Ambulatory Blood Pressure and Metabolic Abnormalities in Hypertensive Subjects With Inappropriately High Left Ventricular Mass

Vittorio Palmieri, Giovanni de Simone, Mary J. Roman, Joseph E. Schwartz, Thomas G. Pickering, Richard B. Devereux

Abstract—Appropriateness of left ventricular (LV) mass to cardiac workload can be evaluated by the ratio of observed LV mass to the value predicted for an individual’s gender, height2.7, and stroke work at rest (%PLVM). It is unclear which pathophysiological factors are associated with inappropriately high LV mass in hypertensive subjects. Adequate LV mass was defined by the 90% confidence interval (73% to 128%) of the distribution of %PLVM in 393 normal-weight normotensive subjects. In 185 hypertensive subjects (aged 56 ± 11 years; 60% male, 29% black), according to %PLVM, 164 (88%) had adequate LV mass, 16 (9%) had inappropriately high LV mass (%PLVM > 128%), and 5 (3%) had %PLVM < 73% (low LV mass). Age, gender, smoking habit, proportion of never-treated subjects, total cholesterol, triglycerides, and creatinine levels did not differ significantly between subjects with adequate and inappropriately high LV mass. Body mass index, fasting glucose, and proportion of black subjects were higher (all \( P < 0.05 \)), while HDL cholesterol was lower (\( P < 0.05 \)) in subjects with inappropriately high LV mass. Blood pressure at the echocardiogram was comparable between subjects with adequate and inappropriately high LV mass, but the latter group had higher ambulatory blood pressure (\( P < 0.01 \)). Subjects with inappropriately high LV mass also had higher aortic root dimension and LV relative wall thickness and relatively lower LV systolic performance than those with adequate LV mass (all \( P < 0.001 \)). Larger aortic root diameter and lower systolic function were also found in hypertensive subjects with inappropriately LV hypertrophy compared with those with adequate LV hypertrophy. In an exploratory case-control study that compared subjects with low %PLVM with age-matched counterparts with adequate LV mass, low %PLVM was associated with lower body mass index, more favorable metabolic profile, and higher LV myocardial contractility. Higher body mass index, larger aortic root, and black race were independent correlates of increased %PLVM. Thus, in arterial hypertension, levels of LV mass inappropriately high for gender, cardiac workload, and height2.7 are associated with higher body mass index, higher ambulatory blood pressure, larger aortic root diameters, and relatively low myocardial contractility. (Hypertension. 1999;34:1032-1040.)

Key Words: hypertrophy, left ventricular ■ hypertension, white coat ■ obesity ■ metabolism ■ echocardiography

Although left ventricular (LV) hypertrophy is an adaptation that preserves cardiac pump function in arterial hypertension, it also represents a preclinical disease strongly predictive of cardiovascular morbidity and mortality.1-2 LV mass growth is related to hemodynamic factors, such as systolic blood pressure (BP), stroke volume, and body size. The ideal amount of lean body mass genetically programmed has been estimated to be proportional to height2.7 in adults. Therefore, height2.7, cardiac workload, and gender have been identified as major physiological determinants of LV growth,3 and, in a reference sample of normal-weight normotensive subjects, they may be used to estimate ideal amount of cardiac muscle. The observed/predicted LV mass ratio may be used to evaluate correlates of the deviation of measured LV mass from predicted LV mass. In a preliminary study, hypertensive subjects with LV mass exceeding values predicted by major physiological correlates (termed “inappropriately high LV mass”) had a higher rate of subsequent cardiovascular death.4

Evaluation of the 24-hour ambulatory BP profile explains the variability of LV mass better than clinic BP5,6 and can assess day-night BP variability,7,8 which is of interest because lack of a nocturnal BP fall has been associated with increased LV mass.8,9 Moreover, “white coat” hypertension can be detected by ambulatory monitoring.10 Furthermore, lower LV contractility,11,12 larger arterial size,13,14 and metabolic abnormalities15-17 have all been associated with higher LV mass. However, whether 24-hour ambulatory BP profile, metabolic

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From the Division of Cardiology and Hypertension Center, Department of Medicine, New York Presbyterian Hospital, Joan and Sanford I. Weill Medical College of Cornell University, New York, NY.
Correspondence to Richard B. Devereux, MD, Division of Cardiology, Box 222, New York Presbyterian Hospital–Weill Medical College of Cornell University, 525 E 68th St, New York, NY 10021. E-mail rbdevere@mail.med.cornell.edu
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abnormalities, and myocardial contractility may contribute to explain levels of LV mass inappropriately high for hemodynamic stimuli, height, and gender in hypertensive subjects is unclear. Accordingly, this study was designed to investigate ambulatory BP and cardiovascular features in hypertensive subjects with adequate or inappropriate LV mass. In addition, metabolic status (fasting glucose, total and HDL cholesterol, and triglyceride levels), LV geometry, and systolic function were also evaluated.

