Acute Myocardial Infarction and Complete Bundle Branch Block at Hospital Admission: Clinical Characteristics and Outcome in the Thrombolytic Era

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Objectives. We sought to assess the outcome of patients with acute myocardial infarction (MI) and bundle branch block in the thrombolytic era.

Background. Studies of patients with acute MI and bundle branch block have reported high mortality rates and poor overall prognosis.

Methods. The North American population with acute MI and bundle branch block enrolled in the Global Utilization of Streptokinase and t-PA [tissue-type plasminogen activator] for Occluded Coronary Arteries (GUSTO-I) trial was matched by age and Killip class with an equal number of GUSTO-I patients without conduction defects.

Results. Of all 26,003 North American patients in GUSTO-I, 420 (1.6%) had left (n = 131) or right (n = 289) bundle branch block. These patients had higher 30-day mortality rates than matched control subjects (18% vs. 11%, p = 0.003, odds ratio [OR] 1.8) and were more likely to experience cardiogenic shock (19% vs. 11%, p = 0.008, OR 1.78) or atrioventricular block/asystole (30% vs. 19%, p < 0.012, OR 1.57) and to require ventricular pacing (18% vs. 11%, p = 0.006, OR 1.73). Bundle branch block also carried an independent 53% higher risk for 30-day mortality. Thirty-day mortality rates for patients with complete, partial and no reversion of the bundle branch block were 8%, 12% and 20%, respectively (two-tailed chi-square test for trend 5.61, p = 0.02, OR 0.34 for complete reversion, OR 0.55 for partial reversion).


Before the widespread use of thrombolysis, up to 30% of patients with acute myocardial infarction (MI) presented to the hospital with bundle branch block or developed it after admission (1–6). These patients had an unfavorable short- and long-term prognosis (6–11). The average in-hospital mortality rate was 30%, with death mainly related to older age and heart failure (3,6,9). In addition, high degree atrioventricular (AV) block complicated the hospital course of 15% of patients with isolated right bundle branch block (12) and of 30% to 46% of those with bifascicular block (9,11).

With the advent of reperfusion therapies, resolution of bundle branch block and AV block have been reported after both primary coronary angioplasty (13,14) and thrombolysis (15). A recent subset analysis of the Global Utilization of Streptokinase and t-PA [tissue-type plasminogen activator] for Occluded Coronary Arteries (GUSTO-I) and Thrombolysis and Angioplasty in Myocardial Infarction (TAMI-9) data bases showed a relatively poorer outcome for patients with acute chest pain who subsequently developed bundle branch block than for those who maintained normal intraventricular conduction throughout the hospital period (16). However, the prognosis of patients presenting to the hospital with acute MI and bundle branch block has not been systematically scrutinized in the thrombolytic era.

Methods

Patients. The study group consisted of all North American patients enrolled in the GUSTO-I trial (17) who had suspected
BUNDLE BRANCH BLOCK AND MI. Patients were included in this study if they had bundle branch block on the admission ECG. Both the admission and predischarge ECGs were analyzed. Right bundle branch and left fascicular blocks were defined according to the classic criteria (19); the diagnosis of left anterior fascicular block in patients with Q wave inferior infarction was made as recommended by Castellanos et al. (20). We used the following definition of left bundle branch block: 1) QRS duration ≥0.125 s in the presence of sinus or supraventricular rhythm; 2) QS or rS complex in lead V1; and 3) R peak time ≥0.06 s without Q waves in lead I, V5 or V6 (21). Patients with intermittent or alternating bundle branch block on the admission ECG were excluded from the study. Information on “new” versus “old” bundle branch block was not available in GUSTO-I.

Infarct location was determined by the attending physicians at time of patient discharge on the basis of all ECG, ventriculographic and clinical data available. Information on in-hospital complications was used as provided in the case report form.

