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## The association between BMI and QCT-derived proximal hip structure and strength in older men: a cross-sectional study

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### Abstract

Although higher body mass index (BMI) is associated with higher bone mineral density, recent evidence indicates that increased BMI may not be consistently associated with reduced hip fracture risk. Moreover, substantial proportions of hip fractures occur among overweight and obese men and women. The role of increased BMI and obesity on bone density, structure, and strength at the hip is not well understood.

We conducted cross-sectional analyses between BMI and various density and structure measures derived from quantitative computed tomography (QCT)-scans of the proximal femur, in 3067 men (mean age: 73 y) from the Osteoporotic Fractures in Men Study (MrOS). Finite element (FE) analysis of hip QCT scans was performed for a subcohort of 672 men to provide a measure of femoral strength for a simulated sideways fall. The impact force was estimated using patient-specific weight and height information. Multivariable general linear models were used to examine the associations between BMI and hip QCT measures.

The relationship of BMI with hip QCT measures was significantly different between men categorized as non-obese and obese ( $P$  for interaction = 0.014). For non-obese men ( $BMI < 30$ ), increasing BMI was associated with higher integral, cortical and trabecular vBMD, integral volume, cross-sectional area, and percent cortical volume (all  $p < 0.001$ ). For obese men ( $BMI \geq 30$ ), increasing BMI was not associated with any of those parameters. In addition, compared to non-obese men, obese men had a higher hip strength, but also a higher ratio of impact force to strength ( $P < 0.0001$ ), in theory increasing their risk of hip fracture despite their increased strength. These results provide a better understanding of hip fracture risk in obese men.

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## Keywords

men; obesity; hip fracture risk; hip structure; hip strength

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## Introduction

While obesity is a well-established risk factor for many chronic diseases, it is generally believed that individuals with higher body mass index (BMI) have a low risk of osteoporosis, in part due to their increased bone mineral density (BMD) <sup>1,2</sup>. However, fracture in obese individuals remains a public health concern <sup>3</sup>. The relationship between obesity and fracture is complex and not well understood. While there are some evidence showing that increases in BMI is associated with reduced risk of fracture <sup>4,5</sup>, more recent studies suggest obesity is not protective and may increase risk for fracture. A study of postmenopausal women with low-trauma fracture reported a high prevalence of obesity despite the fact that BMD was normal in most of the fracture cases <sup>6</sup>. Likewise, among middle aged men, higher waist circumference has been linked to increased risk of hip and wrist fracture <sup>7</sup>. In a large cohort of elderly men, we observed that a substantial proportion of hip and non-spine fractures occur among overweight or obese men <sup>8</sup>. The recent meta-analysis of the association of fracture risk and BMI that was comprised of 398,610 women from 25 countries demonstrated that when adjusted for BMD, high BMI was a risk factor for all osteoporotic fractures<sup>9</sup>. In view of this, understanding the relationships of skeletal strength and the mechanisms of fracture in obese individuals should provide insights for improving preventive and therapeutic approaches for obese populations.

Bone structure and the relative amount of bone in the cortical and trabecular compartments contribute to femoral strength <sup>10</sup>. Evaluations of bone structure <sup>11–13</sup> and strength <sup>14–17</sup> provide mechanistic insight into the etiology of hip fracture. Measures of femoral structure from hip structure analysis (HSA) using DXA scans and measures of distal radius/tibia strength from finite element analysis using peripheral QCT scans are reduced relative to body weight in overweight and obese older women<sup>18,19</sup>. However, these associations have not been studied in men, and hip structural analysis from DXA is not as refined for analysis of femoral strength as is finite element analysis of CT scans <sup>20</sup>. The purpose of this study was to investigate the associations between BMI and QCT-derived hip bone density and structural measurements and to further evaluate the association of BMI with finite element-estimated hip strength and load to strength ratio in older men participating in the Osteoporotic Fractures in Men Study (MrOS). We hypothesized that obesity may have deleterious effects on bone structure or volumetric BMD, and that in the obese bone strength may not be sufficient to protect against the increased impact force exerted on bone during a fall.

## Materials and methods

### Subjects

MrOs is a prospective cohort study designed to determine risk factors for fracture in men aged 65 years and older. The design and recruitment have been previously described <sup>21,22</sup>.

