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Relationship of adiposity to bone volumetric density and microstructure in men and women across the adult lifespan

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Abstract

Recent evidence suggests that adipose tissue may negatively impact bone health, challenging the traditional paradigm that increased fat mass, through mechanical loading or endogenous estrogen production, is beneficial to the skeleton. We hypothesized that it is primarily the visceral compartment of body fat that is detrimental to bone metabolism, resulting in impaired bone density and architecture. In an age-stratified population sample of 218 women and 291 men (age 20–97 years), we assessed visceral (VAT) and subcutaneous (SAT) adipose tissue areas at the L2–L3 interspace level by single slice quantitative computed tomography (QCT) and measured total body fat mass (TBF) by dual-energy X-ray absorptiometry. We then correlated these findings with volumetric bone mineral density (vBMD) at the femoral neck (FN) and lumbar spine (LS) assessed by central QCT, and with vBMD and microstructural parameters at the ultradistal radius (UDR) by high resolution peripheral QCT (HRpQCT). In unadjusted analyses in postmenopausal women, TBF and SAT were positively correlated with total, trabecular, and cortical vBMD at the FN, LS, and UDR and with trabecular microstructure at the UDR. By contrast, VAT was not correlated with vBMD at the FN or LS but was positively correlated with UDR total and trabecular vBMD but not cortical vBMD. Adjustment for age or for bioavailable estradiol and testosterone levels reduced these correlations, while adjustment for body weight eliminated most positive associations. Assessment of the VAT/SAT ratio, however, demonstrated a negative relationship with vBMD at the FN and LS in postmenopausal women, a relationship eliminated when adjusted for age. Correlations between skeletal parameters and adipose measurements in pre-menopausal women and older men were weaker and mostly non-significant. In younger men, VAT was negatively associated with vBMD, cortical thickness, and trabecular microstructure at the UDR, and with LS vBMD and FN cortical vBMD. These associations generally remained after adjustment, with some negative associations (e.g. UDR cortical area) being accentuated. Similar

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Disclosure statement

The authors have nothing to disclose.

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results were found when the VAT/SAT ratio was correlated with FN vBMD in younger men; in contrast, VAT/SAT was positively correlated with FN vBMD in older men and this relationship was strengthened by age-adjustment. Together, our data suggest that adiposity has associations with bone that are age-, gender-, menopausal status-, adipose depot-, and bone compartment-specific. These novel observations warrant further investigations to establish any causal relationships.

Keywords

adipose tissue; visceral; subcutaneous; bone mineral density; bone microarchitecture

Introduction

An alarming trend towards increasing obesity in many populations has been associated with a plethora of adverse consequences [1]. However, the relationship between obesity and skeletal health, specifically, is less well studied [2]. Although there is a surprisingly high prevalence of obesity in postmenopausal women and older men who present with low-trauma fractures [3], higher body weight has traditionally been considered favorable for skeletal health since mechanical loading produces a positive osteogenic response and adipose tissue enhances estrogen metabolism [4]. Indeed, body weight is one of the strongest predictors of bone mass [5]. However, this paradigm has been called into question by several recent studies. In a large population of Chinese and Caucasian subjects, for example, Zhao et al. [6] showed an inverse relationship between fat mass and bone mass after adjusting for the loading effects of body weight. Similarly, Hsu et al. [7] demonstrated that higher body fat percentage was associated with greater risks of osteoporosis, osteopenia and non-spine fractures in Chinese men and women. In a recent review, Reid [5] explained such negative results as an artifact of adjustment in the analysis for correlates of obesity (e.g., body weight), and he concluded that most previous studies had found a positive association of obesity with bone density.

However, it can be appropriate to adjust for factors on the potential causal pathway between obesity and bone in order to test potential mechanisms. In addition, previous assessments of adiposity have relied mainly on dual-energy x-ray absorptiometry (DXA) to dichotomize soft tissue body composition into fat and lean mass [6, 7]. However, adipose tissue itself is not functionally uniform, and different adipose depots have distinctive characteristics in terms of adipocytokine production [8]. Several earlier studies have indeed suggested that different fat depots may have distinct relationships with bone. Among perimenopausal Korean women, for example, waist-hip ratio was used as a surrogate measure of visceral adiposity and had a negative association with lumbar spine (LS) areal bone mineral density (aBMD) after adjustment for age and weight [9]. Similarly, in a study of Chinese women, the DXA-determined android to gynoid fat mass ratio, a marker of central body fat, was negatively associated with aBMD at multiple skeletal sites in the postmenopausal subpopulation [10].

Moreover, DXA assessment of aBMD can be confounded by adiposity and bone size [11], and DXA does not provide separate information about the cortical versus trabecular compartments of bone. Furthermore, aBMD by DXA is only a surrogate for factors less easily assessed in vivo, e.g., the structural properties that contribute to bone strength and resistance to fracture [12]. In the present population-based, cross-sectional study, we examined the relationship between adiposity and bone, focusing on differences between specific adipose depots and their correlations with volumetric bone mineral density (vBMD)

of both cortical and trabecular bone and with bone structural parameters determined using advanced imaging techniques.

