The Influence of Body Fat Content and Distribution on Bone Mass in Healthy Chinese Adults

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Research Article

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Abstract

Introduction: Many previous studies have reported a close relationship between body mass index (BMI) and bone mineral density (BMD). However, the effects of fat on bone health remain controversial, particularly for fat tissue distribution.

Methods: This study enrolled 18,263 participants who had undergone health examinations. Body composition and BMD were measured using dual-energy X-ray absorptiometry. The relationships of BMI and regional fat percentage with BMD were detected by multiple linear regression and generalized additive models. The risk of low BMD was calculated using logistic regression.

Results: There was a negative relationship between the regional fat percentage and FN BMD or LS BMD in both genders ($P<0.05$). In females, this relationship was bidirectional. Multiple logistic regression analyses showed that the risk for low BMD linearly increased across increasing regional fat percentage quartile categories. In females, the ORs for low LS BMD were 3.095 (95% CI, 2.618-3.658) for hip fat percentage and 1.532 (95% CI, 1.271-1.848) for waist fat percentage. In males, the ORs for low FN BMD were 2.211 (95% CI, 1.831-2.670) for waist fat percentage and 1.998 (95% CI, 1.694-2.355) for hip fat percentage.

Conclusions: Overall, the body fat content was a negative predictor of the BMD, and this effect was gender- and location-dependent. In males, waist fat has a greater effect on the FN BMD, whereas in females, hip fat exerts a more negative influence on the LS BMD, which implies a cross-influence between regional fat content and bone mineral density in males and females.

Introduction

Obesity and osteoporosis are public health problems worldwide due to their high morbidity among ageing populations, and much uncertainty still exists about the relationship between them[1]. The body mass index (BMI) has become one of the most commonly used anthropometric field measures used to determine if an adult is underweight, at a normal weight, overweight or obese[2]. The World Health Organization (WHO) has previously proposed the use of the bone mineral density (BMD) as measured by dual-energy X-ray absorptiometry (DXA) for the diagnosis of osteopenia and osteoporosis[3]. The results from earlier studies demonstrate a strong and consistent association between a lower BMI and fracture risk, and it seems that BMI is a protective factor against fractures in the elderly[4, 5]. Nevertheless, recent literature has emerged that offers contradictory findings about a higher BMI increasing the fracture risk[6, 7]. It is common knowledge that obesity is a complex disorder involving an abnormal or excessive amount of body fat. Body composition can be classified into two main components: lean mass and fat mass, which together represent 95% of body weight[8]. As mentioned above, BMI fails to separate the effects of fat on the BMD from the other factors.

As an indicator of obesity, the role of fat mass in the BMD has received increasing attention in recent years. On the one hand, fat mass increases the mechanical load that stimulates bone formation, leading

to an increase in the bone mass[9]; on the other hand, recent investigators have examined the endocrine effect of adipose tissue on the bone through hormones, adipokines and inflammatory factors[10–12]. To date, however, the effects of fat on bone health remains controversial, particularly regarding the content and distribution of the fat, with the distribution of fat receiving scant attention in the research literature.

In this study, a cross-sectional investigation was conducted on 18,263 participants (8,969 males and 9,294 females) who had undergone routine health examinations, with the aim of evaluating the age-related changes in the BMD and the relationship between the regional fat content and the BMD.

Materials And Methods

Data source and study population

After accessing the healthcare database of Second Affiliated Hospital, Soochow University, we designed a retrospective study of people receiving routine health examinations at the Second Affiliated Hospital, Soochow University from 2018 to 2020. All of them were unrelated participants of eastern Han Chinese ancestry who resided in Suzhou with similar living habits and ethnic backgrounds. Participants with a history of metabolic bone disease (e.g., hyperparathyroidism, hyperthyroidism, Cushing's syndrome, osteomalacia, renal failure & diabetes mellitus, etc.), and participants who took medications (e.g., bisphosphonates, estrogen preparations, antiepileptic drugs, corticosteroids, thyroxine & anticoagulants, etc.) that might influence bone metabolism were excluded prior to the study. Ultimately, a total of 18,263 participants (8,969 males and 9,294 females) aged 20 to 100 years old were recruited.