Briefly, 5994 community-dwelling, ambulatory men were recruited from six US academic medical centers (Birmingham, AL, Minneapolis, MN, Palo Alto, CA, Pittsburgh, PA, Portland, OR, and San Diego, CA) from March 2000 through April 2002. Eligible participants were at least 65 years old, able to walk without assistance from another person, and had not had bilateral hip replacement surgery. The institutional review board at each study site approved the study and written informed consent was obtained from all participants.

### Analytic Sample

A total of 3785 participants (63% of MrOS) were referred for QCT scans as previously reported<sup>23</sup>. Of these, 122 were not eligible for hip scan because of hip replacement and 103 hip scans were not available for processing because they were lost or corrupted during data transfer, leaving 3560 hip scans available for processing. Of the initial 3560 hip scans available for processing, 133 failed image processing for various reasons<sup>23</sup>. A total of 3427 with complete data for femoral neck integral BMD was included in these analyses. We excluded men reporting the use of osteoporosis medications, inhaled or oral corticosteroids and hormone therapy (n=354) or having missing BMI or BMI < 18.5 (n=6). Thus, a sample of 3067 men formed the analytic sample for the association analyses with QCT measures.

Finite element (FE) analysis was performed in QCT scans selected with a stratified sampling plan. Baseline QCT scans was selected at random for 384 men. In addition, FE was performed in baseline QCT for all remaining 378 men from Portland and Birmingham sites whose scans had not been selected for the random sample. Eighty-eight men were excluded for reporting the use of osteoporosis medications, corticosteroid, or androgens, and two men were excluded for having missing BMI measurements or low BMI < 18.5, leaving a total of 672 men for the analyses of FE measures.

### Baseline characteristics

Height was measured on Harpenden stadiometers and weight on standard balance beam or digital scales, with participants wearing light clothing without shoes. Body mass index (BMI) was calculated as weight (kilograms) per square height (meter). Subjects were classified as normal weight (BMI: 18.5 to < 25 kg/m<sup>2</sup>), overweight (25 to < 30 kg/m<sup>2</sup>), obese ( $\geq$  30 kg/m<sup>2</sup>), using World Health Organization categories of BMI. Demographic, lifestyle factors including smoking status and alcohol intake, medical history were obtained from standardized questionnaires. Physical activity level was assessed with the Physical Activity Scale for the Elderly (PASE)<sup>24</sup>. Dietary calcium and vitamin D were assessed using a modified Block Food Frequency Questionnaire<sup>25</sup>. A computerized dictionary, based on the original Established Populations for Epidemiologic Studies of the Elderly (EPESE) coding system<sup>26</sup> was used to categorize medications. All prescription medications validated by the clinics were recorded in an electronic medication inventory database (San Francisco Coordinating Center, San Francisco, CA). Each medication was matched to its ingredients based on the Iowa Drug Information Service (IDIS) Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA).

## DXA and QCT scanning

DXA BMD ( $\text{g}/\text{cm}^2$ ) was measured in using fan-beam DXA (QDR 4500W, Hologic Inc., Waltham, MA, USA) and using standardized procedures and centralized quality control procedures<sup>22</sup>. Hip QCT scans were obtained from the femoral head to 3.5 cm below the lesser trochanter at settings of 80 kVp, 280 mA, 3-mm slice thickness, and  $512 \times 512$  matrix in spiral reconstruction mode. Scanner models used at the sites were described<sup>23</sup>. Calibration standards with known hydroxyapatite concentrations (150, 75, and 0  $\text{mg}/\text{cm}^3$ ; Image Analysis) were included in each scan<sup>23</sup>.

## QCT-derived femoral measures

Image processing was described previously<sup>23</sup>. Briefly, regions of interest (ROIs) in the left proximal femur were identified in the QCT images reformatted along the centroidal axis of the femoral neck. The femoral neck ROI was defined as at the portion of the neck extending from the slice with minimum cross-sectional area (medial boundary) to a point 25% of the proximal distance of the neck axis length toward the maximal cross-sectional area. Within this femoral neck ROI, the following measures were obtained. The cross-sectional area ( $\text{cm}^2$ ) was computed as the area within the periosteal boundary at the minimum cross-section. Integral volume ( $\text{cm}^3$ ) was computed as the total volume within the periosteal boundary. The cortical volume was defined by applying a threshold of 0.35  $\text{g}/\text{cm}^3$  to all voxels between the periosteal boundary and the internal trabecular bone. Medullary volume was computed by subtracting the cortical volume from the integral volume. The percent cortical volume was computed as cortical volume divided by integral volume times 100. Volumetric BMD was computed over all voxels in the integral, trabecular, and cortical volumes.

