Left Ventricular Geometry and Severe Left Ventricular Hypertrophy in Children and Adolescents With Essential Hypertension

Stephen R. Daniels, MD, PhD; Jennifer M.H. Loggie, MD; Philip Khoury, MS; Thomas R. Kimball, MD

Background—Left ventricular (LV) hypertrophy has been established as an independent risk factor for cardiovascular disease in adults. Recent research has refined this relationship by determining a cutpoint of 51 g/m² for LV mass index indicative of increased risk and defining LV geometric patterns that are associated with increased risk. The purpose of this study was to evaluate severe LV hypertrophy and LV geometry in children and adolescents with essential hypertension.

Methods and Results—A cross-sectional study of young patients (n = 130) with persistent blood pressure elevation above the 90th percentile was conducted. Nineteen patients (14%) had LV mass greater than the 99th percentile; 11 of these were also above the adult cutpoint of 51 g/m². Males, subjects with greater body mass index, and those who had lower heart rate at maximum exercise were at significantly (P < .05) higher risk of severe LV hypertrophy. In addition, 22 patients (17%) had concentric LV hypertrophy, a geometric pattern that is associated with increased risk of cardiovascular disease in adults. Seven patients had LV mass index above the cutpoint and concentric hypertrophy. No consistent significant determinants of LV geometry were identified in these children and adolescents with hypertension.

Conclusions—Severe LV hypertrophy and abnormal LV geometry are relatively prevalent in young patients with essential hypertension. These findings suggest that these patients may be at risk for future cardiovascular disease and underscore the importance of recognition and treatment of blood pressure elevation in children and adolescents. Weight loss is an important component of therapy in young patients with essential hypertension who are overweight. (Circulation. 1998;97:1907-1911.)

Key Words: ventricles ■ hypertrophy ■ hypertension ■ pediatrics

Left ventricular (LV) hypertrophy has been established as an independent risk factor for cardiovascular disease morbidity and mortality in adults.1,2 This includes increased risk for myocardial infarction, congestive heart failure, and sudden death. The relationship of obesity and elevated blood pressure to increased LV mass index has also been demonstrated.3-5 However, the relative importance of these factors in determining LV mass compared with the process of normal growth and development in children has been debated.6,7 This has led to some uncertainty regarding the clinical utility of the determination of elevation of LV mass in young patients.

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Abnormalities of LV mass can be defined both by a standard measure above which mass is considered excessive for body size and by geometric patterns associated with increased morbidity. De Simone et al8 established a cutpoint of 51 g/m² for LV mass index, beyond which there is a fourfold greater risk for the development of cardiovascular end points in hypertensive adults. This cutpoint is above the 99th percentile for LV mass index in normal children and adolescents. Classification of hypertensive adult patients by their ventricular geometric pattern may further improve our ability to predict cardiovascular risk.9-12 These patterns, including concentric or eccentric hypertrophy, concentric remodeling, and normal ventricular geometry, have been associated with physiological alterations and may prove to provide clinically useful information. These geometric patterns have not previously been studied in pediatric patients with essential hypertension.

The purposes of this study were (1) to determine whether young patients with essential hypertension have LV mass >51 g/m²; (2) to determine whether there are predictors of severe LV hypertrophy, including sex, body size, blood pressure level, dietary variables, and exercise measures; and (3) to evaluate LV geometry in children and adolescents with essential hypertension.
Methods

Subjects
Subjects for this study were children and adolescents who were followed up in the Hypertension Clinic at Children’s Hospital Medical Center, Cincinnati, Ohio, with a diagnosis of essential hypertension. Criteria for inclusion were a minimum of three blood pressure measurements over a minimum of a 3-month period with systolic or diastolic blood pressure greater than the 90th percentile for age and sex according to the standards of the Second NHLBI Task Force on Blood Pressure Control in Children. Blood pressure measurements in the clinic were made by auscultation in the right arm, with the patient in the sitting position, with an appropriate-size cuff. The onset of the fourth Korotkoff phase was used to indicate diastolic blood pressure in subjects <13 years old. The onset of the fifth Korotkoff phase was used for subjects ≥13 years old. None of the subjects had a known secondary cause of blood pressure elevation as determined by clinical and laboratory examination. Subjects were studied in the Clinical Research Center of the Children’s Hospital Medical Center after informed consent was obtained. This investigation was approved by the Institutional Review Board for Research in Human Subjects of the Children’s Hospital Medical Center, Cincinnati, Ohio.

