ORIGINAL ARTICLE

Associations of fat mass and fat distribution with bone mineral density in pre- and postmenopausal Chinese women

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Abstract

Summary Fat mass (FM) is closely related to bone mineral density (BMD). However, the associations of FM and fat distribution with BMD in pre- and postmenopausal women are still poorly understood. The present study showed android fat mass accumulation after menopause had a negative association with BMD.

Introduction FM is closely related to BMD. However, it is unknown whether FM and central fat distribution have different associations with BMD in pre- and postmenopausal women. The study aims to investigate the associations of FM and fat distribution with BMD in pre- and postmenopausal Chinese women.

Methods Two hundred sixty premenopausal and 267 postmenopausal women aged 18 to 79 years were analyzed. Lean mass (LM), FM, percent body fat (%BF), android FM, gynoid FM, and total and regional BMD were measured using dual-energy X-ray absorptiometry. Fat distribution was assessed by android to gynoid FM ratio (AOI). Multiple

regression analysis was performed to examine the associations of BMD with FM, LM, and AOI.

Results FM, %BF, android FM, and AOI were significantly higher, whereas total and regional BMD were significantly lower in postmenopausal women (all p < 0.01). In premenopausal women, FM was positively associated with total and regional BMD (all p < 0.05). AOI had no significant association with BMD. In postmenopausal women, FM was significantly associated with total and regional BMD even additionally adjusting for LM (all p < 0.01). AOI had significantly negative association with total, head, arm, and leg BMD (all p < 0.05). The results remained unchanged when replacing FM with %BF.

Conclusions There were different associations of FM and fat distribution with BMD in pre- and postmenopausal Chinese women. Increased central body fat had a negative association with BMD. Our findings may have significant implications in the prevention of menopause-related osteo-porosis through reducing centralized fat deposition.

Keywords Bone mineral density \cdot Fat distribution \cdot Fat mass \cdot Menopausal status

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Introduction

Osteoporosis is an important public health problem world-wide due to its high morbidity in aging populations especially for women. Bone mineral density (BMD) has been widely accepted as a surrogate measure for the diagnosis of osteopenia and osteoporosis [1, 2]. A number of genetic and environmental factors have been demonstrated to affect BMD [3, 4]. Body weight is one of the important determinants [5–7]. However, the relative effect



of lean mass (LM) and fat mass (FM), the components of body weight, on BMD remains controversial. In addition, the associations between FM and BMD in different ethnicities are inconsistent. Several studies have reported that FM is positively related to BMD in whites and Japanese women [8-11], whereas other research groups have suggested that excessive FM may not protect against decreases in bone mass [12-15]. In a large-scale sample of Chinese and white subjects, FM of both ethnicities was negatively correlated with bone mass when body weight was adjusted [12]. Although previous studies showed either a positive or negative effect of whole body FM on bone mass, regional fat distribution may also influence bone mass independently of total body FM [16-21]. Yet, the results on BMD and central obesity are inconsistent. These conflicting clinical and epidemiologic studies suggest a complex influence of FM and fat distribution on BMD.

FM is a more important determinant of BMD in women than in men, and the effect of FM on BMD in women may differ according to different menopausal status [9, 22]. Menopause is accompanied by dramatic body composition changes, including an increase in total body and central adiposity (android region), decrease in gynoid fat proportion, and a significant decrease in total and regional BMD [23, 24]. Postmenopausal women with a low body weight, low percent body fat (%BF), or low body mass index are at an increased risk of low bone mass and rapid bone loss, both of which are independent contributing factors to postmenopausal osteoporosis [25]. However, a contrary finding also exists [13]. The roles of FM and fat distribution on BMD in different estrogenic status, i.e., pre- and postmenopause, are still unclear. In addition, studies on the association between postmenopausal fat distribution and BMD based on Asian populations, whose body composition and lifestyle are possibly different from western populations [26], are limited. The aim of the present study was to explore the different associations of FM and central fat distribution with BMD in pre- and postmenopausal Chinese women.

