Early Effects of Mild Hypertension on the Heart
A Longitudinal Study
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SUMMARY M-mode echocardiograms were recorded twice, 1 year apart, in a group of 20 men and four women with mild hypertension (mean diastolic (D) BP of 90 to 104 mm Hg) to assess the cardiac response to this modest increase in pressure load and to study the evolution of any changes at entry in the absence of pharmacological therapy. Results were compared with those collected on normotensive (N) subjects (DBP 80 mm Hg or less) matched at entry for age, sex, and level of activity. Analysis of covariance controlling for body surface area or change in body surface area was used to assess statistical significance of differences between groups; results were expressed as means ± standard error of mean. At entry, the hypertensive (H) group had a significantly smaller left ventricular (LV) internal diameter in diastole (46.0 ± 1.4 mm vs 49.9 ± 0.9 mm, p < 0.003) and in systole (28.4 ± 1.0 mm vs 31.5 ± 1.0 mm, p < 0.001), and a significantly larger left atrial dimension (36.1 ± 0.9 mm vs 33.0 ± 0.9 mm, p < 0.05) compared with values in N subjects. There was no significant difference in the thickness of the LV posterior wall or interventricular septum in either systole or diastole, or in the fractional fiber shortening between the N and H subjects. One year later, in the hypertensive group only, there was a significant increase in the systolic dimension of the left ventricle (p < 0.05) and a reduction, although not statistically significant, in the percent fractional fiber shortening. These findings suggest that in early stages of hypertension before LV hypertrophy can be detected by echocardiography there is a reduction in LV compliance, with subsequent gradual change in contractile function.
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KEY WORDS • heart • mild hypertension • left ventricle • contractility • echocardiography • fiber shortening

ECHOCARDIOGRAPHY is a sensitive and specific method to assess left ventricular wall thickness and cavity dimensions, and close correlation between echocardiographic, angiographic, and morphologic measurements has been documented.1 2 The technique has the advantage of being noninvasive and easily repeatable, and is particularly well suited for serial observations.

Cross-sectional studies of hypertensive individuals have shown that the echocardiogram can identify cardiac abnormalities before changes in the electrocardiogram or chest roentgenogram can be detected.3 4 The role of the echocardiogram in evaluating the cardiac response to mild hypertension, however, has never been investigated systematically.

This study was designed to determine the presence and progression of echocardiographic changes in mildly hypertensive individuals who were untreated, had no clinical evidence of heart disease, and had a normal electrocardiogram and chest roentgenogram. Inasmuch as several variables aside from blood pressure (BP) may affect left ventricular wall thickness, extraneous sources of variance were reduced by a matching process to select an appropriate control group.

Method

Participants were selected from volunteers who underwent primary blood pressure (BP) screening at their place of employment in Metropolitan Toronto. Blood pressure was recorded under standardized conditions of quiet, rest, and posture by trained BP technicians. Details of the BP screening process have been previously described.5 All employees with an average diastolic BP of 95 to 119 mm Hg were asked to return for another BP measurement 1 week later. Employees
with an average diastolic BP from the two screens of 90 to 104 mm Hg were considered for the study if they: 1) were not on medication; 2) had no clinical evidence of cardiac disease or target organ damage; and 3) had no remediable secondary form of hypertension. An electrocardiogram and chest roentgenogram were performed on potentially eligible candidates to exclude those with evidence of heart disease, or with electrocardiographic or roentgenographic features of left ventricular hypertrophy or enlargement. Electrocardiograms were assessed using the Romhilt-Estes scoring system, and a cardiothoracic ratio > 0.5 was considered evidence of left ventricular (LV) hypertrophy.7

The control group was selected by random process from among those who were found to have a diastolic BP of 80 mm Hg or less on BP screening and had no clinical or laboratory evidence of heart disease. Eligible normotensives were matched for age, sex, and level of activity as ascertained by questionnaire (light to moderate, strenuous) with the 31 hypertensive subjects.

One year after entry, the initial assessment was repeated and included a clinical examination, measurement of BP and weight, and echocardiogram. Those normotensives who had a diastolic BP of 90 mm Hg or higher and hypertensives who either became normotensive (diastolic BP < 90 mm Hg) or were on antihypertensive medication were excluded from the final analysis.