Statistical analysis. Baseline characteristics were screened by univariate regression analysis to identify those associated with 30-day mortality. The variables “systolic blood pressure” and “abnormal heart rate” were modeled as suggested by Lee et al. (18), that is, by providing prognostic estimates for each unit of systolic blood pressure <120 mm Hg and by considering a U-shaped relation for heart rate in which a higher mortality is expected at very low and high heart rates. Occasional missing data were replaced by values estimated using a simultaneous imputation technique (18). The association of bundle branch block with in-hospital complications was tested. Criteria that had a univariate statistical significance at p < 0.1 were included into a stepwise logistic regression model to identify independent (p < 0.05) predictors of both 30-day mortality and reversion of bundle branch block. The predictive performance of the logistic model for 30-day mortality was examined using the Hosmer-Lemeshow test. Variable modeling was performed with EGRET software (22), and logistic regression models with EGRET and SAS (23).

Results

Bundle branch block was present on 420 baseline ECGs of the 26,003 North American GUSTO-I patients (1.6%). One hundred and thirty-one patients presented with left bundle branch block and 289 patients presented with right bundle branch block (isolated in 133 patients and associated with left anterior fascicular block in 145 patients and with left posterior fascicular block in 11 patients). Baseline characteristics are listed in Table 1. Male gender and diabetes were more prevalent among patients with bundle branch block.

Most patients with bundle branch block at hospital admission had anterior wall infarction. The association was particularly strong for patients with right bundle branch block (188 [65%] of 289). Patients with left bundle branch block presented more frequently with other infarct locations (anterior infarct in 46 [35%] of 131 patients). Peak total creatine kinase was higher among patients with bundle branch block.

Thirty-day mortality. Patients admitted with bundle branch block had a higher 30-day mortality than their matched control subjects (76 [18%] vs. 46 [11%], p = 0.003, odds ratio [OR] 1.8). The conduction defects associated with most deaths were right bundle branch block plus left anterior fascicular block.

### Abbreviations and Acronyms

- AV = atrioventricular
- ECG = electrocardiogram, electrocardiographic
- GUSTO-I = Global Utilization of Streptokinase and t-PA [tissue-type plasminogen activator] for Occluded Coronary Arteries
- MI = myocardial infarction
- OR = odds ratio
- TAMI-9 = Thrombolysis and Angioplasty in Myocardial Infarction
- t-PA = tissue-type plasminogen activator

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With BBB (n = 420)</th>
<th>Patients Without BBB (n = 420)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>69.54 (61.9, 76.2)</td>
<td>69.53 (61.9, 76)</td>
<td>0.93</td>
</tr>
<tr>
<td>Men</td>
<td>317 (75%)</td>
<td>259 (61%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.8 (68.2, 88.2)</td>
<td>76 (67.6, 85.4)</td>
<td>0.26</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172 (162.5, 180)</td>
<td>170 (160, 177.3)</td>
<td>0.88</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>127 (110, 143)</td>
<td>126 (110, 142)</td>
<td>0.31</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>75 (64, 86)</td>
<td>75.5 (64, 88)</td>
<td>0.39</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>78 (64, 90)</td>
<td>72 (62, 88)</td>
<td>0.07</td>
</tr>
<tr>
<td>Killip class</td>
<td>1.32 ± 0.65</td>
<td>1.32 ± 0.65</td>
<td>1</td>
</tr>
<tr>
<td>Peak CK (IU)</td>
<td>1.964 (717, 3,901)</td>
<td>1.557 (642, 2,736)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>180 (45%)</td>
<td>195 (46%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Diabetes</td>
<td>99 (23%)</td>
<td>70 (17%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Current smoker</td>
<td>120 (28%)</td>
<td>136 (32%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>260 (62%)</td>
<td>253 (60%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Family Hx of CAD</td>
<td>160 (38%)</td>
<td>165 (39%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Previous MI</td>
<td>99 (23%)</td>
<td>81 (19%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>26 (6%)</td>
<td>22 (5%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Ant wall MI</td>
<td>234 (56%)</td>
<td>187 (44%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Time to Tx (min)</td>
<td>165 (120, 235)</td>
<td>184 (125, 244)</td>
<td>0.29</td>
</tr>
<tr>
<td>Tx with accelerated t-PA</td>
<td>109 (26%)</td>
<td>117 (28%)</td>
<td>0.53</td>
</tr>
</tbody>
</table>
(23%, p < 0.001, OR 2.5) and isolated right bundle branch block (21%, p = 0.003, OR 2.17) (Table 2). Among nonsurvivors, time from hospital admission to death (median 2 days) was similar for patients with and without bundle branch block (interquartile bounds 1 to 7.5 and 1 to 7, vs. 2 days, respectively).

