Left Ventricular Wall Stress and Systolic Function in Untreated Primary Hypertension

MARIANNE HARTFORD, JOHN C. M. WIKSTRAND, INGEMAR WALLENTIN, SUSANNE M. G. LIUANGMAN, AND GÖRAN L. BERGLUND

SUMMARY A noninvasive investigation was undertaken in four blood pressure (BP) groups of untreated 49-year-old men derived by screening a random population sample: normotensive men (n = 20) and subjects with borderline (n = 30), mild (n = 45), or moderate BP elevation (n = 24). We here report the findings regarding left ventricular (LV) wall stress, LV wall thickness, and LV systolic function. Although there was an increase in LV wall thickness with hypertension, the raised BP was not compensated for by a sufficient degree of LV wall thickening to keep wall stress within normal limits in the hypertensive groups. Among a subset of individuals with pronounced increase in wall thickness peak systolic wall stress approached the normal range, but end-systolic wall stress was still high. In spite of high wall stress LV systolic function was normal or supranormal in the hypertensive men. The LV ejection phase indices showed a close inverse correlation with end-systolic wall stress (r = −0.67 to −0.84) in all four BP groups, but no correlation or only a weak correlation with peak systolic wall stress (r = 0.18 to −0.40). As judged from the relationship between end-systolic wall stress and ejection phase indices of LV function in the normotensive controls, all hypertensive groups had higher than expected values for LV ejection phase indices, which indicates an increased myocardial contractility secondary to adrenergic stimulation or to a more efficient contractile machinery in the myocardial cells. (Hypertension 7: 97-104, 1985)

Key Words • primary hypertension • wall stress • left ventricular hypertrophy • left ventricular systolic function

To equate the increased cardiac load in hypertension with the arterial blood pressure (BP) is to oversimplify, because the forces against which the myocardial fibers must shorten during ventricular contraction are also functions of the geometry of the left ventricle (i.e., its size, its shape, and the thickness of its wall). Recent interest has therefore been devoted to wall stress defined by BP, left ventricular (LV) wall thickness, and LV internal diameter, as an estimate of afterload in hypertension. Most studies have focused on treated patients with established hypertension, in some of whom coronary heart disease has complicated the picture.

Because little is known about LV wall stress during the development of hypertension from the borderline to the established phase, the aim of the present investigation was to analyze the relation between LV wall stress, LV wall thickness, and changes in LV systolic function in different stages of early untreated primary hypertension. Noninvasive techniques including echocardiography and systolic time intervals were used.

Materials and Methods

Study Population

A detailed presentation of the study population has previously been given. In brief, a random sample of 3205 49-year-old men living in Göteborg, Sweden, were invited to a BP screening. Altogether 2376 (74.1%) attended for examination and, based on diastolic BP, 120 subjects representing the entire BP range were randomly selected. None had ever had antihypertensive therapy. All had primary hypertension and were free from previous or current clinically overt cardiovascular disease.

After the echocardiographic examination 1 normotensive man with extreme bradycardia and a heart rate of 35 beats/minute was excluded from the analysis of cardiac function. The remaining 119 men were divided into four groups according to criteria previously given: one normotensive group (n = 20), one with borderline BP elevation (n = 30), one with mild BP
echocardiograms in patients with no history or signs of
graphic stress measurements "l8 For peak systolic
agreement between echocardiographic and angio-
LVDs)/LVDd
LVDd,
Details about the agreement between ejection
EDV = (EDV - ESV)/
derived by the cube method,
P
WS =
x
or wall ratio as
The percentage of LV fractional

