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Sex- and age-specific characteristics of body composition and its effect on bone mineral density in Chinese adults: a southern China aging study

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Abstract

Objectives: This study was an attempt to investigate the variation trend of body composition with aging and explore the association between regional body composition and bone mineral density (BMD) across a cohort of southern Chinese adults.

Design: Cross-sectional study.

Setting and Participants A total of 5749 healthy adults aged 20-95 years were recruited from 2004-2017.

Primary outcome measures: Whole-body lean mass (LM), fat mass (FM), android FM, gynoid FM, appendicular lean mass (ALM), and the BMD in the lumbar spine, femoral neck, and total hip were obtained by dual-energy X-ray absorptiometry (DXA). The android/gynoid fat mass ratio (A/G FMR) based on DXA scan was calculated as an indicator of adipose distribution. Pearson correlation and multiple linear regression analyses were used to determine the associations between BC, adipose distribution, and BMD of each skeletal site.

Results: Whole-body FM, fat%, Android FM, and A/G FMR consistently increased with age in both genders, especially in females, and appendicular LM began to decrease in the fifth decade for both males and females. In multivariable linear regression models with age, BMI, A/G FMR, and ALM as predictor variables, ALM was associated with the most BMD variance of all skeletal sites in males (standard β 0.207 to 0.388, P <0.01 for all), although not the largest but still a positive predictor of BMD in females (standard β 0.123 to 0.227, P < 0.001 for all). A/G FMR was an inverse predictor of BMD at all skeletal sites for females (standard β -0.052 to -0.236, P <0.01 for all) but not in males.

Conclusions: In this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders. A/G FMR as an indicator of central adipose accumulation was inversely associated with BMD in females but not in males.

Strengths and limitations of this study

- This is the first study to analyze the relationships of regional body composition (muscle and fat distribution) with bone mineral density at multiple sites in different ages, menopausal status in a large population-based sample of southern Chinese adults.

- A limitation of this study is that we did not obtain the actual hormone and cytokine levels, dietary intake, and physical activity, which may influence bone nutrition and metabolism.

- And we only collected cross-sectional data and cannot directly conclude the causality limited by its study design.

Introduction

Body weight is one of the main determinants of bone mass. It is known to be positively correlated with bone mineral density (BMD) and can partly reflect bone health. Body mass index (BMI) has been widely used in epidemiological studies and clinical practice to provide a quick assessment of nutritional status and showed a positive relationship with BMD [1]. Body mass is composed of lean fat and bone mass. LM is linked to significant health consequences, studied mostly in the context of severe muscle depletion (sarcopenia) that occurs with aging and catabolic conditions [2]. Moreover, studies indicate that LM may produce a positive effect on bone mass in both genders [3]. FM has also been shown to be a key predictor of BMD and may affect bone via both loading and hormonal mechanisms [4]. Aging is associated with gradual changes in body composition, and these changes may be entirely different between men and women, as well as premenopausal and postmenopausal women [5, 6]. To further explore the changes in body composition with age is one of the purposes of our study.

Regional body composition changes occur with age, typically characterized by decreases in appendicular LM and increases in central FM. Some studies have reported that appendicular LM (ALM) and central FM may affect bone formation independent of the amount of total body composition, but the results were inconsistent [7-9]. Blain et al. [7] showed that ALM was the most influential factor contributing to BMD of the femoral neck in men, and low ALM (sarcopenia) was considered an independent risk for low BMD (osteoporosis). In contrast, Walsh et al. [10] showed that ALM was not significantly related to BMD after adjusting body weight and physical activity in women.

Android fat represents the visceral (central) adipose tissue while gynoid fat reflects the subcutaneous (appendicular) adipose tissue [11]. As the measurements of central FM used different

methods or indexes, the findings regarding the relationship of central adipose with BMD are more controversial. Several studies indicate that central adipose accumulation is negatively related to BMD [12, 13]. On the contrary, some studies show visceral fat is positively associated with BMD in postmenopausal women [14]. These heterogeneous findings may result from the rather complex mechanisms underlying the relationship between fat and bone, including mechanical loading as well as the hormones and cytokines from adipose tissue, which can indirectly influence bone metabolism to a certain extent. Moreover, gender, age, menopausal status, and skeletal site differences in the relationship between BMD with ALM and central FM have not been well studied.

To our knowledge, only a few other studies have documented the relationships of ALM and A/G FMR with BMD at multiple sites in different ages, menopausal status, and in both genders. In the current study, we aim to investigate the relationship between BMD and body composition, especially the effect of regional body composition on BMD. We also want to examine whether these relationships differ by gender, age, and menopausal status in a large population-based sample of Chinese adults.

Methods

Subjects

The present study included healthy Chinese men and women aged 20 to 95 years old. The participants were recruited from the body composition and osteoporosis study at the First Affiliated Hospital of Jinan University (Guangzhou, China) from 2004-2017. Inclusion criteria for the study were Chinese individuals who appeared to be in good health and functionally independent. Subjects were excluded if they met any of the following criteria: (a) a history of fracture; (b) medication known to affect the musculoskeletal system (anti-osteoporotic drugs, androgens or anti-androgen drugs, corticosteroids, etc.); (c) chronic disease known to affect bone metabolism (hyperthyroidism, hyperparathyroidism, rheumatoid arthritis, chronic renal insufficiency, etc.); (d) metal implants (pacemakers, joint replacement device, etc.); (e) inability to determine the menstruation state or non-natural menopause (natural menopause was designated if there was a complete natural cessation of menses for more than twelve months). In the end, 1703 men and 4046 women were included in our study. All subjects provided written informed consent to participate in the study, which was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University.

Anthropometry, BMD and body composition measurement

A research physician obtained information on medical history, medication use, smoking, and alcohol history in a personal interview. Height and body weight were obtained based on standard methods; height was measured without shoes to the nearest 0.1 cm, weight with only light clothing to the nearest 0.1 kg. Body mass index (BMI) was calculated as body weight divided by height squared (kg/m^2). Subjects underwent dual-energy X-ray absorptiometry (DXA; software version enCORE10.50.086; GE-lunar Prodigy, WI, USA) scans to measure the whole body, lumbar spine, femoral neck, and total hip BMD. Total and regional LM and FM were obtained through whole body scans. Android and Gynoid regions were automatically attained using the software provided by the manufacturer. Android region is defined as the portion of the abdomen included between the line joining the two superior iliac crests, extending cranially up to 20% of the distance between this line and the chin. Gynoid region is defined as the portion of the legs leaving from the femoral greater trochanter, directed caudally up to twice the height of the android region. The appendicular region is defined as the areas including both the left and right arms and legs. Daily quality assurance scans were performed by scanning the spine phantom according to the manufacturer's instructions; the same trained technologist conducted all DXA measurements throughout the study. The precision error (%CV) was less than 2% for total LM, FM, total, lumbar spine, femoral neck, and total hip BMD, and less than 3% for regional (trunk, appendicular, android, and gynoid) LM and FM, was determined by duplicate scans with repositioning between each measurement in 30 volunteer subjects.

Statistical analyses

Subjects were categorized into four groups according to gender, age, and menopausal status (786 men＜50years, 917 men ≥50years, 1534 premenopausal women, and 2512 postmenopausal women). The values of continuous variables were presented as the mean ± standard deviation (SD). Unpaired-sample *t*-tests were used to evaluate the mean differences between different groups, and Pearson's correlation coefficients (*r*) were conducted to determine the linear relationships among various parameters. We performed linear regressions to assess the association strength between ALM, A/G FMR, and BMD. In the regression models, BMD (different skeletal sites) measurements were used as dependent variables, and ALM and A/G FMR were treated as independent variables; age, height, and lifestyle factors (smoking and alcohol history) were also included. When we performed linear

regression analyses, we chose the stepwise methods and expressed the results as standard β coefficients; only significant (P <0.05) factors were retained in the models. All tests were two-sided, and P <0.05 was considered statistically significant. All statistical analyses were performed using the statistical package for social sciences (Version 19.0) (SPSS Inc., Chicago, IL, USA).

Patient and Public Involvement

There was no patient or public involvement in this study.

Results

Basal characteristics of subjects

Table 1 details the subject characteristics in each group. Males ≥50years had higher BMI, whole-body FM, fat%, trunk FM, and appendicular FM, but lower weight and lumbar spine BMD than males＜50years (P <0.001). Postmenopausal females had higher values for whole-body FM, whole-body LM, trunk FM, appendicular FM, and A/G FMR, and lower BMD at each site than premenopausal females (P <0.05).

Changes of BMD and body composition with age

To further explore the distribution characteristics of body composition and BMD regarding age, we divided the subjects into multiple subgroups and set ten years as one subgroup. As shown in Table 2 and Figure 1, whole-body FM, fat%, android FM, and A/G FMR showed a consistent increase in both genders. Overall, the highest values of whole-body, lumbar spine, femoral neck, and total hip BMD were observed in the second decade and then decreased slightly with age in males. BMD at each skeletal site increased steadily and reached a peak until perimenopause in the fourth decade in females, and then decreased dramatically after menopause. Interestingly, appendicular LM started to decline after 50 years old in both males and females.

Associations of BMD with whole and regional body composition in different groups

In Pearson's correlation analyses, significant positive correlations were found between BMD at all sites with height, weight, BMI, whole-body LM, whole-body FM, FAT%, Android FM, Gynoid FM, and ALM in all groups (r=0.218-0.616, P <0.05). A/G FMR showed positive correlations with whole-body, lumbar spine, femoral neck, and total hip BMDs in men <50years and ≥50years old (r=0.089~0.318, P<0.001). However, A/G FMR was negatively correlated with whole-body and femoral neck BMDs in postmenopausal females, though the correlation strengths were weak (r=-

0.075, P<0.001 and r=-0.091, P<0.001, respectively). A/G FMR was insignificantly correlated with BMD in premenopausal females (Shown in supplemental table 1-4).

To further explore the independent predictive value of A/G FMR and ALM for BMD at all sites in every group, covariates such as ages, BMI, smoking, and alcohol consumption that associated with BMD were also included in the multiple linear regression analyses (shown in Table 3). Overall, the significant variables accounted for 10.7~37.4% of the variability in BMD.

The effect sizes of A/G FMR and ALM on BMD were different according to the skeletal site and age group. A/G FMR had inverse associations with whole-body, lumbar spine, femoral neck, and total hip BMDs in both premenopausal and postmenopausal women (standard β=-0.236~-0.052), while men had no significant relationship between A/G FMR and each part of BMD after adjustment. ALM was positively associated with whole-body, lumbar spine, femoral neck, and total hip BMDs in both males and females, and the correlations were higher in males (standard β=0.207~0.388) than that in females (standard β=0.123~0.227), in both younger adults and older adults after adjustment.

Discussion

The global epidemic of obesity has become a significant concern in our daily life as it not only has a close relationship with cardiovascular and cerebrovascular diseases but also influences bone health [15]. As a part of body composition, bone density was mainly determined by body weight and BMI. Low BMI had been regarded as a risk factor for osteoporotic hip fracture in both males and females [16]. In this study, we investigated a wide range of healthy Chinese adults aged 20 to 90 years old to further explore the factors that may influence bone health. We divided the participants into different age groups to investigate the changes in body composition and BMD with age in males and females. We also performed multivariable regression analyses to confirm that whether A/G FMR and ALM were independent predictors for BMD after adjusting for age, BMI, smoking, and alcohol consumption. The current report provided more detailed and impressive results which were different from previous studies performed in America [13] and Australia [1]. We found that ALM positively correlated with BMD in both genders, and low ALM was related to low BMD. A/G FMR as an indicator of central adipose accumulation was inversely associated with BMD in females but not in males. These results, based on a large population of Chinese adults, were convincing.

In this study, we found that whole-body LM reached a peak level in the 40-49 years group, and

then decreased gradually in both genders, whereas whole-body FM steadily increased from youth to older age in both genders. After analyzing the baseline characteristics, we found that the decreased whole-body LM in older men was primarily due to a decrease in ALM. Moreover, the increased whole-body FM in older men and women mainly arose from the increase of Trunk FM. In the meantime, we found that the A/G FMR increased with age in both males and females. Men had an earlier whole-body, lumbar spine, femoral neck, and total hip BMD peaks than women. BMD at all sites decreased slightly in older men, but more obviously in postmenopausal women. These results provided us a healthy bone mass for each age group in both men and women. The BMD at each region lower than the guidance ranges in the respective age group should alarm the physician for appropriate intervention.

In our study, the results showed that both total LM and total FM are positively associated with BMD in both genders. The effect size of total LM and total FM to BMD was different according to gender, menopausal status, and age. Total LM is a stronger protective factor to BMD at all sites in men and premenopausal women. Total FM is a stronger contributor to BMD at all sites in postmenopausal women. Several potential theories may explain the observed findings. The influences of LM on BMD may attribute to the direct mechanical effects of muscle, which produces a positive osteogenic response to bone formation. For one hand, whole-body LM, which accounted for a large proportion of body weight in both males and females, would perform a gravitational loading on the bone. On the other hand, the contraction strength of lean muscle should also be considered a specific mechanism of action. A previous study reported that the augmentation and thickening of bone trabecula was an adaption to increased mechanical stress. However, whole-body FM only accounted for a small proportion of body weight in both males and females, but it still performed a significant and positive correlation with BMD, especially in postmenopausal women, in whom a higher standard β value with BMD in all the skeletal sites was shown compared with whole-body LM. Several mechanisms could explain the association between fat tissue and BMD. The outcomes of fat acting on the bone may be influenced not only by weight-bearing effects but also by non-weight bearing effects, including the hormonal metabolism of adipocytes. We speculate that this fat-related mechanism may help to interpret this finding, as the postmenopausal women also had the highest whole-body FM, more than males and premenopausal women in our study. Several hormones, including insulin, leptin, adiponectin, and adipocytic estrogens, were found to be secreted from

adipose tissue, which can influence bone metabolism through the endocrine pathway. Also, the enzyme aromatase in adipose tissue can convert androgen to estrogen and result in an elevated estrogen level. These bone protective hormones led to a positive influence on bone formation via stimulating the differentiation of osteoblasts and preventing osteoclast-mediated bone resorption. This finding further confirmed the results from previous studies that FM should have a positive relationship with bone mass [8, 17].

Though both whole-body LM and FM were found to be positively associated with BMD in both genders, how regional body compositions and differences in fat distribution influence bone metabolism aroused our curiosity. To investigate the effect of ALM and A/G FMR on BMD with various ages, the factors including gender, age, BMI, smoking, and alcohol consumption, which may have close relationships with BMD, were considered in multiple linear regression analyses. In the current study, we found that ALM was positively related to BMD at all sites after adjustment for BMI and age in both genders. ALM is considered one of the most important indexes of the diagnostic criterion for sarcopenia [18, 19]. A study of 679 men aged 40-79 years suggested low ALM was associated with low BMD (whole body, femoral neck, total hip, and lumbar spine) and osteoporosis independent of age, height, physical activity, and other lifestyles [20]. Blain et al. [7] also found that ALM was most strongly associated with femoral neck BMD independent of nutritional, hormonal factors, and other lifestyles in men. There are several mechanisms that may explain the observed association between ALM and BMD. The amount of ALM was smaller than trunk LM in this study, suggesting ALM may affect on bone via contraction strength instead of gravitational loading, especially in males younger than 50 years old, in whom the strongest relationships with BMD in all sites were demonstrated, compared with other groups. Systemic factors that simultaneously involve both ALM and bone metabolism may exist as the decline of ALM was almost parallel with BMD in both genders. For example, the hormone estrogen can strengthen the synthesis of muscle protein and promote calcium deposition in bone tissue, which leads to an increased LM and BMD concurrently [21]. However, a prospective study is needed to explore the potential mechanism further.

