Heart

Electrocardiographic and Echocardiographic Detection of Myocardial Infarction in Patients with Left-Ventricular Hypertrophy

The LIFE Study

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Background: Left-ventricular hypertrophy (LVH) is a recognized risk factor for myocardial infarction (MI). However, detection of MI by standard electrocardiographic (ECG) criteria may be hampered in patients with LVH. In this setting of hypertensive LVH, the accuracy of two-dimensional (2D) echocardiography in detecting incident MI is unknown. Thus, we compared the accuracy of 2D echocardiography with Minnesota-code ECG criteria in detecting incident MI, adjudicated during serial evaluation in patients with hypertension and LVH.

Methods: In the ECG substudy of the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) Study, complete baseline wall-motion (WM) evaluation was obtained in 904 hypertensive patients with ECG LVH who did not have a left-bundle branch block. Electrocardiography and echocardiograms obtained at annual follow-up visits were evaluated for ECG Q-waves by Minnesota codes and WM abnormalities, respectively (mean follow-up, 4.8 ± 0.9 SD years). Occurrence of incident clinical MI during follow-up was adjudicated by an expert end-point committee.

Results: In two logistic models adjusting for confounders, incident MI was independently associated with either incident Q-waves by the Minnesota code (odds ratio [OR], 6.1; 95% confidence interval [CI], 2.4–15.3) or incident and worsened WM abnormalities (OR, 11.9; 95% CI, 4.5–32.0), and the association was stronger for WM abnormalities than for Q-waves (P < .0001). Detection of incident MI by ECG or 2D echocardiography was obtained with sensitivities of 29% and 68% and specificities of 95% and 84%, respectively.

Conclusions: Wall-motion abnormalities on serial 2D ECGs recognize incident MI better than do Minnesota-code ECG criteria during follow-up of patients with hypertension and LVH. Am J Hypertens 2007;20:771–776 © 2007 American Journal of Hypertension, Ltd.

Key Words: Echocardiography, electrocardiography, myocardial infarction, hypertrophy.

Left-ventricular hypertrophy (LVH) is independently associated with an increased risk of myocardial infarction (MI).1–3 Although highly desirable in the setting of LVH, accurate, noninvasive identification of a previous MI is still a major problem in clinical practice.4 The detection of MI-related alterations in electrocardiograms (ECGs) represents the most clinically applicable method for noninvasive recognition of a previous MI. However, it was demonstrated that a clinically symptomatic Q-wave MI may be undetectable in later ECGs because of a masking effect of LVH on pathological Q-waves.5 There is no information on the ability of echocardiographic wall-motion (WM) analysis as compared with ECGs to detect incident MI in patients with LVH. Accordingly, we compared the relations of two-dimensional (2D) echocardiographic and ECG (Minnesota code) findings to...
incident MIs during serial evaluation in patients with hypertension and LVH enrolled in the echocardiography substudy of the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) Study.

**Methods**

**Population**

The protocol was approved by the relevant ethics committees, and all patients gave written, informed consent. Hypertensive patients, aged 55 to 80 years, with LVH on ECG and a mean sitting blood pressure of 160–200/95–115 mm Hg were enrolled in the LIFE Study after 1 to 2 weeks of placebo treatment. Exclusion criteria included MI or stroke within the past 6 months before enrollment, severe aortic stenosis or a known ejection fraction <40%, and the need for open-label treatment with a beta-blocker, angiotensin-converting-enzyme inhibitor, or angiotensin-receptor antagonist. The LIFE echocardiography substudy enrolled 960 LIFE participants who underwent echocardiography at baseline and annually during the follow-up. The mean follow-up in this population was 4.8 ± 0.9 SD years.

**Clinical Definition of Myocardial Infarction**

The occurrence of incident, clinical MI (including ST-elevation and non-ST-elevation MIs) during follow-up was initially identified by the investigators caring for patients by using standardized clinical questionnaires, together with ECG, clinical, and laboratory signs. Thereafter, the occurrence of MI was adjudicated by the Endpoint Classification Committee of the study through a blind review of the clinical records. Investigator-reported MIs not confirmed by the committee were not included, and disagreements between committee members about the classification of end points were resolved by joint in-person reviews.

