Ambulatory Blood Pressure and Left Ventricular Mass Index in Hypertensive Children

Jonathan M. Sorof, Gina Cardwell, Kathy Franco, Ronald J. Portman

Abstract—To determine whether ambulatory blood pressure is more predictive of left ventricular hypertrophy than is casual blood pressure in hypertensive children, echocardiography and ambulatory blood pressure data from 37 untreated hypertensive children were analyzed. Left ventricular mass was calculated using the Devereux equation, left ventricular mass index was calculated as left ventricular mass (in grams)/height2.7 (in meters), and left ventricular hypertrophy was defined as left ventricular mass index >51 g/m2.7. Average blood pressure, blood pressure load, and blood pressure index (average blood pressure divided by pediatric ambulatory blood pressure 95th percentile) were calculated. Left ventricular mass index was strongly correlated with 24-hour systolic blood pressure index \( r = 0.43 \), \( P = 0.008 \) and was also correlated with 24-hour systolic blood pressure \( (r = 0.34, P = 0.037) \), 24-hour systolic blood pressure load \( (r = 0.38, P = 0.020) \), wake systolic blood pressure load \( (r = 0.37, P = 0.025) \), sleep systolic blood pressure \( (r = 0.33, P = 0.048) \), and sleep systolic blood pressure load \( (r = 0.38, P = 0.021) \). Left ventricular mass index did not correlate with age, weight, clinic blood pressure, or ambulatory diastolic blood pressure. The overall prevalence of left ventricular hypertrophy was 27%. The prevalence of left ventricular hypertrophy was 47% (8 of 17) in patients with both systolic blood pressure load \( > 50\% \) and 24-hour systolic blood pressure index \( > 1.0 \), compared with 10% (2 of 20) in patients without both criteria \( (P = 0.015) \). These data suggest ambulatory blood pressure monitoring may be useful for the clinical assessment of hypertensive children by identifying those at high risk for the presence of end organ injury. (Hypertension. 2002;39:903-908.)

Key Words: children ■ blood pressure monitoring, ambulatory ■ hypertrophy, left ventricular ■ cardiovascular disease ■ risk factors

The most recent update from the Task Force on High Blood Pressure in Children and Adolescents provided population-based 95th percentile blood pressure values in children adjusted for age, gender, and height. These pediatric normative data have guided the interpretation of blood pressure values and provided criteria for the diagnosis of hypertension in children. However, the paucity of data in children linking this statistically based definition of hypertension with evidence of hypertensive end-organ injury has created uncertainty regarding the indications for initiating antihypertensive medication in children whose blood pressure exceeds these threshold values. Because overt morbidity cardiovascular events are rare in the majority of hypertensive children, attention has focused on other markers of hypertensive injury, such as increased left ventricular mass index (LVMI) and the presence of left ventricular hypertrophy (LVH). Studies of normal and hypertensive children have found that systolic blood pressure (SBP) and LVMI are positively associated across a wide range of blood pressure values, with no clear blood pressure threshold to predict pathologically increased LVMI. Thus, studies of hypertensive children have reported prevalences of LVH that vary widely. Although these data suggest that children with elevated blood pressure do suffer end-organ injury, its prediction using current hypertension definitions remains uncertain.

In hypertensive adults, ambulatory blood pressure parameters are reported to be better correlated with LVMI and more predictive of LVH than are casual blood pressure values. Although a previous study of mildly hypertensive children confirmed that ambulatory blood pressure is better correlated with LVMI than is casual blood pressure, neither casual nor ambulatory blood pressure values differentiated patients with and without LVH. To determine the ambulatory blood pressure monitoring (ABPM) variables most closely associated with LVMI and/or predictive of the presence of LVH in hypertensive children, echocardiography and ABPM data from children referred to a pediatric hypertension clinic for evaluation were analyzed.

Methods

The records of children with blood pressure >95th percentile, previously documented by a referring physician and confirmed in pediatric hypertension clinic, were reviewed. Inclusion criteria were echocardiography and ABPM for initial diagnostic assessment ≤3 months apart, no known secondary causes of hypertension, and no...
antihypertensive medications during ABPM. A comparison group of normotensive children who had echocardiography during the same period for other indications was identified. Inclusion criteria were technically adequate m-mode measurements for LVMI calculation, no history of elevated blood pressure, no previously documented structural cardiac abnormalities, and no current abnormalities other than trivial tricuspid or mitral regurgitation. Indications for echocardiography in the normotensive group included syncope, chest pain, murmurs, arrhythmias, and rule-out of coronary artery aneurysms secondary to Kawasaki’s disease. The study was approved by an institutional review committee.

