Left Ventricular Mass and Geometry in Adolescence
Early Childhood Determinants

Hanna Hietalampi, Katja Pahkala, Eero Jokinen, Tapani Rönnermaa, Jorma S.A. Viikari, Harri Niinikoski, Olli J. Heinonen, Pia Salo, Olli Simell, Olli T. Raitakari

Abstract—It is not known whether birth weight and early childhood growth are associated with the development of cardiac left ventricular mass (LVM) in healthy adolescents. Left ventricular growth and geometric remodeling may have long-term consequences on cardiovascular health later in life. We studied the determinants of LVM and patterns of geometric remodeling in adolescents with specific emphasis on birth size and growth in early childhood. Left ventricular measurements were obtained with echocardiography in 418 adolescents at the age of 15 years in a prospective atherosclerosis prevention study, Special Turku Coronary Risk Factor Intervention Project (STRIP). Birth weight \( (P=0.0004) \), current pulse pressure \( (P=0.013) \), physical activity level \( (P=0.0024) \), weight \( (P<0.0001) \), and male sex \( (P<0.001) \) had an independent direct association with LVM in adolescents explaining 47% of the variation. Growth in early childhood was not associated with LVM in adolescents. Birth weight \( (P=0.0066) \), current weight \( (P<0.0001) \), and physical activity level \( (P=0.0017) \) were directly associated with left ventricular posterior wall thickness. Current weight was also directly associated with septal thickness \( (P<0.0001) \). Boys had a thicker septum than girls \( (P=0.0092) \). Normal relative wall thickness and increased left ventricular mass index (eccentric remodeling) \( (P<0.0001) \), as well as increase in both variables (concentric, increased LVM) \( (P=0.0003) \), were associated with higher body mass index. Our results indicate that birth weight has a long-lasting impact on LVM and normal body weight is beneficial for cardiac structure in adolescents. (Hypertension. 2012;60:1266-1272.)

Key Words: echocardiography  ■  cardiac structure  ■  birth weight  ■  cardiovascular health  ■  adolescence

Left ventricular hypertrophy is a strong independent predictor of cardiovascular disease morbidity and mortality in adulthood.\(^1\) Subclinical cardiovascular disease begins to evolve in childhood, even as early as during fetal life. Epidemiological studies show that impaired growth during infancy is associated with increased cardiac left ventricular mass (LVM), and impaired fetal growth is linked to increased risk for coronary heart disease in adults.\(^2\)\(^,\)\(^3\) Childhood obesity is associated with eccentric left ventricular hypertrophy in adults.\(^4\) The mechanisms underlying these associations are largely unknown. In obese adolescents, left ventricular growth is thought to be a compensatory response for increased cardiac workload, but nonhemodynamic metabolic factors (eg, insulin levels) also seem to play a significant role.\(^5\) In healthy children, birth weight is associated with LVM at age 2 years.\(^6\) A recent study showed that early growth affects LVM at this age.\(^7\) However, studies investigating the effect of birth weight or early growth on LVM in adolescents are limited. Also, studies where the combined effect of several determinants of adolescent LVM is reported are scarce.

We hypothesized that birth size and early childhood growth affect LVM and patterns of geometric remodeling at age 15 years. To gain more insight into the effect of childhood blood pressure on LVM and geometric remodeling, blood pressure since age 7 months was also assessed. Several determinants were studied simultaneously to define their independent role on LVM and left ventricular geometry in adolescents.

Methods

Design and Subjects

The present study is part of the ongoing Special Turku Coronary Risk Factor Intervention Project for Children (STRIP).\(^8\)\(^,\)\(^9\) Briefly, families of 5-month-old infants were recruited to the study at the well-baby clinics in Turku, Finland, between February 1990 and June 1992. At the age of 7 months, 1062 infants were randomized to an intervention group (n=540) or to a control group (n=522). The intervention group has repeatedly received individualized dietary and lifestyle counseling to reduce the exposure of the intervention children to the environmental risk factors of atherosclerosis. This study was composed of those children for whom cardiac ultrasound data were available at the age of 15 years.