**ECG Analysis**

Patients underwent ECG examinations at baseline and at 6 months and 1, 2, 3, 4, and 5 years after enrollment. Minnesota coding, a standardized code system employed for ECG reporting, was used to describe the abnormalities detected in ECGs. Patients with a left-bundle branch block in their baseline ECG (Minnesota code 7.1.1) were excluded from the analysis because of the inability to correctly diagnose Q-wave MIs in these patients. Major Q-waves as a marker of incident MIs were defined by Minnesota codes that identify MIs hierarchically based on Q-wave duration, amplitude of Q and R deflections, and the presence of QS complexes (codes 1.1 and 1.2). Findings of abnormal repolarization on ECG, ie, ST junction-segment depression (Minnesota codes 4.1 and 4.2) and T-wave abnormal amplitude (Minnesota codes 5.1 and 5.2), were also considered signs of incident, non-ST-elevation MIs.

In the present analysis, incident, pathological Q-waves (Minnesota codes 1.1 and 1.2) and incident ECG ST-T findings (Minnesota codes 4.2, 4.2, 5.1, and 5.2) during follow-up were examined separately in the first ECG available after the clinical MI, to assess the accuracy of these findings for the detection of MIs. For all patients without a clinically ascertained MI during follow-up, the last available ECG was evaluated for incident Q-waves and incident repolarization abnormalities, to define the association of these findings in regularly scheduled ECGs with clinical MIs.

**Echocardiographic Analysis**

The standardized echocardiographic procedures adopted in the LIFE Study were previously described. Echocardiograms were performed within the same week as ECGs, using commercially available, phased-array echocardiographs with M-mode, 2D, pulsed, and continuous-wave Doppler capability. The correct orientation of imaging planes was verified using the standard procedure. All measurements and evaluations were verified by, or primarily made by, experienced investigators blinded to the clinical data.

Wall motion was assessed by a visual, semiquantitative method in parasternal long- and short-axis views and in apical views. According to the Mayo Clinic criteria, in the short-axis view, the left ventricle is divided into five segments at the base and at the papillary muscles (the anterior and posterior septum, and the anterior, lateral, and inferior walls) and four segments at the apex (the septum, and the anterior, lateral, and inferior walls). As previously described, 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; and 0 was assigned to akinetic and −1 to dyskinetic segments. Segmental WM abnormalities were considered significant if they were present in two contiguous segments in a vascular territory. Wall-motion abnormality was defined as global when all segments were hypokinetic.

The presence of WM abnormalities was examined routinely at 1, 2, 3, 4, and 5 years after study enrollment by assigning a score to each segment, as described above. Incident, segmental WM abnormalities, including moderate hypokinesis to dyskinesis, if absent at baseline, and the worsening of preexisting segmental WM abnormalities, in comparison with those at baseline, were analyzed. The first 2D echocardiogram available after a clinical MI and the last 2D echocardiogram available during the trial in patients not suffering MIs during follow-up were included in the statistical analyses, to establish the sensitivity and predictive value of 2D echocardiographic findings for clinically ascertained MIs.
**Statistical Analysis**

Analyses were performed using SPSS 12.0 (SPSS, Inc., Chicago, IL). Results are presented as mean ± SD, and frequencies are expressed as percentages. The study population was dichotomized into groups with versus without clinical MIs. Differences in continuous variables between groups were assessed by nonpaired Student’s t-tests; differences in proportions between groups were tested by \( \chi^2 \) distribution (using the Monte Carlo method to compute exact, two-tailed \( \alpha \)-values when appropriate). Logistic regression models were developed to assess the odds ratios (ORs) and 95% confidence intervals (CIs) of incident, clinically ascertained MIs associated with ECG or 2D echocardiographic findings, adjusting for variables significantly associated with an increased risk of MI, including age, body mass index (BMI), sex, history of a previous MI, and the presence of Q-waves on baseline ECG. The first multivariate logistic model considered the presence or absence of incident Q-waves on ECGs. The second multivariate logistic model considered the presence or absence of incident and worsened WM abnormalities. The resultant logistic models were compared using \(-2 \log \) likelihood statistics to test whether the fit to data was better with one method or the other, using \( \chi^2 \) distribution.\(^{15} \) Additional logistic regression models were developed in subsets of patients without either Q-waves or segmental WM abnormalities at baseline and in patients without a history of previous MIs. In these models, incident Q-waves were compared with incident WM abnormalities as covariates. Two-tailed \( P < .05 \) was considered statistically significant.

