

Is adiposity advantageous for bone strength? A peripheral quantitative computed tomography study in late adolescent females¹⁻³

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ABSTRACT

Background: Whereas excess adiposity is presumed to be advantageous for the skeleton, studies investigating relations between bone strength and fat during youth have been equivocal.

Objectives: Relations of percentage body fat (BF) and bone strength indexes were assessed in late adolescent females, taking into consideration surrogates of muscle force [ie, muscle cross-sectional area (MCSA) and bone length]. Bone measurements in the normal- and high-fat groups were also compared.

Design: Late adolescent females ($n = 115$; aged 18.2 ± 0.4 y) participated in this cross-sectional study. Fat-free soft tissue mass, fat mass, and percentage BF were measured with the use of dual-energy X-ray absorptiometry. Tibial and radial peripheral quantitative computed tomography measurements were taken at the 4% (trabecular bone), 20% (cortical bone), and 66% (for measurement of MCSA) sites from the distal metaphyses.

Results: Percentage BF was inversely related to radial cortical bone area, total bone cross-sectional area (CSA), cortical bone mineral content (BMC), periosteal circumference, and strength-strain index (SSI) (20% site; all $P < 0.05$). After control for MCSA and limb length, negative relations remained between percentage BF and radial measurements and were also observed at the tibia (20% site). Unadjusted bone measures were not different between groups. After control for MCSA, the high- compared with the normal-fat group had lower bone measures at the 20% site (cortical bone area and cortical BMC at the tibia, total bone CSA at the radius, and SSI at both the tibia and radius; $P < 0.05$ for all).

Conclusion: Excess weight in the form of fat mass does not provide additional benefits, and may potentially be negative, for adolescent bone. *Am J Clin Nutr* 2007;86:1530–8.

KEY WORDS Peripheral quantitative computed tomography, PQCT, late adolescent, bone strength, body composition, obesity

INTRODUCTION

Childhood and adolescence are critical stages for developing optimal bone strength. Most bone acquisition occurs between 12 and 18 y of age, when there is a convergence of genetic, hormonal, and environmental influences interacting to enhance skeletal mineralization, expansion, and linear growth (1). Any disorder or condition that alters bone formation or enhances bone resorption during the maturational period will lead to suboptimal skeletal development and presumably a greater risk of osteoporotic fracture later in life (2, 3). Given that the prevalence of child

and adolescent overweight has increased almost 3-fold since the early 1970s (4, 5) combined with recent evidence suggesting that being overweight may contribute to skeletal fractures in children and adolescents (6–8), it is vital to understand the effects of excess fat mass on bone development.

Studies that have investigated skeletal strength with dual-energy X-ray absorptiometry (DXA) in overweight youth have shown mixed results. Some reports indicate that overweight children and adolescents have higher bone mass relative to height, maturation, or fat-free soft tissue (FFST) mass compared with nonoverweight peers (9–11) or that fat mass is a positive contributor to bone mass (12, 13). Others conclude that pediatric overweight is linked to lower bone mass (14, 15) or that the extra weight from fat mass had no influence on bone mass (11).

Although it is possible that the inconsistencies in those studies can be attributed to the statistical evaluation and presentation of either adjusted (eg, for body size, sex, maturity) or unadjusted bone mass data (16, 17), it is also likely that small changes in bone size or shape can lead to significant changes in bone strength, independent of changes in bone mass (18). Ideally, predicting bone strength (or ultimately, a bone's failure load) requires knowledge of both the material (eg, mineral density) and geometric (eg, size and shape) properties of bone (19, 20). Whereas DXA-derived outcomes reflect only a 2-dimensional view of bone and do not represent true density or bone geometry, peripheral quantitative computed tomography (pQCT) is a 3-dimensional imaging technique that measures size, shape, and mineral density of bone and was shown to predict failure load at the radius more accurately than DXA (21, 22). Notably, pQCT depicts an image of the muscle cross-sectional area (MCSA) bordering the bone, which is considered an acceptable surrogate of muscle strength (23, 24). Because the rate of bone formation during growth is highly influenced by mechanical loading generated by muscle forces (25), it has been proposed to not only

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consider the absolute bone measurements but also those measures relative to surrogates of muscle strength and bone length (17, 23, 26).

To our knowledge, no studies have assessed the relations between body fatness and distinct skeletal compartments (ie, trabecular and cortical) with the use of pQCT, while taking into account the muscle-to-bone relation. The study cohort was selected to minimize the influence of differences in age, sex, and maturational status. The primary objective of this study was to examine the relations of percentage body fat (BF) and pQCT-derived tibial and radial measurements in late adolescent females (ie, after maturation), before and after controlling for mechanical loading effects (eg, MCSA and bone length for each respective site). The second objective was to compare these tibial and radial bone measurements between 2 adiposity groups defined as having normal and high percentages BF.

SUBJECTS AND METHODS

Study participants

Late adolescent females ($n = 115$), aged 18–19 y, enrolled in their first semester at The University of Georgia and who had participated in the Fighting Osteoporosis in College Using Soy intervention study, served as participants for this investigation. This age group was selected to minimize any influence of sexual maturation on the bone outcome variables. Thus, all participants must have reported normal menstruation (eg, ≥ 4 menstrual periods in the past 6 mo) for inclusion in the study. Participants were excluded if they reported significant weight loss or gain in the past 6 mo ($\pm 10\%$ initial body weight), participation in National Collegiate Athletic Association Division I athletics, diagnosis of eating disorders, present illness or chronic disease, and use of medications or herbal supplements known to affect body weight, BF, or bone metabolism. Procedures were approved by the Institutional Review Board for Human Subjects at The University of Georgia, and all participants provided written consent.

