Fat Mass Is Not Beneficial to Bone in Adolescents and Young Adults

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Context: Although muscle mass is beneficial to bone, studies on the effect of fat mass on bone have yielded conflicting results.

Objective: The aim of this study was to assess the relations between lean and fat mass and bone structure.

Design: This study was cross-sectional.

Setting: The study was conducted in a general community.

Subjects: Subjects included 300 healthy sexually mature adolescents and young adults (150 males and 150 females) between the ages of 13 and 21 yr.

Main Outcome Measure: We investigated the relation between dual-energy x-ray absorptiometry (DXA) measures of total body fat and lean mass and bone values obtained with DXA (legs and lumbar spine bone mineral density and bone mineral content) and computed tomography (CT) (cross-sectional and cortical bone areas of the femurs and cross-sectional area and cancellous bone density of the vertebrae).

Results: Simple and multiple linear regression analyses showed significant positive relations between DXA lean mass and all CT and DXA measures of bone in the axial and appendicular skeletons (all $P < 0.005$). In contrast, whereas Pearson correlations between DXA measures of fat mass and bone parameters were generally positive, multiple regression analyses showed that fat mass, after accounting for lean mass, trunk height/leg length, had a negative, or no, correlation with CT and DXA values for bone.

Conclusions: Our findings provide compelling evidence that, despite increased mechanical loading and independent of lean mass, adipose tissue is not beneficial to bone structure. (*J Clin Endocrinol Metab* 92: 143–147, 2007)

INCREASED FAT DURING adolescence is a major public health concern, is associated with the metabolic syndrome, and is a risk factor for many common adult conditions, such as cardiovascular disease, diabetes, hypertension, and cancer (1–3). However, most, but not all, studies examining the possible relations between fat mass and bone mass have found a positive association between these two tissues, regardless of age (4–9). Indeed, available data suggest that increased fat enhances bone mass and may protect against osteoporosis in both children and adults (9–12). This positive fat–bone relation is credited not only to stresses from mechanical loading but also to the metabolic effects of bone–active hormones secreted or regulated by adipocytes (13). Leptin, a satiety-regulating hormone that is produced by adipocytes, increases the proliferation and differentiation of osteoblasts in adult patients (14). Additionally, aromatization of androgen to estrogen by fatty tissue results in reduced osteoclast activity and possibly increased bone mass in children (13). In contrast, two studies in females from childhood to young adulthood reported fat mass to be negatively associated with bone mass (8, 15).

Discrepancies in the results from previous studies assessing the relation between fat and bone may be related to differences in the cohorts studied and to the use of dual-energy x-ray absorptiometry (DXA) to simultaneously obtain fat and bone measures. Although DXA allows for accurate determinations of body fat and lean mass, DXA bone values are influenced by the amount and distribution of fatty tissues around the bone (16). In this investigation, the potentially confounding effects of age, pubertal stage, gender, and ethnicity were controlled by only enrolling white sexually mature males and females. Additionally, to account for the possible influence of soft tissues on bone measurements, the effects of fat and lean mass on bone were assessed by both DXA and computed tomography (CT).

Subjects and Methods

Subjects

The institutional review board for clinical investigations at Childrens Hospital Los Angeles approved the investigational protocol, and informed consent was obtained from all parents and/or subjects. A total of 300 healthy white teenagers and young adults (150 males and 150 females) between the ages of 13 and 21 yr were recruited from schools of Los Angeles County and enrolled in this study.

Study subjects had no known diagnosis of any chronic illness; no history of medical disorders resulting in a period of illness that interrupted their usual physical activity and/or nutritional status for more than 1 month in the 2 yr before enrollment; no intake of any medications, vitamin preparations, or calcium supplements within the previous 6 months; and no hospitalization since birth.