Echocardiography
LV mass was determined from echocardiographic measurements of the left ventricle by standard techniques with subjects in the supine position. Studies were performed with two-dimensional guided M-mode echocardiography with transducer frequencies appropriate for body size. Measurements of the LV internal dimension, interventricular septal thickness, and posterior wall thickness were made during diastole according to methods established by the American Society of Echocardiography. LV mass index was calculated by dividing LV mass by height in meters raised to the power of 2.7. Relative wall thickness was measured at end diastole as the ratio of the posterior wall thickness plus septal thickness over LV internal dimension. LV mass index and relative wall thickness in the patients with hypertension were compared with standards and percentiles based on measurements in normal children and adolescents by previously published methods.

Cutoff levels for LV mass and relative wall thickness were created to evaluate LV geometry. The sex-specific 95th percentile for LV mass index from normal children and adolescents was used as one cutoff. A relative wall thickness of 0.41 was used, which represents the 95th percentile for relative wall thickness for normal children and adolescents. This value was also used by Ganau et al for partitioning by relative wall thickness in adults. This results in four categories: normal, concentric remodeling, eccentric hypertrophy, and concentric hypertrophy. Patients with normal geometry had LV mass and relative wall thickness below the 95th percentile. Concentric remodeling was defined as normal LV mass index but elevated relative wall thickness; eccentric hypertrophy was defined as elevated LV mass index with normal relative wall thickness; and concentric hypertrophy was defined as both LV mass index and relative wall thickness greater than the 95th percentile.

The cutoff level used to define the most severe LV hypertrophy was an LV mass index of 51 g/m². This value, which represents approximately the 97.5th percentile for LV mass index in adults, was shown by de Simone et al to be associated with a 4.1-fold risk of cardiovascular disease in adults. Patients above the 99th percentile were considered to have severe LV hypertrophy. Patients below the 90th percentile for LV mass index based on previous studies of normal subjects were considered to have normal LV mass index. These two groups were compared with respect to various independent variables. Next, stepwise multiple logistic regression analysis was performed to assess whether there were independent predictors of severe LV hypertrophy. ANOVA and χ² analysis were used to evaluate differences among the LV geometry groups. A value of P=.05 was used to indicate statistical significance.

Results
One hundred thirty patients 6 to 23 years old were studied. The mean duration of blood pressure elevation during follow-up in the Hypertension Clinic was 2 years (range, 3 months to 12 years). Of the patients studied, 98 (75%) were male, 32 (25%) were female, 69 (53%) were white, and 61 (47%) were black. Descriptive statistics for the study population are presented in Table 1.

The distribution of patients by percentile of LV mass index is presented in Table 2. Eleven of the 130 patients (8%) were found to have LV mass index greater than the cutpoint of 51 g/m². Of these patients, 9 were male, 2 were female, 6 were black, and 5 were white. An additional 8 patients had LV mass greater than the 99th percentile but less than 51 g/m². Fifty-eight patients (45%) had LV mass index below the 90th percentile. They would be considered to have normal LV mass.

The comparison of patients with LV mass index below the 90th percentile and patients with severe LV hypertrophy above the 99th percentile with respect to various independent

Dietary Sodium Intake
Subjects were allowed to select their diet while in the Clinical Research Center. The type and amount of foods consumed were observed by a trained dietitian. The intake of sodium during a 24-hour period was then calculated from the sodium composition of each food and added salt according to the Nutrition Data Coding System of the University of Minnesota, Minneapolis.