Participants were divided into 2 groups on the basis of their percentage BF: normal-fat ($< 32\%$ BF; $n = 93$) and high-fat ($\geq 32\%$ BF; $n = 22$). These classifications were selected based on amounts of BF associated with cardiovascular risk factors (27, 28). By grouping participants by percentage BF, we exclude the possibility of misclassification of those with high amounts of BF that may have otherwise been classified as normal weight if body mass index (BMI; in kg/m^2) had been used for the grouping procedure. Participant ethnicity (Hispanic or Latino–Non-Hispanic or Latino) and race (American Indian or Alaska Native, Asian, black or African American, Native Hawaiian, or other Pacific Islander, white, or any combination of race) were classified with the use of the National Institutes of Health Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research (29). Within the normal-fat group, 78 participants were white, 10 were Asian, 3 were Hispanic, and 2 were black; whereas, in the high-fat group 20 participants were white and 2 were Hispanic. When race was included as a covariate in the analyses of bone outcomes between the normal- and high-fat groups, it did not have a significant effect; therefore, the Asian, Hispanic, and black participants were included in all analyses.

Anthropometry

Height and body weight measurements were collected by a trained laboratory technician. Participants were measured for height and weight in light indoor clothing after the removal of shoes. Height was measured to the nearest 0.1 cm with the use of a wall-mounted stadiometer (Novel Products Inc, Rockton, IL). Body weight was measured to the nearest 0.1 kg with the use of an electronic scale (Seca Bella 840, Columbia, MD). Before testing each week, the scale was checked for accuracy with the use of known weights. Recalibration of the scale was not required during the testing sessions. Limb lengths were measured with anthropometric tape (Rosscraft, Inc, Surrey, Canada) to the nearest 0.10 mm at the tibia (the distal edge of the medial malleolus to the tibial plateau) and forearm (distance between the ulnar styloid process and olecranon).

Body composition

Body composition variables [fat mass (in kg), FFST mass (in kg), and percentage BF] were measured with the use of DXA (Delphi A; S/N 70467; Hologic Inc, Bedford, MA). The same technician analyzed all scans with the use of HOLOGIC WHOLE BODY ANALYSIS software (version 11.2; Hologic Inc). Quality assurance for fat mass, FFST mass, and percentage BF measured by DXA was performed by calibration against a 3-step soft tissue wedge (Hologic anthropomorphic spine phantom, model DPA/QDR-1; SN 9374) composed of different thicknesses of aluminum and lucite, calibrated against stearic acid (100% fat) and water (8.6% fat). In our laboratory, a CV of 0.36% was observed from 648 scans of the spine phantom during a 3-y period. On the basis of a one-factor random effects model, single measure intraclass coefficients (ICCs) were calculated in 5 women, aged 18–30 y, scanned twice in our laboratory during a 7-d period for fat mass, FFST mass, and percentage BF (all $R \geq 0.87$).

Peripheral quantitative computed tomography

PQCT (Stratec XCT-2000; Stratec Medizintechnik GmbH, Pforzheim, Germany) measurements were taken of the nondominant tibia and radius. Tibial measures were taken at the 4% and 20% sites of the total tibial length from the distal metaphysis and represent areas high in trabecular and cortical bone, respectively. Measurements were also assessed at the 4% and 20% sites of the forearm length, proximal to the distal radial metaphysis. Each scan was acquired with a 0.4-mm voxel and at a slice thickness of 2.4 mm. The positioning of the 2 cross-sectional measurements from the tibia and radius were determined in a scout view with their medial endplate as an anatomic marker and automatically set by the software at 4% or 20% sites. Image processing and calculation of the various bone indexes and MCSAs were determined with the use of the STRATEC software (version 5.50d; Stratec Medizintechnik). Total and trabecular volumetric bone mineral density (BMD; in mg/mm^3) and total bone cross-sectional area (in mm^2) were calculated for tibia and radius 4% sites with the use of contour mode 2 and peel mode 2. The following variables were assessed at the tibia and radius 20% sites: cortical volumetric BMD (in mg/mm^3), cortical bone area (in mm^2), total bone cross-sectional area, cortical bone mineral content (BMC; in mg), cortical thickness (in mm), periosteal circumference (in mm), endosteal circumference (in mm), and polar strength-strain index (SSI; in mm^3). Cortical bone variables



for both 20% sites were assessed with the use of cort mode 1 and the default threshold of 710 mg/cm³. The SSI was calculated with cort mode 1 and a threshold of 280 mg/cm³.

A third measurement was taken at the 66% site of both the tibia and radius to assess MCSA (in mm²), an estimate of muscle strength. The proximal two-thirds site was chosen because in this region the muscle has the highest circumference and cross-sectional area (30, 31). The MCSA was measured by placing a region of interest within the subcutaneous fat tissue. Contour mode 3 with a threshold of 34 mg/cm³ and peel mode 1 was used to obtain the "area of muscle plus bone" (ie, muscle + tibia + fibula or muscle + radius + ulna). Next, the analysis was performed with contour mode 1, threshold of 280 mg/cm³ and peel mode 1, to obtain the "area of bone" (ie, tibia + fibula or radius + ulna). The MCSA is finally obtained by subtracting the area of bone from the area of muscle plus bone.

