PATHOPHYSIOLOGY AND NATURAL HISTORY

HYPERTENSION

Left ventricular hypertrophy in patients with hypertension: importance of blood pressure response to regularly recurring stress

RICHARD B. DEVEREUX, M.D., THOMAS G. PICKERING, M.D., PH.D.,
GREGORY A. HARSHFIELD, PH.D., HOLLIS D. KLEINERT, PH.D., LORRAINE DENBY, M.S.,
LINDA CLARK, B.A., DARYL PREGIBON, PH.D., MICHAEL JASON, M.D., BEAT KLEINER, PH.D.,
JEFFREY S. BORER, M.D., AND JOHN H. LARAGH, M.D.

ABSTRACT  Left ventricular hypertrophy (LVH), a target organ response in essential hypertension, is only weakly related to clinical measurements of blood pressure. To determine whether blood pressure measured under basal or stress conditions more closely determines LVH, we compared echocardiographic left ventricular mass index and relative wall thickness with clinical blood pressure and with 24 hr recordings (home, work, and sleep) in 19 normal subjects and 81 patients with mild hypertension. Only a weak correlation was observed in the entire group between left ventricular mass index and clinical measurements of systolic and diastolic blood pressure (r = .24, p < .02; r = .20, p < .05, respectively), which was only slightly improved by use of systolic and diastolic blood pressure readings taken in the home (r = .31, p < .005; r = .21, p < .05, respectively). Sleep and total 24 hr blood pressure also related poorly to left ventricular mass index. In contrast, substantially higher correlations existed between left ventricular mass index and systolic and diastolic blood pressure measured by portable recorder in 60 subjects at work (r = .50, p < .001; r = .39, p < .01, respectively). Similarly, work diastolic blood pressure bore the closest relationship to relative wall thickness (r = .59, p < .001). Home blood pressure readings taken on a work day also showed a moderate relationship with indices of LVH, whereas weaker correlations were found in employed subjects whose blood pressure was recorded on a non-workday, and no relationship between blood pressure and LVH existed in subjects who were not employed. We conclude that hypertensive LVH is poorly related to clinical or home measurements of blood pressure but that a substantially closer relationship exists between LVH and blood pressure during recurring stress at work and between LVH and home blood pressure on a workday. Thus hypertensive cardiac hypertrophy appears to be more closely related to blood pressure during stressful situations than to basal blood pressure.


NUMEROUS STUDIES have demonstrated that the risk of disease and death increases as blood pressure rises. However, despite the consistency of this finding and its high statistical significance in large populations, the actual correlations between blood pressure measurements and the incidence of morbid events have generally been relatively low. One possible explana-

From the Division of Cardiology, The Hypertension Center, and the Department of Neurology, The New York Hospital–Cornell Medical Center, New York, and the Department of Statistics and Data Analysis Research, Bell Laboratories, Murray Hill, NJ.

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Address for correspondence: Richard B. Devereux, M.D., Division of Cardiology, Box 222, The New York Hospital, 525 East 68th St., New York, NY 10021.

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CIRCULATION
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recordings on a workday, we also stratified our subjects according to employment status. A total of 60 subjects worked on the day of recording, 28 were employed but had recordings performed on a non-workday, and 12 were not employed. As seen in table 1, these groups differed only slightly with regard to age and sex, except for a higher number of women in the unemployed group, and had similar 24 hr blood pressure measurements.

Echocardiographic methods. Echocardiograms were performed with standard techniques previously reported from this laboratory.29, 30 Echocardiographic tracings were coded and read blindly and in random order. End-diastolic measurements of interventricular septal thickness (IVS), left ventricular internal dimension (LVID), and posterior wall thickness (PWT) were made according to the Penn Convention protocol to measure left ventricular mass.24 This was calculated by a simple anatomically validated formula:

\[ LVM = 1.04((IVS + LVID + PWT) - LVID)^3 - 13.6 \]

To minimize the impact of variation in body size on left ventricular mass, it was indexed for body surface area. End-diastolic and end-systolic measurements were also made according to the recommendations of the American Society of Echocardiography.31 End-diastolic relative wall thickness32 was calculated from these values.

Blood pressure by portable recorder. The 24 hr blood pressure recordings were obtained with the Del Mar Avionics Ambulatory Blood Pressure Monitor II. Subjects were fitted with the recorder on the morning of the day of the recording, and a minimum of five readings were taken with the subject in the sitting position. These had to be within 5 mm Hg of simultaneous readings obtained with a stethoscope and mercury column for the recording to be considered acceptable. The recorder was then set to take readings at 15 min intervals, and subjects were
during each stage of maximum upright treadmill exercise tests by the Bruce protocol.