M-mode echocardiograms were recorded by the use of a Picker cardiac imager or an Irex ultrasonoscope and a 2.25 megahertz transducer, 1.5 cm in diameter and obtained in the standard manner with the patient in the left lateral position. All measurements were averaged over three cardiac cycles. Interventricular septum and LV posterior wall thickness was measured at the tips of the mitral valve leaflets at the onset of the QRS complex (end-diastole) and at the maximal anterior motion of the LV posterior wall (end-systole). The LV internal dimensions were measured by standard methods at end-diastole and end-systole, and the percent fractional fiber shortening was derived from these measurements.8 Left atrial size was measured at end-systole. Evaluation of the echocardiograms was performed by a single interpreter who had no knowledge of the group designation, BP or health status of the participants.

Analysis of covariance controlling for body surface area or change in body surface area was used to assess statistical significance, with a p value (two-tailed) < 0.05 indicating a statistically significant difference. Statistical tests for unpaired data were used because the number excluded from the final analysis vitiated the use of paired data tests. The reproducibility of the echocardiographic results was determined by recording echocardiograms twice within 1 week in eight individuals. Variance due to unknown biological factors was assessed by correlating the results of the entry echocardiogram with those at the year end in the normotensive group. The results were expressed as means ± standard error of the mean (SEM).

Results

Selected characteristics of the study subjects are given in table 1. Despite exclusions and dropouts, differences between the two groups, apart from BP, were small, indicating the effectiveness of the matching procedure. Echocardiographic data are given in table 2. The systolic and diastolic dimensions of the LV were significantly smaller (p < 0.001 and < 0.003 respectively) and the left atrial dimension was significantly larger (p < 0.05) in the hypertensive group compared with values in control subjects. There was no significant difference in the thickness of the LV posterior wall or interventricular septum in either systole or diastole, or in the percent fractional fiber shortening between the normotensive and hypertensive subjects. In the hypertensive group only, the systolic dimension of the LV at the year end increased significantly compared with the value at entry (p < 0.05). In addition, there was a fall in the percent fractional fiber shortening in this group, although the change was not statistically significant. Correlation coefficients of measurements of LV dimension at end-diastole in normotensive subjects at entry and year end (0.79 and 0.62 respectively) and in eight individuals recorded twice within 1 week (0.97 and 0.92 respectively) were highly significant (p < 0.001); this finding indicated the low biological variability and good reproducibility of these echocardiographic parameters.

**Table 1** Comparability of Normotensive (N) and Hypertensive (H) Individuals at Entry by Selected Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
<th>H</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>27*</td>
<td>24†</td>
</tr>
<tr>
<td>Average age (yrs)</td>
<td>47.9 ± 1.8</td>
<td>47.0 ± 1.8</td>
</tr>
<tr>
<td>Men (%)</td>
<td>74.1</td>
<td>83.3</td>
</tr>
<tr>
<td>Black (%)</td>
<td>3.7</td>
<td>4.2</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>114.8 ± 2.1</td>
<td>142.0 ± 2.1</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>70.1 ± 11</td>
<td>97.5 ± 6.1</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>85.0 ± 1.3</td>
<td>112.3 ± 1.0</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.86 ± 0.03</td>
<td>1.93 ± 0.05</td>
</tr>
</tbody>
</table>

*Excludes three subjects who became hypertensive during the study and one dropout
†Excludes three individuals who were on antihypertensive medication at the year-end assessment, two who became normotensive, and two who dropped out of the study
‡Significant difference from values in normal subjects (p value < 0.001).

