Patients With Prolonged Ischemic Chest Pain and Presumed-New Left Bundle Branch Block Have Heterogeneous Outcomes Depending on the Presence of ST-Segment Changes

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OBJECTIVES  The purpose of this research was to examine the prognostic value of ST-segment changes (concordant ST-segment elevation and/or precordial V1 to V3 ST-segment depression) during presumed-new left bundle branch block (LBBB) in patients receiving fibrinolytic therapy.

BACKGROUND  These patients are often considered high-risk, but their outcome is not well-defined.

METHODS  The Hirulog and Early Reperefusion or Occlusion (HERO)-2 trial compared bivalirudin with heparin in patients receiving streptokinase for ST-segment elevation or presumed-new LBBB. Each patient with LBBB was matched with a control (with normal intraventricular conduction) for age, gender, pulse rate, systolic blood pressure, Killip class, and region.

RESULTS  A total of 300 patients had LBBB (92 with and 208 without ST-segment changes) and 15,340 had normal conduction. Acute myocardial infarction (AMI) occurred in 80.7% of LBBB patients and 88.7% of controls (p = 0.006). ST-segment changes were specific (96.6%) but not sensitive (37.8%) for enzymatic diagnosis of AMI. Mortality at 30 days was similar in LBBB patients with ST-segment changes (21.7%) and controls (25.0%, p = 0.563), but lower in LBBB patients without ST-segment changes than in controls (13.5% vs. 21.6%, p = 0.022). In the whole HERO-2 cohort, the LBBB patients with ST-segment changes had higher mortality than patients with normal conduction (odds ratio [OR] 1.37, 95% confidence interval [CI] 0.78 to 2.42). The LBBB patients without ST-segment changes had lower mortality than patients with normal conduction (OR 0.52, 95% CI 0.33 to 0.80).

CONCLUSIONS  ST-segment changes during LBBB are specific for the diagnosis of AMI and predict 30-day mortality; LBBB patients without ST-segment changes have lower adjusted 30-day mortality than those with normal conduction. Trials are required to determine the best treatment for high-risk and low-risk patients with LBBB. (J Am Coll Cardiol 2005;46:29–38) © 2005 by the American College of Cardiology Foundation

Repolarization changes occurring with left bundle branch block (LBBB) can obscure the classical electrocardiographic changes of ST-segment elevation in patients presenting with acute myocardial infarction (AMI). Treatment guidelines recommend reperfusion therapy for patients presenting with LBBB and a history suggestive of AMI, regardless of associated ST-segment changes (1,2). Although these patients have generally been considered to be at higher risk, it is uncertain if LBBB, in itself, predicts an adverse outcome independently of other prognostic factors.

When LBBB is present, delayed left ventricular activation occurs due to electrical activity spreading rapidly from the terminations of the right bundle branch. Normally the ST segment is depressed or elevated in the opposite direction to the main QRS deflection due to secondary repolarization changes (3). Manifestation of concordant ST-segment elevation (with a positive QRS complex) or ST-segment depression in leads V1 to V3 (with a negative QRS complex) during LBBB requires large ST-segment shifts, which may reflect severe transmural myocardial ischemia (4).

Using a raised creatine kinase-myocardial band (CK-MB) level as the “gold standard” for the diagnosis of AMI, Sgarbossa et al. (4) studied a cohort of patients from the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO)-I...
Abbreviations and Acronyms

AMI = acute myocardial infarction  
CI = confidence interval  
CK = creatine kinase  
GUSTO = Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries  
HERO = Hirulog and Early Reperfusion or Occlusion  
LBBB = left bundle branch block  
OR = odds ratio  
RBBB = right bundle branch block  
ULN = upper limit of normal

trial, and found that two features occurring during LBBB had independent diagnostic value for AMI. ST-segment elevation measuring ≥1 mm concordant with (i.e., in the same direction as) the QRS complex in any lead had the highest diagnostic value, followed by ST-segment depression measuring ≥1 mm in any lead from V1 to V3. ST-segment elevation measuring ≥5 mm discordant with the QRS complex was not, in itself, diagnostic of AMI. These criteria have recently been tested in community and emergency room studies, and were found to be specific, but not sensitive, for the diagnosis of AMI (5,6). In the large, international Hirulog and Early Reperfusion or Occlusion (HERO)-2 trial (7), electrocardiograms were recorded at randomization and repeated 60 min after commencing streptokinase, allowing identification of serial changes during LBBB. In this substudy, we examined the prognostic value (for 30-day mortality) of concordant ST-segment elevation or ST-segment depression in leads V1 to V3 during LBBB.

