Lean mass predicts hip geometry in men and women with non-insulin-requiring type 2 diabetes mellitus

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INTRODUCTION

In men and women with type 2 diabetes mellitus (T2DM), BMD alone may not be the best predictor of bone strength (1, 2). Despite having higher BMD compared to weight-matched controls, individuals with T2DM are at increased of hip fracture (1, 3, 4). This risk appears more pronounced in those with later-stage, insulin-requiring disease than in those with impaired glucose tolerance, suggesting that with progressive insulin resistance, bone quantity and quality begin to diverge (5). Because BMD and other measures of bone quantity do not necessarily predict of skeletal status in T2DM, in this population, it is important to explore novel measures of bone quality and strength.

Bone strength is a composite of tissue mineral density, architecture and geometry. Fracture occurs with the compromise of one or more of these components (6). While dual x-ray absorptiometry (DXA) is used to quantify bone density and computed tomography (CT) helps to define bone architecture, the geometry of bone and its response to external forces is derived from established principles of hip structure analysis (HSA). Section modulus describes hip bending strength, and buckling ratio is used to describe hip cortical stability under compressive loads. Cross-sectional area represents the degree of hip mineralization in cross-section (7). To date, there has been limited application of HSA and evaluation of hip geometry in those with T2DM. Furthermore, modifiable contributors to hip geometry in T2DM have not been identified.

Though BMI is one of the strongest determinants of bone density, recent analyses in both healthy and diabetic men and women suggest that the fat and lean components of BMI differentially affect bone metabolism (8, 9). Greater lean mass enhances muscle contractile forces on bone with resultant mechanoreceptor and osteoblast activation (10). Adipokines

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and sex hormones derived from adipose tissue may also independently influence bone remodeling through their positive and negative effects on osteoblast and osteoclast activity (11–14). Limited data in healthy subjects also show that fat and lean mass have differential effects on hip geometry. While greater lean mass appears to be associated with favorable proximal femur strength in populations of adult men and women, these same associations are yet to be investigated in those with T2DM (15, 16). Because fracture risk appears to increase with worsening insulin resistance, this association is particularly important to understand in diabetic populations with non-insulin requiring disease in whom an early intervention may be able to confer fracture protection (5).

In this study, we investigated the independent contributions of fat and lean mass to hip geometry parameters in middle-aged subjects with non-insulin-requiring T2DM. We hypothesized that increased lean mass would be significantly associated with favorable hip section modulus, cross-sectional area, and buckling ratio estimates. Further, we examined the associations of total, abdominal, subcutaneous (SQ) and visceral fat on these same HSA estimates. We then evaluated possible mechanical means by which lean mass could influence hip geometry by examining the relationship between section modulus, cross sectional area and buckling ratio and total and lower extremity muscle strength. Finally, we looked for additional associations between hip geometry and measures of glycemic control, insulin resistance and medications in study subjects.

MATERIALS AND METHODS

Study design and subjects

For this cross-sectional study, baseline data were used from Sugar, Hypertension and Physical Exercise (SHAPE-2, NCT 00212303, ClinicalTrials.gov), a randomized trial investigating the effects of a 6-month exercise intervention on cardiovascular parameters in sedentary men and women with uncomplicated T2DM and mild hypertension. The study was approved by The Johns Hopkins University School of Medicine Institutional Review Board, and subjects provided informed consent prior to study entry. Men and women were aged 40–65 years and were recruited from the Baltimore area. Subjects were eligible if they were being actively treated for hypertension or had a systolic blood pressure 130–159 mmHg or diastolic blood pressure 80–99 mmHg (17). Exclusion criteria for the study included moderate or severe hypertension, BMI greater than 35 kg/m^2, cigarette smoking in the last six months, alcohol abuse, pregnancy or any other major organ dysfunction to include cardiovascular, renal, pulmonary or thyroid disease. For this analysis, men and women were additionally excluded if they were taking glucocorticoids, bisphosphonates, anti-epileptic agents or other medications that might interfere with bone metabolism.