All pQCT measures were performed and analyzed by one trained operator. The pQCT operator scanned the phantom daily to maintain quality assurance. Test-retest measurements were performed in 5 women, aged 18–24 y, to determine reliability of the pQCT in our laboratory. The one-factor random effects model ICCs for all pQCT measurements were calculated to be $R \leq 0.97$.

Physical activity

Information on physical activity for the past week was collected with the interviewer-administered 7-d recall questionnaire (32), which has been validated in females within this age group (33). Participants reported the amount of time spent sleeping as well as time spent performing moderate, hard, and very hard activities during the previous week. Light physical activity was calculated from the remaining time. From this questionnaire, each participant's average daily energy expenditure (in kcal/d) was estimated.

Dietary intake

Three-day diet records were used to estimate average intakes of daily energy, macronutrients, calcium, and vitamin D per day. The 3 d included 2 weekdays and 1 weekend day. The 3-d diet records were analyzed by FOOD PROCESSOR for WINDOWS software (version 8.0; ESHA Research, Salem, OR). In our laboratory, the reliability of diet records was investigated in a previous study of females 6–10 y of age ($n = 10$) who completed 3-d diet records twice during a 2-wk period. In that investigation, one-factor random effects model ICCs were computed for 3-d energy intake ($R = 0.47$) and 3-d calcium intake ($R = 0.71$).

Statistical analyses

Data were analyzed with the use of SPSS version 11.0.2 (SPSS Inc, Chicago, IL) for the Mac OS X. Normal distribution and homogeneity of variances were confirmed by Shapiro-Wilks W and Levene's tests, respectively. Pearson's bivariate correlations were used to examine the associations of percentage body fat, fat mass, and FFST mass with various measures of bone response variables. Partial Pearson's correlation coefficients were also computed between these same outcome variables, with control for MCSA and limb length. A $P < 0.05$ was considered statistically significant.

Group differences for anthropometric, body composition, physical activity, dietary intake, and unadjusted bone response

variables were determined with the use of unpaired (ie, independent samples) 2-tailed t tests if data were distributed normally and Mann-Whitney U tests otherwise. Descriptive statistics for raw variables are presented as mean \pm SD if not stated otherwise. Group differences for categorical variables (eg, oral contraceptive use) were tested with the use of chi-square tests. An F test was performed to test the assumption of homogeneity of regression slopes for the interaction between the independent variables (ie, adiposity groups) and the covariate (ie, MCSA). Because there was no interaction, analysis of covariance was used to compare the differences in bone response variables between the normal-fat and high-fat groups after adjusting for MCSA differences. Estimated means of bone variables in the adjusted analyses are reported as mean \pm SE. Statistically significant differences are reported if $P < 0.05$.

RESULTS

Participant characteristics

Mean age, weight, height, BMI-for-age, BMI percentile, total FFST mass and fat mass, percentage BF, tibial and forearm lengths and MCSA, oral contraceptive use, and unadjusted bone variables of the participants are provided in **Table 1**. Age and height values were not statistically different between adiposity groups; however, body weight, BMI-for-age, BMI-for-age percentiles, fat mass, and percentage BF were significantly higher in the high-fat group than in the normal-fat group (all $P < 0.05$). Total FFST mass as well as tibial and forearm lengths were not different between groups. The MCSA at the tibia, but not at the forearm, was significantly higher in the high-fat group than in the normal-fat group ($P < 0.05$). No significant difference was found between groups in the percentage of women reporting oral contraceptive use. Among the bone variables, no significant tibial or radial differences were seen at any site between adiposity groups.

Bivariate correlations between body composition and bone measurements

Percentage BF was not associated with total volumetric BMD, trabecular volumetric BMD, or total bone cross-sectional area at the 4% site of the tibia and radius (**Table 2**). In contrast, at the 20% site of the radius, but not the tibia, percentage BF was negatively correlated with cortical bone area, total bone cross-sectional area, cortical BMC, periosteal circumference, and SSI (all $P < 0.05$). Positive relations were observed between total fat mass and total bone cross-sectional area at the 4% site of the tibia and between total fat mass and cortical bone area ($P = 0.054$), total bone cross-sectional area ($P = 0.010$), periosteal circumference ($P = 0.009$), endosteal circumference ($P = 0.041$), and SSI ($P = 0.009$) at the 20% site of the tibia. Positive associations were also found between total FFST mass and total bone cross-sectional area of the 4% site as well as cortical bone area, total bone cross-sectional area, cortical BMC, periosteal circumference, endosteal circumference, and SSI of the 20% sites of both the tibia and radius (all $P < 0.05$). An inverse relation, however, was observed between total FFST mass and cortical volumetric BMD of the tibia ($P = 0.013$).