Subjects and methods

Subjects

A total of 547 healthy women aged from 18 to 79 years old were included from the participants in a community-based chronic disease prevention study conducted by the Obesity and Body Composition Research Center of Zhejiang University School of Public Health from 2008 to 2009. Women with known metabolic bone diseases or those under any medications likely to influence BMD were excluded from the study. Twenty women were excluded because of

hysterectomy. In the end, 260 premenopausal women and 267 postmenopausal women were included in the analysis. Written informed consent was obtained and the study was approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University.

Variable definition

Subjects completed a questionnaire on demographic, lifestyle, and menopausal information. Smoking was categorized as nonsmokers and smokers. Drinking was coded as yes or no. Drinkers were those who drank an alcoholic beverage less than one time per day during the past month. Nondrinkers were those who drank no beer, wine, or hard liquor during the past month. None of the subjects were heavy drinkers. Regular menstruation was defined as the 25–35-day interval between menstrual on-set. Menopause was designated if there was a complete natural cessation of menses for more than 12 months. Years since menopause (YSM) for postmenopausal women were recorded.

Anthropometry and body composition measurement

Physical measurements were obtained based on standardized protocol. Height was measured without shoes to the nearest 0.1 cm, weight with only light clothing to the nearest 0.1 kg (Detecto, USA). All values were recorded as the mean of three measures. Body mass index (BMI) was calculated as body weight (in kilograms) divided by height (in meters) squared.

Dual-energy X-ray absorptiometry (DXA; software version 11.40.004; GE-lunar Prodigy, WI, USA) was used to measure LM, FM, percent body fat (%BF), android FM, gynoid FM, and total and regional BMD through wholebody scans. For the android region, the lower boundary is at pelvis cut. The upper boundary is above pelvis cut by 20% of the distance between pelvis and femoral neck cuts. Lateral boundaries are the arm cuts. The gynoid region is defined by the upper boundary below the pelvis cut line by 1.5 times the height of the android region. The height of the gynoid region is equal to two times the height of the android region. Lateral boundaries are the outer leg cuts. Body fat distribution was assessed by android to gynoid fat ratio (AOI). Regional BMD refers to the mean bone density in the regions of head, rib, arm, spine, trunk, hip, and leg. DXA was calibrated daily using a standard phantom provided by the manufacturer. Measurements were maintained within the manufacturer's precision standards of $\leq 0.8\%$.

Statistical analysis

Basic characteristics of subjects were compared by Student's t test for continuous variables and by X^2 test for categorical



variables. Because a significant interaction between AOI and menopausal status was found for the total and regional BMD, pre- and postmenopausal women were analyzed separately to evaluate the associations of BMD with AOI, FM, and LM in multiple regression models. In model 1, we first explored the associations of FM and AOI with total body and regional BMD. We then added LM into model 1 to investigate the associations of LM with total body and regional BMD with the presence of FM and AOI in the model (model 2). In addition, the regression was rerun replacing FM with %BF. Covariates such as age, height, smoking, drinking, and YSM in postmenopausal women were included in the regression models. SPSS (version 16.0 for Windows, SPSS Inc., Chicago, IL, USA) was used for analysis. All statistical tests were two-tailed, and p < 0.05 was considered significant.

Results

Descriptive statistics

The basic characteristics of the subjects are shown in Table 1. Compared to premenopausal women, postmenopausal women were older, shorter, weighed more, and had a higher BMI (all p < 0.01). There was no significant difference in drinking and smoking habits between the two groups (both p > 0.05). FM, %BF, android FM, and AOI were significantly higher in postmenopausal women than in premenopausal women (all p < 0.01). LM and gynoid FM had no significant difference (both p > 0.05). Total body and regional BMD were significantly lower in postmenopausal women than in premenopausal women (all p < 0.01).

