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# Metabolic syndrome reduces bone mineral density in overweight adolescents☆

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A B S T R A C T

Growing concern has focused on the occurrence of metabolic syndrome (MetS) and its effects on bone mass. There is little information available in the literature concerning the relationship between MetS and BMD in adolescents. The aim of this study was to evaluate the effects of MetS and its components on bone mineral density (BMD) in overweight adolescent boys and girls. This cross-sectional study assessed 271 overweight adolescents with or without MetS (age 10 to 16 years). Anthropometric and biochemical tests were performed. Lumbar spine, proximal femur and total and subtotal body BMD values were obtained by bone densitometry with dual-energy X-ray absorptiometry. MetS was observed in 14% of the adolescents. Overweight adolescents of both genders who were positive for MetS presented with significant decreases in BMD ($g/cm^2/kg$ bodyweight) at all sites evaluated ($p < 0.01$). Female adolescents with large waist circumference, low HDLc, hypertriglyceridemia and high blood pressure showed significant reductions in BMD at all sites evaluated ($p < 0.01$) and, with the exception of increased triglycerides (which had no effect on BMD, $p > 0.05$), the same pattern was observed in male adolescents. Linear regression analyses revealed that waist circumference was negatively correlated with BMD in both genders and that triglycerides were negatively correlated with BMD only in female adolescents. Our results suggest that overweight adolescents with MetS have lower BMD than adolescents without MetS. Among all MetS components measured, increased waist circumference had the strongest relationship with reductions in BMD.



## Introduction

Adolescence is considered a critical period for increases in bone mass. Major bone growth occurs during this phase and peak bone mass is reached during or immediately after this phase [1]. Impairment of bone mass increases during this period may lead to suboptimal bone mass peaks and increase the risk for developing osteopenia/osteoporosis and fractures during old age [2,3]. In recent years, growing concern has focused on the occurrence of metabolic syndrome (MetS) and its effects on bone mass [4,5].

MetS is a clinical condition characterized by the association of abdominal obesity, changes in glucose metabolism, dyslipidemia, and hypertension. These metabolic alterations predispose affected individuals to the development of cardiovascular diseases and type 2 diabetes mellitus [6,7].

The prevalence of MetS among American teenagers is 8.6% according to NHANES data (2001–2006), and higher prevalences are observed among males (10.8%) and Latin Americans (11.2%) [8]. In China, the prevalence of MetS among obese and overweight adolescents is approximately 14.3% and 3.7%, respectively [9]. In a study conducted in Brazil, 321 adolescents who were considered overweight, obese or extremely obese were evaluated and approximately 18% of the population studied had MetS [10].

There is no consensus definition of MetS that can be used to determine the difference in prevalence rates between children and adolescents or the long-term effects of this condition in children and adolescents. However, the use of the criteria suggested by the International Diabetes Federation (IDF) has been recommended [6].

*Abbreviations:* WC, waist circumference; BMC, bone mineral content; BMD, bone mineral density; DXA, dual-energy X-ray bone densitometry; HDLc, HDL cholesterol, HOMA-IR, homeostasis model assessment of insulin resistance; IDF, International Diabetes Federation; BMI, body mass index; MetS, metabolic syndrome; DBP, diastolic blood pressure; SBP, systolic blood pressure.

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A negative correlation between MetS and bone mineral density (BMD) has been demonstrated in adults [11–14]. However, there is little information available in the literature concerning the relationship between MetS and BMD in adolescents [4,5].

Osteoporosis and obesity are major problems with major impacts on global health, and the prevalences of both increase in adults. Individuals are becoming overweight at younger ages [15], which has resulted in an increased prevalence of MetS [10]. The aim of this study was to evaluate the effects of MetS and its components on BMD in overweight adolescent of both genders.

## Material and methods

This is a cross-sectional study involving overweight adolescents with or without MetS selected at the time of the first visit to the Adolescent Botucatu Medical School Clinical Hospital (SP, Brazil) between August 2011 and December 2012. Informed consent and approval were obtained from all participating adolescents and their parents or guardians. This study was approved by the Research Ethics Committee of the Botucatu Medical School, UNESP (Protocol 3928/11 CEP).

Considering that 15% of overweight adolescents present criteria for the diagnosis of MetS [16], the estimated sample size for this study was 190 individuals. This calculation was performed by setting the significance level to 5% for a confidence interval of 95% as determined for a normal distribution with $z = 1.96$ [17]. The sample of the present study consisted of 271 adolescents.