**Results**

Out of 960 patients with baseline echocardiograms, 904 (95%) with complete baseline WM assessment from 2D echocardiograms were included in the analysis, after the exclusion of patients with a left-bundle branch block at baseline ECG (\( n = 51 \)) or absent or incomplete WM data (\( n = 5 \)).

**Univariate Association of ECG and 2D Echocardiographic Variables with Incident MI**

During follow-up, a clinical MI was adjudicated in 35 patients (4%), at a mean interval from recruitment into the study of 30 ± 18 months. On ECG analysis, 56 patients (6%) had incident Q-waves, and 91 patients (10%) had incident repolarization abnormalities. Incident or worsened 2D echocardiographic WM abnormalities were detected in 197 patients (23%). Among these, 146 patients had segmental WM abnormalities, and 51 had global WM abnormalities.

Among 35 patients with an adjudicated clinical MI during follow-up, WM could be detected by echocardiography in only 25 patients (at a mean interval of 6.9 ± 2.7 months after occurrence of the clinical MI), because cardiovascular death had occurred in 8 participants, and 2 patients had MIs after the last scheduled echocardiogram. In the group of patients adjudicated with a clinical MI, 29% (10/35 patients) had incident pathological Q-waves on their next ECG, and 68% (17/25 patients) had incident or worsened segmental WM compared with their baseline evaluation.

The odds of a clinically ascertained MI were sevenfold higher for incident Q-waves on ECG (\( \chi^2 = 31.4; \) OR, 7.2; 95% CI, 3.2–15.8; \( P < .0001 \)) and 11-fold higher for incident and worsened segmental WM abnormalities (\( \chi^2 = 46.0; \) OR, 11.3; 95% CI, 4.8–26.7; \( P < .0001 \)). Incident repolarization abnormalities were no more frequent in patients with a clinical MI at follow-up (\( \chi^2 = 0.7; \) OR, 1.5; 95% CI, 0.6–4.0; \( P = \text{NS} \)). Of note, incident Q-waves, and incident and worsened segmental WM abnormalities, were also observed in 46 (5%) and 129 (16%) patients, respectively, without a clinically documented MI during follow-up. As a consequence, the sensitivity, specificity, positive predictive value, and negative predictive value for incident MIs were 29%, 95%, 18%, and 97% for ECGs, and 68%, 84%, 12%, and 99% for 2D echocardiography, respectively.

**Multivariate Analyses for Identification of Incident MI Correlates**

Multivariate logistic models for the prediction of incident MIs are shown in Table 1. In the first logistic analysis, which included the presence or absence of incident Q-waves as an independent variable, the adjusted OR of an incident MI was 6.1 for incident ECG Q-waves, without significant associations with previous MI, older age, higher BMI, male sex, or Q-waves on baseline ECG. In a similar model, which included the presence or absence of incident and worsened WM abnormalities as an independent variable, the adjusted OR of incident MI was 11.9 for incident and worsened 2D echocardiographic segmental WM abnormalities, again without significant associations with previous MI, age, BMI, sex, or the presence of Q-waves on baseline ECG. Comparison between the \(-2 \log \) likelihood values of the two logistic models demonstrated that incident WM abnormalities were statistically more potent for the detection of clinically ascertained MIs during follow-up than were incident Q-waves (\( P < .0001 \)).

