



## Original Full Length Article

## Increased fat mass is associated with increased bone size but reduced volumetric density in pre pubertal children

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## ABSTRACT

Recent studies have shown that obesity is associated with an increased risk of fracture in both adults and children. It has been suggested that, despite greater bone size, obese individuals may have reduced true volumetric density; however this is difficult to assess using two dimensional techniques such as DXA. We evaluated the relationship between fat mass, and bone size and density, in a population cohort of children in whom DXA and pQCT measurements had been acquired.

We recruited 530 children at 6 years old from the Southampton Women's Survey. The children underwent measurement of bone mass at the whole body, lumbar spine and hip, together with body composition, by DXA (Hologic Discovery, Hologic Inc., Bedford, MA, USA). In addition 132 of these children underwent pQCT measurements at the tibia (Stratec XCT2000, Stratec Biomedical Systems, Birkenfeld, Germany).

Significant positive associations were observed between total fat mass and both bone area (BA) and bone mineral content (BMC) at the whole body minus head, lumbar spine and hip sites (all  $p < 0.0001$ ). When true volumetric density was assessed using pQCT data from the tibia, fat mass (adjusted for lean mass) was negatively associated with both trabecular and cortical density ( $\beta = -14.6 \text{ mg/mm}^3$  per sd,  $p = 0.003$ ;  $\beta = -7.7 \text{ mg/mm}^3$  per sd,  $p = 0.02$  respectively).

These results suggest that fat mass is negatively associated with volumetric bone density at 6 years old, independent of lean mass, despite positive associations with bone size.

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## Introduction

Weight and body composition are major determinants of bone size and density throughout life, reflecting adaptation of skeletal modelling to loading and endocrine influences. This is reflected in positive associations between fat mass and BMD in adults and the negative correlation between risk of fracture and weight in the elderly [1].

**Abbreviations:** BMC, bone mineral content; BA, bone area; aBMD, areal bone mineral density; DXA, dual X-ray absorptiometry; pQCT, peripheral quantitative computed tomography; BMI, body mass index.

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Studies of children have yielded conflicting results with regard to the relationships between fat mass, and bone size, density and fracture risk. Thus some studies have shown positive relationships between fat mass and bone size [2,3], with others additionally demonstrating negative associations with bone mineral content [4–7], suggesting a failure of the skeleton to achieve adequate adaptation to the excess load resulting from obesity. Further studies have shown associations which varied by the age and sex of the child and whether the relationships were assessed cross-sectionally or longitudinally [8,9]. Given the increasing prevalence of obesity and the epidemiological data suggesting a positive relationship between obesity and risk of fracture in children [10], it is important to understand these relationships more fully.

These data have been difficult to disentangle because of the imperfect correction for body size afforded by DXA, and the existence of few data from the use of pQCT. In this study we therefore aimed to evaluate the relationship between fat mass and bone size and volumetric density among pre-pubertal children within a narrow age range, recruited from a free-living population cohort, the Southampton Women's Survey (SWS) and who had undergone assessment with DXA and pQCT.

## Methods

### Participants

The Southampton Women's Survey is a prospective cohort study of 12,583 women aged 20–34 years recruited from the general population [11]. At enrolment the participants were characterised in detail in terms of diet, lifestyle, health, physical activity and anthropometric measurements. 3159 of these women were followed through a subsequent pregnancy and delivered a live born infant. The children are being followed and characterised at regular intervals. Of the 1268 eligible families contacted during the study period for a 6 year follow up 530 attended for DXA, forming the cohort presented in this paper.

### 6 year DXA assessment

The mother and child were invited to visit the Osteoporosis Centre at Southampton General Hospital for assessment of bone mass and body composition. At this visit written informed consent for the DXA scan was obtained from the mother or father. The child's height (using a Leicester height measurer, Seca Ltd, UK) and weight, using calibrated digital scales (Seca Ltd, UK) were measured. Whole body (including body composition) and lumbar spine scans were obtained, using a Hologic Discovery instrument (Hologic Inc., Bedford, MA, USA). To encourage compliance, a suitably bright sheet with appropriate pictures was laid on the couch and to help reduce movement artefact, the children were shown a suitable DVD. The total radiation dose for the scans were as followed: whole body (paediatric scan mode) 4.7  $\mu$ Sv, spine (L1–L4) 1.5  $\mu$ Sv and hip 7.3  $\mu$ Sv. The manufacturer's coefficient of variation (CV) for the instrument was 0.75% for whole body bone mineral density, and the experimental CV when a spine phantom was repeatedly scanned in the same position 16 times was 0.68%. All scans were checked for movement and clothing artefact resulting in 499 suitable for analysis.