METHODS

The HERO-2 trial has been described previously (7). Patients presenting with >30 min of ischemic chest discomfort and either ST-segment elevation or presumed-new-onset LBBB (i.e., with no previous record of LBBB) within 6 h of symptom onset were randomized to receive either bivalirudin or unfractionated heparin as adjunctive therapy with streptokinase and aspirin. All patients gave written, informal consent. The primary end point was 30-day mortality, which did not differ between the two treatment groups. The electrocardiograms (ECG) recorded at randomization (i.e., before fibrinolytic therapy) and 60 min after commencement of fibrinolytic therapy were sent to a core laboratory at Green Lane Hospital for analysis by experienced readers. Enzymatic confirmation of AMI was also used to compare the incidence of enzymatically confirmed AMI in patients randomized with LBBB and the matched control patients. McNemar’s test (for two levels) or Bowker’s test (for more than two levels) for categorical variables, and the Wilcoxon signed rank test for continuous variables. McNemar’s test was also used to compare the incidence of enzymatically confirmed AMI in patients randomized with LBBB and the matched control patients. Also tested were the sensitivity, specificity, positive predictive accuracy, and negative predictive accuracy (for diagnosing AMI) of the three different criteria for ST-segment deviation during LBBB (i.e., concordant ST-segment elevation measuring ≥1 mm, ST-segment depression measuring ≥1 mm in leads V1 to V3, and discordant ST-segment elevation measuring ≥5 mm).

Logistic regression analysis was used to establish whether any of these three criteria independently predicted 30-day mortality.

Logistic regression analysis was also done including all patients with normal intraventricular conduction in HERO-2 and incorporating the baseline variables described above, including the time from symptom onset. The model calculations were repeated using the GUSTO prognostic
risk score, which takes into account the heart rate, systolic blood pressure, AMI location, previous AMI, and the interaction between age and Killip class (8).

Unadjusted and adjusted 30-day survival curves were generated using Cox regression analysis to visualize survival rates for three groups of patients: LBBB with ST-segment changes, LBBB without ST-segment changes, and normal intraventricular conduction. In these models, the factor “ST-segment changes” was treated as a stratifying factor rather than as a covariate. The GUSTO score (continuous variable) and region (five levels) were entered as covariates in the adjusted model. The p values were generated by fitting extra Cox models, in which ST-segment change was entered as a covariate rather than as a stratum, as well as the GUSTO score and region. The assumption was that hazards were proportional to the baseline hazard, and this was tested graphically and statistically (data not shown). Cox regression analysis was done using S-Plus 4.5 software (MathSoft Inc., Cambridge, Massachusetts), and the rest of the analysis was done using SAS 8.01 software (SAS Institute Inc., Cary, North Carolina).

RESULTS

Of the 17,073 patients randomized into HERO-2, 300 (1.76%) had LBBB at randomization. Of these 300, 41 had resolution of LBBB within 60 min (36 patients changed to normal intraventricular conduction and 5 changed to right bundle branch block [RBBB]). A total of 15,340 patients had normal intraventricular conduction at both randomization and 60 min. Another 26 patients (25 with normal intraventricular conduction and 1 with RBBB at randomization) developed new LBBB within 60 min. Table 1 describes the baseline characteristics, in-hospital interventions, and 30-day mortality of the 300 patients with LBBB at randomization, the 300 matched control patients, and the 15,340 patients with normal intraventricular conduction at both time points. Of the 300 patients with LBBB, 148 received bivalirudin and 152 received heparin, and their 30-day mortality rates were 16.2% and 15.8%, respectively (p = 0.92).

When compared with the 15,340 patients with normal intraventricular conduction, patients with LBBB were older and had a greater prevalence of previous AMI and other cardiovascular risk factors, a higher pulse rate, and a higher Killip classification at randomization, as reflected by a higher GUSTO risk score. The 30-day mortality rates were 16% in patients with LBBB and 9.1% in those with normal intraventricular conduction (p < 0.001), and approximately 40% of these deaths occurred within the first 24 h (Table 1). However, patients with LBBB had a lower 30-day mortality rate than matched control patients (16% vs. 22.7%); in 67% of matched pairs, both the LBBB patient and the control patient survived; in 5.7% of matched pairs, both patients died; in 17% of matched pairs, only the control patient died; and in 10.3% of matched pairs, only the LBBB patient died (p = 0.027).

