Outcomes in patients with chronicity of left bundle-branch block with possible acute myocardial infarction

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Introduction

Guidelines derived from patients in clinical trials indicate that emergency department patients with likely myocardial infarction (MI) who have new left bundle-branch block (LBBB) should undergo rapid reperfusion therapy. Whether this pertains to lower risk emergency department patients with LBBB is unclear.

Methods

A total of 401 consecutive patients with LBBB undergoing an MI rule-out protocol were included. Left bundle-branch blocks were classified as chronic; new; or, if no prior electrocardiogram (ECG) was available, as presumably new. Left bundle-branch blocks were considered concordant if there was ≥1 mm concordant ST elevation or depression. Rates of MI, peak MB values in MI patients, and 30-day mortality were compared across groups.

Results

A majority of patients (64%) had new (37%) or presumably new LBBB (27%). A total of 116 patients (29%) had MI, with no significant difference in prevalence or size of MI among the 3 ECG groups. Myocardial infarction was diagnosed in 86% of patients with concordant ECG changes versus 27% of patients without concordant ECG changes (P < .01). Peak MB was >5× normal in 50% who had concordant ST changes compared to none of those who did not. Concordant ST changes were the most important predictor of MI (odds ratio 17, 95% CI 3.4-81, P < .001) and an independent predictor of mortality (odds ratio 4.3, 95% CI 1.3-15, P < .001); new or presumably new LBBB was neither.

Conclusions

Most patients with possible MI with new or presumably new LBBB do not have MI. Concordant ECG changes were an important predictor of MI and death. Current guidelines regarding early reperfusion therapy for patients with LBBB should be reconsidered. (Am Heart J 2011;161:698-704.)
ECGs were read independently by 2 interpreters unaware of the clinical variables and patient outcome. Disagreements were resolved by a third interpreter (3% of cases). The chronicity of the LBBB was determined by comparison with the most recent previous ECG available in our hospital’s computerized ECG records. An LBBB was considered new if the most recent available ECG was not LBBB. If no prior ECG was available for comparison, patients were classified as having presumed new LBBB. Patients who had LBBB on the most recent prior ECG were classified as having chronic LBBB.

**Definitions**

All patients underwent serial sampling of total creatine kinase (CK)-MB (CK-MB) and troponin I (TnI). Diagnosis of MI required at least 1 TnI value that exceeded the reference range (coefficient of variation <10% for that assay) with a serial rise and fall. Five different assays for CK-MB and TnI were used: the Opus Magnum Analyzer (Boston, MA) (diagnostic value 1.0 ng/mL, June 1996-May 1998), the Bayer Immuno One assay (Tarrytown, NY) (diagnostic value 0.3 ng/mL, May 1998-April 2000), the DPC assay (Los Angeles, CA) (diagnostic value 1.0 ng/mL, April 2000-December 2002), the Bayer Tnl assay (Tarrytown, NY) (diagnostic value 0.5 ng/mL, December 2002-April 2007), and the Bayer Tnl Ultra Assay (Tarrytown, NY) (diagnostic value 0.1 ng/mL, April 2007-end of the study). Because different Tnl assays were used, infarct size was estimated using peak CK-MB values obtained during the initial 24 to 36 hours after admission. The number of patients who had CK-MB MI (CK-MB >6 ng/mL) in conjunction with an elevated Tnl was also determined. Size of MI was described based on multiples of peak CK and CK-MB. To compare relative MI size, patients with LBBB and MI were compared with 547 patients with STElevation MI (STEMI) and 2,467 patients with non-STEMI admitted during the same period.

**Renal failure** was defined as a creatinine clearance <60 mL/ min, estimated using the Cockcroft-Gault equation,14 using the initial creatinine. **Significant coronary disease** was defined as a stenosis ≥50% in a coronary artery or its branches or in a coronary bypass graft.

**Statistical analysis**

Comparisons were made among patients with chronic LBBB, new LBBB, and presumed new LBBB. Because patients with new or presumed new LBBB are considered candidates for early reperfusion treatment, they were combined for several analyses.

Student t test or \( \chi^2 \) analysis was used for categorical and proportional variables, respectively. \( P < .05 \) was considered statistically significant. Significant univariate variables at \( P < .10 \) were included in a multivariate analysis to identify independent predictors of acute MI and 30-day mortality. Statistical analysis was performed with a standard statistical software package (SAS 6.11, SAS, Cary, NC).

The authors are solely responsible for the design and conduct of this study, all study analyses, and the drafting and editing of the paper and its final contents.

**Results**

**Clinical characteristics**

From 1994 to 2009, 401 consecutive patients who underwent evaluation for possible acute coronary syndrome had LBBB on the initial ECG and were included in this analysis. In general, the patient population was older (median age 66 years), with frequent comorbidities (Table 1). Ejection fraction (EF) was available in 360 patients (90%), of whom 76% had an EF <50% and with 61%, <40%.