## Estimation of femoral strength and the load-to-strength ratio ( $\Phi$ )

FE analyses were performed as described previously<sup>17,16</sup>. Briefly, FE models were created to simulate a fall to the side of the hip, the diaphysis angled at  $15^\circ$  with respect to the ground with  $15^\circ$  of internal rotation. This represents a severe, unprotected, fall to the side of the hip, which is known to be associated with a high risk of fracture. Strength was calculated from the resulting nonlinear force–deformation curve as the force at 4% deformation of the femoral head with respect to the greater trochanter. The load-to-strength ratio ( $\Phi$ ) was calculated for a simulated sideways fall orientation and impact directly on the greater trochanter. The *in vivo* impact force (the “load”) on the side of the trochanter was estimated for each subject from biomechanical theory using patient-specific weight and height information. A uniform value of trochanteric soft-tissue thickness was assumed for all men. The resulting expression for the load-to-strength ratio was directly proportional to patient mass and the square root of patient height and was inversely and non-linearly proportional to the FE-derived strength<sup>27</sup>. Theoretically, if the *in vivo* impact force is correctly calculated for each patient, when  $\Phi \geq 1$ , a fracture is predicted to occur, whereas no fracture is predicted when  $\Phi < 1$ <sup>27</sup> regardless, higher values of  $\Phi$  denote a greater risk of fracture.

## Statistical Analyses

We compared the baseline characteristics of men across BMI category using ANOVA tests for continuous variables or chi-square tests for categorical variables. To examine the association between BMI and hip QCT measures, we used multivariable general linear models (GLM) to estimate least square (LS) means of each QCT outcome variable by BMI categories and performed linear trend tests. To test our hypothesis of differential associations of BMI with QCT parameters between non-obese and obese individuals, we specifically evaluated the interactions between obesity and BMI, and stratified obese status to assess the relationships between BMI and QCT parameters expressed as SD change per unit increase of BMI in each stratum. We generated Loess curves to further visualize the nonlinearity in the associations between BMI and QCT measurements. A logistic regression model was used to evaluate the OR and 95% CI of having a theoretical biomechanical fracture threshold (defined as a load-to-strength ratio  $>1.0$ ) according to obese status. Covariates for all analyses included age, race, enrollment site and physical activity. Other potential confounders included calcium and vitamin D intake, baseline history of diabetes and fracture after age 50 and were assessed by their change in the associations between BMI categories and each QCT and FE measures by 10% or more. A two-tailed alpha of 0.05 was used.

Because of two different sampling strategies involved in FE samples, we first evaluated potential sampling effect on the associations. We examined the associations of BMI with FE strength and load-to-strength ratio in the random sample and the sample from Portland and Birmingham sites separately (Supplemental table 1a and 1b), and then compared the point estimates from two samples. We found no significant difference of point estimates for both strength and load-to strength ratio between two samples ( $P$  for interaction  $> 0.05$ ) (Supplemental table 1c). We further evaluated the associations between BMI and FE-derived biomechanical measurements stratified by obese status in the random sample and the sample from Portland and Birmingham sites separately (Supplemental table 2a and 2b). The point estimates were compatible between the two samples. Thus the two samples were combined for the association analyses, and results from the combined samples were presented.

## Results

Baseline characteristics of the 3067 men included in these analyses are presented in Table 1. Compared to men in lower BMI categories, those in higher BMI categories were younger and physically less active and had lower intakes of calcium and vitamin D. A greater proportion of obese men reported poor health status in general and had a history of chronic diseases than did men in lower BMI categories. There was no difference in race, smoking status and alcohol consumption across BMI categories.

All bone density and geometry parameters at the femoral neck were significantly different across BMI categories adjusted for age, race and clinical center (Figure 1). Compared with normal weight men, those who were overweight or obese had greater volumetric and areal BMD, greater total bone size (minimal cross-sectional area and integral volume) and cortical thickness (percent cortical volume).