Type 2 diabetes mellitus

All subjects in SHAPE-2 had non-insulin requiring diabetes mellitus and were on one or more oral diabetes medications. Those on hormone therapy (HT) and thiazolidinediones (TZDs) were included in the analysis. Diabetes was verified by medical records, a health care provider, or test results indicating a fasting glucose > 7.0 mmol/L (126 mg/dL), random plasma glucose of >11.1 mmol/L (200 mg/dL) or a 2- hour plasma glucose > 11.1 mmol/L (200 mg/dL) following a 75g glucose load.(18) Men or women with a HbA1c > 11% or random plasma glucose > 22.2 mmol/L (400mg/dL) were excluded.

Anthropometrics, BMD and body composition

Subjects' baseline weight and height were recorded from a calibrated digital scale and stadiometer, respectively. BMI was calculated as weight (kg) divided by height (cm) squared, and waist to hip ratio was derived from the appropriate circumferential

measurements. Bone density at the total body, proximal femur and tricompartmental body composition (fat, lean, mineral) were measured by DXA (GE Lunar Prodigy, General Electric Medical Systems, Milwaukee, WI, USA, Encore 2010, version 13.31.016). Abdominal total, visceral and SQ fat compartments were assessed by 3-slice axial spin-echo series magnetic resonance imaging (MRI, Siemens Medical Systems, Iselin, NJ, USA). To calculate abdominal fat compartments, blinded readers used inversion recovery methods on MRI to optimize the signal contrast between aqueous and adipose tissue. Previous studies using this technique have demonstrated an intraobserver coefficient of variation of 1.6% for SQ fat and 6.5% for abdominal visceral fat (19).

Hip geometry measurements

Hip geometry was quantified using HSA software developed by Beck and colleagues, as previously described (20). Calculations were based on DXA scan measurements at the narrowest point of the femoral neck, or narrow neck (NN) region. With these HSA equations and mineral mass information derived from DXA, BMD was calculated in addition to cross-sectional area (average mineral density with soft tissue spaces removed), bone width and cross-sectional moment of inertia (CSMI) at the NN. Section modulus, a measure of bending strength, was calculated as CSMI divided by the maximum distance from the center of mass to the medial or lateral cortical margin (d_{max}). Cortical thickness was estimated from an annulus model of the NN with a fixed fraction of measured mass at the cortex. Buckling ratio, the propensity of cortical buckling under compressive loads, was estimated as d_{max} divided by mean cortical thickness.

Strength and additional measurements

At baseline, total, upper and lower body muscle strength were measured for each subject using 1- repitition maximum (1-RM) on each of seven different resistance exercises (Hoist 6000 multi-station weight machine, Hoist Fitness, San Diego, CA) (21). Subjects' serum was also sent for baseline fasting insulin (CV: 6%; Linco Research Inc., St. Louis, MO), glucose (CV: 1.5%; Beckman Diagnostics, Fullerton, CA), 25-hydroxy vitamin D (CV: 8%; DiaSorin, Stillwater, MN) and hemoglobin A1C (HbA1c) (CV: 6%; Tosoh A1c 2.2 Plus HPLC, Foster City, CA) values. Quantitative insulin sensitivity check indices (QUICKI) were calculated on all men and women, calculated using the following equation: 1/[log (fasting insulin, mU/L) + log (fasting glucose, mg/dL)] (22).

Statistical analysis

A p-value < 0.05 was considered significant for all analyses, with values presented as mean ± standard deviation. All data were normally distributed. Differences amongst continuous variables describing the baseline characteristics of pre and post-menopausal women and men were determined by ANOVA. Pearson correlation coefficients were used to describe the associations of these continuous variables with section modulus, cross-sectional area and buckling ratio in men and women. Associations between categorical variables and hip geometry outcomes were evaluated with unpaired Student's t-tests. For those variables which demonstrated significant correlations in bivariate analysis, generalized linear modeling (GLM) was utilized to determine whether these variables predicted measures of hip geometry. For the initial analysis, the effects of lean and fat mass on hip geometry parameters were evaluated in both men and women, with the model was adjusted for gender and menopausal status (model 1). In secondary analysis, men and women were evaluated separately to determine sex-specific body composition predictors of section modulus, cross-sectional area and buckling ratio. Due to the known effects of HT on bone metabolism in women, all models were then constructed both excluding and including women on HT (n=50 vs. n=56). The multivariate models including women on HT were then adjusted for HT use and are reported here (model 2). If fat mass appeared to be significantly associated

with a measure of hip geometry, a final series of models were created to determine the independent contribution of lean mass in addition to total or SQ or abdominal visceral fat to hip geometry following adjustment for HT use and menopausal status. This series of analyses were also used to determine the associations between strength measurements and hip geometry. All analyses were carried out using the JMP 8.0.1 statistical software package (SAS Institute, Inc.).

