Published in final edited form as:

Skeletal Radiol. 2016 June ; 45(6): 813–819. doi:10.1007/s00256-016-2363-1.

Body composition predictors of skeletal integrity in obesity

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Abstract

Objective—To determine body composition predictors of skeletal integrity in overweight/obese subjects using DXA. We hypothesized that visceral adiposity would be negatively, and lean mass positively, associated with DXA measures of skeletal integrity in obesity.

Materials and Methods—Our study was IRB approved and HIPAA compliant and written informed consent was obtained. We studied 82 overweight or obese but otherwise healthy premenopausal women and men of similar age who were part of a clinical trial (mean age: 37±10 years, mean BMI: 34±7kg/m²). All subjects underwent DXA of the spine and hip for assessment of bone mineral density (BMD), trabecular bone score (TBS), and hip structural analysis (HSA) and of the whole body for assessment of body composition, including estimated visceral adipose tissue (VAT).

Results—Sixty-three subjects (77%) had normal BMD and 19 subjects (23%) had osteopenia. There were strong age-, sex-, and BMD-independent positive associations between lean mass and HSA parameters ($r=0.50$ to $r=0.81$, $p<0.0001$), while there was no association with TBS. There were strong age-, sex- and BMD-independent inverse association between total fat and VAT mass and TBS ($r=-0.60$ and $r=-0.72$, $p<0.0001$ for both correlations), while there were no associations with HSA parameters.

Conclusion—Lean mass is a positive predictor of hip geometry while fat and VAT mass are negative predictors of trabecular microarchitecture in overweight/obese subjects.

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Clinical trials number: NCT01724489

Compliance with Ethical Standards

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Keywords

Obesity; DXA; trabecular bone score; hip structural analysis; visceral adipose tissue; lean mass

Introduction

Obesity is associated with increased risk for the development of type 2 diabetes, cardiovascular disease, and premature death [1]. Although conventional teaching is that obesity is protective against the development of osteoporosis via mechanical loading and peripheral aromatization of androgens to estrogen [2, 3], recent studies have shown that accumulation of fat, particularly visceral adiposity, is associated with bone loss and fractures [4–10]. Most studies on osteoporosis have focused on the elderly or patients with conditions predisposing for bone loss, such as anorexia nervosa, and body composition predictors of skeletal integrity in young overweight or obese young individuals have not been studied.

Dual energy X-ray absorptiometry (DXA) is usually performed to assess bone mineral density (BMD) and body composition [11, 12] due to its wide availability, minimal radiation dose, and relative low costs. However, BMD measured by DXA is limited in its ability to predict fractures, and patients with fragility fractures often have normal BMD [13]. In addition, the accuracy of DXA has been shown to be decreased in obesity [14, 15]. The limitations of BMD alone to predict fracture risk have led to the development of additional parameters of skeletal integrity. DXA-based hip structural analysis (HSA) is a simple method that can be used to assess proximal femoral geometry [16] and has been shown to improve the prediction of hip fracture risk [17]. Trabecular bone score (TBS), a grey-level texture parameter obtained from DXA images of the lumbar spine, can distinguish patients with and without fragility fractures independent of BMD [18], however this technique has not been validated in obese subjects. Furthermore, a new DXA method for assessment of visceral adipose tissue (VAT) has recently been validated [19].

The purpose of our study therefore was to determine body composition determinants of traditional and novel DXA parameters of skeletal integrity. We hypothesized that visceral adiposity would be negatively, and lean mass positively, associated with HSA parameters and TBS in this population.

Materials and Methods

Our study was IRB approved and complied with HIPAA guidelines. Written informed consent was obtained from all subjects after the nature of the procedure had been fully explained.

Subjects

Data presented here are from subjects who were being screened for eligibility for a clinical research study on obesity and bone and were recruited through advertisements. Inclusion criteria for the study presented here were ages 18–50 years, premenopausal status for women, and BMI ≥ 25 kg/m². Subjects were phone screened prior to the screening visit and subjects who had had hypothalamic or pituitary disorders, diabetes mellitus, rheumatoid arthritis or

other chronic illness, chronic glucocorticoid use, or on other medications that are known to affect bone metabolism or bone mineral density (BMD) were not invited to the screening visit.

All subjects were examined during one study visit at our Clinical Research Center. BMI was calculated by using the formula $BMI = W/H$, where W is weight in kilograms and H is height in square meters. A complete history was recorded and a physical examination was performed.

