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Association between Relative Fat Mass and Lumbar Bone Mineral Density in the US Adults: Evidence from National Health and Nutrition Examination Survey (NHANES), 2011 - 2018

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Abstract

Relative Fat Mass (RFM) is an innovative obesity metric that provides a more precise evaluation of body fat distribution than conventional methods. This study aims to explore the relationship between RFM and lumbar Bone Mineral Density (BMD) in adults from 2011 to 2018.

Weighted multivariate logistic regression, subgroup analysis, and interaction tests were employed to examine the relationship between RFM and lumbar BMD, utilizing data derived from the 2011 to 2018 National Health and Nutrition Examination Survey (NHANES). This study included a total of 11,410 participants. Weighted multiple linear regression analysis revealed a significant negative correlation between RFM and lumbar BMD among adults aged 20 to 59 years. This negative correlation persisted even when RFM was analyzed by quartiles, with individuals in the highest RFM quartile exhibiting lumbar BMD levels 0.046 g/cm2 lower compared to those in the lowest quartile. However, this negative association varied across several specific subgroups. Our findings indicate a significant negative correlation between RFM and lumbar BMD in US adults aged 20-59, offering fresh perspectives and research targets for clinical analysis.

Keywords: NHANES; Osteoporosis; Lumbar bone mineral density; Relative fat mass

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Introduction

Osteoporosis represents a significant global health issue, impacting over 200 million people worldwide [1-4]. Central to osteoporotic feature is diminished bone mineral density (BMD), pivotal in both the evaluation of skeletal health and the diagnosis of the condition [1,5]. In addition to significantly increasing the risk of fractures, osteoporotic fracture is also among the leading cause of disease and mortality in older adults [1]. Therefore, considering that the risk of osteoporosis increases with the aging of the general population, exploring the risk factors and protective elements associated with osteoporosis is crucial for the development of early preventive and management strategies.

Obesity, a complex metabolic disorder, has been steadily increasing in global prevalence in recent years [6,7]. While acknowledged as a major contributor to various chronic diseases, the relationship between obesity and bone density still remains controversial. Previous evidence suggested a positive correlation between obesity and bone density [8,9]. However, recent studies have indicated a possible inverse relationship [8-11]. Body Mass Index (BMI) is commonly used to measure obesity but may not adequately reflect fat distribution, potentially leading to inaccuracies in assessing individual health risks [2]. To better evaluate obesity, researchers have developed a new indicator known as Relative Fat Mass (RFM). RFM incorporates gender, height, and Waist Circumference (WC) to provide a more accurate estimate of total body fat percentage compared to BMI [12]. Additionally, RFM has been associated with several diseases, such as depression, coronary heart disease, hypertension, and type 2 diabetes [13-15], underscoring the importance of RFM in comprehensively assessing health risks associated with obesity. However, the relationship between

RFM and bone metabolism has not been previously explored. Therefore, the aim of this study was to investigate the association between RFM and lumbar BMD in US adults using data from the National Health and Nutrition Examination Survey (NHANES) conducted between 2011 and 2018, providing to better implement the public advocacy of early detection, early diagnosis, and early treatment.

Methods

Survey description and Study participants

The National Health and Nutrition Examination Survey (NHANES), implemented by the National Center for Health Statistics (NCHS), focuses on assessing the physical and nutritional status of Americans. NHANES utilizes a complex stratified multi-stage sampling design to accurately represent the non-institutionalized civilian population across the United States [16]. Each participant is required to provide informed consent after receiving detailed information about the study's objectives and methods. We used NHANES data from 2011 to 2018 for our analyses.

The initial cohort consisted of 39,156 individuals. After excluding 24,222 individuals not aged between 20 and 59 years, 3,403 individuals with incomplete data on lumbar bone mineral density, and 121 individuals with incomplete data on RFM data, a total of 11,410 participants were included in the study (Figure 1).