Left ventricular mass (LVM) was calculated from 2D-guided m-mode echocardiographic measurements of the left ventricle. Measurements of the left ventricle internal dimension, interventricular septal thickness, and posterior wall thickness were made during diastole according to methods established by the American Society of Echocardiography. LVM was calculated using the Devereux equation.\(^{26}\) LVMI was calculated by dividing LVM by height\(^{17}\) to minimize effects of age, gender, ethnicity, and overweight status.\(^{28-30}\) LVH was defined as LVMI >51 g/m\(^2\); a value greater than the pediatric 99th percentile that is associated with a 4.1-fold risk of cardiovascular morbidity in hypertensive adults.\(^{31}\)

ABPM was performed as previously described.\(^{32}\) ABPM data were analyzed by calculating average blood pressure, blood pressure load, and blood pressure index for the entire 24-hour period, wake period, and sleep period. Average blood pressure was calculated by averaging the blood pressure values during the monitoring period. Blood pressure load was calculated as the percentage of each patient’s blood pressure values that exceeded the pediatric ambulatory 95th percentile blood pressure specific for that patient (derived from a study of ABPM values from 1141 healthy children\(^{33}\)). Blood pressure index was calculated by dividing the average blood pressure for each patient by the 95th percentile blood pressure value specific for that patient. Calculated in this manner, a blood pressure index of 1.1 would correspond to blood pressure that was 10% above the 95th percentile, and thus provides an index of the relative severity of blood pressure elevation.\(^{34}\) In addition, blood pressure dipping was calculated by subtracting the average sleep blood pressure from the average wake and dividing the sum by the average wake blood pressure.

Descriptive statistics are presented as percentages, means, and SDs. Univariate analyses for group comparisons of continuous variables were performed using Student’s \(t\) test. Multivariate analyses for group comparisons were performed using ANOVA. The correlation between LVMI and continuous demographic, clinical, and hemodynamic variables was determined using the Pearson correlation coefficient. Multiple regression analysis was used to determine the strength of association between LVMI and multiple independent variables. Fisher’s exact test was used to compare the LVH percentage between groups. \(P>0.05\) indicated statistical significance.

Results

Demographic and clinical data for 37 hypertensive patients who underwent echocardiography and ABPM are shown in Table 1. The mean time interval between ABPM and echocardiography was 36±32 days. Ninety-five percent (35 of 37) of the patients had systolic hypertension, and 30% (11 of 37) of the patients had diastolic hypertension. On average, clinic blood pressure values were above the 95th percentile for SBP by 11±10 mm Hg and below the 95th percentile for diastolic blood pressure by 5±9 mm Hg. The group of 37 hypertensive patients was compared with a group of 33 normotensive patients who underwent echocardiography for other indications. LVMI was significantly greater in the hypertensive group than in the normotensive group (41.5±12.0 versus 32.5±8.1, \(P<0.001\)). Multivariate analysis showed that LVMI remained significantly higher in the hypertensive

<table>
<thead>
<tr>
<th>TABLE 1. Characteristics of Hypertensive Patients</th>
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<tbody>
<tr>
<td>Demographic*</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>13.5±3.7</td>
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<tr>
<td>Gender, m/f</td>
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<tr>
<td>28/9</td>
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<tr>
<td>Weight, kg</td>
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<tr>
<td>77.5±27.1</td>
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<tr>
<td>Height, cm</td>
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<tr>
<td>161±20</td>
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<tr>
<td>Body mass index, kg/m²</td>
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<tr>
<td>29.1±7.1</td>
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<tr>
<td>Hemodynamic (SBP/DBP)</td>
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<tr>
<td>Clinic blood pressure, mm Hg</td>
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<tr>
<td>138.7±14.3/77.2±8.5</td>
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<tr>
<td>Mean blood pressure, mm Hg</td>
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<tr>
<td>126.2±13.5/72.3±7.7</td>
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<tr>
<td>24-hour</td>
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<tr>
<td>132.6±14.7/78.1±8.7</td>
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<tr>
<td>Wake</td>
</tr>
<tr>
<td>116.1±13.1/63.5±7.4</td>
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<tr>
<td>Sleep</td>
</tr>
<tr>
<td>51.4±31.4/32.0±23.6</td>
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<tr>
<td>Blood pressure load, %‡</td>
</tr>
<tr>
<td>52.4±33.5/31.5±26.7</td>
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<tr>
<td>47.1±32.4/32.0±25.7</td>
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<tr>
<td>Dipping, %‡</td>
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<td>12.4±4.6/18.3±7.5</td>
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<tr>
<td>Echocardiographic</td>
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<tr>
<td>LVMI, gm</td>
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<td>152.2±57.6</td>
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<tr>
<td>LVMI, gm/m(^2)</td>
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<td>41.5±11.9</td>
</tr>
</tbody>
</table>

*Ethnicity of patients was as follows: white 13, hispanic 12, black 8, other 3, and Asian 1. Values are mean±SD.  
†Load=percentage of BP values that exceed the pediatric ambulatory 95th percentile.  
‡Dipping=(average wake BP−average sleep BP)/average wake BP.

group after controlling for differences in gender, age, weight, and height (\(P=0.023\)). The prevalence of LVH was 27% (10 of 37) in the hypertensive group and 0% (0 of 33) in the normotensive group (\(P=0.001\)).

