The Role of Overweight and Obesity on Bone Health in Korean Adolescents with a Focus on Lean and Fat Mass

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As the associations between pediatric overweight/obesity and bone health remain controversial, we investigated the effects of overweight/obesity as well as lean mass (LM) and fat mass (FM) on bone parameters in adolescents. Bone parameters were evaluated using dual-energy X-ray absorptiometry (DXA) data of 982 adolescents (aged 12–19 years) from the Korea National Health and Nutrition Examination Survey (2009–2010). Z-scores for LM, FM, bone mass, bone mineral density (BMD), and bone mineral apparent density (BMAD) using Korean pediatric reference values were used for analysis. Adolescents with overweight/obesity had significantly higher bone mass and density of the total-body-less-head (TBLH), lumbar spine, and femur neck than underweight or normal-weight adolescents ($P < 0.001$) after adjusting for vitamin D deficiency, calcium intake, and insulin resistance in both sexes. LM was positively associated with bone parameters at all skeletal sites in both sexes ($P < 0.001$). FM was negatively related to TBLH BMD in boys ($P = 0.018$) but was positively associated to BMD and BMAD of the lumbar spine and femur neck in girls. In conclusion, overweight/obesity and LM play a positive role in bone health in adolescents. The effect of FM on bone parameters is sex- and site-specific.

Keywords: Pediatric Obesity; Body Composition; Bone Density; Adolescent; Korea

INTRODUCTION

Overweight/obesity in adolescents is being recognized as an important health issue as its prevalence has been increasing worldwide. In Korea, the proportions of adolescents with overweight/obesity increased from 12.2% in 2011 to 17.3% in 2016 according to 12th Korean Youth Risk Behavior Web-based Survey in 2016 (1). As lifelong bone health, including future fracture risk, depends on pediatric bone mass acquisition (2), the effect of childhood overweight/obesity on bone health has been of interest.

It remains controversial whether overweight/obesity during childhood is beneficial or harmful for the acquirement of bone mass (3-5). Individuals with similar body mass index (BMI) were shown to have differences in bone density depending on their proportions of fat mass (FM) and lean mass (LM) (6). While the beneficial effect of LM on bone health is well understood, it remains unclear whether FM has a beneficial or harmful effect on bone mass and density; moreover, different results have been reported according to sex (7). Despite a higher body mass, adolescents with overweight/obesity have several risk factors for low bone density such as insufficient calcium intake, sedentary lifestyle, vitamin D deficiency, and insulin resistance (8,9).

Due to the significant differences in body and bone sizes within and across different ages, adjustment using the height Z-score or estimation of volumetric bone mineral density (BMD) is recommended when interpreting bone mass in the growing child (10). The recommended scanning sites in pediatric dual-energy X-ray absorptiometry (DXA) examination are the total-body-less-head (TBLH) and lumbar spine (10). Lower bone mass of the femur neck, as measured by DXA, is also associated with fracture risk in children (11). Recently, age- and sex-specific DXA reference values for bone mineral measures, including volumetric BMD and body composition, were reported for the Korean pediatric population (12). Therefore, Z-scores of bone mass and areal and volumetric BMD of the TBLH, lumbar spine, and femur neck can now be evaluated in Korean adolescents. In this study, we investigated the effects of overweight/obesity on bone mass and density of the TBLH, lumbar spine, and femur neck after adjusting for potential confounders. Moreover, the associations between FM and LM and bone mass and density were evaluated according to sex.

MATERIALS AND METHODS

Study populations

The present study is based on data from the third year (2009) of the Korea National Health and Nutrition Examination Survey

(KNHANES) IV and the first year (2010) of the KNHANES V with permission of the Korea Centers for Disease Control and Prevention. The KNHANES is a cross-sectional national survey with a stratified, multistage, clustered probability sampling design and includes a health interview survey, nutrition survey, and health examination. Among 264,186 primary sampling units (based on the 2005 National Census Registry), 200 and 192 sampling units were randomly selected, sampling of 23 and 20 households from each of the units; this yielded 4,600 and 3,840 households in 2009 and 2010, respectively. In 2009, 12,722 individuals were sampled, with 10,078 participating in health interviews and examinations and 9,397 participating in the nutrition survey. In 2010, 10,938 individuals were sampled with 8,473 participating in the health interviews and examinations and 8,027 participating in the nutrition survey.

Among the 1,998 study participants aged 12–19 years, 1,303 underwent DXA. We excluded participants with missing fasting measures and/or those who failed to fast for > 8 hours (n = 166), those who had a history of diabetes (n = 1), and those with missing values for daily calcium intake (n = 153) and/or blood pressure (n = 1). No participants had fasting glucose levels ≥ 126 mg/dL. In total, 982 participants (508 boys) were included in the final sample (Fig. 1).

