Lack of association between left bundle-branch block and acute myocardial infarction in symptomatic ED patients

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Abstract

Objective: Guidelines recommend treating patients with a new or presumed new left bundle-branch block (LBBB) similar to those with an acute ST-segment elevation myocardial infarction. It is often unclear which emergency department (ED) patients with potentially ischemic symptoms actually have an acute myocardial infarction (AMI), even in the setting of LBBB. Our null hypothesis was that in ED patients with potential AMI, the presence of a new or presumed new LBBB would not predict an increased likelihood of AMI.

Methods: This was an observational cohort study. Patients older than 30 years who presented with chest pain or other ischemic equivalent and had an electrocardiogram (ECG) to evaluate potential acute coronary syndrome (ACS) were enrolled. Data collected include demographics, history, ECG, and cardiac markers. Electrocardiograms were classified according to the standardized guidelines, including LBBB not known to be old (new or presumed new LBBB), LBBB known to be old, or no LBBB. The hospital course was followed, and 30-day follow-up was performed on all patients. Our main outcome was AMI.

Results: There were 7937 visits (mean age, 54.3 ± 15 years, 57% female, 68% black): 55 had new or presumed new LBBB, 136 had old LBBB, and 7746 had no LBBB. The rate of AMI was not significantly different between the 3 groups (7.3% vs 5.2% vs 6.1%; \( P = .75 \)). Revascularization (7.8% vs old 5.2% vs 4.3%; \( P = .04 \)) and coronary artery disease were more common in patients with new or presumed new LBBB (19.2% vs 11.9% vs 10.1%; \( P = .0004 \)).

Conclusions: Despite guideline recommendations that patients with potential ACS and new or presumed new LBBB should be treated similar to STEMI, ED patients with a new or presumed new LBBB are not at increased risk of AMI. In fact, the presence of LBBB, whether new or old, did not predict AMI. Caution should be used in applying recommendations derived from patients with definite AMI to ED patients with potential ACS that may or may not be sustaining an AMI.

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1. Introduction

The American College of Cardiology and American Heart Association guidelines recommend treating patients with new or presumed new left bundle-branch block (LBBB) on electrocardiogram (ECG) similarly to patients with ST-elevation myocardial infarction (STEMI) [1,2]. This recommendation was based on the Fibrinolytic Therapy Trialists’ systematic review of major randomized clinical trials of fibrinolysis vs placebo [3], which found that individuals with a bundle-branch block had higher baseline mortality and had the greatest incremental improvement in survival. However, in the 9 large trials included, only the GISSI trial reported LBBB as a separate entity, whereas 5 other studies did not discriminate between left and right bundle-branch blocks [3-10].

A subsequent analysis by Gallagher [10] concluded that treating all patients with LBBB and suspected acute myocardial infarction (AMI) with fibrinolysis was the preferred strategy for selecting patients for fibrinolytic therapy, and determination of whether the LBBB was new or old did not improve selection accuracy. An analysis by Shlipak et al [11] concluded that treating all patients with LBBB and suspected AMI was preferred over the use of ECG criteria to select patients for fibrinolytic therapy. However, these analyses were dependent on the assumed incidence of AMI in the setting of LBBB and used estimates between 13% and 30% [10-13].

There is, however, significant discrepancy in the reported incidence of AMI in patients presenting with a new or presumed new LBBB [3,12,14-16]. Fibrinolytic therapy is only beneficial in patients with AMI but has significant costs and risks in all patients exposed to treatment [1,3,17]. The purpose of our study was to determine the prevalence of AMI in patients who present with chest pain or an ischemic equivalent and have a new or presumed new LBBB.

2. Methods

2.1. Study design

We conducted an observational cohort study of patients presenting to the ED with symptoms of a potential acute coronary syndrome (ACS) to compare the prevalence of AMI in patients with no, old, or new or presumed new LBBB on the initial ECG.

2.2. Study setting

This study was conducted at the Hospital of the University of Pennsylvania, a university teaching hospital that has an annual census of approximately 57,000 adult patient visits per year. Data were collected after approval by the University of Pennsylvania Committee on Research Involving Human Subjects.

