Echocardiographic Wall Motion Abnormalities in Hypertensive Patients With Electrocardiographic Left Ventricular Hypertrophy
The LIFE Study

Vittorio Palmieri, Peter M. Okin, Jonathan N. Bella, Eva Gerdt, Kristian Wachtell, Julius Gardin, Vasilios Papademetriou, Markku S. Nieminen, Björn Dahlöf, Richard B. Devereux

Abstract—There is limited information on correlates of left ventricular wall motion (WM) abnormalities in ambulatory patients with hypertension and ECG left ventricular hypertrophy by Cornell voltage-duration product and/or Sokolow-Lyon voltage criteria. Therefore, we assessed the prevalence and the correlates of echocardiographic global and segmental left ventricular WM abnormalities in 942 hypertensive patients with hypertrophy enrolled in the Losartan Intervention For End-point reduction in hypertension (LIFE) echo substudy. Patients were separated into groups of those with normal WM or those with segmental or global WM abnormalities. Segmental and global WM abnormalities were mostly of mild degree and were detected in 7% and 6% of the study sample. Compared with subjects with normal motion, those with WM abnormalities were mostly men and had higher prevalences of self-reported coronary heart disease, ECG signs of myocardial infarction, ST-strain pattern, and higher Cornell voltage-duration product, echo-left ventricular mass, and albuminuria, but lower total and high-density lipoprotein cholesterol. Blood pressure was similar among groups. No significant differences were found between patients with global or segmental WM abnormalities. Only half of patients with WM abnormalities had a history or ECG signs of coronary heart disease. Independent correlates of WM abnormalities were higher albuminuria and Cornell voltage-duration product, male gender, and echo-left ventricular hypertrophy, but lower cholesterol. In a subanalysis restricted to patients with WM abnormalities, those with evident cardiovascular disease had a higher prevalence of ST-strain pattern than those with subclinical WM abnormalities, but other clinical, ECG, or echocardiographic parameters were indistinguishable between the 2 groups. Thus, in hypertensives with ECG left ventricular hypertrophy, WM abnormalities, mostly of mild degree, occurred in one eighth of the patients and were associated with male gender, left ventricular hypertrophy, and albuminuria. No significant differences were found between patients with global or segmental wall motion abnormalities. (Hypertension. 2003;41:75-82.)

Key Words: hypertension, arterial risk factors

Coronary heart disease (CHD) is the leading cause of morbidity and mortality in hypertension.1 Myocardial infarction or severe ischemia are the most common causes of left ventricular (LV) wall motion (WM) abnormalities,2 which may reduce LV pump function.3-4 However, information on the prevalence and correlates of WM abnormalities in ambulatory high-risk hypertensive patients is limited.5

Hypertension is a major determinant of LV hypertrophy1 and is associated with increased prevalence of LV systolic dysfunction.6 However, global LV ejection fraction (EF), a measure of LV chamber function highly useful as an indicator of LV systolic dysfunction, can be normal despite segmental WM abnormalities, especially when EF is estimated from linear echocardiographic LV dimensions at mid-cavity level,7 or from single-plane contrast ventriculograms.

Two-dimensional echocardiography allows semi-quantitative assessment of WM abnormalities2-4,8,9 which are pathophysiologically associated with CHD.4 Assessment
of the prevalence of echocardiographic segmental and global WM abnormalities and their electrocardiographic, laboratory, and echocardiographic correlates may help identify subjects with higher cardiovascular event rates in hypertension. Therefore, we examined the prevalence and correlates of echocardiographic systolic WM abnormalities in a large sample of hypertensive adults with LV hypertrophy by ECG.