Methods

Study Population
A total of 185 hypertensive individuals were studied, of whom 76 were referred from the Hypertension Center of The New York Hospital from January 1990 to July 1995, 104 were referred from a worksite-based study, and 5 were identified in a population survey of elderly volunteers from the community. Criteria for diagnosis of hypertension were clinic systolic BP ≥140 (or ≥160 mm Hg for subjects older than 65 years) or diastolic BP ≥90 mm Hg. Subjects underwent 24-hour ambulatory BP monitoring, echocardiogram, and metabolic screening; 41% of the subjects had not been previously treated, while the others had stopped antihypertensive treatment 3 weeks to 6 years before the study protocol. All subjects were free of clinical, echocardiographic, or laboratory evidence of coronary or valvular heart disease, diabetes mellitus, cerebrovascular disease, or secondary hypertension. Subjects with awake ambulatory BP <134/90 mm Hg were considered to have white coat hypertension. Informed consent was obtained from all subjects included.

BP Determination
Clinic BP was estimated by a mercury sphygmomanometer as the average of at least 3 measurements by a physician or qualified nurse. Echo BP is BP measured at the end of the echocardiogram, after ~30 minutes of supine rest in a dark room. Ambulatory BP monitoring was recorded during a routine day by a SpaceLabs 90207 device. Briefly, the monitor was placed on the nondominant arm and set to take BP readings every 15 minutes during the working day and every 30 or 60 minutes during sleep. Subjects were instructed to record their activity and location after each awake in a diary to permit identification of the awake and sleep time. The sleep-awake BP fall was assessed as the absolute and relative changes between sleep and awake systolic and diastolic BP.

Echocardiography
All subjects underwent standard M-mode and 2-dimensional echocardiography by a skilled research technician using commercially available echocardiography equipped with 2.5- to 3.5-MHz transducers. LV dimensions were assessed from 2-dimensionally guided M-mode tracings (American Society of Echocardiography) or, if available echocardiography equipped with 2.5- to 3.5-MHz transducers. LV mass and volume were calculated with the use of Teichholz’s method. Aortic root diameter was measured at the maximal diameter of the sinuses of Valsalva. Observed LV mass was calculated by the adjusted American Society of Echocardiography method and indexed for height. Body surface area, LV hypertrophy was defined with the use of gender-specific cut points (LV mass/height2.7 >47 g/m2 in women; LV mass/height2.7 >50 g/m2 in men). Predicted values of LV mass were derived by an equation previously developed in a reference population of 393 normal-weight, normotensive adults, aged 18 to 85 years, which includes an indicator variable for gender (men = 2; women = 1), height, and stroke work as a measure of cardiac workload [echo systolic BP × Doppler stroke volume × 0.01443]: predicted LV mass = 18.1 × gender + 0.64 × stroke work + 6.63 × height2.7 + 55.7. This equation provides estimates of LV mass expected for cardiac workload, height, and gender. The observed/predicted LV mass ratio × 100 (%PLVM) was estimated in the reference population to identify the 5th and 95th percentiles of its distribution (73% to 128%). With the use of the aforementioned equation, the %PLVM was then computed in hypertensive subjects. Subjects with %PLVM >128% (16 of 185 subjects [9%]) were classified as having inappropriately high LV mass, whereas LV mass was considered adequate if %PLVM was between 73% and 128% (164 of 185 subjects [88%]). Subjects with %PLVM <73% (5 of 185 subjects [3%]) were classified as having inadequate LV mass but were not considered in primary analyses because of the likelihood of unstable results with such small cell size. Relative wall thickness was calculated as twice posterior wall in diastole divided by internal diameter and was used as an estimate of LV geometry. Midwall circumferential end-systolic stress (ESS) was assessed as previously reported. Endocardial fractional shortening (FS), midwall fractional shortening (MWS), as well as 2 estimates of afterload-independent LV systolic function, the percentage of predicted midwall shortening for a given circumferential ESS (termed stress-corrected MWS), a measure of myocardial contractility, and the ratio ESS/LV end-systolic volume index (ESS/ESVi), a measure of LV systolic chamber function, were derived as previously described.