Depot-specific fat has been known to play a different role in terms of obesity and metabolism. A previous study indicated that different fat depots might have distinct relationships with bone mass [22]; Marques reported appendicular FM (AFM) had a positive association with femoral neck BMD

in older women [23]. Inconsistent with that, several studies stated AFM had no [24] or a negative [25] relationship with BMD. Freitas et al. [26] showed that central fat was positively associated with BMD and regarded as an independent and protective factor on the presence of osteoporosis or osteopenia. Sharma et al. [27] reported that a bigger trunk (central) FM was associated with increased BMD in total hip and femoral neck, regardless of HIV status in women. Fat distribution difference seems to produce a meaningful but contradicted effect on bone mass based on previous studies. To further confirm this finding, we performed Pearson's correlation to assess the relationship between Android FM, Gynoid FM, and each part of BMD with a large sample size. The results suggested that both Android FM and Gynoid FM positively correlated with BMD in all males and females, which was partly consistent with previous studies [22, 24]. In contrast, some studies reported abdominal fat and android fat measured by CT or DXA had a negative association with BMD after adjusting for total LM or BMI, suggesting central fat deposition was not beneficial for bone [13]. Surprisingly, we found that A/G FMR showed a diverse correlation with BMD in males and females. The results revealed that A/G FMR was positively correlated with each part of BMD in males <50 years and older group. But in postmenopausal females, A/G FMR had an inverse association with whole-body (r=-0.075, P<0.001) and femoral neck BMD (r=-0.091, P<0.001), and had no relationship with each part of BMD in premenopausal females. Kim et al. [22] also reported that A/G FMR was inversely associated with the trabecular bone score after age adjustment (r=-0.288, P<0.05), which was similar with our findings. Android fat mainly represents visceral fat in the epigastric region, while gynoid fat reflects peripheral (or subcutaneous) fat in the leg. A higher A/G FMR indicating a higher visceral fat or a lower peripheral fat revealed that subjects with a higher A/G FMR had a lower BMD in postmenopausal females, whose ovarian hormones tend to be depleted and lead to a higher subcutaneous lipoprotein lipase activity ratio and predominant fat storage in visceral fat depots [28]. Kim et al. [29] found that visceral fat has a negative association among postmenopausal Korean women with lumbar spine BMD after adjustment for weight. Zhu et al. [17] reported trunk-to-limb fat mass ratio (a surrogate of visceral fat) had a negative association with total body bone mass in young adults [17]. Gilsanz et al. [30] suggested that subcutaneous and visceral fat had opposite effects on femoral bone structure and strength in healthy young females, and proposed that subcutaneous fat may be beneficial to the bone, whereas visceral fat may have a negative association with bone. These heterogeneous findings may be related to the use of diverse

methods for measuring body composition and BMD, disparities in study design, or the different criteria for group division. Moreover, the inconsistency of findings may be due to the rather complex mechanisms underlying the relationship between fat and bone. As a result, we subdivided the Chinese people into different age and gender groups and found that android fat increased with age, especially in females, whose android fat accounted for a more substantial proportion of body weight and had a stronger relationship with BMD in our study. To avoid multicollinearity, we included A/G FMR instead of the total and regional body composition into the same multiple regression analysis when we explored the associations of regional fat depots with BMD, which provided a more reliable result.

Limitations

This study had several limitations. First, we did not obtain a blood sample from participants; thus, the actual hormone and cytokine levels were unknown. The potential mechanisms acting on bone mass mainly referenced in previous reports based on our data and the statistical results. Second, we only collected cross-sectional data and cannot directly conclude the causality limited by its study design. Third, though we evaluated the relationships of body composition and fat distribution with BMD by adjusting age, smoking, and alcohol consumption, other confounders such as socioeconomic status, dietary intake, and physical activity, which may influence bone nutrition and metabolism, were not considered as covariates in the multivariable regression analyses. Fourth, a more substantial amount of visceral fat mass was found in Asians compared with the European people for a given amount of body fat [31]. Therefore, ethnic differences should be considered when interpreting the findings.

Conclusions

In summary, in this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders and suggesting that low ALM is related to low BMD and may be considered an independent risk for osteoporosis. A/G FMR an indicator of central adipose accumulation was inversely associated with BMD in females but not in males.

Contributors

Xiao participated in collection, analysis, interpretation of data, and the writing of the paper. Xu, Principal Investigator, innovator for the project, participated in the conception, design, and revision of the manuscript.

Conflict of interest

The authors have no conflicts of interest.

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Ethics approval

The study was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University.

Data sharing statement

Data will be made available on request.

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Abbreviations

BMD: bone mineral density; LM; lean mass; FM: fat mass; ALM: appendicular lean mass; DXA: dual-energy X-ray absorptiometry; A/G FMR: android/gynoid fat mass ratio; BMI: body mass index.

Figure legend

Fig.1 The age-related change in whole-body lean mass (WBLM), appendicular lean mass (ALM), percentage of whole-body fat mass (fat%), A/G FMR, and bone mineral density in males and females. A/G FMR, Android/Gynoid fat mass ratio; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

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Table 1 Baseline characteristics of subjects

	Male		Female	
	Age＜50years	Age≥50years	Premenopausal	Postmenopausal
No. of subjects	786	917	1534	2512
Age (years)	36.8±8.7	65.8±10.0[c]	37.4±8.7	63.9±9.1[c]
Weight (kg)	63.9±12.4	63.8±10.8 [c]	52.7±9.1	55.0±8.9
Height (cm)	168.8±5.8	166.7±6.1	158.0±4.9	155.9±5.3[c]
BMI (kg/m^2)	22.4±3.9	22.9±3.3 [c]	21.1±3.3	22.6±3.3
Body composition measures (Kg)				
Whole body FM	13.7±7.6	15.2±6.5 [c]	16.7±6.0	18.9±6.2[b]
Whole body LM	47.6±6.0	46.1±5.9	33.8±4.3	34.2±4.0[a]
Fat%	20.2±8.3	23.0±7.3[c]	30.1±6.7	33.6±6.8
Trunk FM	8.2±5.0	9.3±4.4[c]	8.7±3.6	10.6±3.7[b]
Trunk LM	22.4±3.0	22.4±2.9	16.4±2.2	17.1±2.1
Appendicular FM	5.0±2.6	5.3±2.1 [c]	7.3±2.5	7.5±2.6[c]
Appendicular LM	21.4±3.2	19.9±3.1	14.4±2.2	14.0±2.1
A/G FMR	0.57±0.17	0.69±0.19	0.42±0.10	0.56±0.15[c]
Bone mineral density (g/cm^2)				
Whole body	1.105±0.109	1.109±0.105	1.085±0.094	0.994±0.106[c]
Lumbar spine	1.114±0.162	1.099±0.200[c]	1.124±0.155	0.950±0.186[c]
Femoral neck	0.921±0.140	0.839±0.140	0.907±0.122	0.760±0.132[b]
Total hip	0.941±0.150	0.911±0.147	0.942±0.132	0.817±0.144[b]
Current Smoker (%)	17.9%	13.0%	2.4%	2.8%
Current alcohol user (%)	15.4%	12.8%	2.3%	1.5%

Note. Values are presented as number, mean ± standard deviation or percentage.

BMI, body mass index; FM, fat mass; LM, lean mass; Fat%, percentage of whole body fat mass; A/G FMR, android/gynoid fat mass ratio. *P* value was determined by the unpaired-sample *t*-tests. [a]$P < 0.05$; [b] $P< 0.01$; [c]$P < 0.001$. Compared with the same gender of the different age group (unpaired-sample t-tests or chi-squared test).

Table 2 Distributions of age-related change in body composition and bone mineral density

Age (years)	n	WBLM (Kg)	WBFM (Kg)	Fat %	Android FM(Kg)	Gynoid FM(Kg)	A/G FMR	ALM (Kg)	WBBMD (g/cm^2)	LSBMD (g/cm^2)	FNBMD (g/cm^2)	THBMD (g/cm^2)
Male												
20-29	199	47.3±6.0^c	12.1±8.2^c	18.1±9.0^c	1.2±0.9^c	2.4±1.3^c	0.47±0.14^c	21.6±3.3^c	1.102±0.103	1.126±0.151	0.958±0.140	0.954±0.153
30-39	254	47.0±5.9^c	12.8±7.3^c	19.4±8.2^c	1.4±0.9^c	2.4±1.3^a	0.55±0.16^c	21.0±3.3^c	1.090±0.113^c	1.110±0.149	0.909±0.140^b	0.922±0.154^c
40-49	333	48.3±6.0^c	15.4±7.2^c	22.1±7.6^c	1.7±0.9^c	2.6±1.0	0.63±0.17^c	21.5±3.2^c	1.119±0.108^b	1.111±0.178	0.908±0.137	0.947±0.147
50-59	313	48.1±6.1^c	15.2±6.5	22.2±7.2^a	1.7±0.8^c	2.5±0.9	0.67±0.18^c	21.0±3.2^c	1.122±0.110	1.096±0.192	0.895±0.140	0.946±0.154^a
60-69	281	46.9±5.4^c	15.5±6.5	23.0±7.3^a	1.8±0.8^c	2.5±0.9	0.71±0.19^c	20.4±2.8^c	1.122±0.098	1.116±0.190	0.843±0.120	0.924±0.125
70+	323	43.6±5.2^c	15.0±6.5	23.8±7.5	1.7±0.9^b	2.4±0.9	0.70±0.19^c	18.4±2.7^c	1.086±0.101	1.086±0.215^c	0.783±0.135^c	0.863±0.147^a
Female												
20-29	369	32.5±4.2	15.5±6.1	30.1±7.1	1.3±0.6	3.2±1.0	0.38±0.09	14.0±2.1	1.048±0.090	1.103±0.135	0.891±0.126	0.912±0.138
30-39	456	33.5±4.0	16.0±6.0	30.2±6.7	1.4±0.6	3.2±1.0	0.42±0.11	14.3±2.0	1.084±0.090	1.131±0.152	0.917±0.119	0.942±0.123
40-49	709	34.7±4.4	17.8±5.8	31.9±6.4	1.5±0.6	3.5±0.9	0.45±0.10	14.7±2.2	1.105±0.093	1.131±0.165	0.908±0.122	0.958±0.131
50-59	1004	34.6±4.0	19.0±6.3	33.4±6.6	1.8±0.7	3.4±1.0	0.52±0.13	14.4±2.1	1.039±0.103	1.008±0.186	0.828±0.126	0.880±0.137
60-69	805	34.5±3.9	19.1±6.1	33.7±7.1	1.9±0.7	3.3±0.9	0.57±0.15	14.2±2.0	0.986±0.095	0.931±0.171	0.749±0.113	0.814±0.128
70+	703	33.2±3.9	18.4±6.1	33.8±7.1	1.9±0.7	3.1±0.9	0.59±0.16	13.3±1.9	0.939±0.094	0.889±0.177	0.672±0.105	0.732±0.125

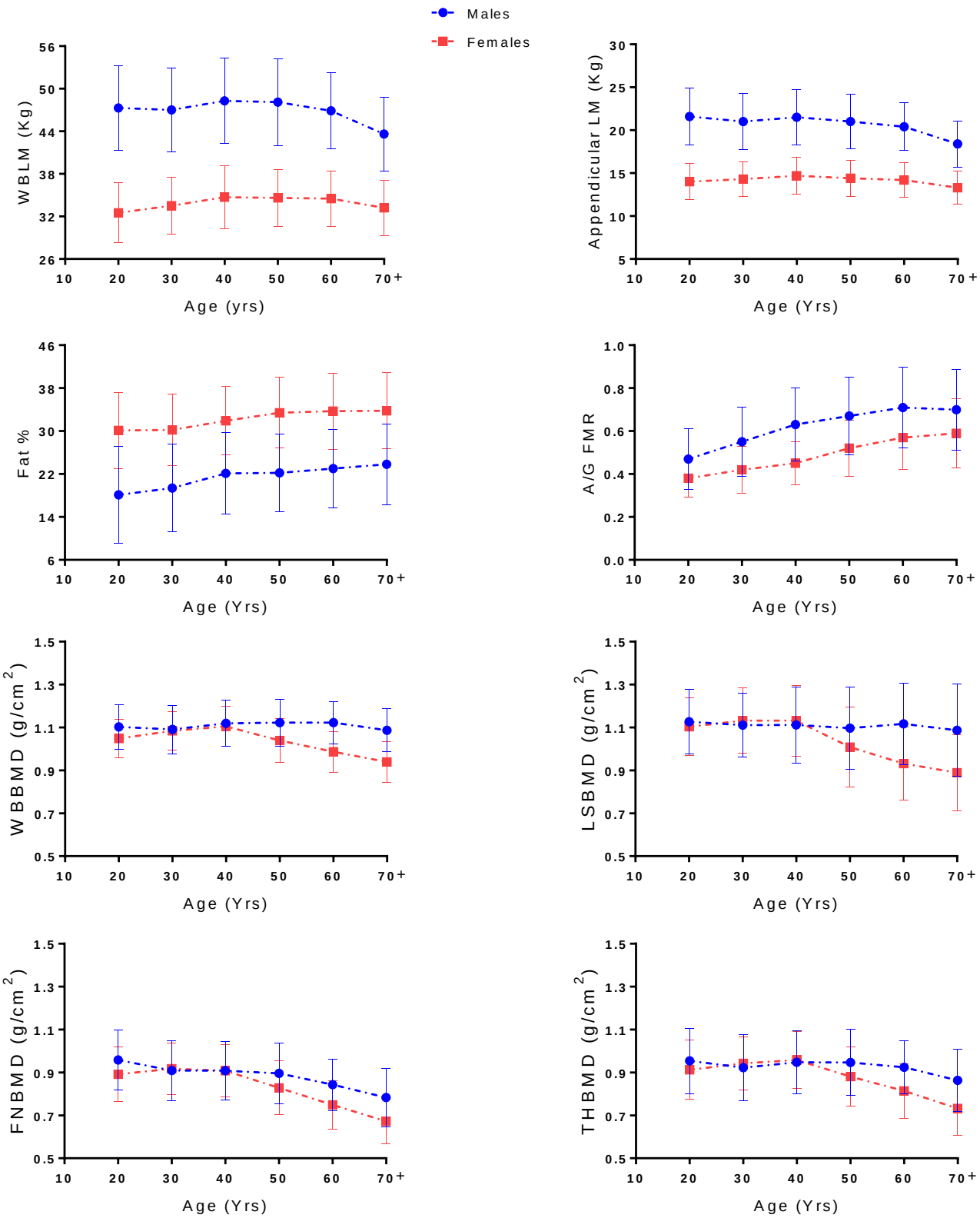
Note. Values are presented as number or mean ± standard deviation. WBLM, whole body lean mass; WBFM, whole body fat mass; Fat % = whole body fat mass/body weight×100; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density. $^aP < 0.05$; $^bP < 0.01$; $^cP < 0.001$. Compared with female of the same age group (unpaired-sample t-tests).

Table 3 Multiple regression analyses of bone mineral density at different skeletal sites with age, BMI, A/G FMR, and appendicular LM (adjusted smoke and alcohol).

