

Obesity during childhood and adolescence augments bone mass and bone dimensions¹⁻³

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ABSTRACT

Background: Studies of the effect of childhood obesity on bone accrual during growth have yielded conflicting results, largely related to the failure to adequately characterize the confounding effects of growth, maturation, and body composition.

Objective: The objective of this study was to determine the effect of childhood obesity on skeletal mass and dimensions relative to height, body composition, and maturation in males and females.

Design: In 132 nonobese (body mass index < 85th percentile) and 103 obese (body mass index \geq 95th percentile) subjects aged 4–20 y, whole-body and vertebral bone mineral content (BMC) was determined by using dual-energy X-ray absorptiometry, and bone area, areal bone mineral density (BMD), and fat and lean masses were measured. Vertebral volumetric BMD was estimated as BMC/area^{1,5}.

Results: Obesity was associated with greater height-for-age, advanced maturation for age, and greater lean mass for height (all $P < 0.001$). Sex-specific multivariate regressions with adjustment for maturation showed that obesity was associated with greater vertebral areal BMD for height, greater volumetric BMD, and greater vertebral BMC for bone area (all $P < 0.05$). After adjustment for maturation and lean mass, obesity was associated with significantly greater whole-body bone area and BMC for age and for height (all $P < 0.001$).

Conclusions: In contrast with the results of prior studies, obesity during childhood and adolescence was associated with increased vertebral bone density and increased whole-body bone dimensions and mass. These differences persisted after adjustment for obesity-related increases in height, maturation, and lean mass. Future studies are needed to determine the effect of these differences on fracture risk. *Am J Clin Nutr* 2004;80:514–23.

KEY WORDS Adolescent, child, obesity, body composition, bone mineral density, bone mineral content, dual-energy X-ray absorptiometry

INTRODUCTION

During childhood and adolescence, bone mineral accretion results in sex- and maturation-specific increases in cortical dimensions and trabecular density (1–3). As emphasized in the recent *NIH Consensus Statement* report on osteoporosis, the bone mass attained during growth is a critical determinant of the risk of osteoporosis later in life (4). Persons with higher peak bone mass after adolescence have a greater protective advantage when the inexorable declines in bone mass that are associated

with increasing age take their toll. Peak bone mass is strongly influenced by genetic factors, but the full genetic potential for bone mass is attained only if nutrition, physical activity, and other lifestyle factors are optimized.

Despite the epidemic of childhood obesity, the effect of obesity on bone mineral accrual during growth is poorly understood. Studies using dual-energy X-ray absorptiometry (DXA) to examine the effect of obesity on bone mass in children have yielded conflicting results, largely related to differing approaches to the assessment of two-dimensional projected DXA bone measures relative to age, bone size, and body size. Some studies reported normal or increased bone mineral content (BMC) in obese children (5–8), whereas others concluded that obese children have decreased bone mass relative to bone size and body weight (9, 10). The need for accurate assessment of the structural effects of obesity on bone mineral accretion is underscored by conflicting reports of the effects of increased fat mass and body mass index (BMI) on fracture risk in childhood (11–14). The objective of the present study was to determine the effect of childhood obesity on skeletal mass and dimensions relative to height, body composition, and maturation in a large multiethnic cohort of children and adolescents.

SUBJECTS AND METHODS

Study subjects

Study subjects were identified through 2 different mechanisms. First, 181 children and adolescents aged 4–20 y were enrolled as healthy control subjects for ongoing bone studies in the Nutrition and Growth Laboratory at the Children's Hospital of Philadelphia (CHOP). Subjects were recruited from the general pediatric clinics and the surrounding community by using newspaper advertisements and flyers. Subjects who had chronic

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medical conditions or were taking medications that could affect growth, pubertal development, nutritional status, or dietary intake were excluded. Obesity was not an exclusion criterion. The protocol was approved by the CHOP Institutional Review Board; all subjects and parents provided written informed consent.

Second, additional obese subjects were identified through a systematic review of all clinical DXA scans performed during a 3-y interval in subjects referred from the CHOP Weight Management Program. All children and adolescents seen in the Weight Management Program were routinely referred for lumbar spine and whole-body DXA scans at the time of the initial evaluation. Approval to analyze the DXA scans and review the medical records was obtained from the CHOP Institutional Review Board. Subjects were excluded if they had chronic medical conditions (other than obesity) or were taking medications that could affect growth and development. Seventy-five eligible subjects were identified.

Anthropometry and Tanner staging

All height and weight measurements were performed in the Nutrition and Growth Laboratory at the time of the DXA scans. Weight (in kg) was measured by using a digital electronic scale on which the subjects stood, and height (in cm) was measured by using a wall-mounted stadiometer. Pubertal status was determined by physical examination and classified according to the method of Tanner (15). Tanner staging of the 181 healthy control subjects was performed by trained research staff, and Tanner staging of the additional obese subjects was performed by the Medical Director of the Weight Management Program (AMT).

Age- and sex-specific *z* scores (SD scores) for height, weight, and BMI were calculated by using year 2000 growth data from the National Center for Health Statistics, Centers for Disease Control and Prevention (16). The BMI percentiles were used to classify subjects as follows: healthy weight, 5th–85th BMI percentiles; overweight, 85th–94th BMI percentiles; or obese, ≥ 95 th BMI percentile (17). For the purpose of these analyses, the study was limited to the comparison between the 132 subjects having a healthy weight and the 103 obese children.

Lumbar spine and whole-body DXA scans

Bone mass in the anterior-posterior lumbar spine (L_{1-4}) and in the whole body was measured by using DXA (QDR 2000; Hologic, Waltham, MA) with a fan beam in the array mode. All subjects were measured on the same machine. The measurements were performed by using standard positioning techniques. Quality-control scans were performed daily by using a simulated L_{1-4} lumbar spine made of hydroxyapatite encased in epoxy resin. In our institution, the *in vitro* CV was $<0.6\%$, and the *in vivo* CV in adults was $<1\%$.