The associations between BMI and QCT measures (except for medullary volume) were nonlinear as shown in Supplemental figure 1 (Loess curve of femoral neck integral vBMD and percent cortical volume are shown as examples), and were significantly different between non-obese and obese men (Table 2) ( $P$  for interaction  $\leq 0.014$ ). For men with BMI  $< 30$ , there was a linear relationship between BMI and most QCT measures. In those men, increasing BMI was associated with higher integral, cortical and trabecular vBMD, integral volume, cross-sectional area, and percent cortical volume (SD increase per unit of BMI: 0.05 for integral vBMD, 0.042 for cortical vBMD and 0.002 for trabecular vBMD, 0.027 for integral volume, 0.03 for cross-sectional area and 0.042 for percent cortical volume, all  $P < 0.001$ ). However, among men with BMI  $\geq 30$ , increasing BMI was not associated with further increases in those parameters. Although increasing BMI was associated with increases in areal femoral neck DXA BMD for both non-obese and obese men, the increment in femoral neck BMD per unit increase in BMI was less for obese men than for non-obese men (SD increase per unit of BMI: 0.035 for obese men vs 0.105 for non-obese men,  $P$  for interaction  $< 0.0001$ ). Inclusion of potential confounders had no substantial effect on these associations.

FE analyses suggested there was a statistically significant linear trend for increasing hip strength from the normal to the obese categories (Figure 2A). Compared to normal-weight men, obese men had higher strength (mean: 6130N vs 5300N,  $P < 0.0001$ ). However, there was also a higher load-to-strength ratio in obese men (mean: 0.79 for obese men vs 0.66 for the normal weight,  $P < 0.0001$ ) (Figure 2B). The increment in femoral strength per unit increase in BMI for obese men was not significantly different from that for non-obese men (SD increase per unit BMI:  $-0.03$  vs  $0.06$ ,  $P$  for interaction  $= 0.36$ ) (Table 3). Similarly, there was no significant difference of the increment in load-to-strength ratio between obese and non-obese men (SD increase per unit BMI: 0.14 vs 0.1,  $P$  for interaction  $= 0.99$ ) (Table 3). Further, using the load-to-strength ratio  $= 1.0$  as a theoretical value of the fracture threshold, 24% in the obese vs 14% in the non-obese had a load-to-strength ratio greater than the threshold. Obese men were 4 times more likely to have a load-to-strength ratio  $> 1.0$  compared to normal-weight men (OR: 4.66; 95% CI: 2.16–10.05;  $P < 0.0001$ ).

## Discussion

In this cross-sectional analysis of BMI and QCT-derived structural and densitometric measures of proximal femur in older men, the relationship between BMI and hip QCT measures was significantly different between men categorized as non-obese and obese. Whereas for non-obese subjects, BMI was associated with a linear increase in femoral neck volumetric BMD, percent cortical volume, and minimal cross-sectional area, for obese men there was no further increase in these measures as BMI increased. Furthermore, compared to normal-weight men, obese men had higher hip strength but also higher load-to-strength ratio, suggesting that in obese men increments in strength with increased BMI might not be sufficient to counter the higher forces involved in a fall.

In theory, individuals with high BMI may accrue more bone and greater bone strength to support a greater body mass<sup>1,2</sup>. In fact, in this study men meeting the criteria for obesity based on their BMI did have greater femoral neck volumetric BMD, bone size and cortical

thickness compared to the overweight and normal weight men. However, the relationship of increasing BMI with progressive increases in those QCT measures appeared to reach a plateau at BMIs of 30 kg/m<sup>2</sup>, with no additional increment in those QCT parameters with further increases in BMI. Previous studies of older women also found that relative to their body weight, heavier individuals have lower BMD and weaker radial and tibial geometry compared to those with normal weight <sup>18</sup>. Together, these findings provide evidence that increments in hip BMD and structural elements in the older obese men are not commensurate with their higher weight. Because these QCT-derived structural and densitometric parameters have been shown to significantly affect bone strength <sup>10,28–31</sup> and are associated with hip fracture risk independent of areal BMD <sup>11</sup>, our findings may have some important implications for understanding the pathophysiology of hip fracture in subjects with high BMI. In addition, our finding could be of clinical importance regarding fracture prediction. The FRAX algorithm uses a series of clinical risk factors, including BMI as a continuous variable, to calculate fracture risk <sup>32</sup>. It has been noted that FRAX may underestimate fracture probability in obese individuals and thus the US-based FRAX-based intervention thresholds (eg, >20% probability of a major osteoporotic fracture or >3% probability of hip fracture in the following 10 years) may be too high for obese subjects <sup>33</sup>. Therefore, incorporating the non-linear association of BMI with bone measures in FRAX model may improve the identification of individual at risk for fracture in the obese populations.