	WBBMD	LSBMD	FNBMD	THBMD
	Standard β	Standard β	Standard β	Standard β
Male				
<50years	R^2=0.376	R^2=0.150	R^2=0.215	R^2=0.283
Age	0.034	-0.019	**-0.137**[c]	-0.025
BMI	**0.276**[c]	**0.148**[a]	**0.121**[a]	**0.185**[c]
A/G FMR	0.011	-0.084	-0.048	-0.003
Appendicular LM	**0.379**[c]	**0.301**[c]	**0.371**[c]	**0.388**[c]
≥50years	R^2=0.290	R^2=0.190	R^2=0.269	R^2=0.263
Age	-0.015	**0.087**[b]	**-0.220**[c]	**-0.124**[c]
BMI	**0.260**[c]	**0.268**[c]	**0.190**[c]	**0.261**[c]
A/G FMR	0.008	0.027	-0.054	-0.035
Appendicular LM	**0.321**[b]	**0.207**[c]	**0.264**[c]	**0.256**[c]
Female				
Premenopausal	R^2=0.280	R^2=0.140	R^2=0.133	R^2=0.177
Age	**0.167**[c]	-0.001	-0.021	**0.062**[a]
BMI	**0.351**[c]	**0.328**[c]	**0.232**[c]	**0.295**[c]
A/G FMR	**-0.236**[c]	**-0.183**[c]	**-0.155**[c]	**-0.153**[c]
Appendicular LM	**0.227**[c]	**0.123**[c]	**0.206**[c]	**0.192**[c]
Postmenopausal	R^2=0.348	R^2=0.209	R^2=0.344	R^2=0.332
Age	**-0.337**[c]	**-0.222**[c]	**-0.438**[c]	**-0.389**[c]
BMI	**0.315**[c]	**0.274**[c]	**0.185**[c]	**0.266**[c]
A/G FMR	**-0.135**[c]	**-0.086**[c]	**-0.083**[c]	**-0.052**[b]
Appendicular LM	**0.186**[c]	**0.152**[c]	**0.180**[c]	**0.166**[c]

Note. Results expressed as standard *β* coefficients. Multiple linear regression analyses including age, BMI, A/G FMR, appendicular lean mass, smoke and alcohol. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

[a]$P < 0.05$; [b]$P < 0.01$; [c]$P < 0.001$.


Males
Females
WBLM (Kg)
Age (yrs)
Appendicular LM (Kg)
Age (Yrs)
Fat %
Age (Yrs)
A/G FMR
Age (Yrs)
WBBMD (g/cm2)
Age (Yrs)
LSBMD (g/cm2)
Age (Yrs)
FNBMD (g/cm2)
Age (Yrs)
THBMD (g/cm2)
Age (Yrs)

SUPPLEMENTARY INFORMATION

Sex- and age-specific characteristics of body composition and its effect on bone mineral density in Chinese adults: a southern China aging study

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Keywords: body composition; aging; bone mineral density; fat distribution; appendicular lean mass.

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Table S1. Pearson's correlation between study variables in males <50years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.092*											
Weight	.161***	.460***										
BMI	.216***	.126***	.917***									
WBLM	.083*	.571***	.851***	.706***								
WBFM	.189***	.265***	.905***	.893***	.549***							
Fat%	.207***	.155***	.788***	.810***	.364***	.962***						
A/G FMR	.407***	.062	.594***	.641***	.363***	.656***	.667***					
ALM	.005	.555***	.822***	.681***	.950***	.541***	.372***	.308***				
WBBMD	.101**	.306***	.610***	.547***	.567***	.489***	.407***	.318***	.569***			
LSBMD	-.019	.245***	.358***	.294***	.355***	.258***	.203***	.096***	.375***	.741***		
FNBMD	-.127***	.274***	.394***	.314***	.423***	.266***	.182***	.089***	.438***	.715***	.662***	
THBMD	.017	.232***	.495***	.443***	.500***	.363***	.280***	.226***	.513***	.842***	.696***	.872***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

$^{*}P < 0.05$; $^{**}P < 0.05$; $^{***}P < 0.001$.

Table S2. Pearson's correlation between study variables in males ≥50years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.165***											
Weight	-.212***	.511***										
BMI	-.160***	.087***	.898***									
WBLM	-.355***	.581***	.835***	.671***								
WBFM	-.016	.287***	.860***	.850***	.438***							
Fat%	.089**	.125***	.668***	.717***	.162***	.941***						
A/G	.042	.028	.446***	.505***	.198***	.548***	.575***					
ALM	-.385	.546***	.807***	.658***	.945***	.442***	.191***	.164***				
WBBMD	-.180***	.307***	.545***	.479***	.501***	.395***	.280***	.193***	.499***			
LSBMD	-.035	.230***	.451***	.407***	.352***	.381***	.307***	.203***	.356***	.772***		
FNBMD	-.354***	.291***	.447***	.373***	.459***	.281***	.172***	.077***	.466***	.760***	.631***	
THBMD	-.267***	.235***	.473***	.433***	.456***	.323***	.221***	.134***	.471***	.848***	.702***	.913***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

$^{*}P < 0.05$; $^{**}P < 0.05$; $^{***}P < 0.001$.

Table S3. Pearson's correlation between study variables in premenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.031											
Weight	.222***	.424***										
BMI	.260***	.072***	.932***									
WBLM	.217*	.510***	.795***	.671**								
WBFM	.166***	.246***	.896***	.890***	.445***							
Fat%	.116***	.078***	.656***	.697***	.084***	.909***						
A/G	.261***	.002	.449***	.494***	.251***	.489***	.465***					
ALM	.153***	.519***	.769***	.640***	.947***	.444***	.111***	.181***				
WBBMD	.230**	.200***	.453***	.423***	.444***	.314***	.142***	.022	.434***			
LSBMD	.053*	.179***	.347***	.315***	.285***	.276***	.175***	.000	.299***	.775***		
FNBMD	.028	.181***	.316***	.281***	.309***	.218***	.095***	-.009	.323***	.704***	.661***	
THBMD	.126***	.111***	.361***	.358***	.355***	.249***	.112***	.043	.363***	.814***	.714***	.894***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

$^{*}P < 0.05$; $^{**}P < 0.05$; $^{***}P < 0.001$.

Table S4. Pearson's correlation between study variables in postmenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.285***											
Weight	-.129***	.452***										
BMI	-.011	.038	.905***									
WBLM	-.172***	.542***	.774***	.608***								
WBFM	-.050*	.273***	.909***	.889***	.442***							
Fat%	.022	.098***	.703***	.746***	.113***	.924***						
A/G	.204***	-.049*	.300***	.359***	.193***	.311***	.315***					
ALM	-.253***	.538***	.729***	.558***	.907***	.435***	.139***	.076***				
WBBMD	-.413***	.332***	.474***	.374***	.419***	.361***	.226***	-.075***	.436***			
LSBMD	-.281***	.299***	.421***	.330***	.345***	.339***	.236***	-.201	.354***	.824***		
FNBMD	-.501***	.336***	.375***	.260***	.344***	.275***	.168***	-.091***	.387***	.785***	.668***	
THBMD	-.442***	.277***	.423***	.344***	.370***	.327***	.218***	-.021	.408***	.830***	.720***	.912***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

$^{*}P < 0.05$; $^{**}P < 0.05$; $^{***}P < 0.001$.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Sex- and age-specific characteristics of body composition and its effect on bone mineral density in southern Chinese adults: a cross-sectional study

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Primary Subject Heading:	Nutrition and metabolism
Secondary Subject Heading:	Public health
Keywords:	body composition, aging, bone mineral density, fat distribution, appendicular lean mass

Sex- and age-specific characteristics of body composition and its effect on bone mineral density in southern Chinese adults: a cross-sectional study

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Keywords: body composition; aging; bone mineral density; fat distribution; appendicular lean mass.

Word count: 5048

Abstract

Objectives: This study was an attempt to investigate the variation trend of body composition with aging and explore the association between regional body composition and bone mineral density (BMD).

Design: Cross-sectional study.

Setting and Participants A total of 5749 healthy adults aged 20-95 years were recruited from 2004-2017.

Primary outcome measures: Whole-body lean mass (LM), fat mass (FM), android FM, gynoid FM, appendicular lean mass (ALM), and the BMD in the lumbar spine, femoral neck, and total hip were obtained by dual-energy X-ray absorptiometry (DXA). The android/gynoid fat mass ratio (A/G FMR) based on DXA scan was calculated as an indicator of adipose distribution. Pearson correlation and multiple linear regression analyses were used to determine the associations between body composition, adipose distribution, and BMD of each skeletal site.

Results: Whole-body FM, percentage of whole-body fat mass, Android FM, and A/G FMR consistently increased with age in both genders, especially in females, and appendicular LM began to decrease in the fifth decade for both males and females. In multivariable linear regression models with age, body mass index, A/G FMR, and ALM as predictor variables, ALM was associated with the most BMD variance of all skeletal sites in males (standard β ranged from 0.207 to 0.405, P <0.001), although not the largest but still a positive predictor of BMD in females (standard β ranged from 0.074 to 0.186, P < 0.05). A/G FMR was an inverse predictor of BMD at all skeletal sites for females (standard β ranged from -249 to -0.052, P <0.01) but not in males.

Conclusions: In this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders. A/G FMR as an indicator of central adipose accumulation was inversely associated with BMD in females but not in males.

Strengths and limitations of this study

- This is the first study to analyze the relationships of regional body composition (muscle and fat distribution) with bone mineral density at multiple sites in different ages, menopausal status in a large population-based sample of southern Chinese adults.

- A limitation of this study is that we did not obtain the actual hormone and cytokine levels, dietary intake, and physical activity, which may influence bone nutrition and metabolism.

- And we only collected cross-sectional data and cannot directly conclude the causality limited by its study design.

Introduction

Body weight is one of the main determinants of bone mass. It is known to be positively correlated with bone mineral density (BMD) and can partly reflect bone health. Body mass index (BMI) has been widely used in epidemiological studies and clinical practice to provide a quick assessment of nutritional status and showed a positive relationship with BMD [1]. Body mass is composed of lean mass (LM), fat mass (FM) and bone mass. LM is linked to significant health consequences, studied mostly in the context of severe muscle depletion (sarcopenia) that occurs with aging and catabolic conditions [2]. Moreover, studies indicate that LM may produce a positive effect on bone mass in both genders [3]. FM has also been shown to be a key predictor of BMD and may affect bone via both loading and hormonal mechanisms [4]. Aging is associated with gradual changes in body composition, and these changes may be entirely different between men and women, as well as premenopausal and postmenopausal women [5, 6]. To further explore the changes in body composition with age is one of the purposes of our study.

Regional body composition changes occur with age, typically characterized by decreases in appendicular LM and increases in central FM. Some studies have reported that appendicular LM (ALM) and central FM may affect bone formation independent of the amount of total body composition, but the results were inconsistent [7-9]. Blain et al. [7] showed that ALM was the most influential factor contributing to BMD of the femoral neck in men, and low ALM (sarcopenia) was considered an independent risk for low BMD (osteoporosis). In contrast, Walsh et al. [10] showed that ALM was not significantly related to BMD after adjusting body weight and physical activity in women.

Android fat represents the visceral (central) adipose tissue while gynoid fat reflects the subcutaneous (appendicular) adipose tissue [11]. As the measurements of central FM used different

methods or indexes, the findings regarding the relationship of central adipose with BMD are more controversial. Several studies indicate that central adipose accumulation is negatively related to BMD [12, 13]. On the contrary, some studies show visceral fat is positively associated with BMD in postmenopausal women [14]. These heterogeneous findings may result from the rather complex mechanisms underlying the relationship between fat and bone, including mechanical loading as well as the hormones and cytokines from adipose tissue, which can indirectly influence bone metabolism to a certain extent. Moreover, gender, age, menopausal status, and skeletal site differences in the relationship between BMD with ALM and central FM have not been well studied.

To our knowledge, only a few other studies have documented the relationships of ALM and android/gynoid fat mass ratio (A/G FMR) with BMD at multiple sites in different ages, menopausal status, and in both genders. In the current study, we aim to investigate the relationship between BMD and body composition, especially the effect of regional body composition on BMD. We also want to examine whether these relationships differ by gender, age, and menopausal status in a large population-based sample of Chinese adults.

Methods

Subjects

The present study included healthy Chinese men and women aged 20 to 95 years old. The participants were recruited from the body composition and osteoporosis study at the First Affiliated Hospital of Jinan University (Guangzhou, China) from 2004-2017. Inclusion criteria for the study were Chinese individuals who appeared to be in good health and functionally independent. Subjects were excluded if they met any of the following criteria: (a) a history of fracture; (b) medication known to affect the musculoskeletal system (anti-osteoporotic drugs, androgens or anti-androgen drugs, corticosteroids, etc.); (c) chronic disease known to affect bone metabolism (hyperthyroidism, hyperparathyroidism, rheumatoid arthritis, chronic renal insufficiency, etc.); (d) metal implants (pacemakers, joint replacement device, etc.); (e) inability to determine the menstruation state or non-natural menopause (natural menopause was designated if there was a complete natural cessation of menses for more than twelve months). And the current smoking and drinking situation has also been recorded. In the end, 1703 men and 4046 women were included in our study. All subjects provided written informed consent to participate in the study, which was approved by the Ethics

Committee of the First Affiliated Hospital of Jinan University.

Anthropometry, BMD and body composition measurement

A research physician obtained information on medical history, medication use, smoking, and alcohol history in a personal interview. Height and body weight were obtained based on standard methods; height was measured without shoes to the nearest 0.1 cm, weight with only light clothing to the nearest 0.1 kg. BMI was calculated as body weight divided by height squared (kg/m^2). Subjects underwent dual-energy X-ray absorptiometry (DXA; software version enCORE10.50.086; GE-lunar Prodigy, WI, USA) scans to measure the whole body, lumbar spine, femoral neck, and total hip BMD. Total and regional LM and FM were obtained through whole body scans. Android and Gynoid regions were automatically attained using the software provided by the manufacturer. Android region is defined as the portion of the abdomen included between the line joining the two superior iliac crests, extending cranially up to 20% of the distance between this line and the chin. Gynoid region is defined as the portion of the legs leaving from the femoral greater trochanter, directed caudally up to twice the height of the android region. The appendicular region is defined as the areas including both the left and right arms and legs. Daily quality assurance scans were performed by scanning the spine phantom according to the manufacturer's instructions; the same trained technologist conducted all DXA measurements throughout the study. The coefficient of variation was less than 2% for total LM, FM, total, lumbar spine, femoral neck, and total hip BMD, and less than 3% for regional (trunk, appendicular, android, and gynoid) LM and FM, was determined by duplicate scans with repositioning between each measurement in 30 volunteer subjects.

Statistical analyses

Subjects were categorized into four groups according to gender, age, and menopausal status (786 men＜50years, 917 men ≥50years, 1534 premenopausal women, and 2512 postmenopausal women). The values of continuous variables were presented as the mean ± standard deviation (SD). Unpaired-sample *t*-tests were used to evaluate the mean differences between different groups, and Pearson's correlation coefficients (*r*) were conducted to determine the linear relationships among various parameters. We performed linear regressions to assess the association strength between ALM, A/G FMR, and BMD. In the regression models, BMD (different skeletal sites) measurements were used as dependent variables, and ALM and A/G FMR were treated as independent variables; age, BMI,

and lifestyle factors (smoking and alcohol history) were also included. When we performed linear regression analyses, we chose the enter methods and expressed the results as standard β coefficients. All tests were two-sided, and P <0.05 was considered statistically significant. All statistical analyses were performed using the statistical package for social sciences (Version 19.0) (SPSS Inc., Chicago, IL, USA).

Patient and Public Involvement

There was no patient or public involvement in this study.

Results

Basal characteristics of subjects

Table 1 details the subject characteristics in each group. Males ≥50years had higher BMI, whole-body FM, percentage of whole-body fat mass (fat%), trunk FM, and appendicular FM, but lower weight and lumbar spine BMD than males < 50years (P <0.001). Postmenopausal females had higher values for whole-body FM, whole-body LM, trunk FM, appendicular FM, and A/G FMR, and lower BMD at each site than premenopausal females (P <0.05).