Dual-energy X-ray absorptiometry

All subjects underwent DXA (Discovery A; Hologic Inc., Bedford, MA, USA) for assessment of BMD, hip structural analysis (HSA), trabecular bone score (TBS), and body composition. Examinations of lateral lumbar spine were excluded from analysis if the thickness score was ≤ 1 as recommended by the manufacturer.

Bone mineral density—BMD of the posterior-anterior (PA) and lateral lumbar spine and hip was determined. Coefficient of variation of DXA has been reported as less than 1% for BMD [20]. Osteopenia was defined by a T-score of -1.0 -2.5 and osteoporosis was defined by a T-score of < -2.5 [21].

Hip structural analysis—Hip structural analysis (HSA) was performed from properties of hip DXA images at the narrow neck (NN; narrowest part of the femoral neck), the intertrochanteric region (IT; along the bisector of the angle of the axes of NN and FS), and the femoral shaft (FS; across the shaft 1.5 cm from the NN to the intersection of the neck and shaft axes) to estimate hip geometry and strength indices [22]. The following HSA parameters were obtained: cross-sectional area (CSA; index of resistance to axial forces); cross-sectional moment of inertia (CSMI; estimate of resistance to bending forces in a cross-section); section modulus (Z; index of bending strength); cortical thickness; subperiosteal width; endocortical width; and buckling ratio (BR; index of susceptibility to cortical buckling under compressive loads). Higher values are associated with greater predicted femoral strength for all HSA-derived parameters except for BR, for which higher values are predictive of inferior strength.

Trabecular bone score—Trabecular bone score (TBS) was calculated as a mean value of the measurements for vertebrae L1–L4 at the same ROI as spine BMD using TBS iNsite software (Medimaps SA, France). TBS was evaluated by determining the variogram of the trabecular bone projected image as previously described [23]. The mean value of the individual measurements for L1–L4 represents the lumbar spine TBS (unitless) [23]. Reported *in vivo* precision for TBS ranges from 1.1% to 2.05% [24–26].

Body composition—Whole-body DXA was used to assess total lean mass and total fat mass. Coefficients of variation of DXA have been reported as 4.1% for body fat mass, and 1.0% for lean body mass [27, 28]. Estimated visceral adipose tissue (VAT) was assessed using Hologic APEX 4.0 software (Hologic Inc., Bedford, MA) as previously described [19, 29].

Statistical Analysis

Statistical analysis was performed using JMP software (version 11, SAS Institute, Cary, NC). Data are presented as mean $\pm$ standard deviation (SD). Nonparametric linear regression analyses were performed to determine body composition determinants of BMD, TBS, HSA and Spearman rho values are reported. Analyses were adjusted for age, sex, and BMD using multivariate standard least squares regression modeling. P values for univariate regression were corrected for multiple comparisons by the Bonferroni method. $P < 0.05$ indicated statistical significance.

Results

Subject characteristics and body composition are shown in Table 1. Our study group was comprised of 82 overweight/obese but otherwise healthy subjects with a mean age of 37 ± 10 years and a mean BMI of 34 ± 7 kg/m². Twenty-four subjects (29%) were overweight (BMI 25 kg/m²–30 kg/m²) and 58 (71%) were obese (BMI ≥ 30 kg/m²). There were 41 men and 41 women.

Sixty-three subjects (77%) had normal BMD (T-score > -1.0) and 19 subjects (23%) had osteopenia (T-score -1.0 – -2.5) based on hip or spine BMD, which is higher than what would be expected in a normal population (T-score < -1 SD = 15.8%). None of the subjects had osteoporosis. Within the women, 29 (71%) had normal BMD and 12 (29%) had osteopenia. Within the men, 34 (83%) had normal BMD and 7 (17%) had osteopenia.

In the overweight group (n=24), 8 (33%) had osteopenia and 16 (67%) had normal BMD, while in the obese group (n=58) 11 (19%) had osteopenia and 47 (81%) had normal BMD.

TBS correlated positively with PA lumbar spine BMD ($r=0.40$, $p=0.005$) and lateral lumbar spine BMD ($r=0.31$, $p=0.01$).

