Sex differences in the effect of body-composition variables on bone mass in healthy children and adolescents[1–3]

Asma Arabi, Hala Tamim, Mona Nabulsi, Joyce Maalouf, Hassan Khalifé, Mahmoud Choucair, Reinhold Vieth, and Ghada El-Hajj Fuleihan

ABSTRACT

Background: Prophylactic interventions against osteoporosis require a determination of the factors that influence the accumulation of bone mass during growth.

Objective: The objective was to determine the independent sex-specific contribution of lean mass and fat mass to bone mineral content (BMC), after adjustment for anthropometric variables and lifestyle factors, in healthy children and adolescents.

Design: Healthy schoolchildren (184 boys and 179 girls) aged 10–17 y ($\bar{x}\pm$ SD: 13.0 $\pm$ 2.1 y) participated in this cross-sectional study. Total and regional (lumbar spine, femoral neck, and distal one-third of the radius) BMC and body composition were measured by dual-energy X-ray absorptiometry.

Results: A significant effect of anthropometric variables and lifestyle factors on BMC was observed at all skeletal sites. Lean mass and fat mass showed robust correlations with BMC, even after adjustment for anthropometric variables and lifestyle factors. Lean mass contributed to 6–12% of the variance in BMC in boys and to 4–10% in girls. Fat mass accounted for 0.1–2% of BMC variance in boys and to 0.1–6.5% in girls.

Conclusions: Both lean mass and fat mass are consistent predictors of BMC at multiple skeletal sites in healthy children and adolescents. The contribution of lean mass to BMC variance was larger in boys than in girls. In both sexes, the highest contribution of lean mass to BMC was observed at the femoral neck. *Am J Clin Nutr* 2004; 80:1428–35.

KEY WORDS Adolescents, bone mineral content, osteoporosis, children, lean mass, fat mass, puberty

INTRODUCTION

Osteoporosis is a major health problem, and the pediatric origin of the disease has gained interest in recent years. It has been recognized that persons with a high peak bone mass are at lower risk of having osteoporotic fractures later in life (1). Thus, prophylactic interventions against osteoporosis require a determination of the factors that influence the accumulation of bone tissue during growth to optimize peak bone mineral accretion, which thereby decreases the prevalence of osteoporotic fractures later in life.

Studies of twins and families have shown that peak bone mass is largely inherited or influenced by genetic factors (2–4). Puberty has a powerful effect on areal bone mineral density (aBMD) and to a much lesser extent on volumetric BMD (5). Patients with abnormal pubertal development and men with delayed puberty have osteopenia (6). However, many environmental and lifestyle factors influence BMD and possibly affect one's genetically determined BMD (7). Nutrition, particularly dietary calcium intake in early life, affects mineral accretion (7–10). A positive correlation between sun exposure and bone density has been reported in prepubertal children (11). Other major determinants are body weight, physical activity, and, particularly, weight-bearing activity (7, 8, 11–13). Body-composition variables (ie, fat mass and lean mass) have been shown to be associated with BMD in adults. In children, both lean mass and fat mass were shown to be correlates of bone mineral content (BMC) and BMD (14–18), and it has been shown that triceps strength is a remarkably good predictor of bone density in men (19). These studies in adolescents were, however, limited by the relatively small sample size (14), the wide age range distribution of study subjects exceeding the critical pubertal period for areal BMD changes (15, 17), or the inclusion of girls only (15, 17, 18). Finally, studies evaluating bone mass in the pediatric age group have used aBMD, BMC, or both in their analyses (14–18). aBMD does not reflect true density, and it has been reported that beyond the small increment in true density that Gilsanz et al (5) clearly defined at the lumbar spine across puberty, little change in true density occurs during growth (20). Therefore, it has been suggested that BMC, rather than aBMD is a superior method for evaluating bone mass in the growing skeleton (21); however, opinions differ as to whether growth and size should be adjusted for (22).

The purpose of this study was to investigate the effect of sex, if any, on the relative contribution of body-composition variables to bone mass in children and adolescents, taking into account anthropometric and lifestyle factors.

[1] From the Calcium Metabolism and Osteoporosis Program, Department of Internal Medicine (AA, MC, JM, and GE-HF), the Faculty of Health Sciences, Department of Epidemiology and Population Health (HT), and the Department of Pediatrics (MN and HK), American University of Beirut, Lebanon; and Mt Sinai Hospital, University of Toronto (RV).

[2] Supported in large part by an educational grant from the Nestle Foundation and by a grant from Merck KGaA.