The STRIP study was conducted according to the guidelines of the Declaration of Helsinki, and the study protocol was approved by the local ethics committee. Written informed consent was obtained from the parents at the beginning of the study and from the children at the age of 15 years.
Cardiac Ultrasound Imaging

At the age of 15 years, echocardiography was performed in 426 children. Successful left ventricular measurements were obtained from 418 children. A single sonographer did the echocardiography and the same observer analyzed the data. Transthoracic 2-dimensional echocardiography was performed with Acuson Sequoia 512 (Acuson, Mountain View, CA) ultrasonography, using 3.5 MHz scanning frequency phased-array transducer. Linear measurements of end-diastolic interventricular septal wall thickness (SWTd), end-diastolic posterior wall thickness (PWTd), and end-diastolic left ventricular internal diameter (LVIdd) were obtained from M-mode tracings. The uncorrected formula to calculate LVM was 1.04[(LVIdd+PWTd+SWTd)/LVIDd]-LVIdd. LVM correction was made according to the formula recommended by American Society of Echocardiography: 0.81[(LVIdd+PWTd+SWTd)/LVIDd]-0.6 g.10,11 LVM index (LVMI) was calculated as LVM/height2 and relative wall thickness (RWT) at end-diastole as (SWTd+PWTd)/LVIDd.12 To assess reproducibility of the ultrasound measurements, we reread the analyses in a subgroup of 57 subjects. The between-observer coefficient of variation for LVM was 8.5%.

Patterns of Left Ventricular Geometry

Left ventricular geometric patterns were defined using LVMI and RWT.13 For left ventricular geometric patterns in adolescents, there are no recommended cutoff points. Therefore, we used cutoff points derived from the cohort. LVMI of 34.02 g/m2.7 in girls and 37.08 g/m2.7 in boys represented the sex-specific 90th percentiles in the cohort. RWT >0.36 for boys and girls in the cohort represented the 90th percentile. On the basis of the 90th percentiles of LVMI and RWT in our subjects, we constructed 4 groups for left ventricular geometric patterns: (1) LVMI <34.02 g/m2.7 for girls and <37.08 g/m2.7 for boys, and RWT ≤0.36 was classified as normal left ventricular geometry; (2) normal LVMI with increased RWT (>0.36) was classified as concentric remodeling; (3) increased LVMI (girls ≥34.02 g/m2.7, boys ≥37.08 g/m2.7) and normal RWT (<0.36) was defined as eccentric remodeling; and (4) increase in both variables identified concentric, increased LVM (Figure 1).

Physical Examination and Physical Activity

At the age of 15 years, weight was measured to the nearest 0.1 kg using an electronic scale (Soehnle S10; Soehnle, Murrhardt, Germany). Height was measured to the nearest 0.1 cm using Harpenden stadiometer (Holtain, Crymych, United Kingdom). Body mass index (BMI) was calculated as kilograms per meter squared. The adolescents were classified as being overweight if their BMI exceeded the international sex-specific 90th percentile. Of the BMI values, the values were ≥34.02 g/m2.7 in girls and ≥37.08 g/m2.7 in boys, and puberty status was classified using Tanner staging (M1 through M5 in girls; G1 through G5 in boys), M1/G1 were considered prepubertal and others were considered pubertal. Leisure-time physical activity was assessed with a self-administered questionnaire. Leisure-time physical activity was calculated as metabolic equivalent hours per week by multiplying the mean frequency, duration, and intensity of the physical activity as described.13 From the leisure-time physical activity data, tertile cutoff points were calculated and the adolescents were divided into 3 groups of physical activity level: (1) ≤11.8 metabolic equivalent h/wk (level 1), (2) ≥11.8 and <32.0 metabolic equivalent h/wk (level 2), and (3) ≥32.0 metabolic equivalent h/wk (level 3).

Birth Size and Early Growth

Data on birth size of the child were collected from the records of the well-baby clinics. Fetal growth restriction was defined as a birth weight below the 10th percentile for gestational age and sex of the total STRIP-cohort. Supine lengths were recorded on a baby-board until the age of 2 years (Bekvil, Paljarinen, Helsinki, Finland). Weights of the infants were measured on an infant scale until age of 15 months (Seca 725 Hamburg, Germany). Increases in weight and height from birth to 7 months, 13 months, and 2 years were analyzed separately.