Study Protocol
The heart investigations, which were part of a 2-day
examination of cardiac and kidney function, were car-
ried out within 1 month of screening and before any
antihypertensive treatment was instituted. The meth-
ods and recording and analyzing techniques have been
described earlier.11-14
The BP was measured in four different situations:
(1) at screening, (2) in the hypertension unit, (3) dur-
ing the noninvasive investigation in the laboratory, and
(4) during isometric exercise.11 In the first two situa-
tions BP was measured with a mercury manometer and
stethoscope; in the latter two situations a phonographic
technique was used. Diastolic BP was registered as
phase 5 (i.e., when the Korotkoff sounds disap-
peared).
M-mode echocardiograms of satisfactory quality
were obtained in 108 men. Recording and measure-
ments of interventricular septum (IVS), LV posterior
wall (LVPW), and LV diameters (LVD) in systole
(LVD s) and diastole (LVD d) have been described pre-
viously and the reliability of the measurements has
been tested.11-15
Left ventricular wall thickness to radius ratio was
defined as (IVS + LVPW)/LVD, and radius to posteri-
or wall ratio as LVD/(2 × LVPW). The percentage of
fractional wall thickening was calculated as 100 ×
(IVS + LVPW - IVS d + LVPW d)/(IVS + LVPW).
For calculation of ejection fraction (EF), end-diastolic
volume (EDV) and end-systolic volume (ESV) were
derived by the cube method, EF = (EDV - ESV)/
EDV. Details about the agreement between ejection
fraction calculated from LV angiograms and M-mode
echocardiograms in patients with no history or signs of
myocardial infarction have been published recently
from our laboratory.16 The percentage of LV fractional
shortening was calculated as 100 × (LVD s - LVD d)/
LVD d, and mean velocity of circumferential fiber
shortening (mean V cf) was calculated as (LVD s
- LVD d)/LVD d × LV ejection time (see next section).
Left ventricular meridional wall stress (WS) was esti-
mated with the formula WS = 1.332 × P × D/4h
(1 + h/D) 10 dynes/cm 2. This formula was derived by
Sandler and Dodge1 as a modification of the basic
Laplace expression. Several groups have found good
agreement between echocardiographic and angio-
graphic stress measurements.17 18 For peak systolic
wall stress D = LVD s, h = (IVS s + LVPWS)/2 and P
= resting systolic BP. The dimensions of the left ven-
tricle were taken from end diastole, on the assump-
tion that there would have been no significant change
in these dimensions from end diastole to peak stress, as
peak systolic wall stress usually occurs early in ejec-
tion.19 20 For end-systolic wall stress D = LVD d, h
= (IVS S + LVPW S)/2. P was obtained by estimating
end-systolic BP from the carotid pulse tracing, where
systolic and diastolic BP, as determined with the
phonographic cuff method, were assigned to the peak
and nadir of the carotid curve respectively, and end-
systolic BP was estimated by linear interpolation to
the height of the dicrotic notch.31
The LV ejection time and the isovolumetric con-
traction time (ICT) were calculated as previously de-
scribed from simultaneous recordings of ECG lead II
and the phonocardiogram, apexcardiogram, or carotid
pulse tracing.14 The ratio between resting laboratory
diastolic BP and isovolumetric contraction time (DBP/
ICT) was calculated as a measure of isovolumetric
pressure rise velocity.14 Because LV ejection time is
influenced by heart rate, this interval also was ex-
pressed as a percentage of the expected value at the
observed heart rate with the regression equation: LV
ejection time = 390 - 1.51 × heart rate, which was
previously obtained from a control group of middle-
aged normotensive men.14 Because no significant cor-
relation between isovolumetric contraction time and
heart rate was found in the range of heart rates studied
at rest, no heart rate correction of this interval was
performed.

Statistical Methods
All statistics were handled by Minitab (University
Park, PA) in a PDP 11/34 computer. The hypothesis of
no differences in means between two samples was
tested with Student's t test if n was greater than 10 in
either group, otherwise the Mann-Whitney U test was
used. The hypothesis of no difference in proportions
test between two groups was tested in a fourfold table
analysis. Only two-tailed tests were used, and differ-
ences were considered significant for p < 0.05.
As the indices of LV systolic function (ejection frac-
tion, fractional shortening, and mean V cf) are reported
to vary with the level of end-systolic wall stress,20 the
regression equations for the relationships between
these indices and end-systolic wall stress in the normo-
tensive group were used for calculation of their expect-
ed values for the observed levels of wall stress in all
individuals. Differences in means between expected
observed values for the given end-systolic wall stress
in the three hypertensive groups and the two sub-
groups with moderate BP elevation were tested with
paired tests as described previously.