Research variables

RFM served as the exposure variable in this study. As an estimator of total body fat percentage, RFM is computed using the formula: RFM = 64−(20 × height / waist circumference) + (12 × sex), where sex is assigned a value of 0 for men and 1 for women. The height and waist circumference were calculated in centimeters [12]. Height and waist circumference (accurate to 0.1 cm) were meticulously assessed by certified health professionals at a Mobile Examination Center (MEC) using rigorous procedures to ensure accuracy. Measurements were conducted with precision to maintain consistency and reliability [17]. Lumbar BMD was analyzed as the dependent variable, considering it as a continuous outcome. It was assessed by accredited radiologists using dual-energy X-ray absorptiometry with specialized instrumentation.

Covariates

Based on previous research [9,10,17], we incorporated several covariates, including age, gender, race, education level, smoking status, income-to-poverty ratio (PIR), vitamin D (25OHD2 + 25OHD3), total calcium, diabetes, hypertension and Chronic Kidney Disease (CKD).

Statistical analysis

In this study, categorical variables were presented as percentages, and continuous variables as mean ± standard deviation. Participant demographics across RFM quartiles were analyzed using the chi-square test and t-test. Weighted multiple linear regression was employed to examine the relationship between RFM and lumbar BMD across three models. Model 1 was unadjusted for covariates, while Model 2 adjusted for age, gender, and race. Model 3 included all covariates listed in Table 1 except BMI. Subsequently, smoothed curve fitting was used to explore the potential nonlinear relationship between RFM and lumbar BMD. Additionally, subgroup analyses and interactions were conducted for age, gender, race, education level, smoking status, diabetes, hypertension, and chronic kidney disease. Missing data were imputed through multiple imputations. Statistical analyses were performed using R (version 4.2) and Empowerstats (version 2.0). Two-sided tests were applied, and statistical significance was defined as $p<0.05$.

Results

Baseline characteristics

This study included 11,410 participants with a mean (SD) age of 39.32 (11.45) years, comprising 48.74% females and 51.26% males. The mean (SD) RFM and BMI for all participants were 34.54 (8.97) and 29.06 (6.95) kg/m^2, respectively, while the mean (SD) lumbar BMD was 1.04 (0.16) g/cm^2. The interquartile ranges for RFM were 7.76-27.98, 27.95 to 33.72, 33.72 to 41.73, and 41.80 to 56.68. Compared to participants in the lowest RFM quartile, those individuals in the highest quartile were more likely to be female and elderly. Additionally, participants in the highest RFM quartile showed a higher prevalence of diabetes, hypertension, and chronic kidney disease. They also exhibited lower levels of education, PIR, 25(OH)D, total calcium, and lumbar BMD ($P<0.001$) (Table 1).

Associations of RFM with lumbar BMD

The associations between RFM and BMD are displayed in Table 2. Both unadjusted and adjusted models demonstrated a negative correlation between increasing RFM as a continuous variable and decreasing lumbar BMD. Specifically, in the fully adjusted model, each unit increase in RFM was associated with a decrease of 0.002 g/cm^2 in lumbar BMD (β=-0.002; 95% CI: -0.002, -0.001; $P<0.0001$). In the multivariable linear regression analysis of RFM quartiles, individuals in the highest RFM quartile exhibited a lumbar BMD 0.046 g/cm^2 lower than those in the lowest quartile (β=-0.046; 95% CI: -0.058, -0.034; $P<0.0001$). Moreover, smooth curve fitting confirmed a negative relationship between RFM and lumbar BMD (Figure 2).

Subgroup analyses

To evaluate the consistency of the relationship between RFM and lumbar BMD across diverse demographic subgroups (age, gender, race, and disease conditions), we conducted subgroup analyses stratified accordingly, alongside interaction tests. Table 3 presents the outcomes of these subgroup analyses. We found statistically significant variations in the association between RFM and lumbar BMD across different age groups, as well as in individuals with

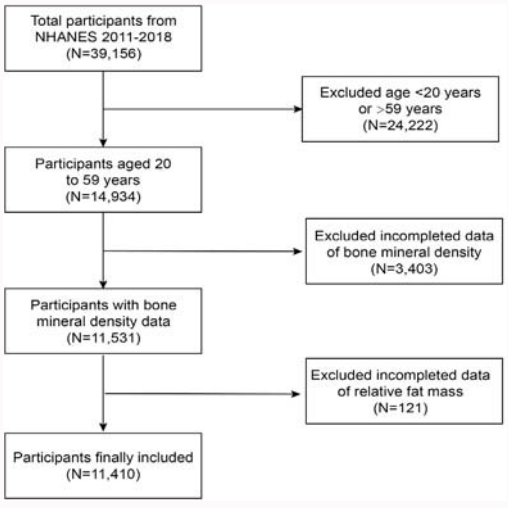

Figure 1: Flowchart inclusion of study participants.