The association between echocardiographic and ABPM variables was determined by univariate and multivariate analyses. LVMI showed the strongest correlation with ambulatory SBP index (\(r=0.43\), \(P=0.008\)) (Figure) among all demographic and clinical variables analyzed. LVMI also showed significant correlations with 24-hour SBP (\(r=0.34\), \(P=0.01\)) among all demographic and clinical variables analyzed. LVMI also showed significant correlations with 24-hour SBP (\(r=0.34\), \(P=0.01\)).
P = 0.037), 24-hour SBP load (r = 0.38, P = 0.020), wake SBP load (r = 0.33, P = 0.048), and sleep SBP load (r = 0.38, P = 0.021). LVMI did not correlate significantly with age, weight, clinic blood pressure, clinic blood pressure index, or any ambulatory diastolic blood pressure parameters. Interventricular septal thickness showed significant univariate correlations with 24-hour SBP (r = 0.43, P = 0.008), wake SBP (r = 0.44, P = 0.007), and sleep SBP (r = 0.39, P = 0.017). Similarly, left ventricular posterior wall thickness showed significant univariate correlations with 24-hour SBP (r = 0.41, P = 0.012), wake SBP (r = 0.39, P = 0.016), and sleep SBP (0.41, P = 0.012). Both septal thickness and posterior wall thickness also showed significant univariate correlations with age and weight. Multiple regression analysis controlling for age and weight showed significant correlations between septal thickness and 24-hour SBP (P = 0.04) and between septal thickness and wake SBP (P = 0.04).

Comparisons of demographic and clinical data between patients with and without LVH are shown in Table 2. Patients with and without LVH did not differ in age, gender distribution, height, weight, or body mass index. Patients with LVH had significantly higher 24-hour SBP (P = 0.035), sleep SBP (P = 0.024), and ambulatory SBP index (P = 0.022) compared with those values in patients without LVH and tended to have higher 24-hour SBP load (P = 0.080), wake SBP load (P = 0.058), wake SBP load (P = 0.077), and sleep SBP load (P = 0.050). Patients with and without LVH did not differ in clinic blood pressure or in any diastolic hemodynamic parameters.

The prediction of LVH by ABPM parameters was assessed by defining threshold values for blood pressure load and blood pressure index. A higher prevalence of LVH was found when SBP load was \( > 50\% \) (P = 0.038) or when ambulatory SBP index was \( > 1.0 \) (P = 0.024). When both SBP load was \( > 50\% \) and ambulatory SBP index was \( > 1.0 \), the prevalence of LVH was 47\% (8 of 17). When both criteria were not met, the prevalence of LVH was 10\% (2 of 20, P = 0.015). The sensitivity and specificity for this combination of ABPM criteria for predicting LVH were 80\% and 67\%, respectively.
Discussion

One of the most difficult issues in the care of children with elevated casual blood pressure is determining whether to initiate antihypertensive medication. Although the presence of elevated blood pressure in children likely represents a cardiovascular risk factor, blood pressure values of hypertensive children tend to normalize with repeated measurements over time without pharmacological treatment. A study of children with persistent mild to moderate blood pressure elevation suggested that although casual blood pressure values allow detection of children with elevated blood pressure, they do not allow differentiation between patients who have white coat hypertension, persistent hypertension, or persistent hypertension with target organ injury. Demonstration of LVH by echocardiography in children who have elevated casual blood pressure suggests more strongly the need for pharmacological therapy. The use of echocardiography to evaluate every child with elevated blood pressure, however, is impractical and expensive. The data from the current study show that ambulatory blood pressure may better quantitate the risk of significant LVH than casual blood pressure and thereby be used as a valuable clinical tool in the assessment of hypertensive children.

The results from the current study are consistent with those of previous studies that show positive associations between ambulatory SBP parameters and LVMI in hypertensive children. In separate studies of children and young adults with mild blood pressure elevation, LVMI was reported to be positively correlated with ambulatory awake SBP and with 24-hour, wake, and sleep SBP. Consistent with these previous studies, the current study found that only ambulatory SBP parameters, and not diastolic blood pressure parameters, were correlated with LVMI. Studies of hypertensive adults have found that blood pressure load is more closely associated with cardiac function than mean blood pressure. The current study showed that ambulatory blood pressure index (a measure of relative ambulatory hypertension severity) was more strongly associated with LVMI than casual blood pressure, mean ambulatory blood pressure, or blood pressure load. This finding suggests that ambulatory blood pressure index may be a more robust indicator of the severity of blood pressure elevation over a 24-hour period than is blood pressure load, which describes only the percentage of blood pressure values that are abnormal.

