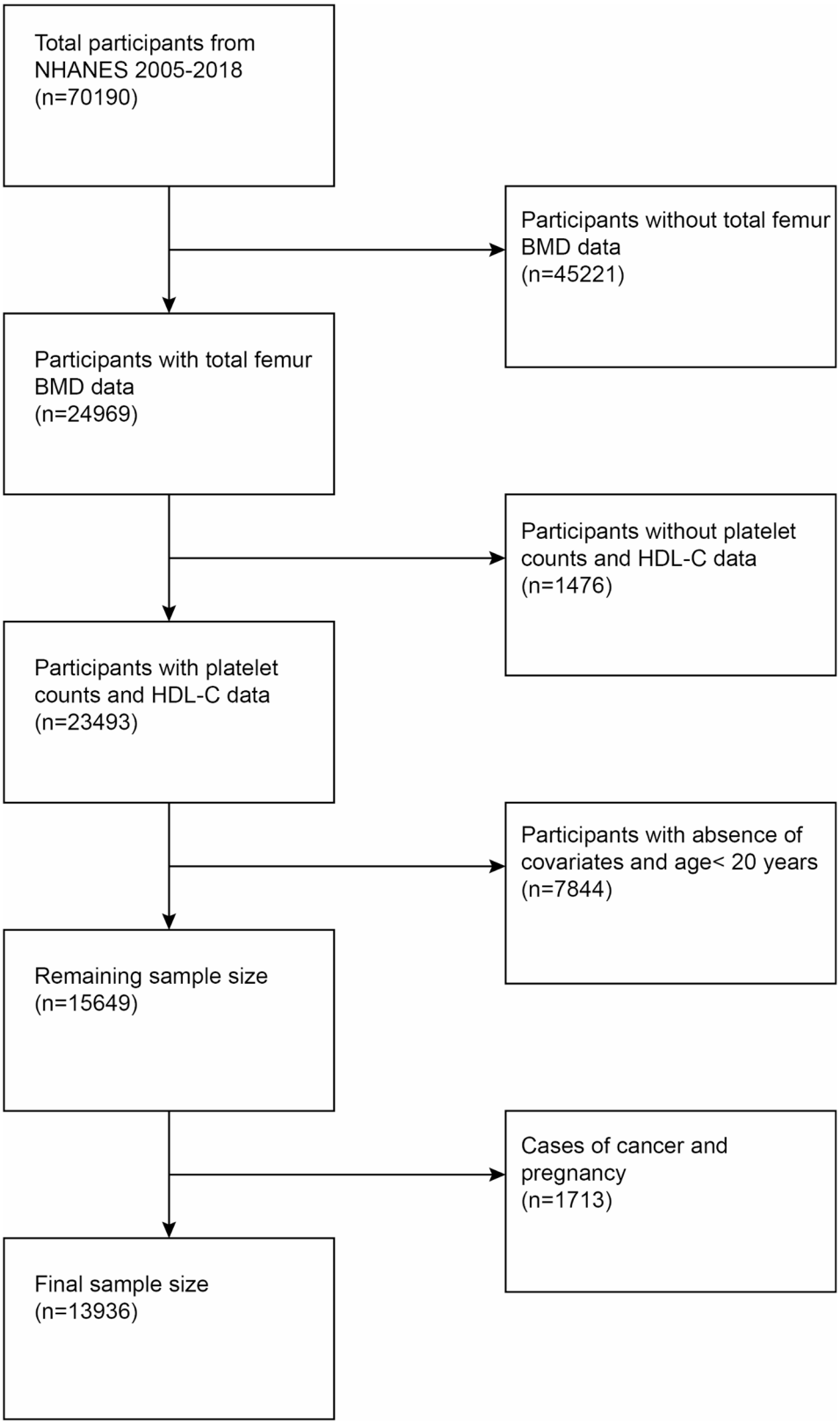

Fig. 1 Flowchart illustrating participant selection. *Legend* BMD, bone mineral density; NHANES, National Health and Nutrition Examination Survey; HDL-C, High-density lipoprotein cholesterol

then divided by 10 to determine the PHR [18]. For PC and HDL-C, calculations were done in 1000 cells/uL and mmol/L, respectively.