Multiple regression analysis

The results of multiple linear regression analysis are shown in Table 2. In model 1, both in pre- and postmenopausal women, FM was significantly positive association with total body and regional BMD (all p<0.05), whereas AOI had no significant relationships with total body and regional BMD except for head BMD in postmenopausal women (p<0.05). When additionally adjusted for LM (model 2), in premenopausal women, the significant association between FM and BMD was eliminated except for the regional BMD of rib, spine, and trunk. While AOI did not have any significant associations with total body and regional BMD, LM had a significantly positive association with BMD in all body regions (all p<0.01). In postmenopausal women, FM was significantly associated with total body and regional BMD, even after additionally adjusting for LM

Table 1 Characteristics of the subjects by menopausal status

	Premenopausal (n=260)	Postmenopausal (n=267)	p value		
Age (years)	38.0±8.6	61.0±7.2	< 0.01		
Height (cm)	157.5 ± 5.5	155.4±5.4	< 0.01		
Weight (kg)	55.8 ± 8.3	58.1 ± 8.0	< 0.01		
BMI (kg/m ²)	22.5 ± 3.1	24.1 ± 3.0	< 0.01		
Body composition measures					
FM(kg)	16.9 ± 5.4	19.5 ± 5.4	< 0.01		
Android FM (kg)	1.6 ± 0.6	2.0 ± 0.6	< 0.01		
Gynoid FM (kg)	3.2 ± 0.8	3.2 ± 0.8	0.96		
LM (kg)	36.3 ± 3.8	36.3 ± 3.6	0.80		
%BF (%)	29.7 ± 5.8	33.0 ± 5.5	< 0.01		
AOI	0.5 ± 0.1	$0.6 {\pm} 0.2$	< 0.01		
Body mineral density	measures (g/cm ²)				
Total body	1.12 ± 0.08	1.03 ± 0.10	< 0.01		
Head	2.25 ± 0.28	2.02 ± 0.32	< 0.01		
Rib	0.64 ± 0.05	0.60 ± 0.06	< 0.01		
Arm	0.82 ± 0.06	0.75 ± 0.08	< 0.01		
Spine	1.04 ± 0.11	0.92 ± 0.12	< 0.01		
Trunk	0.89 ± 0.07	0.82 ± 0.08	< 0.01		
Hip	1.08 ± 0.09	0.99 ± 0.10	< 0.01		
Leg	1.18 ± 0.10	1.09 ± 0.12	< 0.01		
Drinkers (%)	27	28	0.51		
Smokers (%)	4	3	0.39		

Student's t test for continuous variables and X^2 test for categorical variables

(all p < 0.01). LM was also significantly associated with total body and regional BMD (all p < 0.05). AOI had a significantly negative association with total body, head, arm, and leg BMD in postmenopausal women (all p < 0.05), while such an association was not found in premenopausal women. We further replaced FM with %BF and reran the regression models (Table 3). The results were almost identical. %BF was significantly associated with BMD in post- but not in premenopausal women. When additionally adjusting for LM, the associations between %BF and BMD had no changes in pre- and postmenopausal women. LM was significantly associated with BMD both in pre- and in postmenopausal women. AOI was negatively associated with total body, head, arm, and leg BMD in postmenopausal women. Covariates such as smoking, drinking, and YSM had no significant associations with BMD in regression models. Height had a positive association with BMD, but such an association was eliminated when there was additionally adjusted for LM. Age showed a positive association in premenopausal women with BMD and a negative association in postmenopausal women with BMD (data not shown).



