J Musculoskel Neuron Interact 2004; 4(1):105-108

Review Article

Hylonome

Muscle mass during childhood – Relationship to skeletal development

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Abstract

Bone densitometric data often are difficult to interpret in children and adolescents because of large inter- and intraindividual variations in bone size. Here, we propose a functional approach to bone densitometry that addresses two questions: Is bone strength normally adapted to the largest physiological loads, that is, muscle force? Is muscle force adequate for body size? To implement this approach, forearm muscle cross-sectional area (CSA) and bone mineral content (BMC) of the radial diaphysis were measured in 349 healthy subjects from 6 to 19 years of age (183 girls), using peripheral quantitative computed tomography (pQCT). This functional approach to pediatric bone densitometric data should be adaptable to a variety of densitometric techniques.

Keywords: Muscle, Musculoskeletal, Bone Mass, Growth, Bone Density

Introduction

Bone densitometry currently is one of the mainstays in the evaluation of systemic bone diseases in adults[1] and also is increasingly used to assess bone disorders in children and adolescents[2]. The purpose of doing densitometric studies in such circumstances is to measure densitometric indicators of bone stability[3]. Following procedures that were established for diagnosing adult osteoporosis, a decrease in densitometric surrogates of bone stability usually is interpreted as indicating increased fracture risk. The most basic densitometric parameter is bone mineral content (BMC), which can be measured with most densitometric techniques. BMC is either defined as the mass of mineral contained in an entire bone (g) or as the mass of mineral per unit bone length (g/cm). Although mineral mass can be expected to be a good surrogate of bone stability, BMC obviously is a size-dependent parameter. This is a drawback, because short children will have a lower BMC than their healthy age-matched peers, even if their (smaller) bones are otherwise completely normal.

How then can densitometric data in children and adolescents be evaluated in a rational way? We propose a functional approach to this fundamental problem, which takes into account the balance between bone strength and the forces that normally challenge bone stability. The largest physiological loads on a bone result from muscle contraction[4,5]. Therefore, bone stability needs to be adapted to muscle force. This functional muscle-bone relationship could be used for diagnostic purposes, when densitometric surrogates of bone strength are compared with indicators of muscle force.

The aim of this study was to develop a simple diagnostic algorithm to evaluate musculoskeletal adaptation and thus create an index of the "functional muscle-bone unit"[6]. We established height-dependent reference ranges for muscle CSA at the forearm and muscle-related reference data for radial BMC at the same site.

Materials and methods

Healthy subjects

The reference population comprised 349 healthy children and adolescents aged 6–19 years (183 girls and 166 boys). Anthropometric data and age-dependent pQCT results of these individuals have been described previously[7-9].

The authors have no conflict of interest.