Incidence of enzymatically confirmed AMI in patients randomized with LBBB. Patients with LBBB had a lower incidence of enzymatically confirmed AMI than matched control patients (80.7% vs. 88.7%, p = 0.006) or unselected patients with normal intraventricular conduction (80.7% vs. 92.1%, p < 0.001; Table 2). These differences persisted when deaths within 24 h were assumed to be due to AMI and when a lower CK cut-point (>1.5 times the ULN) was used as the criterion for detection of myocyte necrosis (Table 2).

Peak cardiac enzyme levels were lower in patients with LBBB than in matched control patients, and this finding was also present when only patients with enzymatically confirmed AMI were included in the analysis (Table 2).

Usefulness of concordant ST-segment elevation or lead V1 to V3 ST-segment depression during LBBB for diagnosis of enzymatically confirmed AMI. The criterion of concordant ST-segment elevation measuring ≥1 mm on the randomization ECG had high specificity (98.3%) but low sensitivity (33.5%) for the diagnosis of enzymatically confirmed AMI. The criterion of ST-segment depression measuring ≥1 mm in any of the V1 to V3 leads had similarly high specificity, but only 14.1% sensitivity. Lowering the cut-point for ST-segment changes to ≥0.5 mm for each of the two criteria did not improve sensitivity. When both criteria were combined (i.e., concordant ST-segment elevation or lead V1 to V3 ST-segment depression), the specificity for detection of enzymatically confirmed AMI was 96.6%, and the sensitivity was 37.2% (Table 3). The criterion of discordant ST-segment elevation measuring ≥5 mm had 58.6% specificity and 29.3% sensitivity.

Conduction and ST-segment changes between baseline and 60 min. Of the 41 patients with baseline LBBB that resolved within 60 min after commencing fibrinolytic therapy, 26 had ST-segment elevation at 60 min, and 15 did not. Together with the 26 patients who had ST-segment elevation at randomization and subsequently developed new LBBB within 60 min, a total of 52 patients had LBBB on one ECG and a pattern of ST-segment elevation without LBBB on the other ECG (50 had enzymatically confirmed AMI, and 1 without enzymatic confirmation of AMI died within 24 h). Using these 52 cases as having a confirmed “ST-segment elevation acute coronary syndrome,” we evaluated the diagnostic sensitivity of ST-segment changes during LBBB for enzymatically confirmed AMI. The sensitivity of discordant ST-segment elevation measuring ≥1 mm during LBBB was 44.2% (53.9% in the 26 patients developing new LBBB within 60 min), while the sensitivity of ST-segment depression measuring ≥1 mm during LBBB in any of the V1 to V3 leads was 23.1% (30.8% in the 26 patients developing new LBBB).

In 14 of the 82 patients (17%) with concordant ST-segment elevation measuring ≥1 mm during LBBB at randomization, ST-segment elevation in the lead showing
maximum concordant ST-segment elevation became discordant within 60 min after the start of fibrinolytic therapy because the net QRS deflection became negative (Fig. 1).

**ST-segment changes during LBBB and 30-day mortality.** A total of 92 patients had concordant ST-segment elevation measuring ≥1 mm or lead V1 to V3 ST-segment depression measuring ≥1 mm during LBBB, and 208 patients did not (Table 4). Significantly, peak cardiac enzyme levels were more than twice as high in patients with ST-segment changes during LBBB than in those without, and this finding persisted when the analysis excluded patients without enzymatically confirmed AMI (Table 4).