Changes of BMD and body composition with age

To further explore the distribution characteristics of body composition and BMD regarding age, we divided the subjects into multiple subgroups and set ten years as one subgroup. As shown in Table 2 and Figure 1, whole-body FM, fat%, android FM, and A/G FMR showed a consistent increase in both genders. Overall, the highest values of whole-body, lumbar spine, femoral neck, and total hip BMD were observed in the second decade and then decreased slightly with age in males. BMD at each skeletal site increased steadily and reached a peak until perimenopause in the fourth decade in females, and then decreased dramatically after menopause. Interestingly, appendicular LM started to decline after 50 years old in both males and females.

Associations of BMD with whole and regional body composition in different groups

In Pearson's correlation analyses, significant positive correlations were found between BMD at all sites with height, weight, BMI, whole-body LM, whole-body FM, fat%, Android FM, Gynoid FM, and ALM in all groups (r=0.218-0.616, P <0.05). A/G FMR showed positive correlations with whole-body, lumbar spine, femoral neck, and total hip BMDs in men <50years and ≥50years old (r=0.089~0.318, P<0.001). However, A/G FMR was negatively correlated with whole-body and

femoral neck BMDs in postmenopausal females, though the correlation strengths were weak (r=-0.075, P<0.001 and r=-0.091, P<0.001, respectively). A/G FMR was insignificantly correlated with BMD in premenopausal females (Shown in supplemental table 1-4).

To further explore the independent predictive value of A/G FMR and ALM for BMD at all sites in every group, covariates such as ages, BMI, smoking, and alcohol consumption that associated with BMD were also included in the multiple linear regression analyses (shown in Table 3 and 4). Overall, the significant variables accounted for 10.7~37.4% of the variability in BMD. Considering the dynamic change of BMD between period of bone modeling (20-29 years) and that of bone remodeling (30-50 years), and the subjects aged 20-29 years were excluded in the regression analyses. The effect sizes of A/G FMR and ALM on BMD were different according to the skeletal site and age group. A/G FMR had inverse associations with whole-body, lumbar spine, femoral neck, and total hip BMDs in both premenopausal and postmenopausal women (standard β=-0.249~-0.052), while men had no significant relationship between A/G FMR and each part of BMD after adjustment. ALM was positively associated with whole-body, lumbar spine, femoral neck, and total hip BMDs in both males and females, and the correlations were higher in males (standard β=0.207~0.405) than that in females (standard β=0.074~0.186), in both younger adults and older adults after adjustment.

Discussion

The global epidemic of obesity has become a significant concern in our daily life as it not only has a close relationship with cardiovascular and cerebrovascular diseases but also influences bone health [15]. As a part of body composition, bone density was mainly determined by body weight and BMI. Low BMI had been regarded as a risk factor for osteoporotic hip fracture in both males and females [16]. In this study, we investigated a wide range of healthy Chinese adults aged 20 to 90 years old to further explore the factors that may influence bone health. We divided the participants into different age groups to investigate the changes in body composition and BMD with age in males and females. We also performed multivariable regression analyses to confirm that whether A/G FMR and ALM were independent predictors for BMD after adjusting for age, BMI, smoking, and alcohol consumption. The current report provided more detailed and impressive results which were different from previous studies performed in America [13] and Australia [1]. We found that ALM positively correlated with BMD in both genders, and low ALM was related to low BMD. A/G FMR

as an indicator of central adipose accumulation was inversely associated with BMD in females but not in males. These results, based on a large population of Chinese adults, were convincing.

In this study, we found that whole-body LM reached a peak level in the 40-49 years group, and then decreased gradually in both genders, whereas whole-body FM steadily increased from youth to older age in both genders. After analyzing the baseline characteristics, we found that the decreased whole-body LM in older men was primarily due to a decrease in ALM. Moreover, the increased whole-body FM in older men and women mainly arose from the increase of Trunk FM. In the meantime, we found that the A/G FMR increased with age in both males and females. Men had an earlier whole-body, lumbar spine, femoral neck, and total hip BMD peaks than women. BMD at all sites decreased slightly in older men, but more obviously in postmenopausal women. These results provided us a healthy bone mass for each age group in both men and women. The BMD at each region lower than the guidance ranges in the respective age group should alarm the physician for appropriate intervention.

In our study, the results showed that both total LM and total FM are positively associated with BMD in both genders. The effect size of total LM and total FM to BMD was different according to gender, menopausal status, and age. Total LM is a stronger protective factor to BMD at all sites in men and premenopausal women. Total FM is a stronger contributor to BMD at all sites in postmenopausal women. Several potential theories may explain the observed findings. The influences of LM on BMD may attribute to the direct mechanical effects of muscle, which produces a positive osteogenic response to bone formation. For one hand, whole-body LM, which accounted for a large proportion of body weight in both males and females, would perform a gravitational loading on the bone. On the other hand, the contraction strength of lean muscle should also be considered a specific mechanism of action. A previous study reported that the augmentation and thickening of bone trabecula was an adaption to increased mechanical stress. However, whole-body FM only accounted for a small proportion of body weight in both males and females, but it still performed a significant and positive correlation with BMD, especially in postmenopausal women, in whom a higher standard β value with BMD in all the skeletal sites was shown compared with whole-body LM. Several mechanisms could explain the association between fat tissue and BMD. The outcomes of fat acting on the bone may be influenced not only by weight-bearing effects but also by non-weight bearing effects, including the hormonal metabolism of adipocytes. We speculate that this fat-related

mechanism may help to interpret this finding, as the postmenopausal women also had the highest whole-body FM, more than males and premenopausal women in our study. Several hormones, including insulin, leptin, adiponectin, and adipocytic estrogens, were found to be secreted from adipose tissue, which can influence bone metabolism through the endocrine pathway. Also, the enzyme aromatase in adipose tissue can convert androgen to estrogen and result in an elevated estrogen level. These bone protective hormones led to a positive influence on bone formation via stimulating the differentiation of osteoblasts and preventing osteoclast-mediated bone resorption. This finding further confirmed the results from previous studies that FM should have a positive relationship with bone mass [8, 17].

Though both whole-body LM and FM were found to be positively associated with BMD in both genders, how regional body compositions and differences in fat distribution influence bone metabolism aroused our curiosity. To investigate the effect of ALM and A/G FMR on BMD with various ages, the factors including gender, age, BMI, smoking, and alcohol consumption, which may have close relationships with BMD, were considered in multiple linear regression analyses. In the current study, we found that ALM was positively related to BMD at all sites after adjustment for BMI and age in both genders. ALM is considered one of the most important indexes of the diagnostic criterion for sarcopenia [18, 19]. A study of 679 men aged 40-79 years suggested low ALM was associated with low BMD (whole body, femoral neck, total hip, and lumbar spine) and osteoporosis independent of age, height, physical activity, and other lifestyles [20]. Blain et al. [7] also found that ALM was most strongly associated with femoral neck BMD independent of nutritional, hormonal factors, and other lifestyles in men. There are several mechanisms that may explain the observed association between ALM and BMD. The amount of ALM was smaller than trunk LM in this study, suggesting ALM may effect on bone via contraction strength instead of gravitational loading, especially in males younger than 50 years old, in whom the strongest relationships with BMD in all sites were demonstrated, compared with other groups. Systemic factors that simultaneously involve both ALM and bone metabolism may exist as the decline of ALM was almost parallel with BMD in both genders. For example, the hormone estrogen can strengthen the synthesis of muscle protein and promote calcium deposition in bone tissue, which leads to an increased LM and BMD concurrently [21]. However, a prospective study is needed to explore the potential mechanism further.

Depot-specific fat has been known to play a different role in terms of obesity and metabolism. A previous study indicated that different fat depots might have distinct relationships with bone mass [22]; Marques reported appendicular FM (AFM) had a positive association with femoral neck BMD in older women [23]. Inconsistent with that, several studies stated AFM had no [24] or a negative [25] relationship with BMD. Freitas et al. [26] showed that central fat was positively associated with BMD and regarded as an independent and protective factor on the presence of osteoporosis or osteopenia. Sharma et al. [27] reported that a bigger trunk (central) FM was associated with increased BMD in total hip and femoral neck, regardless of HIV status in women. Fat distribution difference seems to produce a meaningful but contradicted effect on bone mass based on previous studies. To further confirm this finding, we performed Pearson's correlation to assess the relationship between Android FM, Gynoid FM, and each part of BMD with a large sample size. The results suggested that both Android FM and Gynoid FM positively correlated with BMD in all males and females, which was partly consistent with previous studies [22, 24]. In contrast, some studies reported abdominal fat and android fat measured by CT or DXA had a negative association with BMD after adjusting for total LM or BMI, suggesting central fat deposition was not beneficial for bone [13]. Surprisingly, we found that A/G FMR showed a diverse correlation with BMD in males and females. The results revealed that A/G FMR was positively correlated with each part of BMD in males <50 years and older group. But in postmenopausal females, A/G FMR had an inverse association with whole-body ($r=-0.075$, $P<0.001$) and femoral neck BMD ($r=-0.091$, $P<0.001$), and had no relationship with each part of BMD in premenopausal females. Kim et al. [22] also reported that A/G FMR was inversely associated with the trabecular bone score after age adjustment ($r=-0.288$, $P<0.05$), which was similar with our findings. Android fat mainly represents visceral fat in the epigastric region, while gynoid fat reflects peripheral (or subcutaneous) fat in the leg. A higher A/G FMR indicating a higher visceral fat or a lower peripheral fat revealed that subjects with a higher A/G FMR had a lower BMD in postmenopausal females, whose ovarian hormones tend to be depleted and lead to a higher subcutaneous lipoprotein lipase activity ratio and predominant fat storage in visceral fat depots [28]. Kim et al. [29] found that visceral fat has a negative association among postmenopausal Korean women with lumbar spine BMD after adjustment for weight. Zhu et al. reported trunk-to-limb fat mass ratio (a surrogate of visceral fat) had a negative association with total body bone mass in young adults [17]. Gilsanz et al. [30] suggested that subcutaneous and

visceral fat had opposite effects on femoral bone structure and strength in healthy young females, and proposed that subcutaneous fat may be beneficial to the bone, whereas visceral fat may have a negative association with bone. These heterogeneous findings may be related to the use of diverse methods for measuring body composition and BMD, disparities in study design, or the different criteria for group division. Moreover, the inconsistency of findings may be due to the rather complex mechanisms underlying the relationship between fat and bone. As a result, we subdivided the Chinese people into different age and gender groups and found that android fat increased with age, especially in females, whose android fat accounted for a more substantial proportion of body weight and had a stronger relationship with BMD in our study. To avoid multicollinearity, we included A/G FMR instead of the total and regional body composition into the same multiple regression analysis when we explored the associations of regional fat depots with BMD, which provided a more reliable result.

Limitations

This study had several limitations. First, we did not obtain a blood sample from participants; thus, the actual hormone and cytokine levels were unknown. The potential mechanisms acting on bone mass mainly referenced in previous reports based on our data and the statistical results. Second, we only collected cross-sectional data and cannot directly conclude the causality limited by its study design. Third, though we evaluated the relationships of body composition and fat distribution with BMD by adjusting age, BMI, smoking, and alcohol consumption, other confounders such as socioeconomic status, dietary intake, and physical activity, which may influence bone nutrition and metabolism, were not considered as covariates in the multivariable regression analyses. Fourth, a more substantial amount of visceral fat mass was found in Asians compared with the European people for a given amount of body fat [31]. Therefore, ethnic differences should be considered when interpreting the findings.

Conclusions

In summary, in this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders and suggesting that low ALM is related to low BMD and may be considered an independent risk for osteoporosis. A/G FMR an indicator of central adipose accumulation was

inversely associated with BMD in females but not in males.

Contributors

Xiao,Tan, Shang, Cheng and Tang participated in collection, analysis, interpretation of data; and Xiao, Guo and Gong wrote the paper. Xu, Principal Investigator, innovator for the project, participated in the conception, design, and revision of the manuscript.

Conflict of interest

The authors have no conflicts of interest.

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Ethics approval

The study was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University.

Data sharing statement

The deidentified participant data will be available upon reasonable request from Prof. Xu (txh@jnu.edu.cn).

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Abbreviations

BMD: bone mineral density; LM; lean mass; FM: fat mass; ALM: appendicular lean mass; DXA: dual-energy X-ray absorptiometry; A/G FMR: android/gynoid fat mass ratio; BMI: body mass index.

Figure legend

Fig.1 The age-related change in whole-body lean mass (WBLM), appendicular lean mass (ALM), percentage of whole-body fat mass (fat%), A/G FMR, and bone mineral density in males and females. A/G FMR, Android/Gynoid fat mass ratio; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

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Table 1 Baseline characteristics of subjects

	Male		Female	
	Age＜50years	Age≥50years	Premenopausal	Postmenopausal
No. of subjects	786	917	1534	2512
Age (years)	36.8±8.7	65.8±10.0[c]	37.4±8.7	63.9±9.1[c]
Weight (kg)	63.9±12.4	63.8±10.8 [c]	52.7±9.1	55.0±8.9
Height (cm)	168.8±5.8	166.7±6.1	158.0±4.9	155.9±5.3[c]
BMI (kg/m^2)	22.4±3.9	22.9±3.3 [c]	21.1±3.3	22.6±3.3
Body composition measures (Kg)				
Whole body FM	13.7±7.6	15.2±6.5 [c]	16.7±6.0	18.9±6.2[b]
Whole body LM	47.6±6.0	46.1±5.9	33.8±4.3	34.2±4.0[a]
Fat%	20.2±8.3	23.0±7.3[c]	30.1±6.7	33.6±6.8
Trunk FM	8.2±5.0	9.3±4.4[c]	8.7±3.6	10.6±3.7[b]
Trunk LM	22.4±3.0	22.4±2.9	16.4±2.2	17.1±2.1
Appendicular FM	5.0±2.6	5.3±2.1 [c]	7.3±2.5	7.5±2.6[c]
Appendicular LM	21.4±3.2	19.9±3.1	14.4±2.2	14.0±2.1
A/G FMR	0.57±0.17	0.69±0.19	0.42±0.10	0.56±0.15[c]
Bone mineral density (g/cm^2)				
Whole body	1.105±0.109	1.109±0.105	1.085±0.094	0.994±0.106[c]
Lumbar spine	1.114±0.162	1.099±0.200[c]	1.124±0.155	0.950±0.186[c]
Femoral neck	0.921±0.140	0.839±0.140	0.907±0.122	0.760±0.132[b]
Total hip	0.941±0.150	0.911±0.147	0.942±0.132	0.817±0.144[b]
Current Smoker (%)	17.9%	13.0%	2.4%	2.8%
Current alcohol user (%)	15.4%	12.8%	2.3%	1.5%

Note. Values are presented as number, mean ± standard deviation or percentage.

BMI, body mass index; FM, fat mass; LM, lean mass; Fat%, percentage of whole body fat mass; A/G FMR, android/gynoid fat mass ratio. *P* value was determined by the unpaired-sample *t*-tests. [a]$P < 0.05$; [b] $P< 0.01$; [c]$P < 0.001$. Compared with the same gender of the different age group (unpaired-sample t-tests or chi-squared test).