Outcome variable

Qualified radiologists conducted dual-energy X-ray absorptiometry (DXA) exams utilizing the QDR 4500 A fan-beam densitometer (Hologic, Inc.). The total femur's BMD was obtained from these hip DXA scans [20].

Covariable

Potential variables with confounding effects on BMD were considered based on previous epidemiologic studies [21, 22]. The demographic variables included age, education, gender, race, marital status, and income-to-poverty ratio. Lifestyle variables included drinking habit, smoking status, diabetes, and hypertension. Laboratory variables included alkaline phosphatase, serum phosphorus, and serum calcium levels. Body measurement data included body mass index (BMI). Information on these covariables was gathered through surveys, physical exams, and laboratory testing. The methodology for calculating these variables is explained in detail on the NHANES website (https://www.cdc.gov/nchs/nhanes/). According to the World Health Organization (WHO), a person is classified as obese if their BMI is 30 kg/m² or higher. Age (<50/≥50 years), gender (male/female), diabetes (yes/no/threshold), BMI (<30/≥30), hypertension (yes/no), drinking habit (yes/no), and smoking status (yes/no) were also considered as stratification variables in this study.

Statistical analysis

Sampling weights are frequently utilized in NHANES to account for complex study designs. Proportions are used to portray categorical data, while means and standard deviations (SD) are utilized to express continuous variables. Both continuous and categorical variables based on quartiles were used to analyze the PHR index. The range of PHR for the four quartiles was as follows: quartile 1 (<14.28), quartile 2 (14.28–18.63), quartile 3 (18.63–24.03), and quartile 4 (>24.03). Weighted Student's t-tests for continuous variables and weighted chi-square tests for categorical variables were used to evaluate differences between groups. To explore the relationship between the PHR index and total femur BMD, a *multivariable* linear regression model was employed. Model 1 was unadjusted. Age, gender, and race adjustments were made to Model 2. Model 3 was adjusted for all potential covariables, including age, gender, race, education level, marital status, income-to-poverty ratio, total calcium, phosphorus, alkaline phosphatase, alcohol status, diabetes, hypertension, body mass index, and smoking status. Nonlinear associations between the PHR index and total femur BMD were examined using smooth curve fitting and generalized additive models. When nonlinear relationships were identified, threshold effects were used to determine the points of change in the relationship between the PHR index and total femur BMD. To evaluate the stability of the findings, additional interaction and subgroup analyses were carried out, analyzing thresholds for the age and sex subgroups. Packager (http://www.r-project.org) and EmpowerStats (http://www.empowerstats.com) were used for all analyses, and $P<0.05$ was used as the statistical significance criterion.

Results

Study population features

The sample of our study consisted of 13,936 individuals; 52.09% were men and 47.91% were women. Study participants were on average, 51.19±16.65 years old. The mean PHR value was 19.94±7.98. Our analysis revealed that total femur BMD increased with rising PHR. Among the PHR quartiles, all covariables were statistically significant ($P<0.05$), except for total calcium, which was not statistically significant ($P>0.05$) (Table 1).

Connection of PHR index with total femur BMD

Table 2 illustrates the association between total femur BMD and the PHR. To provide a comprehensive understanding of this association, our study utilized multivariable linear regression analyses across three distinct models. The results consistently demonstrated that participants in PHR quartiles Q2 to Q4 exhibited progressively greater levels of Total Femur BMD compared to those in the lowest quartile, with a statistically significant trend across all three models (all P for Trend<0.0001). Specifically, in model 3, participants in the PHR index Q4 group had a statistically significant increase in Total Femur BMD of 0.0464 units (β=0.0464, 95% CI: 0.0400, 0.0528; *P* for Trend<0.0001) compared to those in the lowest quartile of the PHR index.