Patients with hypertension. Eighty-one subjects with mild essential hypertension were studied. There were 70 men and 11 women (ages 18 to 66 years, mean 43). Mean clinical blood pressure was 152 ± 15/96 ± 7 mm Hg; the duration of hypertension was 5.5 ± 5.5 years. Treadmill exercise tests were performed in 55 hypertensive patients, and radionuclide cineangiograms were obtained in nine subjects.

Employment status. In view of the potential importance of the blood pressure response to occupational stress in causing target organ manifestations of hypertension and of the emphasis placed by Sokolow et al.12 on obtaining daytime blood pressure recordings on a workday, we also stratified our subjects according to employment status. A total of 60 subjects worked on the day of recording, 28 were employed but had recordings performed on a non-workday, and 12 were not employed. As seen in table 1, these groups differed only slightly with regard to age and sex, except for a higher number of women in the unemployed group, and had similar 24 hr blood pressure measurements.

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<table>
<thead>
<tr>
<th>Employment status of subjects</th>
<th>n</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>24 hr BP</th>
<th>LVMI (g/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects who worked on day of recording</td>
<td>60</td>
<td>43 ± 11</td>
<td>52 M</td>
<td>132 ± 18</td>
<td>106 ± 27</td>
</tr>
<tr>
<td>Employed subjects who wore recorder on non-workday</td>
<td>28</td>
<td>42 ± 13</td>
<td>23 M</td>
<td>133 ± 17</td>
<td>109 ± 26</td>
</tr>
<tr>
<td>Subjects who were not employed</td>
<td>12</td>
<td>34 ± 20</td>
<td>5 M</td>
<td>131 ± 19</td>
<td>90 ± 22</td>
</tr>
</tbody>
</table>

BP = blood pressure; LVMI = left ventricular mass index.
instructed to follow their normal daily routine after they left the laboratory. Each time a reading was taken subjects were instructed to remain motionless and then to record their activity on a diary sheet. After 24 hr they returned to the Hypertension Center, where five additional readings were taken. The tapes were played back into an Avionics Electrocardioscanner (Model 660A) and analyzed on a LSI 11/03 microcomputer (Digital Equipment Corp.) by a method described previously,10–21,24–25 whereby each reading was checked for validity, and the patient’s activity from the diary sheet was entered into the computer.

Components of blood pressure. A minimum of three technically satisfactory blood pressure measurements in a setting were required for a median measurement to be calculated. A sufficient number of measurements were available for 98 patients in the Hypertension Center at the beginning and end of the period of ambulatory monitoring, from which the median “clinic” systolic and diastolic pressures were computed. All but one subject had enough measurements at home to calculate median levels of “home” systolic and diastolic pressure. A total of 60 subjects had “work” blood pressure calculated from a minimum of three blood pressure measurements recorded during a normal workday. 67 subjects had “sleep” blood pressure calculated, and the remaining 33 subjects either removed the pressure recorder during sleep or slept in positions that resulted in a high proportion of artifactual readings. Mean levels of blood pressure throughout the 24 hr period were calculated for all patients.

Statistical analysis. The strength of the association between various measures of blood pressure and left ventricular mass index was assessed by the product moment correlation coefficient and its test of significance.33 No significant difference existed between normotensive and hypertensive subjects in the relationship between blood pressure measurements and indices of LVH, and analyses were therefore performed on the entire study population. Differences between blood pressure under different circumstances in the same patient were assessed by the paired t test. The significance of differences between correlations was determined by use of the Z statistic.34

Results

Relationship of clinical blood pressure measurements to LVH. Only a weak correlation existed between left ventricular mass index and clinical measurements of systolic blood pressure (r = .24, p < .02) (figure 1) or diastolic blood pressure (r = .20, p < .05). A similar weak relationship was observed between end-diastolic relative wall thickness and clinical systolic or diastolic blood pressure (r = .24, p < .02; r = .11, p = NS, respectively). Posterior wall thickness was even more weakly related to blood pressure measurement (r = .19, p = NS for systolic pressure, for example). In addition, no relationship was observed between left ventricular mass index and either the duration of hypertension (r = .01, p = NS) or age (r = .08, p = NS), other factors that might influence severity of hypertensive cardiac hypertrophy.