Materials and Methods

Study subjects

Subjects were recruited from an age-stratified, random sample of Rochester, MN, residents age 21 to 97 years and included 375 women and 325 men [13], of whom 349 women and 297 men had adipose tissue assessments. This community is highly characteristic of the U.S. white population, but other groups are underrepresented [14]; reflecting the ethnic composition of the community, 98% of subjects were white by self-report. Of the 349 women, 131 were excluded from this analysis because they were receiving oral contraceptives, bisphosphonates, selective estrogen receptor modulators or estrogen therapy, leaving 78 premenopausal and 140 postmenopausal (absence of menses for > 6 months) women for study. High-resolution peripheral quantitative computed tomography (HRpQCT) scans were performed on 193 of these 218 women. Of the 297 men, 6 were excluded because they were receiving testosterone or bisphosphonate treatment. Thus, 122 men < 50 years and 169 men ≥ 50 years of age were available for study, and HRpQCT scans were done on 257 of the 291 men. All studies were approved by the Mayo Clinic Institutional Review Board, and written informed consent was obtained from all subjects prior to evaluation.

Quantitative computed tomography (QCT) of the central skeleton

Single-energy QCT scans at the proximal femur and lumbar spine (LS) were made with a multi-detector scanner (LightSpeed QX/i; GE Medical Systems, Waukesha, WI, USA) as previously described [13]. For the LS, we analyzed single slices from the L₁, L₂, and L₃ vertebrae and used the mean of these values. For the femoral neck (FN), we assessed a reformatted section at the mid-portion between the superior aspect of the head and the inferior aspect of the lesser trochanter. Calibration standards scanned with the patient were used to convert Hounsfield units (HU) directly to equivalent vBMD (mg/cm³); the correlation between vBMD results by our algorithm and that of the European Spine Phantom (QRM GmSH, Möhrendorf, Germany) was $r = 0.998$, with an estimated coefficient of variation (CV) of 0.7%. Mayo-developed software for the analysis of bone structure, geometry, and volumetric density from the QCT images has been described elsewhere [15]. We note that partial volume averaging occurs as a reflection of the resolution permitted by the scanner. Accordingly, vBMD as reported throughout the manuscript is more accurately 'apparent' vBMD. For simplicity, however, we have chosen to use vBMD within the text as is typically done. In addition, 2-dimensional FN aBMD was estimated from 3-dimensional FN vBMD data using commercial software (Mindways Software, Inc., Austin, TX, USA).

HRpQCT of the ultradistal radius

As previously described [16], the non-dominant wrist was scanned using a prototype of the XtremeCT (Scanco Medical AG, Bassersdorf, Switzerland). Image acquisition and analysis has been extensively described and validated. Briefly, trabecular bone volume/tissue volume (BV/TV) is derived from the trabecular vBMD, and thickness-independent structure extraction is used to assess the 3-D ridges (center points of the trabeculae) [17]; trabecular number (TbN, 1/mm) is then taken as the inverse of the mean spacing of the ridges [18]. Trabecular thickness (TbTh, mm) is derived as (BV/TV)/TbN and trabecular separation (TbSp, mm) as $(1 - BV/TV)/TbN$, as in standard histomorphometry. In comparison with gold-standard 28-μm resolution microCT (μCT) [19], correlation with BV/TV, TbN, TbTh, and TbSp by HRpQCT is very high ($R = 0.96 - 0.99$). Cortical measures, including cortical vBMD, cortical bone area (BA, mm²), and cortical thickness (CTh, mm) are also obtained

[18]. Excellent correlation ($R=0.98$) has also been shown with CTh measurements by μ CT [20]. To assess short-term precision of the measurements, 20 volunteers (age, 19–40 years) were scanned twice on the same day after repositioning, and the following CVs were observed: cortical vBMD, 1.3%; CTh, 5.1%; BV/TV, 1.2%; TbN, 2.2%; TbTh, 1.8%; and TbSp, 3.4% [16].

Adipose tissue measurements

Height (m) was measured by stadiometer and weight (kg) on an electronic scale; body mass index (BMI) was defined as kg/m^2 . Total body fat (TBF) mass was assessed by total body DXA using the Prodigy instrument (GE Medical Systems, Madison, WI) and software version 6.10.029. In addition, we measured subcutaneous (SAT, cm^2) and visceral (VAT, cm^2) adipose tissue areas from LS QCT using commercial software (TomoVision, Montreal, Canada). The program allows one to select the area to be measured by “painting” with a virtual brush and a user-defined HU range on a single cross-sectional image taken at the L_2 – L_3 interspace. SAT was defined as the area between the skin and the abdominal and back muscles. VAT was defined as the area of adipose tissue within the abdominal cavity; structures indicating the outermost surface of the abdominal cavity were the vertebral body, psoas major, quadratus lumborum, transversus abdomini and rectus abdomini muscles, linea alba, and the connecting fascia. Previous studies have demonstrated that VAT area measured by single slice QCT can reliably predict ($R^2 > 0.9$) total VAT volume [21]. The same investigator (ACN) performed all manual measurements.