Statistical Methods

STRIP study group was not associated with LVM, and therefore we studied the STRIP intervention and control groups as a single cohort. To study sex differences (Table 1), t test was used for continuous and Cochrane-Mantel-Haenszel $\chi^2$ test for categorical response variables. Univariate linear regression analyses were performed to assess determinants of LVM (Table 2). Furthermore, a multivariable model adjusted for sex and weight was used (Table 2). From the sex- and weight-adjusted models, significant determinants of LVM were further entered into a multivariable linear regression analysis with backward selection (exclusion criteria $P<0.15$) to assess independent determinants of LVM (Table 3). In the final model, birth height and current waist circumference were also used instead of birth weight and current weight, respectively. Linear regression analysis was used to study associations of the septal and posterior wall thickness with the determinants of LVM (Table 4), as well as continuous determinants of left ventricular geometric patterns (Table 5). Cochrane-Mantel-Haenszel $\chi^2$ test was used to study associations between categorical determinants of left ventricular geometric patterns (Table 5). Post hoc analyses within ANOVA model main effects were Tukey-Kramer adjusted.

Results

Boys had a greater LVM than girls at age 15 years (131.4 versus 106.9 g, Table 1). Birth weight and height were also greater in boys than in girls. In univariate analyses, birth weight, birth height, and early growth (child’s weight gain from birth to the age of 2 years and increase in height from birth to the age of 7 months) were directly associated with LVM at age 15 years (Table 2). LVM was directly associated with male sex, current weight, height, BMI, and waist circumference. Adolescents who were overweight had 16.6 g greater LVM (mean, 134.4 g) than those with normal BMI (mean, 117.8 g) ($P<0.0001$). LVM increased with increasing systolic and diastolic blood pressures. Of the blood pressure variables, pulse pressure showed the strongest association with LVM. Pulse pressure since 7 months of age until the age of 15 years (lifetime pulse pressure) was also directly associated with LVM.

![Figure. Patterns of left ventricular geometry. Left ventricular mass index (LVMI) and relative wall thickness (RWT) are used to define left ventricular geometric patterns (modified from Ganau et al).13 There are no recommended cutoff points for LVMI and RWT in adolescents. In this study, cutoff points derived from the cohort were used (sex-specific 90th percentile). LV indicates left ventricle.](image-url)
in adolescents. LVM increased with advancing pubertal stage and increasing physical activity level. Participation in STRIP intervention had no association with LVM.

Because of the sex difference in LVM and the strong impact of weight on LVM, adjustment was made for sex and weight (Table 2; for waist circumference and BMI, the adjustment was made only for sex). After the adjustment, current height (P=0.017), waist circumference (P<0.0001), BMI (P<0.0001), systolic blood pressure (P=0.016), pulse pressure (P=0.0021), and physical activity level (P=0.0006) remained associated with LVM. For every 1-mm Hg increase in pulse pressure, LVM increased by 0.50 g. Birth weight (P=0.0001) and birth height (P=0.0014) also remained associated with LVM after adjusting for sex and weight. For 100-g increase in birth weight, LVM increased by 0.77 g. Early growth, pubertal status, and diastolic blood pressure were no longer associated with LVM after the adjustment. The results remained similar when BMI was used instead of weight (data not shown).

Variables that were associated with LVM after adjusting for sex and weight were entered into a multivariable model. For parallel variables (eg, systolic blood pressure, diastolic blood pressure, and pulse pressure) that had a strong correlation (r>0.75), only the one with the highest P value was used in the model. Thus, sex, weight, height, pulse pressure, physical activity level, and birth weight were included in the final model (Table 3). Birth weight was directly associated with LVM regardless of sex and current weight, pulse pressure, and physical activity level (P=0.0004). Male sex (P<0.0001), weight (P<0.0001), pulse pressure (P=0.013), and physical activity level (P=0.0024) were also independently associated with LVM. The results were similar when weight was replaced with waist circumference (model R²=0.44) or when birth height was used instead of birth weight (model R²=0.46) in the final model shown in Table 3 (data not shown for waist circumference and birth height). The associations remained similar when the final model was further adjusted for gestational age (data not shown).