Relationship of blood pressure measurements by portable recorder to left ventricular mass index. Weak relationships were observed between left ventricular mass index and recorder systolic blood pressures in the clinic (r = .33, p < .001) (table 2), at home (r = .31, p < .005), during miscellaneous activities such as shopping and traveling (r = .29, p < .05), and during sleep (r = .10, p = NS). Despite the poor correlations of each of these components of blood pressure with left ventricular mass index there was a slightly closer relationship between 24 hr systolic blood pressure and left ventricular mass index (r = .38, p < .001). As depicted in table 2, comparable weak correlations were observed between diastolic blood pressure measurements under each of these conditions and left ventricular mass index.

In contrast, a substantially higher correlation existed between work systolic blood pressure and left ventricular mass index in the 60 patients who went to work (r = .50, p < .001) (figure 2). This correlation was significantly closer than that between left ventricular mass index and clinical blood pressure measurements (p < .05). Significant correlations also existed between left ventricular mass index and work diastolic blood pressure (r = .39, p < .005) as well as pulse pressure at work, calculated from the difference between systolic and diastolic pressure (r = .42, p < .001).

Relationship between blood pressure measurements by portable recorder and left ventricular relative wall thickness. Clinical blood pressure measurements and blood pressure levels during various times of day showed a similar pattern of relationship to that observed for left ventricular mass index (table 3), with the closest corre-
TABLE 2

Relationship of blood pressure to left ventricular mass index

<table>
<thead>
<tr>
<th></th>
<th>Correlation coefficient with:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic pressure</td>
</tr>
<tr>
<td>n</td>
<td></td>
</tr>
<tr>
<td>Physician-measured</td>
<td>100</td>
</tr>
<tr>
<td>Automatic recorder</td>
<td></td>
</tr>
<tr>
<td>Clinic</td>
<td>98</td>
</tr>
<tr>
<td>Work</td>
<td>60</td>
</tr>
<tr>
<td>Home</td>
<td>99</td>
</tr>
<tr>
<td>Sleep</td>
<td>67</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>74</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

Statistical comparisons: <sup>A</sup>p < .05; <sup>B</sup>p < .01; <sup>C</sup>p < .001.

TABLE 3

Relationship of blood pressure to left ventricular relative wall thickness

<table>
<thead>
<tr>
<th></th>
<th>Correlation coefficient with:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic pressure</td>
</tr>
<tr>
<td>n</td>
<td></td>
</tr>
<tr>
<td>Physician-measured</td>
<td>100</td>
</tr>
<tr>
<td>Automatic recorder</td>
<td></td>
</tr>
<tr>
<td>Clinic</td>
<td>98</td>
</tr>
<tr>
<td>Work</td>
<td>60</td>
</tr>
<tr>
<td>Home</td>
<td>99</td>
</tr>
<tr>
<td>Sleep</td>
<td>67</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>74</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

Statistical comparisons: <sup>A</sup>p < .05; <sup>B</sup>p < .01; <sup>C</sup>p < .001.

lations observed with work diastolic blood pressure (r = .59, p < .001) (figure 3). A similar pattern of relationships was observed for posterior wall and interventricular septal thickness.

Effect of employment status on relationships between blood pressure and LVH. To elucidate further the relationship between LVH and blood pressure responses to occupational stress, separate analyses were performed in the three previously delineated groups: subjects whose readings were obtained on a workday (n = 60), employed subjects who chose to wear the recorder on a non-workday (n = 28), and subjects who were not employed (n = 12). As seen in table 4, the closest relationships between left ventricular mass index and each component of blood pressure during the day were observed in the 60 subjects whose recordings were made on a workday. The weakest relationships were observed in the subjects who were not employed, and intermediate relationships were seen in the employed subjects who chose to wear the blood pressure recorder during a weekend or vacation day. The relationship between home systolic blood pressure and left ventricular mass index in the three groups is illustrated in figure 4. Analyses of variance revealed that these differences could not be attributed to the age or sex of subjects in the different groups nor to differences in the variety of activities at home (eating, moving about,

![FIGURE 2](image-url)  
**FIGURE 2.** A closer relationship exists between automatic recorder measurements of systolic blood pressure at work (horizontal axis) and left ventricular mass index (vertical axis).