In our study, increasing BMI was associated with progressive increase in QCT measures in non-obese men, but that positive association of BMI appears to reach plateau in the men categorized as obese, in whom there was not a continuing improvement in bone density and structural parameters with increasing BMI. Although we didn't observe significant deleterious effect of obesity on bone structure or volumetric BMD, our finding provides support that adiposity in obese individual may not be beneficial to bone health. The beneficial effect of fat mass on bone is to some extent mediated through its mechanical loading and hormones secreted from either the pancreatic beta cell or the adipocyte <sup>1,2</sup>. However, both experimental and human studies have suggested the inverse relationship between fat, in particular visceral fat, and BMD<sup>34,35</sup> and that adipocyte-derived adipokine, chemokines and cytokines may impair bone remodeling processes <sup>36</sup>. A recent study in obese men reported that those with high visceral adipose tissue had weak QCT-derived microarchitecture and mechanical properties compared with those with low visceral adipose tissue <sup>37</sup>. Another study reported that when the mechanical loading effect of body weight is statistically removed, higher body fat mass is correlated with lower bone mass <sup>38</sup>. Moreover, although weight loss overall may lead to greater bone loss <sup>39,40</sup>, there is evidence that the loss of fat mass in particular may increase BMD <sup>41</sup> and bone strength<sup>42</sup>, supporting the negative impact of fat mass on bone. Our findings, together with evidence from these other reports, suggest that adverse effects of excess fat in the obese may outweigh the benefit of increased mechanic loading on bone density and structure <sup>34</sup>. On the other hand, lean mass is associated with high BMD and bone strength <sup>43,44</sup>. Because lean mass is progressively smaller fraction of total mass as BMI increases <sup>18</sup>, reducing lean mass relative to total body mass in the obese may also explain no additional benefit on QCT measures with increasing

BMI among obese men in our study. Finally, obese men have more medical conditions, and more limited activity, that may impair the potential to respond to mechanical stimuli.

FE analysis of hip QCT scans showed that both hip strength and load-to-strength ratio increased with increasing BMI. That trend seemed to be similar in men categorized as obese and non-obese, although the power to detect differences in this relationship between obese and non-obese men may have been limited due to the relatively fewer men with FE analyses than in the full cohort. However, it was clear that the load-to-strength ratio was higher in obese men. In fact, compared to non-obese men, a high proportion of obese men had load-to-strength ratios greater than the theoretical biomechanical fracture threshold  $^{27}(\Phi=1.0)$  (24% in the obese vs 14% in the non-obese). Those findings suggest that in obese men the increase in strength with increasing BMI might not be sufficient to compensate for fall forces that increase in direct proportion to body weight. As a result, obese individuals may be more likely to suffer fracture with a sideways fall.

Our study has several strengths. It is the first evaluation of volumetric and structural properties derived from hip QCT scans across BMI categories in a large population of older men. Analysis of QCT scans provides a more accurate assessment of hip structural characteristics than does HSA analysis of DXA images  $^{45}$ . Moreover, biomechanical analysis using FE provides an estimate of femoral strength in a clinically relevant type of fall  $^{17}$ , the load-to-strength ratio accounts for subject-specific estimates of force encountered by the hip in a fall, and FE-derived femoral strength and load-to-strength ratio also predict hip fracture $^{16,17}$ .