Of the variables showing independent association with LVM (Table 3), weight was associated with left ventricular septal thickness and posterior wall thickness (Table 4). Also, physical activity level and birth weight were directly associated with posterior wall thickness. Boys had a thicker septum than girls. RWT was not associated with sex, current body

<table>
<thead>
<tr>
<th>Study Variables</th>
<th>Girls</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight, g</td>
<td>3494.9±461.4</td>
<td>201</td>
</tr>
<tr>
<td>Birth height, cm</td>
<td>50.1±2.0</td>
<td>201</td>
</tr>
<tr>
<td>Height, cm</td>
<td>166.5±6.0</td>
<td>201</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>57.8±10.0</td>
<td>201</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>20.8±3.0</td>
<td>201</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>71.8±7.5</td>
<td>197</td>
</tr>
<tr>
<td>sBP, mm Hg</td>
<td>109.0±7.3</td>
<td>201</td>
</tr>
<tr>
<td>dBP, mm Hg</td>
<td>62.0±4.7</td>
<td>201</td>
</tr>
<tr>
<td>PP, mm Hg</td>
<td>47.0±6.0</td>
<td>201</td>
</tr>
<tr>
<td>Stage of puberty (M/G), %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M/G2</td>
<td>0</td>
<td>200</td>
</tr>
<tr>
<td>M/G3</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>M/G4</td>
<td>51.5</td>
<td></td>
</tr>
<tr>
<td>M/G5</td>
<td>36.0</td>
<td></td>
</tr>
<tr>
<td>Physical activity, MET h/wk</td>
<td>20.3±27.6</td>
<td>178</td>
</tr>
<tr>
<td>In STRIP intervention group, %</td>
<td>48.2</td>
<td>199</td>
</tr>
<tr>
<td>LVM uncorrected, g</td>
<td>132.9±26.0</td>
<td>201</td>
</tr>
<tr>
<td>LVM, g</td>
<td>106.9±20.8</td>
<td>201</td>
</tr>
<tr>
<td>LVMI, g/m²²</td>
<td>27.0±5.3</td>
<td>201</td>
</tr>
<tr>
<td>Septal thickness, cm</td>
<td>0.72±0.09</td>
<td>201</td>
</tr>
<tr>
<td>Posterior wall thickness, cm</td>
<td>0.75±0.09</td>
<td>200</td>
</tr>
<tr>
<td>Septal/posterior wall thickness</td>
<td>0.96±0.12</td>
<td>200</td>
</tr>
<tr>
<td>RWT</td>
<td>0.32±0.04</td>
<td>200</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure; PP, pulse pressure; MET, metabolic equivalent; STRIP, Special Turku Coronary Risk Factor Intervention Project; LVM, left ventricular mass; LVMI, left ventricular mass index; RWT, relative wall thickness at end-diastole; FGR, fetal growth restriction.

Data are given as mean±SD, median (interquartile range) for physical activity, or % for male sex, STRIP intervention group, FGR.
size, blood pressure, pubertal stage, physical activity level, or birth size (data not shown).

LVM geometric patterns were associated with weight, BMI, and waist circumference (Table 5). Adolescents who had eccentric remodeling or concentric, increased LVM had a higher BMI than those with normal left ventricular geometry.

**Discussion**

To our knowledge, this is the first study to show the direct association between birth weight and LVM in adolescents, independent of current weight, pulse pressure, and physical activity level. In line with previous studies, weight, pulse pressure, and physical activity level of the child were also directly associated with LVM. Eccentric and concentric left ventricular remodeling were associated with increased weight, BMI, and waist circumference of the child.

In contrast to our study, previous studies did not find association between birth weight and LVM in subjects aged 8 through 24 years or in elderly men. Discrepancy in the results may in part be explained by the smaller study cohorts and a wider age range in the previous studies. In a recent population-based prospective cohort study, LVM at the age of 2 years, however, increased with increasing birth weight in line with our results.

LVM is mainly determined by the number of cardiomyocytes (hyperplasia) in early infancy. After the age of 1