Hormonal measurements

Fasting serum samples were obtained on all subjects at the time of the QCT measurements. As previously described [22], we used liquid chromatography-tandem mass spectrometry (LC-MS/MS; API 5000, Applied Biosystems-MDS Sciex, Foster City, CA) to measure serum estradiol (E_2) and testosterone (T). Values as low as 1.25 pg/mL for E_2 and 1 ng/dL for T are detectable by this method, with interassay CVs of 8% and 6% for E_2 and T, respectively. Sex hormone binding globulin (SHBG) was assessed using a chemiluminescent immunoassay (Diagnostic Products Corporation, Los Angeles, CA; interassay CV < 8%), and the non-SHBG bound (bioavailable) fraction of total E_2 and T was measured as previously described [23]; interassay CVs for bioavailable E_2 (bio E_2) and T (bio T) were each < 12%.

Statistical analyses

Bone density and microstructural parameters, as well as adipose tissue measures and sex steroid levels, were summarized using medians and interquartile ranges (IQR; 25–75%). The Wilcoxon rank-sum test was used to compare adipose tissue measures between the men and women. Correlations of hormones, body weight and fat depot results with the skeletal parameters were evaluated using Spearman’s simple and partial correlation coefficients. Linear regression models were also fit and a variance inflation factor value greater than 10 was taken to indicate significant collinearity [24]. Ridge regression was also run on models with weight and fat to determine whether the coefficients were similar when penalization was added to the model. The R function lowess, essentially a type of moving average, was used to explore the data in the figures [25]. Analyses were performed using SAS (SAS Institute Inc., Version 9. Cary, NC) and R [26], and a p-value of <0.05 was considered significant.

Results

Altogether, 29% of the men and 28% of the women were obese (BMI ≥ 30). As shown in Fig. 1A, there was a gradual, age-related rise in TBF among the women, reaching a peak

around the 7th decade of life, with a subsequent decline thereafter. In men, however, TBF remained relatively stable across the adult life-span. SAT in both men and women followed patterns similar to those observed for TBF (Fig. 1B). In these cross-sectional data, VAT (Fig. 1C) increased with age up to approximately the 7th decade in men and roughly the 8th decade in women but remained consistently higher in men than women at all ages ($p < 0.001$). Since the direction of these changes seemed to differ between young and old, we divided the study population into men 20–49 years old, along with the premenopausal women, and contrasted them with the postmenopausal women and the men ≥ 50 years of age. Since the median age at menopause in these women was 48 years, age 50 years seemed a comparable cut-point for the men. The anthropomorphic, hormonal, adipose tissue and bone density/structural data for these four groups are summarized in Table 1.

In unadjusted analyses among the postmenopausal women, TBF was positively correlated with FN aBMD, as well as total, trabecular and cortical vBMD at the FN, LS and UDR and with trabecular microstructure in the UDR; very similar results were seen for SAT (Table 2). By contrast, VAT was not correlated with FN aBMD or with vBMD of the FN or LS. At the UDR, however, VAT was positively correlated with total vBMD and trabecular vBMD but not cortical vBMD; this was associated with increases in UDR BV/TV, TbN and TbTh and a reduction in TbSp. Adjustment for age (to accommodate potential confounding) and more so adjustment for bio E₂ levels (on the causal pathway between fat and bone) reduced these associations among the postmenopausal women, and results were similar when adjustments were also made for bio T (data not shown). However, adjustment for body weight (to account for the effect of mechanical loading) eliminated the original positive or negative associations and, indeed, reversed the sign (from positive to negative or vice versa) for most of them, suggesting that for subjects with similar body weight, those with less fat (and thus more lean mass) have a higher bone density than those with more fat. Simultaneous adjustment for age, bio E₂, height, and weight produced results generally like those for the weight adjustment alone (data not shown).

Compared to postmenopausal women, correlations with the various adipose measures among the older men were weaker and mostly non-significant except for positive correlations of TBF, SAT and VAT with cortical thickness at the FN and LS, as well as cortical area and TbN at the UDR, with a corresponding reduction in TbSp (Supplemental Table 1). Again, the various adjustments, especially that for weight, eliminated these positive relationships.

Likewise, among the premenopausal women, TBF, SAT and VAT were positively associated with cortical thickness but not vBMD at the FN and LS (Supplemental Table 2). At the UDR, positive associations were also seen with trabecular vBMD and related microstructure. Adjustments for age and bio E₂ had less impact on the associations seen among the premenopausal women, but adjustment for weight eliminated all of them.

Quite different results were seen in the younger men (Table 3), where VAT was negatively associated with UDR vBMD, cortical thickness and trabecular microstructure (except for TbN where the correlation was positive), along with LS vBMD and cortical vBMD at the FN. Among these younger men, generally negative associations of TBF, SAT and VAT with FN aBMD, FN trabecular and cortical vBMD, LS total and trabecular vBMD and UDR total, trabecular and cortical vBMD remained after various adjustments, although some were no longer statistically significant. Indeed, adjustment accentuated some negative correlations (e.g., UDR cortical area).

