

The ‘muscle-bone unit’ during the pubertal growth spurt

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Abstract

Mechanostat theory postulates that developmental changes in bone strength are secondary to the increasing loads imposed by larger muscle forces. Therefore, the increase in muscle strength should precede the increase in bone strength. We tested this prediction using densitometric surrogate measures of muscle force (lean body mass, LBM) and bone strength (bone mineral content, BMC) in a study on 70 boys and 68 girls who were longitudinally examined during pubertal development. On the level of the total body, the peak in LBM accrual preceded the peak in BMC accretion by an average of 0.51 years in girls and by 0.36 years in boys. In the arms, the maximal increase in LBM was followed by arm peak BMC accrual after an interval of 0.71 years in girls and 0.63 years in boys. In the lower extremities, the maximal increase in LBM was followed by peak BMC accrual after an interval of 0.22 years in girls and 0.48 years in boys. A multiple regression model revealed that total body peak LBM velocity, but not peak height velocity and sex, was independently associated with total body peak BMC velocity ($r^2 = 0.50$; $P < 0.001$). Similarly, arm and leg peak LBM velocity, but not peak height velocity and sex, were independently associated with arm and leg peak BMC velocity, respectively ($r^2 = 0.61$ for arms, $r^2 = 0.41$ for legs; $P < 0.001$ in both cases). These results are compatible with the view that bone development is driven by muscle development, although the data do not exclude the hypothesis that the two processes are independently determined by genetic mechanisms.

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Introduction

It has been known for more than three decades that muscle mass and bone mass are closely associated [1]. More recently, analogous correlations have been found by using densitometric surrogate measures of muscle mass (lean body mass, LBM) and bone mass (bone mineral content, BMC). The correlation between these two parameters is especially close during growth and development [2–6]. It has also been observed that the sequence of timing for peak accrual in the soft tissues and BMC is similar in both sexes [7].

Mechanostat theory postulates that the statistical association between LBM and BMC reflects a direct cause-and-

effect relationship [8,9]. According to this hypothesis, the skeleton continually adapts its strength to the loads to which it is exposed to keep bone deformation within safe limits. The largest physiological loads on the skeleton result from muscle contraction, which puts several fold larger stresses on the skeleton than the simple effect of gravity [10,11]. Mechanostat theory therefore predicts that the increasing muscle mass (and thus muscle force) during development creates the stimulus for the increase in bone mass (and thus in bone strength).

Although mechanostat theory primarily is an attempt to explain bone physiology and pathophysiology, its conclusions have direct implications on how bone disorders in children are assessed and treated. If muscle forces drive bone development, then analyses of muscle function should be added to the armamentarium of clinicians diagnosing bone disorders. Many bone disorders may at least partly be due to muscle disuse or dysfunction, opening a new field of potential targets for therapeutic interventions [12]. Given

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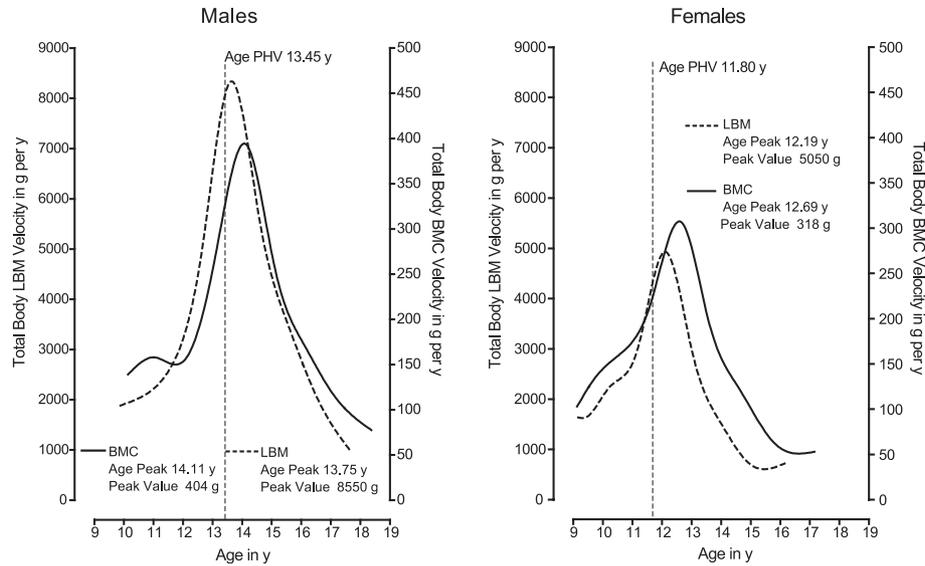