Hip BMD correlated positively with CSA, CSMI, Z and cortical thickness ($r=0.32$ to $r=0.73$, $p=0.003$ to $p<0.0001$) and inversely with BR ($r=-0.36$ to $r=-0.44$, $p=0.0008$ to $p<0.0001$) while there were no associations between hip BMD and subperiosteal or endocortical width ($p>0.07$).

In order to assess BMD-independent predictors of skeletal integrity, associations between measures of body composition and TBS and HSA were controlled for lumbar spine and hip BMD, respectively.

There was a positive age- and sex-independent association between BMI and total hip BMD and an inverse association with TBS, which remained significant after controlling for lateral and AP lumbar spine BMD ($p<0.0001$). There were positive associations between BMI and HSA parameter cortical thickness and inverse association with BR however, the associations lost significance after controlling for multiple comparisons, age, sex and BMD. There were no significant associations between BMI and lumbar spine BMD (Table 2). There was no association between TBS and hip BMD ($p=0.3$).

There were age- sex- and BMD-independent positive associations between lean mass and hip BMD and most HSA parameters (Table 2, Fig. 1), while there were no age- and sex-independent associations between lean mass and TBS or lumbar spine BMD. There were strong age-, sex- and BMD-independent inverse associations between total fat and VAT mass and TBS (Table 2, Fig. 2), while there were no associations between total fat and VAT mass and HSA parameters or BMD.

As the accuracy of TBS and HSA may decrease with increasing BMI, we performed a secondary analysis between TBS and HSA and body composition measures after excluding subjects with severe (class II and III) obesity (BMI >35 kg/m²) (n=29). There were inverse associations between TBS and VAT (r= -0.51, p=0.0005) and total fat mass (r= -0.30, p=0.05) and there was a trend of an inverse association between VAT and lumbar spine BMD (r= -0.22, p=0.1), while there was no association between lean mass and TBS (p=0.6). Strong positive associations between lean mass and hip BMD and HSA parameters (r=0.25 to r=0.85, p<0.04 to p<0.0001) persisted, while there were no associations between hip BMD and VAT or total fat mass (p>0.5).

Discussion

Recent data demonstrate that the epidemic of obesity is complicated by bone loss and fractures [6, 9, 30, 31]. Studies have suggested that excess fat mass, particularly visceral fat, may be a risk factor for bone loss and increased fracture risk in obesity [4–10]. Advances in DXA techniques allow assessment of proximal hip geometry by HSA [16] and surrogates of lumbar spine microarchitecture by TBS to better assess fracture risk [17, 18]. Furthermore, quantification of VAT mass by DXA has been shown to correlate well with values from computed tomography (CT) [19]. While most studies on DXA and fracture risk have focused on the elderly or populations at risk for bone loss, we focused on overweight/obese but otherwise healthy premenopausal women and men of similar age, a group which was thought to be protected from bone loss. We aimed to assess body composition predictors of traditional and novel measures of skeletal integrity by DXA.

In our study, BMI and fat mass were inversely associated with TBS. The inverse association between BMI and TBS is consistent with a large population study examining TBS in 29,407 women [25] and a study in healthy men and women across a wide age (30 to 80 years) and BMI range (15 to 47 kg/m²) [26]. We found strong inverse associations between VAT and fat mass and TBS, independent of age, sex, and lumbar spine BMD, which remained significant after excluding subjects with BMI >35 kg/m². However, there was no significant association between VAT mass and lumbar spine BMD, suggesting that high BMI and VAT mass disproportionately affect trabecular bone. Our findings of impaired microarchitecture in abdominal adiposity are consistent with a transiliac bone biopsy study, which found impaired bone microarchitecture and strength with lower bone formation in premenopausal women with abdominal adiposity [32]. Potential mechanisms for the detrimental effects of excess fat, and particularly VAT, on bone in obesity include dysregulation of the GH/IGF-1 axis with low GH and IGF-1 levels, which are important regulators of bone homeostasis [33–35], and the release of proinflammatory cytokines by VAT, which stimulate osteoclast

activity [36, 37]. Additionally, low vitamin D levels are often found in obese individuals [38, 39].

We found no association between lean mass and TBS or lumbar spine BMD, suggesting that lean mass has no significant effects on lumbar spine microarchitecture or lumbar spine BMD, possibly because there is less mechanical traction of muscle on the lumbar spine compared to extremities. Our data are consistent with a recent study in a healthy Italian population across a wide age-spectrum that found no association between TBS and lean mass [40].