Results
A detailed description of the findings in the four BP
groups and the two subgroups with moderate BP eleva-
tion is given in Table 1. The most important findings
are further illustrated in the figures.
<table>
<thead>
<tr>
<th>Measurement</th>
<th>Normal (n = 16-20)</th>
<th>Borderline (n = 28-30)</th>
<th>Mild (n = 43-45)</th>
<th>All (n = 21-24)</th>
<th>Subgroup A (n = 6-8)</th>
<th>Subgroup B (n = 14-15)</th>
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<tbody>
<tr>
<td><strong>Screening</strong></td>
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<tr>
<td>Systolic BP (mm Hg)</td>
<td>130 ± 11</td>
<td>158 ± 14‡</td>
<td>167 ± 15‡</td>
<td>190 ± 16‡</td>
<td>182 ± 14‡</td>
<td>192 ± 16‡</td>
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<tr>
<td>Diastolic BP (mm Hg)</td>
<td>85 ± 7</td>
<td>107 ± 8‡</td>
<td>117 ± 9‡</td>
<td>128 ± 12†</td>
<td>124 ± 10†</td>
<td>128 ± 10†</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>77 ± 11</td>
<td>82 ± 13</td>
<td>83 ± 13</td>
<td>86 ± 12*</td>
<td>87 ± 14</td>
<td>85 ± 13</td>
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<td><strong>Hypertension unit</strong></td>
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<td>Systolic BP (mm Hg)</td>
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<td>139 ± 11‡</td>
<td>152 ± 10‡</td>
<td>175 ± 16‡</td>
<td>170 ± 10‡</td>
<td>179 ± 18‡</td>
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<td>Diastolic BP (mm Hg)</td>
<td>76 ± 6</td>
<td>85 ± 6‡</td>
<td>99 ± 3‡</td>
<td>114 ± 7†</td>
<td>114 ± 41†</td>
<td>116 ± 84†</td>
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<td>Heart rate (beats/min)</td>
<td>72 ± 10</td>
<td>72 ± 10</td>
<td>76 ± 9</td>
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<td><strong>Isometric exercise</strong></td>
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<td>Systolic BP (mm Hg)</td>
<td>144 ± 14</td>
<td>170 ± 23‡</td>
<td>173 ± 18‡</td>
<td>199 ± 25‡</td>
<td>189 ± 10‡</td>
<td>204 ± 30‡</td>
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<tr>
<td>Diastolic BP (mm Hg)</td>
<td>86 ± 10</td>
<td>103 ± 14‡</td>
<td>108 ± 13‡</td>
<td>126 ± 14‡</td>
<td>115 ± 9*</td>
<td>p &lt; 0.05</td>
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<tr>
<td>Heart rate (beats/min)</td>
<td>76 ± 11</td>
<td>79 ± 14</td>
<td>81 ± 10</td>
<td>82 ± 9</td>
<td>84 ± 10</td>
<td>89 ± 9</td>
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<td><strong>NI laboratory</strong></td>
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<tr>
<td>Systolic BP (mm Hg)</td>
<td>112 ± 11</td>
<td>127 ± 12‡</td>
<td>136 ± 12‡</td>
<td>157 ± 24‡</td>
<td>151 ± 14‡</td>
<td>161 ± 29‡</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>63 ± 9</td>
<td>73 ± 10‡</td>
<td>83 ± 10‡</td>
<td>96 ± 15‡</td>
<td>93 ± 14‡</td>
<td>97 ± 16‡</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>63 ± 8</td>
<td>64 ± 7</td>
<td>70 ± 11†</td>
<td>69 ± 8*</td>
<td>71 ± 8*</td>
<td>68 ± 7</td>
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<tr>
<td>LVDd (mm)</td>
<td>51 ± 3.5</td>
