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Association between fat mass and bone mineral density among Brazilian women differs by menopausal status: The Pró-Saúde Study

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Abstract

Objective: To investigate the association between bone mineral density (BMD) and fat mass in a multiethnic population of Brazilian women, and to evaluate the influence of total body mass and lean mass on this association.

Methods: This is a cross-sectional study nested within the Pro-Saúde Study (EPS), a prospective cohort of university civil servants in Rio de Janeiro. Participants were pre (n=100) and postmenopausal (n=166) women. Total fat, lean mass and BMD of total body, lumbar spine and femoral neck were measured using dual energy X-ray absorptiometry (DXA).The association of BMD with fat mass was investigated after adjustment for total body mass (model 1) and lean mass (model 2) and potential confounding variables using multivariate linear regression models.

Results: In model 1, fat mass was inversely associated with BMD at total body (*B*=-0.010; $p<0.01$) and at femoral neck (*B*= -0.009 $p<0.05$) in premenopausal women. No association between fat mass and BMD was observed in postmenopausal women. Model 2 yielded direct associations between fat mass and BMD (total and specific-sites) (*B*= 0.003 to 0.008; $p<0.01$) only in postmenopausal women.

Conclusions: Independently on the adjustment used, our results suggest the absence of an inverse association between fat mass and BMD in postmenopausal women. Additionally, when adjusted for lean mass, a direct association between fat and bone mass can be observed suggesting that for postmenopausal women being slightly obese does not confer excessive risk of bone loss, and may even result in bone density advantage.

Key words: Fat mass; lean mass; bone mineral density; DXA; regression models.

Introduction

Obesity and osteoporosis are both chronic conditions that share aspects such as multifactorial etiology, the high and still growing prevalence worldwide, and the consequent expensive health care costs associated with their clinical complications [1-4]. Their main biological manifestations, fat mass accumulation and bone mineral loss, respectively, are processes determined by a complex interaction among genetic, environmental and hormonal factors. Furthermore, normal aging is frequently associated with both adiposity increase and higher incidence of osteoporosis, especially in women after the occurrence of menopause [2-5].

Osteoporosis diagnosis is often based on measurement of bone mineral density (BMD) which is under the influence of several factors, including body mass [1,6,7]. Low body mass is recognized as an important risk factor for osteoporosis [8,9] and, conversely, several studies have demonstrated that higher body mass or body mass index (BMI) correlates with higher BMD [6,10,11]. However, there is some evidence that the direct association between body mass and BMD not necessarily reflects a beneficial effect of fat mass on bones.

Total body mass is composed mainly by fat and lean mass. It is well established that lean mass exerts a positive influence on BMD, mainly by a mechanical loading effect on bones [12-15]. On the other hand, the effect of fat mass on the BMD remains controversial [5,6,16,17]. The lack of consensus may be attributed, at least in part, to different statistical approaches, especially the adoption of different adjustment variables, and to the fact that the association between BMD and fat mass appears to depend on age and gender of the studied population. Some authors recently reported that after adjusting for the mechanical loading effects of total body mass, the direct

association between fat mass and BMD was no longer present [2,12] or became inverse [5,16,18,19], depending on the age-gender groups studied.

This issue is of major concern given the scenario of the obesity pandemic. Most studies investigating the relationship between body composition and bone mass focused on a specific population stratum, predominantly postmenopausal women. Few studies, which were restricted to Asian populations, have simultaneously examined women in different ages or menopausal status [16,17]. The aim of this study was to investigate the association between BMD and fat mass in a multiethnic population of Brazilian women. Additionally, we evaluated the influence of total body mass and lean mass on the association between BMD and fat mass.

Methods

Study design and population

This cross-sectional study was nested within the Pro-Saúde Study (EPS), a prospective cohort study of university civil servants in Rio de Janeiro, Brazil, focusing on the investigation of social determinants of health and health-related behavior [20]. Four waves of data collection have been conducted among 3253 participants (1999, 2001, 2006, and 2012).

In parallel with wave 4, a random sample of 520 participants stratified by sex, age (less than 50 yrs vs. 50 yrs or more) and education level (less than high school vs. high school or more) from the Pró-Saúde baseline population was selected to perform additional interview and anthropometric and body composition assessment by dual energy X-ray absorptiometry (DXA). Considering the aim of the present study, only premenopausal (n=100) and postmenopausal (n=166) women were included in the

analyses. Postmenopausal condition was defined as the self-reported cessation of natural menses for at least 12 months. Data collection occurred between July 2012 and October 2013.