Clinical measurements

Height without shoes were recorded to the nearest 0.1 cm and were measured with heels, buttocks, upper back, and head touching the vertical plane. The weights were recorded to the nearest 0.1 kg and were measured with the participants lightly clothed (t-shirt and shorts) and shoeless. BMI (kg/m2) was calculated as the body weight in kilograms divided by the squared height in metres. Absolute value of the BMD (g/cm2) at specific bone sites: the antero-posterior L1-L4 lumbar spine (LS) and the left femoral neck (FN) were measured using dual-energy X-ray absorptiometry (DXA; GE-Lunar, Madison, WI, USA). The soft tissue body composition (regional percentage of body fat mass [%, hip fat percentage and waist fat percentage]) was derived from the scan at the site of the lumbar spine and left hip. The scans were analysed using enCORE version 13 (GE Health) software with an automatic inspection of the regions of interest. T-scores (number of standard deviations [SD] above or below young adult mean BMD) and Z-scores (number of SDs above or below age-matched mean BMD) were calculated automatically with normative data from the NHANES reference database on Caucasian females. Based upon the WHO classification, a low BMD (osteopenia or osteoporosis) was defined as a T-score<-1.0 in females and males aged above 50 years or a Z-score<-1.0 in females and males aged below 50 years. The tests were performed by a trained technician on appropriately calibrated equipment before every session.

Densitometers showed stable long-term performances [coefficient of variation [CV] < 0.5%] and satisfactory in vivo precision (CV 0.8% for lumbar spine, 0.9% for femoral neck).

Statistical analysis

Descriptive statistics were used to describe the subject characteristics. Continuous variables are presented as the mean ± standard deviation. Comparisons between the males and females were made by Student's t-test. Linear regression analysis was used to evaluate the relationships between the BMI, hip and waist fat percentage in each gender, with the BMD of the lumbar spine and femoral neck as dependent variables; BMI, hip and waist fat percentage as predictor variables; and age, weight (except for the model for BMI), height as covariates. To obtain a greater flexibility in representing the relationships between the dependent variable and predictor variables compared with linear regression, generalized additive models (GAMs) were used to generate graphic representations of the dose-response relations of BMI, hip and waist fat percentage with BMD in each gender, adjusted for the covariates listed above for linear regression models. We performed multiple logistic regression analyses to generate odds ratios (ORs) (95% CI) that compared the odds of low BMD (T-score <-1.0) for participants in each of the higher three fat percentage quartile categories to the odds of the participants in the lowest quartile category after adjusting for age, weight, height and BMI. All analyses were performed using IBM SPSS (version 17, IBM, Chicago, Illinois, USA) and R (version 3.4.3, R Foundation for Statistical Computing, Vienna, Austria), and $p < 0.05$ (two-tailed) was considered statistically significant. Collinearity was not observed in any of the models based on a variance inflation factor (VIF) value less than 10. The normality and independence of the residuals and the homogeneity of variance of each model were checked using residual plots (normal probability plot and plot of residuals vs. predicted values).

Results

General Characteristics of the participants

The basic characteristics of the anthropometric measures and DXA measures of 18,263 participants according to the gender are summarized in Table 1. The mean age (± SD) of the participants was 48.336 ± 13.404 years for males and 52.585 ± 14.266 years for females. Males were taller and heavier than females and had a slightly higher BMI (24.704 ± 3.142 vs. 23.013 ± 3.265). Females had higher hip and waist fat percentages than males, especially hip fat percentages (25.587 ± 5.389 vs. 18.840 ± 4.533), and males had higher waist fat percentages than hip fat percentages (26.323 ± 8.115 vs. 18.840 ± 4.533). The average FN BMD was lower than the LS BMD regardless of gender. Both FN BMD and LS BMD were significantly higher in males than in females. Statistically significant differences were found in the above data ($P < 0.001$, Student's t-test).