Our study also has several limitations. It has been estimated that alteration of body composition can result in artifacts in the assessment of BMD by both DXA and QCT  $^{46}$ , but the impact of changes in body composition on QCT seems to be small  $^{47}$ . A recent study using simulated increases in body fat suggested that whereas fat layering introduces error and decreases the reproducibility of both DXA and QCT BMD measurements, the error in QCT is smaller and more uniform than with DXA  $^{47}$ . However, the extent to which excess fat tissue in obese individuals influence the quality of QCT image remains unclear. In addition, proximal femur QCT scans in our study were obtained at a relatively low energy dose which may increase the possibility of image artifacts in participants with large body mass. Our estimates of the hip impact force did not account for any patient-specific variations in cushioning effects of trochanteric fat thickness, and instead assumed a constant value of trochanteric fat thickness for all subjects, which may have led to a relative overestimation of the load-to-strength ratio in overweight and obese men, who presumably have higher values of trochanteric fat tissue. While increased fat thickness should reduce the impact force to some degree, however, it is not clear if very large values of fat thickness add any further cushioning or protective effect $^{48,49}$ . Future studies are needed to incorporate real fat thickness measurements, and the associated biomechanics, into these analyses. Different sampling strategies involved in FE sub-cohort may bias the association of FE measures with BMI. Also, although BMI is widely used and accepted method to define obesity, it is not a precise measure of excess body fat and does not reflect fat distribution, particularly among older population. Future study using more precise assessment of body fat, such as QCT measures, may better characterize the relationship between obesity and hip structures. In

addition, the cross-sectional design of the study makes it impossible to assess causality in the observed associations. Finally, our participants were older men, and most were of European ancestry. The generalizability of our findings to older women, other races /ethnic groups or younger populations is unknown.