The study protocol was registered at the Brazilian National Research Ethics System, and approved by the Ethics Committee of the Social Medicine Institute, at the State University of Rio de Janeiro (CAAE : 04452412.0.0000.5260). All participants provided their written informed consent.

Data Collection

Height was measured with a stadiometer to the nearest 0.1 cm (Seca, Brazil) with subjects without shoes. Weight was measured to the nearest 0.1 kg (Filizola, Brazil). Height and weight were used to derive body mass index (BMI, Kg/m^2) and participants were classified according to the WHO BMI categorization [21]. Hip circumference, at the level of the greater trochanter, and waist circumference, at the level of the umbilicus, were measured with a non-stretchable tape.

Bone mineral density (BMD, g/cm^2) of total body, lumbar spine (LS) (L1–L4) and femoral neck were measured by (DXA) (Lunar iDXA, GE Healthcare, WI). All scans were performed by the same properly trained operator, analyzed by the same certified clinical densitometrist (MC; CCD™, ISCD) and followed standard quality control procedures according to the manufacturer. Measurements on the calibration block (daily) and on the calibration spine phantom (weekly) supplied by the manufacturer had coefficients of variation <0.5%. BMD coefficients of variation were derived from three repeated measurements in 50 subjects were 0.47%, 0.87% and 0.62% for total body, lumbar spine (L1–L4) and femoral neck BMD, respectively.

As recommended by the International Society of Clinical Densitometry [22], osteoporosis was diagnosed in postmenopausal women if the *T* score of the lumbar spine or femoral neck was -2.5 or less. Those with *T* score -1.0 or less were classified as having osteopenia or low bone mineral density. In women prior to menopause, *Z* score values were used to define individuals ‘‘below the expected range for age’’ (when *Z* score was -2.0 or lower) and ‘‘within the expected range for age’’ (*Z* score above -2.0). Fat mass (FM) and non-bone lean mass (referred to as ‘lean mass’) were derived from the total body scan and estimated by the software *enCore* 2008 version 12.20. Total body mass was obtained by sum of absolute values of non-bone lean mass, fat mass and bone mineral content.

Calcium intake was estimated by using a previously validated food frequency questionnaire (FFQ) with 81 items that queried about habitual food intake in the last six months [23]. Habitual calcium intake (mg/day) was calculated using the USDA National Nutrient Database for Standard Reference. The FFQ was administered in person-to-person interviews conducted by trained interviewers.

Fasting blood samples were drawn between 07.00 and 09.00 AM, and serum samples were stored at -80ºC until analysis. Serum 25-hydroxyvitamin D [25(OH)D] was measured by chemiluminescent immunoassay (CLIA) (Liaison, Diasorin, MN, USA). Intra- and interassay coefficients of variation were 4.9% and 5.8%, respectively.

Race/skin color assessment was based on official classification adopted by the Demographic Census conducted by the Brazilian Institute of Geography and Statistics [24]. Participants answered a multiple-choice question to self-classify their race/skin color in one of the following categories: White, Brown, Black, Yellow and Indigenous.

Data analysis

Data were assessed for normality using the Kolmovorov-Smirnov test. Results are presented as mean ± standard deviation for continuous variables and as frequencies and percentages for categorical variables. Comparisons between women by menopausal status were conducted by Student´s *t* test for continuous variables or by chi-square test for categorical variables. Associations between BMD and fat mass were initially investigated by bivariate linear regression considering BMD at total body, lumbar spine and femoral neck as dependent variables and fat mass as independent variable.BMD association with fat mass was further investigated after adjustment for total body mass (model 1) or lean mass (model 2) using multivariate linear regression models.

Confounding variables were identified by using multiple linear regression with backward elimination of those that were statistically non-significant (P>0.10), and used as covariates in both models. Independent variables tested were age, height, skin color/race, calcium intake and serum 25(OH)D. All the potential confounding variables tested, except serum 25(OH)D, appeared as a relevant covariate in at least one bone site. Postmenopausal period (i.e. number of years since cessation of menstruation) was an additional covariate in the case of postmenopausal women. Fat mass collinearity with total body mass and lean mass was checked by calculating the variance inflation factor (VIF) in both linear regression models (1 and 2).

Statistical analyses were conducted using the statistical package SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA) and statistical significance was as set at $p \leq 0.05$.

