Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. 17, no. 1, 163−169, 2014

1094-6950/17:163−169/$36.00
http://dx.doi.org/10.1016/j.jocd.2013.02.009

Section V: Bone Patho-Physiology

Comparison of the Relationship Between Bone Marrow Adipose Tissue and Volumetric Bone Mineral Density in Children and Adults

Wei Shen,[*,1,2] *Gilbert Velasquez,*[2] *Jun Chen,*[2] *Ye Jin,*[2] *Steven B. Heymsfield,*[3] *Dympna Gallagher,*[2] *and F. Xavier Pi-Sunyer*[2]

[1]*Department of Pediatrics, College of Physicians and Surgeons, Columbia University, New York, NY, USA;* [2]*New York Obesity Nutrition Research Center, St. Luke's-Roosevelt Hospital and Institute of Human Nutrition, Columbia University, New York, NY, USA; and* [3]*Pennington Biomedical Research Center, Baton Rouge, LA, USA*

Abstract

Several large-scale studies have reported the presence of an inverse relationship between bone mineral density (BMD) and bone marrow adipose tissue (BMAT) in adults. We aim to determine if there is an inverse relationship between pelvic volumetric BMD (vBMD) and pelvic BMAT in children and to compare this relationship in children and adults. Pelvic BMAT and bone volume (BV) was evaluated in 181 healthy children (5−17 yr) and 495 healthy adults (≥18 yr) with whole-body magnetic resonance imaging (MRI). Pelvic vBMD was calculated using whole-body dual-energy X-ray absorptiometry to measure pelvic bone mineral content and MRI-measured BV. An inverse correlation was found between pelvic BMAT and pelvic vBMD in both children ($r = -0.374$, $p < 0.001$) and adults ($r = -0.650$, $p < 0.001$). In regression analysis with pelvic vBMD as the dependent variable and BMAT as the independent variable, being a child or adult neither significantly contribute to the pelvic BMD ($p = 0.995$) nor did its interaction with pelvic BMAT ($p = 0.415$). The inverse relationship observed between pelvic vBMD and pelvic BMAT in children extends previous findings that found the inverse relationship to exist in adults and provides further support for a reciprocal relationship between adipocytes and osteoblasts.

Key Words: Bone marrow adipose tissue; bone mineral density; dual-energy X-ray absorptiometry; magnetic resonance imaging; volumetric.

Introduction

An inverse relationship between bone mineral density (BMD) and bone marrow adipocyte levels has been documented in animal and human studies *(1−7)*. This relationship has been attributed to the ability of mesenchymal stem cells (MSCs) to differentiate into either adipocytes or osteoblasts *(8,9)*. Preferential differentiation into a given lineage is dependent on the extracellular environment of the MSC and the presence of osteoblast or adipocyte stimulatory factors *(9,10)*.

This cellular relationship is supported by recent studies analyzing BMD and bone marrow adipose tissue (BMAT) in large cohorts of young and old adult populations *(6,7,11−14)*. A recent study by Shen et al *(13)* in 2012 in young adults who had reached peak bone mass and older adults undergoing potential bone loss, a similar inverse relationship was shown between BMD and BMAT. These data support the presence of a competitive relationship between osteoblasts and adipocytes even before the beginning of bone loss. This inverse relationship has not been established in childhood, a stage during which bone mass is accrued.

Dual-energy X-ray absorptiometry (DXA) is commonly used to measure BMD in adults. The output measure of areal

Received 01/29/13; Accepted 02/13/13.
*Address correspondence to: Wei Shen, MD, New York Obesity Nutrition Research Center, St. Luke's-Roosevelt Hospital and Institute of Human Nutrition, Columbia University, 1090 Amsterdam Avenue, 14th Floor, New York, NY 10025. E-mail: WS2003@Columbia.edu

BMD (aBMD) produced by DXA, although accurate for adults, is error prone when being used for the assessment of BMD in children *(15)*. Because bone size and thickness increases substantially during childhood development, it is necessary to use volumetric BMD (vBMD) measures *(15)*. Current studies commonly use quantitative computed tomography (QCT) to obtain vBMD; however, caution is required when using QCT extensively in children because of the potential adverse health effects related to CT scans *(16)*.