Statistical Analysis
Data were stored and analyzed with SPSS 8.0 (SPSS Inc). Continuous variables, expressed as mean ± SD, were log-transformed when necessary to better satisfy distributional assumptions before parametric tests were used. Student’s t test for independent groups was used to compare subjects with inappropriately high or adequate LV mass. ANCOVA was used to adjust the results for age, body mass index (BMI), gender, and race (blacks versus nonblacks), and adjusted means and SDs are provided in parentheses in the tables. Two-tailed Fisher’s exact tests were used to test the null hypothesis for categorical variables. Pearson correlations were used to investigate relationships between LV mass, %PLVM, and demographic, metabolic, and echocardiographic data. The relationships of %PLVM to aortic root diameter and LV systolic performance, controlling for age, BMI, and diastolic ambulatory BP, were investigated with partial correlation. In an exploratory analysis, the small group classified as having inadequate LV mass was matched by age ± 1 year with subjects having adequate LV mass. Gender was not considered because it was included in the equation to predict LV mass. To maximize statistical power, we matched on average 7 subjects with adequate LV mass to each subject having relatively low LV mass. ANOVA, weighted to simulate an equal number of control subjects per case, was used to test differences between these 2 groups. A 2-tailed P < 0.05 was considered statistically significant.

Results

Comparisons Between Hypertensive Subjects With Adequate Versus Inappropriately High LV Mass

Demographic and Metabolic Characteristics
The sample for the primary analyses comprised 180 clinically hypertensive subjects (mean age, 56 ± 11 years; range, 30 to 81 years; 111 men [62%]; 54 blacks [30%]), of whom 164 had adequate and 16 inappropriately high LV mass (Table 1). No significant differences were found in age, gender, height, proportion of never-treated subjects, or smoking habit. BMI and the proportion of blacks were higher in subjects with inappropriately high LV mass. Total cholesterol, triglyceride, and creatinine levels were comparable between the 2 groups, while fasting glucose was higher and HDL cholesterol was lower in subjects with inappropriately high LV mass. Adjustment for covariates eliminated differences in fasting glucose and HDL cholesterol.
TABLE 1. Demographic and Metabolic Characteristics of Hypertensive Subjects With Adequate vs Inappropriately High LV Mass

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adequate LV Mass (n=164)</th>
<th>Inappropriately High LV Mass (n=16)</th>
<th>P</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>56±11</td>
<td>54±8</td>
<td>NS</td>
<td>...</td>
</tr>
<tr>
<td>Male, %</td>
<td>60</td>
<td>81</td>
<td>NS</td>
<td>...</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.4±3.8</td>
<td>30.3±4.1</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Height [m]²</td>
<td>4.2±0.6 (4.2±0.6)</td>
<td>4.2±0.5 (4.2±0.6)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Black, %</td>
<td>27</td>
<td>63</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
<td>Current smokers, %</td>
<td>9</td>
<td>13</td>
<td>NS</td>
<td>...</td>
</tr>
<tr>
<td>Never-smokers, %</td>
<td>56</td>
<td>63</td>
<td>NS</td>
<td>...</td>
</tr>
<tr>
<td>Former smokers, %</td>
<td>35</td>
<td>25</td>
<td>NS</td>
<td>...</td>
</tr>
<tr>
<td>Never-treated patients, %</td>
<td>42</td>
<td>25</td>
<td>NS</td>
<td>...</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>4.9±0.8 (4.9±0.9)</td>
<td>5.3±0.8 (5.1±0.8)</td>
<td>0.03</td>
<td>NS</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.84±1.14 (5.84±1.16)</td>
<td>5.59±1.06 (5.74±1.14)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.37±0.39 (1.37±0.39)</td>
<td>1.16±0.34 (1.14±0.36)</td>
<td>0.03</td>
<td>NS</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>143±112 (143±114)</td>
<td>142±96 (138±111)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>88±19 (88±17)</td>
<td>96±15 (89±16)</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SD unadjusted (and adjusted).

