Early Identification of Children Predisposed to Low Peak Bone Mass and Osteoporosis Later in Life*

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ABSTRACT

The amount of bone that is gained during adolescence is the main contributor to peak bone mass, which, in turn, is a major determinant of osteoporosis and fracture risk in the elderly. We examined whether computed tomography measurements for bone density and the volume of bone in the axial and appendicular skeletons could be tracked through puberty in 40 healthy white children (20 girls and 20 boys). Longitudinal measurements of the cross-sectional area and cancellous bone density of the vertebral bodies and the cross-sectional and cortical bone areas of the femurs at the beginning of puberty accounted for 62–92% of the variations seen at sexual maturity; on average, 3 yr later. When baseline values for these bone traits were divided into quartiles, a linear relation across Tanner stages of sexual development was observed in both girls and boys. The regression lines differed among quartiles for each trait, paralleled each other, and did not overlap. Thus, we are now in a position to identify those children who are genetically prone to develop low values for peak bone mass and toward whom osteoporosis prevention trials should be geared. (J Clin Endocrinol Metab 85: 3908–3918, 2000)

RECENT DATA suggest that the genetic susceptibility to osteoporosis may be detectable in early childhood (1). Studies have shown a familial resemblance for bone mineral mass between prepubertal girls and their mothers and that genes linked to osteoporosis and/or fractures in adulthood are associated with low bone mass in prepubertal children (1–3). In addition, peak bone mass, a major determinant of the risk for osteoporosis and fractures in the elderly, is virtually achieved at the end of sexual development in the lumbar spine and the femur (4–6). By the age of 16 yr, most children have completed sexual maturity, and studies have shown that bone mass values in girls by this age are equal or greater to that of their premenopausal mothers (7, 8).

Puberty is the time of life when the greatest acquisition of bone occurs (6, 9). Regardless of gender, bone mass more than doubles during puberty (10). In this study, we used computed tomography (CT) to longitudinally measure the densities of cancellous and cortical bone and the cross-sectional dimensions of bone in the axial and appendicular skeletons of children at each Tanner stage of sexual development from early puberty to sexual maturity. Our aims were to examine whether measures for quantitative phenotypic traits, which contribute to bone mass and bone strength, at sexual maturity can be predicted from values in early puberty and to assess the constancy of a child’s expected measures relative to population percentiles. This knowledge may aid in the early identification of those children who are at risk for osteoporosis and fragility fractures later in life.

Subjects and Methods

Study population

The study subjects were healthy white children who were recruited from schools of Los Angeles County. The investigational protocol was approved by the institutional review board for clinical investigations at Children’s Hospital Los Angeles, and informed consent was obtained from all subjects and their parents.

The children and their parents were asked about their medical history. Candidates were excluded if they had been given a diagnosis of chronic illness, had been ill for longer than 2 weeks during the previous 6 months, had taken any medications regularly within the previous 6 months, or had been hospitalized at any time since birth. Eligible candidates underwent a physical examination by a pediatric endocrinologist to determine their stage of sexual development. The grading system of Tanner was used, which includes assessments of the pattern of development of pubic hair in all children and of breast development in girls and penile and testicular size in boys (11). If discrepancies existed among criteria, greater emphasis was placed on the degree of breast development in girls and on testicular and penile size in boys, for determinations of Tanner stage. Only children in early puberty (Tanner stage 2) were enrolled in this study. Measurements of height, weight, and sitting height were obtained, and thereafter body surface area and body mass indices were calculated (12). Skeletal maturation was assessed on the basis of roentgenograms of the left hand and wrist according to the method of Greulich and Pyle (13), and those in whom skeletal age differed from chronological age by more than 1 yr were excluded from further evaluation. On the same day, measurements of bone size and bone density were obtained by CT. Subsequently, participants were given instructions to record their dietary intake over a 3-day period.
Using this approach, a total of 50 healthy children (25 girls and 25 boys) were enrolled in this study. All participants were asked to return every 6 months for a physical examination, and CT bone measurements were repeated at each change in Tanner stage from baseline (Tanner 2) to sexual maturity (Tanner 5). During the course of the study, 10 children were withdrawn [5 due to residence relocation (2 girls and 3 boys), 2 began taking birth control pills, 1 became pregnant, 1 boy was severely injured in an automobile accident, and another was randomly excluded at completion of the study; 5 due to accident, and another was randomly excluded at completion of the study. Thus, we longitudinally studied the changes in bone density and bone size in the axial and appendicular skeletons of 20 girls and 20 boys from the beginning of puberty to sexual maturity.