Lipids and Lipoproteins
Venipuncture was performed after a 10-hour fast. Measurements of total cholesterol, triglycerides, and HDL cholesterol were performed in a laboratory standardized by the Centers for Disease Control and Prevention. LDL cholesterol was then calculated from those measurements by the Friedewald formula.

Exercise Test
A graded bicycle ergometer exercise test was performed according to the James protocol. Subjects performed at 50%, 75%, and 100% of predicted maximal workload. During the test, the subjects’ heart rate and blood pressure were measured at rest and at each of the workloads. If the subject was able to perform at >100% of the predicted workload, then additional measurements were made at increasing workloads until exhaustion. Values for heart rate and blood pressure at rest and at maximal exercise were used in the analysis. Cardiac output was measured at maximal exercise by the acetylene rebreathing method.

Statistical Analysis
Descriptive statistics, including mean±SD for continuous variables, and proportions for categorical variables are presented for the study cohort. The values for LV mass index were then classified according to whether they were below the sex-specific 90th percentile, between the 90th and 95th percentile, between the 95th and the 99th percentile, between the 99th percentile and the cutpoint of 51 g/m², or above that cutpoint, which has been associated with increased risk of cardiovascular disease in adults. Patients above the 99th percentile were considered to have severe LV hypertrophy. Patients below the 90th percentile for LV mass index based on previous studies of normal subjects were considered to have normal LV mass index. These two groups were compared with respect to various independent variables. Next, stepwise multiple logistic regression analysis was performed to assess whether there were independent predictors of severe LV hypertrophy. ANOVA and χ² analysis were used to evaluate differences among the LV geometry groups. A value of P=.05 was used to indicate statistical significance.

Anthropometric Measurements
Examination included measurement of height and weight. Body mass index was calculated as weight/height² and used as a measure of ponderosity.
TABLE 1. Descriptive Statistics for the Study Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>14.7</td>
<td>3.4</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.66</td>
<td>0.14</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>73.7</td>
<td>21.8</td>
</tr>
<tr>
<td>Body mass index</td>
<td>26.3</td>
<td>6.2</td>
</tr>
<tr>
<td>Duration of BP elevation, y</td>
<td>2.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>135.4</td>
<td>11.7</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>78.6</td>
<td>10.7</td>
</tr>
<tr>
<td>Left ventricular mass index, g/m²</td>
<td>38.0</td>
<td>9.5</td>
</tr>
<tr>
<td>Heart rate at rest, bpm</td>
<td>89.2</td>
<td>16.0</td>
</tr>
<tr>
<td>Heart rate at maximum exercise, bpm</td>
<td>184.4</td>
<td>15.3</td>
</tr>
</tbody>
</table>

variables is presented in Table 3. There were significant differences in body mass index, sodium intake, resting systolic blood pressure, and systolic blood pressure and heart rate at maximum exercise.

The results of the stepwise multiple logistic regression analysis are presented in Table 4. This analysis revealed that significant independent predictors of severe LV hypertrophy were heart rate at maximum exercise, body mass index, and sex. The direction of these associations indicates that among young patients with essential hypertension, those who are male, who are more obese, and who have a lower heart rate at maximal exercise are more likely to have severe LV hypertrophy.

Among the patients with LV mass index greater than the 95th percentile, 22 had concentric hypertrophy and 39 had eccentric hypertrophy. Twelve patients had LV mass less than the 95th percentile but had elevated relative wall thickness, indicating concentric LV remodeling. The remaining 57 patients had normal LV geometry. The group with concentric hypertrophy was made up of 2 females and 20 males, 5 whites and 17 blacks. The group with eccentric hypertrophy was composed of 10 females and 29 males, 5 whites and 16 blacks. Among the patients with LV mass index >51 g/m², 7 had concentric hypertrophy and 4 had eccentric hypertrophy.