Table 1
Descriptive statistics of the study population

	Female (n = 9294)	Male (n = 8969)	P[a]
	Mean ± SD	Mean ± SD	
Age (yr)	52.585 ± 14.266	48.336 ± 13.404	< 0.001
Anthropometric measures			
Height (cm)	158.638 ± 5.428	170.660 ± 5.789	< 0.001
Weight (kg)	57.922 ± 8.688	72.037 ± 10.417	< 0.001
BMI (kg/m^2)	23.013 ± 3.265	24.704 ± 3.142	< 0.001
DXA measures			
FN BMD (mg/cm^2)	860.180 ± 154.448	949.037 ± 137.418	< 0.001
HF (%)	25.587 ± 5.389	18.840 ± 4.533	< 0.001
FN T-score(SD)	-0.582 ± 1.287	-0.223 ± 1.057	< 0.001
FN BMC(g/cm)	3.895 ± 0.811	4.998 ± 0.885	< 0.001
LS BMD (mg/cm^2)	1061.114 ± 198.726	1125.387 ± 166.300	< 0.001
WF (%)	29.227 ± 8.818	26.323 ± 8.115	< 0.001
LS T-score(SD)	-0.699 ± 1.656	0.220 ± 1.386	< 0.001
LS BMC(g/cm)	29.840 ± 7.101	37.049 ± 7.140	< 0.001
Values are mean ± SD unless otherwise stated. To convert BMD from mg/cm^2 to BMD in g/cm^2, divide by 1000.			
FN, femoral neck; LS, lumbar spine			
a. Student's t-test.			

As shown in Fig. 1, the FN and LS BMD as well as hip and waist fat percentages varied with age. Both the average hip and waist fat percentages slowly increased with age in women; the former peaked and then declined when the participants were approximately 80 years of age, but the latter reached a plateau when the participants were 60–70 years of age and then decreased. In contrast, there was a general rising trend in the average hip and waist fat percentages with an increasing age in men.

Associations of BMI, hip and waist fat percentage with BMD in each gender

As Table 2 shows, multiple linear regression models were used to calculate the regression coefficients and the P values with BMI (Model 1), hip fat percentage (Model 2) or waist fat percentage (Model 3) as

the predictor variables. In model 1, the associations between BMI and FN BMD appear stronger than those of BMI and LS BMD, particularly for the FN BMD in females. In model 2, the associations between the hip fat percentage and the LS BMD appeared stronger than those of the hip fat percentage and FN BMD in both females (-0.179 vs. -0.068) and males (-0.138 vs. -0.095), especially for females (-0.179). In model 3, the associations between the waist fat percentage and FN BMD were stronger than those of waist fat percentage and LS BMD in both females (-0.055 vs. -0.039) and males (-0.111 vs. -0.033), particularly for males (-0.111).

Table 2
Regression coefficients of models with BMI (kg/m2), HF (%) or WF (%) as the predictor variable for lumbar spine and femoral neck BMD (mg/cm2)

	Female		**Male**	
	β	**R_{adj}^2**	**β**	**R_{adj}^2**
FN BMD				
Model 1	0.319*	0.456	0.298*	0.232
Model 2	-0.068*	0.459	-0.095*	0.238
Model 3	-0.055*	0.458	-0.111*	0.238
LS BMD				
Model 1	0.197*	0.366	0.165*	0.056
Model 2	-0.179*	0.387	-0.138*	0.070
Model 3	-0.039**	0.366	-0.033***	0.056
Model 1: BMI				
Model 2: HF (%), the hip fat percentage				
Model 3: WF (%), the waist fat percentage				
β: standard regression coefficient				
* P < 0.001, ** P < 0.01, ***P < 0.05 compared with the corresponding linear regression model.				
Covariates adjusted in both linear regression and GAM included age, weight (for models 2 and 3 only), and height.				
Linear regression analysis with BMD as the dependent variable and BMI (Model 1), HF (%) (Model 2) or WF (%) (Model 3) as the predictor variable.				