All eligible participants underwent a physical examination by a pediatrician. Measurements of weight were obtained to the nearest 0.1 kg

TABLE 1. Age, anthropometric characteristics, and bone, lean, and fat measurements in 150 females and 150 males

	Females, mean ± SD (range)	Males, mean ± SD (range)
Age (yr)	17.0 ± 1.7 (13.1 to 20.9)	17.4 ± 1.6 (14.0 to 21.0)
Height (cm)	161.2 ± 5.6 (146.9 to 177.8)	173.1 ± 7.8 (147.7 to 193.0)
Weight (kg)	62.5 ± 14.2 (42.7 to 115.0)	72.4 ± 15.1 (47.6 to 122.6)
Total fat (kg)	21.0 ± 8.8 (8.0 to 53.6)	15.8 ± 8.8 (3.8 to 45.4)
Total lean (kg)	38.2 ± 6.1 (27.4 to 57.7)	52.7 ± 8.0 (35.8 to 80.2)
BMI (kg/m^2)	24.0 ± 5.1 (16.0 to 41.4)	24.1 ± 4.4 (17.2 to 42.4)
BMI z-score	−0.01 ± 1.1 (−1.7 to 3.6)	0.01 ± 0.9 (−1.4 to 3.9)
CT vertebral CSA (cm^2)	8.6 ± 1.1 (6.0 to 12.5)	10.9 ± 1.4 (8.2 to 14.7)
CT vertebral CBD (mg/cm^3)	176 ± 27 (116 to 232)	169 ± 25 (96 to 234)
CT femoral CSA (cm^2)	5.0 ± 0.7 (3.6 to 7.1)	6.2 ± 0.8 (4.4 to 13.1)
CT femoral CBA (cm^2)	4.1 ± 0.5 (2.5 to 5.5)	5.0 ± 0.7 (3.3 to 6.7)
DXA vertebral BMC (g)	12.4 ± 2.1 (8.0 to 21.4)	14.4 ± 3.1 (7.9 to 23.3)
DXA vertebral BMD (g/cm^2)	1.0 ± 0.1 (0.7 to 1.5)	1.0 ± 0.1 (0.6 to 1.3)
DXA legs BMC (g)	373 ± 67 (234 to 555)	495 ± 94 (306 to 848)
DXA legs BMD (g/cm^2)	1.1 ± 0.1 (0.9 to 1.5)	1.3 ± 0.1 (0.9 to 1.8)

using the Scale-Tronix (Scale-Tronix, Inc., Wheaton, IL), and measurements of height and trunk height were obtained to the nearest 0.1 cm using the Harpenden stadiometer (Holtain Ltd., Crymmych, Wales). For the purposes of this study, leg length was defined as the difference between total height and trunk height. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Tanner stage of sexual development was assessed based on breast development in females and testicular size in males (17); only subjects who had achieved sexual maturity (Tanner V) were included in this study. Skeletal maturation was assessed by the method of Greulich and Pyle (18) from radiographs of the left hand and wrist, and those in whom skeletal age differed from chronological age by more than 2 yr were excluded from further evaluation.

Fat, lean, and bone measurements

Measurements of fat and lean mass of the total body and bone mineral content (BMC) and bone mineral density (BMD) of the first three lumbar vertebrae were obtained using a fan-beam DXA densitometer (Delphi W; Hologic, Inc., Waltham, MA) in array mode and were analyzed with the manufacturer's software. The coefficients of variation for these DXA measurements have been reported to range from 0.7–1.7% (19, 20). The time required for the procedure was approximately 6 min and the radiation exposure was negligible.

On the same day and by the same technologist, CT bone measurements using the same scanner (CT Highlite Advantage; General Electric Co., Milwaukee, WI) and the same mineral reference phantom (CT-T bone densitometry package; General Electric Co.) were obtained. For this study, in the appendicular skeleton, measurements of cross-sectional area (CSA) and cortical bone area (CBA) were acquired at the midshafts of the femurs. In the axial skeleton, measurements of CSA and cancellous bone density (CBD) were obtained at the midportions of the first three lumbar vertebral bodies. Measurements of CBD in the axial skeleton represent the tissue density of bone and are the correlates of measures of CBA in the appendicular skeleton. The coefficients of variation for these CT measurements in young adults are between 0.6 and 1.5% (19). The time required for this procedure was approximately 10 min, and the effective radiation dose was approximately 8 mrem (21).