A majority of patients (64%) had either a new LBBB (36%) or presumed new LBBB (28%). Clinical...
characteristics of patients with chronic LBBB were similar to those with new or presumably new LBBB, except patients with chronic LBBB were less likely to be male and have prior MI or prior revascularization (Table I).

Myocardial infarction

Myocardial infarction was diagnosed in 116 patients (29%), of whom 23 (6%) had TnI elevations alone without CK-MB elevations, whereas 93 had both TnI and CK-MB elevations (23%). The frequency of MI and was not significantly different in patients with chronic, new, or presumed new LBBB (Table I). In the subgroup of patients who had MI, the size of MI based on peak CK-MB and CK values was relatively similar among the 3 groups, although patients with known LBBB were more likely to have MI without CK-MB elevations (Figure 1A and B). Univariate predictors of MI included older age, concordant ECG changes, congestive heart failure (CHF) at admission, prior MI, prior revascularization, and abnormal renal function (Table II). Multivariate predictors included concordant ECG changes ($P < .001$, odds ratio [OR] 16, 95% CI 3.4-81) and age $\geq$65 years ($P = .02$, OR 1.8, 95% CI 1.1-2.9).

Electrocardiographic criteria

Myocardial infarction was diagnosed in 12 (86%) of 14 patients who had concordant ST changes compared to 109 (28%) of 388 without ECG criteria ($P < .001$). Concordant ST depression was present in 4 patients, and concordant ST elevation was present in 10, of whom 8 had MI (Table III). Of the 2 patients with concordant ST elevation who did not have MI, one had 1 mm of elevation in leads I and L that was new compared to a prior ECG, and the other had 1 mm of elevation isolated to lead V4; no prior ECG was available.

Patients who had concordant ST changes and MI were more likely to have a peak CK-MB and CK $>10$x normal (both $P < .05$) and were less likely to have a peak CK-MB or CK $<1$x normal (both $P < .05$) compared to patients without concordant ST changes. The distribution of peak CK (1,820 [680, 6,020] U/L vs 2,700 [580, 3,460] U/L) and CK-MB values (99 [48, 322] ng/mL vs 200 [44, 290] ng/mL) were similar for patients with concordant ST changes and the control group of patients who had STEMI evaluated during the same period (Figure 2A and B). In patients with MI and LBBB who did not have concordant ECG changes, the distribution of peak CK (240 [120, 490] U/L vs 780 [130, 590] U/L) and CK-MB values (13 [6.8, 29] ng/mL vs 42 [4.9, 38] ng/mL) was similar to the control group of patients with non-STEMI (Figure 2).

Six patients had an ST/T ratio $>25\%$, of whom 4 had MI. Peak MB and CK levels tended to be low; peak MB values were 4.1, 16, 20, and 58 ng/mL, and peak CK values were 89, 187, 372, and 493 U/L.

Univariate predictors of MI are shown in Table II. Multivariate predictors included only concordant ST changes (OR 17, 95% CI 3.4-81, $P < .001$) and age $\geq$65 years (OR 1.7, 95% CI 1.1-2.7, $P = .02$).

Coronary angiographic outcomes

Coronary angiography was performed in 152 patients. This included 59 (51%) of the TnI (+) patients and 93 (33%) of the TnI (−) patients. Significant disease was present in 43 (73%) of the TnI (+) patients, of whom 21 (49%) had revascularization, and 37 (40%) of the TnI (−) patients, of whom 16 (37%) had revascularization. Sixteen patients underwent emergent treatment: 1 patient was treated with fibrinolytics (had MI), and 15 underwent emergent coronary angiography. Significant disease was present in 9, of whom 7 had PCI. 1 had coronary artery bypass surgery (CABG), and 1 was managed medically. Six patients had no significant disease.

Thirty-day mortality

Thirty-day mortality was 11% overall; 6.7% in patients without and 22% in patients with MI. In patients with
MI, 30-day mortality was 50% in those with and 20% in patients without concordant ECG changes (Table IV). Troponin MI was the most important univariate and multivariate predictor of mortality. Other multivariate predictors included concordant ECG changes and male gender.

**Discussion**

We found that there was no difference in the incidence of MI based on the chronicity of the LBBB on the presenting ECG. Patients who had concordant ST changes had a high likelihood of MI. In addition, concordant ECG changes were the most important independent predictor of MI as well as an independent predictor of 30-day mortality.