The DXA scans were analyzed to generate measures of vertebral projected bone area (in cm^2), BMC (in g), and areal bone mineral density (BMD, in g/cm^2). Because the standard software for the analysis of the lumbar spine frequently fails to detect a complete bone map in children, all lumbar spine scans were analyzed with the low-density software as previously described (18). Lumbar spine bone mineral apparent density (BMAD, in g/cm^3), which was calculated as lumbar spine BMC/lumbar spine bone area^{1.5}, was used as an estimate of volumetric BMD (19).

Whole-body scans were analyzed to generate whole-body projected bone area and BMC. Because pediatric whole-body data

may be confounded by variability in relative skull size (20), all whole-body DXA results presented in this study represent the bone area and BMC excluding the skull. Estimates of lean mass (in kg), fat mass (in kg), and percentage body fat were also obtained from the whole-body DXA scan excluding the skull. The lean mass measure excluded bone mass. A single operator (BAW) reanalyzed all DXA scans to standardize the analyses.

Statistics

Analyses were conducted by using STATA 7.0 (Stata Corporation, College Station, TX). Two-sided tests of hypotheses were used, and a *P* value < 0.05 was considered statistically significant. Initial analyses were descriptive and included the calculation of means with SDs for subject characteristics for the nonobese and obese subjects. Mean differences in anthropometric and body-composition variables between the nonobese and obese subjects were assessed by using the *t* test. The sex, race, and Tanner stage distributions were compared by using the chi-square test. DXA bone measures were compared by using the Wilcoxon rank-sum test.

The relations between bone measures, age, height, and body composition were explored graphically. Natural log transformations of the outcomes or explanatory variables were used to improve the fit of models. Body weight, height, fat mass, lean mass, and all bone measures (BMC, bone area, areal BMD, and BMAD) were log transformed. The assumptions of the regression models (linearity, normality of residuals, constant variance) were assessed via graphical checks and the following tests: the Shapiro-Wilk test of normality of the residuals, the Ramsey omitted variable test, and the Cook-Weisburg test for heteroskedasticity.

The log-transformed bone and body-composition measures in the obese subjects were compared with those in the nonobese subjects. Bone measures were first assessed relative to age. Because of the differences in height *z* scores between the obese and the nonobese subjects, the models were subsequently adjusted for height. The log-linear relation between spine BMC and projected bone area is well established, according to the power law relation: $\text{BMC} \propto (\text{Area})^p$ (19, 21, 22). Therefore, spine BMC was assessed by using a log-transformed model adjusted for bone area. For the whole body, bone area and BMC were assessed by using log-transformed models adjusted for height. A prediction model in which this approach was used for whole-body BMC relative to height has been described in children (23). A recent pediatric study showed that a log-transformed model of whole-body BMC adjusted for height was highly correlated with cortical bone strength ($r = 0.63$) as measured with the use of peripheral quantitative computed tomography (pQCT), whereas BMC adjusted for bone area was not correlated with strength (24). Whole-body bone area relative to height was assessed as a measure of bone dimensions or breadth. The recent pediatric pQCT study showed that increased bone area relative to height was correlated with increased cortical cross-sectional area in the mid-shaft of the tibia diaphysis (24). The fit of all final models was assessed via the adjusted R^2 value.

Models were adjusted for Tanner stage (with stage 1 as the referent group) and race (African American compared with all others). Sex differences in bone mineral accretion during growth and maturation are well documented. Therefore, each model was tested for sex interactions. The simplest models assessed DXA bone results relative to age and showed significant interactions



TABLE 1

Characteristics of the nonobese and obese children and adolescents

	Nonobese, 5th–85th BMI percentiles (<i>n</i> = 57 M, 75 F)	Obese, >95th BMI percentile (<i>n</i> = 38 M, 65 F)
Age (y)	9.9 ± 3.9 ¹	9.8 ± 2.9
Race (% black)	36	42
Tanner stage (<i>n</i>)		
1	82	57
2	16	23
3	12	8
4	16	8
5	6	7
Height (cm)	136.8 ± 20.4 (102–181) ²	144.0 ± 15.5 (113–177) ³
Height <i>z</i> score	0.16 ± 1.00	1.17 ± 1.07 ³
Weight (kg)	33.2 ± 13.6 (14.5–70)	60.1 ± 20.1 (23.2–113.8) ³
Weight <i>z</i> score	−0.07 ± 0.78	2.47 ± 0.59 ³
BMI (kg/m ²)	16.9 ± 2.3 (13.0–24.9)	28.1 ± 4.9 (18.2–46.9) ³
BMI <i>z</i> score	−0.19 ± 0.81 (−2.20–1.02)	2.3 ± 0.40 (1.7–4.06) ³
Percentage fat (%)	20.1 ± 7.7	46.4 ± 7.5 ³
Fat mass (kg)	6.2 ± 4.5	26.3 ± 10.9 ³
Lean mass (kg)	22.4 ± 9.6	27.9 ± 9.2 ³

¹ \bar{x} ± SD (all such values).² Range in parentheses (all such values).³ Significantly different from nonobese, *P* < 0.001 (*t* test).

between sex and age for lumbar spine BMD and whole-body BMD. In the multivariate models, significant interactions between height and sex or between Tanner stage and sex were detected for lumbar spine BMC, BMD, and BMAD and whole-body BMD. Given the complexity of the sex interactions in these models and the known sex differences in bone mineral accretion during growth, all bone results are presented stratified by sex. It was beyond the scope of this study to address each observed sex interaction independently of obesity effects. However, all models were tested for obesity-by-sex interactions, and the results are presented here.