Methods

Population
As described elsewhere in detail,10 patients aged 55 to 80 years with seated clinic blood pressure (BP) 160 to 200/95 to 115 mm Hg after 1 and 2 weeks on placebo treatment were recruited into the Losartan Intervention For Endpoint reduction in hypertension study (LIFE) if they had LV hypertrophy identified by ECG criteria (Cornell voltage-duration product or Sokolow-Lyon voltage) as previously reported. Exclusion criteria for LIFE were known severe aortic stenosis or ejection fraction (EF) <40%, myocardial infarction or stroke within 6 months or specific requirement for beta-blocker, angiotensin-converting enzyme inhibitor, or angiotensin receptor antagonist therapy. The LIFE echocardiography substudy enrolled 960 members of the LIFE cohort, who underwent baseline echocardiography before randomization for study treatment.11 Body mass index (BMI) was assessed as body weight/height$^2$. Smoking habit was coded as never, ex-smoker, or current smoker; alcohol consumption was coded as yes/no. Diabetes was identified based on physician report or self-report or use of hypoglycemic medication. Clinically evident CHD included self-reported angina or previous myocardial infarction, coronary revascularization procedures. ECG evidence of myocardial infarction was defined by Minnesota codes 1.1 or 1.2. Repolarization abnormalities in leads V5 and/or V6 indicated typical strain when there was a downsloping convex ST segment with an inverted asymmetrical T wave opposite to the QRS axis.12 ECG readings for the present study were performed at the Helsinki University Central Hospital, Finland. Laboratory evaluation included assessment of fasting plasma glucose, total and high density lipoprotein (HDL) cholesterol, plasma creatinine, and the urinary albumin/creatinine ratio (albuminuria).13 Pathologic albuminuria was defined as urinary albumin/creatinine ≥30 mg/g.

Echocardiography
A standard, reliable methodology was employed in the LIFE Echocardiography study to assess LV structure and function.14 Echocardiograms were recorded on video tapes and centrally read at the Echo-Reading Center following recommendations of the American Society of Echocardiography13,14 by trained physician first readers (V.P., J.N.B.) and by a highly experienced second final arbiter (R.B.D.). Correct orientation of planes for imaging and Doppler recordings was verified using standard procedures.15 Two-dimensionally guided M-mode tracings were used, if correctly oriented, to measure LV structures,13 whereas linear measurements of LV structure were obtained in 2D parasternal long-axis view in the presence of low parasternal windows.14 LV measurements were averaged from 2 to 5 cardiac cycles in which LV diameter was maximized by using anatomically correct views. End-diastolic LV dimensions were used to calculate LV mass by a formula that yields values closely related ($r=0.90$) to necropsy LV weight.16 LV mass calculated by this method has stratified cardiovascular risk in the absence or presence of CHD or heart failure.17-20 LV mass was indexed for height$.^2$. LV hypertrophy was defined as LV mass >46.7 g/m$^2$ in women and >49.2 g/m$^2$ in men. Doppler-derived stroke volume$^{21}$ was used to calculate Doppler EF (Doppler stroke volume/LV end-diastolic volume by the Teichholz formula$^1$) and cardiac index (stroke volume×heart rate/body surface area). Valvular disease was assessed, as previously described, by inspection of valvular morphology and leaflet mobility and Doppler echocardiography.22,23 Diastolic parameters were assessed as previously described.

Assessment of WM Score
WM was assessed semiquantiatively in parasternal long- and short-axis views and apical views. In short-axis views, the LV was divided into 5 segments at the base and at papillary muscle level (anterior and posterior septum; anterior, lateral, and posterior walls) and into 4 segments at the apex (septum, anterior, lateral, and posterior walls).23 WM scoring was based on visual assessment of motion of LV segments in 2 or more views to estimate each segment’s contribution to systolic reduction of LV volume. A score of 4.5 was assigned to each segment with normal thickening (≥30%); scores of 3.5, 2.5, and 1.5 were assigned to mildly (wall thickening 20% to 29%), moderately (wall thickening 10% to 19%), and severely (wall thickening <10%) hypokinetic segments, respectively; 0 was assigned to akinetic and −1 to dyskinetic (no appreciable wall thickening with systolic movement away from the center of the LV) segments. As reported previously,26 EF derived from WM score was calculated by adding the score of each segment; the maximum value was obtained as 4.5×14=63% assumed as normal EF, which was derived as the mean value of EF in an ethnically diverse group of apparently normal adults. In the presence of left-bundle branch block, normal WM was assigned if wall thickening was preserved. In a separate series of 111 echocardiograms repeated twice 1 to 4 weeks apart,27 we found good reliability of the total WM score (intraclass correlation coefficient for single measurement absolute agreement, 0.77; 95% confidence interval, 69 to 84; reliability coefficient $\alpha$, 0.87; $\kappa$ for normal/abnormal WM, 0.6; P<0.001).