Table 2 β coefficients of FM, AOI, and LM for total body and regional BMD from multiple regression analysis in pre- and postmenopausal women

	Total	Head	Rib	Arm	Spine	Trunk	Hip	Leg
Model 1								
Premenop	ausal							
FM	0.209**	0.151*	0.421***	0.166*	0.318***	0.304***	0.219**	0.228**
AOI	0.017	-0.002	0.029	0.021	-0.081	0.019	0.007	0.051
Postmeno	pausal							
FM	0.377***	0.308***	0.553***	0.310***	0.470***	0.461***	0.378***	0.338***
AOI	-0.077	-0.118*	0.075	-0.057	0.002	0.051	0.026	-0.082
Model 2 (a	additional adjuste	d for LM)						
Premenop	ausal							
FM	0.082	0.073	0.272***	0.021	0.226**	0.186*	0.127	0.103
AOI	-0.037	-0.035	-0.033	-0.04	-0.120	-0.031	-0.031	0.000
LM	0.397***	0.244**	0.462***	0.450***	0.286**	0.367***	0.284**	0.388***
Postmeno	pausal							
FM	0.296***	0.264***	0.482***	0.199**	0.418***	0.376***	0.299***	0.268***
AOI	-0.134*	-0.149*	0.025	-0.136*	-0.034	-0.008	-0.029	-0.131*
LM	0.290***	0.158*	0.255***	0.400***	0.184**	0.303***	0.284***	0.249**

Covariates included in the regression model were age, height, smoking status, drinking status, and years since menopause in postmenopausal women

Table 3 β coefficients of %BF, AOI, and LM for total body and regional BMD from multiple regression analysis in pre- and postmenopausal women

	Total	Head	Rib	Arm	Spine	Trunk	Hip	Leg
Model 1								
Premenop	oausal							
%BF	0.076	0.063	0.245**	0.032	0.204**	0.167*	0.099	0.099
AOI	0.087	0.045	0.123	0.092	-0.020	0.091	0.059	0.120
Postmeno	pausal							
%BF	0.275***	0.245***	0.442***	0.189**	0.379***	0.345***	0.287***	0.250***
AOI	-0.035	-0.089	0.128*	-0.013	0.046	0.101	0.066	-0.045
Model 2 (ad	dditional adjusted	l for LM)						
Premenop	oausal							
%BF	0.063	0.055	0.228***	0.018	0.193**	0.154*	0.111	0.086
AOI	-0.035	-0.033	-0.037	-0.040	-0.125	-0.033	-0.035	-0.002
LM	0.424***	0.268**	0.552***	0.457***	0.360***	0.429***	0.326***	0.422***
Postmeno	pausal							
%BF	0.261***	0.236***	0.427***	0.172**	0.367***	0.329***	0.273***	0.238***
AOI	-0.141*	-0.156*	0.013	-0.139*	-0.043	-0.017	-0.038	-0.138*
LM	0.396***	0.252**	0.426***	0.471***	0.333***	0.437***	0.390***	0.345**

Covariates included in the regression model were age, height, smoking status, drinking status, and years since menopause in postmenopausal women

^{*}*p*<0.05; ***p*<0.01; ****p*<0.001



^{*}*p*<0.05; ***p*<0.01; ****p*<0.001

Discussion

It has been known for some time that body weight is a significant predictor of hip fracture risk in women [27]. However, the influence of its major components, FM and LM, on BMD remains unclear. The present study explored the associations of total body FM and fat distribution with BMD in pre- and postmenopausal Chinese women. Our study found that FM and android fat distribution have different associations with BMD in post- but not in premenopausal women. The negative association between android fat distribution and BMD in postmenopausal women yields valuable information that positive control central adiposity deposition during menopause transition has important significance not only to metabolic diseases but also to postmenopausal osteoporosis.

The observed positive association between FM and BMD in postmenopausal women was in accordance with previous studies [8, 22]. Although the precise mechanism of the relationship between FM and BMD in postmenopausal women is not clear, several potential theories have been proposed. One straightforward explanation is that greater FM imposes a greater mechanical stress on bones, and in response, bone mass increases to accommodate the greater load. However, FM accounts for only 25% of body weight in normal-weight women. Therefore, weightassociated gravitational forces may be insufficient to explain the impact of FM on bone [12]. Recent evidence has shown that adipose tissue can release more than 20 adipocytokines into circulation, which led some to suggest that adiposity influences BMD through alternative mechanisms such as adipocyte-dependent hormonal factors [28, 29]. In postmenopausal women, adipocytes are important sources of estrogen production, and estrogen is known to inhibit bone resorption by inducing osteoclasts apoptosis [30]. Adipocyte-derived hormones such as adiponectin and leptin may also play roles in regulating BMD. Vitro studies showed that adiponectin inhibited osteoclasts boneresorption activity [31]. Leptin, produced by adipocytes, is also positively correlated with BMD in women [32, 33].