As recently suggested by Russell and colleagues [27], assessment of the VAT/SAT ratio may be useful to determine the impact of the relative proportion of VAT to SAT on bone

(Supplemental Table 3). In contrast to the results in postmenopausal women when VAT alone was assessed, the VAT/SAT ratio was negatively correlated with aBMD and vBMD at the FN, as well as with vertebral total and trabecular vBMD. Adjustment for weight did not materially affect these results, although age-adjustment eliminated their significance. By comparison, in premenopausal women, there was no relationship between the VAT/SAT ratio and BMD at the FN or with total or trabecular vertebral vBMD, results which were unaffected after adjustment for weight or age. In older men, the VAT/SAT ratio was positively correlated with FN vBMD, a result which was not affected by adjustment for weight and was strengthened following adjustment for age. In contrast, the VAT/SAT ratio was negatively correlated with both FN aBMD and vBMD in younger men, results which were unaffected following adjustment for weight but which were again weakened with adjustment for age.

Discussion

As expected from the extensive literature on the subject [5], TBF and SAT were positively associated with many measures of bone density and structure in postmenopausal women, thus the notion that obesity has protective effects on the skeleton. However, both TBF and SAT began to decline later in life, when bone loss also occurs. Consequently, this relationship might be confounded by age. Indeed, most associations were weaker after we adjusted for age. By contrast, the age-related decline in VAT and SAT was less in men < 50 years of age, whose levels were more stable over life. It may be no coincidence then, that the association between adiposity and skeletal parameters was less in older men and that adjustment for age had less effect on the correlation coefficients, i.e., less confounding by age in men < 50 years old. Likewise, adjusting for bio E₂ had somewhat less effect in the older men compared to the older women, even though bio E₂ is an important determinant of skeletal health in elderly men [28]. Adjusting for body weight, though, eliminated essentially all of these positive associations, as seen in some other recent studies [29]. At a given weight (i.e., adjusted for weight), greater fat mass was negatively correlated with many bone parameters. If weight is fixed, however, the person with greater fat mass also has lower lean mass, which is another determinant of bone mass.

VAT and SAT increased with age among the premenopausal women and younger men, but age-adjustment had little influence on the results seen here. Likewise, the various associations were only marginally reduced by adjustment for bio E₂ or the combination of bio E₂ and bio T (data not shown). Again, however, adjustment for body weight eliminated associations of adiposity with bone density and microstructure among the premenopausal women. By contrast, VAT, and to a lesser degree TBF, had consistent inverse relationships with vBMD measures at all three skeletal sites in men < 50 years of age. Adjustment for body weight had relatively little influence on these associations, and the lack of specificity for weight bearing (FN, LS) versus non-weight bearing (UDR) sites further supports the hypothesis that this relationship is independent of the biomechanical effects of weight. However, a differential pattern in this relationship exists for the axial and appendicular skeleton, i.e., it is the trabecular compartment in the spine, whereas in the femur and radius, it is the cortical compartment that is negatively related to VAT. SAT did not appear to have any significant relationship with bone parameters in men < 50 years of age.

The differences observed in men < 50 years compared to the premenopausal women are likely multifactorial. It is well recognized that bone accrual and achievement of peak bone mass differs by gender [13]. Both periosteal apposition and endosteal resorption, which continue in post-pubertal adults, are greater in males compared to females. Moreover, the trabecular bone loss that occurs in young men (age 20–50 years) is similar to that in premenopausal women with respect to time of onset and rate of loss, but the subsequent

accelerated trabecular loss occurs earlier in women (beginning in the perimenopausal period) compared to men (around age 70 years); by comparison, cortical bone loss begins in midlife in both sexes, but is more rapid in women than in men [30]. It is possible then that the earlier onset of accelerated trabecular bone loss in perimenopausal women has obscured the relatively small negative influence of VAT. This would also be consistent with our observations in the older men and postmenopausal women, in whom accelerated bone loss due to other pathophysiologic processes predominates. Further, with the decline of gonadal sex steroids to low levels, especially estrogen in older women, fat may take on a more favorable role as a peripheral estrogen source [30].

As recently described [27], the VAT/SAT ratio may be useful to assess the relative contributions of VAT to SAT on the skeleton. Whereas the VAT/SAT ratio showed no significant relationship with vBMD at skeletal weight-bearing sites (FN and LS) in premenopausal women, we did find a significant negative correlation at these same sites in postmenopausal women. However, when considered in the context of the well-recognized decline in bone mass that also occurs following the menopause, the fact that adjustment for age eliminated this association in the postmenopausal women suggests that the VAT/SAT ratio may not play a major role in postmenopausal bone loss at either the hip or spine, results consistent with those determined when VAT alone was assessed. By comparison, the VAT/SAT ratio was negatively correlated with BMD at the FN in younger men, but positively correlated with FN vBMD in the older male cohort. In contrast to younger men and postmenopausal women, in whom adjustment for age eliminated the significance at the FN, adjustment for age in older men strengthened the positive correlation between VAT/SAT and vBMD. Although the basis for this difference in older men and women is unclear, it suggests that the relationship between VAT and bone with aging may differ between the sexes.