TABLE 1
Characteristics of the participants¹

	Total sample (N = 115)	Normal-fat group ² (n = 93)	High-fat group ² (n = 22)
Age (y)	18.2 ± 0.4	18.2 ± 0.4	18.4 ± 0.5
Weight (kg)	60.1 ± 7.7	58.3 ± 6.2	67.7 ± 8.5 ³
Height (cm)	164.0 ± 6.0	164.0 ± 6.2	164.6 ± 5.3
BMI-for-age (kg/m ²)	22.3 ± 2.5	21.7 ± 1.9	25.0 ± 2.8 ³
BMI percentile	56.3 ± 21.9	51.3 ± 20.7	75.9 ± 16.0 ³
FFST mass (kg)	41.3 ± 4.4	40.9 ± 4.3	42.7 ± 4.7
Fat mass (kg)	17.7 ± 4.7	16.1 ± 2.8	24.6 ± 4.6 ³
Fat mass (%)	28.8 ± 4.3	27.1 ± 2.9	35.3 ± 3.0 ³
Tibial length (mm)	372.6 ± 20.8	372.9 ± 21.2	372.1 ± 19.0
Forearm length (mm)	257.4 ± 14.2	257.2 ± 14.5	257.8 ± 13.2
Tibial MCSA (mm ²)	7060 ± 1239	6889 ± 1069	7777 ± 1608 ³
Forearm MCSA (mm ²)	2489 ± 358	2472 ± 317	2547 ± 497
Oral contraceptive use (%) ⁴	40.7 ± 0.5	37.9 ± 0.5	52.3 ± 0.5
Bone variables, 4% site			
Tot BMD (mg/mm ³)			
Tibia	313.3 ± 38.6	314.1 ± 37.9	310.2 ± 41.8
Radius	348.8 ± 56.5	348.3 ± 57.4	350.7 ± 53.8
Trab BMD (mg/mm ³)			
Tibia	254.3 ± 26.1	255.0 ± 26.2	251.2 ± 26.2
Radius	212.5 ± 31.5	213.7 ± 31.4	207.5 ± 32.1
Tot area (mm ²)			
Tibia	926.1 ± 107.3	921.7 ± 104.3	944.7 ± 119.9
Radius	271.8 ± 44.8	273.1 ± 41.5	266.5 ± 57.8
Bone variables, 20% site			
Cort BMD (mg/mm ³)			
Tibia	1174 ± 16.2	1173 ± 15.7	1176 ± 18.4
Radius	1193 ± 20.5	1193 ± 18.1	1192 ± 29.1
Cort area (mm ²)			
Tibia	190.7 ± 22.7	191.0 ± 22.1	189.2 ± 25.7
Radius	68.7 ± 8.3	69.0 ± 8.2	67.4 ± 8.8
Tot area (mm ²)			
Tibia	332.7 ± 47.6	333.0 ± 48.5	331.5 ± 44.8
Radius	94.2 ± 14.0	95.0 ± 14.0	90.8 ± 13.9
Cort BMC (mg)			
Tibia	223.7 ± 26.8	224.1 ± 26.0	222.5 ± 30.7
Radius	81.9 ± 10.0	82.3 ± 9.8	80.4 ± 11.0
Cort thk (mm)			
Tibia	3.59 ± 0.5	3.60 ± 0.4	3.58 ± 0.5
Radius	2.65 ± 0.2	2.64 ± 0.2	2.67 ± 0.3
Peri circ (mm)			
Tibia	64.5 ± 4.6	64.5 ± 4.6	64.4 ± 4.5
Radius	34.2 ± 2.8	34.3 ± 2.8	33.7 ± 2.6
Endo circ (mm)			
Tibia	41.9 ± 5.7	41.9 ± 5.7	41.9 ± 5.6
Radius	17.8 ± 3.4	18.0 ± 3.4	16.9 ± 3.1
SSI (mm ³)			
Tibia	1268 ± 244	1270 ± 246	1261 ± 239
Radius	217.9 ± 42.2	220.3 ± 42.1	208.0 ± 41.8

¹ All values are $\bar{x} \pm SD$. FFST, fat-free soft-tissue; MCSA, muscle cross-sectional area; Tot BMD, total volumetric bone mineral density; Trab BMD, trabecular volumetric bone mineral density; Tot area, total bone cross-sectional area; Cort BMD, cortical volumetric bone mineral density; Cort area, cortical bone area; Cort BMC, cortical bone mineral content; Cort thk, cortical thickness; Peri circ, periosteal circumference; Endo circ, endosteal circumference; SSI, strength strain index. Bone variables were measured by peripheral quantitative computed tomography at the 4% (trabecular) and 20% (cortical) sites.

² Cutoffs used to denote normal fat (32% body fat) and high fat ($\geq 32\%$ body fat) were determined with cardiovascular risk factors (27, 28).

³ Significantly different from normal-fat group, $P \leq 0.05$ (2-tailed independent t tests).

⁴ Tests of significance between groups were based on the chi-square test.

Partial correlations between body composition and bone measurements

Consistent with the bivariate correlations, after adjustment for MCSA and limb length, no significant relations were found between percentage BF and total volumetric BMD, trabecular volumetric BMD, and total bone cross-sectional area of the 4% sites of the tibia and radius (**Table 3**). At the 20% site, significant negative associations were found between percentage BF and cortical bone area, total bone cross-sectional area, cortical BMC, periosteal circumference, and SSI of tibia and radius (all $P < 0.05$). An inverse relation was also found between percentage BF and cortical thickness at the tibia at the 20% site ($P = 0.052$). Total fat mass was not associated with total volumetric BMD, trabecular volumetric BMD, and total bone cross-sectional area of the 4% sites of the tibia and radius. However, significant negative correlations were found between total fat mass and cortical bone area and cortical BMC at the tibia and radius (all $P < 0.05$). Positive relations were found between total FFST mass and total bone cross-sectional area at the 4% site and between FFST mass and total bone cross-sectional area, periosteal circumference, endosteal circumference, and SSI of the tibia and radius at the 20% site (all $P < 0.05$). Positive associations were also found at the 20% site for tibial cortical bone area and cortical BMC (both $P < 0.05$). Negative relations were observed at the 20% site between FFST mass and cortical volumetric BMD at the tibia ($P = 0.051$) and at the radius ($P = 0.035$) as well as cortical thickness at the radius only ($P = 0.006$).