2.3. Patient population

All adult patients older than 30 years presenting to the ED with a primary complaint of chest pain or other potential ischemic equivalent consistent with a potential ACS who had an ECG ordered as part of their diagnostic evaluation were evaluated for study eligibility. Patients with chest pain who received an ECG were included regardless of the treating physician’s clinical judgment. Patients with potential ischemic equivalents (shortness of breath) were only included if the treating physician determined that ACS was part of their differential. Patients were eligible whether or not they were admitted to the hospital. Patients were excluded if they were younger than 30 years, did not have chest pain or another potential ischemic equivalent, or did not have an electrocardiogram obtained. Management of all patients was at the discretion of the treating physician and independent of study enrollment.

2.4. Data collection

Study subjects were identified by trained research assistants who were present in the ED 7 days a week from 8:00 AM to midnight. Data were collected in accordance with Standardized Reporting Guidelines [18]. Patients were treated by full-time board-certified or board-eligible emergency physicians in conjunction with housestaff, if present. Information collected included basic demographic information, characteristics of chest pain and associated symptoms, cardiac history and risk factors, medications, treatment, and disposition.

Admitted patients were followed daily through their hospital stay through direct communication between the investigators and the health care team. All patients had telephone follow-up after 30 days, regardless of whether they were initially admitted or discharged. At the time of follow-up, patients or proxies were queried about death, myocardial infarction, and revascularization procedures. Medical records were reviewed when patients or proxies were unable to provide follow-up information. A National Death Index search was conducted for all patients.

2.5. Electrocardiographic data

Electrocardiograms were interpreted in accordance with Standardized Reporting Criteria [18]. The treating physician categorized the ECG based on the presence or absence of ST-segment elevation or depression, T-wave inversions, Q waves, left or right bundle-branch blocks, or nonspecific ECG changes. These interpretations were made in real-time settings, and treatment decisions were made by the treating physician. The treating physician...
determined the presence of left bundle-branch block on ECG. The physician also noted if these changes were known to be old, based on comparison with prior ECGs, when available. When prior ECGs were not available, they were considered “not known to be old” or new or presumed new.

2.6. Cardiac biomarker assays

Cardiac troponin I and creatine kinase–MB assays were performed if requested by the treating physician. During the study period, we used an enzyme-linked immunoassay using an Abbott AxSYM automated analyzer (Abbott Laboratories, Mountain View, Calif).

2.7. Main outcome

Acute myocardial infarction was defined in accordance with the European Society of Cardiology/American College of Cardiology guidelines [19,20]. Mortality data were collected from communication with the treating physician, family members, or record review. Revascularization was defined as percutaneous coronary intervention with or without stent placement or coronary artery bypass grafting. Coronary artery disease was defined as at least one vessel with greater than 70% stenosis or documented AMI (which presumed underlying coronary disease).

2.8. Statistical analysis

Data were imported into SAS statistical software (version 9.1, SAS Institute, Cary, NC) for analysis. Categorical data are presented as the percent frequency of occurrence and continuous data are presented as medians with interquartile ranges or means with SDs, as appropriate. Relative risks and 95% confidence intervals (CIs) are also presented. A P value of .05 was statistically significant. We did not perform multivariable analysis and adjust for comorbidities because the decision to perform reperfusion in the setting of LBBB is not based on these criteria.

3. Results

A total of 7937 patients were enrolled. The mean age was 54 ± 14 years, 57% female, 68% black. On their ECG, 55 had new or presumed new LBBB (0.6%), 136 had old LBBB (1.7%), and 7746 had no LBBB. Patients with a LBBB were older and had more documented cardiac risk factors and past cardiac disease (Table 1). A total of 4742 (60%) of patients were admitted. During the initial hospitalization, overall, 484 patients (6.1%) had an AMI, 331 patients (4.2%) had a revascularization procedure performed, and 738 patients (9.3%) were diagnosed with coronary artery disease. Seven thousand seven hundred four patients (97%) were available

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Presenting characteristics of patients</th>
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</thead>
<tbody>
<tr>
<td>Patient characteristics</td>
<td>No LBBB (n = 7746)</td>
</tr>
<tr>
<td>Age (y ± SD)</td>
<td>54 ± 14</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>4430</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>5306</td>
</tr>
<tr>
<td>White</td>
<td>2168</td>
</tr>
<tr>
<td>Other</td>
<td>269</td>
</tr>
<tr>
<td>Cardiac risk factors</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>4245</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1545</td>
</tr>
<tr>
<td>Elevated cholesterol</td>
<td>1764</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>1398</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>3116</td>
</tr>
<tr>
<td>Medical history</td>
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</tr>
<tr>
<td>History of CAD</td>
<td>1630</td>
</tr>
<tr>
<td>Past MI</td>
<td>1042</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>278</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>185</td>
</tr>
<tr>
<td>TIMI score</td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>4443</td>
</tr>
<tr>
<td>2-3</td>
<td>2097</td>
</tr>
<tr>
<td>≥4</td>
<td>692</td>
</tr>
</tbody>
</table>

CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; LBBB, left bundle branch block.
for follow-up in 30 days. Overall, 101 patients died (1.3%) within 30 days.

There was no difference in the rate of AMI between the 3 groups: patients with a new or presumed new LBBB had 7.3% (relative risk [RR], 1.1; 95% CI, 0.47-2.84), old LBBB 5.2% (RR, 0.84; 95% CI, 0.41-1.69), and patients without a LBBB had a 6.1% rate of AMI.

Our secondary outcome was the rate of revascularization (percutaneous coronary intervention [PCI] or coronary artery bypass grafting). Revascularization within 30 days was different between the 3 groups (Table 2): 7.8% in patients with a new or presumed new LBBB, 5.2% in patients with an old LBBB, and 4.3% in patients without a LBBB (P = .04). Documented coronary disease was more common in patients with new or presumed new LBBB (19.2%, RR 1.90) than the other groups of patients (P = .0004).

### 4. Discussion

We found that new or presumed new LBBB provides limited diagnostic value in identifying patients with AMI. This suggests the criteria recommended in the American College of Cardiology/American Heart Association guidelines to select patients for fibrinolytic therapy may not be useful. The prevalence of LBBB in AMI patients, based on large multihospital registries, is between 6% and 9% [3,4,14,21,22]. The prevalence of AMI in patients with LBBB who present to the ED with symptoms of ACS is less clear and differs depending on the study setting. Sgarbossa et al [14] evaluated more than 26,000 patients enrolled in the GUSTO-I trial (Global Utilization Strategy for Thrombolysis of Occluded arteries) and found 0.6% had a LBBB identified on ECG, but 90% of these patients sustained AMI. Rates of more than 30% have been reported from other series of highly selected patients. More recent reports of selected ED patients with LBBB reveal rates of AMI between 10% and 15% [12,13,15,16]. Accurate determination of these rates is necessary for analysis of costs and benefits of various treatment selection strategies [10].

The initial studies that led to guideline development for treatment of patients with LBBB with reperfusion were based on enrollment of some patients with LBBB in large randomized studies. It is reasonable to assume that patients enrolled in these trials may have been somewhat different than the typical ED patient with symptoms consistent with ACS who have a LBBB, as patients enrolled in clinical trials and registries usually represent a lower-risk patient population [23].

We found the rate of AMI in patients with new or presumed new LBBB to be 7.3%. Our results may more accurately reflect the results in common clinical practice in which all patients with symptoms consistent with ACS receive evaluation. Several decision tree analyses have been published that supported the guideline treatments. Gallagher [10] devised a decision analysis tree to look at the benefits and risks for fibrinolysis for patients with LBBB, using a 13% rate of AMI for patients with LBBB. He found that fibrinolysis for all patients with LBBB did not incur greater risk of morbidity or mortality. For each 1000 patients with a new or indeterminate LBBB, a strategy of fibrinolysis for all patients would lead to approximately 44 deaths, with more than 930 patients having stroke-free survival. Shlipak et al [11] reached the same conclusion using numbers from similar sources but estimated a higher LBBB with AMI rate (30%). Our data suggest that these rates of AMI are overestimates and raise questions about whether these decision analyses are appropriate. We studied a large cohort of undifferentiated ED patients, which we feel is more reflective of the true prevalence of patients with LBBB. We found that the AMI rates of patients with LBBB were no higher than in patients without LBBB, suggesting that treatment should be the same for both groups [24].