Measurements

Anthropometric, bone mass, and body composition data were collected with the subjects wearing light clothes without shoes or jewelry. Height and weight were measured using standard methods, and BMI was calculated as weight divided by height squared. The Z-scores for height, weight, and BMI were assigned on the basis of the 2007 Korean National Growth Charts (13). We defined underweight (< 15th BMI percentile), normal-weight (15–85th BMI percentile), overweight (85–95th BMI percentile), and obesity (> 95th BMI percentile) according to BMI percentiles (14). Vitamin D deficiency was defined as a 25-hydroxyvitamin D level of < 20 ng/mL (15). Self-reported questionnaires

were used to assess the dietary intake of calcium using a single 24-hour dietary recall method. Dietary and supplemental calcium intakes were compared with the dietary recommended intake (DRI) for Korean children and adolescents: 1,000 mg/day for boys and 900 mg/day for girls aged 12–14 years, 900 mg/day for boys and 800 mg/day for girls aged 15–18 years, and 750 mg/day for boys and 650 mg/day for girls aged 19–29 years (16). Calcium intake levels were categorized as sufficient (≥ DRI) or insufficient (< DRI). The participants were asked about the amount and intensity of physical activity during a normal week. The definition of regular physical activity was based on the guideline provided by the U.S. Department of Health and Human Services as moderate- or vigorous-intensity physical activity for at least 60 minutes/day on 7 days/week (17).

Biochemical measurements

Blood samples were obtained by venipuncture, refrigerated immediately, and transported to the central testing institute. Fasting plasma glucose and serum lipids (total cholesterol, high-density lipoprotein cholesterol, and triglycerides) were measured enzymatically with the Hitachi automated analyzer 7600 (Hitachi, Tokyo, Japan), and fasting plasma insulin was determined using a 1470 WIZARD gamma-Counter (Perkin-Elmer, Turku, Finland) and an immunoradiometric assay (Biosource, Fleurus, Belgium). The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as a marker of insulin resistance, as follows:

$$\text{HOMA-IR} = \text{fasting plasma glucose (mg/dL)} \times \text{fasting plasma insulin (μU/mL)}/405$$

The 25-hydroxyvitamin D concentration was measured by radioimmunoassay using a 1470 WIZARD gamma-Counter (Perkin-Elmer) and a 25-hydroxyvitamin D ^{125}I radioimmunoassay kit (DiaSorin, Stillwater, MN, USA). At serum 25-hydroxyvitamin D levels of 8.6, 22.8, 33.1, and 49.1 ng/mL, the inter-assay coefficients of variation (CV) were 11.7%, 10.5%, 8.6%, and 12.5%, respectively, and the intra-assay CVs were 9.4%, 8.2%, 9.1%, and 11.0%, respectively.

Bone mass and body composition measurements

Bone mineral content (BMC) (g) and BMD (g/cm^2) of the TBLH, lumbar spine (L1–L4), and femur neck as well as FM and LM were measured by DXA using the QDR 4500A (Hologic Inc., Waltham, MA, USA) at mobile examination centers operated by licensed trained technicians following a standard protocol. Body and bone size were adjusted using the height Z-score for TBLH or estimation of volumetric BMD for lumbar spine and femur neck (10). TBLH bone mass and density were adjusted using the height Z-score. For the lumbar spine and femur neck, bone mineral apparent density (BMAD) (g/cm^3) was used as an estimate of volumetric BMD and calculated as follows (18):
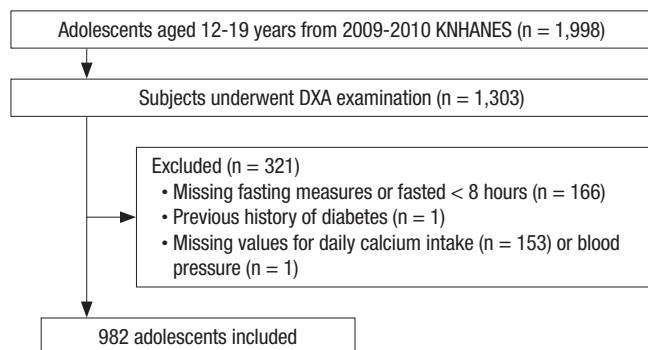

Fig. 1. Flowchart of the study population.
KNHANES = Korea National Health and Nutrition Examination Survey, DXA = dual-energy X-ray absorptiometry.

Lumbar spine BMAD = lumbar spine BMC/(lumbar spine bone area)$^{1.5}$

Femur neck BMAD = femur neck BMC/(femur neck bone area)^2

Finally, we calculated Z-scores (z) of body composition and bone density using the reference values for Korean children and adolescents (12): zFM, zLM, zBMC, zBMD, and zBMAD.