Subgroup analysis

In addition, we performed subgroup analyses to assess the stability of the relationship between the PHR index and total femur BMD across different demographic contexts. These subgroups included age, gender, diabetes, BMI, drinking status, hypertension, and smoking. However, significant interactions (*P*-interaction<0.05) were observed only in the age and gender subgroups, as shown in Supplement 1. This suggests that the relationship between the PHR index and total femur BMD is independent of the remaining stratification variables.

Nonlinear relationship between PHR index and total femur BMD

Using generalized additive models and smoothed curve fitting, we discovered an inverted U-shaped nonlinear

Table 1 Weighted sample characteristics for the study

PHR categories	Q1 < 14.28	Q2 14.28–18.63	Q3 18.63–24.03	Q4 > 24.03	*P*-value
N	3473	3492	3485	3486	
Age	52.70 ± 16.05	49.89 ± 16.05	47.91 ± 15.24	44.79 ± 14.48	< 0.001
Gender (%)					< 0.001
Male	41.21	48.99	56.02	57.21	
Female	58.79	51.01	43.98	42.79	
Race (%)					< 0.001
Mexican American	5.46	6.75	9.08	10.42	
Other Hispanic	3.56	4.08	5.05	5.87	
Non-Hispanic White	73.05	72.30	69.73	68.72	
Non-Hispanic Black	11.60	10.42	9.35	8.70	
Other Race	6.33	6.46	6.79	6.29	
Education level (%)					< 0.001
Less than 9th grade	4.40	4.90	5.70	5.89	
9-11th grade	9.18	10.47	12.16	13.66	
High school graduate/GED or equivalent	21.55	23.30	25.40	27.17	
Some college or AA degree	29.87	29.26	30.55	32.38	
College graduate or above	35.00	32.07	26.19	20.91	
Marital status (%)					0.009
Married or with partner	64.15	67.62	66.62	67.32	
Single	35.85	32.38	33.38	32.68	
Income to poverty ratio	3.29 ± 1.61	3.21 ± 1.63	3.10 ± 1.61	2.94 ± 1.62	< 0.001
Alcohol status (%)					< 0.001
Yes	82.19	79.63	79.47	76.70	
No	17.81	20.37	20.53	23.30	
Hypertension (%)					0.012
Yes	29.45	30.96	33.08	31.57	
No	70.55	69.04	66.92	68.43	
Diabetes (%)					< 0.001
Yes	6.84	8.80	8.58	10.10	
No	91.43	89.18	88.80	88.23	
Borderline	1.73	2.02	2.62	1.68	
Smoking status (%)					< 0.001
Yes	44.00	44.72	46.96	50.42	
No	56.00	55.28	53.04	49.58	
Body mass index (kg/m2, (%))	80.67	71.31	62.58	52.59	< 0.001
< 30	19.33	28.69	37.42	47.41	
>=30					
ALP(IU/L)	65.32 ± 23.66	66.58 ± 20.31	69.77 ± 23.07	71.58 ± 22.23	< 0.001
Total calcium (mg/dL)	9.43 ± 0.35	9.45 ± 0.35	9.44 ± 0.35	9.45 ± 0.37	0.093
Phosphorus(mg/dL)	3.78 ± 0.55	3.74 ± 0.55	3.74 ± 0.57	3.76 ± 0.57	0.004
Total femur BMD (g/cm2)	0.93 ± 0.16	0.96 ± 0.15	0.98 ± 0.15	1.01 ± 0.15	< 0.001