Thirty-day mortality tended to be higher in patients with ST-segment changes during LBBB than in those without.
**Table 2.** Proportion of Patients With Enzymatically Confirmed AMI or Myocardial Necrosis Among Those With LBBB at Randomization

<table>
<thead>
<tr>
<th></th>
<th>LBBB (n = 300)</th>
<th>Controls (n = 300)</th>
<th>p Value vs. LBBB*</th>
<th>Normal Intraventricular Conduction and ST-Segment Elevation (n = 15,340)</th>
<th>p Value vs. LBBB†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzymatically confirmed AMI (CK level &gt;2 × ULN or CK-MB level &gt;ULN), %</td>
<td>80.7</td>
<td>88.7</td>
<td>0.006</td>
<td>92.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Enzymatically confirmed AMI or early death within 24 h, %</td>
<td>82.0</td>
<td>92.7</td>
<td>&lt;0.001</td>
<td>93.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Myocardial necrosis (CK level &gt;1.5 × ULN or CK-MB level &gt;ULN), %</td>
<td>84.0</td>
<td>91.3</td>
<td>0.01</td>
<td>93.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Myocardial necrosis or early death within 24 h, %</td>
<td>85.3</td>
<td>95.0</td>
<td>&lt;0.001</td>
<td>95.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak enzyme level expressed as multiple of ULN‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In all patients (IQR)</td>
<td>4.1 (2.0–9.1)</td>
<td>7.2 (3.1–14.0)</td>
<td>&lt;0.0001</td>
<td>7.5 (3.4–14.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>In matched pairs of patients who both had enzymatically confirmed AMI (IQR)</td>
<td>5.6 (3.0–10.4)</td>
<td>8.1 (4.0–14.9)</td>
<td>&lt;0.0001</td>
<td>8.2 (4.2–14.9)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*p value for comparison between patients with left bundle branch block (LBBB) and matched control patients, as generated from paired comparisons; †p value for comparison between patients with LBBB and those with normal intraventricular conduction; ‡p value for comparison between patients with LBBB and matched control patients, as generated from paired comparisons; †p value for comparison between patients with LBBB and those with normal intraventricular conduction; ‡p value for comparison between patients with LBBB and matched control patients, as generated from paired comparisons.

(21.7% vs. 13.5%, p = 0.067). There was no difference in mortality between the 92 LBBB patients with these ST-segment changes and matched control patients (21.7% vs. 25%, p = 0.563), but mortality was lower in the 208 LBBB patients without these ST-segment changes than in matched control patients (13.5% vs. 21.6%, p = 0.022; Fig. 2).

**Predictors of 30-day mortality.** On univariable analysis of the 300 patients with LBBB, the odds ratio (OR) for 30-day mortality in those with versus those without ST-segment changes (i.e., concordant ST-segment elevation measuring ≥1 mm or lead V1 to V3 ST-segment depression measuring ≥1 mm) was 1.79 (95% confidence interval [CI] 0.95 to 3.37, p = 0.074). The OR for 30-day mortality per 10-U increase in the GUSTO risk score was 1.89 (95% CI 1.49 to 2.41, p < 0.0001).

On multivariable analysis, including the 300 patients with LBBB and the 15,340 patients with normal intraventricular conduction, there was a significant association between the presence of ST-segment changes during LBBB and 30-day mortality (p = 0.007). The ORs for 30-day mortality were 2.65 (95% CI 1.31 to 5.38) in patients with versus patients without ST-segment changes during LBBB, 1.37 (95% CI 0.78 to 2.42) in patients with ST-segment changes during LBBB versus those with normal intraventricular conduction, and 0.52 (95% CI 0.33 to 0.80) in patients without ST-segment changes during LBBB versus those with normal intraventricular conduction. The GUSTO risk score was also a predictor of 30-day mortality (OR 2.18 per 10-U increase, 95% CI 2.09 to 2.28, p < 0.001; Table 5).

When the analysis was repeated excluding patients who had normal enzyme levels and survived for >24 h, the ORs were 2.25 (95% CI 1.08 to 4.67) for LBBB with ST-segment changes versus LBBB without ST-segment changes, 1.36 (95% CI 0.77 to 2.41) for LBBB with ST-segment changes versus normal intraventricular conduction, and 0.61 (95% CI 0.38 to 0.97) for LBBB without ST-segment changes versus normal intraventricular conduction.

Figures 3 and 4 show the unadjusted and adjusted 30-day survival curves for the 92 LBBB patients with concordant ST-segment elevation measuring ≥1 mm or lead V1 to V3 ST-segment depression measuring ≥1 mm, the 208 LBBB patients without these changes, and the 15,340 patients with normal intraventricular conduction.