Because the outcome measures were log transformed, the effect of obesity in each multivariate model is presented as the adjusted ratio of the outcome measure in the obese subjects to the outcome measure in the nonobese control subjects along with the 95% CI. The adjusted ratio and 95% CI were calculated as the exponentiated estimate and the 95% confidence limits, respectively, of the regression parameter for obesity. This approach provided an estimate of the difference in bone measures between the obese and the nonobese subjects across the entire range of values.

RESULTS

Subject characteristics and body composition

Subject characteristics are summarized in **Table 1**. The age, sex, and racial distributions were not significantly different between the obese and nonobese subjects. The Tanner stage distributions and the proportion of children that were prepubertal also did not differ significantly between the 2 groups; however, the obese children were significantly younger at each Tanner stage (Tanner stages 2–5) than were the nonobese children. Height *z* scores and lean and fat masses were significantly greater in the obese subjects than in the nonobese control subjects.

The greater lean mass in the obese subjects may have been due to greater height and advanced maturation. Therefore,

multivariate regression models were used to compare lean mass adjusted for sex, Tanner stage, race, and height between the obese subjects and the nonobese control subjects. No sex interactions were observed. These adjusted models showed that obesity, Tanner stage, and African American race each were independently and significantly associated with greater lean mass for height. The adjusted ratio of lean mass for height in the obese subjects to that in the control subjects was 1.13 (95% CI: 1.11, 1.16; *R*² = 0.95, *P* < 0.001).

Comparison of bone measures between obese and nonobese subjects

The DXA results are summarized in **Table 2**. All lumbar spine and whole-body DXA results were significantly greater in the obese subjects than in the nonobese subjects.

Lumbar spine DXA models

In the male and female obese subjects, lumbar spine bone area, BMC, and areal BMD adjusted for age were significantly greater than those in the nonobese control subjects. The ratios, 95% CIs, and *P* values for the comparison of each vertebral bone measure between the obese and the nonobese subjects are summarized in **Figure 1** and its legend, and the adjusted *R*² values for each of the models presented in **Figure 1** are summarized in **Table 3**.

The greater vertebral bone area, BMC, and areal BMD for age observed in the obese subjects may have been due to greater height for age and advanced maturation for age. Therefore, each lumbar spine measure was assessed relative to height in regression models adjusted for Tanner stage and race. The adjusted models showed that areal BMD relative to height was significantly greater in the obese males and females than in the non-obese control subjects. There were no significant differences in lumbar spine BMC for height between the obese and the non-obese subjects. Bone area for height was significantly lower in

TABLE 2Results of dual-energy X-ray absorptiometry scans in nonobese and obese children and adolescents¹

	Nonobese (<i>n</i> = 132)	Obese (<i>n</i> = 103)
Whole body		
Bone area (cm ²)	975 ± 457 (360–2061)	1372 ± 406 (599–2303) ²
BMC (g)	732 ± 510 (165–2183)	1095 ± 502 (327–2655) ²
Areal BMD (g/cm ²)	0.681 ± 0.153 (0.457–1.104)	0.763 ± 0.128 (0.545–1.153) ²
Lumbar spine		
Bone area (cm ²)	44.7 ± 12.9 (25.9–79.2)	47.0 ± 9.0 (28.7–68.6) ³
BMC (g)	29.5 ± 16.5 (12.7–78.7)	33.1 ± 12.4 (15.1–66.6) ⁴
Areal BMD (g/cm ²)	0.619 ± 0.159 (0.427–1.095)	0.685 ± 0.138 (0.499–1.110) ²
BMAD (g/cm ³)	0.093 ± 0.013 (0.072–0.130)	0.100 ± 0.014 (0.079–0.143) ²

¹ All values are $\bar{x} \pm SD$; range in parentheses. BMC, bone mineral content; BMD, bone mineral density; BMAD, bone mineral apparent density.^{2–4} Significantly different from nonobese (Wilcoxon rank-sum test): ²*P* < 0.0001, ³*P* < 0.02, ⁴*P* < 0.001.

the obese females than in the nonobese females; however, there was no significant difference in bone area for height between the obese males and the nonobese males.

Two approaches were used to examine lumbar spine volumetric BMD: BMAD (19) and BMC relative to bone area (25). The effect of obesity on BMAD in the females is shown in **Figure 2**. Comparable results were seen in the males. In the males and the females, BMAD was significantly greater in the obese children than in the control subjects after adjustment for Tanner stage and

race. In the males and the females, lumbar spine BMC relative to bone area was significantly greater in the obese subjects than in the normal-weight control subjects after adjustment for Tanner stage and race. Both of these approaches used bone area to adjust for differences in skeletal size; therefore, including height as a covariate did not improve the fit of the model, and height was not independently associated with either estimate of volumetric BMD. Including age as a covariate did not improve the fit of any of the multivariate models described above.