Comparisons between the normal- and high-fat groups

Adjusted bone measurements

Group-specific means for each bone variable based on an analysis of covariance that controls for differences in MCSA are summarized in **Table 4**. After controlling for MCSA, the high-fat group had lower bone measures at the 20% site than did the normal-fat group: cortical bone area ($P = 0.015$), cortical BMC ($P = 0.029$), and periosteal circumference ($P = 0.059$) at the tibia; total bone cross-sectional area at the radius ($P = 0.046$); and SSI at both the tibia ($P = 0.039$) and radius ($P = 0.051$).

Physical activity

No significant differences were observed between adiposity groups in reported hours of sleep on in light, moderate, hard, and very hard activities. The high-fat group, however, had significantly higher total daily energy expenditure compared with the normal-fat group (2357 ± 345 compared with 2019 ± 269 kcal/d; $P = 0.010$).

Dietary intake

Energy intakes for the normal-fat and high-fat groups were 1810 ± 426 and 1713 ± 507 kcal/d, respectively ($P = 0.360$). Mean intakes for all macronutrients and micronutrients were not different between groups. Both the normal-fat and high-fat groups met the US recommended dietary allowance for carbohydrate and protein but reported low intakes of calcium (720 ± 324 compared with 626 ± 286 mg, respectively) and vitamin D (98 ± 104 compared with 83 ± 56 IU, respectively). Seventy-four percent (69 of 93) of the normal-fat and 91% (20 of 22) of the high-fat group consumed less than two thirds of the adequate intake for calcium, whereas 76% (71 of 93) of the normal-fat

TABLE 2

Bivariate correlations of bone outcomes at the tibia and radius with percentage body fat, fat mass, and fat-free soft tissue mass¹

	Percentage body fat		Fat mass		Fat-free soft tissue mass	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
4% Site						
Tot BMD (mg/mm ³)						
Tibia	-0.015	0.873	0.009	0.926	0.042	0.657
Radius	-0.032	0.738	-0.003	0.979	0.041	0.663
Trab BMD (mg/mm ³)						
Tibia	0.027	0.774	0.031	0.743	0.053	0.573
Radius	-0.003	0.976	-0.020	0.835	0.008	0.935
Tot area (mm ²)						
Tibia	0.053	0.572	0.286	0.002	0.619	0.001
Radius	-0.089	0.346	0.082	0.384	0.416	0.001
20% Site						
Cort BMD (mg/mm ³)						
Tibia	0.002	0.984	-0.078	0.407	-0.232	0.013
Radius	-0.031	0.741	-0.088	0.347	-0.136	0.146
Cort area (mm ²)						
Tibia	-0.087	0.355	0.180	0.054	0.609	0.001
Radius	-0.191	0.041	0.030	0.750	0.519	0.001
Tot area (mm ²)						
Tibia	-0.016	0.862	0.239	0.010	0.643	0.001
Radius	-0.187	0.045	0.041	0.660	0.542	0.001
Cort BMC (mg)						
Tibia	-0.086	0.361	0.169	0.070	0.576	0.001
Radius	-0.193	0.039	0.018	0.848	0.496	0.001
Cort thk (mm)						
Tibia	-0.102	0.278	0.004	0.966	0.184	0.049
Radius	-0.062	0.509	0.016	0.862	0.181	0.053
Peri circ (mm)						
Tibia	-0.015	0.877	0.243	0.009	0.645	0.001
Radius	-0.199	0.033	-0.015	0.875	0.422	0.020
Endo circ (mm)						
Tibia	0.035	0.713	0.190	0.041	0.428	0.001
Radius	-0.094	0.320	0.063	0.505	0.380	0.001
SSI (mm ³)						
Tibia	-0.026	0.783	0.244	0.009	0.668	0.001
Radius	-0.196	0.035	0.032	0.734	0.535	0.001

¹ Bone variables were measured by peripheral quantitative computed tomography at the 4% (trabecular) and 20% (cortical) sites. Tot BMD, total volumetric bone mineral density; Trab BMD, trabecular volumetric bone mineral density; Tot area, total bone cross-sectional area; Cort BMD, cortical volumetric bone mineral density; Cort area, cortical bone area; Cort BMC, cortical bone mineral content; Cort thk, cortical thickness; Peri circ, periosteal circumference; Endo circ, endosteal circumference; SSI, strength strain index. Pearson's bivariate correlations were used to examine associations of percentage body fat, fat mass, and fat-free soft tissue mass with bone response variables in this sample ($N = 115$).

group and 82% (18 of 22) of the high-fat group consumed less than two thirds of the adequate intake for vitamin D ($P > 0.01$ for both).