*P adjusted for covariates (age, gender, BMI, and race) (ANCOVA).
†P adjusted for gender and race.

Blood Pressure

Subjects with inappropriately high or adequate LV mass had comparable systolic BP at the end of the echocardiogram, whereas diastolic BP tended to be higher (P=0.1) in those with inappropriately high LV mass (Table 2). In contrast, 24-hour, awake, and sleep systolic and diastolic ambulatory BPs were consistently higher in subjects with inappropriately high than in those with adequate LV mass. After adjustment for covariates (age, gender, race, and BMI), differences in ambulatory systolic BP did not reach statistical significance (24 hour, P=0.08; awake, P=0.07; and sleep, P=0.09), while differences in diastolic BP remained statistically significant. The day-night difference in BP was similar in the 2 groups, even when genders were analyzed separately (data not shown; all P>0.1). Pulse pressure was also comparable in subjects with adequate versus inappropriately high LV mass (clinic pulse pressure, 60±16 vs 58±12 mm Hg; awake pulse pressure, 55±11 vs 56±11 mm Hg; all P>0.1).

All 23 subjects (13% of 180) with white coat hypertension, according to previously defined criteria, exhibited adequate LV mass; none had clear-cut LV hypertrophy.

Echocardiographic Findings

As partially expected from the study design, LV mass/height² as well as LV mass/body surface area, used to...
minimize the influence of obesity, were higher in subjects with inappropriately high LV mass than in those with adequate LV mass (Table 3). LV systolic and diastolic dimensions and relative wall thickness were also higher in subjects with inappropriately high LV mass. ESS was similar between the 2 groups. LV endocardial FS, MWS, stress-corrected MWS, and ESS/ESVi ratio were lower in subjects with adequate LV mass (Table 3). LV systolic and diastolic pressures, and Aortic root diameter were also significantly larger in subjects with inappropriately high LV mass than in those with adequate LV mass (Table 3).

### TABLE 3. Echocardiographic Findings in Patients With Adequate or Inappropriately High LV Mass

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adequate LV Mass</th>
<th>Inappropriately High LV Mass</th>
<th>P</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass index, g/m²²</td>
<td>40 ± 8</td>
<td>57 ± 8</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LV mass index, g/m²²</td>
<td>88 ± 17</td>
<td>121 ± 19</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LVIDd, cm</td>
<td>5.0 ± 0.5 (5.0 ± 0.4)</td>
<td>5.2 ± 0.5 (5.1 ± 0.5)</td>
<td>0.02</td>
<td>NS</td>
</tr>
<tr>
<td>LVIDs, cm</td>
<td>3.1 ± 0.5 (3.1 ± 0.4)</td>
<td>3.5 ± 0.5 (3.5 ± 0.5)</td>
<td>&lt;0.0005</td>
<td>0.002</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.37 ± 0.05 (0.37 ± 0.05)</td>
<td>0.43 ± 0.05 (0.42 ± 0.06)</td>
<td>&lt;0.0005</td>
<td>0.001</td>
</tr>
<tr>
<td>Aortic root diameter, cm</td>
<td>3.3 ± 0.4 (3.3 ± 0.4)</td>
<td>3.7 ± 0.4 (3.7 ± 0.04)</td>
<td>&lt;0.0005</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Left atrial dimension, cm</td>
<td>3.4 ± 0.5 (3.5 ± 0.5)</td>
<td>3.6 ± 0.6 (3.4 ± 0.5)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>ESS, kdyne/cm²</td>
<td>146 ± 33 (146 ± 34)</td>
<td>151 ± 40 (151 ± 35)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>FS, %</td>
<td>38 ± 5 (38 ± 5)</td>
<td>33 ± 5 (33 ± 5)</td>
<td>0.002</td>
<td>0.001</td>
</tr>
<tr>
<td>MWS, %</td>
<td>18 ± 2 (18 ± 2)</td>
<td>15 ± 2 (15 ± 2)</td>
<td>&lt;0.0005</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Stress-corrected MWS, %</td>
<td>107 ± 12 (107 ± 12)</td>
<td>87 ± 10 (89 ± 12)</td>
<td>&lt;0.0005</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>ESS/ESVi, kdyne/cm³</td>
<td>7.4 ± 1.5 (7.5 ± 1.4)</td>
<td>5.6 ± 0.8 (5.6 ± 1.4)</td>
<td>&lt;0.0005</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>68 ± 12 (68 ± 12)</td>
<td>72 ± 13 (70 ± 12)</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean ± SD unadjusted (and adjusted). LVIDd indicates LV internal diameter at end-diastole; LVIDs, LV internal diameter at end-systole.