[3] Address reprint requests to GE-HF, Calcium Metabolism and Osteoporosis Program, American University of Beirut, Medical Center, Bliss Street, Beirut, Lebanon. E-mail: gf01@aub.edu.lb.

Received January 5, 2004.

Accepted for publication July 8, 2004.

SUBJECTS AND METHODS

Subjects

Three hundred sixty-three healthy schoolchildren (184 boys and 179 girls) between 10 and 17 y of age were enrolled in a randomized, double-blind, placebo-controlled trial to evaluate the efficacy of vitamin D supplementation on skeletal health. Baseline data detailed previously were used in the analyses of this study (23). Participants were recruited during the period extending between December 2001 and June 2002 from 4 schools in Beirut, Lebanon. Because children of high socioeconomic status do not attend public schools in this community, schools were selected on the basis of school fees in an attempt to have balanced representation from both socioeconomic status strata. We included students from 2 private schools with yearly school fees exceeding US$5000 and 2 public schools with yearly school fees of <US$700. A large proportion of the participants ($n = 196$) had one or more siblings participating in the study. All participants were of Caucasian Lebanese origin.

Subjects were included in the study after a careful physical examination performed by the study physicians (MN, HK, and MC); all subjects had a negative history for any disorders known to affect bone metabolism, including renal disease, liver disease, chronic diarrhea, and gastric or bowel surgery. Also excluded were children receiving a high dose of vitamins within 6 mo of the study, and those taking medications known to affect bone metabolism—such as antiepileptic drugs, rifampicin, cholestyramine, or chronic steroid therapy—were also excluded. At entry, the subjects' serum, calcium, phosphorus, and alkaline phosphatase concentrations were normal for age, and their mean (±SD) 25-hydroxyvitamin concentration was 15.3 ± 7.4 ng/mL. The study was approved by the Institutional Review Board of the American University of Beirut, and informed consent was obtained from all study participants and their parents.

Measurements

At entry, each child underwent a physical examination that included height, weight, pubertal stage assessment, and muscle strength. The subject's standing height was recorded in triplicate (in cm) to the nearest 0.1 cm with the use of a wall stadiometer, and the average value was used. Weight was recorded in kilograms to the nearest 0.5 kg, while the children were wearing light clothing and no shoes, with the use of a standard clinical balance. Mean height and weight were rounded to the nearest integer.

Pubertal status was determined by a physician (MN, HK, or MC) using breast and pubic hair stages in girls and testicular and pubic hair stages in boys, according to the established criteria of Tanner (24). Only the results based on breast and testicular size staging were reported. Exercise frequency, calcium intake, and sun exposure were assessed with the use of questionnaires. The dietary questionnaire used was derived from a more extensive and validated version that we developed in our unit, which showed that 80% of the calcium intake in this age group is from dairy products, as shown by others (25, 26). Therefore, in the current study, we focused on dairy products. The intakes of the following vitamins were also assessed: calcium pills, multivitamins, fluoride, and vitamin D. Physical activity was assessed within 6 mo of study entry and was expressed as the time spent each week in sport activities, as previously reported (12). The sports activities were basketball, baseball, soccer, tennis, bodybuilding, roller blading, dancing, walking, swimming, and biking (27). The children were asked to estimate the time that they were exposed (heads and arms uncovered) to the sun weekly. Veiled girls were considered to have no sun exposure.

Blood was drawn for the measurement of calcium, phosphorus, and alkaline phosphatase by using standard calorimetric methods with a Hitachi 912 analyzer (Boehringer Mannheim, Mannheim, Germany).

BMC (in g); aBMD (in g/cm^2) at the anteroposterior lumbar spine (L1-L4), the left femur (femoral neck), and the whole body; and body composition (ie, fat mass and lean mass) were measured in the supine position and the left distal one-third of the radius was measured in the sitting position by dual-energy X-ray absorptiometry (DXA) with a Hologic 4500A device (Hologic, Bedford, MA) in fast array scanning mode. To avoid differences in measurements related to the use of different software, the pediatric low-density software was applied to all analyses (27–29). In our center, the mean (±SD) precisions expressed as CV (CV%) for 122 serial duplicate scans performed in vivo within the year of the study were as follows: 0.87 ± 0.71% for spine aBMD, 0.82 ± 0.71% for total hip aBMD, 1.40 ± 1.09% for femoral neck aBMD, 1.10 ± 0.84% for trochanter aBMD, and 1.00 ± 0.77% for the distal one-third of the radius aBMD. For BMC, the corresponding values were as follows: 1.14 ± 1.05% for spine BMC, 1.48 ± 2.37% for total hip BMC, 2.00 ± 1.81% for femoral neck BMC, 2.97 ± 2.28% for trochanter BMC, and 1.29 ± 1.35% for the distal one-third of the radius BMC. These values fell within the range of values we and others reported previously (30–32).