Power calculations and statistical analysis

Previous studies indicate that weight explains approximately 80% of the variance in the cross-sectional dimensions at the midshaft of the femur after age, pubertal status, gender, and ethnicity are taken into account (22). Based on these data, 150 males and 150 females were deemed sufficient to allow the detection of a 2% variance with a greater than 80% power. The data were analyzed using simple linear regression and multivariate analyses.

Results

Age, anthropometric parameters, DXA measures, and CT values in females and males are described in Table 1. Ver-

tebral CSA and BMC, femoral CSA and CBA, legs BMC and BMD, height, and total lean mass were significantly higher in males ($P < 0.0001$), whereas measurements of total body fat were higher in females ($P < 0.0001$). Based on current age- and gender-specific Centers for Disease Control reference standards, the BMI of 24% of the females and of 19% of the males was between the 85th and 95th percentiles, and of 12% of the females and of 15% of the males was greater than the 95th percentile.

Overall, moderate correlations were observed between lean and fat mass (r = 0.71 and 0.49 for females and males, respectively; both $P < 0.0001$). However, in subjects with BMI values greater than the 95th percentile, the associations were weaker or not significant [r = 0.52 ($P = 0.019$) and 0.25 ($P = 0.25$) for females and males, respectively].

Measures of bone by CT and DXA were significantly correlated (r between 0.28 and 0.89; Table 2). Regardless of technique, simple linear regressions demonstrated positive associations between measures for bone and values for lean mass in both males and females, with the weakest between CT measures of CBD and lean mass (Figs. 1 and 2 and Table 3). In females, measures of fat mass also correlated with all DXA and CT bone parameters, whereas, in males, these relations were weaker or nonexistent (Figs. 1 and 2 and Table 3).

Multiple regression analysis of the independent effects of lean and fat mass on bone obtained after adjusting for leg length or truncal height confirmed the strong positive effect of lean mass on all bone parameters (Tables 4 and 5). In

TABLE 2. Correlation coefficients for DXA and CT bone measurements

DXA	CT							
	Females				Males			
	Vertebral		Femoral		Vertebral		Femoral	
	CSA	CBD	CSA	CBA	CSA	CBD	CSA	CBA
Vertebral								
BMC	0.50	0.55	0.67	0.66	0.52	0.52	0.53	0.72
BMD	0.28	0.72	0.56	0.59	0.34	0.72	0.47	0.67
Leg								
BMC	0.54	0.42	0.87	0.89	0.51	0.43	0.71	0.89
BMD	0.41	0.55	0.74	0.85	0.32	0.60	0.56	0.80