Statistical analysis

All analyses were performed using sampling weights to report estimates representative of the Korean population. The statistical software package SPSS version 19.0 (SPSS Inc., Chicago, IL, USA) was used to accommodate the complex sampling design with stratification, clustering, and unequal weighting of the KN-HANES sample. A P value < 0.05 was considered significant. All continuous variables are expressed as weighted means with standard errors and categorical variables as numbers and weighted percentages of the participants. Logarithmic conversions were performed for HOMA-IR, daily calcium intake (mg/day), and physical activity (hours/week) to approximate a normal distribution, as these variables were not normally distributed. All analyses were performed in male and female adolescents separately.

The Rao-Scott χ^2 test was used to analyze the associations between categorical variables and categorical BMI groups. We also conducted tests for linear trends (P for linear trend) across the BMI groups. Subgroup analyses were then used to analyze mean differences between groups. Univariate linear regression analyses were used to analyze the associations between baseline characteristics and TBLH, lumbar spine, and femur neck bone parameters. Finally, multivariate linear regression analy-

ses were performed to assess the associations between each categorical group and bone mass or density parameters after adjusting for possible confounders, including age, vitamin D deficiency, calcium intake, physical activity, and HOMA-IR in addition to BMI group or zLM and zFM.

Ethics statement

All study protocols were approved by the Institutional Review Board of the KCDC (Approval No. 2009-01CON-03-2C, 2010-02CON-21-C). All participants volunteered and provided written informed consent prior to participating.

RESULTS

Participant characteristics

Among the 982 adolescents (508 boys) aged 12–19 years (15.6 ± 0.1 years), 146 (14.9%) were underweight, 627 (63.8%) normal-weight, and 209 (21.3%) overweight/obesity. Male participants were taller and had a higher proportion of subjects with sufficient calcium intake and regular physical activity when compared to female participants (P < 0.001 for all). No differences between boys and girls were found in the Z-scores of FM, LM, and bone mass and density of the TBLH, lumbar spine, and femur neck (Table 1).

Table 2 shows the participant characteristics according to BMI groups (underweight, normal-weight, and overweight/obesity groups) for both sexes. HOMA-IR showed a progressive increase from the underweight to normal-weight and overweight/obesity groups for both sexes (P < 0.001 for both).

For both sexes, the overweight/obesity group had significant-

Table 1. Characteristics of participants according to sex

Variables	Total	Male	Female	P
No. of participants	982	508	474	-
Age, yr	15.6 ± 0.1	15.5 ± 0.1	15.7 ± 0.1	0.249
Height Z-score	0.2 ± 0.1	0.7 ± 0.1	0.3 ± 0.1	< 0.001
BMI Z-score	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.825
HOMA-IR	2.8 ± 0.1	2.8 ± 0.1	2.7 ± 0.1	0.451
Vitamin D deficiency	758 (77.9)	380 (76.1)	378 (79.9)	0.217
Sufficient calcium intake	102 (10.4)	68 (14.3)	34 (6.0)	< 0.001
Regular physical activity	123 (11.7)	92 (17.0)	31 (5.8)	< 0.001
FM Z-score, g	0.16 ± 0.05	0.10 ± 0.07	0.23 ± 0.08	0.204
LM Z-score, g	0.19 ± 0.06	0.17 ± 0.07	0.21 ± 0.07	0.635
Total body less head BMC Z-score, g	0.11 ± 0.06	0.17 ± 0.07	0.13 ± 0.08	0.602
Lumbar spine BMC Z-score, g	0.11 ± 0.06	0.14 ± 0.07	0.08 ± 0.07	0.431
Femur neck BMC Z-score, g	0.09 ± 0.05	0.09 ± 0.06	0.10 ± 0.07	0.879
Total body less head BMD Z-score, g/cm^2	−0.05 ± 0.07	0.03 ± 0.07	−0.04 ± 0.08	0.365
Lumbar spine BMD Z-score, g/cm^2	0.03 ± 0.05	0.07 ± 0.06	−0.02 ± 0.07	0.191
Femur neck BMD Z-score, g/cm^2	0.06 ± 0.04	0.04 ± 0.05	0.08 ± 0.06	0.604
Lumbar spine BMAD Z-score, g/cm^3	−0.03 ± 0.05	0.01 ± 0.05	−0.07 ± 0.07	0.255
Femur neck BMAD Z-score, g/cm^3	0.00 ± 0.04	−0.03 ± 0.05	0.04 ± 0.06	0.361

Data are expressed as the mean ± standard error or number (%).
BMI = body mass index, HOMA-IR = homeostasis model assessment-insulin resistance, FM = fat mass, LM = lean mass, BMC = bone mineral content, BMD = bone mineral density, BMAD = bone mineral apparent density.

ly higher zFM and zLM than the underweight and normal-weight groups ($P < 0.001$ for all) (Figs. 2 and 3). Moreover, the zBMC and zBMD of the TBLH, lumbar spine, and femur neck and zB-

MAD of the lumbar spine and femur neck were significantly higher in adolescents with overweight/obesity when compared to underweight and normal-weight adolescents for both sexes