The analysis was repeated in the subset of patients without either Q-waves or segmental WM abnormalities at baseline evaluation. The adjusted OR of incident MI was 21.5 for incident and worsened 2D echocardiographic segmental WM abnormalities (Table 2). In this patient group, the sensitivity, specificity, positive predictive value, and negative predictive value of 2D echocardiographic findings were 68%, 90%, 16%, and 99%, respectively. In the same subset of patients, ECG diagnostic performance was similar to that obtained in the entire study population (adjusted OR, 6.0; 95% CI, 2.4–
Finally, in a further analysis, which excluded patients with a history of previous MI, the adjusted ORs of incident MI were 9.6 (95% CI, 4.2–22.2) for incident Q-waves and 12.5 (95% CI, 5.0–31.2) for incident and worsened 2D echocardiographic segmental WM abnormalities.

**Discussion**

The current study compared the ability of 2D echocardiograms versus ECGs performed at annual reevaluation to detect incident MIs in a prospectively studied population of patients with hypertension and ECG LVH. Our results demonstrated that the evaluation of segmental WM abnormalities is more accurate than ECG Minnesota code findings during serial assessments in identifying incident MIs diagnosed by stringent clinical criteria.

An incident, clinically adjudicated MI was more strongly associated with incident segmental left-ventricular WM abnormalities than with incident Q-waves on ECGs in patients who survived the event. Previous studies conducted in patients surviving a Q-wave MI demonstrated that Q-waves may disappear over time, because of the recovery of superficial layers of injured myocardium within or adjacent to the infarcted area.\(^{16}\) There is evidence that, especially in hypertrophied ventricles, the subendocardium is more sensitive to ischemia with more extensive necrosis, thus leaving superficial myocardium with a better possibility of recovery.\(^{17-19}\) It was also demonstrated that in up to one-third of patients with a Q-wave MI, Minnesota Q-QS ECG codes may undergo complete resolution at long-term follow-up.\(^{20}\) In addition, normalization of preexisting ECG abnormalities may be consequent to their cancellation by new abnormalities generated by necrosis involving the opposite myocardial wall.

The potential inclusion of non-Q-wave MIs among the events adjudicated by the expert LIFE Endpoint Committee may further limit the sensitivity of ECG analysis for the presence of Q-waves in the detection of incident MIs. In some studies, the analysis of ventricular repolarization improved the detection of previous MIs.\(^{21}\) However, in our study, the development of repolarization abnormalities on serial ECGs did not correlate with the occurrence of incident clinical MIs, suggesting that, although repolarization

### Table 1. Multivariate relationships of ECG and echocardiographic findings with clinical MIs

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR [exp(B)]</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incident Q-waves</td>
<td>6.1</td>
<td>2.4–15.3</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>History of MI</td>
<td>2.7</td>
<td>0.9–8.5</td>
<td>.074</td>
</tr>
<tr>
<td>Age</td>
<td>1.1</td>
<td>0.9–1.0</td>
<td>.185</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.1</td>
<td>1.0–1.1</td>
<td>.128</td>
</tr>
<tr>
<td>Sex</td>
<td>0.6</td>
<td>0.3–1.5</td>
<td>.273</td>
</tr>
<tr>
<td>Baseline Q-waves</td>
<td>0.9</td>
<td>0.2–3.3</td>
<td>.895</td>
</tr>
<tr>
<td>B. Incident and worsened segmental WM abnormalities</td>
<td>11.9</td>
<td>4.5–32.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>History of MI</td>
<td>3.0</td>
<td>0.9–9.6</td>
<td>.065</td>
</tr>
<tr>
<td>Age</td>
<td>1.0</td>
<td>0.9–1.1</td>
<td>.919</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.1</td>
<td>1.0–1.2</td>
<td>.231</td>
</tr>
<tr>
<td>Sex</td>
<td>0.6</td>
<td>0.2–1.8</td>
<td>.373</td>
</tr>
<tr>
<td>Baseline Q-waves</td>
<td>0.5</td>
<td>0.1–2.3</td>
<td>.360</td>
</tr>
</tbody>
</table>

CI = confidence interval; ECG = electrocardiogram; MI = myocardial infarction; OR = odds ratio; WM = wall motion.