Administration of fibrinolytic therapy to patients with AMI and ST-segment elevation decreases mortality. The results of the Fibrinolytic Collaborative Group, which included patients with bundle-branch block and presumed AMI, demonstrated a 25% reduction in mortality with treatment with fibrinolytics and thus formed the basis for current treatment recommendations. However, important limitations of this analysis were that patients with right bundle-branch block and LBBB were not differentiated nor was the chronicity of the LBBB determined.

Prevalence of LBBB and MI

Clinical trials that have included patients with LBBB have found that the rate of MI confirmation is significantly lower in patients with LBBB than those who have ST elevation. In the ASSENT 2 and 3 trials, despite...
rigorous entry criteria, 38% of those enrolled with LBBB did not have MI confirmed. Similarly, in the HERO Trial, patients with LBBB were less likely to have MI. In more heterogeneous ED patients, the prevalence of AMI among patients who have LBBB is even lower.

New LBBB

We found that the frequency as well as the size of MI was similar among patients with chronic, new, or LBBB of unknown duration. Although the presence of a new (or presumably new) LBBB is thought to identify patients who have AMI and emergent reperfusion is recommended, data to support these criteria are limited. No references are provided in current guidelines. Some studies, but not all, have shown that a new LBBB is associated with an increased rate of MI. However, even in patients with new LBBB, MI is diagnosed in only a minority. For example, Chang et al found MI in 7.2%, and Li et al found MI in 16% of patients with new or LBBB of unknown duration. Therefore, this criterion appears insufficient for selecting patients for early reperfusion therapy.

The low diagnostic accuracy of the ECG and increased numbers of atypical presentations coupled with the high rate of comorbidities in patients with LBBB can result in diagnostic confusion and likely contribute to the lower rate and increased time to emergent reperfusion in these patients. In an analysis from the National Registry of Acute MI, patients who had LBBB were significantly less likely to undergo early reperfusion treatment, in those who did, door-to-drug time was longer than those with STEMI. Similarly, more recent data in patients undergoing primary PCI from the ACTION-GWTG Registry found that primary PCI rates were significantly lower and were associated with greater delay than that of STEMI patients.

Increasing data indicate that patients with LBBB and MI presenting to the ED represent a heterogeneous group of patients: a minority who have STEMI equivalent, who are likely to benefit from acute reperfusion treatment; patients with non-STEMI equivalent, who have myocardial necrosis but without complete vessel occlusion; and, with increased use of more sensitive assays, patients with acute CHF exacerbation with minor myocardial necrosis who may be mistakenly classified as having MI. Although all may benefit from invasive evaluation, it is only the first group in whom emergent reperfusion treatment is beneficial. Therefore, accurate identification of patients with LBBB who are likely to have an occluded vessel is important.

**Diagnostic ECG changes**

Early diagnosis of MI in patients with LBBB can be improved by applying specific diagnostic ECG criteria. Sgarbossa et al reported that concordant ST elevation or ST depression ≥1 mm was highly specific, although not sensitive, for identifying MI in patients with LBBB. We found similar results; concordant ST changes were specific for MI and were the most important independent predictor of MI. In addition, it was an independent predictor of 30-day mortality; in contrast, a new LBBB predicted neither MI nor mortality.

Our results are concordant with other studies. In a combined analysis of patients with LBBB enrolled in the ASSENT 2 and 3 Trials that included 253 patients with LBBB, MI was diagnosed in only 13% of patients with LBBB without concordant ECG changes compared to 49% of those with concordant ECG changes. Additional analyses that have included patients enrolled in clinical trials or patients admitted from the ED have confirmed the high specificity of these criteria. In a meta-analysis of 10 studies that included 1,614 patients,

### Table IV. 30-day mortality

<table>
<thead>
<tr>
<th></th>
<th>30-day mortality (n = 47)</th>
<th>No 30-day mortality (n = 354)</th>
<th>P</th>
<th>Multivariate P value</th>
<th>OR (95% CI)</th>
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<tr>
<td>ST-T changes</td>
<td>7 (15)</td>
<td>7 (2)</td>
<td>&lt;.001</td>
<td>.02</td>
<td>4.3 (1.3-15)</td>
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<tr>
<td>Age, y</td>
<td>68 ± 17 (70)</td>
<td>66 ± 14 (66)</td>
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<td>Chronic</td>
<td>15 (32)</td>
<td>130 (37)</td>
<td>.52</td>
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<td>New</td>
<td>18 (38)</td>
<td>127 (36)</td>
<td>.74</td>
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<tr>
<td>Unknown</td>
<td>14 (30)</td>
<td>97 (27)</td>
<td>.73</td>
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<tr>
<td>New + unknown</td>
<td>32 (68)</td>
<td>224 (63)</td>
<td>.52</td>
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<td>Age ≥65 y</td>
<td>29 (62)</td>
<td>164 (46)</td>
<td>&lt;.05</td>
<td>.54</td>
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<td>Male</td>
<td>27 (57)</td>
<td>131 (37)</td>
<td>&lt;.01</td>
<td>.005</td>
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<td>Hypertension</td>
<td>32 (68)</td>
<td>280 (79)</td>
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<td>Diabetes</td>
<td>17 (36)</td>
<td>140 (40)</td>
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<td>CHF</td>
<td>17 (36)</td>
<td>89 (25)</td>
<td>.11</td>
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<td>Prior MI</td>
<td>15 (32)</td>
<td>94 (27)</td>
<td>.44</td>
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<td>Prior revascularization</td>
<td>10 (21)</td>
<td>98 (28)</td>
<td>.35</td>
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<td>CrCl &lt;60 mL/min</td>
<td>33 (70)</td>
<td>168 (47)</td>
<td>.004</td>
<td>.03</td>
<td>2.3 (1.1-4.8)</td>
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<td>TnI MI</td>
<td>28 (60)</td>
<td>91 (26)</td>
<td>&lt;.001</td>
<td>.001</td>
<td>3.3 (1.7-6.7)</td>
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</tbody>
</table>