Statistical Analysis
Mean±standard deviation for continuous variables and percentages for discrete variables are reported. The study population was divided into groups of those with normal WM and those with segmental or global systolic dysfunction. Analysis of variance, with correction for multiple comparisons by Scheffe and Dunnett T3 post hoc tests, was used to compare continuous variables among groups. Log transformation was used when needed for parametric tests. Differences in proportions among groups were tested by $\chi^2$ statistic. A series of logistic regression analyses were developed, using a forward method to enter or remove (for $P>0.1$) variables, to assess correlates of WM abnormalities; adjusted odds ratios and 95% confidence intervals were derived; WM abnormalities were the dependent variables, first considered as pooled together; segmental and global abnormalities were subsequently analyzed separately; multivariate logistic models first considered clinical and laboratory data as independent variables, then added ECG variables, and finally added echocardiographic findings to the set of covariates. Cornell voltage-duration product was coded in 2 dummy variables, one indicating Cornell voltage-duration product values between the mean and 1 standard deviation above the mean of the study population (2483 to 3594 mV×ms) and another indicating Cornell voltage-duration products >3594 mV×ms (>1 standard deviation from the mean). Both variables were simultaneously included in logistic models. A supplemental analysis assessed differences between patients with WM abnormalities who had clinical CHD and/or ECG signs of myocardial infarction or who had clinically silent WM abnormalities, using the t test for independent groups and the Fisher exact test for proportions. Two-tailed $P<0.05$ was considered statistically significant.

Results
Of the LIFE patients who underwent echocardiography at baseline, 98% (n=942) had full assessment of WM score, whereas 20 patients were excluded because wall motion scoring was incomplete (n=5, 11 to 13 segments seen) or could not be performed (n=15). As reported in Table 1, 62 patients (7%) had segmental and 56 (6%) had global WM abnormalities. Twenty-nine percent of patients with segmental WM abnormalities had at least 1 LV segment with moderate or severe dysfunction, whereas LV dysfunction was moderate or severe in only 9% of patients with global LV

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Among patients with segmental LV dysfunc-
tion, the anterior septum was most frequently 
involuted, followed by the posterior wall (50% of 
all segmental abnormalities), whereas anterior 
and lateral walls were less commonly involved. 
Isolated apical WM abnormalities and LV dys-
kinesis were rarely seen.

Demographic and Clinical Correlates of Segmental 
and Global Wall Motion Abnormalities

As may be seen in Table 2, patients with global LV WM 
abnormality were slightly older than those with normal LV 
function. The proportion of men in the groups with segmental 
or global dysfunction was greater than in the group without 
WM abnormalities. BMI and prevalence of diabetes did not 
differ among groups, nor did the prevalences of present or 
former smoking or alcohol consumption (data not shown, all 
P=NS).

The prevalence of clinical CHD was almost twice as high 
among patients with segmental or global abnormalities than 
among those with normal LV systolic function. However, 
<40% of patients with WM abnormalities reported CHD 
(Table 2). In particular, self-reported myocardial infarction 
was about 2-fold higher in those with segmental or global 
abnormalities than in those without WM abnormalities. The 
prevalence of myocardial infarction indicated by ECG was 
slightly higher than that by self-report and was 2- to 3-fold 
more frequent with global or segmental WM abnormalities 
than with normal LV systolic function. Clinical CHD or ECG 
signs of myocardial infarction were equally prevalent with 
segmental or global WM abnormalities and also occurred in 
almost one fourth of patients without LV WM abnormalities.