RESULTS

Baseline study population

A total of 134 subjects were included in this analysis. Baseline characteristics including age, anthropometrics, body composition, bone density, strength measures, hip geometry and biochemical data are shown in table 1. Four subjects were excluded from the original SHAPE-2 cohort (n=138) in the present analysis; two men were taking prednisone while two women were taking bisphosphonates at the time of enrollment. Two-thirds of the 56 women in the study were post-menopausal, with 10.8% on HT. Three of the 78 men (3.8%) were taking testosterone at study start.

Glycemic control

QUICKI scores confirmed that subjects had insulin resistance, although 3-month glycemic control was adequate as evidenced by a mean HbA1c was $6.6 \pm 1.2\%$ and $6.8 \pm 1.6\%$ in women and men, respectively. At the time of enrollment, 28.2% of men and 17.9% of women were on TZD monotherapy or in conjunction with other oral medications including metformin, sulfonylureas and/or sitagliptin.

Body composition and muscle strength

There were no significant differences in lean mass, fat mass or abdominal fat compartments between pre and post-menopausal women (data not shown). Taken together, women had significantly higher BMIs compared to men (women, 34.4 ± 5.0 kg/m^2; men, 32.6 ± 4.1, p <0.05), although all subjects were overweight to obese with a BMI range from 29–42 kg/m^2. Women also had significantly greater total, SQ, visceral and abdominal fat than men. Conversely, men had significantly greater lean mass as well as total and lower body muscle strength (table 1).

Bone mineral density and hip geometry

BMD was not significantly different between pre and post-menopausal women. All subjects had normal BMD, defined as falling within one standard deviation of both age-matched mean (Z-score) and young adult mean (T-score) BMD (23). There was no significant difference in BMD between the sexes in the total body, hip or femoral neck. However, men had greater hip mineralization in cross section and bending strength but buckling ratio (9.1 ± 1.6, p<0.05) was increased compared to women, indicating a higher degree of cortical instability when the hip is subjected to compressive forces. Note that the vitamin D status of most subjects was at levels recommended by the Institute of Medicine with mean 25-hydroxy vitamin D levels in women 57.6 ± 22.0 nmol/L (23.1 ± 8.8 ng/mL) and in men 61.9 ± 20.0 nmol/L (24.8 ± 8.4 ng/mL) (24, 25).

Body composition, strength and hip geometry correlations

Correlations between hip geometry measurements and anthropometrics, body composition and strength are shown in table 2. As menopausal status or age did not contribute significantly to body composition or hip geometry in multivariate analysis (data not shown), pre and post-menopausal women were pooled for analysis. In women, increased age was

associated with lower section modulus (r = −0.30) and cross-sectional area (r = −0.31) while BMI was positively associated with these parameters and negatively associated with buckling ratio (r = 0.43, 0.47 and −0.26, respectively). In men, increased BMI was modestly but positively correlated with increased cross-sectional area (r = 0.23). Femoral neck BMD was positively associated with section modulus and cross-sectional area (r = 0.63 and 0.91, respectively) and negatively associated with buckling ratio in both men and women (r = −0.87 and −0.91, respectively). Lean mass was significantly and positively correlated with section modulus (r = 0.45, women and r = 0.55, men) and cross-sectional area (r = 0.47, women and r = 0.53, men) in both sexes and negatively with buckling ratio (r = −0.27) in men alone. In women, abdominal SQ fat mass was associated with section modulus (r = 0.34) and cross-sectional area (r = 0.32); there was no relationship between the other adipose compartments and hip geometry in women. In men, buckling ratio was negatively associated with abdominal SQ fat (r = −0.23). Total and lower body strength were associated with section modulus (r = 0.28) and cross-sectional area (r = 0.36) in men. These significant associations were also seen in women with the exception of the relationship of lower body strength and cross-sectional area. Buckling ratio was only significantly and inversely associated with total strength in men (r = −0.24).