<td>52 ± 4.5</td>
<td>52 ± 5.7</td>
<td>52 ± 7.4</td>
<td>54 ± 5.0</td>
<td>51 ± 4.1</td>
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<tr>
<td>LVDs (mm)</td>
<td>33 ± 4.3</td>
<td>33 ± 4.8</td>
<td>34 ± 5.7</td>
<td>34 ± 5.4</td>
<td>34 ± 5.2</td>
<td>35 ± 5.6</td>
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<tr>
<td>IVSd (mm)</td>
<td>11 ± 1.8</td>
<td>11 ± 2.5</td>
<td>12 ± 3.0</td>
<td>13 ± 3.0</td>
<td>13 ± 3.4</td>
<td>13 ± 3.3</td>
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<tr>
<td>LVNPWd (mm)</td>
<td>10 ± 1.5</td>
<td>10 ± 1.4</td>
<td>11 ± 2.2</td>
<td>11 ± 2.8</td>
<td>8 ± 2.1</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>IVSs (mm)</td>
<td>16 ± 2.5</td>
<td>16 ± 3.2</td>
<td>17 ± 3.4</td>
<td>18 ± 3.1</td>
<td>16 ± 3.3</td>
<td>18 ± 2.8†</td>
</tr>
<tr>
<td>LVNPWs (mm)</td>
<td>17 ± 2.4</td>
<td>18 ± 2.4</td>
<td>18 ± 2.7</td>
<td>19 ± 3.0</td>
<td>18 ± 4.0</td>
<td>19 ± 1.8†</td>
</tr>
<tr>
<td>(IVSd + LVNPWd)/LVDd</td>
<td>0.43 ± 0.07</td>
<td>0.43 ± 0.10</td>
<td>0.45 ± 0.10</td>
<td>0.48 ± 0.13</td>
<td>0.35 ± 0.10</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>LVDd/LV (%)</td>
<td>2.49 ± 0.39</td>
<td>2.49 ± 0.42</td>
<td>2.46 ± 0.50</td>
<td>2.42 ± 0.75</td>
<td>3.24 ± 0.78*</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>PSWS (10³ x dynes/cm²)</td>
<td>145 ± 23</td>
<td>171 ± 42†</td>
<td>178 ± 51‡</td>
<td>190 ± 63‡</td>
<td>259 ± 65‡</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>93 ± 10</td>
<td>104 ± 20*</td>
<td>115 ± 12‡</td>
<td>134 ± 19‡</td>
<td>129 ± 15‡</td>
<td>137 ± 22‡</td>
</tr>
<tr>
<td>(IVSs + LVNPWd)/LVDs</td>
<td>1.01 ± 0.19</td>
<td>1.09 ± 0.26</td>
<td>1.10 ± 0.29</td>
<td>1.12 ± 0.26</td>
<td>1.05 ± 0.25</td>
<td>1.12 ± 0.23</td>
</tr>
<tr>
<td>ESWS (10³ x dynes/cm²)</td>
<td>42 ± 8</td>
<td>46 ± 16</td>
<td>52 ± 18†</td>
<td>55 ± 17†</td>
<td>59 ± 19</td>
<td>55 ± 16†</td>
</tr>
<tr>
<td>FT (%)</td>
<td>56 ± 15</td>
<td>60 ± 15</td>
<td>58 ± 17</td>
<td>57 ± 29</td>
<td>87 ± 35</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>EF</td>
<td>0.70 ± 0.08</td>
<td>0.73 ± 0.10</td>
<td>0.70 ± 0.08</td>
<td>0.70 ± 0.11</td>
<td>0.76 ± 0.06</td>
<td>0.67 ± 0.12</td>
</tr>
<tr>
<td>FS%</td>
<td>34 ± 6</td>
<td>36 ± 7</td>
<td>34 ± 7</td>
<td>34 ± 8</td>
<td>38 ± 5</td>
<td>32 ± 8</td>
</tr>
<tr>
<td>Mean VCF (cmt/s)</td>
<td>1.11 ± 0.18</td>
<td>1.21 ± 0.24</td>
<td>1.17 ± 0.26</td>
<td>1.19 ± 0.27</td>
<td>1.32 ± 0.17*</td>
<td>1.12 ± 0.28</td>
</tr>
<tr>
<td>LVET (ms)</td>
<td>304 ± 19</td>
<td>301 ± 25</td>
<td>288 ± 21†</td>
<td>284 ± 22†</td>
<td>282 ± 22*</td>
<td>286 ± 22*</td>
</tr>
<tr>
<td>LVET (%)</td>
<td>103 ± 4</td>
<td>103 ± 5</td>
<td>100 ± 4†</td>
<td>99 ± 5†</td>
<td>98 ± 5*</td>
<td>99 ± 6*</td>
</tr>
<tr>
<td>ICT (ms)</td>
<td>63 ± 12</td>
<td>63 ± 14</td>
<td>65 ± 12</td>
<td>71 ± 16</td>
<td>67 ± 18</td>
<td>73 ± 16*</td>
</tr>
<tr>
<td>DBP/ICT (mm Hg/s)</td>
<td>1036 ± 194</td>
<td>1187 ± 282*</td>
<td>1316 ± 251†</td>
<td>1423 ± 396‡</td>
<td>1487 ± 515†</td>
<td>1370 ± 336†</td>
</tr>
</tbody>
</table>