A separate analysis was performed among subjects with LV hypertrophy, comparing those with inappropriately high LV mass (inappropriate LV hypertrophy, n = 12) with those with adequate LV mass (adequate LV hypertrophy, n = 19) (Table 4). Subjects with inappropriate LV hypertrophy tended to be younger and have higher BMI than those with adequate LV mass (Table 4).
hypertrophy, but those differences did not reach statistical significance. Women predominated among subjects with adequate LV hypertrophy, whereas no difference was found in race prevalence. Echo BPs (not shown) were similar between groups. However, ambulatory BP tended to be higher in subjects with inappropriately low LV hypertrophy. LV mass/height² or LV mass/body surface area to account for the impact of obesity, relative wall thickness, and aortic root diameter tended to be lower and FS higher in subjects with inappropriately low LV hypertrophy. Endocardial FS, MWS, stress-corrected MWS, and ESS/ESVi were significantly higher and fasting glucose and triglyceride (P<0.05) levels were lower in subjects with inappropriately low LV mass. The difference in HDL cholesterol was not statistically significant.

Comparisons Between Hypertensive Subjects With Inappropriately Low LV Mass and Age-Matched Hypertensive Subjects With Adequate LV Mass

An age-matched pilot case-control study was designed to compare the 5 subjects with relatively low LV mass (%PLVM <73%) with age-matched hypertensive subjects with adequate LV mass (n=36) (Table 5).

Table 5. Comparison Between Age-Matched Patients With Inappropriately Low vs Adequate LV Mass

<table>
<thead>
<tr>
<th>Variables</th>
<th>Inappropriately Low LV Mass (n=5)</th>
<th>Adequate LV Mass (Age-Matched Group)</th>
<th>Difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, kg/m²</td>
<td>25.4±3.1</td>
<td>24.8±3.0</td>
<td>0.6</td>
<td>NS</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>4 (80)</td>
<td>21 (58)</td>
<td>...</td>
<td>NS</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>0</td>
<td>7 (19)</td>
<td>...</td>
<td>NS</td>
</tr>
<tr>
<td>Awake SBP, mm Hg</td>
<td>158±38</td>
<td>150±15</td>
<td>8</td>
<td>NS</td>
</tr>
<tr>
<td>Awake DBP, mm Hg</td>
<td>88±12</td>
<td>89±13</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>LV mass index, g/m²²</td>
<td>36±15</td>
<td>40±9</td>
<td>4</td>
<td>...</td>
</tr>
<tr>
<td>LVIDd, cm</td>
<td>4.7±0.6</td>
<td>4.9±0.5</td>
<td>0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.35±0.04</td>
<td>0.37±0.04</td>
<td>-0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic root diameter, cm</td>
<td>3.0±0.1</td>
<td>3.3±0.4</td>
<td>-0.3</td>
<td>NS</td>
</tr>
<tr>
<td>FS, %</td>
<td>44±6</td>
<td>38±5</td>
<td>6</td>
<td>0.06</td>
</tr>
<tr>
<td>MWS, %</td>
<td>21±2</td>
<td>18±2</td>
<td>4</td>
<td>0.006</td>
</tr>
<tr>
<td>Stress-corrected MWS, %</td>
<td>129±8</td>
<td>109±13</td>
<td>20</td>
<td>0.002</td>
</tr>
<tr>
<td>ESS/ESVi, kdyne/cm²</td>
<td>11.0±3.6</td>
<td>7.7±1.7</td>
<td>4.3</td>
<td>0.02</td>
</tr>
<tr>
<td>Creatinine, µmol/L</td>
<td>94±44</td>
<td>84±20</td>
<td>10</td>
<td>NS</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>4.1±0.3</td>
<td>4.9±0.7</td>
<td>-0.8</td>
<td>0.05</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.73±0.44</td>
<td>1.42±0.47</td>
<td>0.31</td>
<td>NS</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>73±38</td>
<td>151±104</td>
<td>-78</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Abbreviations are as defined in Table 3.