BMI was positively associated with hip BMD, independent of age and sex, while there were no significant independent associations with HSA parameters. This is consistent with studies that have shown adaptive increase in hip BMD in response to increasing BMI [41, 42], while relative to BMI, obese subjects had impaired hip structure compared to normal-weight subjects [41–43], suggesting that hip structure is insufficient to compensate for increasing BMI. However, in a study of older (>65 years) individuals this did not translate into increased risk of developing a major osteoporotic fracture over a follow-up time of 6.2 ± 3.7 years in women and 4.7 ± 3.4 years in men and 4.7 ± 3.4 years [43].

Lean mass was positively associated with hip BMD and HSA parameters, independent of age and sex. Most of the associations between lean mass and HSA parameters remained significant after controlling for hip BMD and after excluding subjects with BMI > 35 kg/m², suggesting that HSA predicts skeletal fragility independent of BMD. Our results are consistent with a recent study by Hu *et al.* that showed lean mass, but not fat mass, to be positively associated with BMD and HSA parameters in Chinese men and women across a wide age spectrum [44]. Beck *et al.* found higher hip BMD, CSA, and section modulus (Z, an engineering index of bending strength), in postmenopausal women with greater BMI, and these effects were proportionate to total body lean mass but not total fat or total body mass [41]. Positive effects of lean mass on bone include skeletal loading at weight-bearing sites, stimulating adaptive increases in BMD and alteration of hip geometry [45]. In a different study, Beck *et al.* demonstrated that despite declines in BMD, subjects with constant skeletal loads maintained section moduli at the femoral neck and shaft, suggesting that mechanical homeostasis in the hip is better characterized by section modulus than bone density [45]. Furthermore, recent studies suggest that several genes and molecular pathways exert a pleiotropic effect on both muscle and bone [46]. For example, bone morphogenic proteins (BMP) are regulators of both bone and muscle formation and homeostasis [47]. *In-vitro* studies have demonstrated that myocytes secrete factors that can protect osteocytes from glucocorticoid-induced cell death through activation of the Wnt/β-catenin pathway, a pathway known to be important for the maintenance of normal bone [48, 49].

Interestingly, 23% of our overweight/obese but otherwise healthy premenopausal women and men of similar age had osteopenia, which is higher than what would be expected in a normal population (t-score < -1SD = 15.8%). Within this group, the prevalence of osteopenia was higher in women compared to men (29% vs 17%) and in overweight subjects compared to obese (33% vs 19%), suggesting that women and overweight subjects are at highest risk of osteopenia.

We did not report the World Health Organization fracture risk assessment tool (FRAX) as our female subjects were premenopausal and the male subjects of similar age and none were taking glucocorticoids, had secondary osteoporosis or rheumatoid arthritis.

Our study had several limitations. First is the cross-sectional study design, which limits our ability to prove causality. Second, we used DXA-derived parameters of lumbar spine microarchitecture (TBS) and hip geometry (HSA) to assess skeletal integrity as well as estimated VAT by DXA instead of CT or MRI. However, studies have shown strong correlations between these variables and equivalent measurements from QCT with less radiation dose [19, 50, 51]. Third, obesity may affect the accuracy of DXA-derived parameters of skeletal integrity and body composition [14, 15]. We therefore excluded examinations with a thickness score of >11. Strengths of our study include the unique population of young, overweight/obese but otherwise healthy men and women and detailed assessment of skeletal integrity and body composition.

In conclusion, lean mass is a positive predictor of hip geometry while fat and VAT mass are negative predictors of trabecular microarchitecture in overweight/obese subjects.

Acknowledgments

Funding: This study was supported by NIH grants R01 DK095792, K24 HL092902 and UL1 RR-025758