*p < 0.05 compared with the normotensive group
†p < 0.01 compared with the normotensive group
‡p < 0.001 compared with the normotensive group

The p values indicate differences between subgroups A and B with moderate BP elevation
BP = blood pressure, NI = noninvasive, LV = left ventricular, LVD = LV diameter, IVS = interventricular septum, LVNPW = LV posterior wall, LVDd = diastolic, LVDs = systolic, PSWS = peak systolic wall stress, ESBP = end-systolic blood pressure, ESWS = end-systolic wall stress, FT% = LV percent fractional wall thickening, EF = ejection fraction, FS% = LV percent fractional shortening, mean VCF = mean velocity of circumferential fiber shortening, LVET = LV ejection time, ICT = isovolumetric contraction time, DBP/ICT = isovolumetric pressure rise velocity.
Blood pressure differed significantly between each of the four groups in all four situations when BP was recorded \((p < 0.05-0.001)\). Blood pressure always tended to be higher in subgroup B than in subgroup A, but only diastolic BP during isometric exercise differed significantly between the two subgroups \((p < 0.05\); Table 1\).

Left ventricular wall thickness increased with BP. In the group with moderate BP elevation the LV posterior wall thickness in systole and the IVS in both diastole and systole were significantly thicker than in the normotensive group \((p < 0.05\); Table 1\). In subgroup B the diastolic wall thickness to radius ratio was significantly increased compared with the normotensive group \((p < 0.01\) and also compared with subgroup A \((p < 0.01\). In the latter subgroup the diastolic wall thickness to radius ratio was significantly lower \((p < 0.05\) than in the normotensive group.

In each of the three hypertensive groups peak systolic wall stress was significantly higher than in the normotensive group \((p < 0.05-0.01\), Figure 1\). Subgroup A had significantly higher peak systolic wall stress in comparison with both the normotensive group and subgroup B \((p < 0.01\), which did not differ significantly from the normotensive subjects (Figure 1). End-systolic wall stress was increased significantly in the groups with mild and moderate BP elevation compared with the normotensive group \((p < 0.01\). In subgroups A and B with moderate BP elevation the level of end-systolic wall stress was similar but, because of the small numbers, subgroup A did not differ significantly from the normotensive group while subgroup B did \((p < 0.01\).

In all the hypertensive groups and also in the two subgroups with moderate BP elevation, LV isovolumetric pressure rise velocity \((\text{DBP/ICT})\) was significantly higher than it was in the normotensive group \((p < 0.05-0.001\). In subgroup A with moderate BP elevation, mean \(V_{CF}\) was significantly increased compared with that of the normotensive group \((p < 0.05\); Figure 2\).

There was a highly significant inverse correlation between the LV ejection phase indices of LV performance and end-systolic wall stress in the four groups (Table 2, Figure 3) These indices showed no correlation or only a weak correlation with peak systolic wall stress in the four groups.