The dose-response relationships of the BMI (Model 1), hip fat percentage (Model 2) or waist fat percentage (Model 3) with the BMD in each gender using generalized additive models are presented in

Fig. 2. There was a positive relationship between the BMI and FN BMD or LS BMD in both males and females, but the associations appeared weaker with higher BMI values. For females, a negative relationship between the hip fat percentage and the LS BMD was apparent, whereas the FN BMD increased at lower values of hip fat percentage and decreased at higher values of hip fat percentage. For males, the negative relationship between waist fat percentage and FN BMD was stronger than those of the hip fat percentage and FN BMD. Nevertheless, both hip fat percentage and waist fat percentage were not strong predictors of the LS BMD in males. The percentage of variation in the BMD measures was apparently higher in females than in males (adjusted R^2: 0.368–0.466 vs. 0.058–0.246). Overall, the percentage of variation in the BMD measures explained by the GAM was slightly higher than those of the linear regression models (Table 2), indicating that the relationships were better represented by the GAM.

Associations of age, hip and waist fat percentage with the odds of low BMD in each gender

As Fig. 3 depicts, multiple logistic regression analyses showed that the risk for low BMD linearly increased across increasing regional fat percentage quartile categories (p for trend < 0.05) after adjusting for confounders, including age, height and BMI. Regarding the location of the body from which the BMD was measured, the risk of low LS BMD was significantly higher in the highest quartile of hip fat percentages than in the lowest quartile in females. The ORs for low LS BMD were 3.095 (95% CI, 2.618–3.658) for hip fat percentage and 1.532 (95% CI, 1.271–1.848) for waist fat percentage. For males, the risk of low FN BMD was significantly higher in the highest quartile of waist fat percentage than in the lowest quartile. The ORs for low FN BMD were 2.211 (95% CI, 1.831–2.670) for waist fat percentage and 1.998 (95% CI, 1.694–2.355) for hip fat percentage.

Discussion

The role of body composition on bone health has been extensively investigated, but the results regarding the effect of fat mass on the BMD have been controversial. In this study of adult Chinese individuals, we found that BMI has shortcomings as a predictor of the BMD because it does not separate lean mass from fat mass and does not explore the influence of the fat distribution on the bone mass. Therefore, we modelled the effect of the regional fat content on the bone mineral density in a large sample size within a healthy population. Our results showed that overall, there was a negative relationship between the regional fat percentage and the FN BMD or the LS BMD in both males and females. Moreover, the tendency and magnitude of this effect depended on the gender, fat content/distribution and bone site.

Our results revealed that the associations between BMI and FN BMD appear stronger than those of BMI and LS BMD in both females and males. A previous study showed that an increasing BMI tended to reduce the risk of hip fractures and the prevalence of vertebral deformity[13]. When the fracture risk was adjusted for the BMD, the BMI appeared to be a predictor only for hip fracture[14]. This might be attributed to the fact that cortical bone rather than trabecular bone is preferentially affected by obesity[15].

In this study, we confirmed that the regional fat content was negatively associated with the BMD in males and females using multiple linear regression models. To further investigate the dose-response relationship between the regional fat content and the BMD, generalized additive models were performed. In females, the data from our study showed that the relationship between the regional fat percentage and the two-site BMD appeared to be n-shaped, indicating that the effect of the regional fat percentage on the BMD is nonlinear. According to these data, we may infer that an increase in the regional body fat is weakly protective against bone loss, but this effect becomes detrimental as we move towards morbid obesity. This suggests that body fat accentuates the mechanical loading on the skeleton and subsequently increases bone mass to a certain extent[16], while morbid obesity induces systemic inflammation due to several conditions, such as metabolic syndrome or insulin resistance, thereby impairing the balance of the body composition, which leads to bone loss[17]. Our results seem consistent with the conclusion from Kim[18] who claimed that overweight may be protective against hip fractures in Asian adults but not morbid obesity, particularly in women. Regardless, more evidence is needed to draw a firm conclusion. For the regional fat content on the BMD in males, the association curve was comparatively complex. Generally, bone mass tends to decline according to the increase in the regional fat percentage. The mechanisms accounting for this association may be, for instance, that the increase of the fat tissue causes the transformation of more androgens into estrogens. Male bone loss is due to decreased circulating androgen, which is necessary for bone health[19]. It was also reported that androgens are solely responsible for normal trabecular bone growth in males[20]. Considering the literature shown above, our study revealed that the more fat tissue is in males, the more bone loss will occur.