Table 1: Basic characteristics of participants by Relative fat mass quartile.

Characteristics	Relative fat mass				P-values
	Q1	Q2	Q3	Q4	
	N=2853	N=2852	N=2852	N=2853	
Age(years)	36.018 ± 11.474	39.860 ± 11.451	39.450 ± 11.295	41.956 ± 10.979	<0.001
Sex, (%)					<0.001
Male	97.827	80.084	26.683	0.456	
Female	2.173	19.916	73.317	99.544	
Race, (%)					<0.001
Non-Hispanic White	34.21	35.273	37.412	30.214	
Non-Hispanic Black	25.061	17.532	19.355	27.55	
Mexican American	8.903	16.339	12.868	19.418	
Other race/multiracial	31.826	30.856	30.365	22.818	
Education level, (%)					<0.001
Less than high school	4.311	7.258	4.839	8.167	
High school	13.109	12.868	9.993	13.109	
More than high school	82.58	79.874	85.168	78.724	
Smoking, (%)					<0.001
Ever	45.005	44.425	33.976	33.789	
Never	54.995	55.575	66.024	66.211	
Diabetes, (%)					<0.001
Yes	3.4	6.942	6.452	12.548	
No	96.6	93.058	93.548	87.452	
Hypertension, (%)					<0.001
Yes	14.686	25.14	21.879	33.789	
No	85.314	74.86	78.121	66.211	
Chronic Kidney Disease, (%)					<0.001
Yes	7.921	10.799	12.868	15.422	
No	92.079	89.201	87.132	84.578	
BMI (kg/m^2)	23.983 ± 2.956	28.363 ± 4.781	28.713 ± 7.349	35.159 ± 6.617	<0.001
PIR	2.557 ± 1.694	2.595 ± 1.675	2.645 ± 1.666	2.195 ± 1.584	<0.001
Total calcium (mmol/L)	2.366 ± 0.084	2.344 ± 0.081	2.333 ± 0.084	2.321 ± 0.089	<0.001
25(OH)D(nmol/L)	60.153 ± 24.211	60.280 ± 23.811	62.918 ± 26.796	57.709 ± 25.874	<0.001
Lumbar BMD (g/cm^2)	1.058 ± 0.162	1.024 ± 0.151	1.045 ± 0.154	1.024 ± 0.148	<0.001

Abbreviations: Q: Quartile; BMI: Body Mass Index; PIR: Ratio of family income to poverty; BMD: Bone Mineral Density

diabetes, hypertension, and chronic kidney disease (P for interaction <0.05). Conversely, no significant differences were observed across genders and races (P for interaction >0.05). Furthermore, within subgroups affected by diabetes, hypertension, and chronic kidney disease, no significant negative association was evident between RFM and lumbar BMD, whereas such a correlation persisted in other subgroups (P for interaction > 0.05).

Discussion

In this study, we identified a negative correlation between RFM and lumbar BMD involving 11,410 participants. Higher RFM was significantly associated with lower lumbar BMD, supported by both continuous and quartile-based analyses. Specifically, each unit increase in RFM is associated with a decrease of 0.002 g/cm^2 in lumbar BMD in our fully adjusted model. Participants in the highest RFM quartile showed a substantial reduction of 0.046 g/cm^2 in lumbar BMD compared to those in the lowest quartile. Subgroup analyses indicated significant variations in the RFM-BMD relationship among different age groups and individuals with diabetes, hypertension, and chronic kidney disease, suggesting potential modifying effects of these conditions on this association. Considering the ability of RFM to effectively assess individual obesity status, these results revealed that managing body fat distribution may hold significant implications for bone metabolism.