Hip geometry and glycemic control correlations

HbA1c was significantly associated with all measures of hip geometry in men. Measures of insulin resistance, or QUICKI, were inversely associated with cross-sectional area (r = −0.25) and positively associated with buckling ratio (r = 0.26) in men. These same associations between measures of glycemic status and HSA were not demonstrated in women. Vitamin D levels were inversely associated with section modulus (r = −0.41) and cross-sectional area (r = −0.39) in women and only cross-sectional area (r = −0.25) in men.

Multivariate analysis

These results are shown in table 3. For the initial analysis, both men and women were entered into a model adjusted for sex. In this model, only lean mass significantly predicted section modulus, cross-sectional area and buckling ratio with no additional contribution of fat mass to hip geometry. Sex was a significant predictor of only buckling ratio in this model. Because of different sample sizes of men and women and the fact that there were significant correlations between fat mass and hip geometry in women, additional models were used to evaluate the sexes separately. In men, lean mass continued to significantly predict all three measures of hip geometry, though this was not the case in women. Rather, fat mass emerged as a significant predictor of section modulus and cross-sectional area while lean mass significantly contributed to only cross-sectional area. Neither fat nor lean mass were associated with buckling ratio in women. To further investigate the relative contribution of fat type to hip geometry in women, an additional series of GLMs was employed. Given the significant colinearity between abdominal total and SQ fat in women (r = 0.92, p<0.01), these fat compartments were entered separately into multivariate models which included lean mass. In this series of models, lean mass, but not abdominal total or SQ fat, significantly contributed to cross-sectional area and section modulus (data not shown). Although total and lower body muscle strength were associated with increased hip geometry in men and women, after controlling for lean mass, strength measures did not independently predict section modulus, cross-sectional area or buckling ratio in either sex. Vitamin D, HbA1c and QUICKI, and TZD use also failed to contribute to hip strength estimates when entered into multivariate analyses (data not shown). Given the known effects of TZD use on both body composition and bone metabolism, we performed subgroup analyses excluding those men and women on PPAR λ agonists (26–28). We re-analyzed the correlations between body composition parameters and hip geometry found that the correlations did not

change in either sex. In addition, we ran multivariate models adjusted for TZD use and found no significant contribution of TZD-use to either body composition or hip geometry.

DISCUSSION

This is the first study to investigate hip geometry in T2DM and its relationship to body composition. Previous studies have explored the relationships between body composition and BMD in T2DM, though none have applied HSA to investigate the effects of fat and lean mass on hip strength (29). Currently postulated mechanisms that explain increased skeletal fragility in individuals with T2DM relate to the micro- and macrovascular complications of longstanding disease, increased fall risk, and diabetic medications such as TZDs (3, 27, 30, 31). Few investigators have considered the influence of bone architecture and strength on fracture risk in this population with otherwise-sufficient BMD. In the multisite Osteoporotic Fractures in Men (MrOS) study, Petit el al found elderly men with diabetes have significantly higher areal BMD than control subjects (32). Despite this elevation in BMD, elderly men with T2DM had lower cortical total bone area and bending strength. This finding was similar to that noted by Beck and colleagues in obese women of the WHI (33). BMD, though related to hip geometry, is not an adequate predictor of hip fracture risk in T2DM. Improved understanding of skeletal fragility in T2DM will require identification of those variables, including body composition, which influence not only BMD but also hip geometry.

There is a paucity of data describing the relationships between fat mass, lean mass and hip geometry in adults. In fact, much of the published literature on the subject involves children and adolescents (34–36). There is no data describing hip geometry and body composition in adults with T2DM. In BACH/Bone, Travison *et al* found that both lean and fat mass correlated with hip strength parameters in healthy men across a wide age spectrum, 30–79 years (16). Only after controlling for lean mass was fat mass found to be inversely associated with proximal femur strength. In a similarly-broad group of men aged 40–79 years, Semanick *et al.* found that *leg* lean mass was significantly and favorably associated with hip section modulus and cross sectional area in Afro-Caribbean men (37). In women, the data are more scarce. Both fat and lean mass were associated with hip geometry in the postmenopausal women (50–79y) of the Women's Health Initiative-Observational Study (WHI-OS) (33). Importantly, measures of hip strength increased with BMI in proportion to increases in lean mass.

