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# 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 $V_1$ to $V_3$ 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 Reperfusion 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.

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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 $V_1$ to $V_3$ (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

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**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 $V_1$ to $V_3$. 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 $V_1$ to $V_3$ 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, informed 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 defined as a CK level exceeding twice the upper limit of normal (ULN) or a CK-MB level exceeding the ULN.

**Electrocardiographic analysis of LBBB.** The diagnostic criteria for LBBB were a QRS duration of ≥0.120 s in the presence of sinus or supraventricular rhythm, a QS or rS complex in lead $V_1$, and an R-wave peak time of ≥0.06 s in leads I, $V_5$, or $V_6$ associated with absence of a Q-wave in the same lead (4). The following measurements were made by a cardiologist blinded to the patients' treatment and outcome, with ST-segment deviation being measured at the J point and compared with the TP segment isoelectric line:

Maximum magnitude of ST-segment elevation in leads with a positive QRS complex (concordant ST-segment elevation).
Maximum magnitude of ST-segment depression in leads $V_1$, $V_2$, or $V_3$.
Maximum magnitude of ST-segment elevation in leads with a negative QRS complex (discordant ST-segment elevation).
Change in net QRS polarity (direction) over 60 min in the lead showing a positive QRS complex and maximum concordant ST-segment elevation at randomization.

**Statistical analysis.** Patients with LBBB were compared with: 1) a matched control group with normal intraventricular conduction, and 2) all patients with normal intraventricular conduction. Each patient with LBBB at randomization was matched (for age, gender, pulse rate, systolic blood pressure, and Killip class at randomization) with a control patient chosen from those in HERO-2 who had normal intraventricular conduction at both randomization and 60 min. As this substudy was performed in 46 countries, the patients were also matched for their recruitment region (Russia, Eastern Europe, Western countries, Latin America, and Asia). After matching for these six variables, further matching was done for diabetes and the time from symptom onset to randomization.

The data are presented as proportions or median values with interquartile ranges where appropriate. Comparisons between groups were done using the chi-square test for categorical variables and the Mann-Whitney *U* test for continuous variables. Comparisons between the LBBB patients and matched control patients were done using 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 $V_1$ to $V_3$, 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