Cornell voltage-duration product and the prevalence of ST 
strain were both higher in patients with WM abnormalities, 
without differences between segmental or global dysfunction 
groups.

**TABLE 2. Demographic and Clinical Correlates of Global and Segmental Wall Motion Abnormalities**

<table>
<thead>
<tr>
<th>Wall Motion</th>
<th>1. Normal WM (n=824)</th>
<th>2. Segmental Abnormalities (n=62)</th>
<th>3. Global Dysfunction (n=56)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>66±7</td>
<td>67±7</td>
<td>68±6</td>
<td>3&gt;1*</td>
</tr>
<tr>
<td>Men, %</td>
<td>56</td>
<td>68</td>
<td>84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>10</td>
<td>18</td>
<td>13</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.4±4.4</td>
<td>28.3±4.7</td>
<td>27.5±4.5</td>
<td>NS</td>
</tr>
<tr>
<td>Self-reported CHD, %</td>
<td>20</td>
<td>37</td>
<td>38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Self-reported MI, %</td>
<td>5</td>
<td>13</td>
<td>11</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>MI on ECG, %</td>
<td>7</td>
<td>21</td>
<td>14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical CVD or ECG MI, %</td>
<td>22</td>
<td>44</td>
<td>39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cornell Voltage-Duration Product, mm/msec</td>
<td>2378±975</td>
<td>3413±1708</td>
<td>3022±1249</td>
<td>2, 3&gt;1†</td>
</tr>
<tr>
<td>ST strain, %</td>
<td>13</td>
<td>30</td>
<td>21</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>174±14</td>
<td>174±16</td>
<td>175±13</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>98±9</td>
<td>99±10</td>
<td>99±10</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>68±12</td>
<td>70±11</td>
<td>66±14</td>
<td>NS</td>
</tr>
<tr>
<td>Total Cholesterol, mg/dL</td>
<td>233±43</td>
<td>218±43</td>
<td>216±43</td>
<td>2*, 3†&gt;1</td>
</tr>
<tr>
<td>HDL Cholesterol, mg/dL</td>
<td>60±18</td>
<td>55±15</td>
<td>52±15</td>
<td>3&lt;†</td>
</tr>
<tr>
<td>U Alb/Crea, log, mg/g</td>
<td>2.73±1.52</td>
<td>3.25±1.64</td>
<td>3.41±1.40</td>
<td>3&gt;†</td>
</tr>
<tr>
<td>Albuminuria ≥30 mg/g, %</td>
<td>27</td>
<td>37</td>
<td>45</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are mean±SD or percentages. WM indicates wall motion; BMI, body mass index; CHD, coronary heart disease; MI, myocardial infarction; CVD, cardiovascular disease; BP, blood pressure; HDL, high-density lipoprotein; and U Alb/Crea, urinary albumin/creatinine ratio.

*P<0.05; †P<0.01.
Systolic and diastolic BP and heart rate did not differ among groups (Table 2). Mean total cholesterol and HDL-cholesterol values were lower in patients with segmental or global LV dysfunction; 7% of subjects without WM abnormalities, 13% of those with segmental, and 4% of those with global abnormalities were on lipid-lowering drugs, mostly statins (P<NS). The total/HDL-cholesterol ratio was minimally higher with segmental and global WM abnormalities (data not shown). Albuminuria was greater in patients with segmental and global abnormalities. The proportion of patients who had taken ACE inhibitors, beta-blockers, calcium channel blockers or diuretics, or nitrates did not significantly differ among the 3 groups (data not shown, all P>0.1). In the group of patients with global WM abnormalities, we found a slightly higher proportion of subjects undergoing treatment with antiplatelet agents (42%) or digitalis (15%) than in the group with normal WM (antiplatelet agents, 25%; digitalis, 2.5%) or segmental WM abnormalities (antiplatelet agents, 38%; digitalis, 2.5%; both P<0.005).