As independent variables, the presence or absence of incident Q-waves is selected in model A (the $-2 \log$ likelihood $= -235.083$), and the presence or absence of incident/worsened WM abnormalities in model B (the $-2 \log$ likelihood $= -160.016$).

### Table 2. Multivariate relationships of echocardiographic findings to clinical MI in patients without either Q-waves or WM abnormalities at baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR [exp(B)]</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident and worsened segmental WM abnormalities</td>
<td>21.5</td>
<td>7.9–58.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>History of MI</td>
<td>2.1</td>
<td>0.6–7.0</td>
<td>.219</td>
</tr>
<tr>
<td>Age</td>
<td>1.0</td>
<td>1.0–1.1</td>
<td>.965</td>
</tr>
<tr>
<td>BMI</td>
<td>1.2</td>
<td>1.0–1.1</td>
<td>.109</td>
</tr>
<tr>
<td>Sex</td>
<td>0.5</td>
<td>0.2–1.6</td>
<td>.242</td>
</tr>
</tbody>
</table>

BMI = body mass index; CI = confidence interval; MI = myocardial infarction; OR = odds ratio; WM = wall motion.

The $-2 \log$ likelihood $= -149.622$. 
abnormalities may reflect myocardial ischemia, they are not a useful ECG sign of new myocardial necrosis in the specific context of LVH, an alternative cause of abnormal repolarization.

When a baseline echocardiogram is available for comparison, incident, segmental WM abnormalities may provide an accurate tool for improving the diagnosis of MI. However, in the present study, 8/25 (32%) MIs adjudicated during follow-up were not identified by 2D echocardiographic evaluation. This is consistent with the reported frequent post-MI normalization of angiographic left-ventricular WM in patients with LVH.22 In our study, 7% of WM abnormalities detected at baseline normalized during follow-up.

An asymptomatic MI is common in LVH patients.23 Thus, a proportion of LIFE patients may have suffered clinically unrecognized MIs. However, other mechanisms, including severe ischemia, may cause resting WM abnormalities without an actual MI in the presence of LVH.24 In some cases, resting WM abnormalities, observed in the absence of a clinically detected MI, may be explained by abnormal myocardial perfusion due to the microcirculatory damage reported in patients with hypertension and LVH.24,25 In addition, in post-MI patients, regional contractile dysfunction may extend to adjacent noninfarcted areas.26

There are limitations to our study. First, this is a post hoc analysis of the LIFE trial data. Second, we cannot determine how many patients with an acute ST-elevation MI were successfully treated with thrombolysis or primary angioplasty. Prompt myocardial reperfusion in such patients may have reduced MI-related ECG and 2D echocardiographic findings. Third, the precision of our estimates is reduced by the limited number of patients who suffered an incident MI in the LIFE echocardiography substudy, as well as by the inability to obtain post-MI echocardiograms in eight patients who died after MI. Nevertheless, our results are consistent with the values of sensitivity and specificity for MI detection by ECG and 2D echocardiographic evaluation. This is consistent with the reported values of sensitivity and specificity for MI detection by ECG and 2D echocardiography in hypertensive patients with electrocardiographic left ventricular hypertrophy: the LIFE Study. Blood Pressure 2001;10: 74–82.

In conclusion, the occurrence of incident MIs is better identified by the detection of incident and worsened WM abnormalities in serial 2D echocardiography than by standardized Minnesota-code ECG criteria during the follow-up of patients with hypertension and LVH. These results may have implications for the management of patients with hypertension and ECG LVH. While the need for echocardiography in hypertensive patients with ECG LVH has been debated, findings from this study suggest that echocardiography at baseline and at intervals during treatment may improve the detection of clinically unrecognized MIs in these patients. It was proposed that echocardiography be performed in hypertensive patients at low or medium risk, because the detection of echocardiographic LVH would accelerate the induction of lifestyle modifications and, in case of beginning antihypertensive drug therapy.29,30

Acknowledgments

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References