Comparisons among the LV geometry groups with respect to various independent variables are presented in Table 5. Few significant differences were observed among the groups; however, the group with concentric remodeling appears to have a significantly longer duration of blood pressure elevation and lower heart rate than the other groups. The group with concentric hypertrophy had the highest sodium intake.

TABLE 2. Distribution by Sex and Race for Percentile Category of Left Ventricular Mass Index

<table>
<thead>
<tr>
<th>LV Mass Index, g/m²</th>
<th>n (%)</th>
<th>Male</th>
<th>Female</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;90th percentile</td>
<td>58 (45)</td>
<td>40</td>
<td>18</td>
<td>35</td>
<td>23</td>
</tr>
<tr>
<td>90th–95th percentile</td>
<td>11 (8 )</td>
<td>9</td>
<td>2</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>95th–99th percentile</td>
<td>42 (32)</td>
<td>32</td>
<td>10</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>99th–51 g/m²²</td>
<td>8 (6)</td>
<td>8</td>
<td>0</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>&gt;51 g/m²²</td>
<td>11 (8 )</td>
<td>9</td>
<td>2</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

TABLE 3. Comparison of Subjects With Normal (<90th%) LV Mass Index and Severe (>99th%) LVH

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal (n=58)</th>
<th>Severe LVH (n=19)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>14.4±3.5</td>
<td>15.4±3.3</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>40/18</td>
<td>17/2</td>
<td>.06</td>
</tr>
<tr>
<td>Race, W/B</td>
<td>35/23</td>
<td>7/12</td>
<td>.06</td>
</tr>
<tr>
<td>BMI</td>
<td>24.7±5.7</td>
<td>27.9±5.9</td>
<td>.04</td>
</tr>
<tr>
<td>Duration, mo</td>
<td>22.5±28.2</td>
<td>20.1±19.5</td>
<td>NS</td>
</tr>
<tr>
<td>Sodium intake, mg/24 h</td>
<td>2920.0±1183.5</td>
<td>3740.7±1426.7</td>
<td>.05</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>104.7±38.8</td>
<td>112.8±25.6</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>49.2±11.9</td>
<td>46.5±7.9</td>
<td>NS</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>133.8±12.7</td>
<td>140.6±8.6</td>
<td>.03</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>77.8±9.6</td>
<td>76.5±14.0</td>
<td>NS</td>
</tr>
<tr>
<td>SBP at maximum exercise, mm Hg</td>
<td>193.0±30.2</td>
<td>209.3±22.2</td>
<td>.03</td>
</tr>
<tr>
<td>Heart rate at maximum exercise, bpm</td>
<td>186.3±15.0</td>
<td>178.0±15.5</td>
<td>.04</td>
</tr>
</tbody>
</table>

LV indicates left ventricular; LVH, LV hypertrophy; W, white; B, black; BMI, body mass index; SBP, systolic blood pressure; and DBP, diastolic blood pressure.

but this difference was not statistically significant. There were no differences in the cardiovascular responses to bicycle exercise or in concentrations of lipids and lipoproteins.

Discussion

These results demonstrate that a small proportion (8%) of children and adolescents with essential hypertension already have LV mass index >51 g/m².² The cutpoint of 51 g/m² has previously been shown to be associated with a fourfold increase in risk for cardiovascular disease in adults. An additional 6% had LV mass between the 99th percentile and the cutpoint; therefore, 14% of the patients had severe LV hypertrophy. In addition, 17% of the patients were found to have concentric LV hypertrophy. This is a geometric pattern that has been associated with increased cardiovascular morbidity in adults. It is possible that these young patients with severe LV hypertrophy and abnormal LV geometry are on a course for early cardiovascular morbidity and mortality. This study was cross-sectional, so it is not possible to determine the extent to which patients crossed percentiles over time. However, the known relationship of elevated blood pressure with LV mass and the fact that 55% of the study population are above the 90th percentile suggest that with a longer duration of hypertension, an even greater proportion of patients may develop severe LV hypertrophy.