Table 2. Characteristics according to the BMI groups (underweight, normal-weight, and overweight/obesity)

Variables	Male (n = 508)				Female (n = 474)			
	Underweight	Normal-weight	Overweight/ obesity	P for trend	Underweight	Normal-weight	Overweight/ obesity	P for trend
No. of participants	77	323	108	-	69	304	101	-
Age, yr	15.8 ± 0.3	15.5 ± 0.2	15.5 ± 0.3	0.685	16.4 ± 0.3*	15.6 ± 0.2	15.6 ± 0.3‡	0.041
Height Z-score	0.4 ± 0.1	0.7 ± 0.1†	1.0 ± 0.1‡	0.001	0.3 ± 0.2	0.3 ± 0.1	0.4 ± 0.1	0.962
BMI Z-score	−1.6 ± 0.1*	0.0 ± 0.0†	1.5 ± 0.0‡	< 0.001	−1.6 ± 0.1*	−0.1 ± 0.0†	1.7 ± 0.1‡	< 0.001
HOMA-IR	2.1 ± 0.1*	2.6 ± 0.1†	4.2 ± 0.2‡	< 0.001	2.2 ± 0.1*	2.6 ± 0.1†	3.5 ± 0.2‡	< 0.001
25-hydroxyvitamin D, ng/mL	6.8 ± 0.3	6.7 ± 0.1	6.6 ± 0.2	0.865	7.3 ± 0.4*	6.3 ± 0.2	6.2 ± 0.3‡	0.031
Vitamin D deficiency	59 (76.9)	237 (76.7)	84 (73.7)	0.885	47 (67.5)	244 (80.0)	87 (87.9)‡	0.006
Calcium intake, mg/day	595.4 ± 57.2	552.8 ± 25.2	584.4 ± 36.0	0.402	431.7 ± 26.2	423.8 ± 21.6	418.2 ± 22.1	0.438
Sufficient calcium intake	10 (17.9)	43 (12.9)	15 (15.9)	0.630	4 (4.2)	24 (5.8)	6 (8.2)	0.612
Physical activity, hours/week	7.0 ± 1.2	7.8 ± 1.2	8.5 ± 1.1	0.961	2.8 ± 1.2	4.6 ± 0.7	6.0 ± 1.4	0.636
Regular physical activity	11 (20.4)	59 (16.5)	22 (15.8)	0.822	0 (0)*	20 (6.0)	11 (9.3)‡	< 0.001

Data are expressed as the mean ± standard error or number (%).
BMI = body mass index, HOMA-IR = homeostasis model assessment-insulin resistance.
*$P < 0.05$ between underweight and normal-weight groups. †$P < 0.05$ between normal-weight and overweight/obese groups. ‡$P < 0.05$ between underweight and overweight/obese groups.
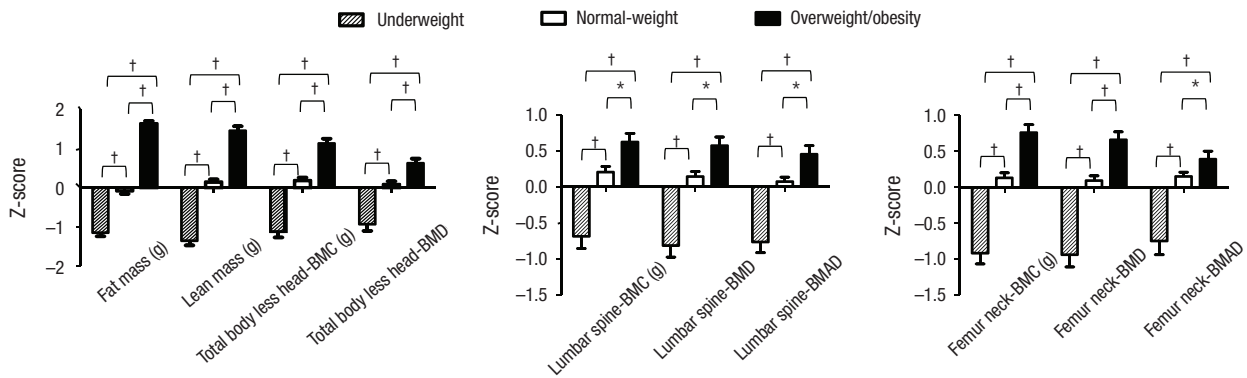
Fig. 2. Comparison of body composition and bone density among the underweight, normal-weight, and overweight/obesity groups in males.
BMC = bone mineral content, BMD = bone mineral density, BMAD = bone mineral apparent density.
*$P < 0.01$. †$P < 0.001$.
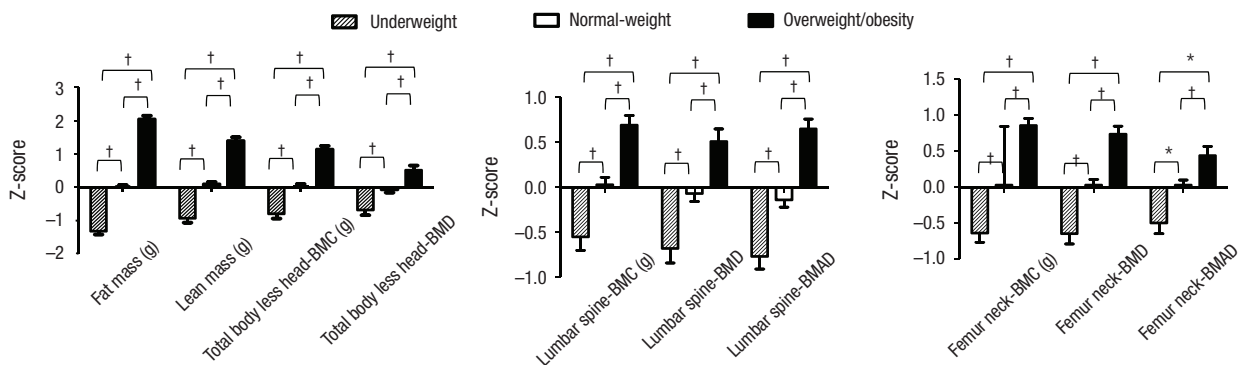
Fig. 3. Comparison of body composition and bone density among the underweight, normal-weight, and overweight/obesity groups in females.
BMC = bone mineral content, BMD = bone mineral density, BMAD = bone mineral apparent density.
*$P < 0.01$. †$P < 0.001$.