DISCUSSION

One of the key findings from this study was that percentage BF was inversely related to pQCT-derived bone measurements assessed at a predominantly cortical site of the radius (cortical bone area, bone cross-sectional area, cortical BMC, periosteal circumference, and SSI) in late adolescent females. When taking into account MCSA and limb length, negative relations not only remained between percentage BF and radial measurements, but they were also observed at the tibia (cortical site). When participants were compared by amount of adiposity, we found that tibial and radial bone measurements were not different between groups. Given that both the high-fat and normal-fat groups had no

significant differences in total FFST mass, it was interesting to find that the additional 9-kg fat mass in the high-fat group provided no advantage for pQCT-derived bone measurements at the tibia and radius. Consistent with the correlational data, after correcting for MCSA differences, the high-fat group had significantly lower tibial cortical bone area, cortical BMC, and SSI, as well as radial total bone cross-sectional area and SSI than did the normal-fat group. Collectively, our data suggest that, contrary to the idea that extra body weight is advantageous for the skeleton, excess weight in the form of fat mass does not provide additional benefits and may potentially be negative for adolescent bone.

The few studies that have examined the relations between overweight and measures of bone, assessed by DXA, show conflicting results. Overweight youth, ranging from 3 to 19 y of age, were reported to either have higher lumbar spine or total body bone mass relative to height, maturation, or FFST mass (9–11) or lower bone mass when corrected for their body weight (14, 15).

TABLE 3

Partial correlations of bone outcomes at the tibia and radius with percentage body fat, fat mass, and fat-free soft tissue mass¹

	Percentage body fat		Fat mass		Fat-free soft tissue mass	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
4% Site						
Tot BMD (mg/mm ³)						
Tibia	-0.066	0.488	-0.062	0.514	0.002	0.983
Radius	-0.034	0.722	-0.062	0.513	-0.159	0.092
Trab BMD (mg/mm ³)						
Tibia	-0.011	0.906	-0.012	0.901	0.061	0.523
Radius	0.006	0.953	-0.034	0.721	-0.073	0.441
Tot area (mm ²)						
Tibia	-0.085	0.369	0.041	0.668	0.438	0.001
Radius	-0.110	0.245	-0.029	0.764	0.285	0.002
20% Site						
Cort BMD (mg/mm ³)						
Tibia	0.063	0.508	0.023	0.811	-0.184	0.051
Radius	-0.027	0.777	-0.087	0.363	-0.198	0.035
Cort area (mm ²)						
Tibia	-0.335	0.001	-0.209	0.026	0.367	0.001
Radius	-0.280	0.003	-0.228	0.015	0.135	0.154
Tot area (mm ²)						
Tibia	-0.229	0.015	-0.115	0.226	0.398	0.001
Radius	-0.238	0.011	-0.138	0.145	0.330	0.001
Cort BMC (mg)						
Tibia	-0.317	0.001	-0.201	0.033	0.329	0.001
Radius	-0.281	0.003	-0.240	0.010	0.098	0.302
Cort thk (mm)						
Tibia	-0.183	0.052	-0.133	0.159	0.093	0.326
Radius	-0.089	0.347	-0.151	0.112	-0.256	0.006
Peri circ (mm)						
Tibia	-0.232	0.013	-0.118	0.213	0.394	0.001
Radius	-0.237	0.011	-0.165	0.081	0.218	0.020
Endo circ (mm)						
Tibia	-0.075	0.431	-0.019	0.841	0.230	0.014
Radius	-0.103	0.276	-0.001	0.991	0.365	0.001
SSI (mm ³)						
Tibia	-0.261	0.005	-0.136	0.150	0.421	0.001
Radius	-0.249	0.008	-0.149	0.116	0.319	0.001

¹ Bone variables were measured by peripheral quantitative computed tomography at the 4% (trabecular) and 20% (cortical) sites. Tot BMD, total volumetric bone mineral density; Trab BMD, trabecular volumetric bone mineral density; Tot area, total bone cross-sectional area; Cort BMD, cortical volumetric bone mineral density; Cort area, cortical bone area; Cort BMC, cortical bone mineral content; Cort thk, cortical thickness; Peri circ, periosteal circumference; Endo circ, endosteal circumference; SSI, strength strain index. Partial Pearson's correlations were used to examine associations of percentage body fat, fat mass, and fat-free soft tissue mass with bone response variables after control for muscle cross-sectional area and limb length in this sample ($N = 115$).

Considering the limitations associated with the 2-dimensional bone measurements of DXA in children and adolescents of different age, sex, body size, body composition, and sexual maturation, adjusted DXA bone outcomes can be difficult to interpret and may explain some of the discrepancies among these studies (9–11). A novel aspect of this study involved the evaluation of pQCT-derived bone measurements relative to limb-specific muscle strength and bone length, a technique that is gaining recognition within the framework of pediatric bone health (17, 23, 26). Because the rate of bone formation is highly influenced by the mechanical stimulation from muscle forces during growth (25, 34), evaluating indexes of bone strength relative to muscle strength and bone length has been recommended (34–36).

From preadulthood to young adulthood, fat mass has been shown to be positively correlated with unadjusted DXA-assessed bone measurements at weight-bearing skeletal sites (13, 37).