Other univariate predictors of 30-day mortality were diabetes (p < 0.001, OR 2.44), anterior infarction (p < 0.001, OR 2.39), abnormal heart rate at hospital admission (heart rate deviating in any direction from a central value of 60 beats/min) (p < 0.001, OR 1.02), hypotension (systolic blood pressure <120 mm Hg) (p < 0.001, OR 0.97), Killip class (p < 0.001, OR 2.5 for class 2, OR 5.2 for class 3, OR 4.48 for class 4), age (p < 0.001, OR 1.04/year) and smoking status (current, ex-smoker or never smoked) (p = 0.004, OR 0.75 for current smoker, OR 0.48 for ex-smoker). Hypertension, weight, history of cerebrovascular disease, previous infarction or coronary artery bypass graft surgery, time to treatment and treatment with accelerated t-PA did not predict mortality.

After adjusting for all relevant baseline prognostic variables (18), bundle branch block carried a 53% higher risk for 30-day mortality (p = 0.050, OR 1.53, 95% confidence interval 1.0 to 2.33). Independent predictors for 30-day mortality are listed in Table 3. The “goodness of fit” of this model was evaluated with the Hosmer-Lemeshow test, which indicated that the model fit well.

In-hospital complications and death. Patients with bundle branch block were more likely than their paired control subjects to experience asystole or AV block, or both (30% vs. 19%, p = 0.012, OR 1.57). The use of ventricular pacing (which in GUSTO-I was based on the attending physician’s judgment) was more frequent in the group with bundle branch block (18% vs. 11%, p = 0.006, OR 1.73). In addition, patients with conduction defects were more likely to develop sustained ventricular tachycardia or fibrillation (11% vs. 7%, p = 0.031, OR 1.73) and cardiogenic shock (19% vs. 11%, p = 0.008, OR 1.78). Acute mitral regurgitation, ventricular septal defect and tamponade affected <3% of patients in either group.

Seventy-four patients with bundle branch block (18%) died during the hospital period, including five who died after 30 days from the index event and excluding seven who died after hospital discharge but within 30 days of the infarct. Sixty-five in-hospital deaths had a cardiac cause and four a noncardiac cause, and in five the cause was not recorded. Of the 420 control subjects, 45 (11%) died in the hospital, including two who died after 30 days and excluding three who died after hospital discharge but within 30 days of the infarct. Of these 45 control subjects, 40 died of a cardiac cause and four of a noncardiac cause, and in one the cause was not recorded.

Only eight autopsy reports were available from the enrolling sites for patients who died in the hospital (six for patients with bundle branch block, two for control subjects). Among patients with bundle branch block, two deaths were caused by cardiac rupture, one by heart failure, one by “asystole,” one by a ruptured aortic aneurysm and one presumably by bilateral aspiration bronchopneumonia.

Post-thrombolysis reversion of the bundle branch block: beneficial effect on mortality. Complete reversion of the bundle branch block was seen in 51 patients (12%), whereas partial reversion occurred in 49 patients (12%) (Table 4). This reversion was not associated with changes in heart rate (86.7 ± 23.5 beats/min at admission vs. 80.46 ± 15.3 beats/min on predischarge ECG; p = 0.12). Predischarge ECGs were not available for 13 patients admitted to the hospital with bundle branch block, 11 of whom died soon after admission. The
remaining 307 ECGs showed persistence or worsening of the bundle branch block (n = 275), nonspecific conduction defects (n = 21), ventricular pacing (n = 9) or agonal rhythm (n = 2). Thirty-day mortality rates for patients with complete and partial reversion of the bundle branch block were 8% and 12%, respectively, whereas patients with persistent bundle branch block had a mortality rate of 18% (two-tailed chi-square test for trend 3.75, p = 0.053, OR 0.39 for complete reversion, OR 0.64 for partial reversion). When patients with missing predischarge ECGs (a nonrandom occurrence) were analyzed in the group of “nonreverters,” the 30-day mortality rate for this group was 20% (two-tailed chi-square test for trend 5.61, p = 0.02, OR 0.34 for complete reversion, OR 0.55 for partial reversion).

