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Bone marrow fat unsaturation in young adults is not affected by present or childhood obesity, but increases with age: A pilot study

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ABSTRACT

Objectives. Obesity increases bone marrow fat (BMF) content. The association between early obesity and bone marrow fatty acid composition is unknown. We measured BMF unsaturation index (UI) in normal-weight and overweight young adults with a known weight status in early childhood and tested the relationship between BMF UI and exercise history, glycemic state, and other clinical characteristics.

Methods. The study included 18 normal-weight (BMI <25 kg/m^2; 2 males, 16 females) and 17 overweight (BMI ≥25 kg/m^2; 9 males, 8 females) young adults aged 15–27 years. BMF UI was assessed with magnetic resonance proton spectroscopy optimized to reduce water interference. Exercise information was obtained with a pedometer accompanied with the history of recent physical activity. Blood samples (insulin, glucose, HbA1c) and body characteristics (BMI, waist-to-hip ratio, body fat composition) were assessed.

Results. BMF UI was not affected by obesity at the time of study or before age 7 years. BMF UI increased with age in normal-weight and overweight subjects ($R = 0.408$, $p = 0.015$) but did not associate with gender, physical activity or body fat composition; a suggestive association was observed with glucose ($R = -0.289$, $p = 0.10$).

Abbreviations: BMI, Body mass index; BMD, Bone mineral density; BMF, Bone marrow fat; UI, Unsaturation index; ^{1}H-MRS, Magnetic resonance proton spectroscopy; PA, Physical activity; BMR, Basal metabolic rate; Insulin, Fasting serum insulin; Glucose, Fasting plasma glucose; HB, Harris-Benedict; HOMA, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR2) index; DXA, Dual-energy X-ray absorptiometry; TE, Echo time.

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Conclusions. The association of BMF UI with age in early adulthood may represent normal maturation of bone marrow. There was a trend toward an association with blood glucose, warranting further studies.

1. Introduction

Obesity, an increasing health concern among children and young adults, has several long-term adverse health effects [1]. It increases the risk for cardiovascular diseases, high blood pressure and type 2 diabetes [2]. Obesity is associated with an increased bone marrow fat (BMF) content [3], which in turn has been linked to osteoporosis [4]. Exercise, on the other hand, reduces femoral BMF content in children [5] and increases tibial bone trabecular density in young female athletes [6]. Similar findings have been obtained in mice; BMF content in femur is suppressed by exercise while bone quantity increases [7]. In these studies mechanical stimulation was induced by running. However, the impact of physical activity (PA) and obesity on BMF composition during young adulthood are unknown.

Human BMF composition can be studied noninvasively with magnetic resonance spectroscopy (^{1}H-MRS) [8]. In the fat spectrum the olefinic, i.e. double bond, proton resonance (at 5.3 ppm) is well resolved from other fat resonances (at 2.8–0.9 ppm). An intense water resonance (at 4.7 ppm) may, however, obscure the olefinic resonance from fat, hampering analysis of fat composition [8]. We have recently introduced a method of using long echo time (TE) MRS to assess fat unsaturation in tissues with an intense water resonance [9]. Using long TE suppresses the intense water resonance, resulting in a well-resolved olefinic resonance, and a more accurate measurement of fat unsaturation [9]. Recently, Troitskaia et al. also applied the long TE MRS method to determine the unsaturation of BMF [10].

There are no previous studies investigating the effect of obesity on BMF unsaturation index (UI). BMF UI is defined as relative amount of double bonds in the fatty acid chains of triglycerides and it relates the proportion of unsaturated fat to saturated fat. Griffith et al. found no association between BMD and BMF UI in subjects with varying BMD [11]. On the contrary, Bredella et al. found that the degree of BMF saturation was inversely associated with BMD in young women with anorexia nervosa [12].

We hypothesized that severe overweight during adolescense and before age 7 years decreases BMF unsaturation, which might indicate impaired obesity-related bone health. To address this question, we measured BMF UI in normal-weight and overweight young adults whose weight status before age 7 years was known and tested the relationship between BMF UI and exercise history, glycemic state and age in this pilot study. BMF UI was assessed with ^{1}H-MRS and exercise information was acquired with a pedometer and history of recent physical activity.

2. Materials and Methods

2.1. Study Design

This study is a part of a research program assessing skeletal and metabolic characteristics of severe early childhood-onset obesity (i.e. obesity developing before age 7 years) and was carried out at Children's Hospital, Helsinki University Central Hospital, Finland. An ethical approval was obtained from the Research Ethics Committee of the Hospital District of Helsinki and Uusimaa (184/13/03/03/2010). Informed written consent was obtained from all study participants. Inclusion criteria for the subjects with severe early-onset obesity were: i) weight-for-height ratio exceeding 60% before age 7 years, according to Finnish growth standards, ii) referral due to severe obesity to Children's Hospital, Helsinki University Central Hospital, during childhood, iii) at the age of 7 years lived in the capital region of Helsinki, and iv) aged between 15 and 27 years at the time of the study.

Altogether 366 patients fulfilling these inclusion criteria were identified in the Children's Hospital patient register during 2011–2013. All were invited to participate in the study and 68 (18.6 %) eligible subjects consented. All participating patients were or had been followed by a pediatrician at Children's Hospital. Common endocrine and genetic causes of obesity were excluded (e.g. Prader Willi syndrome, pseudohypoparathryoidism, hypercortisolism, hypothyroidism). Subjects are referred to as 'subjects with severe early-onset obesity' in the text. For each subject with severe early-onset obesity an age- and sex matched control was selected from the population register. Sampling of controls was limited to the capital region of Helsinki. Exclusion criteria for the controls were obesity (weight-for-height ratio above 40%) before age of 10 years. Altogether 73 controls consented to our study during 2011–2013.

^{1}H-MRS of the tibia was performed to a random subpopulation of 35 subjects, consisting of 18 normal-weight (BMI <25 kg/m^2, 2 male, 16 female) and 17 overweight (BMI ≥25 kg/m^2, 9 male, 8 female) young adults. In this grouping, five subjects (3 females) with no early-onset obesity were classified as overweight due to BMI ≥25 kg/m^2 at the time of the study. One male subject with severe obesity by age 7 years achieved normal weight by young adulthood and was thus included in the normal-weight group. We also performed a second analysis by grouping the subjects based on their BMI by age 7 years: 13 subjects developed severe obesity before age 7 years (7 males, 6 females) while 22 were non-obese at age 7 and were regarded as controls (4 males, 18 females).

2.2. ^{1}H-MRS Cohort Characteristics

The subgroup of subjects with severe early-onset obesity was randomly chosen for ^{1}H-MRS. The sample size was determined based on our earlier MRS study on intramyocellular fat in obese adolescents [13]. A sample size of 35 individuals (17 overweight and 18 normal-weight) would allow us to detect a 15% difference in BMF UI at a significance level of 95% and with 80% power. Subjects were similar in height ($p = 0.9$), BMI ($p = 0.2$), age ($p = 0.6$) and gender ($p = 0.8$) compared to subjects with severe early-onset obesity in the whole cohort. Female subjects were overrepresented in the ^{1}H-MRS