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Lean mass as a predictor of bone density and microarchitecture in adult obese individuals with metabolic syndrome

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ABSTRACT

The effects of obesity and metabolic syndrome (MS) on bone health are controversial. Furthermore, the relationship between body composition and bone quality has not yet been determined in this context. The aim of this study was to investigate the correlations between body composition and bone mineral density (BMD) and bone microstructure in obese individuals with MS. This cross-sectional study assessed 50 obese individuals with MS with respect to their body composition and BMD, both assessed using dual X-ray absorptiometry, and bone microarchitecture, assessed by high-resolution peripheral quantitative computed tomography (HR-pQCT) of the distal tibia and radius. Several HR-pQCT measurements exhibited statistically significant correlations with lean mass. Lean mass was positively correlated with parameters of better bone quality (r: 0.316–0.470) and negatively correlated with parameters of greater bone fragility (r: −0.460 to −0.310). Positive correlations were also observed between lean mass and BMD of the total femur and radius 33%. Fat mass was not significantly correlated with BMD or any HR-pQCT measurements. Our data suggest that lean mass might be a predictor of bone health in obese individuals with MS.

Introduction

Obesity is a clinical condition of epidemic proportions, with a growing number of patients affected across the world [1]. It is associated with many complications such as stroke, coronary heart disease, lung disease and vascular insufficiency [2], but until recently it was considered a protective factor for bone. This concept was based on the higher bone mineral density found in these patients [3,4]. However, new studies have shown a similar incidence of fractures between obese and nonobese individuals [5,6].

Metabolic syndrome (MS) is very common in obese patients and abdominal fat and insulin resistance are involved in its pathophysiology [7]. MS is characterized by a proinflammatory state that negatively affects cardiovascular risk [8]. Chronic inflammatory states are also commonly associated with bone disorders, as demonstrated by studies on osteoporosis in patients with rheumatoid arthritis and systemic lupus erythematosus [9]. The balance between the protection afforded by increased body weight and the damage caused by the inflammatory state has led to controversial results in clinical studies assessing bone mineral density (BMD) [10].

In addition to increased body mass index (BMI), body composition also seems to influence bone quality. Studies, using dual-energy X-ray absorptiometry (DXA), have found positive correlations between lean mass and BMD, whereas the relationship with fat mass has yielded conflicting results, showing positive, negative and no correlations [11].

Although DXA is considered the gold standard and most widely used radiological method to assess bone mass, it has a number of well-known limitations [12]. High-resolution peripheral quantitative computed

Abbreviations: BMD, bone mineral density; MS, metabolic syndrome; HR-pQCT, high-resolution peripheral quantitative computed tomography; BMI, body mass index; DXA, dual-energy X-ray absorptiometry; CRP, C-reactive protein; CTX, carboxy-terminal telopeptide of collagen-1; PTH, parathormone; Dtrab, volumetric BMD of trabecular bone; Dcort, volumetric BMD of cortical bone; Dtot, volumetric BMD of total bone; CTh, cortical thickness; BV/TV, percentage of trabecular bone volume; TbTh, trabecular thickness; TbN, trabecular number; TbSp, trabecular separation; TbSp 1/N SD, standard deviation of trabecular spacing.

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tomography (HR-pQCT) is a new method that provides additional information about the quality of bone microarchitecture [13]. Previous studies have shown associations between deterioration in trabecular and cortical microarchitecture and fractures [14,15].

The aim of the present study was to investigate the relationship between the fat and lean mass distributions (assessed by means of DXA) and bone parameters, assessed by densitometry and HR-pQCT, in obese adults with metabolic syndrome to provide new information regarding this controversial issue.

Material and methods

Participants

Fifty obese (BMI ≥ 30 kg/m^2), non-diabetic, individuals with metabolic syndrome treated at the State Institute of Diabetes and Endocrinology of Rio de Janeiro (IEDE-RJ) were assessed in this study. All patients were under 50 years of age and female participants were at menacme and exhibited regular menstrual cycles. Metabolic syndrome was defined according to the International Diabetes Federation [16], with mandatory criteria including a waist circumference larger than 90 cm for males and 80 cm for females and at least two of the following: (1) triglycerides ≥150 mg/dl (or use of a specific treatment to decrease triglycerides); (2) HDL <40 mg/dl in males and <50 mg/dl in females (or use of a specific treatment for HDL); (3) systolic arterial pressure ≥130 mm Hg and diastolic arterial pressure ≥85 mm Hg (or use of a specific treatment for blood pressure); and (4) fasting blood glucose ≥100 mg/dl.

Patients with a body weight >150 kg were excluded from the study due to the limitations of the densitometry device. In our selection of patients, two were excluded for exceeding the weight limit.

The study protocol was approved by the ethics committee of the IEDE-RJ (CAAE 003-11), and all participants signed an informed consent form that was written in accordance with the second Declaration of Helsinki.