The aim of this study was to determine if an inverse relationship exists between BMD and BMAT in children. To perform this analysis, vBMD was calculated using DXA-measured bone mineral content (BMC) and magnetic resonance imaging (MRI)-measured bone volume (BV). Furthermore, the results of this analysis were compared with the adult populations to determine the vBMD and BMAT relationship present throughout the lifespan. Because the aBMD and BMAT relationship in the adult population has been previously reported *(11,13)*, this article focuses on comparing this relationship in children and adults.

Methods and Materials

Protocol and Design

The primary study cohort consisted of 181 children, aged 5−17 yr. Analysis was also performed on an adult cohort that consisted of 495 study subjects, aged 18 yr or older. All subjects were deemed healthy after completion of a medical history, physical examination, and blood test screening. All subjects underwent a standardized whole-body MRI and DXA scan. Furthermore, the following measures were obtained for each subject: weight, height, age, pubertal or menopausal status, and self-reported ethnicity.

The present study is an analysis of preexisting data. The Institutional Review Board reviewed and approved the exempt status of the present study. All subjects provided written consent to participate in the original study, which was approved by the Institutional Review Board.

Magnetic Resonance Imaging

Whole-body MRI was carried out using a 1.5-T scanner (General Electric, 6X Horizon, Milwaukee, WI) as previously described *(17,18)*. All subjects were scanned with T1-weighted, spin-echo sequence with 210-ms repetition time and a 17-ms echo time. During the scan, subjects remained in a supine position with their arms extended over their heads. The L4−L5 intervertebral disk was used as the point of origin, as 10-mm thick axial slice images were obtained from fingers-to-toes with a 40-mm interslice gap.

The BMAT, BV, subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and skeletal muscle of each individual were segmented by trained technicians using image analysis software (SliceOmatic; TomoVision, Inc., Montreal, QC, Canada). The technicians were blinded to patient demographic and test results. Semiautomated methods (i.e., a combination of threshold method and manual correction) were used to segment BMAT, SAT, VAT, and skeletal muscle as previously described *(11−13)*. Bone regions were manually traced and quality controlled to ensure that nonosseous tissue was omitted from the analysis. Pelvic BMAT and BVs were calculated using the following bones within the region: ilium, sacrum, ischium, pubis, coccyx, and femoral heads. The following equation was used to calculate compartment volumes:

$$V = (t + h)\sum_{i=1}^{N} A_i$$

where V is volume, A_i is each scan's cross-sectional area, h is the between-slice interval, t is the thickness of each slice, and N is the total number of slices. The intraclass correlation coefficient for volume rendering of skeletal muscle, BMAT, BV, SAT, and VAT for the same scan by different analysts are 0.99, 0.99, 0.99, 0.99, and 0.95, respectively.

The pelvic BMC obtained by the DXA scan was divided by the pelvic BV determined by MRI analysis to calculate pelvic vBMD:

$$v\text{BMD} = \frac{\text{BMC}}{\text{BV}}$$

Dual-Energy X-Ray Absorptiometry

The DXA scan (GE Lunar, Madison, WI; adults, DPX software version 4.7e; children, Prodigy software version 6.7) was used to estimate areal BMC from the whole-body scan. Acquisition and analysis of the scans were performed by trained technologists. Values for pelvic BMC (a region contained within the whole-body scan) were used in the current analyses. The estimated precision level for BMD is 1.28% *(19)*. Routine DXA calibration and quality control measures have been previously reported *(20)*.

Statistics

Pearson's correlation coefficients among pelvic BMAT and vBMD, age, weight, body mass index (BMI) percentile, total body fat (TBF), VAT, SAT, and skeletal muscle were calculated for children.

Regression models were established using pelvic vBMD as the dependent variable and pelvic BMAT, weight, TBF, SAT, VAT, and skeletal muscle as the independent variables, with adjustment for demographic factors (age, sex, race, and pubertal or menopausal status) and biologically plausible 2-way interactions (i.e., puberty and BMAT interaction). Multivariable regression models were built using stepwise regression, with a p value of 0.05 for entry and retention.

Equality of variance was assessed using Levene's test, and normality of the residual distributions was determined using the Shapiro-Wilk test. Variable values that did not have a normal distribution were log transformed initially. If the log transformation did not normalize the residual values, the Box-Cox transformations were applied.