<table>
<thead>
<tr>
<th>Study Variables</th>
<th>β±SE</th>
<th>P</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight, g</td>
<td>0.015±0.0025</td>
<td>&lt;0.0001</td>
<td>0.083</td>
</tr>
<tr>
<td>Birth height, cm</td>
<td>3.75±0.58</td>
<td>&lt;0.0001</td>
<td>0.092</td>
</tr>
<tr>
<td>Δweight; birth to 7 mo, kg</td>
<td>6.91±1.65</td>
<td>&lt;0.0001</td>
<td>0.041</td>
</tr>
<tr>
<td>Δweight; birth to 13 mo, kg</td>
<td>6.22±1.41</td>
<td>&lt;0.0001</td>
<td>0.045</td>
</tr>
<tr>
<td>Δheight; birth to 7 mo, cm</td>
<td>1.68±0.64</td>
<td>0.0088</td>
<td>0.017</td>
</tr>
<tr>
<td>Δheight; birth to 13 mo, cm</td>
<td>1.12±0.59</td>
<td>0.056</td>
<td>0.0088</td>
</tr>
<tr>
<td>Male sex</td>
<td>24.5±2.4</td>
<td>0.0001</td>
<td>0.21</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>1.40±0.11</td>
<td>&lt;0.0001</td>
<td>0.29</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>2.95±0.41</td>
<td>&lt;0.0001</td>
<td>0.11</td>
</tr>
<tr>
<td>Waist, cm</td>
<td>1.43±0.16</td>
<td>&lt;0.0001</td>
<td>0.17</td>
</tr>
<tr>
<td>Height, cm</td>
<td>1.71±0.14</td>
<td>&lt;0.0001</td>
<td>0.26</td>
</tr>
<tr>
<td>sBP, mmHg</td>
<td>1.25±0.13</td>
<td>&lt;0.0001</td>
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<td>dBP, mmHg</td>
<td>0.60±0.26</td>
<td>0.024</td>
<td>0.012</td>
</tr>
<tr>
<td>PP, mmHg</td>
<td>1.64±0.16</td>
<td>&lt;0.0001</td>
<td>0.21</td>
</tr>
<tr>
<td>Lifetime PP, mmHg</td>
<td>7.69±2.41</td>
<td>0.0015</td>
<td>0.024</td>
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<tr>
<td>Stage of puberty (M/G)</td>
<td>na</td>
<td>0.044</td>
<td>0.033</td>
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<tr>
<td>Physical activity level (group 1–3)</td>
<td>5.51±1.65</td>
<td>0.0009</td>
<td>0.030</td>
</tr>
<tr>
<td>STRIP intervention group</td>
<td>−0.98±2.66</td>
<td>0.078</td>
<td>0.0003</td>
</tr>
<tr>
<td>FGR</td>
<td>15.2±3.83</td>
<td>&lt;0.0001</td>
<td>0.038</td>
</tr>
</tbody>
</table>

**Table 2. Correlates of LVM (Boys n=217, Girls n=201)**

<table>
<thead>
<tr>
<th>Study Variables</th>
<th>Univariate Model</th>
<th>Adjusted Model*</th>
</tr>
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<tbody>
<tr>
<td>β±SE</td>
<td>P</td>
<td>R²</td>
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<tr>
<td>Birth weight, g</td>
<td>0.015±0.0025</td>
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<tr>
<td>Birth height, cm</td>
<td>3.75±0.58</td>
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<td>Δweight; birth to 7 mo, kg</td>
<td>6.91±1.65</td>
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<td>Δweight; birth to 13 mo, kg</td>
<td>6.22±1.41</td>
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<tr>
<td>Δheight; birth to 7 mo, cm</td>
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<tr>
<td>Δheight; birth to 13 mo, cm</td>
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<tr>
<td>Male sex</td>
<td>24.5±2.4</td>
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<tr>
<td>Weight, kg</td>
<td>1.40±0.11</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>2.95±0.41</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist, cm</td>
<td>1.43±0.16</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Height, cm</td>
<td>1.71±0.14</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>sBP, mmHg</td>
<td>1.25±0.13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>dBP, mmHg</td>
<td>0.60±0.26</td>
<td>0.024</td>
</tr>
<tr>
<td>PP, mmHg</td>
<td>1.64±0.16</td>
<td>&lt;0.0001</td>
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<tr>
<td>Lifetime PP, mmHg</td>
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<td>Stage of puberty (M/G)</td>
<td>na</td>
<td>0.044</td>
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<td>Physical activity level (group 1–3)</td>
<td>5.51±1.65</td>
<td>0.0009</td>
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<td>STRIP intervention group</td>
<td>−0.98±2.66</td>
<td>0.078</td>
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<tr>
<td>FGR</td>
<td>15.2±3.83</td>
<td>&lt;0.0001</td>
</tr>
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</table>