In this study, we demonstrated that lean mass independently predicts hip strength measurements in middle-aged men and women with non-insulin-requiring disease. This finding lends insight into the underlying pathophysiology of increased fracture risk in T2DM despite normal BMD. We speculate, given our findings, that losses in lean mass with progressive T2DM precipitate losses in hip strength and increases in fracture incidence. The significance of lean mass as a predictor of hip strength is particularly intriguing given emerging recognition of sarcopenic obesity in T2DM (38). In Health ABC, Park *et al* found that T2DM in elderly men and women was associated with decreased muscle mass and strength (39). In longitudinal analysis, this same group demonstrated accelerated loss of muscle quantity and strength over time compared to healthy, age-matched controls (40). Decreases in lean mass with T2DM progression can increase fall risk but may also directly and adversely affect bone quality. Lean mass has also been shown to be closely associated with BMD in men and women with early T2DM (29). Therefore, these data further support possible interventions to prevent declines in lean mass which may help prevent reductions in *both* bone density and hip strength. Resistance training builds lean mass and generates forces which mediate mechanoreceptor stimulation and bone remodeling (10). In our subjects, we found significant correlations in total and lower extremity muscle strength and

hip geometry. Thus, resistance exercise may be able to offset losses in hip strength and lean mass over time. Additional trials are required to determine whether changes in lean mass remain associated with changes in hip strength parameters as diabetes progresses and diabetic complications develop. Investigation is also required to determine if building lean mass can improve hip geometry in T2DM.

In addition to the contributions of lean mass to hip geometry, we found that fat mass was associated with section modulus and cross-sectional area in women. This finding may be in part due to significant differences in body composition between sexes. We could also postulate that in middle-aged women with non-insulin requiring diabetes mellitus, both lean and fat mass contribute to hip strength. There is growing realization that adipose tissue may independently influence bone metabolism. Adipokines and fat-derived sex hormones both facilitate and impair bone remodeling (41). Leptin promotes osteoblast differentiation and proliferation locally but may stimulate bone resorption centrally (42). We found no significant correlation between serum leptin and hip geometry in either sex, but we did not investigate other mediators of the fat-bone relationship. For example, adiponectin may also have mixed effects on bone, increasing osteoblastogenesis yet inhibiting osteoprotegerin which bolsters osteoclastogenesis (14). Estrogen, a fat-derived sex hormone, may protect those in the perimenopause from accelerated bone loss (43).

In this study, fat mass contributed to favorable hip geometry in women only. However, with time, increased obesity and more advanced diabetes, the cumulative effects of adipose tissue on hip strength may eventually be deleterious. The WHI-OS showed that at higher BMI's, femoral neck BMD, cross16 sectional area and section modulus decline as a result of overall reduction in lean mass relative to total mass (33). As noted, in BACH/Bone fat mass was negatively associated with proximal femur strength in older men (16). In part, this observation may be due to adverse effects of adipokines on bone. Adipose tissue may also promote the circulation of pro-inflammatory cytokines with subsequent osteoclast activation and suppression of osteoblast differentiation. Resistance exercises to maintain and build lean mass in T2DM combined with interventions designed to reduce overall fat mass could further improve hip geometry in men and women with T2DM as well as have favorable effects on diabetes.

We found modest but significant inverse correlations between HbA1c and hip geometry measures in men, suggesting that suboptimal glycemic control was associated with favorable hip strength. A possible explanation for this relationship is that hyperglycemia induces a hyperinsulinemic state. Insulin is anabolic to bone, stimulating osteoblast growth and proliferation on periosteal surfaces and increasing section modulus, cross-sectional area and buckling ratio (44). Though fasting insulin levels were not significantly correlated with hip geometry, the sample may not have been large enough to detect these relationships. Further, subjects were on insulin sensitizing agents. Vitamin D levels were inversely associated with cross-sectional area in both sexes and section modulus in women. Increased adiposity is associated with vitamin D deficiency, and here we have shown that fat mass is significantly associated with hip strength in women (45). The relationship between vitamin D deficiency and hip strength in men remains unclear.

