# Adolescent Obesity, Bone Mass, and Cardiometabolic Risk Factors

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**Objective** To compare bone mass between overweight adolescents with and without cardiometabolic risk factors (CMR). Associations of bone mass with CMR and adiposity were also determined.

**Study design** Adolescents (aged 14 to 18 years) who were overweight were classified as healthy (n = 55), having one CMR (1CMR; n = 46), or having two or more CMR (≥2CMR; n = 42). CMRs were measured with standard methods and defined according to pediatric definitions of metabolic syndrome. Total body bone mass, fat mass, and fat-free soft tissue mass were measured with dual-energy X-ray absorptiometry. Visceral adipose tissue and subcutaneous abdominal adipose tissue were assessed with magnetic resonance imaging.

**Results** After controlling for age, sex, race, height, and fat-free soft tissue mass, the healthy group had 5.4% and 6.3% greater bone mass than the 1CMR and ≥2CMR groups, respectively (both $P$ values <.04). With multiple linear regression, adjusting for the same co-variates, visceral adipose tissue ($\beta$ = –0.22), waist circumference ($\beta$ = –0.23), homeostasis model assessment of insulin resistance ($\beta$ = –0.23), and high-density lipoprotein cholesterol level ($\beta$ = 0.22) were revealed to be associated with bone mass (all $P$ values <.04). There was a trend toward a significant inverse association between bone mass and fasting glucose level ($P$ = .056). No relations were found between bone mass and fat mass, subcutaneous abdominal adipose tissue, blood pressure, or triglyceride level.

**Conclusion** Being overweight with metabolic abnormalities, particularly insulin resistance, low high-density lipoprotein cholesterol level, and visceral adiposity, may adversely influence adolescent bone mass. *(J Pediatr 2011;158:727-34)*.

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Peak bone mass, which is generally achieved by early adulthood, is an important determinant of adult risk for osteoporosis. Thus any childhood disease or condition that reduces bone mineral accrual during the maturational period may lead to suboptimal peak bone mass and presumably a greater risk of fracture in later life.[1] Recently, there has been a growing concern that childhood obesity may negatively affect bone development, because there is evidence linking childhood obesity to skeletal fractures.[2] However, determining whether excess adiposity is either beneficial or detrimental to the growing skeleton has been challenging. Whereas some studies report greater bone mass in children and adolescents who are overweight compared with their peers who are a healthy weight,[3-5] other studies conclude that obesity is linked to lower bone mass or that extra weight from fat mass had no effect on bone mass.[6-9]

Discrepancies in the aforementioned childhood bone-fat investigations may be attributed, in part, to the methodological limitations when comparing bone mass between overweight and healthy weight children of the same age. At any given age, a wide variation exists in children in stature, body composition, rate of growth, and timing and tempo of biological maturation. Because children who are overweight compared with healthy weight children of the same age are generally further advanced in maturation, their skeletal development is likewise more advanced, because of increased hormonal activity, than their healthy weight peers. In addition, the metabolic effects of obesity could have an impact on bone development. Currently, no studies have investigated the bone-fat relationship in overweight youth, while considering cardiometabolic risk factors (CMR).

The primary aim of this study was to compare total body bone mineral content (BMC) between overweight adolescents with no CMR (healthy group), adolescents with only one CMR (1CMR group), and adolescents with two or more CMRs (≥2CMR group). The secondary aim was to determine associations of total body BMC with CMR and robust measurements of total and central adiposity. We tested the hypotheses that: (1) total body BMC is lower in overweight adolescents with CMR; and (2) total body

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| aBMD | Areal bone mineral density | LDL | Low-density lipoprotein |
| BMC | Bone mineral content | MET | Metabolic equivalent |
| CMR | Cardiometabolic risk factors | MRI | Magnetic resonance imaging |
| DXA | Dual-energy X-ray absorptiometry | PA | Physical activity |
| FFST | Fat-free soft tissue | SAAT | Subcutaneous abdominal adipose tissue |
| HDL | High-density lipoprotein | VAT | Visceral adipose tissue |
| HOMA-IR | Homeostasis model assessment of insulin resistance | | |

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BMC is negatively associated with CMR and central adiposity. Because age, sex, race, height, and muscle mass are known to be independent predictors of bone mass in children and adolescents,[10] these variables were considered as potential confounders in our analyses.

## Methods

Participants in this cross-sectional investigation were 143 overweight adolescents who were recruited from high schools in the Augusta, Georgia, area to participate in an adiposity and cardiovascular fitness study. With approval from superintendents and school principals, flyers were distributed to all students in the high schools. Inclusion criteria for this study were white or black/African-American race, age 14 to 18 years, and overweight (body mass index [BMI] ≥85th percentile for age and sex). Adolescents were excluded when they were taking medications or had any medical conditions that could affect growth, maturation, physical activity, nutritional status, or metabolism. Informed consent and assent were obtained from all parents and adolescents, respectively. The protocol was approved by the Human Assurance Committee at the Medical College of Georgia (institutional review board). All measurements were performed at the Georgia Prevention Institute at the Medical College of Georgia between 2001 and 2005.