Table 3 presents the observed values for ejection fraction, fractional shortening, and mean \(V_{CF}\) along with their expected values for the observed levels of end-systolic wall stress from the regression equations in the normotensive group (ejection fraction expected \(= 1.05 - 0.0084 \times \text{end-systolic wall stress observed}\); fractional shortening expected \(= 60.4 - 0.64 \times \text{end-systolic wall stress observed}\); and mean \(V_{CF}\) expected \(= 1.83 - 0.017 \times \text{end-systolic wall stress observed}\). For all three ejection phase indices the observed values were significantly higher than expected \((p < 0.05-0.001)\) in the three hypertensive groups and the two subgroups.

Discussion

In this study of middle-aged men who represent a wide range of blood pressures, a raised BP was associated with higher levels of wall stress than was a normal BP. Thus, the increase in LV wall thickness, as judged from M-mode echocardiography, in response to the increased tension in the LV wall, was inadequate to maintain wall stress within normal limits. Left ventricular ejection phase indices were higher than expected in all hypertensive groups as judged from the relationship between these indices and end-systolic wall stress in the normotensive group, which indicates an increased myocardial contractility. Thus, our results suggest that during the development of primary hypertension from the borderline to the established phase wall stress is high and LV systolic function is supranormal.
Our findings seem to be at variance with some other studies, which found that wall stress was normal in uncomplicated hypertension and that a high wall stress was associated with signs of LV decompensation.9 10 Our results are supported by two recent studies, however, in which wall stress was high but systolic cardiac performance was normal or enhanced, not depressed.22 23 Differences in results to a large extent may be explained by differences in the studied hypertensive populations. Our hypertensive subjects were representative of a screened, untreated population and were in a much earlier phase of the hypertension disorder than the majority of subjects in other studies. Two findings are open to discussion, however: (1) The apparent lack of an increase in LV diastolic wall thickness in subgroup A and (2) the good LV systolic performance in spite of the high wall stress. Both findings

![Figure 2: Left ventricular isovolumetric pressure rise velocity, ejection fraction, fractional shortening, and mean V_CF in three hypertensive groups and in subgroups A and B (with moderate BP elevation) in relation to the levels in the normotensive group. * = p < 0.05, ** = p < 0.01, *** = p < 0.001 (compared with the normotensive group). The bars represent standard error of the mean.]

![Figure 3: Relationship between LV end-systolic wall stress and LV fractional shortening for the normotensive men, those with borderline, mild, and moderate BP elevation, and subgroups A and B with moderate BP elevation. The linear regression line ± 2 SD in the normotensive group is given.]

### Table 2  Relationship Between Left Ventricular Ejection Phase Indices and Wall Stress

<table>
<thead>
<tr>
<th>Group</th>
<th>Correlation vs peak systolic wall stress</th>
<th>Correlation vs end-systolic wall stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension (n = 16)</td>
<td>Ejection fraction: -0.05, -0.80†</td>
<td>Ejection fraction: 0.25, 0.75†</td>
</tr>
<tr>
<td></td>
<td>Fractional shortening: -0.09, -0.82†</td>
<td>Fractional shortening: 0.40*, 0.84†</td>
</tr>
<tr>
<td></td>
<td>Mean V_CF: -0.05, -0.75†</td>
<td>Mean V_CF: 0.35, 0.78†</td>
</tr>
<tr>
<td>Borderline hypertension (n = 28)</td>
<td>Ejection fraction: -0.36, -0.82†</td>
<td>Ejection fraction: 0.24, 0.75†</td>
</tr>
<tr>
<td></td>
<td>Fractional shortening: -0.40*, 0.84†</td>
<td>Fractional shortening: 0.35, 0.78†</td>
</tr>
<tr>
<td></td>
<td>Mean V_CF: -0.35, -0.78†</td>
<td>Mean V_CF: 0.04, 0.74†</td>
</tr>
<tr>
<td>Mild hypertension (n = 43)</td>
<td>Ejection fraction: -0.25, 0.67†</td>
<td>Ejection fraction: 0.17, 0.68†</td>
</tr>
<tr>
<td></td>
<td>Fractional shortening: -0.24, 0.75†</td>
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<tr>
<td></td>
<td>Mean V_CF: -0.35*, 0.78†</td>
<td>Mean V_CF: 0.04, 0.74†</td>
</tr>
<tr>
<td>Moderate hypertension (n = 21)</td>
<td>Ejection fraction: -0.14, 0.73†</td>
<td>Ejection fraction: 0.17, 0.68†</td>
</tr>
<tr>
<td></td>
<td>Fractional shortening: -0.15, 0.73†</td>
<td>Fractional shortening: 0.18, 0.68†</td>
</tr>
<tr>
<td></td>
<td>Mean V_CF: -0.19*, 0.71†</td>
<td>Mean V_CF: 0.04, 0.74†</td>
</tr>
</tbody>
</table>