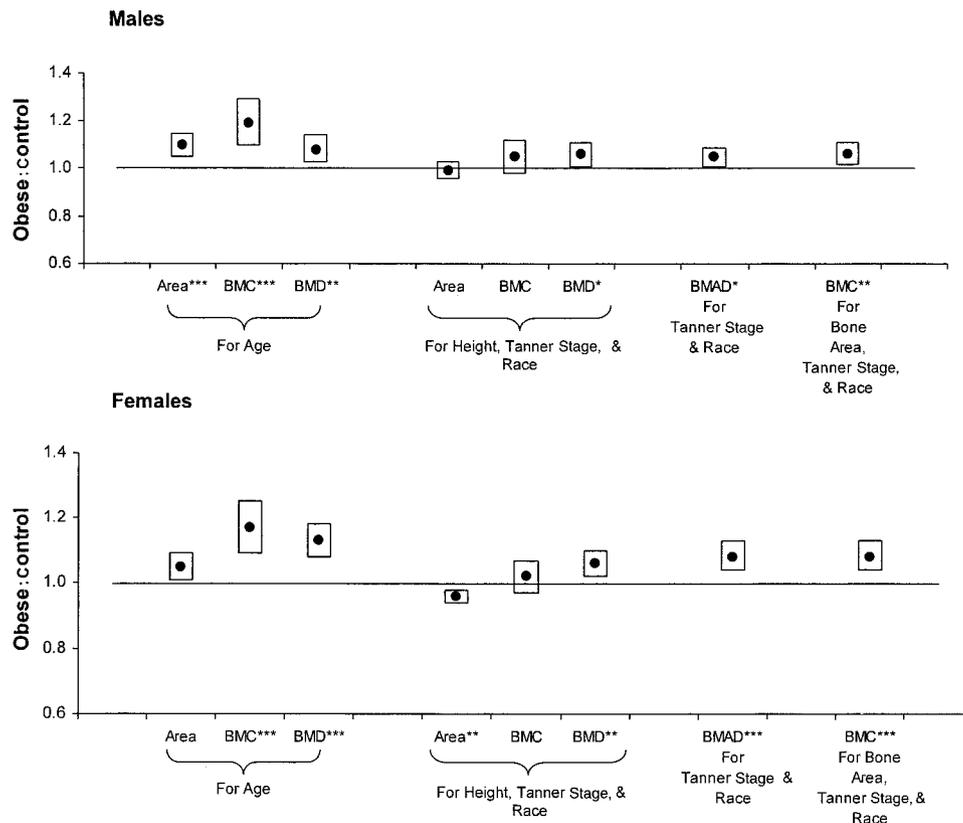


FIGURE 1. The effect of obesity on lumbar spine measures of bone area, bone mineral content (BMC), bone mineral density (BMD), and bone mineral apparent density (BMAD) relative to age, body size (height), and bone size (bone area) obtained with the use of dual-energy X-ray absorptiometry in sex-specific multivariate regressions. The results are presented as the point estimate (●) and 95% CI (□) for the ratio of a given lumbar spine bone measure in the obese subjects to that in the nonobese control subjects. The horizontal line at the ratio of 1.0 represents no difference between the obese and the nonobese subjects. ****Significant effect of obesity: **P* < 0.05, ***P* < 0.01, ****P* < 0.001. Adjusted *R*² values for each model are presented in Table 3. Tests for interaction between obesity and sex were performed for each of the 8 models summarized in the figure. The test for interaction was significant only for lumbar spine bone area adjusted for height, Tanner stage, and race (*P* = 0.02). That is, compared with the respective nonobese subjects, the obese females, but not the obese males, had lower spine area after adjustment for height, Tanner stage, and race.



TABLE 3

Sex-specific regression models for comparison of the results of dual-energy X-ray absorptiometry scans between the obese subjects and the nonobese subjects¹

		<i>R</i> ²	
		Males	Females
Lumbar spine			
Bone area (cm ²)	Age	0.84	0.77
BMC (g)	Age	0.82	0.80
Areal BMD (g/cm ²)	Age	0.65	0.70
Bone area (cm ²)	Height, Tanner stage, race	0.93	0.93
BMC (g)	Height, Tanner stage, race	0.92	0.90
Areal BMD (g/cm ²)	Height, Tanner stage, race	0.78	0.78
BMAD (g/cm ³)	Tanner stage, race	0.28	0.52
BMC (g)	Bone area, Tanner stage, race	0.96	0.95
Whole body			
Bone area (cm ²)	Age	0.91	0.83
BMC (g)	Age	0.91	0.83
Bone area (cm ²)	Height	0.96	0.95
BMC (g)	Height	0.95	0.92
Bone area (cm ²)	Height, Tanner stage, race, lean mass	0.97	0.96
BMC (g)	Height, Tanner stage, race, lean mass	0.97	0.95
BMC (g)	Bone area, Tanner stage, race	0.99	0.99

¹ *n* = 132 nonobese subjects and 103 obese subjects. BMC, bone mineral content; BMD, bone mineral density; BMAD, bone mineral apparent density. Each model included a dummy variable for obesity status, and the exponentiated coefficient for this variable within each model is presented as the ratio of the bone outcome in the obese subjects to that in the nonobese subjects in Figures 1 and 3.

Whole-body DXA models

In the male and female obese subjects, whole-body projected bone area and BMC adjusted for age were significantly greater than those in the nonobese control subjects. The ratios, 95% CIs,

and *P* values for the comparison of the whole-body bone measures between the obese subjects and the control subjects are summarized in **Figure 3** and its legend, and the adjusted *R*² values for the models are summarized in Table 3.

The significantly greater whole-body bone area and BMC for age observed in the obese subjects may have been due to greater height. Therefore, whole-body bone area and BMC were assessed relative to height. Whole-body bone area and BMC for height were significantly greater in the obese subjects than in the nonobese control subjects. The significant differences between the 2 groups in whole-body BMC and bone area for height are shown in **Figures 4** and **5**, respectively.

Lean mass was highly correlated with whole-body BMC and bone area in both the nonobese and the obese subjects (all *R* ≥ 0.93), and the obese subjects had significantly greater lean mass relative to height than did the nonobese subjects, as described above. To determine whether the greater whole-body BMC and bone area for height observed in the obese children was due to greater lean mass for height (ie, greater bone loading by muscle forces), lean mass was included in the multivariate models for whole-body BMC for height and whole-body bone area for height. Whole-body lean mass, Tanner stage, and obesity each were positively and independently associated with greater whole-body bone area for height and whole-body BMC for height.

Whole-body BMC for bone area was significantly lower in the obese subjects than in the normal-weight subjects after adjustment for Tanner stage and race in both the males and the females. Including age as a covariate did not improve the fit of any of the multivariate models described above.