Techniques and definitions of CT measurements

All CT measurements were done with the same scanner (CT-T 9800; General Electric Co., Milwaukee, WI), mineral reference phantom (CT-T bone densitometry package; General Electric Co.), and specially designed software. For determinations in the axial skeleton, the apparent density of cancellous bone and the cross-sectional area were measured at the lumbar vertebrae, and, in the appendicular skeleton, the cross-sectional area, the cortical bone area, and the material density of cortical bone were measured at the midshaft of both femurs, as described previously (14, 15). For this study, the density of cancellous bone was defined as the mean value of the CT unit of measurement (mg/cm³) at the midportion of the first three lumbar vertebral bodies. Because of the relatively small size of the trabeculae when compared with the pixel, CT values for apparent cancellous bone density reflect not only the amount of mineralized bone and osteoid, but also the amount of marrow per pixel (16). These measurements are analogous to in vitro determinations of the volumetric density of trabecular bone, which are obtained by washing the marrow from the pores of a specimen of cancellous bone, weighing it, and dividing the weight by the volume of the specimen, including the pores (17). The density of cortical bone was defined as the amount of bone per pixel (mg/cm³) at the midshaft of the femur. Because of the thickness and the relative lack of porosity of cortical bone in both sexes, the CT values reflect the material or true density of the bone (the amount of collagen and mineral in a given volume of bone) (14). These measurements are analogous to in vitro determinations of the intrinsic mineral density of bone, which are commonly expressed as the ash weight per unit volume of bone (18).

The coefficients of variation for repeated CT measurements of vertebral cross-sectional area, cancellous bone density, femoral cross-sectional area, cortical bone area and cortical bone density were calculated to be between 0.6% and 2.0% (14, 15). The time required for the procedure was ~10 min, and the radiation exposure was ~100–200 mrem (1.5 mSv) localized to the midportions of the first three lumbar vertebrae and the femurs; the effective radiation dose was 10 min, and the radiation exposure was 1.5 mSv localized to the midportions of the first three lumbar vertebrae and the femurs; the effective radiation dose was 1.5 mSv. Differences among quartiles were assessed by linear trend analysis using a repeated measures model with unstructured covariance matrix (22, 23). An α level of 0.05 was accepted for significance in all statistical procedures.

Results

The age and anthropometric characteristics of the children studied at different Tanner stages of sexual development are shown in Table 1. As expected, these parameters increased with advancing sexual development in all children. There were significant gender differences in the duration of puberty and, on average, girls took 2.7 ± 0.54 yr whereas boys took 3.2 ± 0.71 yr to reach sexual maturity from Tanner stage 2 (P = 0.007). Moreover, girls were slightly younger than boys at all Tanner stages of sexual development.

Tables 2 and 3 show the mean values for the 3-day dietary intake records of the children. No significant changes in dietary intake were observed with advancing Tanner stage in girls or boys. Calcium intake was higher in boys than in girls throughout the study; on average, 966 ± 379 mg/day vs. 710 ± 238 mg/day, respectively. These gender differences were significant at Tanner 4 (P = 0.017) and when dietary calcium at all Tanner stages was used as a vector of observation; Hotelling’s T² test (P < 0.003). No significant correlations were found between caloric intake and CT values for any of the bone traits. Additionally, there were no correlations between calcium intake and increases in CT values of the cross-sectional dimensions of the vertebrae or the femurs, the density of cancellous bone in the vertebrae, or the density of cortical bone in the femurs in either boys or girls; all correlation coefficients are between −0.18 and 0.14.

CT values for the cross-sectional dimensions and the density of bone in the axial and appendicular skeletons of girls and boys from Tanner 2 to Tanner 5 are shown in Table 4. Significant increases in values for all skeletal phenotypes were observed with each advancing Tanner stage of sexual development in all children. There was, however, no association between the timing (the age at Tanner 2) or the duration (the difference in age between Tanner 5 and Tanner 2) of puberty and peak values for any of the CT bone measurements.