Values given as mean ± standard error of the mean.
TABLE 2. Comparison of Echocardiographic Results in Normotensive (N) and Hypertensive (H) Individuals at Entry and Year-end

<table>
<thead>
<tr>
<th></th>
<th>Entry</th>
<th>1 Year</th>
<th>Entry</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV dimension in diastole (mm)</td>
<td>49.9 ± 0.9</td>
<td>49.4 ± 1.1</td>
<td>46.4 ± 1.4*</td>
<td>47.7 ± 1.0*</td>
</tr>
<tr>
<td>LV dimension in systole (mm)</td>
<td>31.5 ± 1.0</td>
<td>31.1 ± 0.8</td>
<td>28.4 ± 1.0*</td>
<td>31.2 ± 1.0†</td>
</tr>
<tr>
<td>LVPW in diastole (mm)</td>
<td>9.4 ± 0.2</td>
<td>9.6 ± 0.2</td>
<td>9.6 ± 0.2</td>
<td>9.5 ± 0.4</td>
</tr>
<tr>
<td>LVPW in systole (mm)</td>
<td>16.8 ± 0.4</td>
<td>17.2 ± 0.5</td>
<td>17.4 ± 0.6</td>
<td>17.0 ± 0.5</td>
</tr>
<tr>
<td>IVS in diastole (mm)</td>
<td>10.0 ± 0.2</td>
<td>10.3 ± 0.4</td>
<td>10.7 ± 0.3</td>
<td>10.7 ± 0.3</td>
</tr>
<tr>
<td>IVS in systole (mm)</td>
<td>15.6 ± 0.4</td>
<td>15.6 ± 0.5</td>
<td>16.9 ± 0.5</td>
<td>16.8 ± 0.5</td>
</tr>
<tr>
<td>Left atrial dimension (mm)</td>
<td>33.0 ± 0.9</td>
<td>33.0 ± 0.9</td>
<td>36.1 ± 0.9*</td>
<td>36.5 ± 0.9*</td>
</tr>
<tr>
<td>Fractional fiber shortening (%)</td>
<td>36.9 ± 1.7</td>
<td>37.1 ± 1.0</td>
<td>38.5 ± 1.7</td>
<td>34.5 ± 1.9</td>
</tr>
</tbody>
</table>

LV = left ventricle, LVPW = left ventricular posterior wall, IVS = interventricular septum.
*Significant difference from value in control subjects (p < 0.05).
†Significant difference from value at entry (p < 0.05).

Discussion

Left ventricular hypertrophy is generally considered the hallmark of chronic pressure overload and appears to be an adaptive response to normalize systolic wall stress. Since cardiac performance at rest is normal in patients with compensated essential hypertension, it seems likely that hypertrophy contributes to the maintenance of normal LV function.

In the present report, no increase in LV wall thickness was detected in patients with mild hypertension. However, we did observe a persistent reduction in LV internal diameter in end-diastole, which suggests that there was a decrease in LV end-diastolic volume. It is unlikely that this alteration was a reflection of reduced plasma volume because studies have shown that this measurement is normal in patients with a mean diastolic pressure less than 105 mm of mercury. Moreover, it would be difficult to reconcile such a generalized decrease in volume with the observed increase in left atrial dimension.

Studies in experimental animals have documented an alteration in the Frank-Starling relation in hypertension. The maintenance of normal stroke volume in such circumstances would require either an increased end-diastolic filling pressure or an increased inotropic stimulation or both. It has been shown in cardiac catheterization studies that patients with essential hypertension initially have normal end-diastolic pressure. This would therefore suggest that, early in the course of hypertension, there is an increased inotropic influence to the heart, the manifestations of which would be a reduction in ventricular volume at any given end-diastolic pressure. The nature of the putative inotropic stimulus is speculative at this point although an increased sympathetic drive to the heart is one possibility.

Many investigators have used echocardiographic techniques to assess the heart of hypertensive patients. Comparison of these results with our data, however, was not possible because of significant differences in the clinical characteristics of the patients evaluated. In the cross-sectional study of Dunn and co-workers, they noted that with advancing hypertension along with changes in LV mass and cardiac index, there was a progressive increase in LV systolic dimension and decrease in percent fractional fiber shortening. Similar results were observed in this longitudinal evaluation of our hypertensive group. These results suggest that even when BP is mildly elevated, a subtle but definite change in contractile function can be detected if hypertension is left untreated.

In summary, we have demonstrated that patients with mild hypertension have smaller LV dimensions, normal myocardial wall thickness, and larger left atrial dimension compared to normotensive controls. These findings suggest that in early stages of hypertension, before LV hypertrophy can be detected by echocardiography, there is a reduction in LV compliance with subsequent gradual change in contractile function.

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