Table 2 Distributions of age-related change in body composition and bone mineral density

Age (years)	n	WBLM (Kg)	WBFM (Kg)	Fat %	Android FM(Kg)	Gynoid FM(Kg)	A/G FMR	ALM (Kg)	WBBMD (g/cm^2)	LSBMD (g/cm^2)	FNBMD (g/cm^2)	THBMD (g/cm^2)
Male												
20-29	199	47.3±6.0^c	12.1±8.2^c	18.1±9.0^c	1.2±0.9^c	2.4±1.3^c	0.47±0.14^c	21.6±3.3^c	1.102±0.103	1.176±0.151	0.958±0.140	0.954±0.153
30-39	254	47.0±5.9^c	12.8±7.3^c	19.4±8.2^c	1.4±0.9^c	2.4±1.3^a	0.55±0.16^c	21.0±3.3^c	1.090±0.113^c	1.160±0.149	0.909±0.140^b	0.922±0.154^c
40-49	333	48.3±6.0^c	15.4±7.2^c	22.1±7.6^c	1.7±0.9^c	2.6±1.0	0.63±0.17^c	21.5±3.2^c	1.119±0.108^b	1.171±0.178	0.908±0.137	0.947±0.147
50-59	313	48.1±6.1^c	15.2±6.5	22.2±7.2^a	1.7±0.8^c	2.5±0.9	0.67±0.18^c	21.0±3.2^c	1.122±0.110	1.096±0.192	0.895±0.140	0.946±0.154^a
60-69	281	46.9±5.4^c	15.5±6.5	23.0±7.3^a	1.8±0.8^c	2.5±0.9	0.71±0.19^c	20.4±2.8^c	1.122±0.098	1.116±0.190	0.843±0.120	0.924±0.125
70+	323	43.6±5.2^c	15.0±6.5	23.8±7.5	1.7±0.9^b	2.4±0.9	0.70±0.19^c	18.4±2.7^c	1.086±0.101	1.086±0.215^c	0.783±0.135^c	0.863±0.147^a
Female												
20-29	369	32.5±4.2	15.5±6.1	30.1±7.1	1.3±0.6	3.2±1.0	0.38±0.09	14.0±2.1	1.048±0.090	1.173±0.135	0.891±0.126	0.912±0.138
30-39	456	33.5±4.0	16.0±6.0	30.2±6.7	1.4±0.6	3.2±1.0	0.42±0.11	14.3±2.0	1.084±0.090	1.171±0.152	0.917±0.119	0.942±0.123
40-49	709	34.7±4.4	17.8±5.8	31.9±6.4	1.5±0.6	3.5±0.9	0.45±0.10	14.7±2.2	1.105±0.093	1.171±0.165	0.908±0.122	0.958±0.131
50-59	1004	34.6±4.0	19.0±6.3	33.4±6.6	1.8±0.7	3.4±1.0	0.52±0.13	14.4±2.1	1.039±0.103	1.028±0.186	0.828±0.126	0.880±0.137
60-69	805	34.5±3.9	19.1±6.1	33.7±7.1	1.9±0.7	3.3±0.9	0.57±0.15	14.2±2.0	0.986±0.095	0.991±0.171	0.749±0.113	0.814±0.128
70+	703	33.2±3.9	18.4±6.1	33.8±7.1	1.9±0.7	3.1±0.9	0.59±0.16	13.3±1.9	0.939±0.094	0.889±0.177	0.672±0.105	0.732±0.125

Note. Values are presented as number or mean ± standard deviation. WBLM, whole body lean mass; WBFM, whole body fat mass; Fat % = whole body fat mass/body weight×100; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density. $^aP < 0.05$; $^bP < 0.01$; $^cP < 0.001$. Compared with female of the same age group (unpaired-sample t-tests).

Table 3 Multiple regression analyses of bone mineral density at different skeletal sites with age, smoke, alcohol, BMI, A/G FMR, and appendicular LM in males.

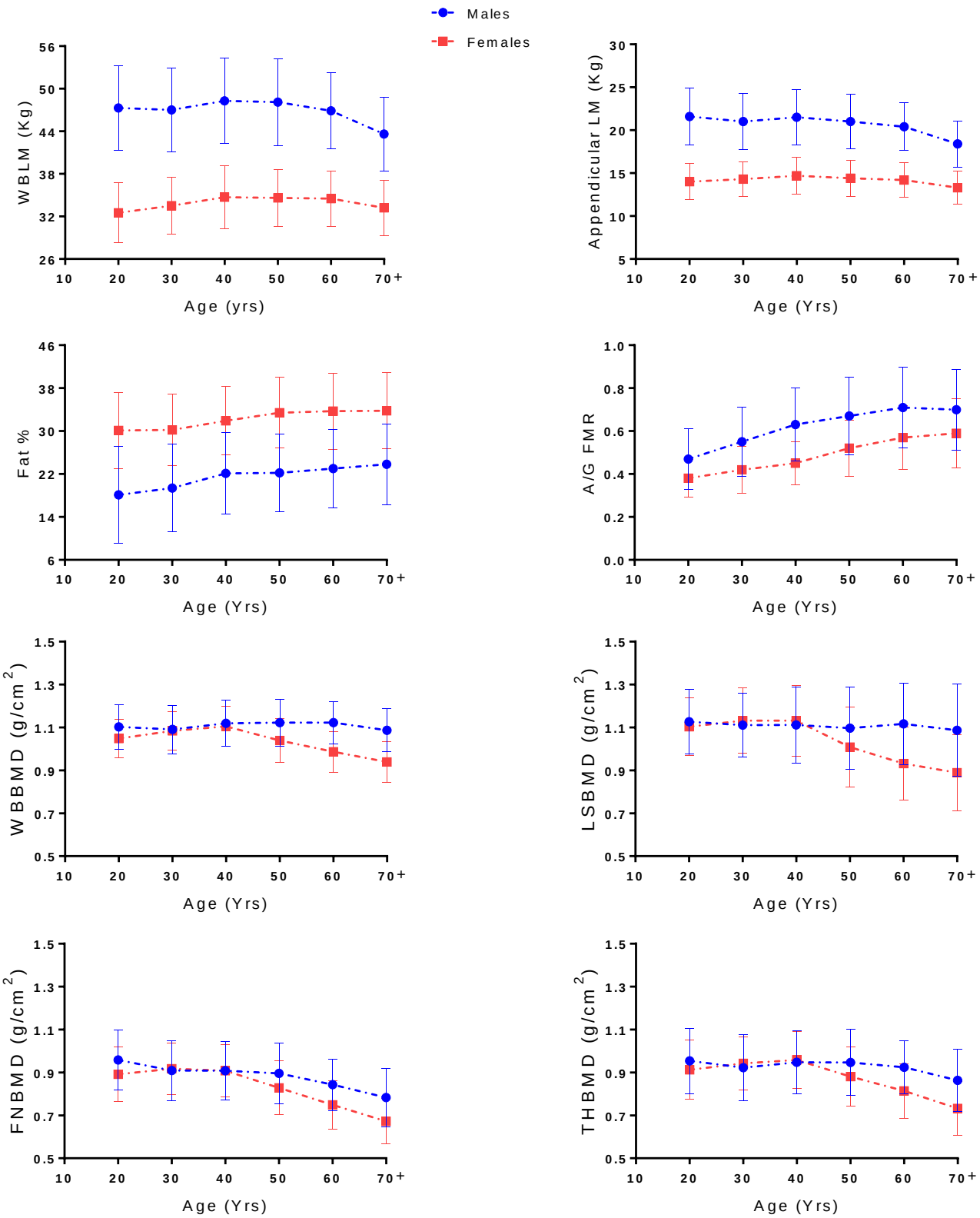
Males	WBBMD			LSBMD			FNBMD			THBMD		
	Standard β	t	Sig.	Standard β	t	Sig.	Standard β	t	Sig.	Standard β	t	Sig.
<50 y												
Age	**0.066**	1.991	0.047	-0.018	-0.459	0.647	-0.044	-1.161	0.246	0.029	0.821	0.412
Smoke	-0.057	-1.783	0.075	-0.043	-1.116	0.265	-0.047	-1.267	0.206	-0.050	-1.473	0.141
Alcohol	**0.063**	1.988	0.047	0.041	1.081	0.280	0.011	0.303	0.762	0.009	0.279	0.780
BMI	**0.266**	4.998	0.000	**0.170**	2.668	0.008	**0.139**	2.269	0.024	**0.222**	3.920	0.000
A/G FMR	0.044	1.028	0.304	-0.063	-1.223	0.222	-0.040	-0.811	0.418	0.014	0.315	0.753
Appendicular LM	**0.402**	9.240	0.000	**0.309**	5.923	0.000	**0.395**	7.872	0.000	**0.405**	8.757	0.000
≥50 y												
Age	-0.015	-0.486	0.627	**0.087**	2.673	0.008	**-0.220**	-7.086	0.000	**-0.124**	-3.989	0.000
Smoke	-0.023	-0.786	0.432	-0.027	-0.865	0.387	0.005	0.165	0.868	-0.006	-0.215	0.830
Alcohol	0.023	0.794	0.427	0.059	1.920	0.055	0.022	0.747	0.455	0.020	0.697	0.486
BMI	**0.260**	5.915	0.000	**0.268**	5.704	.000	**0.190**	4.257	0.000	**0.261**	5.817	0.000
A/G FMR	0.008	0.241	0.809	0.027	0.759	0.448	-0.054	-1.585	0.113	-0.035	-1.032	0.302
Appendicular LM	**0.321**	7.814	0.000	**0.207**	4.719	0.000	**0.264**	6.328	0.000	**0.256**	6.127	0.000

Note. Results expressed as standard β coefficients. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

Table 4 Multiple regression analyses of bone mineral density at different skeletal sites with age, smoke, alcohol, BMI, A/G FMR, and appendicular LM in females.

Females	WBBMD			LSBMD			FNBMD			THBMD		
	Standard β	t	Sig.	Standard β	t	Sig.	Standard β	t	Sig.	Standard β	t	Sig.
Premenopausal												
Age	0.039	1.483	0.138	**-0.074**	-2.665	0.008	**-0.098**	-3.483	0.001	-0.008	-0.278	0.781
Smoke	0.024	0.958	0.338	0.022	0.794	0.427	0.033	1.196	0.232	0.030	1.133	0.258
Alcohol	-0.005	-0.197	0.844	0.008	0.289	0.773	0.013	0.467	0.641	0.012	0.451	0.652
BMI	**0.413**	11.055	0.000	**0.384**	9.659	0.000	**0.277**	6.901	0.000	**0.360**	9.177	0.000
A/G FMR	**-0.249**	-8.421	0.000	**-0.193**	-6.152	0.000	**-0.155**	-4.872	0.000	**-0.157**	-5.083	0.000
Appendicular LM	**0.179**	5.360	0.000	**0.074**	2.099	0.036	**0.159**	4.451	0.000	**0.138**	3.940	0.000
Postmenopausal												
Age	**-0.337**	-19.556	0.000	**-0.222**	-11.701	0.000	**-0.438**	-25.343	0.000	**-0.389**	-22.318	0.000
Somke	-0.024	-1.482	0.139	0.007	.383	0.702	-0.019	-1.146	0.252	-0.024	-1.461	0.144
Alcohol	-0.015	-0.898	0.369	-0.029	-1.649	0.099	-0.008	-0.504	0.614	-0.020	-1.213	0.225
BMI	**0.315**	14.922	0.000	**0.274**	11.767	0.000	**0.185**	8.718	0.000	**0.266**	12.451	0.000
A/G FMR	**-0.135**	-7.585	0.000	**-0.086**	-4.402	0.000	**-0.083**	-4.644	0.000	**-0.052**	-2.867	0.004
Appendicular LM	**0.186**	9.076	0.000	**0.152**	6.744	0.000	**0.180**	8.787	0.000	**0.166**	7.998	0.000

Note. Results expressed as standard β coefficients. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.


Males
Females
WBLM (Kg)
Age (yrs)
Appendicular LM (Kg)
Age (Yrs)
Fat %
Age (Yrs)
A/G FMR
Age (Yrs)
WBBMD (g/cm2)
Age (Yrs)
LSBMD (g/cm2)
Age (Yrs)
FNBMD (g/cm2)
Age (Yrs)
THBMD (g/cm2)
Age (Yrs)

SUPPLEMENTARY INFORMATION

Sex- and age-specific characteristics of body composition and its effect on bone mineral density in Chinese adults: a southern China aging study

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Keywords: body composition; aging; bone mineral density; fat distribution; appendicular lean mass.

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Table S1. Pearson's correlation between study variables in males <50years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.092*											
Weight	.161***	.460***										
BMI	.216***	.126***	.917***									
WBLM	.083*	.571***	.851***	.706***								
WBFM	.189***	.265***	.905***	.893***	.549***							
Fat%	.207***	.155***	.788***	.810***	.364***	.962***						
A/G FMR	.407***	.062	.594***	.641***	.363***	.656***	.667***					
ALM	.005	.555***	.822***	.681***	.950***	.541***	.372***	.308***				
WBBMD	.101**	.306***	.610***	.547***	.567***	.489***	.407***	.318***	.569***			
LSBMD	-.019	.245***	.358***	.294***	.355***	.258***	.203***	.096***	.375***	.741***		
FNBMD	-.127***	.274***	.394***	.314***	.423***	.266***	.182***	.089***	.438***	.715***	.662***	
THBMD	.017	.232***	.495***	.443***	.500***	.363***	.280***	.226***	.513***	.842***	.696***	.872***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

$^{*}P < 0.05$; $^{**}P < 0.05$; $^{***}P < 0.001$.

Table S2. Pearson's correlation between study variables in males ≥50years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.165***											
Weight	-.212***	.511***										
BMI	-.160***	.087***	.898***									
WBLM	-.355***	.581***	.835***	.671***								
WBFM	-.016	.287***	.860***	.850***	.438***							
Fat%	.089**	.125***	.668***	.717***	.162***	.941***						
A/G	.042	.028	.446***	.505***	.198***	.548***	.575***					
ALM	-.385	.546***	.807***	.658***	.945***	.442***	.191***	.164***				
WBBMD	-.180***	.307***	.545***	.479***	.501***	.395***	.280***	.193***	.499***			
LSBMD	-.035	.230***	.451***	.407***	.352***	.381***	.307***	.203***	.356***	.772***		
FNBMD	-.354***	.291***	.447***	.373***	.459***	.281***	.172***	.077***	.466***	.760***	.631***	
THBMD	-.267***	.235***	.473***	.433***	.456***	.323***	.221***	.134***	.471***	.848***	.702***	.913***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

$^{*}P < 0.05$; $^{**}P < 0.05$; $^{***}P < 0.001$.

Table S3. Pearson's correlation between study variables in premenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.031											
Weight	.222***	.424***										
BMI	.260***	.072***	.932***									
WBLM	.217*	.510***	.795***	.671**								
WBFM	.166***	.246***	.896***	.890***	.445***							
Fat%	.116***	.078***	.656***	.697***	.084***	.909***						
A/G	.261***	.002	.449***	.494***	.251***	.489***	.465***					
ALM	.153***	.519***	.769***	.640***	.947***	.444***	.111***	.181***				
WBBMD	.230**	.200***	.453***	.423***	.444***	.314***	.142***	.022	.434***			
LSBMD	.053*	.179***	.347***	.315***	.285***	.276***	.175***	.000	.299***	.775***		
FNBMD	.028	.181***	.316***	.281***	.309***	.218***	.095***	-.009	.323***	.704***	.661***	
THBMD	.126***	.111***	.361***	.358***	.355***	.249***	.112***	.043	.363***	.814***	.714***	.894***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

*$P < 0.05$; **$P < 0.05$; ***$P < 0.001$.