*p < 0.05  †p < 0.001
TABLE 3  Observed and Expected Values for Left Ventricular Ejection Phase Indices

<table>
<thead>
<tr>
<th>LV ejection phase indices</th>
<th>Borderline (n = 28)</th>
<th>Mild (n = 43)</th>
<th>All (n = 21)</th>
<th>Subgroup A (n = 6)</th>
<th>Subgroup B (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observed</td>
<td>0.73 ±0.10†</td>
<td>0.70 ±0.08†</td>
<td>0.70 ±0.11 †</td>
<td>0.76 ±0.06*</td>
<td>0.67 ±0.12†</td>
</tr>
<tr>
<td>Expected</td>
<td>0.67 ±0.14</td>
<td>0.62 ±0.15</td>
<td>0.59 ±0.14</td>
<td>0.56 ±0.16</td>
<td>0.59 ±0.13</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observed</td>
<td>36 ±7†</td>
<td>34 ±7†</td>
<td>34 ±8†</td>
<td>38 ±5*</td>
<td>32 ±8†</td>
</tr>
<tr>
<td>Expected</td>
<td>31 ±11</td>
<td>27 ±11</td>
<td>25 ±11</td>
<td>23 ±12</td>
<td>25 ±10</td>
</tr>
<tr>
<td>Mean VCF (cmt/s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observed</td>
<td>1.21 ±0.24†</td>
<td>1.17 ±0.26†</td>
<td>1.19 ±0.27†</td>
<td>1.32 ±0.17*</td>
<td>1.12 ±0.28†</td>
</tr>
<tr>
<td>Expected</td>
<td>1.04 ±0.28</td>
<td>0.93 ±0.30</td>
<td>0.88 ±0.30</td>
<td>0.81 ±0.33</td>
<td>0.88 ±0.28</td>
</tr>
</tbody>
</table>

*p < 0.05 compared with the expected value
†p < 0.01 compared with the expected value
‡p < 0.001 compared with the expected value

have to be discussed against the background of variables of importance for left ventricle morphology and function (i.e., preload and afterload and the myocardial contractility as defined by autonomic nervous influence and the quality of the contractile machinery in the myocardial cells).

The following explanation could be offered for the lack of increase in LV diastolic wall thickness and the high peak systolic wall stress in subgroup A with moderate BP elevation. As is illustrated in Figure 4, the peak systolic wall stress in subgroup A was higher than in subgroup B owing to a significantly thinner end-diastolic LV wall and also because of a tendency for LV end-diastolic diameter to be larger in subgroup A than in subgroup B. At end systole, on the other hand, the two subgroups with moderate BP elevation did not differ in wall stress, because the fractional thickening of the LV wall during ejection was significantly more pronounced and the fractional shortening of the LV diameter tended to be larger in subgroup A (Figure 4). The most likely explanation for this — and the difference in peak systolic wall stress between the two subgroups with rather similar BP elevation — is a difference in hemodynamic characteristics, subgroup A being volume dependent and subgroup B resistance dependent. This interpretation fits well with diastolic and systolic diameters recorded in the two subgroups and was further supported by plethysmographic findings in these men. Minimal resistance in the calf was significantly increased in subgroup B, which indicates structural vascular changes in arterial resistance vessels in subgroup B but not in subgroup A.11

Evidently the gradual increase in total peripheral resistance, mainly due to increased structural changes