Thus, it was not surprising in our study that fat mass was positively related to unadjusted bone measurements at the tibia (weight-bearing site) but not at the radius (non-weight-bearing site). Because we observed negative associations between radial bone measurements and percentage BF, one could speculate that obesity increases risk of fractures at non-weight-bearing skeletal sites, such as the forearm, given that the mechanical force during a fall is proportional to body weight. This may explain why studies have reported higher forearm fractures in overweight than in normal weight children and adolescents (38–40). Because of the tibia's weight-bearing location, it is also reasonable to expect that the extra weight from fat mass could lead to a greater muscle contraction and eventually greater bone strength compared with the radius. However, when interpreting the relations between percentage BF as well as fat mass with bone measurements at the tibia relative to MCSA and

TABLE 4

Bone measurements of the tibia and radius after adjustment for muscle cross-sectional area in normal-fat and high-fat late adolescent females¹

Bone variable	Normal-fat group ² (n = 93)	High-fat group ² (n = 22)	P value ³
4% Site			
Tot BMD (mg/mm ³)			
Tibia	315.1 ± 4.0 ⁴	305.8 ± 8.4	0.326
Radius	349.0 ± 5.7	348.1 ± 11.7	0.948
Trab BMD (mg/mm ³)			
Tibia	255.7 ± 2.7	248.4 ± 5.7	0.255
Radius	214.0 ± 3.2	206.2 ± 9.3	0.295
Tot area (mm ²)			
Tibia	926.7 ± 10.7	923.7 ± 22.5	0.907
Radius	273.6 ± 4.5	264.4 ± 9.3	0.377
20% Site			
Cort BMD (mg/mm ³)			
Tibia	1173 ± 1.7	1178 ± 3.5	0.206
Radius	1193 ± 2.1	1192 ± 4.4	0.768
Cort area (mm ²)			
Tibia	192.9 ± 2.0	181.3 ± 4.2	0.015
Radius	69.1 ± 0.7	66.5 ± 1.4	0.080
Tot area (mm ²)			
Tibia	336.4 ± 4.4	317.1 ± 9.2	0.063
Radius	95.3 ± 1.2	89.6 ± 2.6	0.046
Cort BMC (mg)			
Tibia	226.1 ± 2.4	213.7 ± 5.0	0.029
Radius	82.6 ± 0.8	79.3 ± 1.7	0.077
Cort thk (mm)			
Tibia	3.61 ± 0.05	3.51 ± 0.09	0.355
Radius	2.65 ± 0.02	2.66 ± 0.04	0.795
Peri circ (mm)			
Tibia	64.9 ± 0.4	63.0 ± 0.9	0.059
Radius	34.3 ± 0.3	33.5 ± 0.5	0.128
Endo circ (mm)			
Tibia	42.1 ± 0.6	41.0 ± 1.2	0.393
Radius	18.1 ± 0.3	16.8 ± 0.7	0.096
SSI (mm ³)			
Tibia	1288 ± 21.7	1181 ± 45.8	0.039
Radius	221.1 ± 3.7	204.2 ± 7.7	0.051

¹ Bone variables were measured by peripheral quantitative computed tomography at the 4% (trabecular) and 20% (cortical) sites. Tot BMD, total volumetric bone mineral density; Trab BMD, trabecular volumetric bone mineral density; Tot area, total bone cross-sectional area; Cort BMD, cortical volumetric bone mineral density; Cort area, cortical bone area; Cort BMC, cortical bone mineral content; Cort thk, cortical thickness; Peri circ, periosteal circumference; Endo circ, endosteal circumference; SSI, strength strain index.

² Cutoffs used to denote normal fat (<32% body fat) and high fat (≥32% body fat) were determined with cardiovascular risk factors (27, 28).

³ Tests of significance between groups were based on group main effect by using ANCOVA.

⁴ $\bar{x} \pm SE$ (all such values) adjusted for muscle cross-sectional area (66% site).

tibial length, negative associations were observed. Therefore, our data suggest that high amounts of BF negatively influence bone independent of its weight-bearing effects, and areas consisting predominantly of cortical bone seem to be affected more than trabecular bone. Whereas additional studies are needed to confirm our interpretation, our findings are consistent with Janicka et al, (41) who showed that fat mass was negatively correlated with computed tomography-derived measures of

bone strength in adolescent males, after accounting for surrogates of muscle force.

Analyses from cellular and molecular studies suggest that the mechanisms involving bone and fat is intricate by nature, because both adipocytes and osteoblasts originate from mesenchymal stem cells in bone marrow. Factors regulating lipid metabolism may also have a significant effect on bone formation. Extra weight in the form of fat mass has not only been shown to stimulate bone growth by direct mechanical actions from increased load (42) but also through increased production of the hormones insulin, estrogen, and leptin, all of which have shown increases in markers of bone formation when administered in vivo (43–47). Alternatively, excess adipose tissue has also been shown to hinder bone growth, in vitro, by enhancing the role of oxidized lipids in accelerating atherogenesis, thus activating calcifying vascular cells and inhibiting osteoblastic differentiation (48). Moreover, bone marrow adipogenesis increases with conditions that induce bone loss, such as estrogen depletion (49), disuse, and hindlimb unloading (50, 51). Future work should continue to explore these potential mechanisms to enhance our knowledge of fat and bone relations.