Echocardiographic Findings in Patients Stratified According to Wall Motion Abnormalities
As reported in Table 3, LV wall thicknesses were similar in groups with or without WM abnormalities. LV diameter, mass, and prevalence of LV hypertrophy were higher with segmental or global WM abnormalities. Prevalence of eccentric LV hypertrophy was higher in the groups with WM abnormalities (73% with segmental, 72% with global) than in the group with no WM abnormalities (P<0.001); prevalence of concentric LV hypertrophy did not differ among the 3 groups (17% with segmental and 20% with global WM abnormalities, 28% with normal WM, P=0.1). Left atrial diameter was greater in the group with global dysfunction than in that without WM abnormalities. No difference in aortic root diameter was seen among groups, but aortic valve fibrocalcification was more frequent with global WM abnormalities. Doppler-derived LV EF and, by definition, EF from WM scores were lower in patients with WM abnormalities and were slightly lower with global compared with segmental abnormalities (Table 3). Doppler-derived cardiac index was equally reduced with segmental or global dysfunction. After adjustment for age and gender, on average, isovolumic relaxation time (123 ms with segmental and 116 ms with global WM abnormalities versus 115 ms with normal WM, all P>0.1) and E wave deceleration time (197 ms with segmental and 203 ms with global WM abnormalities versus 217 ms with normal WM, all P>0.3) did not differ significantly among the 3 groups. E/A ratio was significantly higher in the group with global WM abnormality than in those with normal WM (1.04 versus 0.86, P<0.01), whereas there was no significant difference between those with segmental WM abnormalities and those with normal WM (0.96 versus 0.86, P>0.2).

Mitrail regurgitation, predominantly mild, occurred in 24% to 30% of the 3 groups (NS). Similarly, there was no difference among groups in the prevalence of aortic regurgitation (13% to 21%), aortic stenosis (0% to 3%), or mitral stenosis (0.1%). Mitral annular calcification was detected in 48% to 55% of those in the 3 groups (P=NS).

Multivariate Analysis: Correlates of Wall Motion Abnormalities
A first set of logistic models (Table 4) considered WM abnormalities as the dependent variable and clinical and laboratory information (age, BMI, gender, diabetes, smoking, alcohol consumption, self-reported CHD, pulse pressure, mean BP, albuminuria, and total and HDL cholesterol) as independent variables. Male gender, albuminuria, CHD, and lower total cholesterol were correlates of WM abnormalities (either segmental or global) (Table 4). In a second logistic model, segmental LV dysfunction was related to lower total cholesterol but not to other variables. Another logistic model showed that global WM abnormalities were associated with male gender, CHD, and albuminuria.

A second set of logistic models added myocardial infarction by ECG, ST strain, and Cornell voltage-duration product to the set of independent variables considered above. As shown in Table 5, WM abnormalities (either segmental or...
TABLE 4. Clinical and Laboratory Correlates of Wall Motion Abnormalities: Multivariate Analyses

<table>
<thead>
<tr>
<th></th>
<th>Abnormal Wall Motion*</th>
<th>Segmental Dysfunction*</th>
<th>Global Dysfunction*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total χ² of the model (P)</td>
<td>43 (&lt;0.001)</td>
<td>7.3 (&lt;0.001)</td>
<td>30 (&lt;0.001)</td>
</tr>
<tr>
<td>Independent variables, odds ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>2.5 (1.5–4.2)</td>
<td>—</td>
<td>5.3 (2.0–13.6)</td>
</tr>
<tr>
<td>Log U Alb/Creat, log mg/g</td>
<td>1.2 (1.06–1.4)</td>
<td>—</td>
<td>1.2 (1.02–1.48)</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>0.8 (0.6–0.97)</td>
<td>0.7 (0.5–0.9)</td>
<td>—</td>
</tr>
<tr>
<td>Self-reported CHD</td>
<td>2.0 (1.3–3.2)</td>
<td>—</td>
<td>2.2 (1.1–4.1)</td>
</tr>
</tbody>
</table>

All P<0.01. *Additional variables that did not enter models (forward stepwise method; removed for P>0.1): age, BMI, mean BP, pulse pressure, total and HDL-cholesterol, diabetes, smoking habit, and alcohol consumption.

global) were associated with male gender, albuminuria, lower cholesterol, and higher Cornell voltage-duration product, but not other variables. In a second logistic model, segmental LV dysfunction was associated with lower total cholesterol, greater albuminuria, and Cornell voltage-duration product. A subsequent logistic model showed associations of global WM abnormalities with male gender and albuminuria.

