VIEWPOINT

Evolving Considerations in the Management of Patients With Left Bundle Branch Block and Suspected Myocardial Infarction

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Patients with a suspected acute coronary syndrome and left bundle branch block (LBBB) present a unique diagnostic and therapeutic challenge to the clinician. Although current guidelines recommend that patients with new or presumed new LBBB undergo early reperfusion therapy, data suggest that only a minority of patients with LBBB are ultimately diagnosed with acute myocardial infarction, regardless of LBBB chronicity, and that a significant proportion of patients will not have an occluded culprit artery at cardiac catheterization. The current treatment approach exposes a significant proportion of patients to the risks of fibrinolytic therapy without the likelihood of significant benefit and leads to increased rates of false-positive cardiac catheterization laboratory activation, unnecessary risks, and costs. Therefore, alternative strategies to those for patients with ST-segment elevation myocardial infarction are needed to guide selection of appropriate patients with a suspected acute coronary syndrome and LBBB for urgent reperfusion therapy. In this article, we describe the evolving epidemiology of LBBB in acute coronary syndromes and discuss controversies related to current clinical practice. We propose a more judicious diagnostic approach among clinically stable patients with LBBB who do not have electrocardiographic findings highly specific for ST-segment elevation myocardial infarction. (J Am Coll Cardiol 2012; 60:96–105) © 2012 by the American College of Cardiology Foundation

Patients with a suspected acute coronary syndrome (ACS) in the setting of left bundle branch block (LBBB) present an important diagnostic and therapeutic challenge to the clinician. Not only is the electrocardiographic (ECG) diagnosis of acute myocardial infarction (AMI) difficult because of so-called masking of characteristic ECG changes by altered ventricular depolarization, but also these patients may be at higher risk for AMI, congestive heart failure, and death compared with patients without bundle branch block (BBB) (1–3). Although current guidelines from the American College of Cardiology/American Heart Association (4) and the European Society of Cardiology (5) recommend that patients with new or presumed new LBBB undergo early reperfusion therapy with fibrinolysis or percutaneous coronary intervention (PCI), these recommendations are based on studies performed more than 20 years ago, and the

populations studied may differ notably from contemporary patient subsets.

In this paper, we review the pathophysiologic mechanisms underlying LBBB in AMI and the historical context, epidemiology, and outcomes of the current recommended treatment approach; discuss controversies in clinical practice; and suggest future strategies for improvement in the efficiency and outcomes of care for patients with LBBB.

Pathophysiology of LBBB in AMI

The intraventricular conduction system of the left ventricle is composed of fibers of the bundle of His that become the main left bundle branch and then divide into anterior and posterior fascicles, further branching to become the distal conduction system. In contrast to the right bundle branch, which is a discrete structure that can be injured acutely with a small focal insult, the left bundle branch is a large and diffuse structure that typically requires a large insult to lead to acute injury (6). When a new LBBB is caused by AMI, the site of infarction usually is anterior or anteroseptal (7), with the infarction involving a large myocardial territory. Inferior or posterior infarctions uncommonly may result in a new LBBB from involvement of the more proximal portion of the conduction system supplied by the atrioventricular nodal artery. However, most cases of LBBB in AMI are not a result of focal infarctions, because either a discrete

lesion just distal to the bundle of His or extensive myocardial damage involving a large portion of the distal conduction system including both fascicles would be required to cause LBBB (Fig. 1).

Although LBBB can occur de novo in AMI, it is more often a pre-existing marker of underlying structural heart disease, and thus reflective of the patient's baseline cardiovascular risk. In these cases, LBBB may be the result of an aging or fibrotic conduction system, or both; chronic ischemic heart disease; left ventricular hypertrophy (most commonly from long-standing hypertension); adverse ventricular remodeling resulting from congestive heart failure; or valvular heart disease. It is not possible to determine the chronicity of LBBB without reviewing previous ECG tracings, because the onset of LBBB usually is asymptomatic. LBBB in AMI may be transient or permanent, although early accounts note that most cases of permanent LBBB were not the result of an acute transmural infarction, because true AMI-associated LBBB was associated with very high mortality (8).