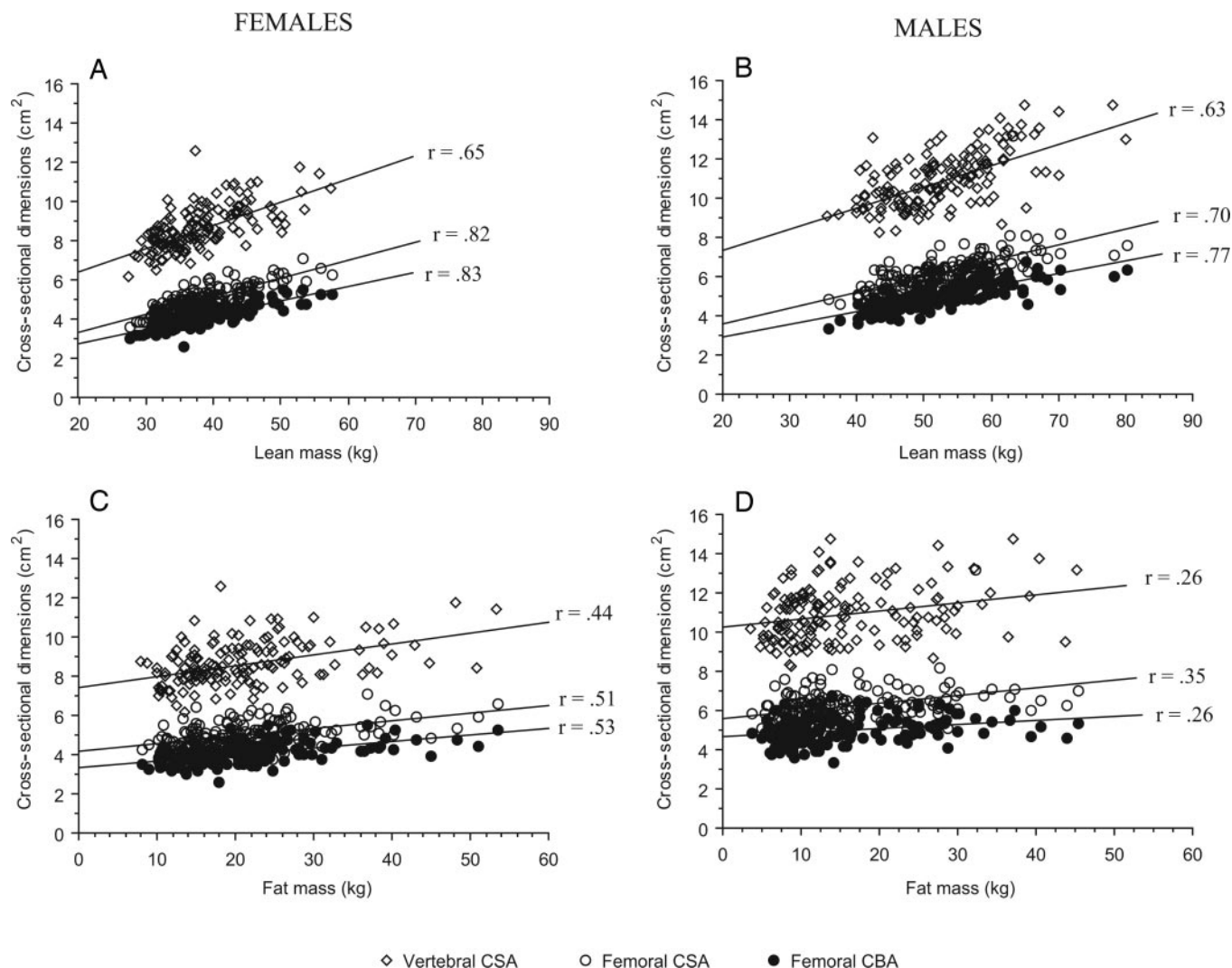All are significant to the value $P < 0.0001$.
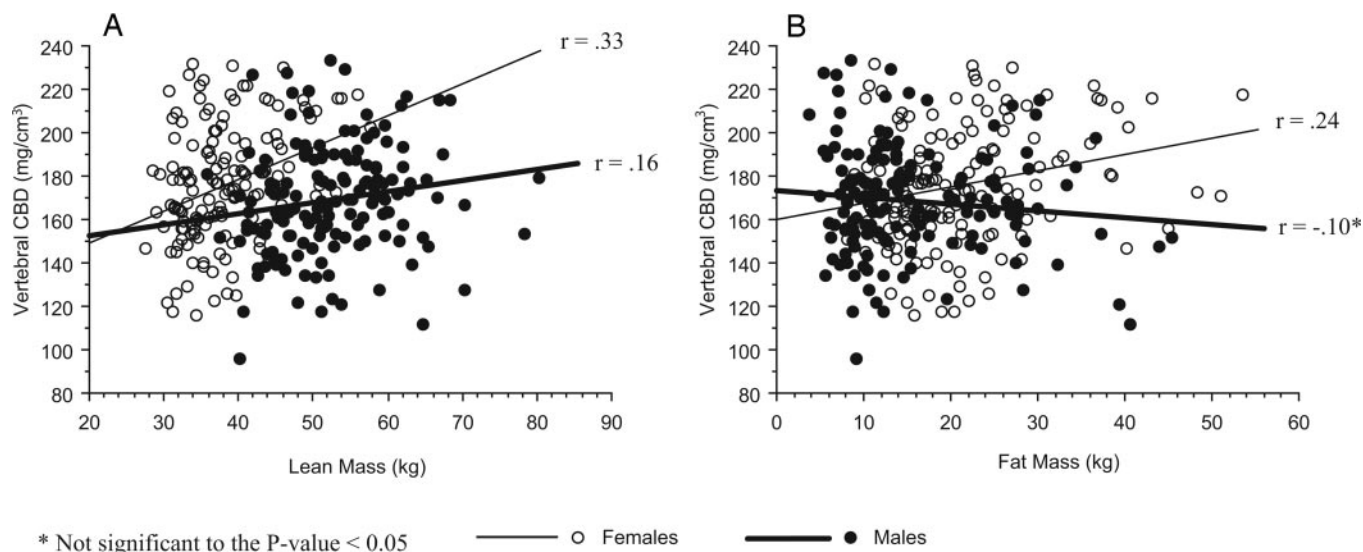
FEMALES