The inclusion criteria were as follows: 10 to 16 years of age, overweight (BMI ≥85th percentile for gender and age), and between the 5th and 95th age- and gender-appropriate height percentiles [18]. Adolescents were excluded from this study for the following reasons: weight exceeding 100 kg (densitometry was not feasible for these potential subjects), a history of prematurity, prolonged therapy with corticosteroids, use of calcium and/or iron supplements in the 12 months preceding this research, presence of chronic diseases, use of drugs that negatively affect bone metabolism such as anticonvulsants or antacids containing aluminum, consumption of an exclusive high-fiber vegetarian diet with fiber content above age-appropriate recommendations (>26 g/day for female adolescents or >31 g/day for male adolescents (9–13 years) or >38 g/day (males and females 14–16 years)) [19], caffeine intakes of >300 mg/day (>3 cups of coffee per day) [20],consumption of more than 500 mL/day of soft drinks [21], and lack of daily consumption of dairy products. Furthermore, the adolescents were neither smokers nor drinkers, were not engaged in any extracurricular sporting activities, and participated in physical education classes in their schools for no more than 2 h/week. Other exclusion criteria were the presence of metabolic, endocrine or genetic diseases (as verified by a history of current disorders, general and specific physical examinations, laboratory or radiological procedures), any changes in menstrual cycle (oligo/amenorrhea, clinical or biochemical hyperandrogenism) that could suggest the presence of polycystic ovary syndrome (PCOS), use of combined oral contraceptives, and pregnancy in girls. These exclusion criteria were established in order to prevent other events or situations described in the literature from interfering with the increase in bone mass in these adolescents.

Adolescents were excluded if they failed to attend all scheduled appointments for either anthropometric measurements or blood sampling or if they did not follow the established sample collection procedures; e.g., if they did not fast for at least 10 h prior to collection.

To assess weight (kg) and height (cm), the adolescents were asked to wear minimal clothing and no shoes following the criteria described by the National Health and Nutrition Examination Survey [22]. BMI (kg/m$^2$) was calculated using body weight and height, and the BMI percentiles were obtained with the Epi Info software 3.5.1., which uses gender and age growth curves as references [18]. Individuals with BMI between the 85th and 95th percentile were considered overweight, individuals between the 95th and 99th percentile were considered obese [23], and individuals above the 99th percentile were considered extremely obese [24]. Waist circumference (cm) was obtained at the midpoint between the last rib and the iliac crest at the end of a regular expiration [22]. Measurements were performed thrice by the same trained evaluator. Blood pressure was measured with the adolescent in a sitting position after a 5-min rest. The mean of three measurements with 3-min intervals was used. Measurements were performed on the right arm by auscultation with a calibrated mercury sphygmomanometer using a cuff that was appropriate for the arm's circumference [25].

Sexual maturity was evaluated by an experienced physician by visual breast evaluation (females) or genital observation (males) and the results are reported using the Tanner scale [26,27]. Skeletal maturation was evaluated using the method of Greulich & Pyle [28].

Blood samples were obtained in the morning after a 10-h fast. Samples were collected by well-trained laboratory technicians and were evaluated at the Central Laboratory. Dry chemistry was used to assess HDLc, triglycerides and fasting glucose in a Vitros 950 (Johnson and Johnson) according to the manufacturer's instructions. Values are expressed as mg/dL.

MetS was defined according to the criteria proposed by the IDF [6] (Table 1). A subject was classified to have MetS if he/she presented with central obesity defined by a large waist circumference (≥90th percentile according to age and gender using the curve proposed by Fernández et al. [29]) and at least two of the four criteria shown in Table 1.

Lumbar spine (L1–L4), proximal left femur, and total and subtotal BMD (g/cm$^2$) were evaluated by attenuating dual-energy X-ray bone absorptiometry (DXA) using a Hologic QDR 4500 Discovery A (Hologic, Inc., Bedford, MA). All evaluations were performed by a single technician that was unaware of the objectives of the study. Additionally, the manufacturer's instructions and the standards of the International Society for Clinical Densitometry (ISCD) [30] were followed. The effect of body size on bone mass can lead to misinterpretations when comparing individuals of different heights and body compositions. In this study, we sought to minimize body size-induced biases in bone mass estimates by using BMD transformed for body weight (g/cm$^2$/kg body weight).

## Statistical analysis

Data were stored in Excel and analyzed using the SAS for Windows software v.9.2. Normality of the quantitative variables was verified by the Shapiro–Wilk test.

We conducted descriptive analyses of the data using frequency distributions and measures of central tendency and dispersion for sample characterization. The chi-square test was used to compare pubertal stages between adolescents with and without MetS.

BMD was analyzed for the whole group of adolescents and stratified by gender. This variable was also considered after being transformed into BMD per kilogram body weight, which reduced the variability of the data; the same comparisons were performed for transformed and non-transformed BMD values [31].

The Student *t*-test was used to compare BMD and transformed BMD values across adolescents with and without MetS and its components were stratified by gender.

Linear regression analysis was used to examine the relationships between the MetS component-related variables and the body and lumbar spine BMD in both genders. Analysis of variance (ANOVA) was used to compare total body BMD adjusted for age, height and weight according to the presence of MetS components, followed by Tukey's post hoc test. Statistical significance was set at $p < 0.05$.