**Table 3. Determinants of LVM at the Age of 15 y in a Multivariable Model**

<table>
<thead>
<tr>
<th>Study Variables</th>
<th>β±SE*</th>
<th>P</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight, 100 g</td>
<td>0.74±0.0021</td>
<td>0.0004</td>
<td>0.025</td>
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<tr>
<td>Male sex</td>
<td>12.0±2.58</td>
<td>&lt;0.0001</td>
<td>0.13</td>
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<tr>
<td>Weight, kg</td>
<td>1.0±0.13</td>
<td>&lt;0.0001</td>
<td>0.29</td>
</tr>
<tr>
<td>Height, cm</td>
<td>0.34±0.18</td>
<td>0.055</td>
<td>0.00</td>
</tr>
<tr>
<td>PP, mm Hg</td>
<td>0.42±0.17</td>
<td>0.013</td>
<td>0.010</td>
</tr>
<tr>
<td>Physical activity level (group 1–3)</td>
<td>3.8±1.23</td>
<td>0.0024</td>
<td>0.016</td>
</tr>
</tbody>
</table>

LVM indicates left ventricular mass; R², partial R²; PP, pulse pressure.

*Data show estimated regression coefficients±SE for a 1-unit change in the covariate.

R² indicates partial R²; BMI, body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure; PP, pulse pressure; na, not applicable; STRIP, Special Turku Coronary Risk Factor Intervention Project; FGR, fetal growth restriction; LVM, left ventricular mass.

Birth weight below the 10th percentile for gestational age and sex of the total STRIP-study cohort.

Data show the difference of group means for dichotomous variables.

Data show estimated regression coefficients±SE for a 1 u change in the covariate.

Data were adjusted only for sex.

Data show the regression coefficients for a change in LVM when the explanatory variable increases 1U.

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year, cardiomyocytes have reached their final number and changes in LVM reflect the growth of myocytes (hypertrophy) as a response to increased pressure or volume load. Physiological growth of the left ventricle (eutrophy) related to child’s somatic growth is mediated through growth factor signaling (e.g., growth hormone and insulin-like growth factor-1), whereas pathological cardiac remodeling is stimulated by neurohormones (e.g., atrial natriuretic peptide and angiotensin) and involves cardiac tissue fibrosis. Somatic growth mainly determines cardiac growth and cardiac structure tracks in children and adolescents. In our study, current weight was the strongest determinant of LVM, explaining 29% of the variation. LVM increased 10 g for every 10 kg increase in weight.

Table 4. Association of the Determinants of LVM With the Septal Thickness and Posterior Wall Thickness of the Left Ventricle

<table>
<thead>
<tr>
<th>Study Variables</th>
<th>Septum β±SE*</th>
<th>P</th>
<th>R²</th>
<th>Posterior Wall β±SE*</th>
<th>P</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight, 100 g</td>
<td>0.0015±0.00098</td>
<td>0.13</td>
<td>0.0061</td>
<td>0.00025±0.000093</td>
<td>0.0066</td>
<td>0.017</td>
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<tr>
<td>Male sex</td>
<td>0.032±0.012</td>
<td>0.0092</td>
<td>0.034</td>
<td>0.020±0.012</td>
<td>0.085</td>
<td>0.024</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>0.0026±0.00059</td>
<td>&lt;0.0001</td>
<td>0.099</td>
<td>0.0027±0.00056</td>
<td>&lt;0.0001</td>
<td>0.12</td>
</tr>
<tr>
<td>Height, cm</td>
<td>0.00010±0.00084</td>
<td>0.90</td>
<td>0.0000</td>
<td>-0.000066±0.00080</td>
<td>0.93</td>
<td>0.0000</td>
</tr>
<tr>
<td>PP, mm Hg</td>
<td>0.00032±0.00080</td>
<td>0.97</td>
<td>0.0000</td>
<td>0.0010±0.00076</td>
<td>0.18</td>
<td>0.0041</td>
</tr>
<tr>
<td>Physical activity level</td>
<td>0.0089±0.0059</td>
<td>0.13</td>
<td>0.0056</td>
<td>0.018±0.0056</td>
<td>0.0017</td>
<td>0.030</td>
</tr>
</tbody>
</table>

LVM indicates left ventricular mass; R², partial R²; PP, pulse pressure.
*Data show estimated regression coefficients±SE for a 1U change in the covariate.