### Table 1. Ages and anthropometric measurements for 20 girls and 20 boys at different Tanner stages of sexual development

<table>
<thead>
<tr>
<th>Tanner stage</th>
<th>Age (yr)</th>
<th>Bone age (yr)</th>
<th>Height (cm)</th>
<th>Sitting height (cm)</th>
<th>Weight (kg)</th>
<th>Surface area (m²)</th>
<th>Body mass index (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>12.3 ± 1.0</td>
<td>12.6 ± 1.0</td>
<td>153 ± 5.7</td>
<td>79.9 ± 3.2</td>
<td>44.0 ± 10.0</td>
<td>1.4 ± 0.2</td>
<td>18.9 ± 3.9</td>
</tr>
<tr>
<td>3</td>
<td>12.9 ± 1.0</td>
<td>13.5 ± 1.1</td>
<td>157 ± 5.6</td>
<td>81.4 ± 3.0</td>
<td>49.9 ± 11.3</td>
<td>1.4 ± 0.2</td>
<td>20.1 ± 4.3</td>
</tr>
<tr>
<td>4</td>
<td>13.6 ± 0.8</td>
<td>14.7 ± 0.8</td>
<td>159 ± 4.8</td>
<td>82.9 ± 2.3</td>
<td>52.8 ± 12.6</td>
<td>1.5 ± 0.2</td>
<td>20.6 ± 4.8</td>
</tr>
<tr>
<td>5</td>
<td>15.0 ± 0.8</td>
<td>15.9 ± 0.6</td>
<td>163 ± 4.4</td>
<td>83.4 ± 2.4</td>
<td>56.5 ± 14.7</td>
<td>1.6 ± 0.2</td>
<td>21.2 ± 5.6</td>
</tr>
<tr>
<td>Boys</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>12.4 ± 0.6</td>
<td>12.2 ± 0.6</td>
<td>155 ± 6.6</td>
<td>81.7 ± 3.0</td>
<td>46.3 ± 11.3</td>
<td>1.4 ± 0.2</td>
<td>19.2 ± 3.7</td>
</tr>
<tr>
<td>3</td>
<td>13.7 ± 0.6</td>
<td>13.2 ± 0.6</td>
<td>164 ± 6.4</td>
<td>84.6 ± 2.9</td>
<td>54.0 ± 13.9</td>
<td>1.5 ± 0.2</td>
<td>20.3 ± 4.5</td>
</tr>
<tr>
<td>4</td>
<td>14.5 ± 0.7</td>
<td>14.3 ± 1.0</td>
<td>168 ± 6.0</td>
<td>86.7 ± 2.8</td>
<td>59.0 ± 14.6</td>
<td>1.6 ± 0.2</td>
<td>21.1 ± 4.6</td>
</tr>
<tr>
<td>5</td>
<td>15.6 ± 0.9</td>
<td>15.7 ± 0.9</td>
<td>173 ± 6.1</td>
<td>87.7 ± 3.3</td>
<td>65.8 ± 18.3</td>
<td>1.7 ± 0.2</td>
<td>22.2 ± 5.7</td>
</tr>
</tbody>
</table>

All values are expressed as mean ± SD.
When all Tanner stages were considered together or when bone and the cross-sectional area of the femurs; this was true when children were positively correlated with the area of cortical bone (r = 0.36 and 0.56).

Changes in standing height (correlation coefficients between 0.63 and 0.72), than with bone areas and gains in body weight (regardless of gender, r = 0.29). In contrast, stronger correlations were seen between increments in the femoral cross-sectional and cortical bone density, there were substantial differences in cross-sectional bone growth between boys and girls. Moreover, gender had a differential effect on cross-sectional bone growth in the axial and appendicular skeletons. At commencement of the study, boys had significantly greater vertebral cross-sectional area than girls (23%; P = 0.001), but not significantly greater femoral cross-sectional or cortical bone area. At completion, gender differences in the appendicular skeleton had increased and boys had significant