Because the inclusion of head BMD in the calculation of total-body BMD may lower the predictive value of some measures for this variable, subtotal body measurements (head excluded) were used in the analyses (33).

Statistical analysis

General linear models were used to explore possible interactions between various predictors for the outcome variable BMC. These models showed interactions between sex and age for the distal one-third of the radius BMC ($P < 0.007$), between sex and height for the distal one-third of the radius BMC ($P = 0.01$), between sex and physical exercise for the femoral neck BMC ($P = 0.04$), between sex and lean mass for BMC at all skeletal sites ($P < 0.01$), between sex and fat mass for total-body BMC ($P = 0.02$), and between sex and Tanner stages at all skeletal sites ($P < 0.01$). Therefore, multivariate analyses were reported separately for boys and girls. Bivariate analyses were reported separately for boys and girls in the event of significant interactions between sex and other predictors on the outcome variables. In the event of no such interaction, the results were expressed for the combined data (data for boys and girls combined).

Bivariate analyses

Because the outcome variables were skewed, Spearman correlation coefficients were used to determine the strength of relations between BMC and the other continuous variables, such as age, height, sun exposure, calcium intake, hours of exercise per week, lean mass, and fat mass. A comparison of variables between groups was performed by using an independent two-tailed *t* test or a chi-square test. The effect of puberty on the outcomes

was assessed by using one-way analysis of variance or analysis of covariance.

Multivariate analyses

Multiple regression models were created by entering the BMC of the specific skeletal site as a dependent variable and the independent variables that were significant correlates of BMC at any skeletal site on bivariate analyses. The models were constructed on the basis of all enter selection procedure, where the independent variables were entered by sequential blocks, and the cumulative R^2 was determined after each block was added. These blocks were entered in the following order: anthropometric variables (age, pubertal stages, and height), lifestyle factors (sun exposure, exercise, and socioeconomic status), and body-composition variables (eg, lean and fat mass) entered as discrete blocks. Fat mass and lean mass were entered last in the models to investigate the strength of their association with BMC, after correction for all the known predictors (anthropometric and lifestyle measures) of bone mass in children. Because both lean mass and fat mass are components of body weight and because BMI is determined by body weight and height, body weight and BMI were not entered in the models to avoid colinearity. Because 201 children had 25 hydroxyvitamin D concentrations <15 ng/mL, and because the effect of hypovitaminosis D (vitamin D concentration between 10 and 20 ng/mL) on the skeleton is not clear, regression analyses were also performed separately in the subgroup of participants who had vitamin D concentrations >15 ng/mL.

All analyses were carried out by using SPSS software (version 11.0; SPSS Inc, Chicago). There were a total of 196 siblings among the participants. Thus, cluster analyses were performed by using STATA (version 7; Stata Corp, College Station, TX) to adjust for the lack of independence of BMC among siblings that was due to heredity and possible familial resemblance. Values were expressed as means ± SDs. P values < 0.05 were considered to be statistically significant.

RESULTS

Clinical characteristics

The clinical characteristics of the study group are shown in **Table 1**. The mean age of the study group was 13.1 ± 2.0 y. Representation by sex was balanced, and there was no significant difference in mean age between the boys and the girls. Fifty-three percent of the boys and 33% of the girls were in the early pubertal stages (I to II), whereas 46% of the boys and 66% of the girls were in more advanced pubertal stages (III to V); the difference in proportion between groups was significant ($P < 0.01$).

Boys had a significantly greater body weight, weekly sun exposure, and daily calcium intake and were more likely to exercise for a longer time than the girls. Lean mass was greater in the boys than in the girls, whereas fat mass was greater in the girls (Table 1).

Correlates of bone mineral content on bivariate analyses

Anthropometric variables

Age and height correlated with BMC at all skeletal sites; the correlation coefficients ranged from 0.61 to 0.90 depending on the predictor and the skeletal site (**Table 2**). In both sexes, there was a significant effect (by analysis of variance) of puberty on BMC at all skeletal sites (**Table 3**).