Fig. 1. Velocities of total body LBM and BMC accretion during the pubertal growth spurt. The age at PHV is shown as a reference point for pubertal development.

these far-reaching implications of mechanostat theory, it is important to evaluate it from as many different angles as possible.

If muscle force during development really drives bone strength as mechanostat theory postulates, then the increase in muscle development must precede and should determine the increase in BMC. Examining the adolescent growth spurts in lean and bone tissue provides a model to test this hypothesis in healthy children. The maximal rates of LBM and BMC accretion during this period can serve as markers to establish the temporal sequence of developmental events. In this longitudinal study, we therefore investigated the relationship between pubertal peak velocity in lean body mass accretion (PVLBM) and peak velocity in bone mineral content accretion (PVBMC). For comparison, peak height velocity (PHV) was also analyzed, as this is a well-established marker of pubertal events.

Materials and methods

Subjects

All subjects were participants in the University of Saskatchewan Pediatric Bone Mineral Study. Of 375 eligible students attending two elementary schools in Saskatoon, Canada, 113 boys and 115 girls, ranging in age from 8 to 14 years, were initially enrolled in this multiyear longitudinal study. Height and weight were taken on all subjects every 6 months. Dual-Energy X-ray Absorptiometry (DXA) scans were performed annually.

Only those subjects who clearly showed a peak in their height and BMC velocity curves were selected for the longitudinal analysis, resulting in a final sample size of 70 boys and 68 girls. Subjects who were excluded were

primarily individuals who were beyond their age of PHV when first measured. All testing was done at the Royal University Hospital (Department of Nuclear Medicine) in Saskatoon. All study procedures were approved by appropriate university and hospital ethics committees and informed consent was obtained as described before [13].

Bone and height measurements

DXA scans (Hologic QDR 2000; Hologic, Waltham, MA, USA) of the whole body were carried out annually in October or November of each year by one of two experienced operators, as described in detail before [14]. Measurements

Table 1

Age of peak velocity and peak velocity values in total body and segmental growth

	Boys (<i>n</i> = 70)		Girls (<i>n</i> = 68)	
	Mean	SD	Mean	SD
<i>Age at peak velocity</i>				
Height (years)	13.45	0.97	11.80	0.86
Total Body LBM (years)	13.75	0.97	12.19	0.96
Total Body BMC (years)	14.11	0.97	12.69	0.90
Arm LBM (years)	13.75	1.03	12.19	1.18
Arm BMC (years)	14.38	1.27	12.90	1.25
Leg LBM (years)	13.56	0.99	12.10	0.97
Leg BMC (years)	14.04	1.20	12.32	0.95
<i>Peak velocity values</i>				
Height (cm/year)	10.4	1.3	8.5	1.1
Total Body LBM (g/year)	8550	1672	5050	1212
Total Body BMC (g/year)	404	91	318	64
Arm LBM (g/year)	1128	282	507	145
Arm BMC (g/year)	64	18	41	10
Leg LBM (g/year)	3213	642	1886	481
Leg BMC (g/year)	174	42	135	31