A trained laboratory technician collected height, body weight, and waist circumference measurements. Participants were measured in light indoor clothing after the removal of shoes. Height (cm) and body weight (kg) were assessed for calculation of sex- and age-specific BMI percentiles.[11] Waist circumference (cm) was then obtained at the midpoint between the lowest rib and the iliac crest. Seated blood pressure was measured 5 times at 1-minute intervals after a 10-minute rest with the Dinamap Pro 100 (Critikon Corporation, Tampa, Florida), and the last 3 measures were averaged. Sexual maturation stage (or Tanner stage) was measured with a 5-stage scale, ranging from I (prepubertal) to V (fully mature) as described by Tanner.[12] With a sex-specific questionnaire, participants reported their pubertal stage by comparing their own physical development to the 5 stages in standard sets of diagrams. A parent or research coordinator then reviewed the results with the children to make sure they understood the questionnaire. When an individual reported discordant stages of pubic hair and breast or genital development, the higher of the two stages was used. In addition, the female participants provided information about their menarcheal status.

Fasting blood samples were obtained from participants for assessment of glucose, insulin, triglyceride, total cholesterol, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol levels. Glucose was measured in 10 μL sera with an Ektachem DT system (Johnson and Johnson Clinical Diagnostics, Rochester, New York) with mean intra-assay and interassay coefficient of variations of 0.61% and 1.45%, respectively. Insulin was assayed in duplicate 100 μL with reagents obtained from Linco (St. Charles, Missouri), with mean intra-assay and interassay coefficient of variations of 5% and 5.6%, respectively. From the measures of glucose and insulin levels, the homeostasis model assessment of insulin resistance (HOMA-IR) was calculated: fasting insulin (μU/mL) x fasting glucose (mg/dL)/405. Triglyceride (mg/dL), total cholesterol (mg/dL), and HDL cholesterol (mg/dL) were measured with the Ektachem DT II system. With this system, HDL cholesterol is analyzed by using a two-reagent system involving stabilization of LDL, very-LDL, and chylomicrons with cyclodextrin and dextrin sulfate and subsequent enzymatic-colorimetric detection of HDL cholesterol. LDL cholesterol (mg/dL) was determined with the Friedewald formula.

Bone outcomes of the total body (BMC [g], bone area [$cm^2$], and areal bone mineral density [aBMD; $g/cm^2$]) were measured with dual-energy X-ray absorptiometry (DXA; QDR-4500W, Hologic, Waltham, Massachusetts). Because of the limitations of aBMD in children and adolescents, total body BMC has been proposed as the most appropriate outcome measure of bone mass status in youth.[13] Therefore, total body BMC was chosen as our primary bone outcome measure for bone mass status. Total body composition was also determined with DXA for fat-free soft tissue mass (FFST; kg) and fat mass (kg). Anthropomorphic phantoms were scanned daily for quality assurance. In this laboratory, with a one-way random effects model, single-measure intraclass correlation coefficients were calculated in 219 adolescents, aged 13 to 18 years. Each participant underwent scanning twice within a 7-day period for BMC, bone area, aBMD, FFST mass, and fat mass (all $R \geq .97$).

Visceral adipose tissue (VAT) and subcutaneous abdominal adipose tissue (SAAT) were measured with a 1.5-T magnetic resonance imaging system (MRI; General Electric Medical Systems, Milwaukee, Wisconsin). Five transverse images were acquired from the lumbar region beginning at the inferior border of the fifth lumbar vertebra and proceeding toward the head; a 2-mm gap between images was used to prevent crosstalk. To calculate volumes for VAT and SAAT, the cross-sectional area ($cm^2$) from each slice was multiplied by the slice width (1 cm), and then the individual volumes ($cm^3$) were summed. The intraclass correlation coefficients for repeat analyses of the same scans on separate days within a 7-day period were $R \geq .98$ for both VAT and SAAT.

The amount of minutes per day spent in moderate and vigorous physical activities (PA) was assessed with MTI Actigraph monitors (model 7164; MTI Health Services, Fort Walton Beach, Florida), uniaxial accelerometers that measure vertical acceleration and deceleration. With epoch length set at 1 minute and expressed as counts per minute, the accelerometers were to begin recording when the subject left our laboratory after the first day of testing. The subjects were instructed to (1) wear the monitor for a period of 7 days; (2) remove it for sleep, bathing, and any activity that may cause harm to either the monitor or another person (eg, during contact sports); and (3) bring the monitor back to us 1 week later. Data from day 1 and day 7 were discarded because a full day of information was not available for those