Table S4. Pearson's correlation between study variables in postmenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.285***											
Weight	-.129***	.452***										
BMI	-.011	.038	.905***									
WBLM	-.172***	.542***	.774***	.608***								
WBFM	-.050*	.273***	.909***	.889***	.442***							
Fat%	.022	.098***	.703***	.746***	.113***	.924***						
A/G	.204***	-.049*	.300***	.359***	.193***	.311***	.315***					
ALM	-.253***	.538***	.729***	.558***	.907***	.435***	.139***	.076***				
WBBMD	-.413***	.332***	.474***	.374***	.419***	.361***	.226***	-.075***	.436***			
LSBMD	-.281***	.299***	.421***	.330***	.345***	.339***	.236***	-.201	.354***	.824***		
FNBMD	-.501***	.336***	.375***	.260***	.344***	.275***	.168***	-.091***	.387***	.785***	.668***	
THBMD	-.442***	.277***	.423***	.344***	.370***	.327***	.218***	-.021	.408***	.830***	.720***	.912***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

$^{*}P < 0.05$; $^{**}P < 0.05$; $^{***}P < 0.001$.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Sex- and age-specific characteristics of body composition and its effect on bone mineral density in southern Chinese adults: a cross-sectional study

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Primary Subject Heading:	Nutrition and metabolism
Secondary Subject Heading:	Public health
Keywords:	body composition, aging, bone mineral density, fat distribution, appendicular lean mass

Sex- and age-specific characteristics of body composition and its effect on bone mineral density in southern Chinese adults: a cross-sectional study

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Keywords: body composition; aging; bone mineral density; fat distribution; appendicular lean mass.

Word count: 5048

Abstract

Objectives: This study was an attempt to investigate the variation trend of body composition with aging and explore the association between regional body composition and bone mineral density (BMD).

Design: Cross-sectional study.

Setting and Participants A total of 5749 healthy adults aged 20-95 years were recruited from 2004-2017.

Primary outcome measures: Whole-body lean mass (LM), fat mass (FM), android FM, gynoid FM, appendicular lean mass (ALM), and the BMD in the lumbar spine, femoral neck, and total hip were obtained by dual-energy X-ray absorptiometry (DXA). The android/gynoid fat mass ratio (A/G FMR) based on DXA scan was calculated as an indicator of adipose distribution. Pearson correlation and multiple linear regression analyses were used to determine the associations between body composition, adipose distribution, and BMD of each skeletal site.

Results: Whole-body FM, percentage of whole-body fat mass, Android FM, and A/G FMR consistently increased with age in both genders, especially in females, and appendicular LM began to decrease in the fifth decade for both males and females. In multivariable linear regression models with age, body mass index, A/G FMR, and ALM as predictor variables, ALM was associated with the most BMD variance of all skeletal sites in males (standard β ranged from 0.207 to 0.405, P <0.001), although not the largest but still a positive predictor of BMD in females (standard β ranged from 0.074 to 0.186, P < 0.05). A/G FMR was an inverse predictor of BMD at all skeletal sites for females (standard β ranged from -249 to -0.052, P <0.01) but not in males.

Conclusions: In this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders. A/G FMR as an indicator of central adipose accumulation was inversely associated with BMD in females but not in males.

Strengths and limitations of this study

- This is the first study to analyze the relationships of regional body composition (muscle and fat distribution) with bone mineral density at multiple sites in different ages, menopausal status in a large population-based sample of southern Chinese adults.

- A limitation of this study is that we did not obtain the actual hormone and cytokine levels, dietary intake, and physical activity, which may influence bone nutrition and metabolism.

- And we only collected cross-sectional data and cannot directly conclude the causality limited by its study design.

Introduction

Body weight is one of the main determinants of bone mass. It is known to be positively correlated with bone mineral density (BMD) and can partly reflect bone health. Body mass index (BMI) has been widely used in epidemiological studies and clinical practice to provide a quick assessment of nutritional status and showed a positive relationship with BMD [1]. Body mass is composed of lean mass (LM), fat mass (FM) and bone mass. LM is linked to significant health consequences, studied mostly in the context of severe muscle depletion (sarcopenia) that occurs with aging and catabolic conditions [2]. Moreover, studies indicate that LM may produce a positive effect on bone mass in both genders [3]. FM has also been shown to be a key predictor of BMD and may affect bone via both loading and hormonal mechanisms [4]. Aging is associated with gradual changes in body composition, and these changes may be entirely different between men and women, as well as premenopausal and postmenopausal women [5, 6]. To further explore the changes in body composition with age is one of the purposes of our study.

Regional body composition changes occur with age, typically characterized by decreases in appendicular LM and increases in central FM. Some studies have reported that appendicular LM (ALM) and central FM may affect bone formation independent of the amount of total body composition, but the results were inconsistent [7-9]. Blain et al. [7] showed that ALM was the most influential factor contributing to BMD of the femoral neck in men, and low ALM (sarcopenia) was considered an independent risk for low BMD (osteoporosis). In contrast, Walsh et al. [10] showed that ALM was not significantly related to BMD after adjusting body weight and physical activity in women.

Android fat represents the visceral (central) adipose tissue while gynoid fat reflects the subcutaneous (appendicular) adipose tissue [11]. As the measurements of central FM used different

methods or indexes, the findings regarding the relationship of central adipose with BMD are more controversial. Several studies indicate that central adipose accumulation is negatively related to BMD [12, 13]. On the contrary, some studies show visceral fat is positively associated with BMD in postmenopausal women [14]. These heterogeneous findings may result from the rather complex mechanisms underlying the relationship between fat and bone, including mechanical loading as well as the hormones and cytokines from adipose tissue, which can indirectly influence bone metabolism to a certain extent. Moreover, gender, age, menopausal status, and skeletal site differences in the relationship between BMD with ALM and central FM have not been well studied.

To our knowledge, only a few other studies have documented the relationships of ALM and android/gynoid fat mass ratio (A/G FMR) with BMD at multiple sites in different ages, menopausal status, and in both genders. In the current study, we aim to investigate the relationship between BMD and body composition, especially the effect of regional body composition on BMD. We also want to examine whether these relationships differ by gender, age, and menopausal status in a large population-based sample of Chinese adults.

Methods

Subjects

The present study included healthy Chinese men and women aged 20 to 95 years old. The participants were recruited from the body composition and osteoporosis study at the First Affiliated Hospital of Jinan University (Guangzhou, China) from 2004-2017. Inclusion criteria for the study were Chinese individuals who appeared to be in good health and functionally independent. Subjects were excluded if they met any of the following criteria: (a) a history of fracture; (b) medication known to affect the musculoskeletal system (anti-osteoporotic drugs, androgens or anti-androgen drugs, corticosteroids, etc.); (c) chronic disease known to affect bone metabolism (hyperthyroidism, hyperparathyroidism, rheumatoid arthritis, chronic renal insufficiency, etc.); (d) metal implants (pacemakers, joint replacement device, etc.); (e) inability to determine the menstruation state or non-natural menopause (natural menopause was designated if there was a complete natural cessation of menses for more than twelve months). The inclusion and exclusion criteria flowchart of study was shown in Figure 1. And the current smoking and drinking situation has also been recorded. In the end, 1703 men and 4046 women were included in our study. All subjects provided written

informed consent to participate in the study, which was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University.

Anthropometry, BMD and body composition measurement

A research physician obtained information on medical history, medication use, smoking, and alcohol history in a personal interview. Height and body weight were obtained based on standard methods; height was measured without shoes to the nearest 0.1 cm, weight with only light clothing to the nearest 0.1 kg. BMI was calculated as body weight divided by height squared (kg/m^2). Subjects underwent dual-energy X-ray absorptiometry (DXA; software version enCORE10.50.086; GE-lunar Prodigy, WI, USA) scans to measure the whole body, lumbar spine, femoral neck, and total hip BMD. Total and regional LM and FM were obtained through whole body scans. Android and Gynoid regions were automatically attained using the software provided by the manufacturer. Android region is defined as the portion of the abdomen included between the line joining the two superior iliac crests, extending cranially up to 20% of the distance between this line and the chin. Gynoid region is defined as the portion of the legs leaving from the femoral greater trochanter, directed caudally up to twice the height of the android region. The appendicular region is defined as the areas including both the left and right arms and legs. Daily quality assurance scans were performed by scanning the spine phantom according to the manufacturer's instructions; the same trained technologist conducted all DXA measurements throughout the study. The coefficient of variation was less than 2% for total LM, FM, total, lumbar spine, femoral neck, and total hip BMD, and less than 3% for regional (trunk, appendicular, android, and gynoid) LM and FM, was determined by duplicate scans with repositioning between each measurement in 30 volunteer subjects.

Statistical analyses

Subjects were categorized into four groups according to gender, age, and menopausal status (786 men＜50years, 917 men ≥50years, 1534 premenopausal women, and 2512 postmenopausal women). The values of continuous variables were presented as the mean ± standard deviation (SD). Unpaired-sample *t*-tests were used to evaluate the mean differences between different groups, and Pearson's correlation coefficients (*r*) were conducted to determine the linear relationships among various parameters. We performed linear regressions to assess the association strength between ALM, A/G FMR, and BMD. In the regression models, BMD (different skeletal sites) measurements were used

as dependent variables, and ALM and A/G FMR were treated as independent variables; age, BMI, and lifestyle factors (smoking and alcohol history) were also included. When we performed linear regression analyses, we chose the enter methods and expressed the results as standard β coefficients. All tests were two-sided, and P <0.05 was considered statistically significant. All statistical analyses were performed using the statistical package for social sciences (Version 19.0) (SPSS Inc., Chicago, IL, USA).

Patient and Public Involvement

There was no patient or public involvement in this study.

Results

Basal characteristics of subjects

Table 1 details the subject characteristics in each group. Males ≥50years had higher BMI, whole-body FM, percentage of whole-body fat mass (fat%), trunk FM, and appendicular FM, but lower weight and lumbar spine BMD than males < 50years (P <0.001). Postmenopausal females had higher values for whole-body FM, whole-body LM, trunk FM, appendicular FM, and A/G FMR, and lower BMD at each site than premenopausal females (P <0.05).

Changes of BMD and body composition with age

To further explore the distribution characteristics of body composition and BMD regarding age, we divided the subjects into multiple subgroups and set ten years as one subgroup. As shown in Table 2 and Figure 2, whole-body FM, fat%, android FM, and A/G FMR showed a consistent increase in both genders. Overall, the highest values of whole-body, lumbar spine, femoral neck, and total hip BMD were observed in the second decade and then decreased slightly with age in males. BMD at each skeletal site increased steadily and reached a peak until perimenopause in the fourth decade in females, and then decreased dramatically after menopause. Interestingly, appendicular LM started to decline after 50 years old in both males and females.

Associations of BMD with whole and regional body composition in different groups

In Pearson's correlation analyses, significant positive correlations were found between BMD at all sites with height, weight, BMI, whole-body LM, whole-body FM, fat%, Android FM, Gynoid FM, and ALM in all groups (r=0.218-0.616, P <0.05). A/G FMR showed positive correlations with whole-body, lumbar spine, femoral neck, and total hip BMDs in men <50years and ≥50years old

(r=0.089~0.318, P <0.001). However, A/G FMR was negatively correlated with whole-body and femoral neck BMDs in postmenopausal females, though the correlation strengths were weak (r=-0.075, P <0.001 and r=-0.091, P <0.001, respectively). A/G FMR was insignificantly correlated with BMD in premenopausal females (Shown in supplemental table 1-4).

To further explore the independent predictive value of A/G FMR and ALM for BMD at all sites in every group, covariates such as ages, BMI, smoking, and alcohol consumption that associated with BMD were also included in the multiple linear regression analyses (shown in Table 3 and 4). Overall, the significant variables accounted for 10.7~37.4% of the variability in BMD. Considering the dynamic change of BMD between period of bone modeling (20-29 years) and that of bone remodeling (30-50 years), and the subjects aged 20-29 years were excluded in the regression analyses. The effect sizes of A/G FMR and ALM on BMD were different according to the skeletal site and age group. A/G FMR had inverse associations with whole-body, lumbar spine, femoral neck, and total hip BMDs in both premenopausal (standard β from -0.249 to -0.155, P <0.001) and postmenopausal women (standard β from -0.135 to -0.052, P <0.01), while men had no significant relationship between A/G FMR and each part of BMD after adjustment. ALM was positively associated with whole-body, lumbar spine, femoral neck, and total hip BMDs in both males and females, and the correlations were higher in males than that in females (standard β from 0.309 to 0.405 of men with <50y vs. standard β from 0.074 to 0.179 of premenopausal women, P <0.001; standard β from 0.207 to 0.321 of males with ≥50y vs. standard β from 0.152 to 0.186 of postmenopausal women, P <0.001).

Discussion

The global epidemic of obesity has become a significant concern in our daily life as it not only has a close relationship with cardiovascular and cerebrovascular diseases but also influences bone health [15]. As a part of body composition, bone density was mainly determined by body weight and BMI. Low BMI had been regarded as a risk factor for osteoporotic hip fracture in both males and females [16]. In this study, we investigated a wide range of healthy Chinese adults aged 20 to 95 years old to further explore the factors that may influence bone health. We divided the participants into different age groups to investigate the changes in body composition and BMD with age in males and females. We also performed multivariable regression analyses to confirm that whether A/G

FMR and ALM were independent predictors for BMD after adjusting for age, BMI, smoking, and alcohol consumption. The current report provided more detailed and impressive results which were different from previous studies performed in America [13] and Australia [1]. We found that ALM positively correlated with BMD in both genders, and low ALM was related to low BMD. A/G FMR as an indicator of central adipose accumulation was inversely associated with BMD in females but not in males. These results, based on a large population of Chinese adults, were convincing.

In this study, we found that whole-body LM reached a peak level in the 40-49 years group, and then decreased gradually in both genders, whereas whole-body FM steadily increased from youth to older age in both genders. After analyzing the baseline characteristics, we found that the decreased whole-body LM in older men was primarily due to a decrease in ALM. Moreover, the increased whole-body FM in older men and women mainly arose from the increase of Trunk FM. In the meantime, we found that the A/G FMR increased with age in both males and females. Men had an earlier whole-body, lumbar spine, femoral neck, and total hip BMD peaks than women. BMD at all sites decreased slightly in older men, but more obviously in postmenopausal women. These results provided us a healthy bone mass for each age group in both men and women. The BMD at each region lower than the guidance ranges in the respective age group should alarm the physician for appropriate intervention.

In our study, the results showed that both total LM and total FM are positively associated with BMD in both genders. The effect size of total LM and total FM to BMD was different according to gender, menopausal status, and age. Total LM is a stronger protective factor to BMD at all sites in men and premenopausal women. Total FM is a stronger contributor to BMD at all sites in postmenopausal women. Several potential theories may explain the observed findings. The influences of LM on BMD may attribute to the direct mechanical effects of muscle, which produces a positive osteogenic response to bone formation. For one hand, whole-body LM, which accounted for a large proportion of body weight in both males and females, would perform a gravitational loading on the bone. On the other hand, the contraction strength of lean muscle should also be considered a specific mechanism of action. A previous study reported that the augmentation and thickening of bone trabecula was an adaption to increased mechanical stress. However, whole-body FM only accounted for a small proportion of body weight in both males and females, but it still performed a significant and positive correlation with BMD, especially in postmenopausal women,

in whom a higher standard β value with BMD in all the skeletal sites was shown compared with whole-body LM. Several mechanisms could explain the association between fat tissue and BMD. The outcomes of fat acting on the bone may be influenced not only by weight-bearing effects but also by non-weight bearing effects, including the hormonal metabolism of adipocytes. We speculate that this fat-related mechanism may help to interpret this finding, as the postmenopausal women also had the highest whole-body FM, more than males and premenopausal women in our study. Several hormones, including insulin, leptin, adiponectin, and adipocytic estrogens, were found to be secreted from adipose tissue, which can influence bone metabolism through the endocrine pathway. Also, the enzyme aromatase in adipose tissue can convert androgen to estrogen and result in an elevated estrogen level. These bone protective hormones led to a positive influence on bone formation via stimulating the differentiation of osteoblasts and preventing osteoclast-mediated bone resorption. This finding further confirmed the results from previous studies that FM should have a positive relationship with bone mass [8, 17].