Results

The general characteristics, anthropometry and body composition of the study participants are summarized in **Table 1**. BMI was on average 27.2 ± 5.4kg/m² in premenopausal women and 28.4 ± 5.1kg/m² in postmenopausal women with no statistically significant difference between menopausal status groups. The distribution in BMI categories was also similar between menopausal status groups with overweight being the most prevalent category in both groups. Premenopausal women had higher lean mass and lower percentage of fat mass than postmenopausal women.

Mean serum 25(OH)D concentration was similar (P>0.05) in premenopausal (18.6 ± 8.6 ng/mL) and postmenopausal women (18.7 ± 7.4ng/mL). Also, no significant difference between groups was observed in distribution by vitamin D status. Calcium intake was on average close to the current recommended intake (1000 mg/ day) (25) in postmenopausal women and represented 85% of the recommended intake for premenopausal women (Table 1).

Mean total body, lumbar spine and femoral neck BMD were higher in premenopausal compared with postmenopausal women (**Table 2**). . In postmenopausal women, the prevalence of osteoporosis (*T* score ≤ -2.5) varied from 2.4 to 10.1% depending on the bone site evaluated, being more prevalent at lumbar spine. Osteopenia (-2.5 >*T* score < -1.0) was more prevalent (34.9%) at femoral neck (Table 2).

Lean mass ('non-bone lean mass') was directly associated with BMD at all bone sites in both pre- and postmenopausal women (Pearson correlation analysis, r>0.40 and p<0.001, data not shown). Lean mass was also directly associated with fat mass in both groups (r=0.71; p<0.001 for both pre- and postmenopausal women). The association between BMD and fat mass was evaluated using regression models (**Table 3**). Initially,

using a bivariate regression model, direct and statistically significant associations were observed between fat mass and BMD (total and specific sites; unadjusted model, table 3) in both pre and postmenopausal women. Subsequently, the multivariate model including total body mass, age, height, calcium intake and race (model 1) and postmenopausal period (when applicable) showed that fat mass was inversely associated with both BMD at total body and femoral neck only in premenopausal women. In this group, the estimated decrease in BMD with each additional kg of fat mass was 10mg/cm² at total body and 9mg/cm² at femoral neck. The model 2, that included total lean mass instead of total body mass, resulted in statistically significant direct associations between fat mass and BMD (total and specific-sites) only in postmenopausal women. In this group, the estimated increase in BMD with each additional kg of fat mass was 3mg/cm² at total body, 8mg/cm² at lumbar spine and 6mg/cm² at femoral neck. Lean mass was significantly and directly associated (*B*=0.005 – 0.011; $p<0.01$) with BMD at all bone sites evaluated in both groups, except at lumbar spine and femoral neck in postmenopausal women.

Discussion

In the present study, we investigated the relationship between BMD and fat mass in Brazilian pre and postmenopausal women. For this investigation we considered the influence of potentially confounding variables. We observed that the use of total body mass or lean mass, as adjustment variables, may alter the direction and strength of the association between BMD and fat mass depending on menopausal status. Independently of the adjustment used, there is no evidence of inverse association between BMD and fat mass in postmenopausal women.

Based on BMI classification, the prevalence of overweight (24.9 < BMI ≤ 29.9 kg/m^2) was 42.2% in women, values that were lower than the observed in equivalent strata in the main Brazilian surveys (48.0% and 60.8% in POF 2008 and VIGITEL 2012, respectively). On the other hand, using data from the same surveys as reference, the prevalence of obesity (BMI >29.9 kg/m^2) in the present study (28.5% in women) was considerably higher. The prevalence of obesity in adult women ranged from 15.6 to 21.0% in POF 2008 and from 18 to 23% in VIGITEL 2012 [26,27].

Data on osteoporosis prevalence in Brazilian population are scarce and based on self-reported information of osteoporosis diagnosis. Data on VIGITEL 2006 showed that 7% of women population (18y or older) reported osteoporosis diagnosis [28]. More recently, the Brazilian Osteoporosis Study (BRAZOS) showed that about 6% of the population older than 40 y reported osteoporosis diagnosis [29]. Our data on measured BMD are quite similar and shows that 6.2% of all women studied (and 10.1% of the postmenopausal) had *T* score values lower than -2.5, indicative of osteoporosis, in at least one of the assessed bone sites.