**DISCUSSION**

This study has two major new findings. First, in patients presenting with LBBB and a history of >30 min of ischemic chest discomfort, the presence of concordant ST-segment elevation or lead V1 to V3 ST-segment depression independently predicted higher 30-day mortality. Sec-

**Table 3.** Application of ST-Segment Criteria for the Diagnosis of AMI in the 300 Patients With LBBB at Randomization

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concordant ST-segment elevation ≥1 mm</td>
<td>82</td>
<td>33.5 (27.6–39.8)</td>
<td>98.3 (89.5–99.9)</td>
<td>98.8 (92.5–99.9)</td>
<td>26.1 (20.6–32.6)</td>
</tr>
<tr>
<td>Lead V1 to V3 ST-segment depression ≥1 mm</td>
<td>35</td>
<td>14.1 (10.1–19.2)</td>
<td>98.4 (89.5–99.9)</td>
<td>97.1 (83.4–99.9)</td>
<td>21.5 (16.8–27.0)</td>
</tr>
<tr>
<td>Concordant ST-segment elevation ≥1 mm or lead V1 to V3 ST-segment depression ≥1 mm</td>
<td>92</td>
<td>37.2 (31.1–43.6)</td>
<td>96.6 (87.0–99.4)</td>
<td>97.8 (91.6–99.6)</td>
<td>26.9 (21.1–33.6)</td>
</tr>
</tbody>
</table>

AMI = acute myocardial infarction; LBBB = left bundle branch block.
ond, patients with LBBB had more high-risk features (e.g., older age, previous AMI, and a higher GUSTO risk score) than patients with normal intraventricular conduction. After adjustment for these baseline risk factors, patients with LBBB did not have a higher 30-day mortality rate. In fact, the absence of concordant ST-segment elevation or lead V1 to V3 ST-segment depression during LBBB independently predicted a lower 30-day mortality rate than that of patients with normal intraventricular conduction. Our analysis focused on risk assessment at the time when patients were first seen and treatment decisions needed to be made, before the results of cardiac enzyme tests were available. When multivariable analysis was performed only on patients who were subsequently confirmed as having abnormal enzyme levels, the findings were identical.

Over 80% of HERO-2 trial patients with LBBB had enzymatically confirmed AMI. As in previous studies (4–6), concordant ST-segment elevation measuring $\geq 1$ mm and lead V1 to V3 ST-segment depression measuring $\geq 1$ mm within the LBBB morphology were both highly specific.

Figure 1. (A) Randomization and (B) 60-min electrocardiograms in a patient in whom concordant ST-segment elevation in lead V3 became discordant ST-segment elevation because the net QRS deflection in lead V3 became negative by 60 min.
for the diagnosis of enzymatically confirmed AMI. Concordant ST-segment elevation had modest sensitivity of 33.5%, and lead V1 to V3 ST-segment depression had only 14.1% sensitivity. The use of a lower ST-segment cut-point of 0.5 mm did not improve diagnostic sensitivity. Discordant ST-segment elevation measuring 5 mm was neither sensitive (29.3%) nor specific (58.6%). In the 45-patient “validation cohort” described in the original report by Sgarbossa et al. (4), the sensitivity of either concordant ST-segment elevation or lead V1 to V3 ST-segment depression for the diagnosis of enzymatically confirmed AMI was 36%, which was consistent with our findings. These criteria had lower sensitivity (<20%) in emergency room and community studies (5,6).

There are several explanations for the relatively infrequent occurrence of concordant ST-segment elevation during LBBB in patients with enzymatically confirmed AMI. First, some patients with enzymatically confirmed AMI and LBBB may have the “equivalent” of non-ST-segment elevation AMI. From serial electrocardiographic recordings, we identified 52 patients who had LBBB on one ECG and ST-segment elevation without LBBB on the other ECG. In these 52 patients with an “ST-segment elevation acute coronary syndrome,” the diagnostic sensitivity of concordant ST-segment elevation measuring ≥1 mm during LBBB was modest (44.2%).

Second, the ST segment may have risen from below the original baseline during AMI, but not enough to be detectable as concordant ST-segment elevation during LBBB. The secondary repolarization changes during LBBB are opposite in direction to those of the main QRS deflection (3), leading to a negative ST-segment baseline, and several millimeters of ST-segment elevation during AMI from this negative baseline may be insufficient to raise the ST segment above the isoelectric line.

Third, the QRS vector changes as AMI progresses over time. In the 17% of our patients who exhibited concordant ST-segment elevation during LBBB at randomization, concordant ST-segment elevation became discordant within 60 min as the net QRS complex became negative. Thus, in some LBBB patients who presented with a more evolved AMI, the concordant ST-segment elevation pattern may have evolved into a discordant ST-segment elevation pattern.