**Angiographic evaluation.** Two-hundred and fifty-six patients with bundle branch block underwent angiographic evaluation after receiving thrombolytic therapy, as part of an angiographic substudy (n = 16) (24) or by recommendation of the attending physician (n = 240). The culprit lesion in patients with right bundle branch block (isolated or with left fascicular block) was observed more often in the left anterior descending coronary artery, whereas the culprit lesion in patients with left bundle branch block was located more often in the right coronary artery (Table 5). Patients with left bundle branch block were slightly more likely to have circumflex occlusion than patients with right bundle branch block (p = 0.051). Information on coronary lesions was not available for 12 patients, three of whom died before undergoing catheterization. Percutaneous transluminal coronary angioplasty was performed in 92 patients with bundle branch block, 19 of whom showed partial or total reversion of their conduction defect after the procedure.

**Discussion**

The main finding of our study is that both 30-day and 1-year survival rates in patients with acute MI and bundle branch block treated with thrombolysis are poorer than those for similar patients with no conduction defects. Previous reports have suggested that this unfavorable prognosis is determined by older age (25,26) or heart failure (9,12,27), or both (6). We found that even when patients were matched with control subjects for age and Killip class, bundle branch block remained an independent predictor of mortality. Although the association had only borderline statistical significance, these patients were 53% more likely to die within 30 days of hospital admission than their matched control subjects. Asystole or AV block, ventricular arrhythmias and cardiogenic shock were also more frequent among patients with bundle branch block.

A recent analysis of the GUSTO-I and TAMI-9 data bases showed a 30-day mortality rate of only 8.7% for patients with bundle branch block (16). This may reflect differences in the groups studied. The previous analysis included only patients who participated in an ischemia monitoring substudy who did not have bundle branch block at hospital admission. Most of those patients (77.6%) had transient blocks, perhaps reflecting ongoing reperfusion, whereas an equivalent proportion of patients in our study (76.2%) had persistent blocks. The subgroup with persistent blocks in the previous study had a mortality rate similar to that found in our study (19.4% vs. 18%). Finally, the association of conduction defects with heart rate was not explored in the previous study, and patients with rate-dependent bundle branch blocks—and higher survival rates—may have been included in the analysis.

The relation between bundle branch block and mortality is complex. Autopsy studies on patients dying shortly after infarction have shown little or no necrosis, edema or inflammation of the conduction system (28,29). This absence of evident injury to the bundle branches, and the fact that the Purkinje fibers are more resistant to ischemia compared with myocytes, points rather to a dynamic phenomenon responsible for the mortality. Experimental observations in the isolated ventricle may provide a biologic rationale for this hypothesis by underscoring the role of the “near-necrotic zone.” When a band of necrotic myocardium is placed on the surface of a normal ventricle from a second animal, myocytes and conducting fibers show functional depression, and excitation and conduction are soon abolished (30). If the near-necrotic zone involves the conduction system, complete AV block or bundle branch block can occur. These functional changes in the conduction system remain after removing the necrotic tissue, and the degree of recovery is a function of the duration of the experiment (30). In addition, the bundle branches receive both sympathetic and vagal innervation (31), which may be interrupted during myocardial ischemia (32). A reentry circuitry provided by the blocked bundle branch, local ionic changes induced by ischemia and functional autonomic denervation all may contribute to ventricular arrhythmias. Death from both “primary” and “late” ventricular fibrillation is well documented in patients with bundle branch block (10,33–36); we found that their risk for ventricular arrhythmias was as high as their risk for cardiogenic shock.

Conduction defects often resolve during the hospital period. The overall reversion rate for bundle branch block of 24% in our study was associated with a 50% relative reduction in 30-day mortality (from 20% to an average of 10%). Thus, patients who recovered normal intraventricular conduction...
had a prognosis similar to that of patients who never developed bundle branch block. This finding also has been reported among subjects not receiving thrombolyis (10,12,27). The graded effect on survival in our study (greater for patients undergoing complete reversion than for those undergoing partial reversion) suggests a myocardial mechanism of death linked to the bundle branch block. Whether the reversion of the conduction defect results from spontaneous or from therapeutically induced reperfusion, it is possible that the final common pathway in reducing mortality involves the salvage of myocardium or changes in the electrophysiologic milieu that tend to prevent ventricular arrhythmias, or both.