It should be recognized that SAT is not just an inactive store of adipocytes, as it can also secrete leptin, adiponectin and inflammatory cytokines [31, 32]. Nevertheless, it is VAT which is more consistently and strongly associated with metabolic abnormalities, insulin resistance, adipokine production and inflammation [8, 33, 34], processes that may be involved in the maintenance of bone mass and structure. The VAT depot releases adipocytokines which stimulate hepatic release of acute phase response proteins such as C-reactive protein (CRP) and is associated with macrophages which secrete inflammatory cytokines including tumor necrosis factor alpha, interleukin-6 (IL-6), monocyte chemoattractant protein-1, and plasminogen activator inhibitor-1 [35, 36]. IL-6 can stimulate osteoclasts to increase the rate of bone resorption [37], while higher circulating CRP levels are associated with higher serum N-terminal telopeptide of type 1 collagen (NTX), a marker of bone resorption [38], and lower bone mass [39]. In a Korean study [40], femoral neck aBMD was significantly lower in subjects with the metabolic syndrome (MS), and aBMD declined as the number of MS components increased; waist circumference (a marker for visceral fat mass) was the most important MS component of this negative association. In multiple linear regression models, waist circumference and fat mass were negatively associated with aBMD, while lean mass was positively associated, suggesting that visceral fat may lead to bone loss. Similarly, in a study of 100 healthy females age 15–25 years, subcutaneous fat had positive associations with bone structure and strength, whereas visceral fat was negatively correlated with most bone macro-structure and strength parameters (e.g., femoral cross-sectional area, cortical bone area, and polar moment of inertia) [41].

The present investigation provides a rigorous examination of the relationship between adiposity and bone across a wide age-range in both men and women. Strengths include the recruitment of subjects from an age-stratified random sample of community residents, and the fact that we were able to obtain detailed information regarding both cortical and

trabecular compartments of bone, based on QCT, and on bone microstructural parameters, based on HRpQCT. In addition, we adjusted for the mechanical loading effect of weight in some analyses to assess the independent associations between adipose depots and bone mass and microstructure, although we remain cognizant of the potential collinearity between body weight and VAT, SAT and TBF, as highlighted in a recent review [5]. Formal statistical diagnostics via the variance inflation factor and exploration of the coefficients with ridge regression confirmed the validity of our regression analyses (data not shown). Additionally, exploratory plots of fat versus bone parameters by subgroups of subjects with similar weight showed patterns that were consistent with those detected by the partial correlations. We also analyzed our data stratified by age and menopausal status; these two factors are potential confounders since increasing age and menopause are associated with an increase in visceral adiposity, as well as a decline in bone mass and sex steroid levels [42]. This also ensured that we did not pool disparate groups and violate necessary assumptions regarding distributions of the variables being studied. The main limitation of our study is the cross-sectional design, from which it is difficult to infer causality. As the study population was nearly completely white, extrapolation of these findings to other ethnic or racial groups is also uncertain. Finally, we were unable to determine whether VAT may be surrogate marker for other factors that are negatively associated with bone density.

In men ≥ 50 years of age and postmenopausal women, we did not observe any significant relationships between adiposity and bone parameters after adjustment for confounding by age and effects of estrogen and body weight on putative causal pathways between adipose tissue and bone. However, potential negative effects of adiposity in the 3rd to 5th decades of life imply that, in order to allow optimal peak bone mass accrual, the prevention of obesity (or more precisely, efforts to limit the accumulation of VAT) must be undertaken early in life. Particularly worrisome is the reduction in cortical area without a compensatory increase in total bone area that is associated with greater VAT in young men, suggesting increased endosteal bone resorption not offset by periosteal skeletal apposition. While males have better bone strength than women due largely to greater bone size, this strength may be compromised by cortical thinning. Further, the decrease in cortical vBMD may represent a true decrease in density of interstitial bone or an increase in intracortical porosity, either of which would be expected to further compromise bone strength. Our data thus suggest that the relationship between visceral and subcutaneous adipose depots with bone is complex and is age-, menopausal status-, gender-, adipose depot- and bone compartment-specific. Longitudinal follow-up of our current cohort for fracture outcomes will clarify whether a higher VAT increases fracture risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Study evaluated visceral and subcutaneous adipose tissue in relation to volumetric bone mineral density across the adult lifespan.
- Total body fat and subcutaneous adipose were positively correlated with volumetric bone mineral density in postmenopausal women.
- Visceral adipose tissue was not correlated with femoral neck or lumbar spine bone mineral density in postmenopausal women.
- Visceral adipose tissue was negatively correlated with lumbar spine and femoral neck volumetric bone mineral density in younger men.
- The relationship between adiposity and bone is affected by age, gender, menopausal status, and adipose and bone compartment site.

Fig. 1. Relationship of (A) total body fat (TBF), (B) subcutaneous adipose tissue (SAT), and (C) visceral adipose tissue (VAT) to age among Rochester, MN men and women 20 to 97 years old.

Table 1
Clinical, hormonal and vBMD/structural parameters of Rochester, MN, men vs. women, overall and stratified by age (median, IQR).