A final set of logistic models added echocardiographic LV hypertrophy and aortic valve fibrocalcification to the clinical, laboratory, and ECG data. WM abnormalities (either segmental or global) were related to male gender, albuminuria, lower total cholesterol, and segmental echocardiographic LV hypertrophy. On the other hand, isolated apical dysfunction or LV aneurysm were uncommon. The 12.5% prevalence of LV WM abnormalities in LIFE echo substudy patients is nearly 3 times higher than the 4.3% reported in hypertensive adults in the Cardiovascular Health Study. One potential explanation is the selection of subjects with ECG LV hypertrophy for LIFE, in view of the known association of higher LV mass with CHD, myocardial infarction, and larger myocardial infarction size. In fact, patients with segmental or global WM abnormalities had greater LV mass, as indicated by both ECG and echocardiographic methods, than those without systolic dysfunction. On the other hand, exclusion from LIFE of hypertensive patients requiring specific treatment with beta-blockers or ACE inhibitors as well as patients with known severe LV dysfunction may have led to underrepresentation of more severe abnormalities, especially dysfunction of the large anterior LV wall.

TABLE 5. Clinical, Laboratory, and ECG Correlates of Wall Motion Abnormalities: Multivariate Analyses

<table>
<thead>
<tr>
<th></th>
<th>Abnormal Wall Motion*</th>
<th>Segmental Dysfunction*</th>
<th>Global Dysfunction*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total χ² of the model (P)</td>
<td>67 (&lt;0.001)</td>
<td>25 (&lt;0.001)</td>
<td>29 (&lt;0.001)</td>
</tr>
<tr>
<td>Independent variables, odds ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>3.2 (1.7–5.9)</td>
<td>—</td>
<td>6.1 (2.1–17.4)</td>
</tr>
<tr>
<td>Log U Alb/Creat, log mg/g</td>
<td>1.3 (1.1–1.4)</td>
<td>1.2 (1.01–1.5)</td>
<td>1.2 (1.03–1.5)</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>0.7 (0.6–0.95)</td>
<td>0.7 (0.5–0.9)</td>
<td>—</td>
</tr>
<tr>
<td>Cornell voltage-duration product 2483–3594 mV×msec</td>
<td>1.9 (1.1–3.2)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cornell voltage-duration product &gt;3594 mV×msec</td>
<td>4.1 (2.1–8.1)</td>
<td>4.2 (2.0–8.8)</td>
<td>—</td>
</tr>
</tbody>
</table>

All P<0.01. *Additional variables that did not enter models (forward stepwise method; removed for P>0.1): age, BMI, mean BP, pulse pressure, total and HDL-cholesterol, diabetes, smoking habit, alcohol consumption, self-reported coronary heart disease, ECG-myocardial infarction, and ST strain.
In our study, fewer than half of patients with segmental or global LV WM abnormalities had overt CHD. Autopsy data suggest low sensitivity of clinical data for significant CHD. In multivariate models, clinical CHD independently predicted WM abnormalities and was more strongly associated with global than with segmental dysfunction (Table 4). However, when ECG and echocardiographic LV hypertrophy were included in the independent variables, self-reported CHD was excluded from multivariate models (Tables 5 and 6). This suggests that target organ damage is more strongly associated with WM abnormalities than with clinical information in hypertensive patients, consistent with previous evidence that echocardiographic findings in hypertensive patients predict cardiovascular events independent of clinical findings. Consequently, risk stratification of those patients, even if screened for LV hypertrophy by ECG, was significantly refined by echocardiography.