**Bundle branch block location.** Most patients with conduction defects in our study had right bundle branch block, alone or in combination with a left fascicular block. This could be because the right bundle branch is a narrow structure, relatively vulnerable to focal ischemia. The blood supply to the proximal segment of the right bundle is derived from the AV node artery, whereas that for the remaining two-thirds of the right bundle and for the left anterior fascicle is provided by the septal branches of the left anterior descending coronary artery (37,38). This and the fact that anterior infarcts portend an intrinsically worse prognosis (39) could explain both the association of right bundle branch block with anterior infarcts and the higher mortality (40,41). Autopsy analysis in these patients has revealed that the infarct area always includes the ventricular septum (33,38).

The less frequent compromise of the left bundle during acute MI has been observed by other investigators (2,16), and it may reflect the diffuse structure of the left bundle. The main left bundle branch and its posterior division receive a dual blood supply from both a septal branch of the left anterior descending coronary artery and the AV node artery (38). Thus, only extensive damage that includes most of the ventricular septum and the anterior wall may interrupt the conduction at the left bundle (42). The greater survival of patients who develop left bundle branch block has not been a consistent finding across studies (2,6,10,33). It might reflect either a predominantly patch-like necrotic process, the fact that most infarcts were nonanterior, or a prehospital survival bias of patients with newly acquired left bundle branch block, which would drive the selective admission of patients with “old,” more benign left bundle branch blocks.

**Study limitations.** The relatively low incidence of bundle branch block (1.6%) among GUSTO-I patients may originate from differences in design from previous studies, which included either patients with late-onset bundle branch block (i.e., developed during the hospital period) (1,16,26), patients with alternating left and right bundle branch blocks (16) or patients with isolated fascicular blocks (1). It may also reflect a selection bias in GUSTO-I, with preferential enrollment of patients in whom the diagnosis of acute MI was obvious despite the presence of the conduction defect; this might explain the prevalent association of left bundle branch block with nonanterior infarcts. Thus, the results of this study may apply best to those patients with acute MI and bundle branch block who are enrolled in clinical trials.

Notwithstanding the relatively small sample size, bundle branch block emerged as an important prognostic factor, and thus our findings may apply better to patients with bundle branch block who have a higher ECG risk.

Patients with bundle branch block probably had larger infarcts than their control subjects. A highly reliable indicator of infarct size was not available in our study. Peak creatine kinase, MB fraction varies with reperfusion status, and its blood level values were not reported in many patients. Peak total creatine kinase, which was higher among patients with bundle branch block, is a nonspecific marker for infarct size (43,44). Killip class may not provide accurate information on heart failure accompanying large infarcts; aside from left ventricular function, other variables may be captured by Killip class. However, Killip class remained a powerful prognostic factor for mortality in the entire GUSTO-I population (18). This suggests that patients with and without bundle branch block would be similarly affected in analyses that include Killip class.

**Clinical implications and conclusions.** The advent of reperfusion therapies has not diminished the strong association between bundle branch block and early mortality in patients with acute MI. Their poor prognosis does not seem to be related exclusively to the development of AV block, a larger infarct size or more severe heart failure. The mechanism ultimately leading to death is complex and appears to involve the conduction defect, because in our study survival was poorer after partial reversion of the bundle branch block than after complete reversion. In addition, the contribution of septal asynergy, late bradyarrhythmias and electrical instability may be more important than previously appreciated.

Recommendations for patients who present with bundle branch block during acute MI have focused on the relief of heart failure and on the appropriateness of prophylactic pacing (2,11,33,45). The use of ventricular pacing has not gained widespread acceptance because it does not seem to improve in-hospital survival and it may be associated with serious complications (2,45); prophylactic placement of external pacing pads seems a more attractive alternative (46). In contrast, therapeutic procedures that optimally restore myocardial perfusion might prevent or reverse the development of near-necrotic lesions in the conduction system altogether by decreasing its time of exposure to ischemia (12,15).

The confirmation of a role for ventricular arrhythmias in the death of patients with bundle branch block could lead to prevention of early mortality by intensifying cardiac monitoring in the coronary unit and by instituting specific measures in those patients at higher risk. Effective antiarrhythmic therapies could include the prophylactic placement of external patches for use with portable automatic external defibrillators and the use of implantable cardioverter-defibrillators.
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References