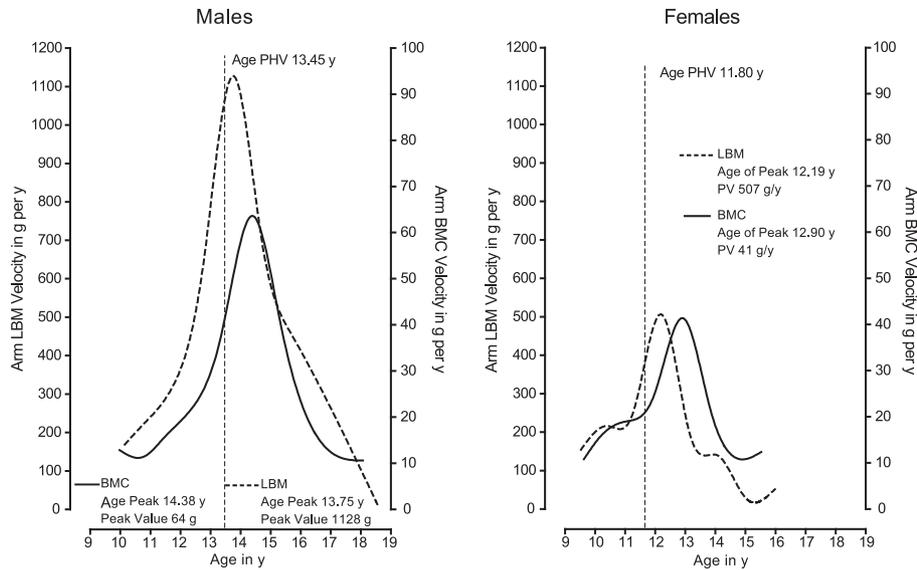


Fig. 2. Velocities of upper extremity LBM and BMC accretion during the pubertal growth spurt. The age at PHV is shown as a reference point for pubertal development.

were done in the array mode using enhanced global software version 7.10. Results for upper and lower extremities correspond to the sum of the results of the right and left sides. Height measures were taken at 6-month intervals and recorded without shoes as stretch stature to 0.1 cm using a wall stadiometer.

Data analysis

Because subjects were not re-measured on exactly the same dates each year, whole-year velocity values were calculated for each subject by dividing the time between the quasi-annual LBM and BMC measurements by the age increment (mean value, 0.998 ± 0.048 years). A cubic

spline fit was then applied to the whole-year height, LBM and BMC velocity values for each child. This allowed the determination of the peak velocity values and the age at which it occurred. Differences between ages at PVLBM and PVBMC were evaluated by paired *t* test. Multiple regression analyses were performed in the stepwise forward mode. A *P* value below 0.05 was considered significant.

Results

PHV preceded the peak in total body LBM by an average of 0.39 (SD 0.57) years in girls and by 0.30 (SD 0.49) years

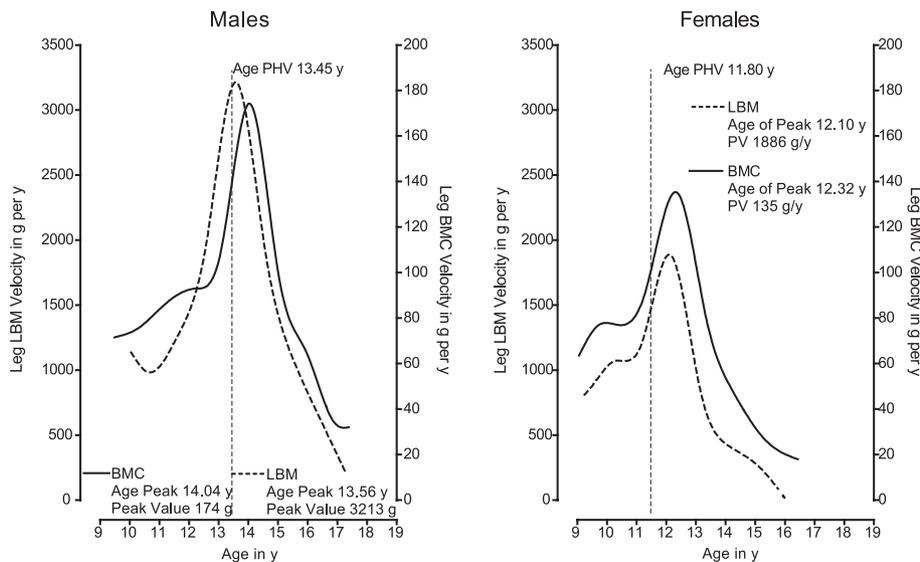


Fig. 3. Velocities of lower extremity LBM and BMC accretion during the pubertal growth spurt. The age at PHV is shown as a reference point for pubertal development.