Segmental WM abnormalities can be related to subclinical coronary artery disease. Up to one third of acute myocardial infarctions can be clinically silent; up to 30% of acute myocardial infarctions never manifest diagnostic Q waves; a diagnostic Q wave disappears in 10% to 30% of Q-wave infarctions or is not diagnostic 2 years after an acute myocardial infarction. Therefore, silent ischemia or myocardial infarction or chronic ischemia/hibernating myocardium may cause WM abnormalities at rest. Although mild hypokinesis may be a normal variant, hypokinesis is strongly associated with significant CHD. Furthermore, even

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### TABLE 6. Clinical, Laboratory, ECG, and Echocardiographic Correlates of Wall Motion Abnormalities: Multivariate Analyses

<table>
<thead>
<tr>
<th></th>
<th>Absent Wall Motion*</th>
<th>Segmental Dysfunction*</th>
<th>Global Dysfunction*</th>
</tr>
</thead>
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<tr>
<td>Total χ² of the model (P)</td>
<td>73 (&lt;0.001)</td>
<td>22 (&lt;0.005)</td>
<td>44 (&lt;0.001)</td>
</tr>
<tr>
<td>Independent variables, odds ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>3.5 (1.8–6.6)</td>
<td>—</td>
<td>7.5 (2.6–21.4)</td>
</tr>
<tr>
<td>Log U Alb/Creat, log mg/g</td>
<td>1.2 (1.02–1.4)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>0.7 (0.6–0.96)</td>
<td>0.6 (0.5–0.9)</td>
<td>—</td>
</tr>
<tr>
<td>Cornell voltage-duration product 2483–3594 mV×msec</td>
<td>1.7 (1.002–3.0)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cornell voltage-duration product &gt;3594 mV×msec</td>
<td>3.9 (2.0–7.7)</td>
<td>4.2 (2.0–8.8)</td>
<td>—</td>
</tr>
<tr>
<td>Echo-LV hypertrophy</td>
<td>3.4 (1.5–7.7)</td>
<td>—</td>
<td>7.5 (1.5–31.6)</td>
</tr>
<tr>
<td>Fibrocalcific aortic valve</td>
<td>—</td>
<td>2.9 (1.5–5.6)</td>
<td>—</td>
</tr>
</tbody>
</table>

All P<0.01. *Additional variables that did not enter models (forward stepwise method; removed for P>0.1): age, BMI, mean BP, pulse pressure, total and HDL-cholesterol, diabetes, smoking habit, alcohol consumption, self-reported coronary heart disease, ECG-myocardial infarction, and ST strain.

### TABLE 7. Demographic and Clinical Correlates of Wall Motion Abnormalities in the Presence or Absence of Overt Coronary Heart Disease

<table>
<thead>
<tr>
<th>Data</th>
<th>With Clinical or ECG Evidence of CHD (n=49)</th>
<th>Without Clinical or ECG Evidence of CHD (n=69)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>69±7</td>
<td>67±6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Men, %</td>
<td>76</td>
<td>75</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>16</td>
<td>15</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.1±4.2</td>
<td>28.5±4.8</td>
<td>NS</td>
</tr>
<tr>
<td>Cornell voltage-duration product, mm/msec</td>
<td>3383±1467</td>
<td>3095±1529</td>
<td>NS</td>
</tr>
<tr>
<td>ST strain, %</td>
<td>41</td>
<td>14</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>175±16</td>
<td>175±13</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>100±10</td>
<td>98±10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>69±11</td>
<td>66±14</td>
<td>NS</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>215±46</td>
<td>216±43</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>54±16</td>
<td>53±15</td>
<td>NS</td>
</tr>
<tr>
<td>U Alb/Creat, log mg/g</td>
<td>3.31±1.64</td>
<td>3.33±1.40</td>
<td>NS</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>279±63</td>
<td>283±60</td>
<td>NS</td>
</tr>
<tr>
<td>Doppler-derived EF, %</td>
<td>43±11</td>
<td>44±12</td>
<td>NS</td>
</tr>
<tr>
<td>WM score-derived EF, %</td>
<td>47.1±7.9</td>
<td>47.3±8.8</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SD or percentages.
mild WM abnormalities may improve with coronary revascularization.4,41