Though both whole-body LM and FM were found to be positively associated with BMD in both genders, how regional body compositions and differences in fat distribution influence bone metabolism aroused our curiosity. To investigate the effect of ALM and A/G FMR on BMD with various ages, the factors including gender, age, BMI, smoking, and alcohol consumption, which may have close relationships with BMD, were considered in multiple linear regression analyses. In the current study, we found that ALM was positively related to BMD at all sites after adjustment for BMI and age in both genders. ALM is considered one of the most important indexes of the diagnostic criterion for sarcopenia [18, 19]. A study of 679 men aged 40-79 years suggested low ALM was associated with low BMD (whole body, femoral neck, total hip, and lumbar spine) and osteoporosis independent of age, height, physical activity, and other lifestyles [20]. Blain et al. [7] also found that ALM was most strongly associated with femoral neck BMD independent of nutritional, hormonal factors, and other lifestyles in men. There are several mechanisms that may explain the observed association between ALM and BMD. The amount of ALM was smaller than trunk LM in this study, suggesting ALM may effect on bone via contraction strength instead of gravitational loading, especially in males younger than 50 years old, in whom the strongest relationships with BMD in all sites were demonstrated, compared with other groups. Systemic factors that simultaneously involve both ALM and bone metabolism may exist as the decline of

ALM was almost parallel with BMD in both genders. For example, the hormone estrogen can strengthen the synthesis of muscle protein and promote calcium deposition in bone tissue, which leads to an increased LM and BMD concurrently [21]. However, a prospective study is needed to explore the potential mechanism further.

Depot-specific fat has been known to play a different role in terms of obesity and metabolism. A previous study indicated that different fat depots might have distinct relationships with bone mass [22]; Marques reported appendicular FM (AFM) had a positive association with femoral neck BMD in older women [23]. Inconsistent with that, several studies stated AFM had no [24] or a negative [25] relationship with BMD. Freitas et al. [26] showed that central fat was positively associated with BMD and regarded as an independent and protective factor on the presence of osteoporosis or osteopenia. Sharma et al. [27] reported that a bigger trunk (central) FM was associated with increased BMD in total hip and femoral neck, regardless of HIV status in women. Fat distribution difference seems to produce a meaningful but contradicted effect on bone mass based on previous studies. To further confirm this finding, we performed Pearson's correlation to assess the relationship between Android FM, Gynoid FM, and each part of BMD with a large sample size. The results suggested that both Android FM and Gynoid FM positively correlated with BMD in all males and females, which was partly consistent with previous studies [22, 24]. In contrast, some studies reported abdominal fat and android fat measured by CT or DXA had a negative association with BMD after adjusting for total LM or BMI, suggesting central fat deposition was not beneficial for bone [13]. Surprisingly, we found that A/G FMR showed a diverse correlation with BMD in males and females. The results revealed that A/G FMR was positively correlated with each part of BMD in males <50 years and older group. But in postmenopausal females, A/G FMR had an inverse association with whole-body ($r=-0.075$, $P<0.001$) and femoral neck BMD ($r=-0.091$, $P<0.001$), and had no relationship with each part of BMD in premenopausal females. Kim et al. [22] also reported that A/G FMR was inversely associated with the trabecular bone score after age adjustment ($r=-0.288$, $P<0.05$), which was similar with our findings. Android fat mainly represents visceral fat in the epigastric region, while gynoid fat reflects peripheral (or subcutaneous) fat in the leg. A higher A/G FMR indicating a higher visceral fat or a lower peripheral fat revealed that subjects with a higher A/G FMR had a lower BMD in postmenopausal females, whose ovarian hormones tend to be depleted and lead to a higher subcutaneous lipoprotein lipase activity ratio and predominant fat

storage in visceral fat depots [28]. Kim et al. [29] found that visceral fat has a negative association among postmenopausal Korean women with lumbar spine BMD after adjustment for weight. Zhu et al. reported trunk-to-limb fat mass ratio (a surrogate of visceral fat) had a negative association with total body bone mass in young adults [17]. Gilsanz et al. [30] suggested that subcutaneous and visceral fat had opposite effects on femoral bone structure and strength in healthy young females, and proposed that subcutaneous fat may be beneficial to the bone, whereas visceral fat may have a negative association with bone. These heterogeneous findings may be related to the use of diverse methods for measuring body composition and BMD, disparities in study design, or the different criteria for group division. Moreover, the inconsistency of findings may be due to the rather complex mechanisms underlying the relationship between fat and bone. As a result, we subdivided the Chinese people into different age and gender groups and found that android fat increased with age, especially in females, whose android fat accounted for a more substantial proportion of body weight and had a stronger relationship with BMD in our study. To avoid multicollinearity, we included A/G FMR instead of the total and regional body composition into the same multiple regression analysis when we explored the associations of regional fat depots with BMD, which provided a more reliable result.

Limitations

This study had several limitations. First, we did not obtain a blood sample from participants; thus, the actual hormone and cytokine levels were unknown. The potential mechanisms acting on bone mass mainly referenced in previous reports based on our data and the statistical results. Second, we only collected cross-sectional data and cannot directly conclude the causality limited by its study design. Third, though we evaluated the relationships of body composition and fat distribution with BMD by adjusting age, BMI, smoking, and alcohol consumption, other confounders such as socioeconomic status, dietary intake, and physical activity, which may influence bone nutrition and metabolism, were not considered as covariates in the multivariable regression analyses. Fourth, a more substantial amount of visceral fat mass was found in Asians compared with the European people for a given amount of body fat [31]. Therefore, ethnic differences should be considered when interpreting the findings.

Conclusions

In summary, in this large cohort of Chinese adults, ALM had a strong positive association with BMD in both genders and suggesting that low ALM is related to low BMD and may be considered an independent risk for osteoporosis. A/G FMR an indicator of central adipose accumulation was inversely associated with BMD in females but not in males.

Contributors

Xiao,Tan, Shang, Cheng and Tang participated in collection, analysis, interpretation of data; and Xiao, Guo and Gong wrote the paper. Xu, Principal Investigator, innovator for the project, participated in the conception, design, and revision of the manuscript.

Conflict of interest

The authors have no conflicts of interest.

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Ethics approval

The study was approved by the Ethics Committee of the First Affiliated Hospital of Jinan University.

Data sharing statement

The deidentified participant data will be available upon reasonable request from Prof. Xu (txh@jnu.edu.cn).

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Abbreviations

BMD: bone mineral density; LM; lean mass; FM: fat mass; ALM: appendicular lean mass; DXA: dual-energy X-ray absorptiometry; A/G FMR: android/gynoid fat mass ratio; BMI: body mass index.

Figure legend

Fig. 1 The study inclusion/exclusion criteria flowchart. DXA, dual-energy X-ray absorptiometry.

Fig.2 The age-related change in whole-body lean mass (WBLM), appendicular lean mass (ALM),

percentage of whole-body fat mass (fat%), A/G FMR, and bone mineral density in males and females. A/G FMR, Android/Gynoid fat mass ratio; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

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Table 1 Baseline characteristics of subjects

	Male		Female	
	Age＜50years	Age≥50years	Premenopausal	Postmenopausal
No. of subjects	786	917	1534	2512
Age (years)	36.8±8.7	65.8±10.0[c]	37.4±8.7	63.9±9.1[c]
Weight (kg)	63.9±12.4	63.8±10.8[c]	52.7±9.1	55.0±8.9
Height (cm)	168.8±5.8	166.7±6.1	158.0±4.9	155.9±5.3[c]
BMI (kg/m^2)	22.4±3.9	22.9±3.3[c]	21.1±3.3	22.6±3.3
Body composition measures (Kg)				
Whole body FM	13.7±7.6	15.2±6.5[c]	16.7±6.0	18.9±6.2[b]
Whole body LM	47.6±6.0	46.1±5.9	33.8±4.3	34.2±4.0[a]
Fat%	20.2±8.3	23.0±7.3[c]	30.1±6.7	33.6±6.8
Trunk FM	8.2±5.0	9.3±4.4[c]	8.7±3.6	10.6±3.7[b]
Trunk LM	22.4±3.0	22.4±2.9	16.4±2.2	17.1±2.1
Appendicular FM	5.0±2.6	5.3±2.1[c]	7.3±2.5	7.5±2.6[c]
Appendicular LM	21.4±3.2	19.9±3.1	14.4±2.2	14.0±2.1
A/G FMR	0.57±0.17	0.69±0.19	0.42±0.10	0.56±0.15[c]
Bone mineral density (g/cm^2)				
Whole body	1.105±0.109	1.109±0.105	1.085±0.094	0.994±0.106[c]
Lumbar spine	1.114±0.162	1.099±0.200[c]	1.124±0.155	0.950±0.186[c]
Femoral neck	0.921±0.140	0.839±0.140	0.907±0.122	0.760±0.132[b]
Total hip	0.941±0.150	0.911±0.147	0.942±0.132	0.817±0.144[b]
Current Smoker (%)	n=141 (17.9%)	n=119 (13.0%)	n=37 (2.4%)	n=70 (2.8%)
Current alcohol user (%)	n=121 (15.4%)	n=117 (12.8%)	n=35 (2.3%)	n=38 (1.5%)

Note. Values are presented as number, mean ± standard deviation or percentage.

BMI, body mass index; FM, fat mass; LM, lean mass; Fat%, percentage of whole body fat mass; A/G FMR, android/gynoid fat mass ratio. *P* value was determined by the unpaired-sample *t*-tests. [a]$P < 0.05$; [b] $P< 0.01$; [c]$P < 0.001$. Compared with the same gender of the different age group (unpaired-sample t-tests or chi-squared test).

Table 2 Distributions of age-related change in body composition and bone mineral density

Age (years)	n	WBLM (Kg)	WBFM (Kg)	Fat %	Android FM(Kg)	Gynoid FM(Kg)	A/G FMR	ALM (Kg)	WBBMD (g/cm^2)	LSBMD (g/cm^2)	FNBMD (g/cm^2)	THBMD (g/cm^2)
Male												
20-29	199	47.3±6.0^c	12.1±8.2^c	18.1±9.0^c	1.2±0.9^c	2.4±1.3^c	0.47±0.14^c	21.6±3.3^c	1.102±0.103	1.176±0.151	0.958±0.140	0.954±0.153
30-39	254	47.0±5.9^c	12.8±7.3^c	19.4±8.2^c	1.4±0.9^c	2.4±1.3^a	0.55±0.16^c	21.0±3.3^c	1.090±0.113^c	1.160±0.149	0.909±0.140^b	0.922±0.154^c
40-49	333	48.3±6.0^c	15.4±7.2^c	22.1±7.6^c	1.7±0.9^c	2.6±1.0	0.63±0.17^c	21.5±3.2^c	1.119±0.108^b	1.171±0.178	0.908±0.137	0.947±0.147
50-59	313	48.1±6.1^c	15.2±6.5	22.2±7.2^a	1.7±0.8^c	2.5±0.9	0.67±0.18^c	21.0±3.2^c	1.122±0.110	1.096±0.192	0.895±0.140	0.946±0.154^a
60-69	281	46.9±5.4^c	15.5±6.5	23.0±7.3^a	1.8±0.8^c	2.5±0.9	0.71±0.19^c	20.4±2.8^c	1.122±0.098	1.116±0.190	0.843±0.120	0.924±0.125
70+	323	43.6±5.2^c	15.0±6.5	23.8±7.5	1.7±0.9^b	2.4±0.9	0.70±0.19^c	18.4±2.7^c	1.086±0.101	1.086±0.215^c	0.783±0.135^c	0.863±0.147^a
Female												
20-29	369	32.5±4.2	15.5±6.1	30.1±7.1	1.3±0.6	3.2±1.0	0.38±0.09	14.0±2.1	1.048±0.090	1.173±0.135	0.891±0.126	0.912±0.138
30-39	456	33.5±4.0	16.0±6.0	30.2±6.7	1.4±0.6	3.2±1.0	0.42±0.11	14.3±2.0	1.084±0.090	1.161±0.152	0.917±0.119	0.942±0.123
40-49	709	34.7±4.4	17.8±5.8	31.9±6.4	1.5±0.6	3.5±0.9	0.45±0.10	14.7±2.2	1.105±0.093	1.151±0.165	0.908±0.122	0.958±0.131
50-59	1004	34.6±4.0	19.0±6.3	33.4±6.6	1.8±0.7	3.4±1.0	0.52±0.13	14.4±2.1	1.039±0.103	1.028±0.186	0.828±0.126	0.880±0.137
60-69	805	34.5±3.9	19.1±6.1	33.7±7.1	1.9±0.7	3.3±0.9	0.57±0.15	14.2±2.0	0.986±0.095	0.991±0.171	0.749±0.113	0.814±0.128
70+	703	33.2±3.9	18.4±6.1	33.8±7.1	1.9±0.7	3.1±0.9	0.59±0.16	13.3±1.9	0.939±0.094	0.889±0.177	0.672±0.105	0.732±0.125

Note. Values are presented as number or mean ± standard deviation. WBLM, whole body lean mass; WBFM, whole body fat mass; Fat % = whole body fat mass/body weight×100; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density. $^aP < 0.05$; $^bP < 0.01$; $^cP < 0.001$. Compared with female of the same age group (unpaired-sample t-tests).

Table 3 Multiple regression analyses of bone mineral density at different skeletal sites with age, smoke, alcohol, BMI, A/G FMR, and appendicular LM in males.