![FIGURE 3](image-url)  
**FIGURE 3.** The closest relationship observed in this study was between automatic recorder measurements of work diastolic blood pressure (horizontal axis) and end-diastolic left ventricular relative wall thickness (vertical axis).
TABLE 4
Correlation coefficients between blood pressure and left ventricular mass index

<table>
<thead>
<tr>
<th>Employment status</th>
<th>SBP</th>
<th>DBP</th>
<th>n</th>
<th>SBP</th>
<th>DBP</th>
<th>n</th>
<th>SBP</th>
<th>DBP</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician-measured</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Automatic recorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic</td>
<td>.26A</td>
<td>.24</td>
<td>60</td>
<td>.16</td>
<td>.21</td>
<td>22</td>
<td>.29</td>
<td>.07</td>
<td>10</td>
</tr>
<tr>
<td>Work</td>
<td>.50C</td>
<td>.49C</td>
<td>60</td>
<td>.05</td>
<td>.35</td>
<td>27</td>
<td>.27</td>
<td>-.14</td>
<td>12</td>
</tr>
<tr>
<td>Home</td>
<td>.50C</td>
<td>.39A</td>
<td>60</td>
<td>-.02</td>
<td>.16</td>
<td>28</td>
<td>.07</td>
<td>-.27</td>
<td>12</td>
</tr>
<tr>
<td>Sleep</td>
<td>.48C</td>
<td>.35B</td>
<td>60</td>
<td>-.06</td>
<td>.23</td>
<td>19</td>
<td>.67</td>
<td>.41</td>
<td>6</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>.43B</td>
<td>.37B</td>
<td>50</td>
<td>-.04</td>
<td>.35</td>
<td>21</td>
<td>-.06</td>
<td>-.52</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>.50C</td>
<td>.45C</td>
<td>60</td>
<td>.008</td>
<td>.25</td>
<td>28</td>
<td>.12</td>
<td>.12</td>
<td>12</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure; DBP = diastolic blood pressure.
Statistical comparisons: Ap < .05; p < .01; p < .001.

relaxing, or conversing). Furthermore, there was no relationship between age and left ventricular mass index in any subgroup, which is consistent with our observation in normal subjects. A similar pattern was observed for the relationships between blood pressure measurements and relative wall thickness, with the closest correlations in the group with workday recordings and the weakest in the unemployed group. In contrast to left ventricular mass index, a significant relationship was observed between age and relative wall thickness in the unemployed group (r = .44, p < .01) but not in the working group (r = .23, p = NS).

Pattern of blood pressure variability in normal and in hypertensive subjects with and without LVH. Similar to the results of previous reports, very small increments in blood pressure between home and clinic or work were observed in normotensive individuals (table 5). In contrast, the hypertensive patients in this study exhibited significant increases in blood pressure over home measurements in the clinic (+6/4 mm Hg for those without LVH, +3/5 for those with; p < .05) and at work (+6/6 mm Hg for those without LVH, +8/6 for those with; p < .05).

Discussion
For many years, considerable attention has been devoted to the role of stress in cardiovascular conditions. Several studies have indicated that stress-prone personality types suffer increased frequencies of complications of coronary artery disease and that there may in fact be a generalized risk of premature death in individuals with maladaptive personality types or whose work involves high demands but little decision making. In contrast, leading experts in hypertension have suggested that blood pressure responses to stress may be misleading, representing a recrudescence of the primative defense reaction, and that basal blood pressures provide a better indicator of risk. However, all studies in support of this hypothesis have suffered from a common flaw — the assumption that the blood...
TABLE 5
Cardiac findings and blood pressure during daily activity in normal and hypertensive subjects with and without LVH\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>Normal (n = 15)</th>
<th>Hypertensive without LVH (n = 31)</th>
<th>Hypertensive with LVH (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVMI (g/m²)</td>
<td>91 ± 26</td>
<td>97 ± 15</td>
<td>140 ± 15</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>3.48 ± 1.19</td>
<td>3.48 ± 0.78</td>
<td>3.47 ± 1.11</td>
</tr>
<tr>
<td>BP (mm Hg)(^b)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic</td>
<td>112 ± 15/78 ± 10</td>
<td>141 ± 18/94 ± 12</td>
<td>144 ± 20/97 ± 12</td>
</tr>
<tr>
<td>Work</td>
<td>116 ± 14/84 ± 7</td>
<td>141 ± 15/96 ± 10</td>
<td>149 ± 13/98 ± 10</td>
</tr>
<tr>
<td>Home</td>
<td>111 ± 9/79 ± 6</td>
<td>135 ± 14/90 ± 11</td>
<td>141 ± 15/92 ± 11</td>
</tr>
<tr>
<td>Sleep</td>
<td>104 ± 6/69 ± 6</td>
<td>124 ± 17/81 ± 10</td>
<td>124 ± 16/84 ± 13</td>
</tr>
<tr>
<td>Total</td>
<td>115 ± 7/80 ± 5</td>
<td>135 ± 15/91 ± 9</td>
<td>139 ± 13/92 ± 11</td>
</tr>
</tbody>
</table>