**TABLE 2.** Dietary intake for 20 girls at different Tanner stages of sexual development

<table>
<thead>
<tr>
<th>Tanner stage</th>
<th>Tanner 2</th>
<th>Tanner 3</th>
<th>Tanner 4</th>
<th>Tanner 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories (kc)</td>
<td>1902 ± 354</td>
<td>1750 ± 350</td>
<td>1776 ± 326</td>
<td>1702 ± 438</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>80 ± 17</td>
<td>71 ± 13</td>
<td>71 ± 15</td>
<td>67 ± 19</td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>250 ± 49</td>
<td>228 ± 55</td>
<td>235 ± 53</td>
<td>227 ± 65</td>
</tr>
<tr>
<td>Sugar (g)</td>
<td>95 ± 22</td>
<td>79 ± 33</td>
<td>82 ± 31</td>
<td>78 ± 24</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>72 ± 18</td>
<td>63 ± 15</td>
<td>63 ± 14</td>
<td>61 ± 19</td>
</tr>
<tr>
<td>Crude fiber (g)</td>
<td>3.79 ± 1.14</td>
<td>3.44 ± 1.58</td>
<td>2.75 ± 1.38</td>
<td>3.22 ± 1.46</td>
</tr>
<tr>
<td>Vitamin D (g)</td>
<td>4.13 ± 1.93</td>
<td>3.45 ± 2.29</td>
<td>3.23 ± 1.24</td>
<td>2.71 ± 1.42</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>777 ± 289</td>
<td>694 ± 288</td>
<td>675 ± 154</td>
<td>693 ± 222</td>
</tr>
<tr>
<td>Phosphorus (mg)</td>
<td>1200 ± 274</td>
<td>1035 ± 255</td>
<td>990 ± 179</td>
<td>1004 ± 320</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>215 ± 48</td>
<td>90 ± 55</td>
<td>182 ± 42</td>
<td>205 ± 69</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>2667 ± 845</td>
<td>2272 ± 640</td>
<td>2568 ± 1291</td>
<td>2183 ± 733</td>
</tr>
</tbody>
</table>

All values are expressed as mean ± sd.

**TABLE 3.** Dietary intake for 20 boys at different Tanner stages of sexual development

<table>
<thead>
<tr>
<th>Tanner stage</th>
<th>Tanner 2</th>
<th>Tanner 3</th>
<th>Tanner 4</th>
<th>Tanner 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories (kc)</td>
<td>2350 ± 310</td>
<td>2310 ± 430</td>
<td>2299 ± 436</td>
<td>2377 ± 460</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>87 ± 20</td>
<td>85 ± 19</td>
<td>85 ± 19</td>
<td>92 ± 16</td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>314 ± 50</td>
<td>305 ± 74</td>
<td>311 ± 65</td>
<td>316 ± 72</td>
</tr>
<tr>
<td>Sugar (g)</td>
<td>11 ± 35</td>
<td>11 ± 35</td>
<td>11 ± 30</td>
<td>12 ± 29</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>85 ± 16</td>
<td>85 ± 25</td>
<td>82 ± 22</td>
<td>84 ± 22</td>
</tr>
<tr>
<td>Crude fiber (g)</td>
<td>5.20 ± 3.87</td>
<td>4.26 ± 1.86</td>
<td>3.99 ± 1.61</td>
<td>4.41 ± 1.89</td>
</tr>
<tr>
<td>Vitamin D (g)</td>
<td>5.52 ± 3.64</td>
<td>4.76 ± 3.41</td>
<td>5.79 ± 3.91</td>
<td>4.53 ± 2.22</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>973 ± 376</td>
<td>965 ± 394</td>
<td>1012 ± 481</td>
<td>915 ± 346</td>
</tr>
<tr>
<td>Phosphorus (mg)</td>
<td>1371 ± 320</td>
<td>1396 ± 370</td>
<td>1366 ± 387</td>
<td>1393 ± 307</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>342 ± 392</td>
<td>245 ± 67</td>
<td>244 ± 76</td>
<td>246 ± 64</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>3284 ± 639</td>
<td>3239 ± 1049</td>
<td>3015 ± 819</td>
<td>2038 ± 979</td>
</tr>
</tbody>
</table>

All values are expressed as mean ± sd.