Relationships of Observed/Predicted LV Mass Ratio to Aortic Root and LV Function

LV mass was not significantly related to age, but %PLVM showed a negative relationship to age, probably reflecting the positive relationships between age and stroke work (r=0.27, P<0.001) that may tend to reduce the increment of observed/predicted LV mass ratio with increasing age (Table 6). BMI was more strongly related to LV mass than to %PLVM. Ambulatory (awake or sleep) and echo diastolic BP were positively related to LV mass, whereas %PLVM showed a positive relationship to ambulatory diastolic BPs (both awake or sleep) but not to echo diastolic BP. After adjustment for age and BMI, awake diastolic BP showed a significant positive relationship to LV mass (partial r=0.36, P<0.001) and %PLVM (partial r=0.20, P<0.005). No significant associations were found between LV mass or %PLVM with systolic or diastolic day-night BP differences. A positive relationship was found between ESS and LV mass but not with %PLVM. Of interest, parameters of LV systolic function (endocardial FS, MWS, stress-corrected MWS, and ESS/
ESVi ratio) had moderate negative correlations to LV mass but were even more strongly negatively related to %PLVM. After adjustment for age, BMI and awake diastolic BP, high values of LV mass, and %PLVM were associated with higher aortic root diameters and lower LV systolic function.

**Discussion**

In the present study we investigated cardiovascular features associated with values of LV mass that are higher than those predicted by gender, height$^2$, and cardiac workload,$^3$ a condition we termed inappropriately high LV mass.$^4$ This study provides initial evidence that inappropriately high LV mass is associated with high BMI even though the formula to predict LV mass accounts for ideal lean body mass for given height (that is, height$^2.7$) and hemodynamic factors (stroke volume and systolic BP) that mediate obesity-associated increases of LV mass.$^30$ Within this clinically hypertensive sample, diastolic ambulatory BP slightly discriminated those with inappropriately high LV mass, even after controlling for obesity and systolic BP (included in stroke work). Inappropriately high LV mass was also associated, independently of age, diastolic awake BP, and BMI, with relatively depressed LV systolic performance, which is documented to have adverse prognostic significance. The association of metabolic abnormalities (high fasting glucose levels and worse lipid profile) with inappropriately high LV mass could be explained by the confounding effect of obesity. The fact that a similar pattern was found in the subset of subjects with LV hypertrophy suggests that inappropriateness of LV mass may represent a marker of a transition from a compensatory to a pathological phenotype of severe LV hypertrophy.

In continuity with our main results, an additional case-control study performed to explore differences between subjects with inappropriately low LV mass and age-matched hypertensive subjects with adequate LV mass provided initial evidence of associations of relatively low LV mass with lower BMI, higher LV systolic performance, and a favorable metabolic profile, characterized by lower fasting glucose and triglyceride levels and higher HDL cholesterol.

**Inappropriately High LV Mass, Obesity, and Metabolic Findings**

Subjects with inappropriately high LV mass had higher BMI, higher fasting glucose levels, and lower mean HDL cholesterol than subjects with adequate LV mass. The strong association of overweight with the observed/predicted LV mass ratio in hypertensive subjects might not be purely an extension of an association between relative body weight and LV mass in apparently normal adults but may reflect, at least in part, the importance of overweight/obesity in the pathophysiology of hypertension. The equation used to predict LV mass was derived in normal-weight subjects and includes body height to the power of 2.7 but not weight. Height$^2.7$ is a marker of the individual’s “ideal” lean body mass programmed for the size of skeleton$^{27–29}$ for which the cardiac muscle might be also genetically programmed and is linearly related to LV mass. However, height$^2$ does not account for the additional increase in lean body mass that usually occurs in obese subjects. Thus, the ratio of observed/predicted LV mass may be particularly sensitive to the effect of overweight-related metabolic abnormalities and hemodynamic impact of increased lean body mass. However, the equation to predict adequacy of LV mass includes both systolic BP and stress volume, which we have previously shown to increase in parallel with body size in overweight and obese individuals.$^{30}$ Therefore, the equation to predict LV mass accounts for hemodynamic stimulus for LV growth in obesity. Obesity-related insulin resistance (as suggested by metabolic findings) and/or elevated blood viscosity$^{31}$ might contribute to increase the ratio of observed/predicted LV mass. Obesity has been repeatedly associated with increased LV mass$^{32–34}$ as well as with hyperinsulinemia and insulin resistance.$^{15,35}$