The prevalence of LVH in the current study was 27% in the hypertensive group using the restrictive LVH definition of LVMI >51 g/m².7 The absence of LVH in any patient in the normotensive comparison group from the same center provides validation of this relatively high prevalence of LVH in the hypertensive group. Previous studies have reported a prevalence of LVH in hypertensive children that ranges from 10% to 38%, depending in part on the method of indexing LV and the criteria used to define pathologically increased LVMI. In the current study, LVMI was calculated by the formula of Devereux and indexed to height to the power of 2.7. This approach to indexing is reported to have a high correlation with LVM/lean body mass and minimizes the effect of overweight status on LVMI. The threshold of 51 g/m² to define LVH corresponds to an LVMI greater than the pediatric 99th percentile (ie, severe LVH) and is reported to be associated with a 4-fold higher risk for the development of cardiovascular endpoints in hypertensive adults. The only previous study reporting the prevalence of LVMI >51 g/m² in hypertensive children found that 8% to 9% of patients (11 of 130) exceeded this threshold. This discrepancy may be because the patients in the current study had evidence of more severe hypertension as shown by higher mean clinic SBP values (138.7 versus 135.4 mm Hg), despite being younger (13.5 versus 14.7 years) and shorter (161 versus 166 cm) than patients in the previous study.

The current study clearly demonstrates hypertensive children with LVH have higher ambulatory blood pressure parameters compared with those of children without LVH. These differences persisted even after controlling for age, gender, and weight. In contrast, no differences were found in clinic blood pressure values. These results differ from those of a previous study of mildly hypertensive children in which no differences in ambulatory SBP parameters and lower ambulatory diastolic blood pressure were found in patients with LVH compared with those without LVH. Previous studies of hypertensive adults have reported that 90% of hypertensive adults with a SBP load >50% had LVH compared with <10% of patients with a SBP load <30%. In the current study, the combined criteria of SBP load threshold of 50% and ambulatory SBP index threshold of 1.0 showed a sensitivity and specificity for LVH of 80% and 67%, respectively. These data suggest that ABPM may predict the presence of LVH in hypertensive children, as has been demonstrated in hypertensive adults.

The current study is limited by several factors. Although the current study is one of the largest to date in children, greater numbers of normotensive and hypertensive patients undergoing both ABPM and echocardiography are needed before the results may be generalized to the overall pediatric population or to the at-risk population of hypertensive children. In addition, there may have been selection bias toward referral of patients to the clinic with more severe or long-standing blood pressure elevation. Thus, the prevalence of LVH in hypertensive children in general is likely to be lower than in this referral-based population. Because the primary aim of the current study was to determine the ambulatory blood pressure parameters that are most closely related to LVMI and predictive of LVH, the study of a more severely affected population of children with an anticipated higher prevalence of LVH is appropriate as an initial approach to the question. Finally, the majority of patients in the current study had systolic hypertension, which may have biased the study results to show a stronger association between SBP and LVMI. However, previous studies have found that the majority of hypertensive children have systolic hypertension, with diastolic hypertension occurring less commonly.

Perspectives

There is little doubt that very young children with extreme blood pressure elevation virtually always require an aggres-
sive approach to their management. However, the changing epidemiology of pediatric hypertension has made these types of patients increasingly less common in the face of a growing epidemic of childhood obesity, inactivity, and poor dietary habits. In a large pediatric hypertension practice, the typical patient demographic is that of an otherwise healthy adolescent with mild to moderate hypertension and some combination of the cardiovascular disease risk factors such of obesity, a family history of hypertension, and an ethnic predisposition to hypertensive disease. In this context, the indications for pharmacological treatment and the target blood pressure values to aim for in response to treatment are unclear based on the current literature. Thus, the practice of evidence-based medicine remains a challenge for physicians who care for hypertensive children. The current study is consistent with studies of adults, showing that ambulatory blood pressure is more closely associated with LVMI and predictive of LVH than is casual blood pressure. In adults, LVH is a potent predictor of cardiovascular morbidity and mortality and, in children, represents an early stage in the progression of cardiovascular disease. It remains to be determined whether treatment of hypertensive children results in regression of LVMI and resolution of the LVH. If so, this would provide additional evidence that early and aggressive treatment of even mild to moderate hypertension in children is warranted.

Acknowledgments

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