Lifestyle factors

In the whole study group, sun exposure and physical exercise correlated modestly with BMC at all sites ($r = 0.14–0.30$), depending on the predictor and skeletal site (Table 2). In the overall group, there was no correlation between calcium intake and BMC (Table 2). At all sites, children of high socioeconomic status had a greater BMC than did those of low socioeconomic status of the same sex (Table 3). This difference persisted at the total body and the femoral neck, even after adjustment for age and for Tanner stages.

Body composition

In both sexes, BMC showed robust correlations with lean mass and to a lesser degree with fat mass at all sites (Table 2). At all sites, the coefficients of correlation with lean mass were significantly greater in the boys than in the girls ($P < 0.01$), whereas the coefficients of correlation with fat mass were greater in the girls than in the boys at the lumbar spine ($P = 0.01$) and the femoral neck ($P = 0.01$). Within sex, the coefficients of correlation with lean mass were significantly greater than those with fat mass ($P < 0.0001$), except at the lumbar spine in girls.

Correlates of bone mineral content on multivariate analyses

In the linear regression analyses, the well-established predictors of bone mass in children—such as age, puberty, and height entered as a block—accounted for a large proportion of BMC variance in the boys (69–85%) and in the girls (63–80%) (**Table 4**). Lifestyle factors such as exercise, sun exposure, and socioeconomic status entered as a block accounted for an additional 0.2–3.2% of BMC variance in boys and for 0.3–0.5% of BMC variance in girls (Table 4). Lean mass was a significant correlate of BMC in both sexes at all skeletal sites. The contribution of lean mass to BMC variance was greater in the boys (5.7–12.3%) than in the girls (4.3–10.5%). In both sexes, the highest contribution of lean mass to BMC was observed at the femoral neck. Fat mass was a significant correlate for BMC at the lumbar spine, for total-body BMC in both sexes, and for femoral neck BMC in the girls. After adjustment for other predictors, it accounted for up to 1.9% of BMC variance in the boys and for up to 6.5% of BMC variance in the girls (Table 4). In both sexes, the β estimates for lean mass were several times those for fat mass at all sites in the boys and at the lumbar spine, distal one-third of the radius, and femoral neck in the girls (Table 4).

When BMD was used in the regression models, similar results were obtained, but with a lesser contribution of the correlates to BMD than of BMC variance ($R^2 = 0.76$ at the spine in both sexes, $R^2 = 0.58$ at the femoral neck in both sexes, $R^2 = 0.65$ in the boys and 0.67 in the girls at the distal one-third of the radius). The contribution of lean mass to BMD variance was greater in the boys (5.6–9.5%) than in the girls (1.5–7.9%). In contrast, fat mass accounted for up to 1.1% of the BMD variance in the boys and up to 6.5% of the BMD variance in the girls.

Subgroup analyses of 162 patients with 25-hydroxyvitamin D concentrations >15 ng/mL showed results similar to those obtained in the whole group. Lean mass contributed to 7.6–13% of BMC variance in the boys and to 2.5–5.7% of BMC variance in

TABLE 1
Clinical characteristics of the study participants[1]

Variable	Boys (n = 184)	Girls (n = 179)	P[2]
Anthropometric measures			
Age (y)	13.0 ± 1.9[3]	13.2 ± 2.1	0.239
Height (cm)	155 ± 13	153 ± 10	0.051
Weight (kg)	52 ± 16	48 ± 12	0.008
BMI (kg/m^2)	21.0 ± 4.1	20.2 ± 3.5	0.048
Menarche (yes/no)	NA	116/63	—
Tanner stage (n)			
I	48	22	0.01
II	49	38	0.01
III	33	52	0.01
IV	34	61	0.01
V	20	6	0.01
Lifestyle factors			
Socioeconomic status (high/low)[4]	62/122	86/93	0.006
Exercise (yes/no)	148/26	105/65	<0.001
Exercise (h/wk)	7.9 ± 6.9	3.7 ± 4.8	0.003
Calcium intake (mg/d)	766 ± 351	679 ± 366	0.021
Sun exposure (min/wk)	547 ± 328	442 ± 332	0.003
Body composition[5]			
Subtotal lean mass (g)	33 027 ± 10547	27 330 ± 5733	<0.001
Subtotal fat mass (g)	12 927 ± 8275	15 309 ± 7499	0.004
Bone mass and scanned area			
Lumbar spine BMC (g)	37.4 ± 13.7	40.5 ± 12.3	0.026
Lumbar spine BMD (g/cm^2)	0.66 ± 0.12	0.73 ± 0.14	<0.001
Lumbar spine area (cm^2)	55.2 ± 9.9	54.2 ± 8.0	0.282
Total-body BMC (g)	1458 ± 469	1384 ± 349	0.095
Total-body BMD (g/cm^2)	0.84 ± 0.11	0.83 ± 0.09	0.125
Total-body area (cm^2)	1900 ± 347	1859 ± 287	0.276
Distal one-third of BMC (g)	1.4 ± 0.3	1.3 ± 0.2	0.008
Distal one-third of BMD (g/cm^2)	0.56 ± 0.07	0.57 ± 0.06	0.271
Distal one-third of area (cm^2)	2.5 ± 0.3	2.3 ± 0.2	<0.001
Femoral neck BMC (g)	3.8 ± 0.9	3.3 ± 0.6	0.001
Femoral neck BMD (g/cm^2)	0.78 ± 0.13	0.72 ± 0.11	<0.001
Femoral neck area (cm^2)	4.8 ± 0.5	4.5 ± 0.5	<0.001