($P < 0.01$ for all) (Figs. 2 and 3).

Associations between BMI and bone parameters

We constructed a multivariate regression model adjusted for age, vitamin D deficiency, calcium intake, physical activity, and HOMA-IR to assess the effect of BMI on bone parameters (Table 3). For both sexes, increasing BMI was correlated with increasing zBMC and zBMD of the TBLH, lumbar spine, and femur neck after adjusting for confounders (all $P < 0.001$ for all). Vitamin D deficiency was a significant risk factor for low bone mass

and density of the TBLH (BMC, $P = 0.016$; and BMD, $P = 0.039$), lumbar spine (BMC, $P = 0.001$; BMD, $P = 0.002$; and BMAD, $P = 0.018$), and femur neck (BMC, $P = 0.037$; BMD, $P = 0.004$; and BMAD, $P = 0.001$) in female adolescents.

Associations between LM, FM, and bone parameters

Next, we included zFM and zLM instead of BMI in the multivariate-adjusted model (Table 4). zLM was positively associated with zBMC and zBMD of the TBLH for both sexes ($P < 0.001$ for all); this remained significant after additionally adjusting for

Table 3. Multivariate-adjusted model to analyze the effect of the BMI group on bone parameters

Variables	Total body less head		Lumbar spine (L1–L4)			Femur neck		
	zBMC	zBMD	zBMC	zBMD	zBMAD	zBMC	zBMD	zBMAD
Male (n = 508)								
Age, yr	−0.05 ± 0.03	−0.06 ± 0.03*	−0.06 ± 0.03*	−0.05 ± 0.03*	−0.03 ± 0.02	−0.05 ± 0.03	−0.04 ± 0.03	−0.01 ± 0.02
Vitamin D deficiency	0.09 ± 0.12	−0.11 ± 0.12	0.04 ± 0.14	0.00 ± 0.12	−0.02 ± 0.11	0.01 ± 0.12	−0.08 ± 0.10	−0.15 ± 0.13
Insufficient calcium intake	−0.30 ± 0.21	−0.37 ± 0.20	−0.44 ± 0.21*	−0.44 ± 0.21*	−0.38 ± 0.19*	−0.26 ± 0.21	−0.24 ± 0.21	−0.15 ± 0.22
Physically inactive	−0.13 ± 0.11	−0.10 ± 0.12	−0.06 ± 0.14	−0.03 ± 0.14	−0.00 ± 0.14	−0.17 ± 0.12	−0.28 ± 0.16	−0.31 ± 0.19
HOMA-IR	−0.02 ± 0.13	−0.13 ± 0.14	−0.29 ± 0.16	−0.22 ± 0.15	−0.13 ± 0.15	−0.14 ± 0.14	−0.13 ± 0.13	−0.09 ± 0.14
BMI group[§]	1.13 ± 0.11[‡]	0.80 ± 0.10[‡]	0.73 ± 0.12[‡]	0.75 ± 0.11[‡]	0.64 ± 0.10[‡]	0.88 ± 0.10[‡]	0.83 ± 0.10[‡]	0.59 ± 0.11[‡]
Female (n = 474)								
Age, yr	0.00 ± 0.02	−0.03 ± 0.02	−0.03 ± 0.03	0.00 ± 0.02	0.01 ± 0.02	0.00 ± 0.02	−0.02 ± 0.02	−0.02 ± 0.03
Vitamin D deficiency	−0.32 ± 0.13*	−0.34 ± 0.16*	−0.48 ± 0.14[†]	−0.45 ± 0.14[†]	−0.38 ± 0.16*	−0.30 ± 0.14*	−0.43 ± 0.14[†]	−0.44 ± 0.13[†]
Insufficient calcium intake	−0.44 ± 0.17[†]	0.04 ± 0.20	−0.18 ± 0.14	−0.22 ± 0.13	−0.17 ± 0.14	−0.31 ± 0.15*	−0.27 ± 0.15	−0.16 ± 0.17
Physically inactive	−0.27 ± 0.18	−0.23 ± 0.17	−0.10 ± 0.20	−0.08 ± 0.20	−0.07 ± 0.18	−0.12 ± 0.26	−0.16 ± 0.27	−0.16 ± 0.27
HOMA-IR	−0.05 ± 0.15	−0.10 ± 0.14	−0.07 ± 0.18	−0.08 ± 0.15	−0.04 ± 0.14	−0.15 ± 0.16	−0.21 ± 0.12	−0.22 ± 0.12
BMI group[§]	1.00 ± 0.09[‡]	0.63 ± 0.12[‡]	0.67 ± 0.09[‡]	0.80 ± 0.08[‡]	0.76 ± 0.09[‡]	0.81 ± 0.09[‡]	0.77 ± 0.10[‡]	0.54 ± 0.10[†]