Total body mass is well recognized as a strong predictor of bone mass and consists mainly of lean mass (with a small contribution of BMC) followed by fat mass [1,7]. However, it is noteworthy that body composition may be modified by age (or menopausal status). Gradual increases in adiposity and decreases in lean mass during adulthood have been noted for both men and women [30,31]. Consistently, in the present study, lower lean mass and higher adiposity was observed in postmenopausal compared to pre-menopausal women.

A recent meta-analysis that investigated the association between body composition components and BMD estimated that lean mass accounts for 21% of variation in total BMD, while fat mass explains approximately 8% of differences in

BMD [6]. Although fat mass has a lower contribution to the variation in BMD, compared with lean mass, it is the component of total body mass that is more susceptible to changes in adulthood. Studies evaluating the association between fat mass and bone mineral density have yielded conflicting results, which may be partially due to different statistical approaches, especially the adoption of different adjustment variables.

Most studies conducted from 1990s until the early 2000s reported direct association between fat mass and bone mass and suggested that it may be attributable to either the weight bearing effect of fat mass or the metabolic and hormonal influences of fat tissue [32,33,34]. Similarly, in the present study we observed a direct association between fat mass and BMD (both at total body and at specific bone sites) in pre and postmenopausal women, when other relevant variables were not controlled for.

Over the last few years, the suggested beneficial effect of fat mass on bone mass began to be questioned. Recent studies have shown that, after adjustment for total body mass, the relationship between bone mineral density and fat mass disappears [2,12] or become inverse depending on the population studied [5,16,18,19]. An inverse association between fat mass and BMD was recently observed in men aged >50y and postmenopausal women after adjustment for total body mass [18]. Using the same adjustment approach, Yoo and coworkers [2] also found inverse association between fat mass and BMD in premenopausal women, but not in men and postmenopausal women. In the present study, when we consider total body mass as covariate, fat mass was inversely associated with BMD at total body and femoral neck only in premenopausal women. No association was observed between fat mass and BMD in postmenopausal women.

It is necessary to consider, however, that the adjustment by total body mass in the relationship between BMD and fat mass may result in potential collinearity among variables. Because fat mass is a component of total body mass, considering total body mass as a covariate may bring together the effect of fat mass itself. Therefore, when both total body and fat mass are considered in a regression model, it will probably give misleading results. In fact, the correlation coefficient between fat mass and total body mass is usually greater than 0.9 (in the present study it was 0.8) and violates the assumptions of multiple regression analysis [35]. Collinearity between total body mass and fat mass was confirmed by calculating VIF, that was greater than 10 in both women groups.

Lean mass is a potential alternative variable for adjustment when investigating the relationship between fat and bone mass. Lean mass is the component that represents the majority of total body mass and its direct effect on BMD is well recognized. The correlation between fat mass and lean mass is usually between 0.3 and 0.4 (in the present study it was 0.2), which should not violate the assumption regarding the independence of variables to enter into a multiple regression analysis [35]. In the present study, VIF between lean mass and fat mass was less than 2 in all groups studied, ruling out the possibility of collinearity between these variables. Therefore, we believe that the most cautious adjustment in the evaluation of the relationship between BMD and fat mass is considering lean mass as a covariate. Few studies have considered lean mass as covariate in the association between BMD and fat mass [36,37,38]. After accounting for lean mass, Janicka and coworkers [36] reported that fat mass was inversely associated or not associated with bone parameters in adolescents and young adults. Also, no association between fat mass and BMD was observed in older men when lean mass was considered as covariate [37]. In our study, considering lean mass as covariate, no

association between fat mass and BMD was observed in premenopausal women. However, in postmenopausal women, we observed that fat mass was directly associated with BMD at the total body and specific bone sites. This is consistent with a recent meta-analysis showing that in postmenopausal women, the effect of fat mass on BMD appears to be equivalent to the direct lean mass effect [6]. More recently, no association between fat mass and BMD was observed in postmenopausal African women after adjustment for lean mass [38], which could raise the doubt of a potential ethnic influence on this association.

There are several plausible mechanisms to explain both detrimental and beneficial effect of fat on bones. On the one hand, there is the potential competition for cell differentiation since adipocytes and osteoblasts originate from a common progenitor, and the systemic inflammatory condition characteristic of obesity with consequent secretion of inflammatory cytokines that may lead to bone resorption [19]. Additionally, obesity is frequently associated with vitamin D insufficiency due to its sequestration in adipose tissue, which in turn negatively affects bone health [39]. On the other hand, the increased aromatization of androgen to estrogen in adipose tissue [31] as well as the high circulating levels of insulin, insulin-like growth factor 1[8] and leptin [33], usually associated with adiposity, appear to favor bone formation.