[1] BMC, bone mineral content; BMD, bone mineral density; NA, not applicable.
[2] Student's t test or chi-square test.
[3] $\bar{x}$ ± SD (all such values).
[4] High socioeconomic status: yearly school fees of ≥ US$5000; low socioeconomic status: yearly school fees of ≤ US$7000.
[5] After exclusion of the head from the analyses.

the girls, whereas fat mass contributed up to 2.5% of BMC variance in the boys and up to 2.8% in the girls. Results of the regression analyses were similar when cluster analyses were done.

DISCUSSION

In this cross-sectional study, both lean mass and fat mass were consistent independent predictors of total and regional areal bone mass in both sexes, even after adjustment for the well-known predictors of BMC in healthy children and adolescents. The effect of lean mass was stronger in the boys, whereas the effect of fat mass was relatively more important in the girls. The effect of lean mass was more substantial than was the effect of fat mass at both the trabecular and cortical sites.

It is well recognized that a greater body weight is associated with a greater BMD. Studies in postmenopausal women related this effect on bone density to lean mass (34, 35), fat mass (36), or both (37). Few studies assessed the contribution of fat mass and lean mass to total-body BMC (14, 15, 17, 18, 38), total-body BMD (16), and regional BMD (15, 17) in children and young adults, and most of these studies were conducted in girls. Whereas the effect of lean mass was consistent across studies (14–18), the effect of fat mass was more variable (16, 38). In the current study, both lean mass and fat mass were significant independent predictors of total body, as well as of regional BMC, even after adjustment for anthropometric and lifestyle factors. Similarly to what was previously reported (14, 15), the effect of lean mass was larger than that of fat mass. The β estimates for the effect of lean mass on BMC at different skeletal sites were up to 20-fold those for the corresponding β estimates for fat mass. The proportional contribution of lean mass to bone mass variance was larger in the boys than in the girls at all skeletal sites. This effect of lean mass may be direct and due to the mechanical loading of the muscle mass and to muscle strength. Muscle strength has been shown to predict bone mass in men (19). Recently, Schoenau and Frost (39) suggested that bone and muscle form a functional "bone-muscle unit" in which changes in momentary muscle strength should and usually do affect bone

TABLE 2
Spearman's correlation coefficients between bone mineral content (BMC) and anthropometric variables (age and height), lifestyle factors (calcium intake, sun exposure, and physical exercise), and body-composition variables (lean mass and fat mass)

	L1-L4 BMC			Total-body BMC			Distal one-third of radius BMC			Femoral neck BMC		
	Boys[1]	Girls[1]	All[2]	Boys[1]	Girls[1]	All[2]	Boys[1]	Girls[1]	All[2]	Boys[1]	Girls[1]	All[2]
Age	—	—	0.78[3]	—	—	0.75[3]	0.79[4]	0.74[4]	—	—	—	0.61[3]
Height	—	—	0.80[3]	—	—	0.90[3]	0.82[4]	0.74[4]	—	—	—	0.78[3]
Calcium intake	—	—	−0.025	—	—	0.057	—	—	0.05	—	—	0.08
Sun exposure	—	—	0.27[3]	—	—	0.30[3]	—	—	0.27[3]	—	—	0.30[3]
Exercise	—	—	0.14[4]	—	—	0.23[3]	—	—	0.24[3]	0.24[3]	0.19[4]	—
Lean mass	0.79[4]	0.62[4]	—	0.96[4]	0.78[4]	—	0.87[4]	0.75[4]	—	0.89[4]	0.82[4]	—
Fat mass	—	—	0.36[3]	0.49[4]	0.56[3]	—	—	—	0.35[3]	—	—	0.41[3]