MALES

FIG. 1. Relations between total lean mass and vertebral CSA (*upper line*), femoral CSA (*middle line*), and CBA (*lower line*) in 150 females (A) and 150 males (B), and between total fat and vertebral CSA (*upper line*), femoral CSA (*middle line*), and CBA (*lower line*) in 150 females (C) and 150 males (D).

FIG. 2. Relations between vertebral CBD and lean mass (A) and fat mass (B) in 150 females (*thin lines*) and 150 males (*thick lines*).

TABLE 3. Correlation coefficients for DXA bone measurements with lean and fat mass

	Females		Males	
	Lean	Fat	Lean	Fat
Vertebral				
BMC	0.60	0.35	0.63	−0.01[a]
BMD	0.54	0.46	0.58	0.13[a]
Leg				
BMC	0.83	0.48	0.79	0.24
BMD	0.74	0.41	0.62	0.10[a]

[a] Not significant to the value $P < 0.05$.

contrast, fat mass had a negative, or no, relation to measures of bone. In males, all DXA measurements and CT measures of vertebral CBD and femoral CBA were negatively related to fat mass, whereas the CSAs of the vertebral body and the femur did not enter into the model. In females, there were no associations between bone and fat determinations, with the exception of a negative relation between DXA leg BMD and fat mass.

Discussion

The findings of this study corroborate previous studies indicating that, regardless of age or gender, lean mass has a strong positive influence on bone mass in the appendicular and axial skeletons (23–25). In contrast, we found that, after taking lean mass into account, measures of body fat had an inverse, or no, relation with parameters related to the structure and strength of bone. These findings are consistent with previous reports showing fat mass to be negatively associated with bone mass (8, 26) and those suggesting that bone strength is primarily determined by dynamic loads from muscle force, not static loads, such as fat mass (25). They, however, disagree with the contention for a beneficial effect of fat mass on bone and investigations, suggesting that fat mass is an even stronger predictor than lean mass of bone density (4, 7, 27).

Overall, analyses using fat mass revealed that the negative contribution of adipose tissue offset its potential benefit as a mechanical load. The basis for the negative effect of fat on bone observed in this study is unknown. However, adipose tissue, once considered a metabolically passive fuel depot for energy substrate and insulation, has recently become apparent as a metabolically active tissue. It secretes multiple proteins (collectively called adipokines) into circulation, which play important roles in the modulation of various biological functions. Further studies are needed to elucidate the role of adipokines and other adipose-modulated biochemical signals as potential mediators of bone structure.