A visual representation is shown in **Figure 1** of the overall effect by which smaller bone dimensions and lesser bone material, as was observed in the high-fat group compared with the normal-fat group, had on the tibial and radial SSI, an estimate of torsional bone strength (52). It is assumed here that MCSA provides an approximate assessment of muscle strength; therefore, it is a surrogate measure of the loads to which the tibial and radial bones are exposed. Why bone strength in the high-fat group was not appropriately adapted to the prevailing loads is unknown; however, modifiable factors such as physical activity and diet not only play an important role in obesity progression but also significantly affect bone strength. It is possible that higher proportions of fat mass could be a marker for reduced physical activity. However, when information about physical activity was collected in this study, no significant differences were found for physical activity levels between groups. The high- and normal-fat groups reported moderate amounts of physical activity (27.2 compared with 29.4 min/d, respectively) lower than the US recommendations for this age group (ie, ≈60 min of moderate intensity activity/d) (53). Specific types of high-impact exercise have been documented as having a positive effect on bone mineral accrual, particularly during growth (54–56). It is unlikely that reported current activity levels explain the group differences in bone strength. However, we did not collect information on the types of activities performed by the participants; therefore, it is uncertain the degree to which participants engaged in high-impact physical activities.

For dietary intake, the groups reported no significant differences in energy, macronutrient, and micronutrient intakes. Mean calcium intakes in both groups were low and less than the US-recommended adequate intake; however, a higher percentage of participants in the high-fat group than in the normal-fat group consumed less than two-thirds adequate intake for calcium. Analysis of covariance was used to assess whether dietary calcium had an effect on the adjusted bone outcomes between groups. After controlling for dietary calcium in addition to MCSA, no significant effect from calcium was observed on the adjusted bone outcomes. The mean intakes for vitamin D were also low in both groups and less than the adequate intake. Because cutaneous synthesis of vitamin D has a greater influence



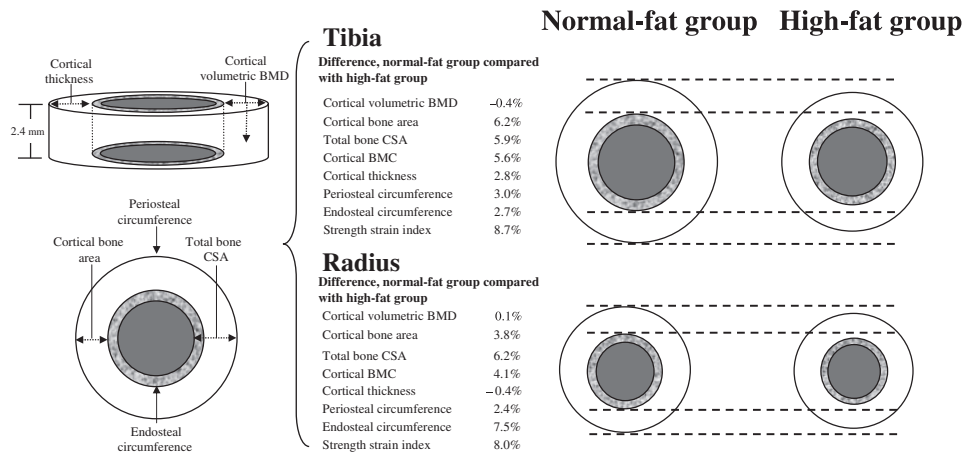


FIGURE 1. Schematic representation of the average magnitude of difference $[A - B/(A + B)/2 \times 100]$ at the 20% site of the tibia and radius, after control for muscle cross-sectional area (CSA), in adolescent females in the normal-fat group ($n = 93$) compared with the high-fat group ($n = 22$). The outer white circles represent cortical bone, the textured circles represent trabecular bone, and the gray circles represent the medullary cavity. BMD, bone mineral density; BMC, bone mineral content.

than does dietary vitamin D on serum 25-hydroxyvitamin D concentrations, it would have been preferable to measure circulating concentrations of serum 25-hydroxyvitamin D to better understand the influences of vitamin D status on bone in these subjects. Because overweight and obese persons tend to have lower concentrations of circulating vitamin D, possibly as a result of vitamin D's partial sequestration in the adipose tissue (57), vitamin D could be a mediating factor in the relation between excess fatness and bone.

Some limitations in our study must be acknowledged. First, it is important to note that the analysis of muscle strength is complex, and the use of MCSA does not reflect the functional status of the entire muscle system, including muscle length, contraction velocity, structure, and coordination (58). Whether the data generated with this technique can be used to predict bone health and risk of skeletal fractures must be validated by subsequent prospective studies. Second, the present study used baseline data from a randomized nutrition intervention trial and was not specifically designed to examine adiposity and bone relations. As a result, the sample was relatively homogenous for BMI. If BMI-for-age percentiles were used in the overweight classification scheme such as other investigators have used (7–10), few participants would have been classified as being at risk of overweight or being overweight (10 of 22 participants in the high-fat group exceeded the 85th BMI-for-age percentile and 1 participant exceeded the 95th BMI-for-age percentile). The homogeneity of this sample for body fatness may partly explain why there were no significant differences in total body FFST mass among the high- and normal-fat groups. The participants in the high-fat group did have greater MCSA of the tibia, and this may be related to the weight-bearing effect at this skeletal site, because no significant differences existed at the radius (nonloading site). An advantage of this sample was that the degree of variability in factors known to influence bone, such as sex, age, and maturational status, were minimized. All participants were healthy females between the ages of 18 and 19 y who reported having regular menstrual cycles.

Although the clinical significance of bone strength lies in the occurrence of fractures, our study provides important insight into the obesity and bone strength relation with the use of pQCT.

Specifically, our results suggest that extra weight in the form of fat mass does not provide additional benefits to material and geometric properties of bone strength in late adolescent females. However, prospective research is needed to confirm a cause-and-effect relation that considers physical inactivity, metabolic diseases, and environmental influences.

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