Interestingly, both Cornell voltage-duration product and anatomic LV hypertrophy were independently associated with WM abnormalities, whereas ST strain did not enter multivariate models. ST strain is associated with LV hypertrophy12 independently of overt CHD.42 In univariate analyses, ST strain was 2- to 3-fold more frequent in the presence of WM abnormalities (Table 2). In subjects with WM abnormalities, ST strain was 4-fold more frequent in those with than in those without CHD, suggesting that ST strain is associated with both LV hypertrophy and overt ischemic disease. Conversely, no clinical, laboratory, or echocardiographic differences were found between subjects with clinically overt or silent WM abnormalities (Table 7). Therefore, WM abnormalities may be independent signs of coronary disease even in asymptomatic patients.

Patients with LV WM abnormalities had greater albuminuria, a potential marker of microangiopathy.43 This finding was confirmed in all multivariate analyses that pooled segmental and global abnormalities, and in some, but not all, multivariate analyses considering segmental or global dysfunction separately. Of particular note, albuminuria was associated with segmental or global LV systolic dysfunction independently of clinically overt CHD.

Surprisingly, total and HDL cholesterol levels were lower in patients with WM abnormalities. Because use of lipid lowering drugs was similar among the 3 groups, unmeasured lifestyle and diet modifications may be responsible for this finding. On the other hand, benefits associated with relatively low cholesterol level may have permitted patients with LV MW abnormalities plus LV hypertrophy to maintain adequate EF (>40%) for enrollment in the LIFE study. Furthermore, the modest inotropic effect of digoxin, used more commonly in patients with global LV WM abnormality, may have slightly diminished the degree of LV systolic dysfunction in this group.

In the study population, men had more LV WM abnormalities than women, as previously reported.4 In multivariate analysis, male gender had a strong association with segmental and especially global WM abnormalities (odds ratios 2.5 to 3.3 and 5.3 to 7.5), independently of covariates, including diabetes, alcohol consumption, and smoking.

A potential limitation of our study is that echocardiographic LV WM was assessed only at rest, because of the nature of the LIFE study. Neither WM abnormalities during stress, nor coronary morphology or myocardial perfusion studies are available. Therefore, pathophysiologic inferences from our results need to be made with caution. Our findings also need extension to patients with milder hypertension. However, it is relevant that subjects with clinically silent WM abnormalities did not differ from those with WM abnormalities and overt CHD in clinical, laboratory, and echocardiographic findings, suggesting that in our study population both “silent” WM abnormalities and those associated with symptoms or ECG signs of CHD are most likely manifestations of coronary artery disease.9

Palmieri et al  Wall Motion Abnormalities in Hypertension

Perspective

In ambulatory patients with long-standing arterial hypertension, wall motion abnormalities, mostly a manifestation of CHD, were associated with male gender, higher Cornell voltage-duration product, and increased echocardiographic LV mass and albuminuria, whereas clinical and ECG information correlated poorly with WM abnormalities.

Conclusions

Echocardiographic LV WM abnormalities occurred in about one eighth of patients with moderately severe hypertension as manifested by BP level and presence of ECG-LV hypertrophy, despite the exclusion of patients with overt heart failure, recent myocardial infarction or stroke, or clinical need for beta-blocker or ACE-inhibitor therapy. WM abnormalities were associated with greater Cornell voltage-duration product and anatomic LV mass, male gender, and microangiopathy independently of overt CHD.

Acknowledgment

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Echocardiographic Wall Motion Abnormalities in Hypertensive Patients With Electrocardiographic Left Ventricular Hypertrophy: The LIFE Study

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