Notes For variables that fluctuate continuously, mean +/- SD: The P-value was calculated using a weighted linear regression model. % is a category variable. The P-value was ascertained by applying the weighted chi-square test. PHR, platelet/high-density lipoprotein cholesterol ratio; ALP, alkaline phosphatase; BMD, bone mineral density

association between the PHR index and total femur BMD (Fig. 2). After fully accounting for confounders, segmented linear regression yielded an inflection point of 33.301 for the PHR index concerning total femur BMD. This result was validated by a log-likelihood ratio test at a significance level of less than 0.05 (Table 3). Based on the analysis, for every unit increase in the PHR index in the general population below the inflection point (33.301), Total Femur BMD increased by 0.0029 units (95% CI: 0.0025, 0.0032). However, beyond this point, Total Femur BMD decreased by -0.0017 units (95% CI: -0.0026, -0.0007) for each additional unit increase in the PHR index, with both trends being statistically significant. We also analyzed age and gender subgroups, and the results in Fig. 3 show a consistent inverted U-shaped association between the PHR index and total femur BMD across

Table 2 PHR and total femur BMD association

	Non-adjusted β(95%CI)*P* value	Adjust I β(95%CI)*P* value	Adjust II β(95%CI)*P* value
PHR quartile			
Q1	Ref.	Ref.	Ref.
Q2	0.0327(0.0255, 0.0399) < 0.0001	0.0170(0.0107, 0.0234) < 0.0001	0.0168(0.0106, 0.0229) < 0.0001
Q3	0.0558(0.0486, 0.0630) < 0.0001	0.0273(0.0210,0.0337) < 0.0001	0.0290(0.0227, 0.0353) <0.0001
Q4	0.0801(0.0729, 0.0873) < 0.0001	0.0421(0.0357, 0.0486) < 0.0001	0.0464(0.0400, 0.0528) <0.0001
P for trend	< 0.0001	<0.0001	< 0.0001

Notes Model 1: Not a single covariable was changed

Model 2: Age, gender and race were adjusted

Model 3: Age, gender, race, education level, marital status, income to poverty ratio, total calcium, phosphorus, alkaline phosphatase, alcohol status, diabetes, hypertension, body mass index and smoking status were adjusted

PHR, platelet/high-density lipoprotein cholesterol ratio; BMD, bone mineral density

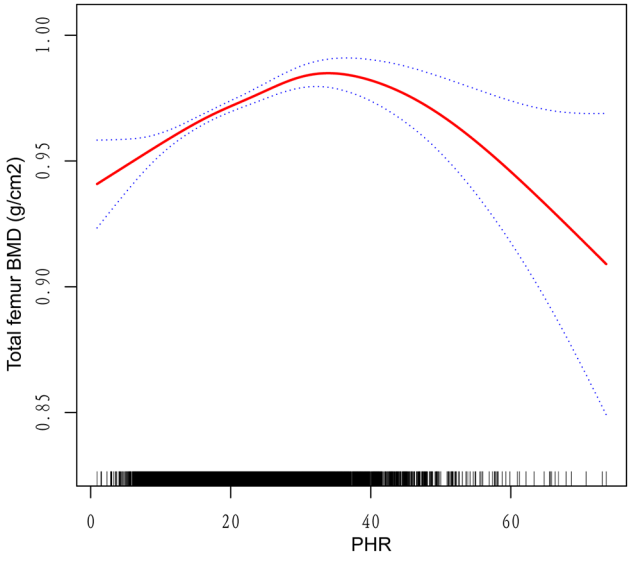

Fig. 2 The association between the PHR index and total femur BMD. *Legend* The smooth red line represents the best possible match between the variables on the curve. The blue shading shows the 95% confidence interval for the fit. All potential confounding variables were eliminated. Y axis do not contain the whole range of the data (it just contains data in range from 0.85-1, while data bellow 0.85 are not proportionally presented)