It is well accepted that both hormonal mechanisms and loading are relevant for the final effect of fat mass on bones, but the relative importance may differ between men and women due to considerably different lean mass [16]. Therefore, it is possible to hypothesize that adipose tissue-related hormonal factors may be more important in compensating for lower lean mass especially in postmenopausal women and, in this case, fat mass would constitute an important determinant of bone mass. It is also important to consider that, in elderly people, although overweight is associated with

increased risk for cardiovascular disease it is also associated with decreased mortality from these diseases [40]. Although postmenopausal women in the present study were not elderly (only n=17 were older than 65 years), it appears that our results somehow reflect this obesity paradox. Given the very complex effect of obesity with aging, intentional weight loss by obese older people may be beneficial only if they have obesity-related morbidities [40], which is not the case of participants in the present study.

Limitations of the present study include its cross sectional design that limits causal inference, the absence of information on physical activity habits, and the restricted information on dietary habits, recognized to influence both BMD and fat mass. It is also important to consider that bone health is not solely determined by BMD. Bone microarchitecture together with biochemical markers of bone metabolism and bone-related hormonal profile, not evaluated in the present study, are also important for bone fragility assessment. Our study strengths include the simultaneous investigation of pre and postmenopausal women not restricted to a specific ethnic group, and the model building strategy with adjustment for the main potential confounders.

It is noteworthy that the results of studies investigating the association between fat and bone mass are influenced by the statistical approaches adopted. As observed by several previous studies, we found that total body mass correction results in inverse association between fat mass and BMD in premenopausal women. However, this inverse association disappears if lean mass is adopted as the adjustment variable. Moreover, our results suggest that independently on the adjustment used, there is no evidence of inverse association between fat mass and BMD in postmenopausal women. Additionally, if lean mass is used instead of total body mass as a covariate, an evidence of direct association between fat and bone mass can be observed in postmenopausal

women. Our results should be interpreted in the light of the complex effects of obesity with aging. Nevertheless, they suggest that for postmenopausal women, being slightly obese does not confer excessive risk of bone loss, and may even result in bone density advantage. This is somehow consistent with the concept, albeit controversial, of the "obesity paradox" in which overweight/obesity would confer a survival advantage for individuals who have been diagnosed with a medical condition. The relationship between fat mass and bones deserves further investigation, including the mechanisms underlying this association, particularly in postmenopausal women, which are subject to a higher risk of developing osteoporosis.

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The authors' responsibilities were as follows: FFB and EF designed and supervised the study; AC and MC conducted DXA analysis and interpretation; AC analyzed the data; AC, EF and FFB wrote the manuscript; AC and FFB had primary responsibility for the final content. All authors read and approved the final manuscript. The authors have no conflicts of interest to declare.

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Table 1: General characteristics and body composition of the study population, according to menopause status. Pró-Saúde Study – Rio de Janeiro, Brazil, 2012-13.

Parameters	Premenopausal (n=100)	Postmenopausal (n=166)	P*
Age (years)	47 ± 5	57 ± 7	<0.001
Years since menopause (y)[a]	--	10 ± 7	na
Total body mass (kg)[a]	71 ± 15	72 ± 14	0.84
Height (m)[a]	1.62 ± 0.07	1.58 ± 0.06	<0.001
BMI categories[b]			
Underweight (≤18,5 kg/m²)	1 (1.0)	2 (1.2)	
Normal (18,5 – 24,9 kg/m²)	33 (33.0)	38 (22.9)	
Overweight (25 – 29,9 kg/m²)	44 (44.0)	70 (42.2)	0.36
Obesity I (30 – 34,9 kg/m²)	13 (13.0)	34 (20.5)	
Obesity II (35 – 39,9 kg/m²)	7 (7.0)	17 (1.2)	
Obesity III (≥ 40 kg/m²)	2 (2.0)	5 (3.0)	
Waist circumference (cm)[a]	94 ± 12	97 ± 12	0.07
Hip circumference (cm)[a]	105 ± 10	106 ± 11	0.52
Waist-to-hip ratio[a]	0.89 ± 0.07	0.91 ± 0.07	<0.05
Total lean mass (kg)[a]	40 ± 6	38 ± 5	<0.05
Total fat mass (kg)[a]	29 ± 10	31 ± 10	0.09
Total fat mass (%)[a]	40 ± 5	43 ± 6	<0.001
Serum 25(OH)D concentration[b]			
<12ng/mL	23 (23.0)	33 (29.2)	
12-20ng/mL	38 (38.0)	63 (38.7)	0.86
>20ng/mL	39 (39.0)	67 (41.1)	
Calcium intake (mg)[a]	847 ± 356	940 ± 443	0.07
Skin color/Race[b]			
White	47 (47.0)	66 (40.5)	
Brown	34 (34.0)	47 (28.8)	<0.05
Black	15 (15.0)	49 (30.1)	