References

1. Rexrode KM, Carey VJ, Hennekens CH, et al. Abdominal adiposity and coronary heart disease in women. *Jama*. 1998; 280:1843–1848. [PubMed: 9846779]
2. Albala C, Yanez M, Devoto E, Sostin C, Zeballos L, Santos JL. Obesity as a protective factor for postmenopausal osteoporosis. *Int J Obes Relat Metab Disord*. 1996; 20:1027–1032. [PubMed: 8923160]
3. Reid IR, Plank LD, Evans MC. Fat mass is an important determinant of whole body bone density in premenopausal women but not in men. *J Clin Endocrinol Metab*. 1992; 75:779–782. [PubMed: 1517366]
4. Bredella MA, Torriani M, Ghomi RH, et al. Determinants of bone mineral density in obese premenopausal women. *Bone*. 2011; 48:748–754. [PubMed: 21195217]
5. Gilsanz V, Chalfant J, Mo AO, Lee DC, Dorey FJ, Mittelman SD. Reciprocal relations of subcutaneous and visceral fat to bone structure and strength. *J Clin Endocrinol Metab*. 2009; 94:3387–3393. [PubMed: 19531595]
6. Goulding A, Jones IE, Taylor RW, Williams SM, Manning PJ. Bone mineral density and body composition in boys with distal forearm fractures: a dual-energy x-ray absorptiometry study. *J Pediatr*. 2001; 139:509–515. [PubMed: 11598596]
7. Hsu YH, Venners SA, Terwedow HA, et al. Relation of body composition, fat mass, and serum lipids to osteoporotic fractures and bone mineral density in Chinese men and women. *Am J Clin Nutr*. 2006; 83:146–154. [PubMed: 16400063]
8. Janicka A, Wren TA, Sanchez MM, et al. Fat mass is not beneficial to bone in adolescents and young adults. *J Clin Endocrinol Metab*. 2007; 92:143–147. [PubMed: 17047019]
9. Nielson CM, Marshall LM, Adams AL, et al. BMI and fracture risk in older men: the osteoporotic fractures in men study (MrOS). *J Bone Miner Res*. 2011; 26:496–502. [PubMed: 20814955]
10. Zhang P, Peterson M, Su GL, Wang SC. Visceral adiposity is negatively associated with bone density and muscle attenuation. *Am J Clin Nutr*. 2015; 101:337–343. [PubMed: 25646331]
11. Cummings SR, Bates D, Black DM. Clinical use of bone densitometry: scientific review. *Jama*. 2002; 288:1889–1897. [PubMed: 12377088]

12. Hangartner TN, Warner S, Braillon P, Jankowski L, Shepherd J. The Official Positions of the International Society for Clinical Densitometry: acquisition of dual-energy X-ray absorptiometry body composition and considerations regarding analysis and repeatability of measures. *J Clin Densitom.* 2013; 16:520–536. [PubMed: 24183641]
13. Premaor MO, Pilbrow L, Tonkin C, Parker RA, Compston J. Obesity and fractures in postmenopausal women. *J Bone Miner Res.* 2010; 25:292–297. [PubMed: 19821769]
14. Evans EM, Mojtahedi MC, Kessinger RB, Misis MM. Simulated change in body fatness affects Hologic QDR 4500A whole body and central DXA bone measures. *J Clin Densitom.* 2006; 9:315–322. [PubMed: 16931350]
15. Yu EW, Thomas BJ, Brown JK, Finkelstein JS. Simulated increases in body fat and errors in bone mineral density measurements by DXA and QCT. *J Bone Miner Res.* 2012; 27:119–124. [PubMed: 21915902]
16. Beck TJ, Ruff CB, Warden KE, Scott WW Jr, Rao GU. Predicting femoral neck strength from bone mineral data. A structural approach. *Invest Radiol.* 1990; 25:6–18. [PubMed: 2298552]