Interestingly, through multiple linear regression models, we found that the associations between the hip fat percentage and the LS BMD appeared stronger than those of the hip fat percentage and the FN BMD in both females and males, especially for females, while the associations between the waist fat percentage and the FN BMD were stronger than those of the waist fat percentage and the LS BMD in both females and males, particularly for males. Additionally, in our multiple logistic regression analyses, we obtained similar results; that is, the risk of low LS BMD was most significant in the participants in the highest quartile of hip fat percentage for females, whereas the risk of low FN BMD was most significant in the highest quartile of waist fat percentage in males. These results were supported by a prospective cohort study from Norway of 23,061 men aged 60 to 79 years. In this study, men in the highest tertile of waist circumference had a 100% higher risk of hip fractures than men in the lowest tertile, which means that abdominal adiposity considerably increased the risk of hip fractures[21]. In another cross-sectional study of 1,011 participants aged 50–80 years, it was reported that women who had at least one vertebral deformity had a greater percentage of trunk fat than women without vertebral deformities[22], which was also consistent with our findings above. Altogether, we may infer that there existed a cross-influence between the regional fat content and the bone mineral density. This result may pave the way for the development of predictive health education that is suitable for clinical practice, which means that men should care more about their waist circumference and avoid abdominal adiposity, while women should pay more attention to their hip circumference. Actually, not all fat depots are the same: site-specific

effects rather than simply total body fat may be crucial in the assessment of the impact of obesity on the BMD[23].

Osteoporosis and obesity, which superficially have no obvious connection, share a common denominator, including a genetic predisposition and a common progenitor cell. Thus, several underlying mechanisms have been proposed to elucidate the harmful effect of fat tissue on bone health. At the molecular genetics level, a genome-wide bivariate analysis of Caucasians of European origin identified some suggestive shared genomic regions for both body fat mass and BMD, therefore implying that those two diseases might be influenced by some shared candidate genes or mutual crosstalk between their phenotypes' gene regulatory networks[24]. At the cellular level, adipocytes and osteoblasts have common progenitor cells, mesenchymal stem cells (MSCs). A shift of the cell differentiation of MSCs to adipocytes rather than osteoblasts will hinder osteogenesis and will consequently result in bone loss[25]. Apart from the causations mentioned above, several adipokines, which are secreted by adipocytes, including adiponectin and leptin, have shown a negative effect on bone metabolism. Serum adiponectin is reported to be inversely correlated with the BMD in both males and females by inhibiting osteoblast proliferation and promoting apoptosis, altogether decreasing bone formation levels[26–28]. Leptin has a detrimental effect on bone formation mainly via the central nervous system, which appears to be mediated by the decreased production of serotonin in hypothalamic neurons[29, 30].

This study also has limitations mainly because it was a retrospective study, and any changes in the sex hormones and adipocytokines were not examined. Therefore, whether these changes are involved in the interactions is still unclear.

In conclusion, there is a cross-influence between the regional fat content and the bone mineral density. The mechanism by which the regional fat content exerts a cross-harmful effect on the hip/lumbar bone mass in females and males is not yet well known. Additional perspective and interventional studies are needed to unravel these gender- and location-dependent mechanisms in this area of study.

Declarations

Acknowledgement

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Ethical approval

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Soochow University (JD-LK-2018-074-01).