[1] Missing data indicate sex-specific correlation coefficients that were not reported because no interactions on the outcome were observed between sex and the corresponding predictor.
[2] Missing data indicate correlation coefficients that were not reported because significant interactions between sex and the corresponding predictor on the outcome were observed.
[3] $P < 0.01$.
[4] $P = 0.01$.

strength predictably and correspondingly. Seeman et al (40) suggested that the association between greater muscle mass and greater BMD is likely to be genetically determined by common genes regulating size. Bone size and lean mass are greater in boys than in girls, which partially explains why boys have a greater BMC at the weight-bearing site (the femoral neck) than do girls.

Young et al (17) investigated these relations in a longitudinal study and showed that during pubertal development in twin girls, and up to 4 y postmenarche, annual changes in BMD at the spine, total hip, and femoral neck increased with annual changes in lean mass, independently of changes in fat mass or height during linear growth. In contrast, a change in fat mass was the predominant predictor during postlinear growth. In the current study, the effect of fat mass was more important in the girls than in the boys at the lumbar spine, the femoral neck, and the total body. This may be explained by the fact that most of the girls in the study were postmenarcheal (65%). The effect of fat mass may be partly mediated by fat-related bone active hormones such as leptin (41) and by estrogen production through aromatization in fat tissue. Estrogens play a more important role than do androgens in bone maturation, as was previously shown by the increased BMD after estrogen therapy in males with an aromatase deficiency (42). In the current study, the effect of fat mass in boys was more pronounced at a trabecular site, the spine.

This study confirmed the well-recognized contribution of anthropometric variables such as age, pubertal stage, and body size (height) on BMC and aBMD in children and adolescents (43–45). After adjustment for other covariates, both age and pubertal development remained significant predictors of BMC at all sites. During puberty, both androgens and estrogens stimulate calcium absorption and retention and result in a net positive flow of calcium into bone, which contributes to bone accumulation (46). Lifestyle factors such as exercise, dietary calcium intake, and sun exposure are well-known correlates of bone mass in children and adolescents, although with weaker contributions (11, 12, 47–49).

In the current study, after adjustment for confounders, exercise remained a significant predictor of femoral neck BMC in the boys only. Boys exercise more than do girls, which partially explains the greater BMC at the femoral neck. Children of a high

TABLE 3
Bone mineral content (BMC) by sex, Tanner stage, and socioeconomic status (SES)[1]

	L1-L4 BMC			Total-body BMC			Distal one-third of radius BMC			Femoral neck BMC		
	Boys	Girls	All[2]	Boys	Girls	All[2]	Boys	Girls	All[2]	Boys	Girls	All[2]
Tanner stage		*g*			*g*			*g*			*g*	
I (n = 48 boys, 22 girls)	27.9 ± 8.1	24.1 ± 4.6	—	1156 ± 295	926 ± 226	—	1.2 ± 0.1	1.0 ± 0.1	—	3.2 ± 0.6	2.3 ± 0.5	—
II (n = 49 boys, 38 girls)	30.1 ± 4.8	30.9 ± 6.0	—	1179 ± 272	1161 ± 226	—	1.2 ± 0.1	1.1 ± 0.2	—	3.3 ± 0.4	2.9 ± 0.4	—
III (n = 33 boys, 52 girls)	35.6 ± 6.1	42.0 ± 8.8	—	1406 ± 258	1403 ± 255	—	1.3 ± 0.2	1.3 ± 0.2	—	3.7 ± 0.5	3.3 ± 0.5	—
IV (n = 34 boys, 61 girls)	51.9 ± 11.1	49.8 ± 8.2	—	1956 ± 347	1642 ± 260	—	1.7 ± 0.2	1.5 ± 0.1	—	4.7 ± 0.9	3.7 ± 0.5	—
V (n = 20 boys, 6 girls)	60.4 ± 8.6	56.9 ± 9.5	—	2157 ± 135	1686 ± 206	—	1.9 ± 0.1	1.6 ± 0.2	—	5.1 ± 0.3	3.9 ± 0.4	—
P[3]	< 0.001	< 0.001		< 0.001	< 0.001		< 0.001	<0.001		<0.001	< 0.001	
SES												
Low (n = 122 boys, 93 girls)	5.2 ± 11.9	36.6 ± 10.9	35.8 ± 1.5	1361 ± 439	1258 ± 327	1310 ± 386	1.3 ± 0.3	1.2 ± 0.2	1.3 ± 0.3	3.6 ± 0.8	3.0 ± 0.6	3.4 ± 0.8
High (n = 62 boys, 186 girls)	41.5 ± 15.9	44.5 ± 12.3	43.3 ± 13.9	1648 ± 471	1520 ± 321	1557 ± 397	1.5 ± 0.3	1.4 ± 0.2	1.4 ± 0.3	4.1 ± 1.0	3.5 ± 0.6	3.7 ± 0.8
P[4]	—	—	<0.001	—	—	<0.001	—	—	<0.001	—	—	<0.001