**TABLE 4.** CT bone measurements for 20 girls and 20 boys at different Tanner stages of sexual development

<table>
<thead>
<tr>
<th>Tanner stage</th>
<th>Girls</th>
<th>Boys</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanner stage</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Cross-sectional area (cm²)</td>
<td>7.56 ± 0.84</td>
<td>7.82 ± 0.86</td>
<td>7.99 ± 0.93</td>
<td>8.10 ± 0.95</td>
<td>9.30 ± 1.20</td>
<td>9.77 ± 1.19</td>
<td>10.14 ± 1.28</td>
</tr>
<tr>
<td>Cortical bone area (cm²)</td>
<td>254 ± 25</td>
<td>270 ± 25</td>
<td>287 ± 27</td>
<td>300 ± 28</td>
<td>248 ± 30</td>
<td>266 ± 39</td>
<td>282 ± 35</td>
</tr>
<tr>
<td>Cancellous bone density (mg/cm³)</td>
<td>4.38 ± 0.54</td>
<td>4.57 ± 0.59</td>
<td>4.72 ± 0.57</td>
<td>4.80 ± 0.51</td>
<td>4.87 ± 0.62</td>
<td>5.39 ± 0.62</td>
<td>5.69 ± 0.66</td>
</tr>
<tr>
<td>Cortical bone density (mg/cm³)</td>
<td>3.43 ± 0.36</td>
<td>3.69 ± 0.37</td>
<td>3.81 ± 0.38</td>
<td>3.90 ± 0.43</td>
<td>3.55 ± 0.49</td>
<td>4.15 ± 0.48</td>
<td>4.47 ± 0.51</td>
</tr>
</tbody>
</table>

All values are expressed as mean ± sd.

Whereas gains in CT values for cancellous bone density correlated weakly with height and weight, cortical bone density values were not influenced by either parameter. Gains in the cross-sectional dimensions of the vertebrae and the femurs correlated significantly with gains in all anthropometric indices. Increments in cross-sectional vertebral area from the beginning to the end of puberty were more closely associated with increases in standing height (r = 0.69 for girls; r = 0.43 for boys) than with changes in body weight (both, r = 0.29). In contrast, stronger correlations were seen between increments in the femoral cross-sectional and cortical bone areas and gains in body weight (regardless of gender, all correlation coefficients between 0.63 and 0.72), than with changes in standing height (correlation coefficients between 0.36 and 0.56).

Overall, values for the vertebral cross-sectional area in all children were positively correlated with the area of cortical bone and the cross-sectional area of the femurs; this was true when all Tanner stages were considered together or when each Tanner stage was evaluated separately (all correlation coefficients were between 0.52 and 0.68). However, no correlation was found between the material density of cortical bone in the femurs and the apparent density of cancellous bone in the vertebral bodies. Values for cortical bone density were eight times higher than those for cancellous bone density, a finding consistent with histomorphometric studies, indicating an equivalent difference in the porosity of these two types of bone (24).

Although there were no gender differences in values for cancellous or cortical bone density, there were substantial differences in cross-sectional bone growth between boys and girls. Moreover, gender had a differential effect on cross-sectional bone growth in the axial and appendicular skeletons. At commencement of the study, boys had significantly greater vertebral cross-sectional area than girls (23%; P = 0.001), but not significantly greater femoral cross-sectional or cortical bone area. At completion, gender differences in the appendicular skeleton had increased and boys had signifi-
cantly greater femoral cross-sectional dimensions than girls (18% and 17% for the cross-sectional and cortical bone areas, respectively; both, $P < 0.0001$). However, multiple regression analysis indicated that the greater increases in the cross-sectional growth of the femurs in boys were related to simultaneous greater gains in height and body weight. In
contrast, gender differences in vertebral cross-sectional area persisted even after accounting for the confounding effects of body size.

Figures 1-4, panel a, shows values for vertebral cross-sectional area, vertebral cancellous bone density, femoral cross-sectional area, and femoral cortical bone area of each
boy and girl at the different Tanner stages. There were strong correlations between the values for each bone trait at the different Tanner stages in all subjects, and measurements in early puberty accounted for 62–92% of the variations seen at sexual maturity (Table 5). Based on the initial CT measurements in both boys and girls, values for vertebral and femoral cross-sectional area, femoral cortical area, and the density of cancellous bone were independently stratified into quartiles;
each quartile represented the mean value for five measurements. Linear trend analyses using a repeated measures model with unstructured covariance matrix revealed a linear regression across the Tanner stages at each baseline quartile for each of these traits. Moreover, regardless of gender, the regression lines across Tanner stages for each phenotype
differed among quartiles and did not overlap (Figs. 1–4, panel b). In contrast, values for femoral cortical bone density at the beginning of puberty did not predict those at sexual maturity and the linear regressions for the different quartiles intersected and were not parallel (Fig. 5).