Table 3 Analysis of the threshold effect of PHR and total femur BMD

	Adjusted β (95% CI), *P*-value
PHR	
Total	
Fitting by the two-piecewise linear model	
Inflection point	33.301
PHR < Inflection point	0.0029 (0.0025, 0.0032) < 0.0001
PHR > Inflection point	-0.0017 (-0.0026, -0.0007) 0.0010
Log-likelihood ratio	< 0.001
Subgroup analysis	
Age < 50	
Fitting by the two-piecewise linear model	
Inflection point	35.1765
PHR < Inflection point	0.0027 (0.0022, 0.0032) < 0.0001
PHR > Inflection point	-0.0020 (-0.0035, -0.0006) 0.0049
Log-likelihood ratio	< 0.001
Age ≥ 50	
Fitting by the two-piecewise linear model	
Inflection point	32.2143
PHR < Inflection point	0.0025 (0.0020, 0.0030) < 0.0001
PHR > Inflection point	-0.0017 (-0.0031, -0.0002) 0.0283
Log-likelihood ratio	< 0.001
Male	
Fitting by the two-piecewise linear model	
Inflection point	35.1351
PHR < Inflection point	0.0021 (0.0016, 0.0026) < 0.0001
PHR > Inflection point	-0.0019 (-0.0033, -0.0004) 0.0128
Log-likelihood ratio	< 0.001
Female	
Fitting by the two-piecewise linear model	
Inflection point	33.0612
PHR < Inflection point	0.0035 (0.0030, 0.0040) < 0.0001
PHR > Inflection point	-0.0018 (-0.0032, -0.0003) 0.0206
Log-likelihood ratio	< 0.001

Notes Age, gender, race, education level, marital status, income to poverty ratio, total calcium, phosphorus, alkaline phosphatase, alcohol status, diabetes, hypertension, body mass index and smoking status were adjusted. The strata variable was not included in the model when stratifying by itself

PHR, platelet/high-density lipoprotein cholesterol ratio; BMD, bone mineral density

these subgroups. Additionally, we analyzed the inflection points of the threshold effects within each subgroup, as determined by the measurements obtained from the two-segment linear regression model (Table 3).

Discussion

This study comprehensively analyzed NHANES data from 2005 to 2018. The connection between PHR and total femur BMD was explored, revealing a complex, nonlinear inverted U-shaped association. And through threshold analysis, we identified that the inflection point was precisely 33.301. This relationship was more pronounced in female or aged 50 years older subjects, as assessed by subgroup analyses and interactions. Moreover, this inverted U-shaped association was also present in subgroups based on sex and age. These findings highlight the potential of PHR as a predictor of BMD, particularly in high-risk groups like women and the elderly.

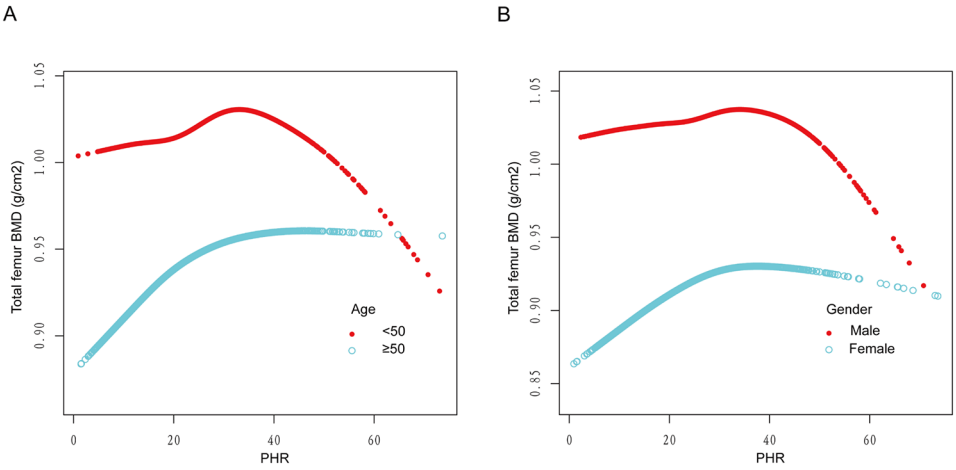

Fig. 3 The association between the PHR index and total femur BMD was stratified by age (**A**) and gender (**B**). *Legend* Y axis do not contain the whole range of the data (it just contains data in range from 0.85-1, while data bellow 0.85 are not proportionally presented)

Notably, this study is the first to examine the association between PHR and total femur BMD.