DISCUSSION

In this comparison of 132 nonobese and 103 obese children and adolescents, obesity was associated with significantly

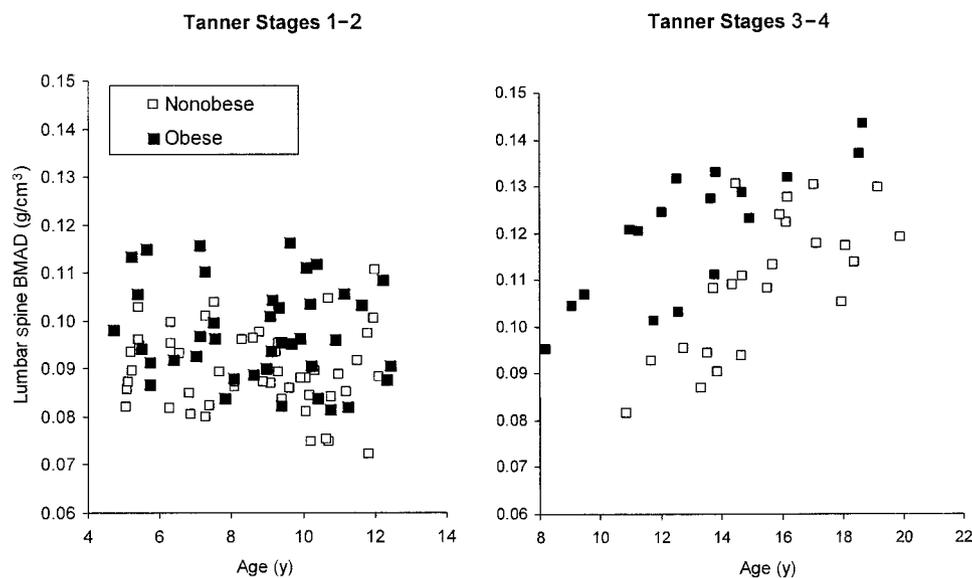


FIGURE 2. Lumbar spine bone mineral apparent density (BMAD) for age in the female obese and nonobese subjects according to Tanner stage. Similar results were seen in the males (data not shown). The data are presented for prepubertal and early pubertal subjects (Tanner stages 1 and 2) and for midpubertal to mature subjects (Tanner stages 3–5). Regressions showed that BMAD for age was significantly greater in the obese subjects than in the nonobese subjects in both pubertal groups (Tanner stages 1 and 2: females, *P* < 0.001; males, *P* < 0.02; Tanner stages 3–5: females, *P* < 0.001; males, *P* < 0.05). Tests for interaction between obesity and sex and between obesity and Tanner stage in the assessment of BMAD for age were not significant.

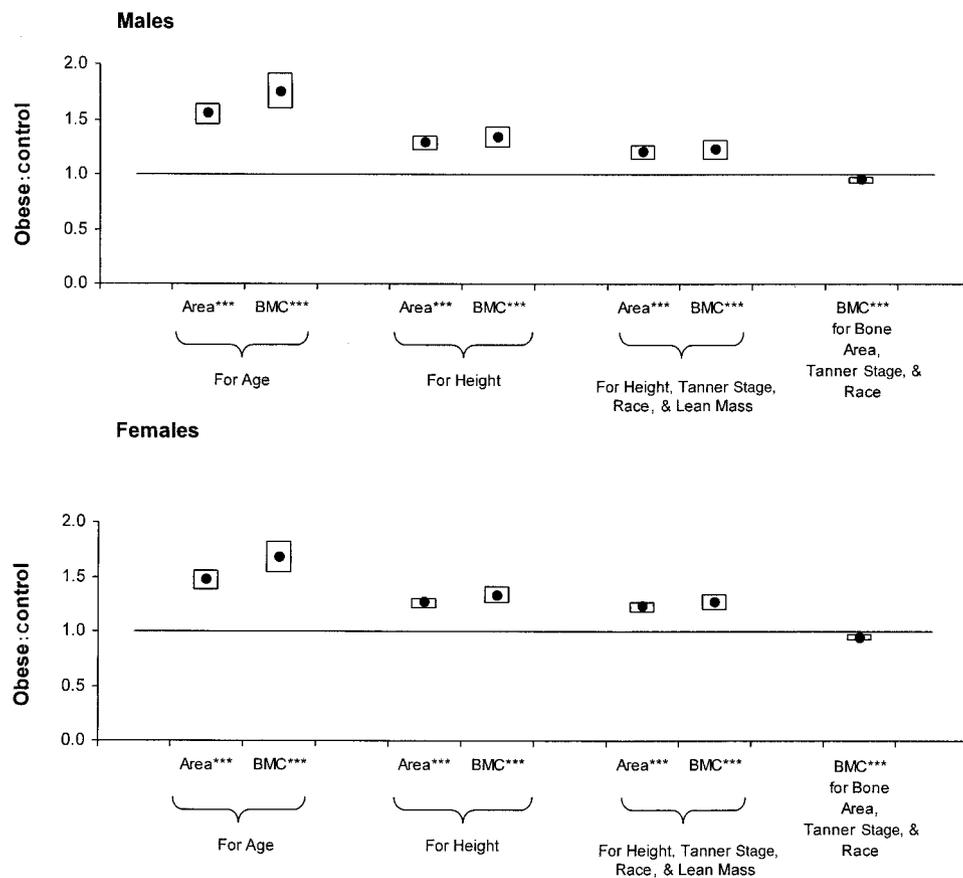


FIGURE 3. The effect of obesity on whole-body measures of bone area and bone mineral content (BMC) relative to age, body size (height), and bone size (bone area) obtained with the use of dual-energy X-ray absorptiometry in sex-specific multivariate regressions. The results are presented as the point estimate (●) and 95% CI (□) for the ratio of a given bone measure in the obese subjects to that in the nonobese control subjects. The horizontal line at the ratio of 1.0 represents no difference between the obese and the nonobese subjects. ***Significant effect of obesity, $P < 0.001$. The adjusted R^2 values for each model are presented in Table 3. Tests for interaction between obesity and sex were performed for each of the 7 models summarized in the figure. No significant sex-by-obesity interactions were detected.

greater vertebral density and whole-body bone area and BMC for height. To date, this is the largest study of bone mass and dimensions in obese children that permits separate evaluation of males and females across all stages of sexual maturation.