**Discussion**

The results of the current study indicate that, in girls and boys, values for the bone traits associated with bone mass and the strength of the bone in the axial and appendicular skeletons at early puberty predict values at sexual maturity. Measurements of the cross-sectional dimensions of the femurs and lumbar vertebral bodies and of the density of cancellous bone at the beginning of puberty accounted for 62–92% of the variations seen at sexual maturity; on average, 3 yr later. Thus, although more than 60% of peak bone mineral mass is gained during puberty (6, 9), children retain their bone phenotypes and tracking for skeletal size, bone volume, and cancellous bone density is maintained throughout sexual development. On average, tracking for these phenotypes during puberty is as striking as that observed for standing height. Furthermore, when values for these bone traits are divided into quartiles, a linear relation across Tanner stages of sexual development at each baseline quartile is observed. The regression lines differ among quartiles for each trait, parallel each other, and do not overlap. These findings indicate that we are now in a position to identify those children who are genetically prone to attain low values for peak bone mass.

In contrast to the other bone phenotypes studied, there was no correlation between CT values for the material density of bone at early puberty and values at sexual maturity in either boys or girls. We found, however, small, but significant, increases in the density of cortical bone at the midshaft of the femur in both boys and girls from Tanner stage 2 to Tanner stage 5, on average, by about 3%. Unfortunately, it remains unclear whether the gains in bone density were due to an increase in mineralization or a decrease in porosity, because the limited resolution of CT scanners cannot correct for inaccuracies related to the number and diameter of the Haversian canals. It should be noted that the findings in the present study conflict with our previously published reports, suggesting that the material density of cortical bone remains constant throughout childhood and is not influenced by puberty (14, 25). This discrepancy is likely the reflection of the cross-sectional nature of the previous investigations and the rather small gains in CT values for cortical bone density that occur during puberty.

Several investigators have proposed that during puberty there is a physiologic and temporary decrease in the material density of bone. The contention is that during puberty there is either an increase in unmineralized osteoid as bone formation outstrips mineral deposition or an increase in bone porosity associated with the greater bone remodeling rate of the growing skeleton (26, 27). However, our results do not support this hypothesis because the material density of bone increases, rather than decreases, during puberty. On the other hand, our findings are in accordance with a previous longitudinal study using dual-energy x-ray absorptiometry that showed parallel increases in standing height and bone mass at the midshaft of the femur in girls during puberty (28).

In the axial skeleton, cancellous bone density in the vertebral increased during puberty, a finding that corroborates previous cross-sectional data (4, 29). Regardless of gender, CT values for cancellous bone density increased with Tanner stage of sexual development, and values at sexual maturity were, overall, 18% higher than at the beginning of puberty. We found no relation between the ages of the subjects at commencement of the study or the duration of puberty and CT values for cancellous bone density at sexual maturity. Due to technical limitations, we were unable to define whether the increases in CT values for cancellous bone density during puberty were a reflection of an increase in the degree of mineralization of the trabeculae, the number of trabeculae, or, as several investigators have suggested, the thickness of the trabeculae (16, 30).

Our findings complement existing evidence indicating that girls and boys have identical cancellous and cortical bone density, emphasizing that gender differences in bone mass in children are due to variations in bone size (15, 31–33). In the axial skeleton, gender differences in vertebral cross-sectional area were present at baseline, increased throughout puberty, and persisted even after accounting for differences in body mass. In contrast, there were no significant differences in femoral cross-sectional dimensions between boys and girls at baseline, but gender differences became apparent and increased during pu-

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**TABLE 5. Correlations between skeletal phenotypes at the beginning of puberty (Tanner 2) with values at midpuberty, late puberty, and sexual maturity (Tanner 3, 4, and 5)**