In conclusion, the relationships between BMI and femoral BMD and structure appear to be nonlinear and are different between men categorized as non-obese and obese. In non-obese men, increasing BMI is associated with increasingly greater bone size, cortical thickness and cortical and trabecular BMDs. In individuals with BMI levels in the obese range, there is no further increase in those volumetric and structure parameters with additional increases in BMI. FE analyses suggest that the increase in strength is not proportionate with increased impact force in obese men. Our data provide some insight into the relationship between skeletal structure and strength and hip fracture risk in obese men.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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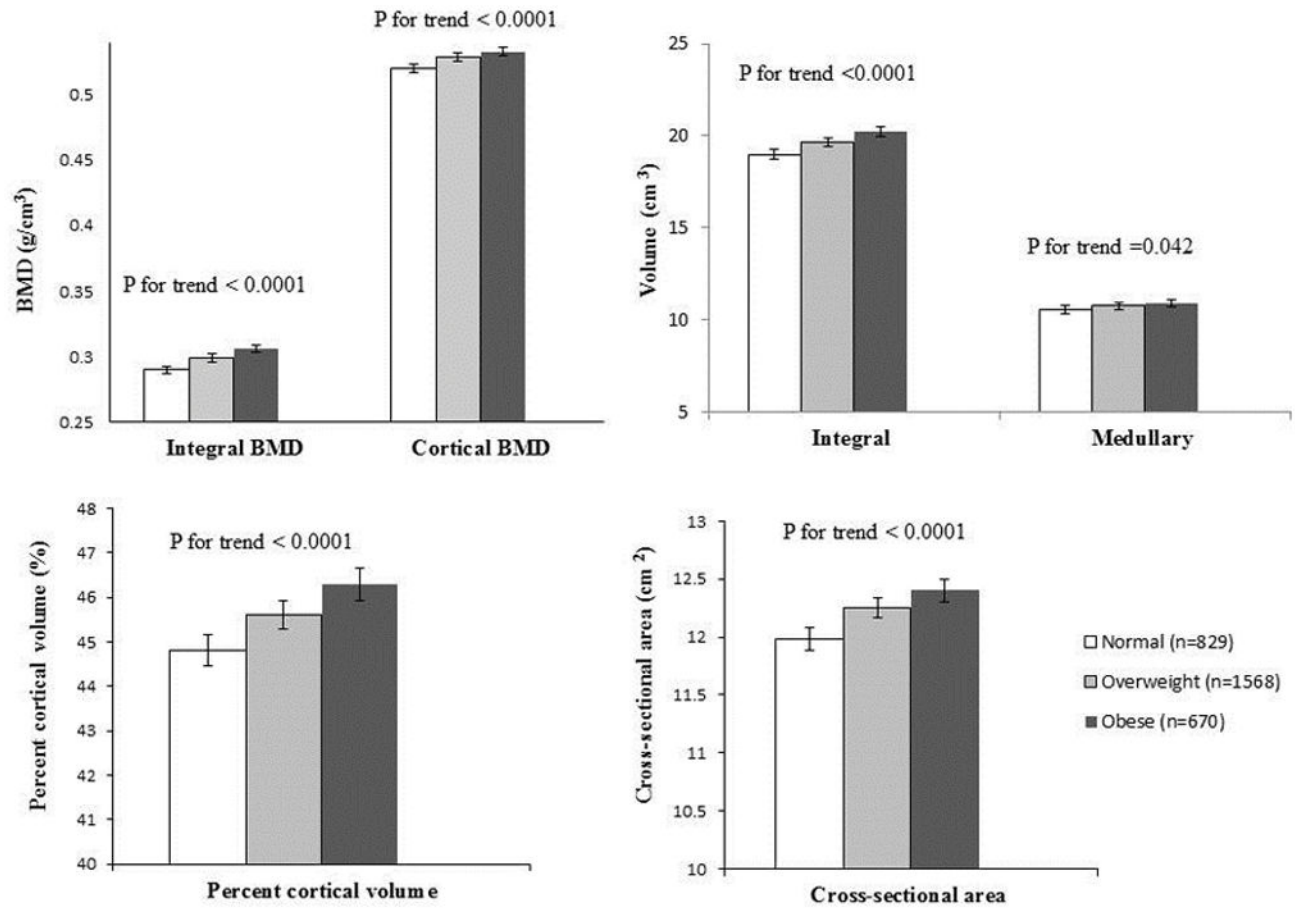
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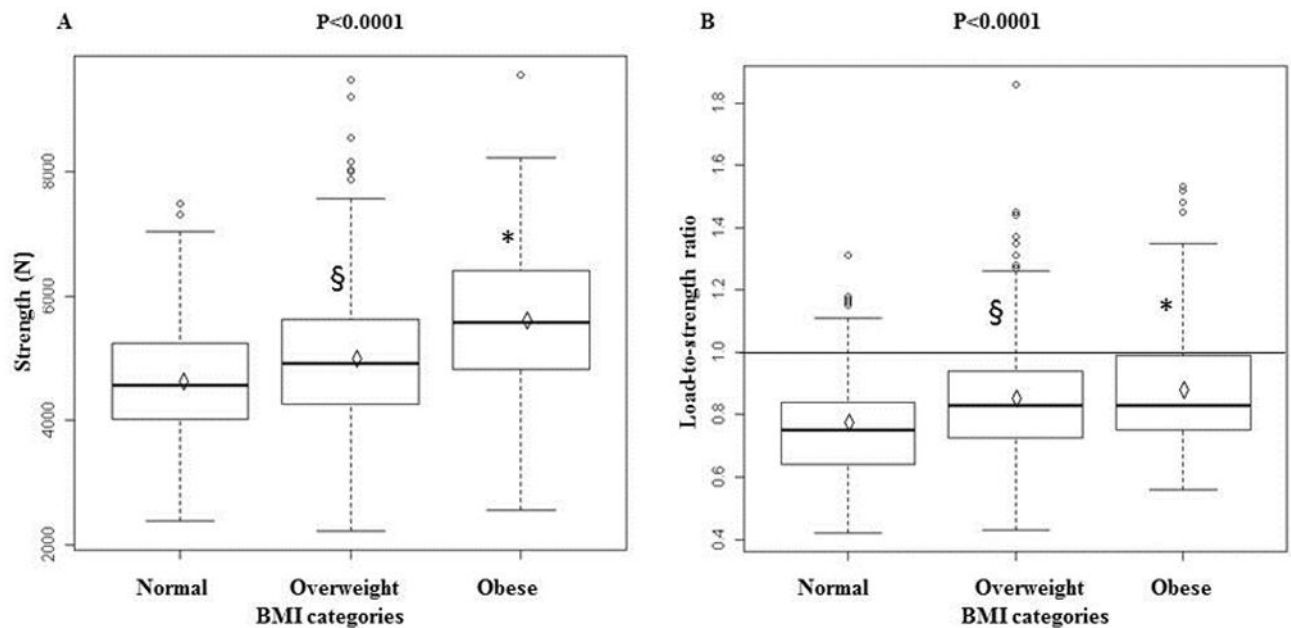
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**Figure 1.**

Least squares means for femoral neck QCT measurements by BMI category adjusted for age, site, race and physical activity in men of the MrOS study. The error bars indicate standard errors.