Table 5. Determinants of Left Ventricle Geometric Patterns

<table>
<thead>
<tr>
<th>Study Variables</th>
<th>Normal LV Geometry (n=344)</th>
<th>Concentric Remodeling (n=33)</th>
<th>Eccentric Remodeling (n=33)</th>
<th>Concentric Increased LVM (n=8)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight, g</td>
<td>3561±505</td>
<td>3638±461</td>
<td>3714±458</td>
<td>3634±709</td>
<td>0.34</td>
</tr>
<tr>
<td>Birth height, cm</td>
<td>50.6±2.2</td>
<td>50.9±2.2</td>
<td>50.6±1.8</td>
<td>50.3±3.0</td>
<td>0.89</td>
</tr>
<tr>
<td>Δweight; birth to 7 mo, kg</td>
<td>5.0±0.8</td>
<td>4.9±0.9</td>
<td>4.9±0.9</td>
<td>4.8±0.9</td>
<td>0.95</td>
</tr>
<tr>
<td>Δweight; birth to 13 mo, kg</td>
<td>6.7±0.9</td>
<td>6.8±1.0</td>
<td>6.6±1.0</td>
<td>7.0±0.8</td>
<td>0.67</td>
</tr>
<tr>
<td>Δweight; birth to 2 y, kg</td>
<td>9.3±1.2</td>
<td>9.6±1.40</td>
<td>9.3±1.4</td>
<td>9.5±0.8</td>
<td>0.72</td>
</tr>
<tr>
<td>Δheight; birth to 7 mo, cm</td>
<td>19.8±2.1</td>
<td>19.4±2.1</td>
<td>19.6±2.3</td>
<td>19.5±2.0</td>
<td>0.76</td>
</tr>
<tr>
<td>Δheight; birth to 13 mo, cm</td>
<td>27.4±2.3</td>
<td>27.4±2.4</td>
<td>26.7±2.0</td>
<td>27.2±2.3</td>
<td>0.51</td>
</tr>
<tr>
<td>Δheight; birth to 2 y, cm</td>
<td>37.9±2.6</td>
<td>37.6±2.4</td>
<td>36.8±2.2</td>
<td>38.1±3.1</td>
<td>0.18</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>52.6</td>
<td>45.5</td>
<td>48.5</td>
<td>62.5</td>
<td>0.77</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>58.8±10.3</td>
<td>60.2±9.7</td>
<td>62.7±10.8</td>
<td>68.7±4.4</td>
<td>0.012*</td>
</tr>
<tr>
<td>Height, cm</td>
<td>170.8±10.3</td>
<td>170.1±7.1</td>
<td>167.1±6.8</td>
<td>168.2±11.8</td>
<td>0.069</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>20.1±2.8</td>
<td>20.8±3.2</td>
<td>22.4±3.6</td>
<td>24.4±4.7</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>72.5±7.5</td>
<td>73.5±7.3</td>
<td>76.0±9.6</td>
<td>80.8±9.9</td>
<td>0.0039*</td>
</tr>
<tr>
<td>sBP mm Hg</td>
<td>113±9</td>
<td>111±10</td>
<td>116±9</td>
<td>113±10</td>
<td>0.20</td>
</tr>
<tr>
<td>dBP, mm Hg</td>
<td>62±5</td>
<td>61±5</td>
<td>64±6</td>
<td>60±5</td>
<td>0.13</td>
</tr>
<tr>
<td>PP, mm Hg</td>
<td>51±8</td>
<td>50±7</td>
<td>53±8</td>
<td>54±7</td>
<td>0.37</td>
</tr>
<tr>
<td>Lifetime PP, mm Hg</td>
<td>-0.015±0.54</td>
<td>-0.067±0.48</td>
<td>0.089±0.68</td>
<td>0.31±0.43</td>
<td>0.24</td>
</tr>
<tr>
<td>Stage of puberty (M/G 1–5)</td>
<td>4.2±0.6</td>
<td>4.2±0.7</td>
<td>4.2±0.7</td>
<td>4.0±0.6</td>
<td>0.84</td>
</tr>
<tr>
<td>Physical activity level</td>
<td>2.0±0.8</td>
<td>2.3±0.7</td>
<td>2.2±0.9</td>
<td>2.3±1.0</td>
<td>0.15</td>
</tr>
<tr>
<td>STRIP intervention group</td>
<td>50.4</td>
<td>56.3</td>
<td>42.4</td>
<td>12.5</td>
<td>0.13</td>
</tr>
<tr>
<td>FGR, %</td>
<td>14.1</td>
<td>15.6</td>
<td>12.5</td>
<td>0.00</td>
<td>0.46</td>
</tr>
</tbody>
</table>

LV indicates left ventricular; LVM, left ventricular mass; BMI, body mass index; sBP, systolic blood pressure; dBP, diastolic blood pressure; PP, pulse pressure; STRIP, Special Turku Coronary Risk Factor Intervention Project; FGR, fetal growth restriction.