This study investigates the relationship between RFM and lumbar BMD for the first time. There has been ongoing debate regarding the association of obesity with bone density and osteoporosis. Previous studies using BMI and WC as indicators have found a positive correlation between obesity and bone density. For instance, an early clinical study noted that increased body weight among Caucasian women aged 25 and older was linked to a reduced risk of hip fractures [18]. Another cross-sectional study involving 11,165 participants

Table 2: The associations between Relative fat mass and bone mineral density.

Exposure	Model 1 [β (95% CI)]	Model 2 [β (95% CI)]	Model 3 [β (95% CI)]
Lumbar BMD (continuous)	-0.001(-0.001, - 0.001), <0.0001	-0.002(-0.002, - 0.001), <0.0001	-0.002(-0.002, - 0.001), <0.0001
RFM (quartile)			
Quartile 1	Reference	Reference	Reference
Quartile 2	-0.027 (-0.035, - 0.020), <0.0001	-0.022 (-0.030, - 0.014), <0.0001	-0.023 (-0.031, - 0.016), <0.0001
Quartile 3	-0.009 (-0.016, - 0.001), <0.05	-0.019 (-0.029, - 0.010), <0.0001	-0.021 (-0.031, - 0.011), <0.0001
Quartile 4	-0.028 (-0.036, - 0.020), <0.0001	-0.046 (-0.058, - 0.034), <0.0001	-0.046 (-0.058, - 0.034), <0.0001
P for trend	<0.0001	<0.0001	<0.0001

Model 1: no covariates were adjusted. Model 2: age, gender, and race were adjusted. Model 3: age, gender, race, education level, smoking status, income-to-poverty ratio, vitamin D (25OHD2 + 25OHD3), total calcium, diabetes, hypertension and chronic kidney disease were adjusted.

Table 3: Subgroup analysis of the association between Relative fat mass and lumbar bone.

Exposure	Lumbar BMD [β (95% CI)]	P for interaction P
Age		0.004
20-39 years old	-0.003 (-0.003, - 0.002)	
40-59 years old	-0.001 (-0.002, - 0.000)	
Sex		0.0674
Male	-0.002 (-0.003, - 0.002)	
Female	-0.001 (-0.002, - 0.001)	
Race		0.6464
Non-Hispanic White	-0.002 (-0.002, - 0.001)	
Non-Hispanic Black	-0.002 (-0.003, - 0.001)	
Mexican American	-0.003 (-0.005, - 0.001)	
Other race/multiracial	-0.002 (-0.003, - 0.000)	
Education level		0.0351
Less than high school	-0.005 (-0.008, - 0.002)	
High school	-0.001 (-0.003, 0.001)	
More than high school	-0.002 (-0.002, - 0.001)	
Smoking		0.1692
Ever	-0.002 (-0.002, - 0.001)	
Never	-0.002 (-0.003, - 0.001)	
Diabetes		0.0042
Yes	0.002 (-0.001, 0.004)	
No	-0.002 (-0.002, - 0.001)	
Hypertension		<0.0001
Yes	0.001 (-0.000, 0.002)	
No	-0.002 (-0.003, - 0.002)	
Chronic Kidney Disease		0.0016
Yes	0.000 (-0.001, 0.002)	
No	-0.002 (-0.003, - 0.002)	

Age, gender, race, education level, smoking status, income-to-poverty ratio, vitamin D (25OHD2 + 25OHD3), total calcium, diabetes, hypertension and chronic kidney disease were adjusted.

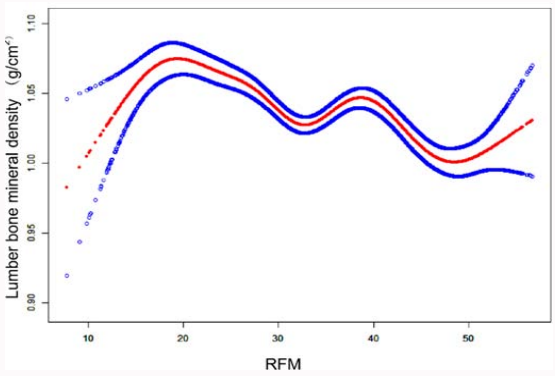

Figure 2: The association between RFM and lumbar bone mineral density.