[1] All values are $\bar{x}$ ± SD.
[2] Missing data indicate that significant interactions ($P < 0.01$) between sex and Tanner stage were observed at all skeletal sites.
[3] Values indicate the difference between Tanner stages within each sex (ANOVA).
[4] Values indicate the difference between SES groups (t test). In columns where no P value is given, no significant interactions between sex and SES group were observed.

TABLE 4
Linear regression models with bone mineral content (BMC) as the outcome and anthropometric measures, lifestyle factors, and body-composition variables as the predictors entered as sequential blocks[1]

	Lumbar spine BMC		Total-body BMC		Distal one third of radius BMC		Femoral neck BMC	
	Boys (n = 179)	Girls (n = 184)	Boys (n = 179)	Girls (n = 184)	Boys (n = 179)	Girls (n = 184)	Boys (n = 179)	Girls (n = 184)
Block 1: anthropometric measures								
Age (y)	1.05 (0.4)[2]	1.5 (0.3)	17 (8.7)	18.4 (6.6)	0.05 (0.01)	0.03 (0.01)	0.07 (0.03)	−0.01 (0.02)
P	0.009	0.01	0.04	0.006	0.01	0.003	0.8	0.5
Height (cm)	−0.02 (0.08)	0.17 (0.08)	5.5 (1.7)	12.2 (1.5)	−0.002 (0.002)	0.01 (0.003)	−0.005 (0.006)	0.004 (0.006)
P	0.8	0.04	0.002	0.001	0.2	0.5	0.3	0.4
Tanner stages	0.6 (0.6)	2.5 (0.6)	−4.7 (13.2)	30.5 (12.1)	−0.01 (0.010	0.04 (0.01)	−0.03 (0.04)	0.1 (0.04)
P	0.3	0.01	0.7	0.013	0.3	0.02	0.4	0.001
R^2	0.771	0.794	0.847	0.797	0.730	0.627	0.686	0.628
Block 2: lifestyle factors								
SES	2.4 (1.0)	−0.05 (0.9)	71 (22.6)	41.8 (18.6)	0.05 (0.02)	0.04 (0.03)	0.1 (0.07)	0.1 (0.06)
P	0.01	0.9	0.002	0.026	0.06	0.1	0.1	0.02
Exercise	−0.09 (0.06)	0.16 (0.08)	1.3 (1.4)	0.3 (1.8)	0.0006 (0.002)	0.01 (0.003)	0.09 (0.005)	0.007 (0.006)
P	0.1	0.06	0.3	0.8	0.7	0.5	0.006	0.2
Sun exposure[3]	0.0004 (0.001)	−0.0009 (0.001)	−0.01 (0.03)	0.004 (0.028)	-3×10^{-5} (0.01)	-4×10^{-5} (0.01)	4×10^{-5} (0.01)	-6×10^{-5} (0.01)
P	0.7	0.5	0.7	0.8	0.4	0.3	0.6	0.5
ΔR^2	0.002	0.005	0.032	0.004	0.004	0.003	0.014	0.005
Block 3: lean mass								
Lean mass (kg)[3]	0.01 (0.01)	0.0008 (0.01)	20 (0.003)	10 (0.002)	3×10^{-5} (0.01)	2×10^{-5} (0.01)	8×10^{-5} (0.01)	7×10^{-5} (0.01)
P	0.01	0.01	0.001	0.001	0.01	0.01	0.01	0.01
ΔR^2	0.057	0.043	0.073	0.047	0.076	0.05	0.123	0.105
Block 4: fat mass								
Fat mass (kg)[3,4]	−0.0003 (0.01)	0.0001 (0.01)	7 (0.001)	10 (0.001)	2×10^{-6} (0.01)	1×10^{-6} (0.01)	4×10^{-6} (0.01)	1×10^{-5} (0.01)
P	0.01	0.009	0.001	0.001	0.1	0.5	0.3	0.01
ΔR^2	0.019	0.03	0.011	0.065	0.002	0.001	0.001	0.01
R^2	0.848	0.872	0.963	0.913	0.812	0.680	0.824	0.748