Data are given as mean±SD, median (interquartile range) for physical activity level, or % for male sex, STRIP intervention group, FGR. Tukey-Kramer adjusted P values for post hoc comparisons.

*Data show normal LV geometry vs concentric increased LVM for weight P=0.0390, BMI P=0.0003, waist P=0.0271.
†Data show normal LV geometry vs eccentric remodeling for BMI P≤0.0001.
associated with the thicknesses of interventricular septum and posterior wall.

Obesity-induced left ventricular growth reflects volume overload, resulting in increased myocardial oxygen consumption and oxidative-wall stress. Adipose tissue may also activate renin–angiotensin-mediated myocardial tissue growth and fibrosis. Childhood obesity predicts increased LVM in adulthood and is an independent risk factor for subclinical left ventricular dysfunction. In this study, adolescents with eccentric or concentric left ventricular remodeling had significantly increased BMI and waist circumference compared with those with normal geometry, in line with previous findings in adults. This suggests that an unfavorable alteration in left ventricular loading changes left ventricle geometry also in adolescents. Because the prevalence of obesity among children is increasing, our study indicates that the role of normal body weight is important in preventing unfavorable cardiac growth and remodeling already in adolescents.

Pulse pressure was associated with LVM but had a weaker explanatory rate on LVM than birth weight. Epidemiologic studies confirm the direct association between childhood blood pressure and LVM in nonhypertensive adolescents. The stronger impact of birth weight on LVM could be explained by possible neurohormonal effect of metabolic factors related to birth size. This study provides further evidence of the importance of blood pressure on LVM.

In our study, physical activity level was directly associated with LVM and posterior wall thickness. Cardiovascular adaptation to exercise is well known. In the athlete’s heart, adaptation to increased hemodynamic load because of physical activity leads to physiological changes in cardiac morphology. Our findings suggest that, in healthy adolescents, too physical activity leads to increase in LVM and is specifically associated with the growth of the left ventricle posterior wall.

Low birth weight is associated with adult risk for cardiovascular disease and also changes in cardiac shape even in childhood. Increased birth weight (macrosomia) relates with ventricular hypertrophy in infants of mothers with diabetic mellitus. Our study shows that the association of birth weight on LVM is evident also in children with normal birth weight for gestational age. The mechanisms that combine birth weight and LVM in later life are largely unknown. Changes in stroke volume, cardiac output, or afterload attributed to hemodynamic factors related to birth weight might contribute to left ventricular growth. It has also been suggested that both low and high birth weight may be associated with a lower probability of undertaking physical activity and subsequently affect LVM. A recent study showed the association of early growth on LVM at 2 years of age. In our study, an increase in weight during early childhood (from birth to 2 years) was not related to LVM, suggesting that the impact of early growth on LVM is not sustained to later life.

The strengths of this study are the large study cohort, 418 healthy 15-year-old adolescents, with a long follow-up time and extensive amount of data collected. Because of the fact that echocardiography was performed only once, conclusions on causality cannot be drawn. For determining LVM, cardiac MRI has become the gold standard. However, echocardiography is still the most used application, particularly in clinical practice to assess LVM.

The study children were participants of the dietary intervention study to prevent atherosclerosis. The intervention has resulted in differences in the diet, lipids, blood pressure, and endothelial function between the intervention and control children. In the present analysis were found no intervention effect on LVM, indicating that the intervention has not impacted adversely on LVM.

Perspectives
Increased LVM predicts cardiovascular disease morbidity and mortality in adults. It is evident that subclinical changes of cardiovascular disease begin to evolve in childhood. To gain more insight on the early life determinants of LVM in adolescents, we assessed echocardiography in 418 healthy adolescents. Our study showed that birth weight together with current pulse pressure, physical activity level, and weight were independently associated with LVM in adolescents explaining 47% of the variation. These results indicate that birth weight has a long-lasting effect on LVM, whereas weight gain during the first 2 years of life does not associate with LVM in adolescents. Normal body weight is beneficial also for the cardiac structure of the adolescents. Our results extend the knowledge of the determinants of LVM from fetal life to adolescence, relevant for the research of early epidemiology and prevention of cardiovascular disease.

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Disclosures
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Left Ventricular Mass and Geometry in Adolescence: Early Childhood Determinants
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