In the American College of Cardiology/American Heart Association guidelines (1), the combination of bundle branch block and a history suggestive of AMI is listed as a class 1 indication for fibrinolytic therapy. This recommendation is based on the findings of placebo-controlled fibrinolytic trials (9–11), which showed that patients with bundle branch block on the randomization ECG had high mortality and benefited significantly from fibrinolytic therapy, with a 21% reduction in mortality. However, these trials did not specify whether the ECG showed RBBB or LBBB.

<table>
<thead>
<tr>
<th>Enzymatically Confirmed AMI</th>
<th>LBBB with ST-Segment Changesa (n = 92)</th>
<th>LBBB and No ST-Segment Changesa (n = 208)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak enzyme level expressed as multiple of ULN</td>
<td>90 (97.8%)</td>
<td>152 (73.1%)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>All patients (IQR)</td>
<td>8.5 (4.0–17.5)</td>
<td>3.2 (1.5–6.2)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>Patients with enzymatically confirmed AMI (IQR)</td>
<td>9.4 (4.2–18.0)</td>
<td>4.4 (2.9–7.5)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>20 (21.7%)</td>
<td>28 (13.5%)</td>
<td>p = 0.067</td>
</tr>
</tbody>
</table>

*ST-segment changes were defined as concordant ST-segment elevation measuring ≥1 mm or ST-segment depression measuring ≥1 mm in electrocardiographic leads V1 to V3 during left bundle branch block (LBBB); †the causes of in-hospital death were classified as cardiac, stroke, bleeding, anaphylaxis, or other causes.

AMI = acute myocardial infarction; IQR = interquartile range; ULN = upper limit of normal. | Figure 2. Thirty-day mortality in 92 patients with ST-segment changes during left bundle branch block (LBBB) versus matched control patients, and in 208 patients without ST-segment changes during LBBB versus matched control patients.
LBBB, whether the conduction abnormalities were new, or whether there were associated ST-segment changes. ST-segment elevation can be detected in patients with RBBB, but in those with LBBB, ST-segment changes reflecting transmural ischemia may be obscured by repolarization changes. There are, therefore, no data available from randomized clinical trials that specifically demonstrate a mortality reduction with fibrinolytic therapy in patients with LBBB.

In the HERO-2 trial, which specified prolonged ischemic chest discomfort lasting \( \geq 30 \) min and presumed-new LBBB as inclusion criteria, enzymatically confirmed cases of AMI were about 10% less frequent in patients with LBBB than in matched control patients. Some of these patients with LBBB who did not have enzymatically confirmed AMI might have had nonischemic chest discomfort or prolonged ischemia without AMI.

When patients have concordant ST-segment elevation or lead V\(_1\) to V\(_3\) ST-segment depression during LBBB, these findings are highly specific (97%) for the diagnosis of enzymatically confirmed AMI. The use of early biomarkers such as myoglobin (12,13) and heart-type fatty-acid binding protein (14) in patients without ST-segment changes may identify a group of patients in whom subsequent confirmation of AMI by cardiac markers is unlikely and in whom fibrinolytic therapy may not prove beneficial.

In contrast with unselected HERO-2 patients with normal intraventricular conduction, the patients with LBBB were older and had a greater prevalence of previous AMI and other cardiovascular risk factors, a higher pulse rate, and

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**Table 5. Multivariable Logistic Regression Models for Predictors of 30-Day Mortality**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GUSTO risk score (every 10-U rise)</td>
<td>2.18</td>
<td>2.09–2.28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ST-segment changes* during LBBB</td>
<td></td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>(A) LBBB with ST-segment changes versus LBBB without ST-segment changes</td>
<td>2.65</td>
<td>1.31–5.38</td>
<td></td>
</tr>
<tr>
<td>(B) LBBB with ST-segment changes versus normal intraventricular conduction</td>
<td>1.37</td>
<td>0.78–2.42</td>
<td></td>
</tr>
<tr>
<td>(C) LBBB without ST-segment changes versus normal intraventricular conduction</td>
<td>0.52</td>
<td>0.33–0.80</td>
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</table>