Study limitations

We recognize that there were limitations to this study. We could describe associations but not causal relationships between body composition and hip strength parameters in this cross-sectional analysis. There was no age-matched control population in this study against whom to compare our findings. Subjects were only enrolled in the study if they had uncomplicated, non-insulin requiring diabetes, but we did not have data on disease duration or microvascular complications. This limitation precludes generalization of our conclusions to

those with insulin-requiring or more complicated disease. Though we had information on medication use at the time of enrollment, we did not have a record of duration of medication use or diabetes medications which may have been discontinued prior to enrollment. Non-prescription medications including multivitamins, calcium and vitamin D intake were not recorded. Using NHANES 2003–2006 data, we assume that in the absence of any supplementation, subjects' daily, dietary intake was *at least* calcium 1000 mg/day and vitamin D 200 IU/day (46). Data from non-diabetic postmenopausal women in the WHI show that calcium 1000mg and vitamin D 400 IU daily supplementation has favorable effects on hip geometry parameters (47). Further studies are needed to determine whether similar supplementation in men and women with T2DM could have similar, beneficial effects on hip strength. We saw no relationship between TZD use and HSA measurements in either men or women, but additional research is needed to determine the effects of prolonged use of PPAR γ agonists on hip geometry in diabetic populations. We believe that the small numbers of men and women on PPAR γ agonists limits our ability to draw definitive conclusions as to the contribution of this class of medication to body composition and hip strength in men and women with T2DM. Similarly, we saw no relationship between HT use and hip geometry in study subjects despite the known positive effects of sex hormones on bone (48). We suspect that this study was not powered to detect the association between HT use and hip geometry, and would propose that this clinical question requires dedicated studies in the future.

SUMMARY AND CONCLUSION

The increased fracture rate observed in T2DM is likely multifactorial and a product of acquired physiologic and biomechanical changes that adversely affect bone. BMD does not explain the skeletal fragility observed in individuals with T2DM and thus it is important to identify other measures of skeletal strength in this population. Identification of modifiable contributors to hip geometry in early diabetes has implications for fracture prevention. We have shown that lean mass is an independent predictor of hip strength in men and women with non-insulin-requiring T2DM. When evaluated separately, fat mass was also associated with hip geometry in women. Additional studies are warranted to determine whether acquisition or maintenance of lean mass through resistance training can modify hip strength in T2DM or potentially prevent fracture.

Acknowledgments

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Table 1

Study subject baseline characteristics

	Women (n=56)	Men (n=78)
Age (years)	55.6 ± 6.2	56.9 ± 5.9
BMI (kg/m^2)	34.4 ± 5.0[*]	32.6 ± 4.1
Waist circumference (cm)	99.8 ± 10.9[*]	106.8 ± 9.3
Waist-hip ratio	0.8 ± 0.1[*]	1.0 ± 0.1
Body fat (%)	44.8 ± 5.4[*]	33.6 ± 5.1
Lean mass (kg)	47.5 ± 6.6[*]	64.3 ± 8.4
Fat mass (kg)	41.9 ± 10.7[*]	34.7 ± 8.2
Abdominal total fat (cm^2)	636.0 ± 158.8[*]	563.6 ± 139.6
Abdominal SQ fat (cm^2)	473.1 ± 132.1[*]	357.7 ± 109.7
Abdominal visceral fat (cm^2)	136.5 ± 57.2[*]	178.3 ± 72.5
Section modulus	1.8 ± 0.3[*]	2.4 ± 0.4
Cross sectional area	3.3 ± 0.5[*]	3.8 ± 0.6
Buckling ratio	8.3 ± 1.4[*]	9.1 ± 1.6
BMD total body (g/cm^2)	1.28 ± 0.11	1.31 ± 0.12
BMD hip (g/cm^2)	1.12 ± 0.15	1.16 ± 0.15
BMD femoral neck (g/cm^2)	1.04 ± 0.15	1.08 ± 0.16
Total strength (kg)	312.5 ± 55.3[*]	484.5 ± 8.7
Lower extremity strength (kg)	186.5 ± 38.2[*]	264.6 ± 5.2
25-hydroxy vit D (nmol/L)	57.6 ± 22.0	61.9 ± 20.0
Fasting glucose (mmol/L)	7.8 ± 2.9	8.1 ± 2.4
Fasting insulin (pmol/L)	157.0 ± 63.9	177.1 ± 134.7
Fasting leptin (mcg/L)	27.5 ± 13.8[*]	11.5 ± 7.5
HbA1c (%)	6.6 ± 1.2	6.8 ± 1.6
QUICKI	0.3 ± 0.02	0.3 ± 0.02