Data are presented as regression coefficient (β) ± standard error.
BMC = bone mineral content, BMD = bone mineral density, BMAD = bone mineral apparent density, HOMA-IR = homeostasis model assessment of insulin resistance, BMI = body mass index, z = Z-scores.
*$P < 0.05$. [†]$P < 0.01$. [‡]$P < 0.001$. [§]BMI group was defined as underweight, normal-weight and overweight/obesity. Underweight group was used as a reference group.

Table 4. Multivariate-adjusted model to analyze the effect of FM and LM on bone parameters

Variables	Total body less head		Lumbar spine (L1–L4)			Femur neck		
	zBMC	zBMD	zBMC	zBMD	zBMAD	zBMC	zBMD	zBMAD
Male (n = 508)								
Age, yr	0.00 ± 0.02	−0.01 ± 0.02	−0.01 ± 0.02	−0.02 ± 0.02	−0.01 ± 0.02	−0.01 ± 0.02	0.00 ± 0.02	0.02 ± 0.02
Vitamin D deficiency	0.01 ± 0.07	−0.19 ± 0.10	−0.03 ± 0.10	−0.06 ± 0.11	−0.08 ± 0.11	−0.07 ± 0.09	−0.15 ± 0.11	−0.20 ± 0.14
Insufficient Ca intake	−0.14 ± 0.13	−0.25 ± 0.17	−0.31 ± 0.16	−0.33 ± 0.18	−0.31 ± 0.18	−0.13 ± 0.16	−0.13 ± 0.19	−0.09 ± 0.22
Physically inactive	−0.09 ± 0.09	−0.07 ± 0.12	−0.04 ± 0.13	0.00 ± 0.14	0.03 ± 0.14	−0.14 ± 0.11	−0.25 ± 0.16	−0.29 ± 0.20
HOMA-IR	−0.25 ± 0.10	−0.13 ± 0.13	−0.40 ± 0.13[†]	−0.26 ± 0.15	−0.11 ± 0.16	−0.22 ± 0.10*	−0.14 ± 0.12	−0.05 ± 0.14
FM Z-score, g	0.05 ± 0.04	−0.12 ± 0.05*	−0.13 ± 0.05	−0.06 ± 0.06	0.00 ± 0.06	−0.08 ± 0.05	−0.03 ± 0.05	0.01 ± 0.06
LM Z-score, g	0.84 ± 0.03[‡]	0.64 ± 0.04[‡]	0.71 ± 0.05[‡]	0.58 ± 0.06[‡]	0.38 ± 0.06[‡]	0.71 ± 0.05[‡]	0.57 ± 0.05[‡]	0.32 ± 0.06[‡]
Female (n = 474)								
Age, yr	−0.01 ± 0.02	−0.02 ± 0.02	−0.03 ± 0.02	−0.00 ± 0.02	−0.00 ± 0.02	0.00 ± 0.02	−0.02 ± 0.02	−0.02 ± 0.02
Vitamin D deficiency	−0.20 ± 0.11	−0.18 ± 0.15	−0.36 ± 0.12[†]	−0.35 ± 0.12[†]	−0.31 ± 0.15*	−0.15 ± 0.12	−0.31 ± 0.13*	−0.38 ± 0.13[†]
Insufficient Ca intake	−0.27 ± 0.14	0.11 ± 0.18	−0.07 ± 0.12	−0.12 ± 0.12	−0.09 ± 0.12	−0.19 ± 0.10	−0.16 ± 0.11	−0.09 ± 0.16
Physically inactive	0.04 ± 0.15	−0.09 ± 0.18	0.11 ± 0.22	0.05 ± 0.21	−0.01 ± 0.18	0.11 ± 0.22	0.01 ± 0.27	−0.09 ± 0.28
HOMA-IR	−0.33 ± 0.13*	−0.15 ± 0.14	−0.22 ± 0.15	−0.16 ± 0.14	−0.05 ± 0.14	−0.30 ± 0.13*	−0.33 ± 0.10[†]	−0.26 ± 0.12*
FM Z-score, g	0.25 ± 0.05	−0.10 ± 0.06	0.04 ± 0.04	0.15 ± 0.05[†]	0.20 ± 0.05[‡]	0.05 ± 0.04	0.10 ± 0.05*	0.13 ± 0.06*
LM Z-score, g	0.61 ± 0.04[‡]	0.59 ± 0.05[‡]	0.55 ± 0.04[‡]	0.37 ± 0.05[‡]	0.18 ± 0.05[‡]	0.62 ± 0.05[‡]	0.45 ± 0.05[‡]	0.19 ± 0.06[‡]