[1] References for discrete variables were as follows: Tanner stage = Tanner I; socioeconomic status (SES) = low SES. There were significant interactions between sex and age on the distal one-third of the radius BMC, between sex and height on the distal one-third of the radius BMC, between sex and physical exercise on the femoral neck BMC, between sex and lean mass on BMC at all skeletal sites, between sex and fat mass at the total-body BMC, and between sex and Tanner stages at all skeletal sites ($P < 0.05$).

[2] β; SE in parentheses (all such values). Values were adjusted for all predictors entered in the models.

[3] For ΔR^2, changes after adding blocks sequentially.

[4] R^2 represents cumulative values.

socioeconomic background, another correlate of lifestyle factors, had a greater BMC than did those of a low socioeconomic background, and this effect remained significant after adjustment for other confounders at many skeletal sites in both sexes. One study in adults noted that osteoporosis might be a disease of males of high socioeconomic status because of their low activity level (50). This situation may very well be different in children because it is plausible that children of a high socioeconomic status may be more involved in sports activities, may have a greater daily intake of calcium, and may have been exposed to a better nutritional environment in utero and in early life compared with children of a low socioeconomic status (51).

A limitation of this study is that bone age, an important predictor of skeletal maturity and bone mass, was not assessed. In children, the increments in BMC are in large part influenced by growth and size. They are also influenced by the amount of soft tissues surrounding bone, another variable that significantly changes with growth. Although the use of computerized tomography to measure bone mass would circumvent these problems, DXA remains the best technique used to assess bone mass in children because of the short scan time and low radiation dose required. Although it has been suggested that the use of DXA-derived BMC, without any size correction, is a superior approach for evaluating bone mass (21, 52), this notion is controversial (22) and was not the usual procedure used in the pediatric studies published to date (14–18, 38). In our study, BMC was used as the primary outcome measure to express bone mass in the growing skeleton and is the most appropriate variable for correlating lean mass and fat mass. Indeed, and as anticipated, body-composition variables contributed more to BMC variance than to aBMD variance.

Most of previous studies that evaluated the effect of body composition on bone mass in children were limited by a lack of control for all well-known predictors of bone density concomitantly (14–16, 38), a small sample size (14), a wide age range exceeding the critical pubertal period for bone accumulation (15, 17), the use of regional (15, 17) or total-body aBMD (16) in the multivariate analyses, and the inclusion of girls only (15, 17, 18). This cross-sectional study confirmed the powerful independent effect of both lean mass and fat mass on BMC, as previously reported in one longitudinal study (17). Discrepancies in the effect of fat mass on BMC between our study results and those of previous studies (16, 38) may be explained by a variety of factors. These include the fact that some studies did not take into account the pubertal stages or lifestyle factors and the different techniques for analyzing the data, such as the inclusion of weight and BMI in the stepwise models. The strengths of the current study were its large sample size, its evaluation of multiple skeletal sites, its inclusion of both sexes, the type of model used, and the adjustment for several important correlates of bone mass.

In conclusion, this study provided strong evidence that both lean mass and fat mass were consistent and independent predictors of BMC in healthy children and adolescents. The relative effect of lean mass was stronger in boys than in girls, whereas the effect of fat mass was stronger in girls, possibly because of their postmenarcheal stage. Our findings have important implications in the development of public health strategies and in the alteration of diet and exercise lifestyles to optimize body composition, and therefore in bone mass, for children and adolescents.

We thank the administrators, school nurses, parents, and students from the American Community School, the International College, Amlieh School, and the Ashbal Al Sahel School for their support in making the study possible. We also thank S Mroueh for her expert technical assistance in the acquisition and analyses of the BMD scans.

AA helped analyze the data and write the manuscript. HT helped analyze the data. JM, MC, and HK helped collect the data. MN helped collect and analyze the data. RV helped design the experiment, provided significant advice, and reviewed the manuscript. GE-HF helped design the experiment, analyze the data, and write the manuscript and provided significant advice. None of the authors had a conflict of interest.

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