Values are mean ± standard deviation (SD)

[*] Mean values different from men (p≤0.05)

Body mass index (BMI); Bone mineral density (BMD); Subcutaneous (SQ); Vitamin (vit); Hemoglobin A1c (HbA1c); Quantitative insulin sensitivity check index (QUICKI)

Table 2

Correlation coefficients

Variable	Section Modulus		Cross Sectional Area		Buckling Ratio	
	Women (n=56)	Men (n=78)	Women (n=56)	Men (n=78)	Women (n=56)	Men (n=78)
Age (years)	−0.30*	−0.20	−0.31*	−0.21	0.11	0.11
BMI (kg/m²)	0.43*	0.20	0.47*	0.23*	−0.26*	−0.21
BMD femoral neck (g/cm²)	0.65*	0.63*	0.91*	0.91*	−0.87*	−0.91*
Lean mass (kg)	0.45*	0.55*	0.47*	0.53*	−0.20	−0.27*
Fat mass (kg)	0.47*	0.10	0.49*	0.12	−0.21	−0.13
Abd. total fat (cm²)	0.24	−0.03	0.22	0.03	−0.04	−0.14
Abd. SQ fat mass (cm²)	0.34*	0.01	0.32*	0.11	−0.08	−0.23*
Abd. vis fat (cm²)	−0.08	−0.10	−0.08	−0.10	0.02	0.04
Total strength (kg)	0.29*	0.32*	0.27*	0.36*	−0.09	−0.24*
LE strength (kg)	0.28*	0.28*	0.22	0.31*	−0.03	−0.21
25-hydroxy vit D (ng/dL)	−0.41*	−0.20	−0.39*	−0.25*	0.20	0.20
HbA1c (%)	0.01	0.25*	0.03	0.35*	−0.20	−0.27*
QUICK-I	−0.01	−0.17	0.01	−0.25*	0.21	0.26*

*
P-value significant, ≤0.05

Body mass index (BMI); Bone mineral density (BMD); Abdominal (Abd.); Subcutaneous (SQ); Visceral (vis); Lower extremity (LE); Vitamin (vit); Hemoglobin A1c (HbA1c); Quantitative insulin sensitivity check index (QUICKI)

Not significantly correlated in either sex (p>0.05): waist-hip ratio, fasting insulin, fasting leptin

Table 3

Multiple linear regressions showing the effects of lean and fat mass on HSA parameters with and without adjustment for sex

| | Men & Women (n=134) | | Women (n=56) | | Men (n=78) | |
| | Model 1[a] | | Model 2[b] | | Model 2[b] | |
	β	P	β	P	β	P
Section Modulus						
Sex	−0.084	0.095				
Lean mass	0.025	<0.001[*]	0.014	0.532	0.029	<0.001[*]
Fat mass	0.002	0.593	0.009	0.031[*]	−0.004	0.431
Cross Sectional Area						
Sex	0.011	0.876				
Lean mass	0.034	<0.001[*]	0.022	0.049[*]	0.038	<0.001[*]
Fat mass	0.005	0.278	0.016	0.021[*]	−0.004	0.619
Buckling ratio						
Sex	−0.721	0.002[*]				
Lean mass	−0.043	0.021[*]	−0.023	0.492	−0.050	0.030[*]
Fat mass	−0.012	0.432	−0.019	0.059	−0.010	0.673

[*] P- value significant, ≤0.05

[a] Adjusted for sex, hormone thrapy (HT)

[b] Adjusted for HT, menopausal status (women only)