Conflicts of Interest

The authors have no conflicts of interest to declare.

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Figures

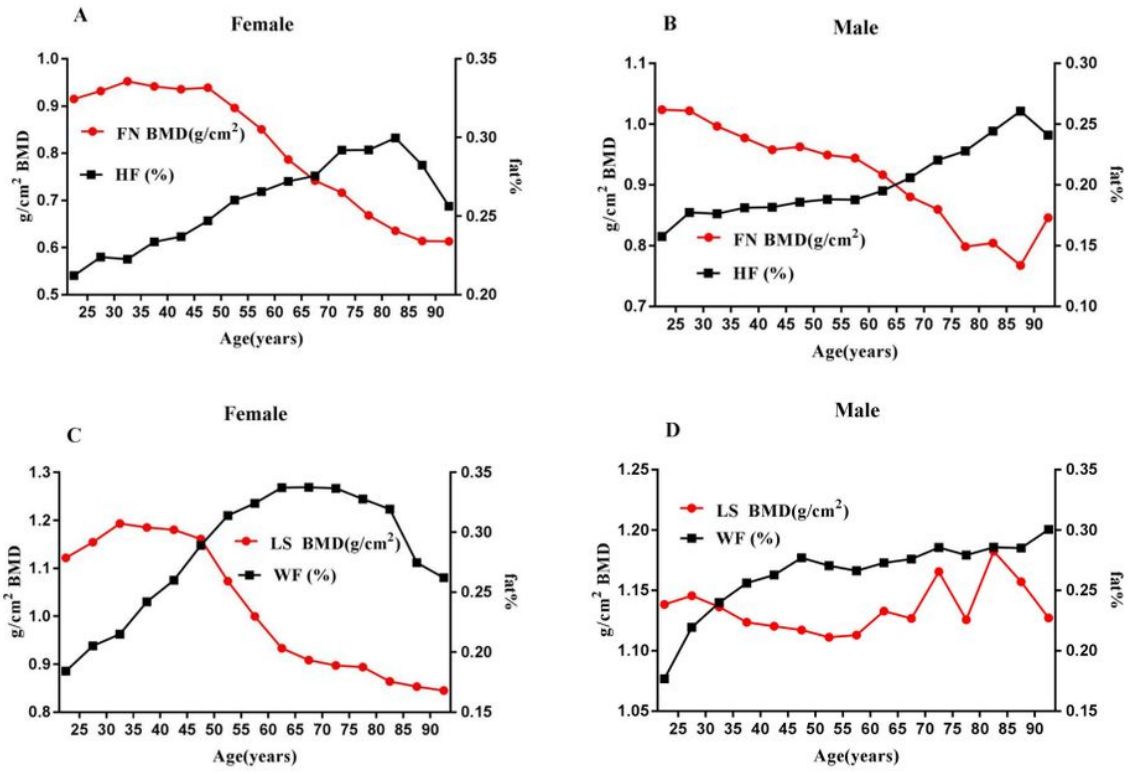

Fig. 1. Curve of FN BMD, LS BMD and regional fat content with age in different genders

Figure 1

See image above for figure legend.