Data are presented as regression coefficient (β) ± standard error.
FM = fat mass, LM = lean mass, BMC = bone mineral content, BMD = bone mineral density, BMAD = bone mineral apparent density, Ca = calcium, HOMA-IR = homeostasis model assessment of insulin resistance, z = Z-scores.
*$P < 0.05$. [†]$P < 0.01$. [‡]$P < 0.001$.

height Z-scores. zLM also showed a positive association with zBMC, zBMD, and zBMAD of the lumbar spine and femur neck for both sexes ($P < 0.001$ for all).

We detected several differences in the associations between zFM and bone density between male and female participants. Although zFM showed a negative association with zBMD of the TBLH for both sexes, this was only statistically significant in male subjects ($P = 0.018$); the association remained significant after additionally adjusting for height Z-scores ($P = 0.018$). In contrast, zFM was positively associated with the lumbar spine zBMD ($P = 0.004$) and zBMAD ($P < 0.001$) as well as the femur neck zBMD ($P = 0.044$) and zBMAD ($P = 0.031$) in female participants only.

Meanwhile, HOMA-IR showed a negative association with the zBMC of the lumbar spine ($P = 0.003$) and femur neck ($P = 0.038$) in male participants and was negatively related to the zBMC of the TBLH ($P = 0.011$) as well as the zBMC ($P = 0.020$), zBMD ($P = 0.002$), and zBMAD ($P = 0.030$) of the femur neck in female participants after adjusting for age, vitamin D deficiency, calcium intake, physical activity, zFM, and zLM.

DISCUSSION

Adolescents with overweight/obesity had significantly higher bone mass and density of the TBLH, lumbar spine, and femur neck than underweight or normal-weight adolescents after adjusting for age, vitamin D deficiency, calcium intake, physical activity, and HOMA-IR. In both sexes, LM was beneficial for bone mass and density of the TBLH, lumbar spine, and femur neck. FM showed a negative association with TBLH bone density in male adolescents, and positive associations with lumbar spine and femur neck bone density in female adolescents.

Studies on the effects of overweight/obesity on bone mass and density in children have been controversial. Whereas some reported increased bone mass and density in overweight or obese children (3,19,20), others reported decreased (4,21) or similar (5,22) bone mass and density when compared to normal-weight children. These conflicting results can be attributed to the various methods used to assess bone health, the different covariates included in the studies, and the different cutoff systems used to define the weight groups and/or various categorization. Adolescents with overweight/obesity often have several risk factors adversely affecting bone health, including vitamin D deficiency, insufficient calcium intake, and a sedentary lifestyle (8). Moreover, the effect of insulin resistance must be included as a covariate in studies assessing the effect of overweight/obesity on bone health (9). Since adolescents with overweight/obesity are usually taller, height Z-score adjustments for the TBLH and calculation of the BMAD for the lumbar spine and femur neck are recommended to adjust for body size (10). We constructed a multivariate regression model adjusted for age, vitamin D deficiency, calcium intake, physical activity, and HOMA-IR and/or body size as covariates; the results of this model confirmed a beneficial effect of overweight or obesity on bone mass and density in both sexes.

Although some earlier studies in children reported higher total body and lumbar spine bone densities in children with overweight/obesity (3,19), the Z-scores of bone mass and density based on pediatric normative reference values could not be used as they were not available at the time. This study is strengthened by the objective assessment of body composition and bone parameters using nationwide pediatric normative reference values (12) as well as adjustments for potential confounders affecting bone health. TBLH, lumbar spine, and femur neck zBMC and zBMD showed consistent increases with increasing BMI in both sexes; this remained significant after adjusting for body size. This positive association between overweight/obesity and lumbar spine and femur neck bone mass and density might be attributable to weight-bearing and the effect of mechanical loading (6,23). In addition, hormonal influences such as increased circulating leptin, which was known to stimulate osteoblast differentiation via direct peripheral effects on stromal precursor cells in vitro and enhance mineralization of bone matrix (24), may play a beneficial role on bone mass and density (25).