17. Karlamangla AS, Barrett-Connor E, Young J, Greendale GA. Hip fracture risk assessment using composite indices of femoral neck strength: the Rancho Bernardo study. *Osteoporos Int.* 2004; 15:62–70. [PubMed: 14605798]
18. Hans D, Goertzen AL, Krieg MA, Leslie WD. Bone microarchitecture assessed by TBS predicts osteoporotic fractures independent of bone density: the Manitoba study. *J Bone Miner Res.* 2011; 26:2762–2769. [PubMed: 21887701]
19. Micklesfield LK, Goedecke JH, Punyanitya M, Wilson KE, Kelly TL. Dual-energy X-ray performs as well as clinical computed tomography for the measurement of visceral fat. *Obesity (Silver Spring).* 2012; 20:1109–1114. [PubMed: 22240726]
20. Barthe N, Braillon P, Ducassou D, Basse-Cathalinat B. Comparison of two Hologic DXA systems (QDR 1000 and QDR 4500/A). *Br J Radiol.* 1997; 70:728–739. [PubMed: 9245885]
21. Kanis JA, Gluer CC. An update on the diagnosis and assessment of osteoporosis with densitometry. Committee of Scientific Advisors, International Osteoporosis Foundation. *Osteoporos Int.* 2000; 11:192–202. [PubMed: 10824234]
22. LaCroix AZ, Beck TJ, Cauley JA, et al. Hip structural geometry and incidence of hip fracture in postmenopausal women: what does it add to conventional bone mineral density? *Osteoporos Int.* 2010; 21:919–929. [PubMed: 19756830]
23. Hans D, Barthe N, Boutroy S, Pothuaud L, Winzenrieth R, Krieg MA. Correlations between trabecular bone score, measured using anteroposterior dual-energy X-ray absorptiometry acquisition, and 3-dimensional parameters of bone microarchitecture: an experimental study on human cadaver vertebrae. *J Clin Densitom.* 2011; 14:302–312. [PubMed: 21724435]
24. Silva BC, Boutroy S, Zhang C, et al. Trabecular bone score (TBS)--a novel method to evaluate bone microarchitectural texture in patients with primary hyperparathyroidism. *J Clin Endocrinol Metab.* 2013; 98:1963–1970. [PubMed: 23526463]
25. Leslie WD, Krieg MA, Hans D. Clinical factors associated with trabecular bone score. *J Clin Densitom.* 2013; 16:374–379. [PubMed: 23452869]
26. Sritara C, Thakkestian A, Ongphiphadhanakul B, et al. Age-Adjusted Dual X-ray Absorptiometry-Derived Trabecular Bone Score Curve for the Lumbar Spine in Thai Females and Males. *J Clin Densitom.* 2015
27. Pintauro SJ, Nagy TR, Duthie CM, Goran MI. Cross-calibration of fat and lean measurements by dual-energy X-ray absorptiometry to pig carcass analysis in the pediatric body weight range. *Am J Clin Nutr.* 1996; 63:293–298. [PubMed: 8602583]
28. van der Sluis IM, de Ridder MA, Boot AM, Krenning EP, de Muinck Keizer-Schrama SM. Reference data for bone density and body composition measured with dual energy x ray absorptiometry in white children and young adults. *Arch Dis Child.* 2002; 87:341–347. discussion 341–347. [PubMed: 12244017]
29. Bredella MA, Gill CM, Keating LK, et al. Assessment of abdominal fat compartments using DXA in premenopausal women from anorexia nervosa to morbid obesity. *Obesity (Silver Spring).* 2013; 21:2458–2464. [PubMed: 23512706]