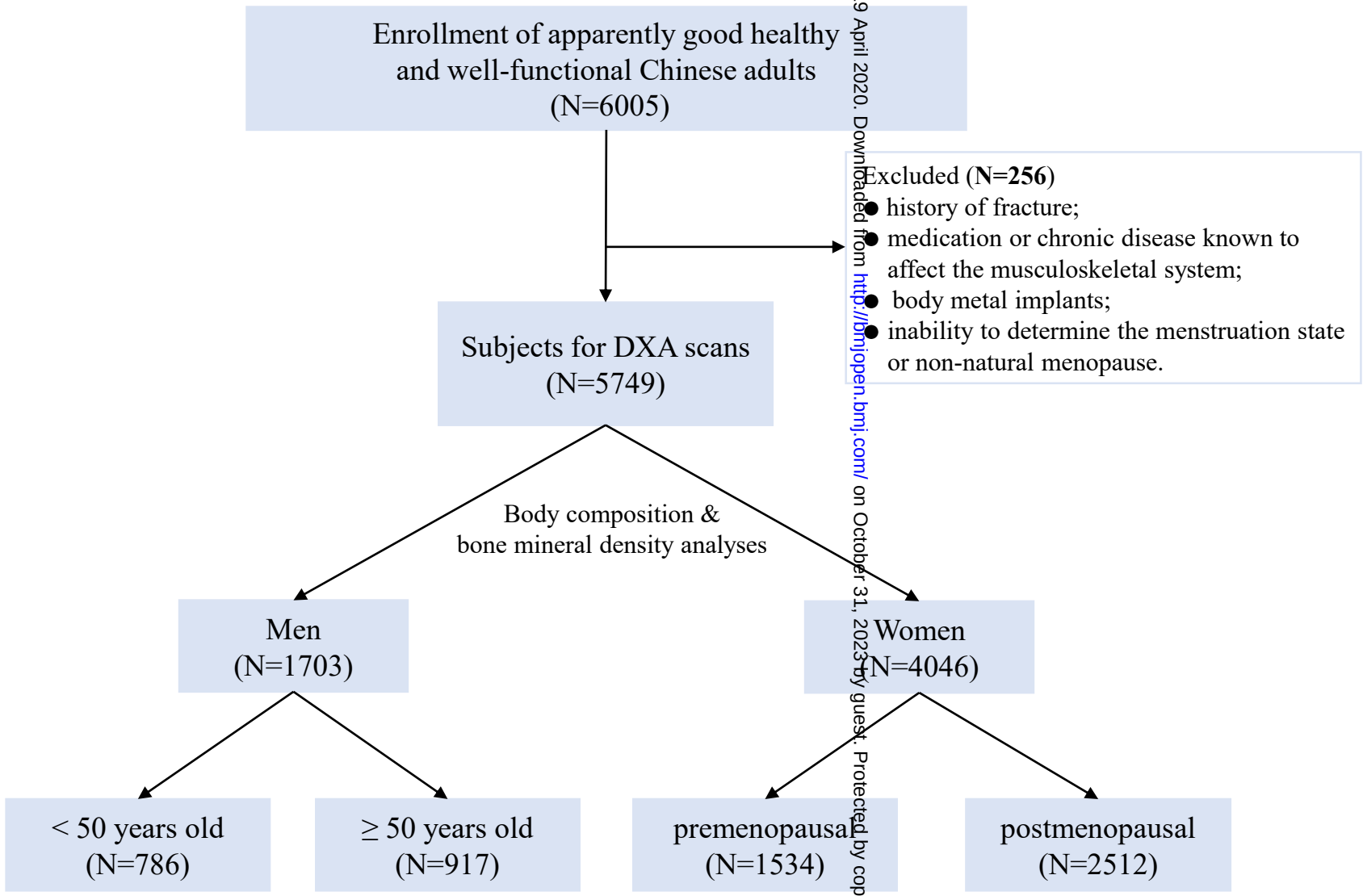
Males	WBBMD			LSBMD			FNBMD			THBMD		
	Standard β	t	Sig.	Standard β	t	Sig.	Standard β	t	Sig.	Standard β	t	Sig.
<50 y												
Age	**0.066**	1.991	0.047	-0.018	-0.459	0.647	-0.044	-1.161	0.246	0.029	0.821	0.412
Smoke	-0.057	-1.783	0.075	-0.043	-1.116	0.265	-0.047	-1.267	0.206	-0.050	-1.473	0.141
Alcohol	**0.063**	1.988	0.047	0.041	1.081	0.280	0.011	0.303	0.762	0.009	0.279	0.780
BMI	**0.266**	4.998	<0.001	**0.170**	2.668	0.008	**0.139**	2.269	0.024	**0.222**	3.920	<0.001
A/G FMR	0.044	1.028	0.304	-0.063	-1.223	0.222	-0.040	-0.811	0.418	0.014	0.315	0.753
Appendicular LM	**0.402**	9.240	<0.001	**0.309**	5.923	<0.001	**0.395**	7.872	<0.001	**0.405**	8.757	<0.001
≥50 y												
Age	-0.015	-0.486	0.627	**0.087**	2.673	0.008	**-0.220**	-7.086	<0.001	**-0.124**	-3.989	<0.001
Smoke	-0.023	-0.786	0.432	-0.027	-0.865	0.387	0.005	0.165	0.869	-0.006	-0.215	0.830
Alcohol	0.023	0.794	0.427	0.059	1.920	0.055	0.022	0.747	0.455	0.020	0.697	0.486
BMI	**0.260**	5.915	<0.001	**0.268**	5.704	<0.001	**0.190**	4.257	<0.001	**0.261**	5.817	<0.001
A/G FMR	0.008	0.241	0.809	0.027	0.759	0.448	-0.054	-1.585	0.113	-0.035	-1.032	0.302
Appendicular LM	**0.321**	7.814	<0.001	**0.207**	4.719	<0.001	**0.264**	6.328	<0.001	**0.256**	6.127	<0.001

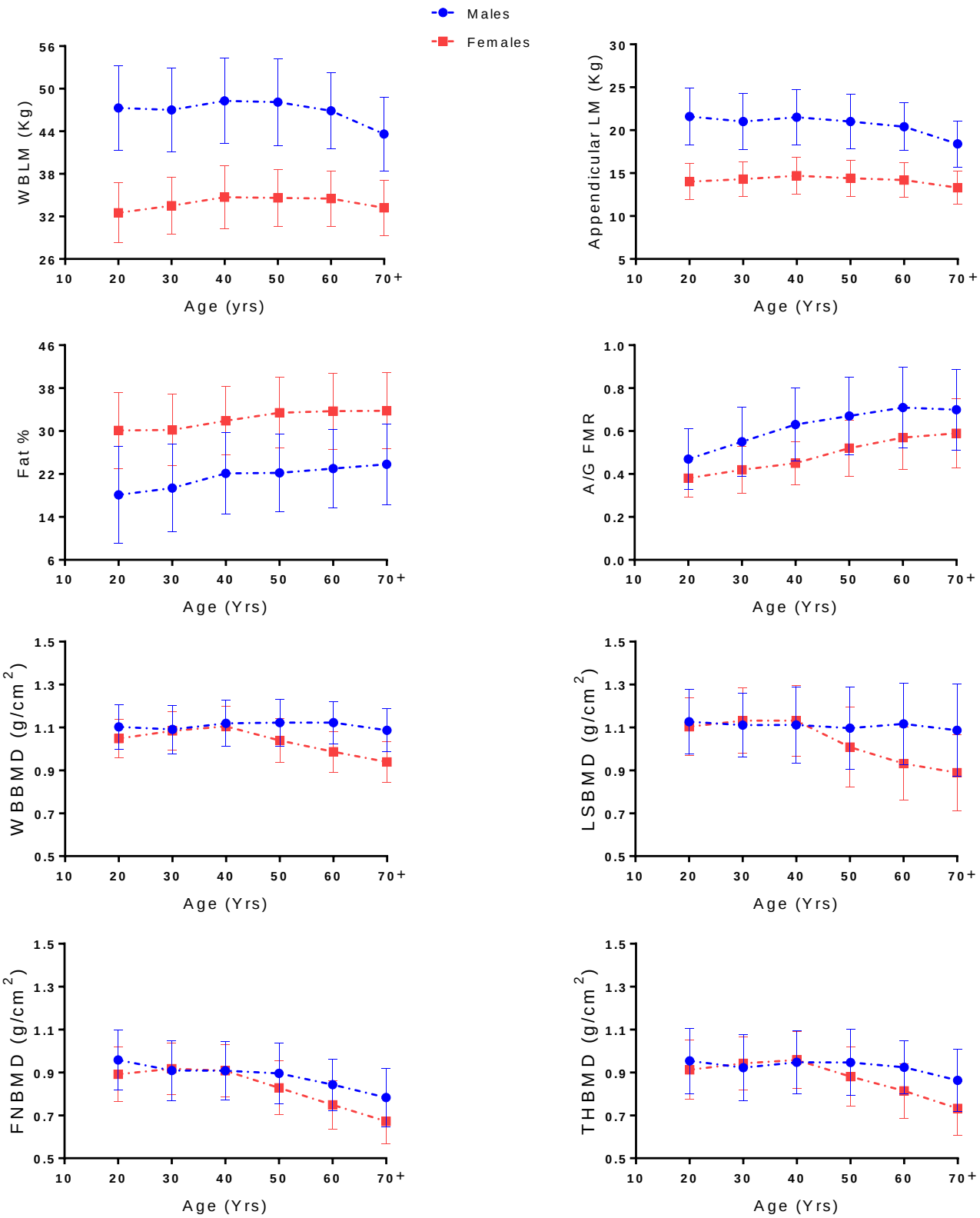
Note. Results expressed as standard β coefficients. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

Table 4 Multiple regression analyses of bone mineral density at different skeletal sites with age, smoke, alcohol, BMI, A/G FMR, and appendicular LM in females.

Females	WBBMD			LSBMD			FNBMD			THBMD		
	Standard β	t	Sig.	Standard β	t	Sig.	Standard β	t	Sig.	Standard β	t	Sig.
Premenopausal												
Age	0.039	1.483	0.138	**-0.074**	-2.665	0.008	**-0.098**	-3.483	0.001	-0.008	-0.278	0.781
Smoke	0.024	0.958	0.338	0.022	0.794	0.427	0.033	1.196	0.232	0.030	1.133	0.258
Alcohol	-0.005	-0.197	0.844	0.008	0.289	0.773	0.013	0.467	0.640	0.012	0.451	0.652
BMI	**0.413**	11.055	<0.001	**0.384**	9.659	<0.001	**0.277**	6.901	<0.001	**0.360**	9.177	<0.001
A/G FMR	**-0.249**	-8.421	<0.001	**-0.193**	-6.152	<0.001	**-0.155**	-4.872	<0.001	**-0.157**	-5.083	<0.001
Appendicular LM	**0.179**	5.360	<0.001	**0.074**	2.099	0.036	**0.159**	4.451	<0.001	**0.138**	3.940	<0.001
Postmenopausal												
Age	**-0.337**	-19.556	<0.001	**-0.222**	-11.701	<0.001	**-0.438**	-25.343	<0.001	**-0.389**	-22.318	<0.001
Smoke	-0.024	-1.482	0.139	0.007	.383	0.702	-0.019	-1.146	0.252	-0.024	-1.461	0.144
Alcohol	-0.015	-0.898	0.369	-0.029	-1.649	0.099	-0.008	-0.504	0.614	-0.020	-1.213	0.225
BMI	**0.315**	14.922	<0.001	**0.274**	11.767	<0.001	**0.185**	8.718	<0.001	**0.266**	12.451	<0.001
A/G FMR	**-0.135**	-7.585	<0.001	**-0.086**	-4.402	<0.001	**-0.083**	-4.644	<0.001	**-0.052**	-2.867	0.004
Appendicular LM	**0.186**	9.076	<0.001	**0.152**	6.744	<0.001	**0.180**	8.787	<0.001	**0.166**	7.998	<0.001

Note. Results expressed as standard β coefficients. BMI, body mass index; A/G FMR, android/gynoid fat mass ratio; LM, lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.




Males
Females
WBLM (Kg)
Age (yrs)
Appendicular LM (Kg)
Age (Yrs)
Fat %
Age (Yrs)
A/G FMR
Age (Yrs)
WBBMD (g/cm2)
Age (Yrs)
LSBMD (g/cm2)
Age (Yrs)
FNBMD (g/cm2)
Age (Yrs)
THBMD (g/cm2)
Age (Yrs)

SUPPLEMENTARY INFORMATION

Sex- and age-specific characteristics of body composition and its effect on bone mineral density in southern Chinese adults: a cross-sectional study

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Keywords: body composition; aging; bone mineral density; fat distribution; appendicular lean mass.

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Table S1. Pearson's correlation between study variables in males <50years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.092*											
Weight	.161***	.460***										
BMI	.216***	.126***	.917***									
WBLM	.083*	.571***	.851***	.706***								
WBFM	.189***	.265***	.905***	.893***	.549***							
Fat%	.207***	.155***	.788***	.810***	.364***	.962***						
A/G FMR	.407***	.062	.594***	.641***	.363***	.656***	.667***					
ALM	.005	.555***	.822***	.681***	.950***	.541***	.372***	.308***				
WBBMD	.101**	.306***	.610***	.547***	.567***	.489***	.407***	.318***	.569***			
LSBMD	-.019	.245***	.358***	.294***	.355***	.258***	.203***	.096***	.375***	.742***		
FNBMD	-.127***	.274***	.394***	.314***	.423***	.266***	.182***	.089***	.438***	.719***	.662***	
THBMD	.017	.232***	.495***	.443***	.500***	.363***	.280***	.226***	.513***	.840***	.696***	.872***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

*$P < 0.05$; **$P < 0.05$; ***$P < 0.001$.

Table S2. Pearson's correlation between study variables in males ≥50years

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.165***											
Weight	-.212***	.511***										
BMI	-.160***	.087***	.898***									
WBLM	-.355***	.581***	.835***	.671***								
WBFM	-.016	.287***	.860***	.850***	.438***							
Fat%	.089**	.125***	.668***	.717***	.162***	.941***						
A/G	.042	.028	.446***	.505***	.198***	.548***	.575***					
ALM	-.385	.546***	.807***	.658***	.945***	.442***	.191***	.164***				
WBBMD	-.180***	.307***	.545***	.479***	.501***	.395***	.280***	.193***	.499***			
LSBMD	-.035	.230***	.451***	.407***	.352***	.381***	.307***	.203***	.356***	.772***		
FNBMD	-.354***	.291***	.447***	.373***	.459***	.281***	.172***	.077***	.466***	.760***	.631***	
THBMD	-.267***	.235***	.473***	.433***	.456***	.323***	.221***	.134***	.471***	.845***	.702***	.913***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

$^{*}P < 0.05$; $^{**}P < 0.05$; $^{***}P < 0.001$.

Table S3. Pearson's correlation between study variables in premenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.031											
Weight	.222***	.424***										
BMI	.260***	.072***	.932***									
WBLM	.217*	.510***	.795***	.671**								
WBFM	.166***	.246***	.896***	.890***	.445***							
Fat%	.116***	.078***	.656***	.697***	.084***	.909***						
A/G	.261***	.002	.449***	.494***	.251***	.489***	.465***					
ALM	.153***	.519***	.769***	.640***	.947***	.444***	.111***	.181***				
WBBMD	.230**	.200***	.453***	.423***	.444***	.314***	.142***	.022	.434***			
LSBMD	.053*	.179***	.347***	.315***	.285***	.276***	.175***	.000	.299***	.777***		
FNBMD	.028	.181***	.316***	.281***	.309***	.218***	.095***	-.009	.323***	.704***	.661***	
THBMD	.126***	.111***	.361***	.358***	.355***	.249***	.112***	.043	.363***	.814***	.714***	.894***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

*$P < 0.05$; **$P < 0.05$; ***$P < 0.001$.

Table S4. Pearson's correlation between study variables in postmenopausal females

	Age	Height	Weight	BMI	WBLM	WBFM	Fat%	A/G FMR	ALM	WBBMD	LSBMD	FNBMD
Height	-.285***											
Weight	-.129***	.452***										
BMI	-.011	.038	.905***									
WBLM	-.172***	.542***	.774***	.608***								
WBFM	-.050*	.273***	.909***	.889***	.442***							
Fat%	.022	.098***	.703***	.746***	.113***	.924***						
A/G	.204***	-.049*	.300***	.359***	.193***	.311***	.315***					
ALM	-.253***	.538***	.729***	.558***	.907***	.435***	.139***	.076***				
WBBMD	-.413***	.332***	.474***	.374***	.419***	.361***	.226***	-.075***	.436***			
LSBMD	-.281***	.299***	.421***	.330***	.345***	.339***	.236***	-.201	.354***	.821***		
FNBMD	-.501***	.336***	.375***	.260***	.344***	.275***	.168***	-.091***	.387***	.785***	.668***	
THBMD	-.442***	.277***	.423***	.344***	.370***	.327***	.218***	-.021	.408***	.839***	.720***	.912***

Note. Results expressed as *r* coefficients. BMI, body mass index; WBLM, whole body lean mass; WBFM, whole body fat mass; Fat%, percentage of body fat mass; FM, fat mass; A/G FMR, android/gynoid fat mass ratio; ALM, appendicular lean mass; WBBMD, whole body bone mineral density; LSBMD, lumbar spine bone mineral density; FNBMD, femoral neck bone mineral density; THBMD, total hip bone mineral density.

*$P < 0.05$; **$P < 0.05$; ***$P < 0.001$.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
Outcome data	15*	Report numbers of outcome events or summary measures	6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7

		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.