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Fat mass is positively associated with bone mass acquisition in children with small or normal lean mass: A three-year follow-up study

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ABSTRACT

The independent impact of fat mass (FM) on bone health is difficult to assess, as FM is correlated with lean soft tissue mass (LSTM). In a previous cross-sectional study, FM was suggested to help promote high bone mass acquisition in adolescents with small LSTM. The present prospective cohort study investigated the effects of FM on bone in pubertal children after stratification by height-normalized index of LSTM (LSTMI). The source population was all 5th grade children enrolled in either one of the two public elementary schools in Hamamatsu, Japan. Of these, 545 children who participated in both baseline (at age 11) and follow-up (at age 14) surveys were included in the present analysis. Body composition and whole body areal bone mineral density (aBMD) were measured using dual-energy X-ray absorptiometry. From baseline to follow-up, significant ($P < 0.05$) differences were observed in changes in aBMD among tertiles of change in FM in both sexes after adjusting for confounding factors including LSTMI. After stratification by tertiles of sex-specific LSTMI, adjusted means of changes in aBMD according to tertiles of change in FM within the lowest and second lowest tertiles of LSTMI in both sexes showed a significant increase from the lower tertiles to the highest tertile of change in FM. In the highest tertile of LSTMI, changes in FM showed no significant association with changes in aBMD. These findings suggest that adipose tissue might help promote high bone mass acquisition in pubertal children with small or normal LSTMI.

1. Introduction

Rapid bone mineral acquisition occurs relatively early in life, and accumulation of bone mass/density in the whole body as well as at multiple skeletal sites is mostly achieved by late adolescence [1,2]. Peak bone mineral accretion occurs at 13 years of age in girls and 14 years in boys [3]. Insufficient bone mass accumulation during late childhood and peripubertal years increases the risk of osteoporotic fractures in later life, as age-related bone loss ensues [4]. Thus, optimization of lifestyle factors known to influence peak bone mass is an important strategy for reducing osteoporosis risk in later life [2].

Body weight is closely associated with bone health during growth [5], with mechanical loading being an essential mechanism for maintaining bone health. Weight-bearing exercise that provides loading to skeletal regions promotes bone growth in pubertal children [6]. Body weight is the sum of bone mass, fat mass (FM), and lean soft tissue mass (LSTM), which includes muscle mass. The mechanical contribution of muscles to skeletal loading includes forces generated by muscle as well as muscle weight. In particular, muscle contraction places the greatest physiological load on bone, and so the stability of bone must be adapted to muscle strength [7]. On the other hand, the mechanical contribution of FM is limited to the weight of FM alone [5].

Previous epidemiological studies regarding the impact of FM on pediatric bone health have yielded conflicting results. While some studies found FM to be a positive determinant of bone health [8–13], other studies showed that FM had no beneficial effects on bone in children and adolescents [14–20]. This discrepancy might be partly due to multicollinearity, given the possible intercorrelation between FM and LSTM in the same multiple linear regression model [21,22]. Correlations between FM and LSTM make it difficult to evaluate the independent impact of FM on bone [23]. Furthermore, several studies have reported that LSTM is more strongly associated with bone mass compared to FM [9,10,23]. The larger effects of LSTM on bone might obscure smaller effects of FM, and indeed, FM appears to differently affect bone health according to LSTM.

Abbreviations: BMC, bone mineral content; aBMD, areal bone mineral density; BMI, body mass index; DXA, dual-energy X-ray absorptiometry; FM, fat mass; FMI, fat mass index; LSTM, lean soft tissue mass; LSTMI, lean soft tissue mass index.

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A previous cross-sectional study analyzed the association between FM and bone mass after stratification by LSTM (i.e., avoiding multicollinearity and larger effects of LSTM) to address these issues, and suggested that FM could help promote high bone mass acquisition in adolescents with relatively small LSTM [23]. In the present prospective cohort study, we investigated the effects of FM on bone health in a population-based sample of children in Hamamatsu City, Japan, stratified by LSTM.

2. Materials and methods

2.1. Subjects

The source population (accessible population) of the present study was all 5th grade public school children enrolled in Aritama Elementary School and Sekishi Elementary School in Hamamatsu City, Japan, as of November or December in 2010, 2011, 2012, and 2013 (1071 students: 557 boys and 514 girls; Hamamatsu Kids Health Study). As there are no other elementary schools, including private schools, in this elementary school district, most children living in this area attend either one of the two elementary schools and go on to Sekishi Junior High School in the same district. Accordingly, we conducted a baseline survey at the two elementary schools and a follow-up survey at Sekishi Junior High School three years later, in December 2013, 2014, 2015, and 2016. Of the 1071 students included in the source population, baseline data were collected from 817 (424 boys and 393 girls). In the present study, data of 545 students (279 boys and 266 girls) who participated in both baseline (at age 11) and follow-up (at age 14) surveys were subject to analysis.

This study was approved by the Ethics Committee of the Kindai University Faculty of Medicine, and performed in accordance with the ethical standards set forth in the Declaration of Helsinki. All parents and guardians of the students received printed information regarding study procedures including the dose of dual-energy X-ray absorptiometry (DXA) radiation exposure, and provided written consent at both baseline and follow-up surveys. Students were also allowed to decline participation on their own accord.