Numerous previous academic studies have delved into the association between multiple CVD risk markers and BMD levels [23, 24], however, the majority of these studies have predominantly focused on non-platelet-related markers, thereby overlooking the potential impact of platelet-related factors. Additionally, they have failed to integrate *platelets* with lipid biochemistry indices in a comprehensive manner to analyze their combined effects on BMD. The roles of high-density lipoprotein cholesterol (HDL-C) and platelets in BMD, despite their established involvement as major players in atherosclerosis, remain unclear and warrant further investigation. For example, one study showed a positive *association* between HDL-cholesterol and BMD [21], while a Korean study demonstrated a similar positive *association* between femoral neck BMD and HDL-C in postmenopausal women [25]. In addition, one study showed a negative *association* between HDL-C and total BMD values [26]. In contrast to HDL-C research, studies investigating the relationship between platelets and BMD are more limited. A Swedish cohort study indicated that high platelet counts were associated with low BMD at all sites [27], a result that is consistent with findings from a South Korean study [28]. In addition, a Chinese study found a positive *association* between circulating platelet concentration and BMD at the right and left hip joints [29]. Therefore, the PHR, which has been proposed in recent years as a potential composite indicator, may offer a more comprehensive approach to predicting BMD. Compared with a single index, PHR accounts for the combined effect of both platelets and HDL-C on BMD and may better explain the inconsistencies in existing studies.

In our study, we observed an inverted U-shaped relationship between PHR and total femur BMD, with an initial increase in total femur BMD as PHR increased, followed by a decline upon reaching the inflection point at PHR 33.301. This pattern may reflect the beneficial effects of moderate platelet and HDL levels on bone health [21, 30]. In addition, we performed subgroup analyses (detailed in Supplementary Material 1) and used threshold effects to identify inflection points based on sex and age subgroups. In the age subgroup, we identified a stronger association between PHR and total femur BMD in subjects aged ≥ 50 years than in those aged < 50 years. However, the inflection point of PHR was lower in those aged ≥ 50 years, consistent with studies showing that thrombocytopenia occurs with increasing age [31]. Furthermore, both atherosclerosis and osteoporosis risks rise with age [32, 33].

In the gender subgroup analysis, we found that PHR was significantly *nonlinearly* correlated with total femur BMD in females, whereas no statistically significant association was observed in males. Additionally, the PHR inflection point was higher in males than in females. Previous studies have shown that the association between cardiovascular risk markers, such as the plasma atherogenic index (AIP), and BMD is stronger in women than in men [24]. Studies have also indicated that platelet counts and reactivity are generally higher in women than in men [34]. These sex differences in platelet function may be partly attributable to the different roles of sex hormones: estrogen in women and testosterone in men play key roles in regulating BMD [26, 35]. These hormonal differences may influence the effect of PHR on BMD across sexes. Consequently, our findings may provide valuable insights for promoting healthy BMD in older adults, particularly older women, by enhancing HDL function and implementing platelet-modulating strategies. This could inform the clinical targeting of lipid-modifying drugs and antiplatelet therapies in this population. In the

remaining subgroup analyses, no significant variability was detected, indicating the stability of the observed relationships across different demographic settings.