	All			Young		Old	
	Men	Women	Men 20-49 years	Premenopausal women	Men 50 years	Postmenopausal women	
N	291	218	122	78	169	140	
Demographic variables							
Age (years)	54.7 (39.6-71.6)	59.3 (45.2-73.4)	36.9 (30.6-43.5)	41.8 (38.0-46.1)	68.7 (59.9-79.7)	68.4 (61.2-81.6)	
Weight (kg)	85.8 (77.0-96.7)	72.0 (62.0-81.0)	90.2 (79.1-102)	65.9 (59.0-81.0)	84.1 (75.8-92.9)	73.8 (63.9-81.0)	
Body mass index (kg/m ²)	27.6 (25.3-30.8)	26.9 (23.5-30.4)	27.7 (25.0-31.3)	24.3 (22.1-28.9)	27.6 (25.6-30.2)	28.3 (24.9-31.1)	
Hormonal variables							
Bioavailable estrogen (pg/ml)	11.0 (8.0-13.7)	2.7 (1.1-14.3)	12.6 (10.6-16.4)	20.2 (10.8-34.6)	9.5 (7.0-12.3)	1.5 (0.8-2.6)	
Bioavailable testosterone (ng/dl)	83.8 (53.9-121)	1.4 (0.9-2.4)	121 (99.2-153)	1.6 (1.1-2.4)	60.6 (45.1-83.6)	1.3 (0.8-2.3)	
Adipose measures							
Total body fat (kg)	28.3 (22.9-35.6)	33.2 (25.5-41.5)	27.8 (20.6-37.3)	28.0 (21.3-38.5)	28.5 (24.2-34.5)	34.6 (27.9-41.8)	
Subcutaneous adipose tissue (cm ²)	158 (118-206)	190 (113-251)	161 (106-218)	142 (98.8-244)	157 (123-195)	203 (146-256)	
Visceral adipose tissue (cm ²)	184 (135-245)	101 (63.0-155)	156 (90.4-204)	57.7 (35.7-108)	214 (151-268)	119 (85.9-172)	
vBMD/Structural parameters							
• Femoral Neck							
aBMD (g/cm ²)	0.73 (0.63-0.82)	0.67 (0.57-0.75)	0.80 (0.72-0.86)	0.75 (0.72-0.88)	0.67 (0.60-0.76)	0.60 (0.51-0.68)	
Total vBMD (mg/cm ³)	301 (256-351)	316 (265-370)	335 (296-361)	371 (345-430)	274 (238-317)	289 (249-320)	
Trabecular vBMD (mg/cm ³)	202 (166-233)	204 (159-247)	230 (202-257)	251 (222-284)	175 (149-210)	178 (142-211)	
Cortical vBMD (mg/cm ³)	554 (504-593)	564 (506-630)	574 (524-618)	626 (565-659)	537 (487-576)	537 (489-587)	
Cortical thickness (mm)	2.78 (2.54-3.07)	2.76 (2.55-3.09)	2.84 (2.61-3.19)	2.89 (2.67-3.26)	2.72 (2.48-2.98)	2.67 (2.48-2.94)	
• Lumbar spine							
Total vBMD (mg/cm ³)	196 (160-225)	191 (146-229)	216 (193-240)	232 (214-257)	173 (144-209)	156 (126-193)	
Trabecular vBMD (mg/cm ³)	156 (126-183)	152 (111-185)	178 (158-199)	188 (172-210)	135 (110-162)	123 (94-152)	
Cortical thickness (mm)	1.87 (1.68-2.02)	1.72 (1.45-1.89)	1.97 (1.85-2.10)	1.88 (1.77-2.05)	1.75 (1.58-1.94)	1.51 (1.35-1.73)	
• Ultradistal Radius							
Total vBMD (mg/cm ³)	330 (284-367)	300 (253-339)	347 (312-379)	329 (301-376)	308 (266-351)	272 (224-310)	
Trabecular vBMD (mg/cm ³)	195 (163-220)	151 (124-174)	209 (185-227)	160 (134-186)	184 (155-206)	145 (116-166)	
Cortical vBMD (mg/cm ³)	832 (786-868)	840 (767-891)	845 (808-878)	895 (856-918)	815 (766-860)	793 (721-854)	

N	All		Young		Old	
	Men	Women	Men 20-49 years	Premenopausal women	Men 50 years	Postmenopausal women
	291	218	122	78	169	140
Cortical thickness (mm)	0.77 (0.62-0.90)	0.67 (0.52-0.81)	0.83 (0.69-0.92)	0.80 (0.70-0.90)	0.71 (0.59-0.89)	0.58 (0.42-0.71)
Total area (mm ²)	375 (329-424)	250 (223-282)	363 (324-411)	245 (219-279)	381 (339-435)	255 (226-293)
Trabecular area (mm ²)	297 (249-348)	196 (169-230)	288 (246-338)	187 (164-214)	305 (256-357)	203 (172-238)
Cortical area (mm ²)	64.9 (54.3-74.5)	45.1 (35.3-54.7)	67.9 (60.1-77.4)	55.4 (47.8-61.0)	62.4 (51.7-72.4)	40.1 (30.8-47.1)
BV/TV	0.16 (0.14-0.18)	0.12 (0.10-0.14)	0.17 (0.15-0.19)	0.13 (0.11-0.16)	0.15 (0.13-0.17)	0.12 (0.10-0.14)
Trabecular number (1/mm)	2.76 (2.55-2.92)	2.53 (2.35-2.69)	2.69 (2.48-2.88)	2.55 (2.40-2.73)	2.79 (2.61-2.94)	2.49 (2.26-2.66)
Trabecular thickness (mm)	0.059 (0.050-0.066)	0.049 (0.042-0.056)	0.065 (0.057-0.073)	0.052 (0.046-0.058)	0.055 (0.047-0.062)	0.048 (0.040-0.055)
Trabecular separation (mm)	0.31 (0.29-0.33)	0.35 (0.32-0.38)	0.31 (0.29-0.33)	0.34 (0.31-0.37)	0.30 (0.29-0.33)	0.35 (0.33-0.39)

IRQ, interquartile range.