### pQCT

A consecutive subgroup of 172 children was invited back to the Osteoporosis Centre to have an additional assessment of bone mass using a pQCT peripheral quantitative computed tomography scanner (Stratec XCT 2000, Software version 6.00 B 00.61, threshold for cortical bone 710 mg/cm<sup>3</sup>, Stratec Biomedical Systems, Birkenfeld, Germany) following the DXA visit. After written informed consent was obtained the child's lower leg length was measured from the medial malleolus to the tibial tuberosity in order to demarcate the correct scan position. The child was then asked to place their right lower leg into the pQCT instrument; the laser guidance system on the instrument was used to position the medial malleolus correctly. The foot was secured into place in order to reduce movement artefact. A suitable DVD was used in order to occupy the child and again reduce movement artefact.

A scout view was obtained to find the distal end of the tibia. A reference line was then placed; the 4% site was used to assess trabecular density and the 38% site for cortical density. The total radiation dose for the scans was 1.5  $\mu$ Sv. All scans were checked for movement, and excluded if the circumference was interrupted. 148 children underwent pQCT assessment. Of these, 132 scans were suitable for trabecular bone analysis (4% site); 125 were also suitable for analysis of cortical bone indices (38% site).

### Statistical analysis

Bone outcomes from DXA at 6 years included: bone area (BA), bone mineral content (BMC), areal bone mineral density (aBMD) at the whole body minus head and lumbar spine. Bone indices from pQCT included total area, trabecular content and trabecular density at

4% site; at the 38% site total area, cortical area, content, thickness and density were assessed, together with stress–strain index. Children were classified as either normal weight, overweight or obese using the method of Vidma et al. [12]. This classification incorporates height, weight, age and gender based on records derived from the 1990 British Growth Reference and the 2000 US CDC Growth Reference data, to give outcomes appropriate to growing children. All fat mass variables were positively skewed, and so were log-transformed. For ease of interpretation, and to allow comparison of relationships, these values, and those for lean mass variables, were converted to within group z-scores. *T*-test and Wilcoxon–Mann Whitney tests were used to explore differences in anthropometric characteristics, pQCT and DXA measurements between males and females. Linear regression models were fitted to explore the relationships between body composition and bone indices. Both age at DXA/pQCT and gender of the child were associated with bone indices, hence all bone indices were adjusted for age at scan, and gender. All analyses were also conducted unadjusted for gender, but incorporating a gender–predictor interaction term to explore the role of the child's sex in potentially modifying any relationships observed. Since more adipose children also tend to have greater lean mass (more muscle is required to enable locomotion in a heavier individual), and lean mass may have a positive effect on bone through loading, lean mass was considered to be a potential mechanistic mediator in any relationship between fat and bone. Analyses were therefore conducted unadjusted and adjusted for lean mass. Statistical analyses were performed using Stata 11.0 (Statacorp, Texas, USA).

The Southampton Women's Survey was approved by the Southampton and South West Hampshire Local Research Ethics Committee. Written consent was obtained from parents/carers of all participants.

## Results

### Characteristics of the children

Analyses are based on 499 children with complete DXA data at 6 years. Table 1 summarises the characteristics of the children. Despite similar height and weight at age 6 years, there were differences in bone indices by gender. Additionally, girls had a greater mean total fat mass compared with the boys ( $p < 0.0001$ ). 395 children were of normal weight (equivalent to adult BMI  $< 25$  kg/m<sup>2</sup>), 50 were overweight (equivalent to adult BMI between 25 and 30 kg/m<sup>2</sup>) and 17 were obese (equivalent to adult BMI  $> 30$  kg/m<sup>2</sup>). All, apart from 18 children were of white Caucasian ethnicity. There was no difference in the anthropometric measures at birth and at age 1 year between those children who did or did not participate in this study; however study participants' mothers tended to be of higher social class ( $p = 0.004$ ) and were less likely to smoke ( $p = 0.03$ ). The subgroup of children who underwent pQCT were slightly younger than the overall group who underwent DXA (6.5 years versus 6.6 years in the overall DXA group,  $p < 0.01$ ), but otherwise were broadly similar.

### Relationships between body composition and bone mass

Table 2 summarises the relationships between body composition and bone indices. Both total fat mass and total lean mass were positively associated with whole body minus head BA, BMC and aBMD. When lean mass was included in regression models, these relationships were somewhat attenuated, but remained statistically significant; the associations between fat mass and bone indices at the lumbar spine became non-significant after inclusion of lean mass. There was evidence of gender differences in the relationships between lean adjusted fat mass and the bone outcomes, which were stronger in male than female children ( $p$  value for the lean adjusted fat mass–gender interaction terms with whole body BA, BMC, aBMD all  $< 0.05$ ). Similar

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