in boys (Fig. 1; Table 1). The peak in total body PVLBM preceded the peak in total body PVBMC ($P < 0.001$ in both sexes) by an average of 0.51 (SD 0.47) years in girls and by 0.36 (SD 0.47) years in boys. Total body PVLBM occurred before total body PVBMC in 59 (87%) of the girls and in 54 (77%) of the boys. A multiple regression model that tested sex, PHV, and total body PVLBM as predictors of total body PVBMC revealed that only PVLBM was independently associated with total body PVBMC ($r^2 = 0.50$; $P < 0.001$).

Analogous analyses of the upper extremities showed that PHV preceded arm PVLBM by 0.39 years in girls and by 0.30 years in boys (Fig. 2). Arm PVLBM was followed by arm PVBMC after an interval of 0.71 years in girls and 0.63 years in boys. A multiple regression model that tested sex, PHV, and arm PVLBM as predictors of arm PVBMC revealed that only arm PVLBM was independently associated with arm PVBMC ($r^2 = 0.61$; $P < 0.001$).

In the lower extremities, PHV preceded PVLBM by 0.30 years in girls and by 0.11 years in boys (Fig. 3). Leg PVLBM was followed by leg PVBMC after an interval of 0.22 years in girls and 0.48 years in boys. A multiple regression model that tested sex, PHV, and leg PVLBM as predictors of leg PVBMC revealed that only leg PVLBM was independently associated with leg PVBMC ($r^2 = 0.41$; $P < 0.001$).

Discussion

In this study, we compared the maximal accretion rates for a marker of muscle force (LBM) and a surrogate measure of bone strength (BMC). Both at the level of the entire body and in the upper and lower extremities, the maximal rate of LBM accrual occurred a few months before the maximal increase in BMC, and the peak rates of change in these two measures were closely correlated. These observations are in accordance with the postulate from mechanostat theory that the increase in muscle force drives the increase in bone strength during development.

It must be acknowledged that the present data do not establish a direct cause-and-effect relationship between muscle force and bone strength. It can be argued that both parameters are independently controlled by other factors, notably genetic determinants [15]. However, a functional relationship between mechanical forces and bone development is supported by the clinical observation that disease processes interfering with muscle development (e.g., muscle dystrophy, spina bifida, poliomyelitis) invariably have a negative effect on bone development [16–18]. Conversely, orthopedic surgeons make use of the fact that a ‘weak’ bone such as the fibula can hypertrophy to replace the much stronger tibia, if mechanically needed [19]. These observations are hardly compatible with the idea that bone development is genetically programmed to be independent of mechanical requirements. In any case, the main factors

determining the mechanical forces to which the skeleton is exposed (muscle forces, length of lever arms, body weight), as well as the bones’ mechanosensitivity are certainly genetically determined to a large extent. Therefore, the distinction between ‘genetic’ and ‘mechanical’ factors may not be helpful for evaluating determinants of bone development.

In this study, the maximal rate of LBM accrual at each site was related to the maximal rate of bone mass accumulation, whereas PHV was not independently associated with peak bone mass accretion. This mirrors recent findings by Ruff [20], who found that PHV was a weak predictor of changes in humerus and femur diaphysis strength, as estimated from serial radiographs.

One obvious limitation of the present study stems from the use of DXA for assessing the muscle–bone relationship. BMC was used as a surrogate marker of bone strength, which does not take into account determinants of bone strength other than bone mass, such as bone geometry. Similarly, we did not analyze the actual forces generated by muscle action, but used LBM as a surrogate measure. Therefore, our results are a first approximation rather than a precise evaluation of the muscle–bone unit.

In conclusion, this study is in accordance with the hypothesis derived from mechanostat theory that muscle development precedes bone development during the pubertal growth spurt. However, the data do not exclude the view that the two processes are independently determined by genetic mechanisms. Thus, further studies are required to establish a cause-and-effect relationship between muscle and bone development.

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