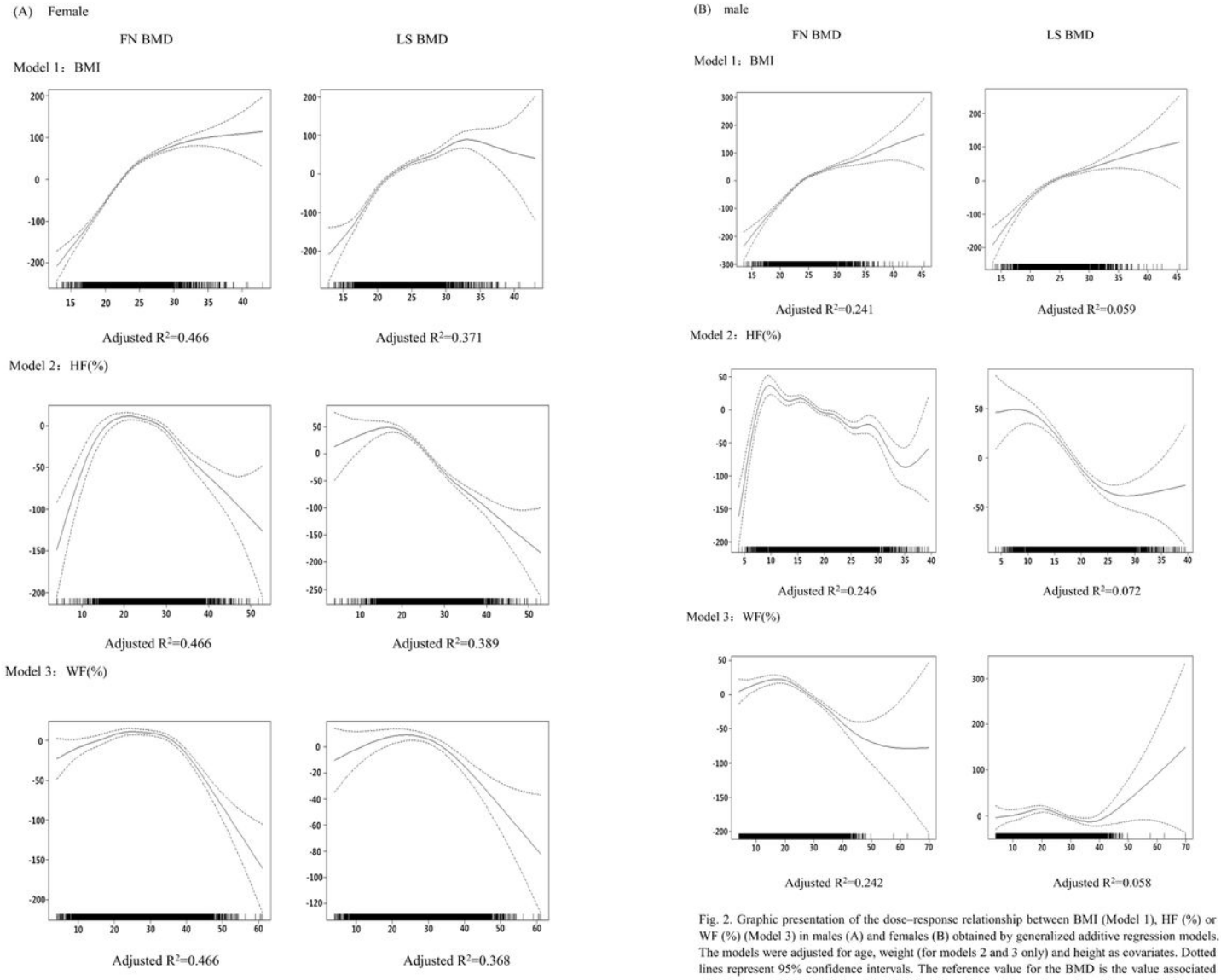

Fig. 2. Graphic presentation of the dose–response relationship between BMI (Model 1), HF (%) or WF (%) (Model 3) in males (A) and females (B) obtained by generalized additive regression models. The models were adjusted for age, weight (for models 2 and 3 only) and height as covariates. Dotted lines represent 95% confidence intervals. The reference value for the BMD is the value associated with the mean BMI, HF (%) or WF (%) for all participants in each gender. The rug plot along the bottom of each graph depicts each observation.

Figure 2

See image above for figure legend.