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Accepted 23 May 2003

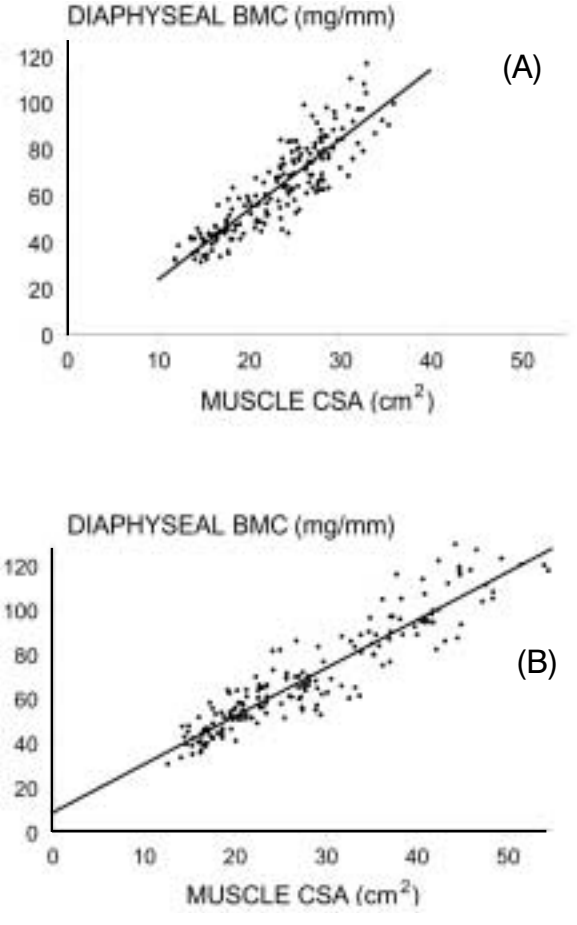

Figure 1. Relationship between muscle CSA and BMC at the proximal forearm in (A) girls and (B) boys. Regression equations: girls, BMC (mg/mm) = - 6.60 + 3.03 x muscle CSA (cm^2), $r = 0.89$; boys, BMC = 8.52 + 2.13 x muscle CSA, $r = 0.92$; $p < 0.001$ each. Reproduced from J Bone Miner Res 2002; 17:1095-1101 with permission of the American Society for Bone and Mineral Research.

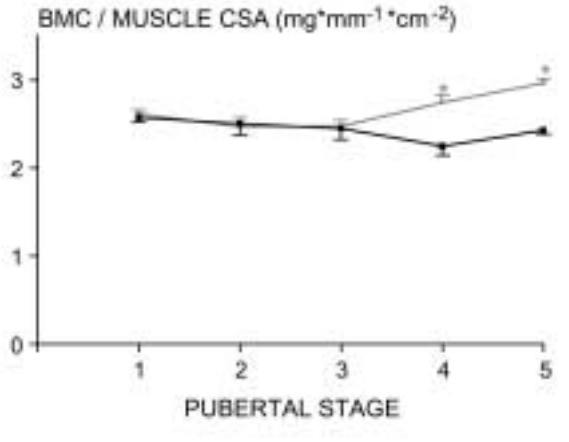

Figure 2. Variation with pubertal stage (mean and SE) in the ratio between BMC and muscle CSA in healthy girls and boys. Significant differences between the genders are indicated by an asterisk ($p < 0.01$ in both cases). The variation between pubertal stage groups are significant in both genders (girls $p < 0.0001$; boys $p = 0.003$ by Kruskal Wallis test). Reproduced from J Bone Miner Res 2002; 17:1095-1101 with permission of the American Society for Bone and Mineral Research.

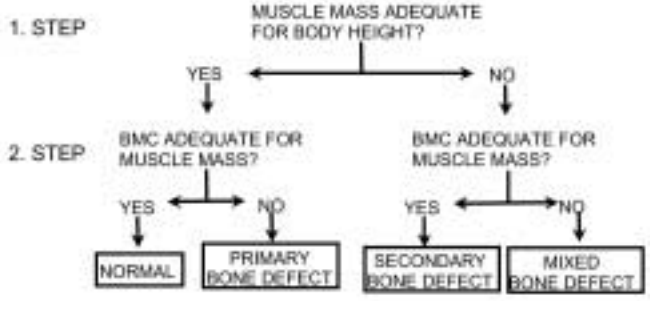

Figure 3. Proposed diagnostic algorithm. Reproduced from J Bone Miner Res 2002; 17:1095-1101 with permission of the American Society for Bone and Mineral Research.

Peripheral quantitative computed tomography

Peripheral quantitative computed tomography (pQCT) measurements were performed at the proximal nondominant forearm, as described in detail before[8-10]. Briefly, an XCT-2000 scanner (Stratec, Inc., Pforzheim; Germany) was used, which is equipped with a low-energy (38 keV) X-ray tube. The measurement was performed at a site in which the distance to the ulnar styloid process corresponded to 65% of forearm length.

Results

Regression analysis between body height and muscle CSA at the proximal forearm revealed a power relationship between the two parameters (regression equations: girls, muscle CSA [cm2] = 0.0021 * height 1.85 [cm], $r = 0.90$; boys, muscle CSA = 0.0004 * height 2.20, $r = 0.90$; $p < 0.0001$ each). Mean and SD of muscle CSA were calculated for height groups spanning 10 cm each (Table 1). Muscle CSA was larger in boys than in girls from 120 to 139 cm and from 160 to 179 cm.

There was a linear relationship between muscle CSA and BMC of the radial diaphysis (Fig. 1). Possibly, the simplest indicator of the muscle-bone relationship that can be derived from these data are the ratio between BMC and muscle CSA. Table 2 shows the variation with age in this ratio.

There was no gender difference in the BMD/muscle CSA ratio until pubertal stage 3, but girls had significantly higher values thereafter (Fig. 2).