Regardless of the mechanisms involved in the fat-bone association, a link between these tissues is suggested by recent studies demonstrating that osteoblasts and adipocytes originate from the same mesenchymal stem cells. These stem cells, through alternative activation of reciprocal transcriptional programs, differentiate into either cell lineage in a mutually exclusive way (28). In bone marrow, this could lead to a reciprocal relation between fat and bone, depending on the local milieu. The balance between osteoblast and adipocyte differentiation could be disrupted by environmental

TABLE 4. Multiple linear regressions showing the simultaneous effects of lean and fat mass after adjusting for leg length/truncal height on CT bone measurements in the appendicular and axial skeletons of 150 females and 150 males

	Females		Males	
	β	P	β	P
Vertebral CSA				
Trunk height	0.052	0.024	0.045	0.156
Fat mass	−0.008	0.497	−0.010	0.390
Lean mass	0.111	<0.0001	0.101	<0.0001
Vertebral CBD				
Trunk height	−0.250	0.724	−1.384	0.052
Fat mass	0.041	0.906	−0.730	0.006
Lean mass	1.502	0.005	1.306	0.001
Femoral CSA				
Leg length	0.017	0.018	0.018	0.147
Fat mass	−0.007	0.177	0.005	0.519
Lean mass	0.096	<0.0001	0.072	<0.0001
Femoral CBA				
Leg length	0.000	0.966	0.000	0.128
Fat mass	−0.007	0.093	−0.010	0.034
Lean mass	0.082	<0.0001	0.066	<0.0001

factors; decreased bone formation accompanied by increased adipogenesis occurs with immobility, whereas the opposite is associated with increased weight-bearing exercise (29).

The relatively large number of well-characterized subjects and the use of two techniques for the accurate and independent assessment of the contributions of lean and fat tissues on bone structure are major strengths of this study. Contrary to our notion that discrepancies among previous investigations were a reflection of the influence of soft tissues on DXA bone determinations, we found similar results regardless of the technique used. There are several limitations in this study, including its cross-sectional design and the inability to extrapolate our findings to other racial groups or elderly subjects. Future studies are needed to determine whether the deleterious effects of fat on vertebral and femoral bone in young healthy white subjects can be extended to other cohorts.

TABLE 5. Multiple linear regressions showing the simultaneous effects of lean and fat mass after adjusting for leg length/truncal height on DXA bone measurements in the appendicular and axial skeletons of 150 females and 150 males

	Females		Males	
	β	P	β	P
Vertebral BMC				
Trunk height	0.157	0.001	0.134	0.029
Fat mass	−0.042	0.060	−0.146	<0.0001
Lean mass	0.211	<0.0001	0.284	<0.0001
Vertebral BMD				
Trunk height	0.002	0.361	−0.002	.583
Fat mass	0.002	0.154	−0.003	0.005
Lean mass	0.008	<0.0001	0.011	<0.0001
Leg BMC				
Leg length	2.308	0.001	3.653	<0.0001
Fat mass	−0.947	0.063	−1.527	<0.010
Lean mass	9.706	<0.0001	8.803	<0.0001
Leg BMD				
Leg length	−0.001	0.286	0.000	.930
Fat mass	−0.003	0.001	−0.004	0.001
Lean mass	0.017	<0.0001	0.013	<0.0001

In conclusion, the pervasive negative health consequences of obesity involve many organ systems and medical subspecialties, as well as a large proportion of the population. However, despite the dire repercussions of obesity, the traditional paradigm suggests that adiposity is beneficial to the skeleton and could protect against osteoporosis. Our findings challenge this widely held view and provide compelling evidence that despite increased mechanical loading, adipose tissue is not beneficial to bone structure in young men and women.

Acknowledgments

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