Measurements

All participants underwent a structured medical interview and physical examination. A number of factors that might interfere with bone health were investigated, including smoking, alcohol use, physical activity, previous fractures, chronic diseases and use of medications (e.g., thiazides, corticoids, contraceptives, and anticonvulsants). Premenopausal state was assessed based on clinical records. BMI values were calculated using the weight/height^2 ratio and expressed as kg/m^2. Abdominal circumference was expressed in centimeters and measured at the midpoint between the rib cage border and the iliac crest. Blood samples were collected after a 12-hour fast to measure glucose, lipid profiles, insulin (measured by routine methods), C-reactive protein (CRP, immunoturbidimetry, normal range [NR] <3 mg/l), bone alkaline phosphatase (chemiluminescence, NR: men: 6–30 μg/ml; women at menacme: 3–19 μg/ml), carboxy-terminal telopeptide of collagen-1 (CTX, electrochemiluminescent immunoassay, NR: men under 50 years: ≤0.584 ng/ml and women at menacme: ≤0.573 ng/ml), parathormone (PTH, chemiluminescence, NR: 12–65 pg/ml) and 25-OH-vitamin D (chemiluminescence; normal: ≥30 ng/ml, insufficiency: 21–29 ng/ml, deficiency: ≤20 ng/ml).

A Prodigy-GE densitometer (GE Lunar Prodigy Advance, GE Healthcare Madison, WI, USA) was used to assess body composition and BMD by means of DXA. Lean body mass (grams) and body fat mass (grams and percentage) were measured for the entire body. BMD was measured at the lumbar spine, femoral neck, total femur, and the radius 33% (proximal third of the radius) and was expressed in absolute values (g/cm^2) and as standard deviations (SDs) from the expected BMD for the age-matched population (Z-score). The reference standard from which the T-score was calculated was the National Health and Nutrition Examination Survey III (NHANES III) database, which was corrected for male sex when men were evaluated. Values of Z-scores ≤−2.0 were considered to be lower than the expected bone mass. The coefficient of variation of BMD measurements at our institution is 1.5% at the lumbar spine and 2.3% at the femoral neck.

Volumetric BMD and bone microarchitecture were measured on appropriately immobilized non-dominant distal forearm and tibia using a 3D HR-pQCT system (XtremeCT, SCANCO Medical AG, Brüttisellen, Switzerland). This system employs a 2D detector combined with a 0.08-mm point-focus X-ray tube, which enables the acquisition of several CT sections with an 82-μm nominal resolution. A total of 110 sections were obtained at each site, generating a 9-mm 3D representation of the axial direction. The radiation dose was similar to that used in standard DXA procedures (less than 3 μSv per measurement). The attenuation data were transformed to equivalent hydroxyapatite (HA) densities. The data were assessed for artifacts and excluded when necessary; the analysis was performed with 49 radial and 45 tibial images. More details of the image acquisition and analysis have been previously described [17]. The same accredited technician analyzed all of the images.

The variables included in the analysis were as follows: volumetric BMD (g HA/cm^3) in the trabecular (Dtrab) and cortical (Dcort) areas, as well as the total area (Dtot); cortical thickness (CTh, mm); percentage of trabecular bone volume (BV/TV, %); trabecular thickness (TbTh, mm); trabecular number (TbN, mm^{-1}); trabecular separation (TbSp, mm); and standard deviation of trabecular spacing (TbSp 1/N SD, mm). TbTh and TbSp were calculated based on TbN and BV/TV [TbTh = BV/TV / TbN and TbSp = (1 − BV/TVd) / TbN]. CTh was calculated by dividing the cortical volume by the external bone surface. The variability of density-based measurements is typically less than 1% and between 3% and 5% for bone structural parameters [13].

Statistical analysis

The statistical analysis was performed with SAS® System software, version 6.11 (SAS Institute, Inc., Cary, NC, USA). The results were expressed as the mean and standard deviation, median and interquartile range or number and percentage. Correlations among the clinical, metabolic, bone densitometry, body composition, and HR-pQCT variables were analyzed by Pearson's correlation coefficient or the Spearman correlation coefficient, as appropriate. Student's *t* test was used for independent samples.

Multivariate analysis was performed to investigate the association between variables and possible confounders and to assess the impact of multiple covariates in the same model. A multiple linear regression including lean mass (g), fat mass (g), age, gender, 25-OH-vitamin D and CRP was used to identify the independent variables that influence the HR-pQCT measurements. A p-value less than 0.05 was considered significant. After Bonferroni adjustments, the significant p-value was 0.008.

Results

The study population comprised 40 women and 10 men. The primary clinical, anthropometric, laboratory and densitometry data are described in Table 1. The distribution of participants according to BMI ranges was as follows: 11 exhibited grade 1 obesity (BMI = 30–34.9); 16 displayed grade 2 obesity (BMI = 35–39.9); and 23 showed grade 3 obesity (BMI ≥ 40). All participants were sedentary. None reported a previous history of fractures. None of the participants were smokers or consumed more than 20 g of alcohol per day.

Only six participants exhibited a Z-score ≤−2, and all lower than expected bone mass value were observed at the lumbar spine. Higher than expected BMD values were observed in five participants (Z-score ≥ 2): one at the lumbar spine, one at the femoral neck, and three at the total femur.