In contrast, subjects with relatively low LV mass tended to be lean and to have low fasting glucose, total cholesterol, and
triglyceride levels as well as high HDL cholesterol, which are hallmarks of potentially optimal glucose tolerance. Furthermore, differences in BMI and other metabolic findings between subjects with adequate versus inappropriately high LV mass approached statistical significance among the small subgroup (n=31) of subjects with LV hypertrophy, which suggested associations of a magnitude that could be pathophysiologically important. 17

Contribution of Ambulatory Blood Pressure to Inappropriately High LV Mass
LV mass is more closely correlated with ambulatory BP than conventional clinic BP measurements. 5,6,8–10 Although BP evaluated at the end of the echocardiogram under standardized resting conditions may be more reliable than usual measures of clinic BP, in our study only ambulatory BP statistically differentiated the 2 groups, independently of age, gender, race, and BMI. In the analysis of subjects with LV hypertrophy, ambulatory BPs tended to be higher than conventional BP (P<0.05) at systolic pressure waveform because of vascular stiffening 4 may mediate the stronger relation of LV mass with aortic root diameter. 45,46 A relationship between larger aortic root size and inappropriately high LV mass may depend on increased proximal aortic stiffness, by enhancing LV wall stress in early systole as a result of loss of aortic elastic reserve. 47 Changes in the arterial pressure waveform because of vascular stiffening may mediate the stronger relation of LV mass with aortic root dimension than with BP, with possible additional contributions of a nonhemodynamic nature. 13,49

Additionally, inappropriately high LV mass was associated with lower myocardial function as well as lower afterload-independent LV systolic chamber function, which are strong independent predictors of cardiovascular events. 50,51 Those differences remained highly significant even when we compared inappropriately high LV mass with adequate LV hypertrophy, while subjects with relatively low observed/predicted LV mass had high LV systolic performance. Our findings support previous observations of a potentially bidirectional relationship between myocardial contractility and adaptation of LV muscle to growth stimuli. 11,14,26

Conclusions
In hypertensive adults, values of LV mass that exceeded the ones predicted by individual gender, height, 17, and stroke work were associated with higher BMI, metabolic abnormalities, black race, higher ambulatory BP (but not with different day-night BP profile), larger aortic root diameter, concentric LV geometry, and lower LV systolic performance. These characteristics were also confirmed in the subgroup of subjects with LV hypertrophy. Our findings also extend previous observations in which lower myocardial contractility was associated with less favorable metabolic profile, impaired arterial compliance, and higher arterial wall thickness. 52 Genetic factors may have an additional role in LV adaptation to workload and body size. 53

Echocardiographic Findings
The larger aortic root diameters in subjects with inappropiate as opposed to adequate LV mass suggest morphological and functional relationships between the proximal arterial tree and appropriateness of LV mass. The difference in aortic root diameter remained significant (P<0.01, data not shown) after adjustment for age, gender, race, and BMI as potential covariates of aortic root diameter, as well as in alternative analyses that considered systolic, diastolic, or pulse pressure alternatively as covariates. Thus, the between-group difference in aortic root diameter is independent of BP differences between subjects with inappropriate or adequate LV mass. It is also notable that this difference was still present in the subset of subjects with LV hypertrophy. Mean aortic root diameter showed a significant positive trend (from 3.0 to 3.3 to 3.8 cm) from subjects with relatively low %PLVM, to subjects with adequate LV mass, and to those with inappropriate LV hypertrophy. Parallel changes in cardiac and large-artery structure have been previously documented for smaller-capacitance arteries, 44 and a positive relationship between BP and aortic root size has also been reported. 45,46 A relationship between aortic root diameters and LV mass has been recently reported in a population-based study. 14 Although pulse pressure was comparable in the 2 groups, the association between larger aortic root size and inappropriately high LV mass may depend on increased proximal aortic stiffness, by enhancing LV wall stress in early systole as a result of loss of aortic elastic reserve. 47 Changes in the arterial pressure waveform because of vascular stiffening may mediate the stronger relation of LV mass with aortic root dimension than with BP, with possible additional contributions of a nonhemodynamic nature. 13,49

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