A multistaged approach was needed because of the limitations of DXA and the nature of the differences between obese and nonobese children. DXA is a two-dimensional approach that provides an estimate of density expressed as grams per projected area (areal BMD, in g/cm^2). This estimate is not a measure of volumetric density (g/cm^3) because it provides no information about bone depth. Bones in taller persons are longer, wider, and deeper; however, DXA bone area only captures the bone length and width and not the greater depth. Therefore, areal BMD inherently overestimates the volumetric BMD of tall persons (26). Consequently, assessment of areal BMD for age is biased by increased stature in obese children. BMAD (19) and regression of BMC against bone area (21) were used to estimate vertebral volumetric BMD in the present study. Both strategies showed significantly greater vertebral BMD in the obese subjects than in the nonobese subjects.

The differences in body size, body composition, and maturation between the obese and the nonobese subjects dictated the need for multivariate models that account for these potential confounders. Although our results showed greater vertebral

BMC for bone area in the obese subjects, Goulding et al (9) recently reported significantly lower vertebral BMC for bone area in 18 obese children than in healthy-weight control subjects after adjustment for height, weight, and Tanner stage. These contradictory conclusions regarding the effect of obesity are explained by the fact that the authors included both weight and height in their regression models and failed to consider the joint distribution of weight, height, and obesity status in interpreting their findings.

Our interpretation takes the joint distribution of lean mass and height into account in the sense that obesity status is assessed relative to the values of these covariates. In our model, the coefficient for obesity status represents the difference in expected outcome between obese and nonobese subjects of the same height, Tanner stage, race, and lean mass. This interpretation is possible because 2 subjects of the same height, Tanner stage, race, and lean mass may differ in their obesity status. However, if our model also included weight, then this interpretation of the regression coefficient for obesity status would not be possible, because, by definition, both of 2 subjects with the same height and weight would be either obese or nonobese. In a model that includes both height and weight, the effect of obesity, therefore, cannot be assessed solely by the regression coefficient for obesity status; the regression coefficients for weight and height must be

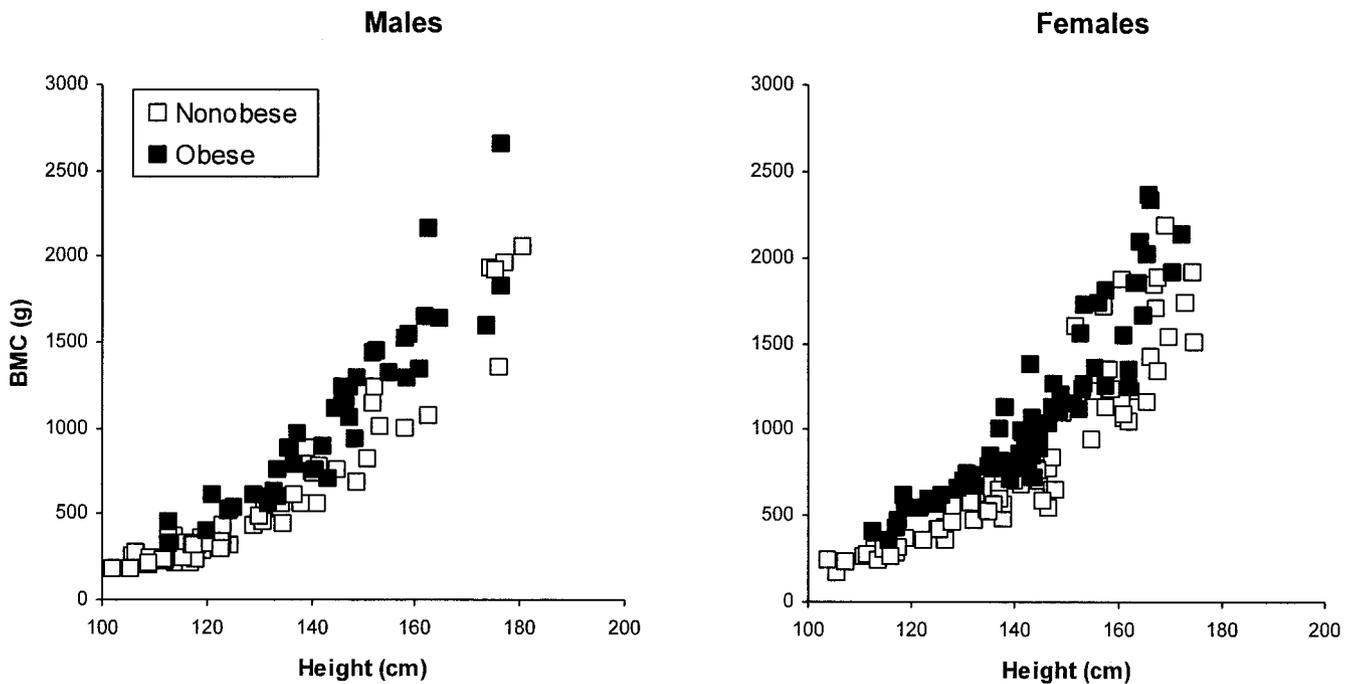


FIGURE 4. Whole-body bone mineral content (BMC) for height obtained with the use of dual-energy X-ray absorptiometry in obese and nonobese children and adolescents according to sex. Regressions showed that BMC for height was significantly greater in the obese subjects than in the nonobese subjects (females, $P < 0.001$; males, $P < 0.001$). Tests for sex-by-height, sex-by-obesity, obesity-by-height, and sex-by-obesity-by-height interactions were not significant.

considered. A mathematical illustration of these effects in which the model reported by Goulding et al (9) is used is provided in **Appendix A**.