Table 2

Correlation of bone density and structural parameters at different skeletal sites with adiposity measures among postmenopausal Rochester, MN women (unadjusted/adjusted for age/adjusted for serum bioavailable estradiol [E₂]/adjusted for body weight).

Skeletal site	TBF	SAT	VAT
Femoral neck			
aBMD (g/cm ²)	0.40[§]/0.33[§]/0.27[‡]/–0.24[‡]	0.36[§]/0.30[§]/0.23[‡]/–0.09	0.07/0.14/–0.07/– 0.33[§]
Total vBMD (mg/cm ³)	0.34[§]/0.27[‡]/0.19[‡]/–0.21[‡]	0.33[§]/0.27[‡]/0.19[‡]/–0.05	0.06/0.13/–0.08/– 0.28[‡]
Trabecular vBMD (mg/cm ³)	0.37[§]/0.30[§]/0.23[‡]/–0.16	0.34[§]/0.27[‡]/0.20[‡]/–0.05	0.04/0.12/–0.11/– 0.32[§]
Cortical vBMD (mg/cm ³)	0.23[‡]/0.17/0.15/–0.18[‡]	0.21[‡]/0.16/0.14/–0.06	0.10/0.14/0.04/–0.11
Cortical thickness (mm)	0.33[§]/0.30[§]/0.17/–0.11	0.32[§]/0.29[§]/0.17/–0.01	0.15/ 0.18[‡] /0.03/–0.11
Lumbar spine			
Total vBMD (mg/cm ³)	0.33[§]/0.23[‡]/0.17/–0.18[‡]	0.28[‡]/0.17/0.11/–0.13	0.04/0.10/–0.12/– 0.30[§]
Trabecular vBMD (mg/cm ³)	0.35[§]/0.25[‡]/0.19[‡]/–0.17	0.30[§]/0.19[‡]/0.14/–0.11	0.05/0.10/–0.11/– 0.30[§]
Cortical Thickness (mm)	0.36[§]/0.27[‡]/0.19[‡]/–0.20[‡]	0.34[§]/0.25[‡]/0.17/–0.09	0.11/0.16/–0.07/– 0.25[‡]
Ultradistal radius			
Total vBMD (mg/cm ³)	0.28[‡]/0.22[‡]/0.16/0.03	0.19[‡]/0.13/0.06/–0.06	0.20[‡]/0.24[‡]/0.11/0.04
Trabecular vBMD (mg/cm ³)	0.39[§]/0.39[§]/0.28[‡]/–0.02	0.28[‡]/0.28[‡]/0.17/–0.07	0.30[§]/0.30[§]/0.21[‡]/0.08
Cortical vBMD (mg/cm ³)	0.14/0.02/0.01/–0.03	0.10/–0.03/–0.03/–0.08	0.04/0.08/–0.08/–0.10
Cortical thickness (mm)	0.20[‡]/0.11/0.10/–0.00	0.13/0.03/0.02/–0.09	0.12/0.17/0.03/–0.03
Total area (mm ²)	0.22[‡]/0.22[‡]/0.16/–0.30[§]	0.21[‡]/0.22[‡]/0.16/–0.10	0.14/0.14/0.09/–0.10
Trabecular area (mm ²)	0.15/0.17/0.12/– 0.25[‡]	0.17/ 0.18[‡] /0.14/–0.06	0.10/0.10/0.07/–0.08
Cortical area (mm ²)	0.30[§]/0.23[‡]/0.19[‡]/–0.06	0.22[‡]/0.12/0.09/–0.12	0.19[‡]/0.27[‡]/0.09/–0.04
Bone volume/total volume	0.39[§]/0.39[§]/0.28[‡]/–0.03	0.28[‡]/0.28[‡]/0.17/–0.07	0.30[§]/0.30[§]/0.21[‡]/0.07
Trabecular number (1/mm)	0.45[§]/0.43[§]/0.35[§]/–0.07	0.34[§]/0.30[§]/0.21[‡]/–0.16	0.36[§]/0.38[§]/0.27[‡]/0.06
Trabecular thickness (mm)	0.29[‡]/0.31[§]/0.20[‡]/0.01	0.20[‡]/0.22[‡]/0.11/–0.02	0.22[‡]/0.22[‡]/0.15/0.08
Trabecular separation (mm)	–0.44[§]/–0.42[§]/–0.34[§]/0.07	–0.33[§]/–0.30[§]/–0.21[‡]/0.14	–0.36[§]/–0.38[§]/0.27[‡]/–0.07

[‡] p<0.05;

[‡] p<0.01;

[§] p<0.001.