The association between the three groups (ST-segment changes\* present during left bundle branch block (LBBB), ST-segment changes\* absent during LBBB, and normal intraventricular conduction) was similar when the recruitment region and the time from symptom onset were also entered into the model: (A) odds ratio (OR) 2.70, 95% confidence interval (CI) 1.33–5.49; (B) OR 1.38, 95% CI 0.79–2.44; (C) OR 0.51, 95% CI 0.33–0.80. The results were also similar when the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) risk score in the model was replaced by age, sex, pulse, systolic blood pressure, and Killip class: (A) OR 2.73, 95% CI 1.33–5.62; (B) OR 1.44, 95% CI 0.81–2.54; (C) OR 0.53, 95% CI 0.33–0.83. The results were also similar when the analysis was repeated excluding patients who had a normal enzyme level and survived for \( > 24 \) h: (A) OR 2.25, 95% CI 1.08–4.67; (B) OR 1.36, 95% CI 0.77–2.41; (C) OR 0.61, 95% CI 0.38–0.97. *ST-segment changes were defined as concordant ST-segment elevation measuring \( \geq 1 \) mm or ST-segment depression measuring \( \geq 1 \) mm in electrocardiographic leads V\(_1\) to V\(_3\) during LBBB.

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**Figure 3.** Nonadjusted 30-day survival curves in 92 patients with either concordant ST-segment elevation or lead V\(_1\) to V\(_3\) ST-segment depression during left bundle branch block (LBBB), 208 patients without concordant ST-segment elevation or lead V\(_1\) to V\(_3\) ST-segment depression during LBBB, and 15,340 patients with normal intraventricular conduction (\( p = 0.029 \) for normal conduction vs. LBBB without ST-segment changes; \( p < 0.001 \) for normal conduction vs. LBBB with ST-segment changes; \( p = 0.07 \) for LBBB without ST-segment changes vs. LBBB with ST-segment changes).
a higher Killip classification at randomization. Although their 30-day mortality rate was higher than that of unselected patients with ST-segment elevation and normal conduction (16% vs. 9.1%, p < 0.001), it was lower than that of matched control patients (16% vs. 22.7%, p = 0.027). In patients with LBBB, concordant ST-segment elevation or lead V₁ to V₃ ST-segment depression during LBBB independently predicted the risk of 30-day mortality, which was 2.65 times higher in patients with associated ST-segment changes than in those without these features, after adjustment for other prognostic factors (Table 5). These ST-segment changes may have represented large shifts from the original baseline ST-segment level during LBBB (3,15,16), reflecting more severe ischemia.

Although some patients with LBBB and no ST-segment changes did not have enzymatic confirmation of AMI, this cannot fully explain their better outcome because the results were similar when multivariable analysis was repeated after excluding patients with normal enzyme levels who survived for >24 h. The better 30-day prognosis in these patients with LBBB and no ST-segment changes may be at least partly explained by smaller infarct sizes as reflected by lower peak enzyme levels, and/or by the possibility that their infarction was more characteristic of non-ST-segment elevation AMI than ST-segment elevation AMI. In the North American cohort of patients with LBBB randomized into the GUSTO-I trial, 30-day mortality was identical in the 131 patients with LBBB and control patients matched for age and Killip class (17), but further subgroup analysis of the LBBB patients was not performed.

Both LBBB and AMI are more common in elderly patients, and, with increasing longevity, the diagnostic and management challenges posed by patients presenting with LBBB accompanying prolonged ischemic chest discomfort will arise more frequently. In the HERO-2 trial, LBBB at the time of randomization was presumed to be new unless the patient had a previous record of LBBB. Our findings suggest that the presence of LBBB (even when judged clinically to be new) in a patient with symptoms compatible with AMI should not in itself be regarded as an independent marker of higher risk. Instead, patients with LBBB may be risk-stratified by the presence or absence of concordant ST-segment elevation or lead V₁ to V₃ ST-segment depression.

Although patients with ST-segment changes during LBBB had a higher 30-day mortality rate than those without ST-segment changes during LBBB, the latter subgroup of LBBB patients actually had a lower adjusted 30-day mortality rate than the majority of patients with ST-segment elevation AMI and normal intraventricular conduction. These lower-risk patients with LBBB and no associated ST-segment changes may have had no AMI, a smaller AMI, or an event more characteristic of non-ST-segment elevation AMI with normal intraventricular conduction. Further studies are needed to test different management strategies in patients presenting with symptoms compatible with AMI accompanied by LBBB with or without ST-segment changes.

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REFERENCES