Next, we investigated the independent effects of LM and FM on bone mass and density in male and female adolescents. When LM and FM were included in a multivariate-adjusted model instead of BMI, LM was a positive predictor for bone mass and density of the TBLH, lumbar spine, and femur neck. Increasing loads imposed by bigger muscles that exert higher tensile forces on their attaching bones might explain the beneficial role of LM on bone mass and density (26-28). Meanwhile, significantly lower bone mass and density in underweight adolescents when compared to normal-weight individuals in this study were associated with lower LM rather than insufficient calcium intake or vitamin D deficiency. This result supports the importance of adequate LM for bone health in childhood (29).

The literature on the effect of FM on bone health is controversial; this can be attributed to differences in the study participants' age and sexes, the measured skeletal sites, and the covariates used in the models (7). In the present study, we found sex- and skeletal site-specific differences in the effect of FM on bone health, after adjusting for all possible confounders, including LM. FM was negatively associated with TBLH BMD in both sexes, although this was only statistically significant in male adolescents. In contrast, FM showed a positive association with lumbar spine and femur neck BMD and BMAD in female adolescents only. The positive association between FM and lumbar spine BMD is consistent with a previous study in female adolescents aged 14–16 years (30). FM is not only part of weight-bearing component of the body but also affects bone as a metabolically active organ (31). A positive association between FM

and bone parameters was shown for weight-bearing sites (lumbar spine and femur neck), whereas a negative association was shown for non-weight-bearing sites (TBLH) (32). Possible mediators for the negative effect of FM on bone density include inflammatory cytokines, which are released from fat cells, in particular from the visceral fat component, promoting bone resorption by stimulating the differentiation of osteoclasts (33). Although it is unclear why the association between FM and the bone density of weight-bearing bone sites differs by sex, FM might have a differential effect on the bone density of the lumbar spine and femur neck according to sex due to sex-specific differences in FM percentage and distribution, and hormonal changes during the pubertal period. Women are known to have higher adiposity and more subcutaneous adipose tissue than men (34). Moreover, estrogen inhibits bone resorption during rapid pubertal growth and promotes bone formation after menarche (35).

Meanwhile, insulin resistance, expressed as HOMA-IR, was negatively associated with bone mass and density after adjusting for age, vitamin D deficiency, calcium intake, physical activity, zFM, and zLM in both sexes in our study. Possible mechanisms explaining the adverse effect of insulin resistance on bone density include increased proinflammatory cytokines levels (36), decreased uncarboxylated osteocalcin levels (37), and impaired insulin signaling in osteoblasts (38).

This study has several limitations. The cross-sectional design cannot provide evidence for causal relationships between LM and FM and peak bone accrual in adolescence. Further longitudinal research is required to gain more knowledge on the consequences of childhood overweight or obesity on the quality and strength of the bones. The effect of pubertal stage on bone health could not be evaluated since the KNHANES database did not include these data. Although quantitative computed tomography (QCT) is a three-dimensional technique to quantify true volumetric BMD, we could not measure volumetric BMD using QCT because the KNHANES database only includes DXA data. However, QCT is also limited by the absence of standardized scan techniques and a paucity of reference data (39). Instead, we used the Z-scores of BMC and BMD of the TBLH, lumbar spine and femur neck using DXA and their estimates of volumetric BMD, as recommended by the International Society for Clinical Densitometry (10). The clinical significance of altered bone mineral accrual lies in the association with fractures. Although we could not analyze the forearm, which is known as the most common fracture site in childhood, lumbar spine and femur neck BMADs were related to wrist and forearm fractures in a pediatric population-based fracture study (11); moreover, low TBLH BMD predicted subsequent fracture risk in a large prospective cohort study in children (40).

In conclusion, overweight/obesity had a positive effect on bone mass and density. LM was associated with higher bone mass and density in both, male and female adolescents. Sex- and site-specific differences for the effects of FM on bone density were found. These findings suggest that interventions to increase LM are helpful to augment bone health in adolescents with overweight/obesity. Future longitudinal studies, taking into account LM, pubertal state, and hormonal changes according to sex, are needed to evaluate the effects of FM on bone health in adolescents.

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DISCLOSURE

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Conceptualization: Kim HY, Jung HW, Kim JH, Shin CH, Yang SW, Lee YA. Data curation: Kim HY, Hong H, Shin CH, Lee YA. Investigation: Kim HY, Jung HW, Hong H, Kim JH, Shin CH, Yang SW, Lee YA. Writing - original draft: Kim HY. Writing - review & editing: Kim HY, Jung HW, Hong H, Kim JH, Shin CH, Yang SW, Lee YA.

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