Significant Spearman correlations are bolded.

Table 3

Correlation of bone density and structural parameters at different skeletal sites with adiposity measures among Rochester, MN men age 20–49 years (unadjusted/adjusted for age/adjusted for serum bioavailable estradiol [E₂]/adjusted for body weight).

Skeletal site	TBF	SAT	VAT
Femoral neck			
aBMD (g/cm ²)	0.05/0.08/0.04/–0.26 [‡]	0.11/0.11/0.09/–0.11	–0.13/–0.04/–0.13/–0.41 [§]
Total vBMD (mg/cm ³)	–0.06/–0.04/–0.08/–0.17	0.01/0.01/–0.01/–0.02	–0.17/–0.08/–0.17/–0.28 [‡]
Trabecular vBMD (mg/cm ³)	–0.04/–0.01/–0.07/–0.18	0.02/0.02/–0.01/–0.05	–0.17/–0.05/–0.18/–0.31 [§]
Cortical vBMD (mg/cm ³)	–0.18 [‡] /–0.17/–0.19 [‡] /–0.23 [‡]	–0.14/–0.14/–0.15/–0.10	–0.23 [‡] /–0.21 [‡] /–0.23 [‡] /–0.24 [‡]
Cortical thickness (mm)	0.27 [‡] /0.30 [‡] /0.27 [‡] /–0.13	0.30 [‡] /0.31 [§] /0.29 [‡] /–0.04	0.15/0.24 [‡] /0.15/–0.19 [‡]
Lumbar spine			
Total vBMD (mg/cm ³)	–0.19 [‡] /–0.17/–0.22 [‡] /–0.22 [‡]	–0.14/–0.15/–0.19 [‡] /–0.14	–0.28 [‡] /–0.22 [‡] /–0.30 [‡] /–0.33 [§]
Trabecular vBMD (mg/cm ³)	–0.19 [‡] /–0.18/–0.23 [‡] /–0.24 [‡]	–0.15/–0.16/–0.20 [‡] /–0.16	–0.28 [‡] /–0.21 [‡] /–0.30 [§] /–0.33 [§]
Cortical thickness (mm)	0.19 [‡] /0.21 [‡] /0.17/–0.19 [‡]	0.22 [‡] /0.23 [‡] /0.19 [‡] /–0.10	0.08/0.14/0.07/–0.24 [‡]
Ultradistal radius			
Total vBMD (mg/cm ³)	–0.17/–0.17/–0.18/–0.11	–0.14/–0.14/–0.14/–0.02	–0.23 [‡] /–0.23 [‡] /–0.23 [‡] /–0.18
Trabecular vBMD (mg/cm ³)	–0.13/0.11/–0.14/–0.15	–0.11/–0.11/–0.12/–0.10	–0.23 [‡] /–0.17/–0.23 [‡] /–0.27 [‡]
Cortical vBMD (mg/cm ³)	–0.20 [‡] /–0.21 [‡] /–0.20 [‡] /–0.08	–0.15/–0.16/–0.15/0.02	–0.23 [‡] /–0.28 [‡] /–0.24 [‡] /–0.14
Cortical thickness (mm)	–0.15/–0.16/–0.15/–0.16	–0.12/–0.12/–0.11/–0.07	–0.20 [‡] /0.23 [‡] /–0.20 [‡] /–0.18
Total area (mm ²)	0.20 [‡] /0.19 [‡] /0.20 [‡] /–0.21 [‡]	0.14/0.14/0.15/–0.26 [‡]	0.16/0.16/0.16/–0.12
Trabecular area (mm ²)	0.21 [‡] /0.21 [‡] /0.21 [‡] /–0.15	0.16/0.16/0.16/–0.21 [‡]	0.19/0.20 [‡] /0.19/–0.07
Cortical area (mm ²)	–0.09/–0.10/–0.08/–0.24 [‡]	–0.07/–0.07/–0.06/–0.18	–0.13/–0.17/–0.13/–0.23 [‡]
Bone volume/total volume	–0.13/–0.11/–0.14/–0.15	–0.11/–0.11/–0.12/–0.10	–0.23 [‡] /–0.17/–0.23 [‡] /–0.27 [‡]
Trabecular number (1/mm)	0.28 [‡] /0.26 [‡] /0.28 [‡] /0.01	0.24 [‡] /0.25 [‡] /0.24 [‡] /–0.02	0.24 [‡] /0.18/0.24 [‡] /0.03
Trabecular thickness (mm)	–0.24 [‡] /–0.22 [‡] /–0.25 [‡] /–0.16	–0.21 [‡] /–0.23 [‡] /–0.23 [‡] /–0.10	–0.32 [§] /–0.23 [‡] /–0.31 [‡] /0.26 [‡]
Trabecular separation (mm)	–0.21 [‡] /–0.20 [‡] /–0.21 [‡] /0.03	–0.19 [‡] /–0.19 [‡] /–0.19 [‡] /0.04	–0.14/–0.11/–0.15/0.06

[‡]p<0.05;

[‡]p<0.01;

[§]p<0.001.

Significant Spearman correlations are bolded.