**Figure 2.**

BMI and FE-derived biomechanical measurements (A) Strength (B) Load-to-strength ratio, adjusted for age, site, race and physical activity in the men of the MrOS study. P is for trend test. § P < 0.05 and \* P < 0.0001 compared with normal-weight men.

Sample size: N for normal weight=202; N for overweight=380; N for obese=90

The length of the box represents the interquartile range (the distance between the 25th and 75th percentiles). The symbol in the box interior represents the group mean. The horizontal line in the box interior represents the group median. The whiskers on the boxes depict the extreme values.

**Table 1**

Characteristics of men in MrOS study by BMI category (N = 3067)

	Normal (18.5–24.9 kg/m <sup>2</sup> )	Overweight (25–29.9 kg/m <sup>2</sup> )	Obese (30–50.7 kg/m <sup>2</sup> )	P
N (%)	829(27.0)	1568(51.1)	670 (21.9)	
Age (yr)	74.5(6.3)	73.4(5.8)	72.2(5.2)	<0.0001
Caucasian, n (%)	716(86.4)	1386(88.4)	574(85.7)	0.14
Current smoker, n (%)	32(3.9)	64(4.1)	15(2.2)	0.09
Alcohol (drinks/wk)	4.0(5.8)	4.3(7.0)	4.0(6.7)	0.39
Physical activity score	152(70)	149(65)	144(67)	0.08
Self-reported good health, n (%)	740(89.3)	1376(87.8)	536(80)	<0.0001
Calcium intake (mg)	1,206(620)	1,136(589)	1066(557)	<0.0001
Vitamin D intake (IU)	408(243)	392(246)	367(233)	0.005
Self-reported medical history				
Osteoporosis, n (%)	12(1.5)	30(1.9)	13(1.9)	0.68
Diabetes, n (%)	55(6.6)	152(9.7)	137(20.5)	<0.0001
Arthritis, n (%)	319(38.5)	717(45.7)	367(54.8)	<0.0001
Fracture after age 50, n (%)	404(48.7)	851(54.3)	379(56.6)	0.005

Values are means (SD) unless otherwise noted. P values for categorical variables are from chi-square tests (Fisher's exact test for small expected frequencies); P values for continuous variables were calculated using one-way ANOVA.

**Table 2**

The association of BMI with proximal femoral QCT measurements stratified by obesity status in men of the MrOS study

	BMI < 30 (n=2397)		BMI ≥ 30 (n=670)		P for Interaction *
	SD increase per unit of BMI	P	SD increase per unit of BMI	P	
<b>Femoral neck</b>					
BMD (g/cm <sup>3</sup> )					
Integral	0.05 ± 0.008	<0.0001	-0.012 ± 0.014	0.39	0.0003
Cortical	0.042 ± 0.008	<0.0001	-0.008 ± 0.013	0.54	0.002
Trabecular	0.002 ± 0.0004	<0.0001	-0.0008 ± 0.0006	0.18	0.0005
Volume (cm <sup>3</sup> )					
Integral	0.027 ± 0.008	0.001	-0.015 ± 0.014	0.28	0.014
Medullary	0.006 ± 0.009	0.47	-0.011 ± 0.014	0.45	0.33
Percent cortical volume	0.042 ± 0.008	<0.0001	-0.009 ± 0.013	0.49	0.002
Cross-sectional area (cm <sup>2</sup> )	0.03 ± 0.009	0.0005	-0.02 ± 0.014	0.14	0.003
DXA BMD	0.105 ± 0.008	<0.0001	0.035 ± 0.014	0.011	<0.0001

P-value was adjusted for age, site, race and physical activity.

\* The interaction was to test the difference of point estimates between the non-obese and the obese.

**Table 3**  
The association of BMI with FE-derived measures stratified by obesity status in men of the MrOS study

	BMI < 30 (n=582)		BMI ≥ 30 (n=90)	
	SD increase per unit of BMI	P	SD increase per unit of BMI	P
Strength	0.056 ± 0.014	0.0002	-0.03 ± 0.064	0.69
Load-to-strength ratio	0.094 ± 0.015	<0.0001	0.14 ± 0.07	0.06
				P for Interaction*
				0.36
				0.99

P-value was adjusted for age, site, race and physical activity.  
\*The interaction was to test the difference of point estimates between the non-obese and the obese.