30. Armstrong ME, Spencer EA, Cairns BJ, et al. Body mass index and physical activity in relation to the incidence of hip fracture in postmenopausal women. *J Bone Miner Res.* 2011; 26:1330–1338. [PubMed: 21611971]
31. Compston JE, Watts NB, Chapurlat R, et al. Obesity is not protective against fracture in postmenopausal women: GLOW. *Am J Med.* 2011; 124:1043–1050. [PubMed: 22017783]
32. Cohen A, Dempster DW, Recker RR, et al. Abdominal fat is associated with lower bone formation and inferior bone quality in healthy premenopausal women: a transiliac bone biopsy study. *J Clin Endocrinol Metab.* 2013; 98:2562–2572. [PubMed: 23515452]
33. Bredella MA, Gerweck AV, Barber LA, et al. Effects of growth hormone administration for 6 months on bone turnover and bone marrow fat in obese premenopausal women. *Bone.* 2014; 62:29–35. [PubMed: 24508386]
34. Menagh PJ, Turner RT, Jump DB, et al. Growth hormone regulates the balance between bone formation and bone marrow adiposity. *J Bone Miner Res.* 2010; 25:757–768. [PubMed: 19821771]
35. Mukherjee A, Murray RD, Shalet SM. Impact of growth hormone status on body composition and the skeleton. *Horm Res.* 2004; 62(Suppl 3):35–41. [PubMed: 15539797]
36. Cartier A, Lemieux I, Almeras N, Tremblay A, Bergeron J, Despres JP. Visceral obesity and plasma glucose-insulin homeostasis: contributions of interleukin-6 and tumor necrosis factor- α in men. *J Clin Endocrinol Metab.* 2008; 93:1931–1938. [PubMed: 18319319]
37. Pou KM, Massaro JM, Hoffmann U, et al. Visceral and subcutaneous adipose tissue volumes are cross-sectionally related to markers of inflammation and oxidative stress: the Framingham Heart Study. *Circulation.* 2007; 116:1234–1241. [PubMed: 17709633]
38. Kremer R, Campbell PP, Reinhardt T, Gilsanz V. Vitamin D status and its relationship to body fat, final height, and peak bone mass in young women. *J Clin Endocrinol Metab.* 2009; 94:67–73. [PubMed: 18984659]
39. Young KA, Engelman CD, Langefeld CD, et al. Association of plasma vitamin D levels with adiposity in Hispanic and African Americans. *J Clin Endocrinol Metab.* 2009; 94:3306–3313. [PubMed: 19549738]
40. Bazzocchi A, Ponti F, Diano D, et al. Trabecular bone score in healthy ageing. *Br J Radiol.* 2015; 88:20140865. [PubMed: 26148778]
41. Beck TJ, Petit MA, Wu G, LeBoff MS, Cauley JA, Chen Z. Does obesity really make the femur stronger? BMD, geometry, and fracture incidence in the women's health initiative-observational study. *J Bone Miner Res.* 2009; 24:1369–1379. [PubMed: 19292617]
42. Shen J, Nielson CM, Marshall LM, Lee DC, Keaveny TM, Orwoll ES. The Association Between BMI and QCT-Derived Proximal Hip Structure and Strength in Older Men: A Cross-Sectional Study. *J Bone Miner Res.* 2015; 30:1301–1308. [PubMed: 25565555]
43. Shen J, Leslie WD, Nielson CM, Majumdar SR, Morin SN, Orwoll ES. Associations of Body Mass Index With Incident Fractures and Hip Structural Parameters in a Large Canadian Cohort. *J Clin Endocrinol Metab.* 2016; 101:476–484. [PubMed: 26670128]
44. Hu WW, Zhang H, Wang C, et al. Lean mass predicts hip geometry and bone mineral density in chinese men and women and age comparisons of body composition. *J Clin Densitom.* 2012; 15:434–442. [PubMed: 22521541]
45. Beck TJ, Oreskovic TL, Stone KL, et al. Structural adaptation to changing skeletal load in the progression toward hip fragility: the study of osteoporotic fractures. *J Bone Miner Res.* 2001; 16:1108–1119. [PubMed: 11393788]
46. Cianferotti L, Brandi ML. Muscle-bone interactions: basic and clinical aspects. *Endocrine.* 2014; 45:165–177. [PubMed: 23990248]
47. Sartori R, Sandri M. Bone and morphogenetic protein signalling and muscle mass. *Curr Opin Clin Nutr Metab Care.* 2015; 18:215–220. [PubMed: 25807347]
48. Jahn K, Lara-Castillo N, Brotto L, et al. Skeletal muscle secreted factors prevent glucocorticoid-induced osteocyte apoptosis through activation of beta-catenin. *Eur Cell Mater.* 2012; 24:197–209. discussion 209-110. [PubMed: 22972510]
49. Kramer I, Halleux C, Keller H, et al. Osteocyte Wnt/beta-catenin signaling is required for normal bone homeostasis. *Mol Cell Biol.* 2010; 30:3071–3085. [PubMed: 20404086]