[a]Values were expressed as mean ± SD. [b]Values were expressed as n (%). BMI = Body mass index; na = not applicable. *p-values were obtained by Student t test for continuous variables or by chi-square test for categorical variables.

Table 2: Bone parameters of Brazilian women, according to menopause status. Pró-Saúde Study – Rio de Janeiro, Brazil, 2012-13.

Parameters	Premenopausal (n=100)	Postmenopausal (n=166)	p*
Total body			
BMD (cm^2)[a]	1.142 ± 0.095	1.077 ± 0.117	<0.001
T score <-1.0[b]	--	30 (18.1)	
T score ≤-2.5[b]	--	4 (2.4)	
Z score≤-2.0[b]	0 (0.0)	--	
Lumbar spine (L1-L4)			
BMD (cm^2)[a]	1.199 ± 0.157	1.109 ± 0.174	<0.001
T score <-1.0[b]	--	46 (27.7)	
T score ≤-2.5[b]	--	17 (10.1)	
Z score≤-2.0[b]	2 (2.0)	--	
Femoral Neck			
BMD (cm^2)[a]	1.008 ± 0.131	0.939 ± 0.136	<0.001
T score <-1.0[b]	--	58 (34.9)	
T score ≤-2.5[b]	--	5 (3.0)	
Z score≤-2.0[b]	0 (0.0)	--	

[a] Values were expressed as mean ± SD. [b] Values were expressed as n (%).*p-values were obtained by Student's t-test for continuous variables or by chi-square test for categorical variables.. BMD = Bone mineral density.

Table 3: Association by linear regression models between bone mineral density and fat mass among Brazilian women. Pró-Saúde Study – Rio de Janeiro, Brazil, 2012-13.

	Premenopausal (n=100)			Postmenopausal (n=166) *		
	B(95%CI)	t	P	*B*(95%CI)	t	P
TBMD (g/cm²)						
Unadjusted	0.003 (0.002; 0.005)	3.942	<0.001	0.005 (0.003; 0.007)	5.964	<0.001
Model 1	-0.010 (-0.015; -0,004)	-3.453	0.001	-0.002 (-0.008; 0.005)	-0.521	0.603
Model 2	0.000 (-0.005; 0.002)	-0.852	0.397	0.003 (0.001; 0.005)	2.764	0.007
LSBMD (g/cm²)						
Unadjusted	0.005 (0.002; 0.008)	3.343	0.001	0.008 (0.005; 0.010)	5.959	0.005
Model 1	-0.007 (-0.018; 0.005)	-1.191	0.237	0.001 (-0.010; 0.011)	0.130	0.897
Model 2	0.002 (-0.002; 0.006)	1.003	0.318	0.008 (0.005; 0.010)	5.898	<0.001
FNBMD (g/cm²)						
Unadjusted	0.003 (0.001; 0.006)	2.528	0.013	0.006 (0.004; 0.008)	6.482	<0.001
Model 1	-0.009 (-0.018; 0.000)	-2.203	0.030	0.000 (-0.008; 0.008)	-0.004	0.997
Model 2	0.000 (-0.004; 0.003)	-0.205	0.838	0.006 (0.004; 0.008)	6.222	<0.001

TBMD = Total bone mineral density; LSBMD = Lumbar spine bone mineral density; FNBMD = Femoral neck bone mineral density
Model 1: Adjusted by total body mass, age, height, calcium intake and race.
Model 2: Adjusted by lean mass, age, height, calcium intake and race.
*In postmenopausal women, postmenopausal period was also included in the models.

Highlights

- BMD was associated with fat mass (FM) differently in pre and postmenopausal women
- Adjustments for total body or lean mass modified the direction and strength of the BMD-FM association
- There was no evidence of inverse association between BMD and FM in postmenopausal women
- Adjusting for lean mass, a direct association between fat and BMD was observed in these women