Discussion

In this study we present a new diagnostic approach to evaluate densitometric data in children and adolescents. The theoretical background for this approach is provided by

Height range (cm)	n	*Girls*	n	*Boys*
120-129	27	15.8 ± 1.4*	26	17.1 ± 2.0
130-139	22	18.1 ± 2.4*	17	20.3 ± 2.5
140-149	18	20.8 ± 2.5	22	22.4 ± 3.7
150-159	38	24.8 ± 3.0	27	24.6 ± 4.0
160-169	43	27.4 ± 3.5*	21	30.5 ± 4.8
170-179	24	28.0 ± 3.3*	31	36.6 ± 6.3
180-189			12	40.8 ± 5.1

Values are mean ± SD.
A significant difference between results in girls and boys of the same height group ($p < 0.01$ in each case).
The variation between height groups was significant at $p < 0.0001$ in both genders (Kruskal Wallis test).

Table 1. Height dependent results for muscle CSA (cm^2) at the 65% site of the proximal forearm. Reproduced from J Bone Miner Res 2002; 17:1095-1101 with permission of the American Society for Bone and Mineral Research.

Age (years)	n	*Female*	n	*Male*
6-7	28	2.59 ± 0.29	27	2.54 ± 0.34
8-9	27	2.62 ± 0.38	22	2.55 ± 0.31
10-11	30	2.59 ± 0.35	31	2.58 ± 0.30
12-13	31	2.64 ± 0.40	27	2.47 ± 0.43
14-15	25	2.90 ± 0.35*	27	2.39 ± 0.32
16-17	23	2.91 ± 0.31*	21	2.36 ± 0.26
18-19	20	2.96 ± 0.36*	11	2.44 ± 0.26
p		<0.0001		0.09

Values are mean ± SD.
A significant difference between results in girls and boys of the same age group ($p < 0.001$ in each case).Value of p indicates the significance of the variation between age groups (Kruskal-Wallis test).

Table 2. Variation with age in the ratio between BMC (mg/mm) and muscle CSA (cm^2). Reproduced from J Bone Miner Res 2002; 17:1095-1101 with permission of the American Society for Bone and Mineral Research.

the mechanostat theory, which proposes that bones adapt their strength to keep the strain caused by physiological loads close to a set point[11,12]. We found that during puberty, the BMC/muscle CSA ratio increases in girls but not in boys. This mirrors our earlier observation that girls and boys have a similar muscle-bone relationship regarding external bone size, but girls have a relatively smaller marrow cavity[10]. These observations are in accordance with the hypothesis that estrogen lowers the mechanostat set point on endosteal bone surfaces[13]. The changes in BMC/muscle CSA during female puberty could be an example of how hormonal factors can modulate the muscle-bone relationship[13]. Regarding the application of the muscle-bone relationship to clinical practice, we propose the two-step diagnostic algorithm shown in Fig. 3. Required are a measure of muscle force or size and a measure of BMC at a corresponding location. The results can be combined into four diagnostic groups. In the first situation, muscle force or size is adequate for height. If BMC is adapted normally to the muscle system, the result is interpreted as "normal". If BMC is lower than expected for muscle force or size, a "primary bone defect" is diagnosed. In the second situation, muscle force or size is too low for height. Even if BMC is adapted adequately to the decreased mechanical challenge, this means that bone mass and presumably strength are still too low for body height. Therefore, a "secondary bone defect" is diagnosed. If muscle force or size is abnormally low and BMC is even lower than expected from a normal muscle bone relationship, a "mixed bone defect" (primary and secondary) is present. This diagnostic procedure resembles a classification of disorders with low bone mass that was proposed by Frost. That classification distinguished "true osteoporosis," "physiological osteopenia," and "combination states"[14]. We prefer the qualifications "primary" and "secondary" to "true" and "physiological," because even physiological osteopenia may result in serious morbidity.

It should be possible to adapt the general idea of this diagnostic approach to densitometric techniques other than pQCT. Body height and BMC are routine measures, but probably many pediatric densitometry units do not yet perform concomitant analyses of local muscle force or size.

Further studies are needed to work out the methodological details when devices other than pQCT are used for this purpose.

In conclusion, we are proposing a new diagnostic approach to pediatric bone diseases, which is based on the analysis of the balance between bone strength and the physiological challenge to bone strength.

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