FIGURE 4. Values for peak and end-systolic (ES) wall stress, LV fractional wall thickening, and mean VCF in relation to LV diastolic and systolic wall thickness and diameter in the normotensive group (N) and in subgroups A and B with moderate BP elevation. For explanation, see text. SBP = systolic blood pressure; frac thick = fractional wall thickening.
in the peripheral resistance vessels, but also influenced by structural changes in the great arteries with increasing rigidity, complicates the situation for the left side of the heart, especially toward the end of systole in resistance-dependent hypertension. At high resistance the proportional decrease in LV diameter from end diastole to end systole will be reduced, and the increase in LV wall thickness during ejection will also be smaller (see Figure 4). A greater compensatory increase in LV diastolic wall thickness is therefore necessary to maintain a constant end-systolic wall stress in hypertension owing to high total peripheral resistance than when a similar blood pressure rise is secondary to increased cardiac output. The consequence is that major differences in peak systolic wall stress may be observed at different stages of primary hypertension, including the early stages, despite the fact that the end-systolic wall stress and BP do not differ. This finding can therefore be explained by great variations in structural cardiovascular changes between volume- and resistance-dependent primary hypertension. The apparent lack of an increase in LV end-diastolic wall thickness in subgroup A with moderate BP elevation is probably explained by a more favorable loading situation, especially during end systole, than in subgroup B. Thus, afterload in early primary hypertension seems to be better characterized by LV end-systolic wall thickness, wall tension, and wall stress than by the end-diastolic and peak systolic values.

Subgroup A had a significant increase in mean \( V_{cf} \) compared with the normotensive group, which indicates an enhanced LV performance. As the end-diastolic diameter tended to be slightly larger in this subgroup than in the normotensive group, with no difference in end-systolic diameters, an increase in preload and utilization of the Frank-Starling mechanism probably would explain the higher mean \( V_{cf} \). On the other hand, some of the LV ejection phase indices in subgroup B showed a nonsignificant tendency toward lower levels than in the normotensive group. A possible explanation is that, owing to increased stiffness of the hypertrophied LV wall, the end-diastolic prestretch of the average myocardial cell was inadequate for the excessive afterload. Thus, preload seems to be of great importance for differences in LV ejection phase indices in these two subgroups.

Another factor of importance in this respect is myocardial contractility. By studying the relationship between end-systolic wall stress and LV ejection phase indices, it is possible to evaluate the contractility of the myocardium independent of loading conditions. This evaluation is possible because the relation between end-systolic wall stress and the extent of LV shortening is independent of preload and the inclusion of end-systolic wall stress in the equation compensates for differences in afterload. In agreement with other recent studies on wall stress in normotensive and hypertensive men, we found a close inverse correlation between end-systolic wall stress and ejection phase indices of LV function, such as ejection fraction, fractional shortening, and mean \( V_{cf} \), in all four groups. These indices showed no or only a weak correlation with peak systolic wall stress.

As judged from the relationship between end-systolic wall stress and ejection phase indices in the normotensive controls, all hypertensive groups had higher than expected values for LV ejection phase indices. This finding thus could not be explained by differences in preload, but rather by an enhanced LV contractility secondary to an increase in adrenergic influence or to a more efficient contractile machinery in the myocardial cells in the hypertensive men.

**Conclusion**

The present study demonstrated that a high peak systolic and end-systolic wall stress may be present early in the course of hypertensive disease. Because of alternative mechanisms that increase the myocardial contractility, LV systolic function is normal or even supranormal at this stage. In more advanced LV hypertrophy peak systolic wall stress may be normalized but end-systolic wall stress is often high in this situation as well, as the high resistance to LV ejection makes fractional shortening of the LV diameter — hence, also fractional thickening of the wall during systole — difficult. In both early and advanced hypertension high wall stress means augmented cardiac work and increased myocardial oxygen demand. Actions to lower the BP are essential to protect the myocardium. As suggested by Dreisin and colleagues the ideal antihypertensive treatment should be designed to reduce not only BP but also cardiac work and myocardial oxygen consumption.

**Acknowledgments**

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