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Girls</th>
<th></th>
<th></th>
<th>Boys</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tanner 3</td>
<td>Tanner 4</td>
<td>Tanner 5</td>
<td>Tanner 3</td>
<td>Tanner 4</td>
<td>Tanner 5</td>
</tr>
<tr>
<td>Standing height</td>
<td>0.94</td>
<td>0.89</td>
<td>0.84</td>
<td>0.82</td>
<td>0.81</td>
<td>0.79</td>
</tr>
<tr>
<td>Sitting height</td>
<td>0.88</td>
<td>0.79</td>
<td>0.78</td>
<td>0.82</td>
<td>0.66</td>
<td>0.46</td>
</tr>
<tr>
<td>Body weight</td>
<td>0.94</td>
<td>0.92</td>
<td>0.81</td>
<td>0.94</td>
<td>0.93</td>
<td>0.90</td>
</tr>
<tr>
<td>Vertebral CSA</td>
<td>0.99</td>
<td>0.98</td>
<td>0.96</td>
<td>0.98</td>
<td>0.96</td>
<td>0.94</td>
</tr>
<tr>
<td>Femoral CSA</td>
<td>0.94</td>
<td>0.86</td>
<td>0.84</td>
<td>0.91</td>
<td>0.86</td>
<td>0.84</td>
</tr>
<tr>
<td>Femoral CBA</td>
<td>0.87</td>
<td>0.78</td>
<td>0.78</td>
<td>0.86</td>
<td>0.83</td>
<td>0.83</td>
</tr>
<tr>
<td>Cancellous BD</td>
<td>0.92</td>
<td>0.84</td>
<td>0.79</td>
<td>0.85</td>
<td>0.92</td>
<td>0.88</td>
</tr>
</tbody>
</table>

CSA, Cross-sectional area; CBA, cortical bone area; BD, bone density.
Multiple regression analysis revealed that the greater gains in femoral cross-sectional growth of boys were related to simultaneous greater gains in height and body weight. The results of the current study corroborate previous studies indicating that, although femoral cross-sectional bone acquisition is primarily driven by mechan-
ical load related to increasing body mass, vertebral cross-
sectional growth is not only associated with increasing
body mass, but is also strongly influenced by gender (34, 35).

Nutritional analyses revealed that dietary calcium intake
did not correlate with baseline values or changes in any of
the skeletal phenotypes in girls, in boys, or when all children
were considered together. However, the relatively small
number of subjects studied and the inherent limitations as-
associated with food questionnaires make comparisons among
studies relating nutrition to bone accretion during growth
prone to inaccuracy. Previous studies have yielded conflicting
results. Whereas some found that persons who consume
large quantities of calcium early in life have greater bone
mass later in adulthood (36), others show no beneficial effect
of dietary calcium supplementation on bone accretion during
puberty (10, 37).

Because of difficulties in longitudinally studying sub-
jects from childhood to an elderly age, the contention that
senile osteoporosis is the result of inadequate bone acquisi-
tion during growth remains unproven. This notion is
supported, however, by recent data showing that there is
a strong resemblance between mother-daughter bone traits and that this resemblance is present even before the
daughters have begun puberty (1, 38). Additional support
for this concept comes from the knowledge that genes associated with the normal variations in bone mass in elderly women are also related to variations in bone density
in children (2, 3, 39). If bone loss was the exclusive
determinant of late life bone mass, one would not expect
such a strong resemblance in bone traits between girls and
their mothers or an association between candidate genes
in the same genealogy between the rates of standing height gain and bone mass accumulation in children (38). If bone loss were the primary factor, one would expect
such a resemblance to be weaker or absent in girls and
their mothers or an association between candidate genes
in the same genealogy.

In conclusion, the findings of this study indicate that
values for the apparent density of cancellous bone and the
cross-sectional dimensions of bone in the axial and appen-
dicular skeletal structures at early puberty predict values at
sexual maturity. Whereas our results suggest that the
genetic susceptibility for osteoporosis is present very early
in life, they do not preclude the notion that tracking for
bone traits can be altered by changing environmental fac-
tors. Rather, they suggest that osteoporosis prevention
trials should start in early childhood and should be geared
toward those children who have the highest risk for de-
veloping osteoporosis and fragility fractures later in life.

Additional studies are needed to establish whether track-
ing for quantitative bone traits associated with weaker
bones can be altered and/or whether baseline values in
early puberty will change percentiles by sexual maturity
as a result of simple nutritional, mechanical, or pharma-
cological intervention.

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