The specific mechanisms explaining the association between the PHR index and BMD remain unknown and may be related to the fact that osteoporosis and atherosclerosis share traditional cardiovascular risk factors and pathophysiologic mechanisms [36]. HDL has anti-inflammatory and antioxidant properties. Chronic inflammation is a common pathophysiological pathway in cardiovascular disease and osteoporosis [37–39]. By reducing inflammation, HDL helps protect bone density, shields osteoclasts (bone-forming cells) and osteoblasts (mature bone cells) from oxidative damage, and reduces osteoclast (bone resorption cells) activity [40, 41]. Excess cholesterol in bone disrupts the balance between bone formation and resorption, leading to bone loss [42]. HDL helps maintain this balance by facilitating reverse cholesterol transport and supporting healthy bone remodeling [43]. Additionally, studies have shown that HDL enhances the differentiation of MSCs into osteoblasts, which are responsible for bone formation [44], and increases the availability of nitric oxide (NO) to improve endothelial cell function. This strengthens blood flow to the skeleton and ensures the necessary supply of nutrients and oxygen [45]. These mechanisms emphasize the importance of HDL in cardiovascular protection and support its role in maintaining BMD and preventing osteoporosis. *More research is required to clarify the precise mechanisms of platelets in bone metabolism.* However, their role can be explained in terms of pro-inflammatory and growth factor secretion. Platelets play an important role in the inflammatory response by releasing pro-inflammatory cytokines, which increase osteoclast activity and promote bone resorption, thereby decreasing BMD [46]. By producing a lot of reactive oxygen species (ROS), they also worsen oxidative stress, which in turn increases osteoclast activity and formation and lowers bone mineral density (BMD) [47]. Additionally, platelets contain a variety of growth factors that are released upon activation and promote the proliferation and differentiation of osteoblasts [30]. Thus, platelet-HDL interactions significantly affect BMD. Overall, elevated PHR negatively affects BMD by increasing oxidative stress, inflammation, and endothelial dysfunction.

Limitation and strengths

Our study includes several noteworthy advantages. Firstly, this is the first study that we are aware of that evaluates the association between femoral BMD and the PHR index, which could be a useful predictor of BMD in clinical settings. Secondly, as we selected a nationally representative sample, our results have broad applicability to the whole population. Furthermore, we were able to conduct subgroup analyses of PHR indicators with BMD across all genders and races thanks to our sizable sample size. These findings are particularly valuable for high-risk populations, such as the elderly and women. However, it is critical to recognize the limitations of this study. The cross-sectional design limits inferences about causality between the PHR index and femoral BMD in adults. Despite adjusting for known confounders, unmeasured variables may have influenced the observed associations. Future longitudinal studies are needed to confirm these findings and explore potential mechanisms in more detail. Additionally, patients with malignant tumors and pregnant women were excluded because cancer and pregnancy can significantly impact BMD. Lastly, our study could not account for sex hormone levels due to the lack of this information in the 2005–2018 NHANES database.

Conclusion

Our study identified a complex, nonlinear inverted U-shaped connection between PHR and total femur BMD. Notably, total femur BMD decreased when the PHR threshold of 33.301 was exceeded. Therefore, maintaining PHR levels within a certain range may help preserve healthy BMD and guide the clinical use of lipid-modulating and antiplatelet drugs. This information is especially valuable for the elderly and women, who are at high risk for both cardiovascular disease and osteoporosis.

Abbreviations

BMD	Bone mineral density
HDL-C	High-density lipoprotein cholesterol
PHR	The platelet/high-density lipoprotein cholesterol ratio
GAM	Generalized additive model
NHANES	National Health and Nutrition Examination Survey
SD	Standard deviation
BMI	Body mass index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02291-x.

Supplementary Material 1

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Author contributions

HY: Conceptualization, Methodology, Formal analysis, Writing – original draft, Visualization. ZC: Conceptualization, Software, Writing – review & editing. KL: Software, Visualization, Data curation.YZ: Validation, Data curation, Formal analysis. H L: Software, Visualization. N T: Writing – review & editing, Supervision, Project administration.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The US Centers for Health Statistics Ethics Review Board authorized the NHANES protocols, and each participant gave written informed permission at the time of the survey.

Competing interests
The authors declare no competing interests.

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