2.2. Body composition measurement

FM (kg), LSTM (kg), areal bone mineral density (aBMD, g/cm^2), and bone mineral content (BMC, g) in the whole body were determined with a single DXA scanner (QDR-4500A, Hologic Inc., Bedford, MA, USA) mounted on a mobile examination car in each school. Quality control of the DXA scanner was performed using the Step Phantom scan for body composition throughout the surveys. Subjects wore light clothing without metal objects while undergoing whole-body scanning. A single experienced radiological technologist performed all scans and scan analyses. Height-normalized index of whole-body FM (fat mass index, FMI; kg/m^2) was calculated as total body FM divided by height squared (m^2) and used as an index of whole body adiposity independent of overall body size [24,25]. Similarly, height-normalized index of whole-body LSTM (lean soft tissue mass index, LSTMI; kg/m^2) was calculated. Changes in bone variables and fat variables were calculated by subtracting baseline values from follow-up values.

2.3. Other variables

Body weight, height, and waist circumference were measured in light clothing with no shoes at the same time as the body composition measurements. Body mass index (BMI, kg/m^2) was also calculated by dividing total body weight (kg) by height squared (m^2) to examine baseline characteristics and to determine whether subjects were overweight or underweight. International BMI cut-offs for child overweight (based on the adult BMI cut-off of 25 kg/m^2; boys, >20.55 kg/m^2; girls, >20.74 kg/m^2) [26] and child underweight (based on the adult BMI cut-off of 18.2 kg/m^2; boys, <14.97 kg/m^2; girls, <15.05 kg/m^2) were used [27].

Information regarding pubic hair appearance and time spent doing sedentary activities, such as watching television, playing video games, using a mobile phone, and using a computer, was obtained by a self-reported questionnaire comprising multiple-choice single-answer questions. Participants with parents/guardians were allowed to choose only one of predefined options (pubic hair appearance: 3rd grade, 4th grade, 5th grade, or no appearance; sedentary behavior: <1 h/day, ≥1 and <2 h/day, ≥2 and <3 h/day, ≥3 and <4 h/day, or ≥4 h/day).

2.4. Statistical analysis

Differences in characteristics between follow-up and dropout subjects were evaluated using the unpaired *t*-test or Mann-Whitney *U* test. A repeated measures ANOVA was used to evaluate differences in bone mass change among tertiles of change in FM from baseline to follow-up. In addition, subjects were stratified by sex-specific LSTMI at the baseline survey before assessing relationships between FM variables and bone variables. The lowest, second-lowest, and highest tertiles of LSTMI were defined as "relatively small LSTMI," "relatively normal LSTMI," and "relatively large LSTMI" groups, respectively. A repeated measures ANCOVA was used to evaluate differences in bone mass change, after adjusting for tertiles of LSTMI, height, sedentary behavior, and pubic hair appearance at the baseline survey. Simple regression analysis was performed to evaluate trends from the lowest tertile group of LSTMI (LSTMI T1; relatively small LSTMI) to the highest tertile group of LSTMI (LSTMI T3; relatively large LSTMI). The dependent variable was measurement, and the independent variable was LSTMI tertile. The relationship between bone mass and FMI was evaluated within each tertile of LSTMI using a multiple regression model, after adjusting for potential confounding factors such as sedentary behavior and pubic hair appearance at the baseline survey. The relationship between bone mass and FM was also evaluated within each tertile of LSTMI, after adjusting for height, sedentary behavior, and pubic hair appearance at the baseline survey. Mean changes in aBMD according to tertiles of change in FM within each tertile of LSTMI were calculated using a general linear model after adjusting for height, sedentary behavior, and pubic hair appearance at the baseline survey. For trend tests on aBMD change from the lowest to highest tertile of change in FM within each tertile of LSTMI, multiple linear regression analysis was performed after adjusting for potential confounding factors. $P < 0.05$ was considered statistically significant. All analyses were performed using SPSS Statistics Desktop for Japan, Version 22 (IBM Japan, Ltd., Tokyo, Japan).

3. Results

Table 1 summarizes the baseline characteristics of follow-up subjects (study population) and dropout subjects at the baseline survey. The study population was 66.7% of the baseline population. There were no significant differences between the study population and the dropout population (33.3% of the baseline population). Table 2 shows differences in bone mineral parameters among tertiles of change in FM from baseline to follow-up. Significant differences were observed in aBMD and BMC among tertiles of change in FM in both sexes after adjusting for confounding factors including LSTMI.

Table 3 shows baseline and follow-up characteristics of body composition stratified by sex-specific LSTMI at the baseline survey, and relationships between LSTMI and FM parameters, and between LSTMI and bone mineral parameters at baseline and follow-up surveys. Trend tests showed a significant increase in aBMD from the lowest tertile to the highest tertile of LSTMI in both sexes at the baseline and follow-up surveys. FMI also showed a significant increase from the lowest to highest tertile of LSTMI in both sexes at the baseline and follow-up surveys. Table 4 shows the relationship between bone mass and FMI within each tertile of LSTMI. In boys, baseline FMI was significantly and