**Categorical data are presented as n (%). Continuous data are presented as mean ± SD (median).**
the presence of concordant ECG changes had a specificity of 98%, with a positive likelihood ratio of 7.9 for predicting MI.\textsuperscript{16}

We also found that patients with LBBB who had MI and concordant ECG changes had significantly larger infarcts, likely contributing to the higher mortality. Peak CK and CK-MB values were similar to that of STEMI patients and significantly higher than that in non-STEMI patients. Similar results were reported in the HERO Trial; as peak CK values were more than twice to those with concordant ECG changes, mortality was similar to the STEMI patients and almost twice as high as LBBB patients without concordant ST changes.\textsuperscript{10}

Requiring diagnostic ECG changes could induce complexity into the decision making. However, a high agreement between cardiologists and emergency medicine physicians for diagnosing MI using these criteria has been reported,\textsuperscript{17} indicating that emergency physicians could be able to accurately use these criteria.

In the absence of concordant ST elevation or depression, the ability to rapidly identify MI is difficult. Standard tools, such as cardiac markers or emergent imaging, are limited. Body-surface potential ECG mapping\textsuperscript{18,19} has shown promise but has not gained wide-spread use. Therefore, use of specific ECG criteria appears to be the best available tool for rapid selection of patients who are most likely to benefit from emergent reperfusion.

Performance measures

Only a subset of guidelines should be considered performance measures—those specifically intended for public reporting, external comparisons, and pay-for-performance programs.\textsuperscript{30} They should be limited to those that meet the highest level of evidence, with substantial data that the treatment is beneficial and that failure to treat appropriate patients is associated with worse outcomes.\textsuperscript{21} However, we and others\textsuperscript{7,8} found that MI is diagnosed in only a minority of patients with new LBBB. The size of MI was relatively small in most patients who had MI and therefore less likely to benefit from emergent reperfusion, especially if treated with fibrinolytics.\textsuperscript{15} In addition, attempts to meet the 90-minute door-to-balloon time could lead to inadvertent patient harm. There is a high false-positive rate in patients with LBBB undergoing emergent coronary angiography for presumed STEMI.\textsuperscript{22} The risk of emergent angiography may outweigh the benefits given the high rates of underlying CHF, renal insufficiency, and other comorbidities that increase the risk of contrast nephropathy.\textsuperscript{23} Use of troponins may inadvertently classify patients with CHF as having MI and therefore subject to this performance measure. Because most patients with a new LBBB do not have MI, clinical judgment and use of objective ECG criteria offer the best way to determine the need for early reperfusion.

Limitations

Although patient data from an extended period were used, the criteria for emergent reperfusion in patients with LBBB have been present because guidelines were published in 1996. We used CK and CK-MB to estimate peak MI size because of the multiple different TnI assays used during the study period. In addition, use of CK and CK-MB allows comparison across other studies, a technique used in clinical trials.

Despite these limitations, our study has several strengths. These include the large consecutive cohort of patients with LBBB, the ability to assess the chronicity of the LBBB, the ability to determine 30-day rather than just in-hospital mortality, and use of standardized diagnostic criteria for MI, including use of troponins, instead of CK or CK-MB.

Conclusions

Most patients who present to the ED with possible AMI who have an underlying LBBB do not have an MI. In those who do, MI size is relatively small and therefore are unlikely to benefit from emergent reperfusion treatment. The diagnostic use of a new LBBB was low. Specific ECG criteria, concordant ST depression or elevation, had a high specificity and identified patients who had large MIs. The use of emergent reperfusion treatment in patients with new LBBB as a performance indicator should be reconsidered.

Disclosures

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References


