Changes in Volumetric Bone Density and Strength at the Tibial Midshaft in Boys and Girls during Growth

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Introduction
- The greater incidence of fragility fractures in older women compared to men may be related to the differences in sex-specific patterns of bone strength development during growth (1,2).
- We have compared the adaptation at the periosteal and endocortical surfaces of the tibial midshaft in boys and girls during puberty (Ahamed et al, unpublished data). Although all children increased bone size through periosteal apposition; boys had substantially larger increases than girls (2≤0.01), while girls experienced greater endocortical apposition (p≤0.001).
- As geometry has a large contribution to bone strength, boys may have a greater resistance to structural failure due to their larger but less dense bones (3,4).
- Although bone density, bone mineral content, bone size and shape contribute to bone strength (5), their relative contribution during growth in boys and girls is unknown.
- The aim of the current study was to examine the sex-specific changes in volumetric bone density and bone strength across 5 years of growth in children aligned on a common maturation landmark (PHV).

Objective
To compare a) how volumetric bone density (vBMD) at the tibial midshaft is accrued in boys and girls across 5 years of growth and b) to compare sex differences in bone strength accrual (SSI).

We hypothesized that girls would exhibit greater gains in vBMD compared with boys across growth; whereas, boys would exhibit greater gains in bone strength.

Healthy Bones Study (HBS)
- Participants were enrolled in the HBS in Richmond, B.C., Canada (6). This prospective trial initially involved a 1.5 year exercise-based intervention. We found no significant difference in pQCT bone parameters between Control and Intervention groups at the end of the intervention (7). Thus, for the purpose of this study, groups were collapsed to prospectively monitor change over 5 additional years.

Subjects
Participants:
- n=170 (80 boys, 90 girls)
  - Mean Age: 12.1±0.5 years at baseline (50); 16.5±0.6 years at final (50)

Imaging
- Instrument: Peripheral QCT ( XCT-2000, Stratec, Medizintechnik GmbH, Pforzheim, Germany) (Fig. 1 Top)
  - Slice: Tibial midshaft (50% site, Fig. 1 Bottom)

Primary Outcomes:
- Volumetric Bone Density
- CoD (mg/cm³)
- Strength Strain Index
- SSI (mm²) = S S D

Maturity Adjustment
- Peak Height Velocity (PHV):
  - Based on aligning children on a common maturation landmark (8).
  - Height velocity by mean age was plotted using GraphPad Prism (Version 5.0)
  - Cubic spline curves were used to fit ≥ 2 data points to determine greatest growth period (peak) in height velocity (PHV).
  - Age at PHV was determined for all participants
  - Natural offset in years was defined relative to age at PHV
  - For example: maturity offset of -1 to 1 year prior to PHV, maturation offset of +1 to 1 year post PHV

Statistical Analysis
- Multi-level modeling (MLM):
  - Dependent variables = CoD, SSI
  - Independent variables = Maturity Offset
  - Fixed effect = Sex, random effect = slope and intercept
  - Sex X Maturity Offset interaction included
  - MLM analysis was performed with STATA (Version 9.2)

Results

<table>
<thead>
<tr>
<th></th>
<th>Boys (n=80)</th>
<th>Girls (n=90)</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>60 months</td>
</tr>
<tr>
<td>Age (years)</td>
<td>12.1 (5.0)</td>
<td>16.7 (6.5)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157.1 (6.8)</td>
<td>176.4 (7.9)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>46.3 (12.4)</td>
<td>70.4 (13.3)</td>
</tr>
<tr>
<td>Tibia Length (mm)</td>
<td>366.2 (24.9)</td>
<td>418.4 (25.6)</td>
</tr>
<tr>
<td>CoD (mg/cm³)</td>
<td>1083.4 (11.4)</td>
<td>611.3 (29.3)</td>
</tr>
<tr>
<td>SSI (mm²)</td>
<td>1395.2 (466.2)</td>
<td>2271.0 (666.7)</td>
</tr>
</tbody>
</table>

Table 1: Descriptive figures for anthropometric and bone variables at baseline and end of study. *Significant differences at baseline (p≤0.05). Mean (SD).

Summary
- CoD: Boys and girls exhibited gains in CoD during adolescent growth (Table 1, Figure 2). The magnitude of this increase was significantly greater in girls compared with boys (p≤0.001).
- There was no difference in the rate of change in CoD between boys and girls (1.3% vs 1.0%) over the measurement time frame (p=0.03).
- SSI: Boys and girls exhibited increases in bone strength accrual during adolescents (Table 1, Figure 3).
- Boys had significantly greater SSI (16%) than girls at maturity offset=0 (p≤0.001).
- Boys had greater increases in SSI (55%) than girls over the study period (p≤0.001).

Conclusion
- Girls exhibited greater increases in CoD; however, no significant difference in the rate of change in CoD was observed between the two sexes.
- Boys exhibited greater increases in strength as measured by SSI which can partly be explained by their larger bone size.
- This is the first study to examine change in CoD and SSI in a longitudinal cohort followed over a 5 year period.
- This study provides valuable insight into sex-specific differences in bone geometry during growth.

References