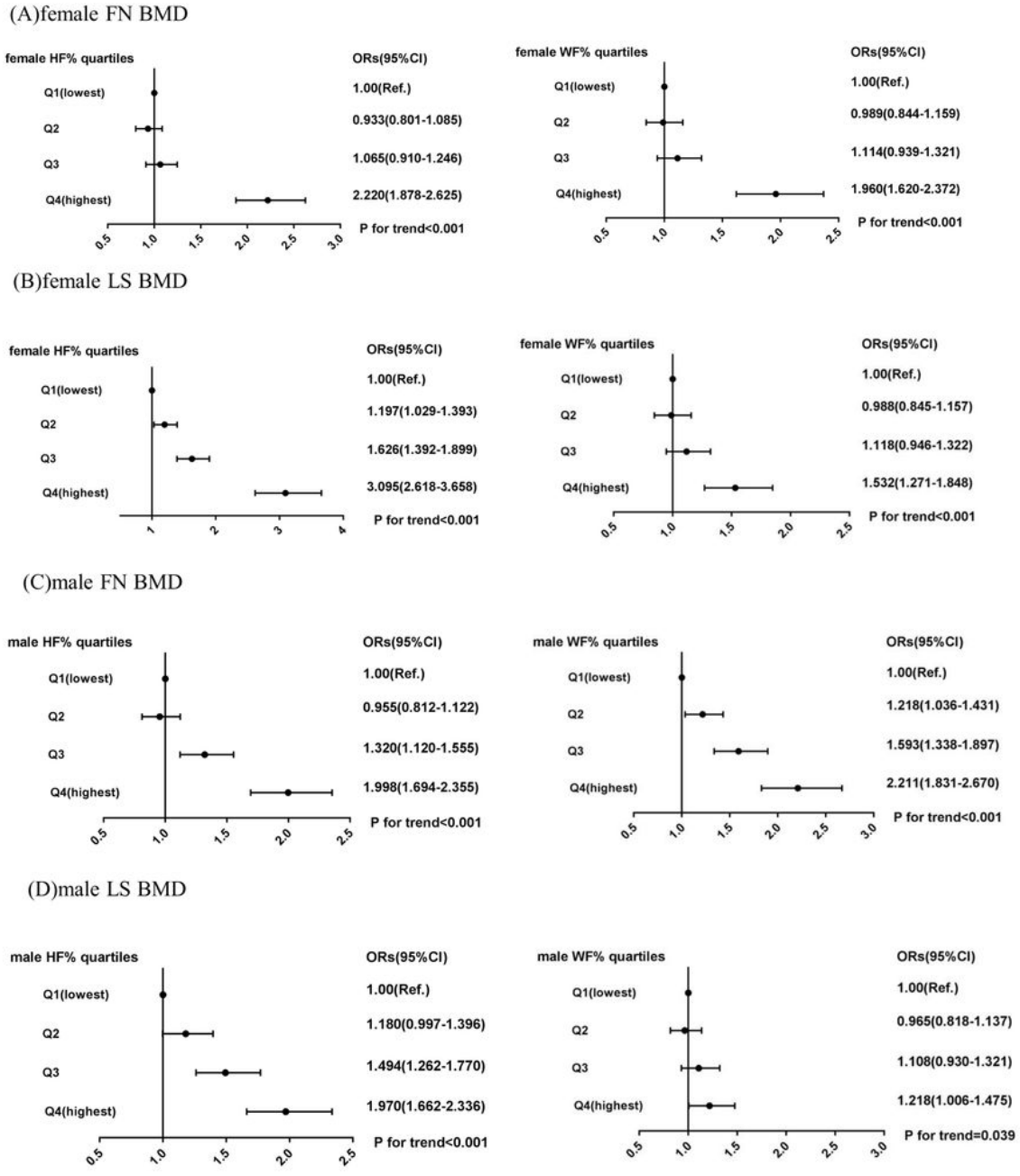

Fig. 3. Risk of low BMD (T-score <-1.0) across quartiles of male HF (%), male WF (%), female HF (%), and female WF (%). (A) female FN BMD. (B) female LS BMD. (C) male FN BMD. (D)male LS BMD. ORs (95% CI) were calculated using multivariate logistic regression after adjusting for age, height and BMI; OR, odds ratio; CI, confidence interval.

Figure 3

See image above for figure legend.