The interpretation of whole-body DXA measures requires similar considerations. Cortical bone constitutes 80% of whole-body bone mass. We recently compared varied analytic

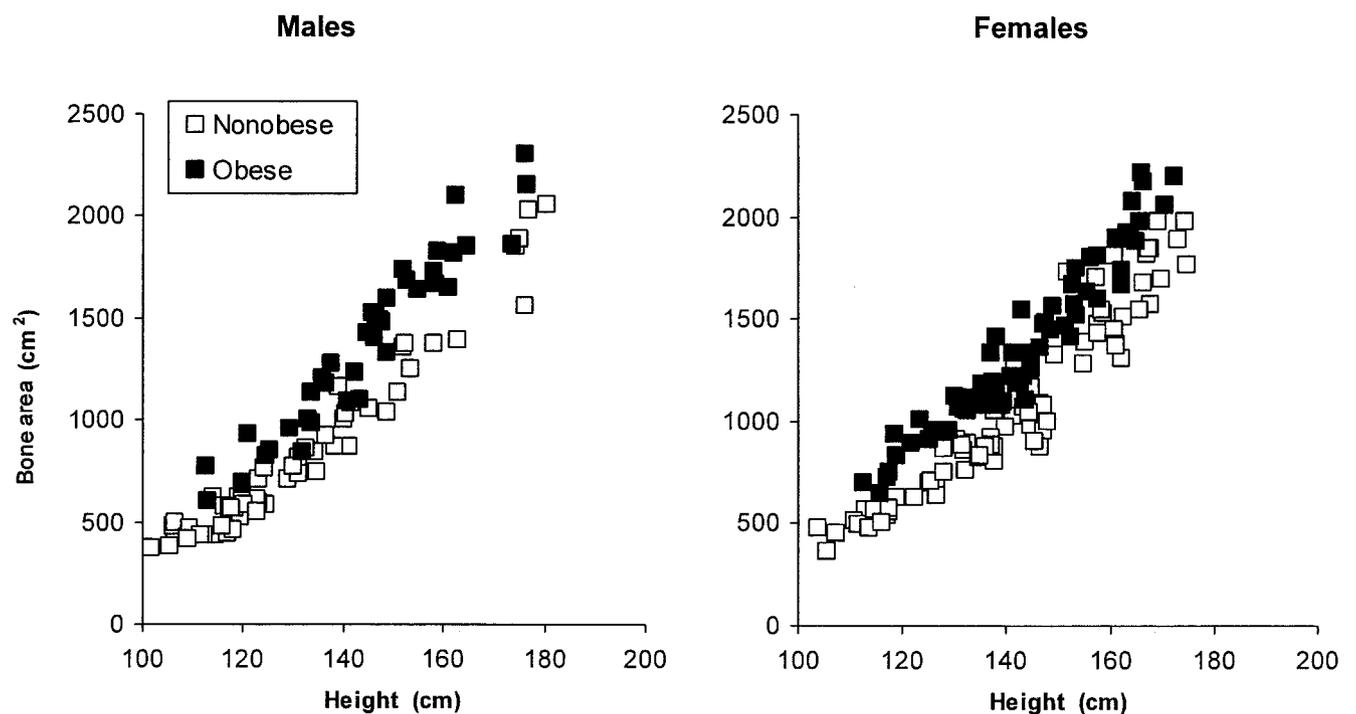


FIGURE 5. Whole-body bone area for height obtained with the use of dual-energy X-ray absorptiometry in obese and nonobese children and adolescents according to sex. Regressions showed that bone area for height was significantly greater in the obese subjects than in the nonobese subjects (females, $P < 0.001$; males, $P < 0.001$). Tests for sex-by-height and sex-by-obesity interactions were negative. However, the test for interaction between obesity and height was significant ($P < 0.01$) in the females. Although bone area was significantly greater in the obese females than in the nonobese females across the range of heights, the increase in bone area with an increase in height (slope) was not as great in the obese females as in the nonobese females.

strategies for whole-body DXA results with pQCT measures of cortical cross-sectional area and strength in 150 healthy children (24). DXA whole-body bone area for height and BMC for height were both strongly and positively associated with pQCT cross-sectional area and strength, which suggests broader bones with less resistance to bending. DXA bone area for weight, BMC for weight, and BMC for bone area were poor predictors of bone cross-sectional area and strength.

As summarized in Figure 3, the obese subjects in the present study had markedly greater whole-body bone area and BMC relative to age and height than did the nonobese subjects. In contrast with our findings, other investigators have reported normal (8) or decreased (10) whole-body BMC and bone area relative to body size. Again, this relates to the choice of body size covariates. Manzoni et al (8) reported no differences in whole-body bone measures between obese children and nonobese control subjects after adjustment for height, weight, lean mass, and fat mass. As detailed above, it is not appropriate to fix height and weight in the comparison between obese and non-obese subjects. Goulding et al (9) reported lower whole-body bone area and BMC relative to body weight in obese children. We were able to reproduce this result within our data; however, we believe this is inappropriate because it results in the comparison of children of different stature. An obese child will be substantially shorter than a nonobese child of the same weight, and this difference in BMC and bone area will reflect differences in bone length rather than width.