The variables that independently predicted LV mass above the 99th percentile in this study were sex, body mass index,
and heart rate at maximal exercise. These results are consistent with previous studies of the determinants of LV hypertrophy in adults and children. Studies of normal children as well as those with hypertension have documented increased LV mass in boys compared with girls.3,6,20 DeSimone et al21 showed that this sex difference in LV mass is relatively small in normal children before puberty but becomes much larger after puberty and parallels the sex differences in growth in body size. They speculated that because initial LV mass and probably the number of cardiac myocytes are similar in boys and girls early in life, the fact that normal adult myocardial mass is ≈30% greater in men than in women indicates that a state of relative hypertrophy apparently exists even in normal men. Thus, it is not surprising that a significantly greater proportion of male subjects in our study of children and adolescents with blood pressure elevation had an elevation of LV mass above the 99th percentile.

The finding that increased body mass index is associated with increased LV mass index is also consistent with other studies. For example, MacMahon et al22 reported a reduction of LV mass after weight reduction in young, obese hypertensive subjects. Previous studies have shown that body mass index is a significant correlate of LV mass in both normal children and adults as well as in children and adults with elevated blood pressure.5,7,16,20 There has been some controversy over the relative importance of body growth, obesity, and elevated blood pressure in determining LV mass. The findings from the present study confirm the importance of weight control for children with elevated blood pressure who are overweight. Excess body mass may contribute both to the elevation of blood pressure and to the development of severe LV hypertrophy.

The association of lower heart rate at maximum exercise and severe LV hypertrophy remains unexplained. One possibility is that the patients with excessive hypertrophy were not able to achieve as high a level of exercise as those without hypertrophy. However, a comparison of exercise performed standardized by the expected level for age showed no significant difference between the groups. It is likely that the patients with severe hypertrophy have greater stroke volume with exercise because they had similar cardiac output at maximum exercise (data not shown) in comparison with the patients with normal LV mass index.

Studies in adults have evaluated the pathophysiology of patients with hypertension who are classified by the geometric pattern of the left ventricle.23 It has been shown that adult patients with concentric hypertrophy or remodeling have higher blood pressure.17,24 In our study of young patients with essential hypertension, individuals with concentric remodeling and hypertrophy had higher systolic blood pressure than those with eccentric hypertrophy, but the difference was not statistically significant. Previous studies suggest that adult patients with eccentric hypertrophy may consume more sodium in their diet and have greater circulating volume.24,25 In our study, however, the children with eccentric hypertrophy were intermediate in their level of sodium consumption. It is likely that adults with essential hypertension have had a longer duration of hypertension and have had some evolution of their LV geometric pattern over time. Longer-term studies will be necessary to understand the evolution of LV geometry and the associated physiological changes in children.

Several studies have shown that adults with hypertension and concentric LV hypertrophy have increased risk of cardiovascular morbidity, those with eccentric hypertrophy and concentric remodeling form an intermediate-risk group, and those with normal geometry form a relatively low-risk group. Verdecchia et al9 showed that risk stratification by characterization of LV geometry is independent of the conventional risk factors. Our study indicates that, on the basis of this classification, more than half of the young patients with essential hypertension fall into the intermediate- or high-risk group. One caveat is that it is unclear in adults to what extent increased cardiovascular risk is associated with LV geometry alone as opposed to the physiological abnormalities with which they are associated.23 In addition, the risk associated with these findings in children and adolescents will not be fully understood until complete growth of the body and the heart is achieved.

The results of the present study underscore the importance of the recognition and treatment of elevated blood pressure in children and adolescents. It appears that males are more prone to severe LV hypertrophy and that weight loss may be an important nonpharmacological method to ameliorate severe LV hypertrophy. Further research will be needed to better understand the evolution and importance of LV geometric patterns in young patients with elevated blood pressure.

Acknowledgments

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