demonstrated positive correlations between WC and both femoral and lumbar spine BMD, suggesting a protective effect against osteoporosis [9]. Despite traditional views suggested that obesity may prevent osteoporosis or osteoporotic fractures, recent evidence contradicted this notion [10,19,20]. A prospective study in 2012 indicated a significantly increased risk of proximal humerus fractures among women over 50 years old due to obesity [19]. Additionally, a clinical study focusing on women found that after adjusting for various risk factors, underweight or normal-weight women had lower rates of distal radius fractures compared to overweight women [21]. It is noteworthy that recent clinical studies employing novel obesity indicators have also indicated a negative correlation between obesity and bone density at various sites [10,20]. RFM, as a novel obesity index, is not only highly feasible for measurement but also has been shown to effectively predict whole-body fat percentage in adults aged 20 years and older [13-15,22]. Furthermore, multiple studies have demonstrated correlations between RFM and various diseases [23]. Therefore, we posit that utilizing RFM may better reflect the relationship between obesity and bone density.

Subgroup analyses revealed variations in the relationship between RFM and lumbar BMD among populations with specific diseases, including diabetes, hypertension, and CKD. Several studies have indicated that individuals with diabetes tend to exhibit higher lumbar and femoral BMD compared to non-diabetic individuals, despite an increased risk of fragility fractures [24-26]. Overall, while the impact of diabetes on bone health is complex, it may exert a partially positive effect on bone density. A multicenter cross-sectional study from Canada found that hypertension is associated with higher lumbar BMD in adults aged 50 and older [26]. Moreover, another study involving 4,306 participants demonstrated that individuals with hypertension had increased lumbar BMD compared to controls [27]. The mechanisms through which hypertension affects bone density remain unclear; however, one potential biological mechanism is that hypertension may stimulate the secretion of various hormones, such as parathyroid hormone, which could promote bone formation and thereby increase bone density [28]. CKD, identified as an independent risk factor for osteoporosis, may influence bone density through

multiple factors, although the specific relationships are not yet fully understood [29-31].

In recent years, the association between obesity and osteoporosis has attracted significant research attention. Despite numerous studies on this relationship, the precise mechanisms through which obesity influences bone density remain unclear. Potential mechanisms encompass several aspects. Firstly, increased subcutaneous and visceral fat tends to induce inflammation, potentially elevating the risk of osteoporosis through various direct or indirect pathways [32, 33]. Secondly, adipose tissue-derived cytokines such as interleukin-6, tumor necrosis factor α, and acute phase proteins play crucial roles in the interplay among obesity, osteoporosis, and fractures [34]. These cytokines may enhance bone resorption rates by stimulating osteoclasts through multiple pathways [35,36]. Additionally, some studies have demonstrated that adipose tissue secretes various adipokines and hormones contributing to osteoporosis, including leptin and adiponectin [37,38]. Moreover, researches indicated a higher risk of vitamin D deficiency in obese populations, potentially leading to secondary hyperparathyroidism and consequently increasing the risk of osteoporosis [39,40]. Furthermore, alterations in the bone microenvironment due to obesity may impair specific cells and affect bone health. Increased oxidative stress and accumulation of senescent cells in the bone microenvironment are factors that could potentially lead to dysfunction of bone marrow stromal cells [41-43].

Our study possesses certain strengths. Firstly, we incorporated a large sample size, thereby enhancing the representativeness of our findings. Secondly, adjustments were made for multiple confounding factors that could potentially influence the outcomes, thereby improving the reliability of our results. However, several limitations should be acknowledged. Firstly, due to the cross-sectional nature of this study, establishing a causal relationship between lumbar BMD and RFM was not feasible. Secondly, despite adjusting for multiple covariates, there are numerous other factors influencing bone health that warrant more comprehensive investigation to validate our findings. Lastly, our data were derived from participants in the United States, which may limit the generalizability of our conclusions to other populations.

Conclusion

Our study identified a negative correlation between RFM and lumbar BMD in US adults, providing a novel index for early evaluation of osteoporosis. This finding improves our understanding of the association between RFM and lumbar BMD and provides new evidence for the complex relationship between obesity and bone metabolism.

Flow chart of participants selection. NHANES, National Health and Nutrition Examination Survey Flow chart of participants selection. NHANES, National Health and Nutrition Examination Survey.

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