Prior investigators have proposed assessing whole-body BMC relative to bone area as an approach to adjust for differences in skeletal size (27). Although this approach may be valid in the lumbar spine, application to the whole body is problematic, as shown by our comparison between DXA and pQCT (24). The skeleton is a composite of many tube-like (eg, limbs) and broad (eg, pelvis) structures that vary in depth and thickness. Therefore, bone area is a poor measure of the volume of bone over which the BMC is distributed. Second, DXA bone area is a function of subject height and bone width. In a child with broad bones for height, assessment of BMC for bone area will result in the comparison of that child with a significantly taller child of comparable bone area, and this difference in BMC and bone area will reflect differences in bone length rather than width. Therefore, the lower whole-body BMC for bone area observed in obese children may not represent a deficit in bone mass.

A final technical limitation of DXA relates to the potential for projection error in the assessment of bone measures in obese subjects. DXA manufacturers have largely converted to fan beams that introduce magnification errors in measures of bone area and BMC. In the case of Hologic scanners, as the bone is elevated a greater distance off the table (as occurs with obesity), bone geometry and BMC are underestimated (28). However, in the present study, whole-body bone area and BMC were increased for age and height in childhood obesity. These findings cannot be attributed to projection error because such an error would result in an underestimation of BMC and bone area. Rather, our observation of increased whole-body bone area and BMC likely underestimates the true magnitude of the increases seen in obesity. Note that the lower vertebral bone area for height in the obese females than in the nonobese females may have been due to magnification error. Sex differences in fat distribution

(subcutaneous or visceral) (29) may have differing effects on regional elevation of the skeleton.

There are several possible mechanisms for increased bone mass in childhood obesity. Hormonal influences, such as increased conversion of androstenedione to estrogen or increased circulating leptin concentrations, may play a role (30). Leptin acts as a growth factor on the chondrocytes of skeletal growth centers via insulin-like growth factor I receptor expression and thereby potentially contributes to the increased linear growth and skeletal mass observed in childhood obesity (31). During puberty, estrogen promotes accrual of bone mass on the cortical endosteal surface and in trabecular bone (32).

Increased biomechanical loading due to increased body weight and increased lean muscle mechanical forces may also have contributed to the increased bone dimensions and mass observed in the obese subjects. Increased loading of long bones produces the greatest mechanical stresses on the subperiosteal surface and stimulates bone formation by subperiosteal expansion (33). For example, loading in the playing arm in racquet sports induces significant increases in bone dimensions and mass (34). The effect of weight gain on bone loading has been examined in adults. A longitudinal study in postmenopausal women showed that women who gained weight experienced a significant increase in hip cortical section modulus through periosteal expansion (35). A QCT study in healthy children suggested that weight bearing and mechanical stresses are important determinants of cortical bone mass, whereas trabecular bone density is influenced by hormonal factors associated with sexual development (36).

A study of bone biomechanics in adult male rats with dietarily induced obesity showed significantly greater bone strength in the obese rats than in the controls (37). The cross-sectional geometry and ultimate fracture load of the femur were higher in the obese rats than in the controls.

Ultimately, the clinical significance of altered bone mineral accrual lies in the occurrence of fractures. Studies on the effect of fat mass and BMI on fracture risk have yielded conflicting results (11–14). We propose that the increased BMC in childhood obesity results in increased bone strength but that this increase is not sufficient to overcome the significantly greater forces generated when an obese child falls on an outstretched arm. Although childhood obesity may result in an increased risk of childhood forearm fractures, the effect of obesity on life-long fracture risk is unknown.

Future studies using 3-dimensional imaging techniques such as QCT are needed to determine the effect of obesity on bone mass and dimensions, to determine whether the onset of obesity before completion of puberty results in greater bone mineral accretion than does obesity later in life, to determine whether the increases in spine and whole-body BMC are sustained into adulthood, and to further evaluate the mechanisms for increased bone mass relative to pubertal stage and muscle mass in obese children and adolescents. 

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APPENDIX A

For assessment of the effect of obesity, it is not possible to fix both height and weight, because height and weight determine obesity status. However, one can fix the values of height and other explanatory variables and compare obese, and necessarily heavier, subjects with nonobese subjects. This is illustrated with the use of the multivariate regression reported by Goulding et al (1):

$$\ln(\text{BMC}) = \text{constant} + \ln(\text{bone area}) + \ln(\text{height}) \\ + \ln(\text{weight}) + \text{Tanner stage} + \text{obesity group} \quad (A1)$$

The regression coefficients reported for obesity status and weight were -0.129 and 0.389 , respectively. For consideration of the joint effects of the negative obesity status coefficient and the positive weight coefficient, the ratio of vertebral BMC in obese subjects to that in nonobese subjects who have similar values for all variables (bone area, height, and Tanner stage) except weight must be used. This ratio can be expressed as follows:

$$\text{BMC}_{\text{obese}}/\text{BMC}_{\text{nonobese}} = (e^{-0.129}) \\ \times (\text{weight}_{\text{obese}}/\text{weight}_{\text{nonobese}})^{0.389} \quad (A2)$$

This means that the ratio of BMC in obese subjects to that in nonobese subjects will exceed 1.0 and indicate a beneficial effect



of obesity as long as the ratio of weight in the obese group to that in the nonobese group exceeds 1.40, ie, the obese subjects weigh $\geq 40\%$ more than do the nonobese subjects of a given height. In the present study, the obese subjects weighed, on average, 46% more than did the nonobese subjects of the same height, which is consistent with the positive effect of obesity on vertebral BMC for bone area.

Note that the regressions for BMC showed that obesity was negatively associated with BMC for height and that weight was positively associated with BMC for height, so that the results of

the analysis differ if only the regression coefficient for obesity is assessed. In contrast, in our analyses, both lean mass and obesity were positively associated with BMC for height, which simplified the interpretation of the regressions.

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