LVMI = left ventricular mass index; BP = blood pressure.
\(^a\)Subjects who had recordings on a work day (n = 60).
\(^b\)Obtained by automatic recorder. Expressed as systolic/diastolic.

pressure response to clinical measurement (made by the physician) represented an appropriate index of blood pressure reactivity to stress.

With the development of techniques for continuous recording of blood pressure, it has become possible to test this hypothesis. We have also tested an alternative hypothesis in this study — that the blood pressure response to regularly recurring stresses such as employment is pathophysiologically important in determining the cardiovascular effects of mild-to-moderate hypertension. At first glance, our studies appear to confirm the finding of Caldwell et al.\(^{13}\) that there is little difference between casual and near basal (home) blood pressure measurements in terms of their relationship to target organ manifestations of hypertension. In our entire study population, only weak relationships existed between left ventricular mass index and either home blood pressure or clinical measurement of blood pressure, as has been previously reported for the latter.\(^{30, 39}\) However, our findings indicate that the relationship between home blood pressure recordings and left ventricular mass index differs substantially according to whether or not recordings were made on a workday. Thus home measurements on a workday showed highly significant correlations (p < .001) with left ventricular mass index, whereas home measurements on a non-workday or in unemployed subjects did not. The present findings are consistent with another of our studies,\(^{40}\) in which we found that home blood pressure values, the majority of which were taken on a workday, correlated more closely than clinical values with LVH.

The finding that measurements of hypertensive LVH are most closely related to blood pressure at work, a regularly recurring stress, and to home, blood pressure on a workday is new and potentially important in several regards. First, it suggests an explanation for the weak relationship between clinical measurements of blood pressure and hypertensive LVH in that blood pressure during the daily stress of work appears to be of greater importance. This finding is not unprecedented. In the classic study of Sokolow et al.,\(^{12}\) in which subjects were encouraged to go to work during much of the 10 to 12 hr period of recording, a similar correlation (r = .55) was observed between ambulatory blood pressure and severity of LVH. Furthermore, Rowlands et al.\(^{17}\) recently reported a comparable correlation between left ventricular mass and 24 hr blood pressure recorded by intra-arterial catheter in the hospital, a situation that might recreate the blood pressure response to the workplace. Additional precedent is provided by evidence that athletes\(^{41-42}\) develop moderate LVH, although exercise rarely occupies more than a few hours a day. In our patients, physical training effects can be excluded as an explanation of variability in LVH. By the nature of the apparatus we employ for portable blood pressure recording, accurate readings cannot be obtained during strenuous exercise and hence individuals with physically demanding occupations were not included in this study. Further, we excluded subjects who were highly physically conditioned.

Second, the combination of a closer relationship between LVM and work blood pressure and the tendency for work blood pressure to be farther above basal pressure in hypertensive than normotensive individuals may explain the tendency for resting cardiac function to be slightly elevated in uncomplicated hypertension.\(^{29, 43}\) At this stage, corresponding to the "physiological hypertrophy" of Linzbach\(^{44}\) or Meerson's stage of hyperfunction,\(^{45}\) the heart with increased muscle mass to adapt to elevated levels of blood pressure during stress may function with low levels of resting left ventricular wall stresses.\(^{30}\) Since systolic ventricular performance is inversely related to left ventricular wall stress, the low levels of wall stress would result in supernormal systolic function.

Finally, our findings provide a potential pathophysiological mechanism for the often-suggested relationship between stress-responsive personality patterns and risk of cardiovascular diseases, including hypertension.\(^{6, 38}\) It is appealing to speculate that individuals prone to high levels of anxiety or with type A personality\(^{6}\) might have an enhanced propensity to elevated blood pressure in response to psychological stress. This exaggerated blood pressure response to stress could in turn
cause accelerated end-organ damage. Further studies are needed to test this hypothesis.

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