In most studies, AMI patients with a new or presumed new LBBB have a worse outcome than patients without a new LBBB [3,11,14,22,23,25-30]. Guerrero et al [26], in a post hoc analysis of the Primary Angioplasty in Myocardial Infarction database, found that patients with LBBB had lower ejection fraction and more multivessel disease than other patients who received primary PCI. This is consistent with our data where we found a higher likelihood of coronary

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**Table 2** Outcomes of patients with no, old, or new LBBB

<table>
<thead>
<tr>
<th></th>
<th>No LBBB * (n = 7746)</th>
<th>Old LBBB (n = 136)</th>
<th>New LBBB (n = 55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI</td>
<td>% (n)</td>
<td>% (n) RR (95% CI)</td>
<td>% (n) RR (95% CI)</td>
</tr>
<tr>
<td>Admit to CCU</td>
<td>6.1% (473)</td>
<td>5.2% (7) 0.84 (0.41-1.69)</td>
<td>7.3% (4) 1.19 (0.47-2.84)</td>
</tr>
<tr>
<td>Revascularization</td>
<td>11.1 (858)</td>
<td>20.6% (28) 1.86 (1.31-2.56)</td>
<td>27.3% (15) 2.46 (1.55-3.65)</td>
</tr>
<tr>
<td>(PCI or CABG) within 30 d</td>
<td>4.3% (320)</td>
<td>5.2% (7) 1.22 (0.59-2.44)</td>
<td>7.8% (4) 1.84 (0.72-4.37)</td>
</tr>
<tr>
<td>Coronary artery disease diagnosed within 30 d</td>
<td>10.1% (759)</td>
<td>11.9% (16) 1.17 (0.73-1.8)</td>
<td>19.2% (10) 1.90 (1.06-3.17)</td>
</tr>
<tr>
<td>Death within 30 d</td>
<td>1.5% (106)</td>
<td>3.0% (4) 2.10 (0.81-5.32)</td>
<td>2.0% (1) 1.39 (0.24-7.37)</td>
</tr>
<tr>
<td>Composite (AMI, revascularization, CAD, death) at 30 d</td>
<td>11.0% (829)</td>
<td>14.8% (20) 1.34 (0.88-1.99)</td>
<td>19.2% (10) 1.74 (0.98-2.91)</td>
</tr>
</tbody>
</table>

* Indicates baseline comparison.

Coronary artery disease is defined as more than one vessel with more than 70% stenosis or documented AMI.
disease in the patients with LBBB. There was an increased rate of revascularization in patients with LBBB regardless of whether it was new or old.

Guidelines recommend reperfusion for new or presumed new LBBB [1,2]. Our data suggest that fibrinolysis may not be the optimal approach because the rate of AMI is not higher in patients with LBBB than in patients without. Perhaps primary PCI might be a better approach because it will allow both diagnosis and intervention. It is accepted practice to overtriage patients for activation of the cardiac catheterization lab for presumed STEMI, as the benefits of primary PCI has been documented [1]. Larson et al recently reported on “false-positive” cardiac catheterization activation in more than 1300 patients [25]. In this analysis there were 36 patients with a new or presumed new LBBB, most of whom did not have a lesion explaining the presenting symptoms. There was no culprit lesion in 44% of these patients, and another 27% did not have significant coronary artery disease. Despite these results, the 30-day mortality for these patients was still double that of the rest of their study cohort [25]. This study and others like ours suggest that primary PCI may be useful in patients with new or presumed new LBBB to make a definitive diagnosis and to allow intervention when appropriate without incurring the risk of fibrinolysis.

Our study has some limitations that merit discussion. Although we did not have a very large number of patients with LBBB, the frequency of LBBB was consistent with the few prior studies, and the number of LBBB in our study was as much or more than most of these prior studies. We classified LBBB as not known to be old but did not specify between definitely new and presumed new (ie, no old ECG for comparison). It is possible that the subset with definitely new LBBB might be higher risk for AMI, but we could not assess this due to the method of ECG classification. The ECG readings were not interpreted in a core laboratory but were interpreted by the treating physician in the ED. Prior ECGs are limited to those in our medical records system; however, it is noteworthy that other local hospitals are within our health system and we have easy access to their records through the same medical records system. There may have also been “workup” bias in the evaluation of patients with new or presumed new LBBB. However, despite a possibility of increased evaluation in patients with new or presumed new LBBB, the prevalence of AMI was still not increased.

In conclusion, we found that patients with and without LBBB had similar rates of AMI. This suggests guidelines calling for fibrinolytic therapy of patients with new LBBB should be reevaluated. Past decision analyses were based on an overestimate of the likelihood of sustaining AMI.

References