50. Ramamurthi K, Ahmad O, Engelke K, et al. An in vivo comparison of hip structure analysis (HSA) with measurements obtained by QCT. *Osteoporos Int.* 2012; 23:543–551. [PubMed: 21394495]
51. Roux JP, Wegrzyn J, Boutroy S, Buxsein ML, Hans D, Chapurlat R. The predictive value of trabecular bone score (TBS) on whole lumbar vertebrae mechanics: an ex vivo study. *Osteoporos Int.* 2013; 24:2455–2460. [PubMed: 23468074]

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Fig. 1.

Regression analysis between lean mass and section modulus (Z, index of bending strength) at the narrowest part of the femoral neck. There is a positive association between lean mass and Z, which remained significant after controlling for multiple comparisons, age, sex, and hip BMD ($p=0.02$).

Fig. 2. Regression analysis between visceral adipose tissue (VAT) mass and trabecular bone score (TBS). There is an inverse association between VAT mass and TBS, which remained significant after controlling for age, sex, and lumbar spine BMD ($p < 0.0001$).

Table 1Clinical characteristics and body composition of study subjects, mean $\pm$ SD and (range)

	Subjects (n=82)
Age (years)	37 $\pm$ 10 (18 – 50)
Women/men (n)	41/41
Weight (kg)	101 $\pm$ 21 (64 – 157)
BMI (kg/m²)	34 $\pm$ 7 (25 – 50)
Total lean mass (kg)	60 $\pm$ 13 (39 – 98)
Total fat mass (kg)	39 $\pm$ 14 (13 – 73)
Visceral adipose tissue mass (kg)	0.7 $\pm$ 0.3 (0.2 – 1.9)

Table 2

Associations between measures of body composition and skeletal integrity in overweight/obese subjects.

	BMI			Lean mass			Total fat mass			VAT mass		
	r	p		r	p		r	p		r	p	
TBS (L1-L4)	-0.55	<0.0001 ^{***}		-0.17	0.2		-0.60	<0.0001 ^{***}		-0.72	<0.0001 ^{***}	
HSA NN CSA	0.17	0.1		0.66	<0.0001 ^{***}		0.06	0.6		0.07	0.5	
HSA IT CSA	0.16	0.1		0.71	<0.0001 ^{***}		0.05	0.7		0.16	0.2	
HSA FS CSA	0.15	0.2		0.74	<0.0001 ^{***}		0.03	0.8		0.14	0.2	
HSA NN CSMI	0.01	0.9		0.79	<0.0001 ^{***}		-0.08	0.5		0.06	0.6	
HSA IT CSMI	0.06	0.6		0.81	<0.0001 ^{***}		-0.05	0.7		0.12	0.3	
HSA FS CSMI	0.03	0.8		0.70	<0.0001 ^{***}		-0.11	0.3		0.04	0.7	
HSA NN Z	0.005	1.0		0.76	<0.0001 ^{***}		-0.03	0.8		0.05	0.7	
HSA IT Z	0.10	0.4		0.78	<0.0001 ^{***}		-0.06	0.6		0.18	0.1	
HSA FS Z	0.02	0.8		0.69	<0.0001 ^{***}		-0.06	0.6		0.08	0.5	
HSA NN cortical thickness	0.22	0.05		0.29	0.007		0.12	0.3		0.10	0.4	
HSA IT cortical thickness	0.30	0.006		0.43	<0.0001 ^{***}		0.19	0.09		0.29	0.01	
HSA FS cortical thickness	0.16	0.2		0.35	0.001 [*]		0.04	0.7		0.19	0.1	
HSA NN subperiost. width	0.04	0.7		0.55	<0.0001 ^{***}		0.02	0.8		0.01	0.9	
HSA IT subperiosteal width	-0.04	0.7		0.70	<0.0001 ^{***}		-0.09	0.4		0.04	0.7	
HSA FS subperiosteal width	0.03	0.8		0.62	<0.0001 ^{***}		-0.02	0.9		0.02	0.8	
HSA NN endocortical width	0.01	0.9		0.46	0.004		0.02	0.8		0.008	1.0	
HSA IT endocortical width	-0.08	0.5		0.65	<0.0001 ^{***}		-0.11	0.3		0.03	0.8	
HSA FS endocortical width	-0.11	0.3		0.25	0.02		-0.05	0.7		-0.12	0.3	
HSA NN BR	-0.14	0.2		-0.04	0.7		-0.06	0.6		-0.08	0.5	
HSA IT BR	-0.33	0.002		0.07	0.5		-0.25	0.02		-0.29	0.02	
HSA FS BR	-0.12	0.3		0.09	0.4		-0.04	0.7		-0.12	0.3	
L-spine BMD AP	0.22	0.05		0.31	0.005		0.09	0.4		0.10	0.4	
L-spine BMD Lat	0.15	0.2		0.28	0.02		0.03	0.8		-0.13	0.3	

BMI			Lean mass			Total fat mass			VAT mass		
r	p		r	p		r	p		r	p	
Total hip BMD											
0.38	0.0004	^{*,‡}	0.50	<0.0001	^{*,‡}	0.24	0.03		0.31	0.008	

^{*}: significant after controlling for multiple comparisons;

[‡]: significant after controlling for multiple comparisons, age and sex;

[‡]: significant after controlling for multiple comparisons, age, sex and lumbar spine BMD (for TBS) and hip BMD for HSA parameters

HSA: hip structural analysis; NN: narrow neck; IT: intertrochanteric; NS: femoral shaft; CSA: cross-sectional area; CSMI: cross-sectional moment of inertia; Z: section modulus; BR: buckling ratio