Although bone mass increased with total body FM in our study, BMD was negatively associated with central adiposity accumulation, indicated as AOI, in postmenopausal women. A prospective study showed the significant association between increased intra-abdominal fat and change of C-reactive protein, tissue plasminogen activator antigen, leptin, and adiponectin in women going through the menopausal transition [34]. These visceral adiposity-associated inflammatory markers and adipokines may exert detrimental influence on bone metabolism [33, 35–38]. A recent study using computerized tomography to measure abdominal fat found a negative effect of visceral fat on femoral bone phenotypes [20]. In the present study,

adipocyte-derived hormonal factors were not measured. The associations between FM and fat distribution with BMD in postmenopausal women could not be explained in terms of either biomechanical or biochemical function of FM. Further studies should be conducted to address the underlying mechanism.

The findings of this study confirmed previous studies that LM has a strong positive effect on bone mass [39, 40]. The positive effect of FM on BMD in premenopausal women was eliminated when additionally adjusting for LM. This implies that bone strength is primarily determined by the dynamic loads from muscle force, but not by the static loads, such as FM [41]. Furthermore, the effect of ovarian estrogen may override the effect of aromatized estrogen derived from FM on BMD in premenopausal women [42]. After menopause, some changes, including a decrease in LM and increase in FM, occur in body composition, and the biochemical functions of FM may become prominent.

The major strength of the present study is that fat distribution was examined using a regional analysis of whole-body DXA scan. Android to gynoid fat ratio, which is closely related to metabolic disturbance in a previous study, is significantly greater in postmenopausal women than in premenopausal women [43]. We used AOI as the central adiposity indicator to investigate the association with BMD rather than waist-hip circumference ratio and trunk-leg fat ratio [16, 17] and found that an android type of fat distribution in postmenopausal women was negatively associated with the BMD of total body and major body regions. This is the first study to explore the association between AOI and BMD. The significant association between AOI and BMD suggests that central adipose tissue is not only correlated with metabolic diseases but also with bone health.

Limitations to the present study should be noted. First, although this is the first study using AOI to show the associations with BMD in women, the subjects are all Chinese and the results may not be generalized to other ethnicities. Second, our data are cross-sectional, so that we are not able to draw the cause and effect relationship between FM and fat distribution with BMD. Third, in the present study, we did not measure the femoral neck or lumbar spine sites to define the diagnosis of osteoporosis. Several studies have used mean BMD to explore the association between body composition and osteoporosis [13, 19, 44, 45]. In addition, as identified in the studies, the diagnostic differentiation of the total body BMD is similar to that of the lumbar spine and femoral neck sites BMD in women [46–48]. Finally, body weight was not included as a controlling variable due to its collinearity with FM and LM. The correlation coefficients between FM and body weight and between LM and body weight are 0.91 and 0.85, respectively, in our data. Including body weight in the



regression model with the presence of LM and FM caused a high multicollinearity in the regression models. In addition, a newly published study on osteoporosis in specific body composition phenotypes indicated that controlling for weight may not be an appropriate adjustment when investigating the influence of FM on BMD [49].

In conclusion, our study showed that there were different associations of FM and fat distribution with BMD in pre- and postmenopausal women. Android fat mass accumulation after menopause had a negative association with BMD. From the public health point of view, rational control weight gain and the prevention of centralized fat deposition during menopause may have significant implications in decreasing menopause-related osteoporosis.

Conflicts of interest None.

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