Historical Perspective

Recognition of LBBB in AMI dates back to 1917 in an account by Oppenheimer and Rothschild (9). Early descriptions of BBB in AMI reported an incidence of 10% to 15% and a mortality rate of 42% to 63% (10). Patients with BBB tended to be significantly older and to have an increased frequency of hypertension, congestive heart failure, previous myocardial infarction, and cardiogenic shock. It is, therefore, difficult to discern if historical studies documenting the significantly increased mortality risk (approximately 2-fold) in BBB were confounded by age and comorbid conditions. Additionally, studies included patients with both LBBB and right BBB, recorded ECG data at widely varied time points, lacked discrimination between new and old infarction, and had limited diagnostic resources to confirm AMI at presentation (11).

For more than 60 years, clinicians have recognized that a diagnosis of AMI in the setting of LBBB is especially challenging (12). Because left ventricular activation occurs much later in LBBB and the initial septal activation advances from right to left (opposite of the normal situation), septal Q waves indicative of an AMI are absent. Additionally, secondary ST-T wave abnormalities that occur in LBBB obscure the recognition of injury currents in ischemia and infarction. Despite the suggestion of multiple criteria for diagnosis of AMI in the setting of LBBB, it generally was believed that clinicians remained largely blind to ECG changes in patients with LBBB (12). In 1996, Sgarbossa et al. (13) published an analysis from the GUSTO-1 (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries-1) trial evaluating multiple different ECG criteria that had been suggested as being potentially useful for the diagnosis of AMI in the setting of LBBB. Of these, ST-segment

elevation concordant with the major QRS deflection in any lead and ST-segment depression in leads V_1, V_2, or V_3 had odds ratios for AMI of 25.2 (95% confidence interval [CI]: 11.6 to 54.7) and 6.0 (95% CI: 1.9 to 19.3), respectively; discordant ST-segment elevation of 5 mm or more in any lead had a weaker association (odds ratio: 4.3, 95% CI: 1.8 to 10.6). When combined, these 3 ECG criteria yielded a sensitivity and specificity of approximately 78% and 90%, respectively. Subsequent validation studies have confirmed that ST-segment concordance criteria are highly specific for AMI, but generally have reported much lower sensitivities than the initial study (14,15). Currently, the Sgarbossa criteria are used most extensively to diagnose AMI in the setting of a known chronic LBBB. Although data exist to support use of the Sgarbossa criteria in new or indeterminate-age LBBB, current guidelines

Abbreviations and Acronyms

ACS = acute coronary syndrome(s)

AMI = acute myocardial infarction

BBB = bundle branch block

CI = confidence interval

ECG = electrocardiography

LBBB = left bundle branch block

NSTEMI = non–ST-segment elevation myocardial infarction

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction
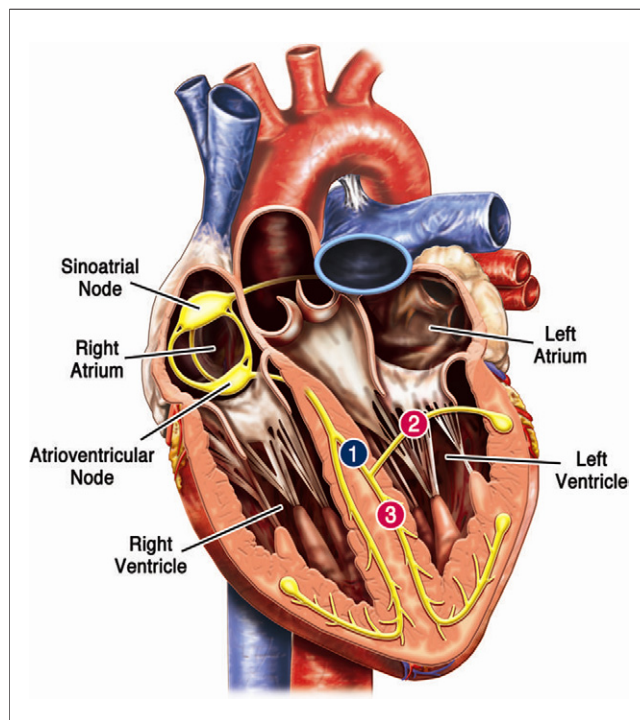
Figure 1   Anatomy of the Left Bundle Branch

The left bundle branch comprises the main left bundle and distal anterior and posterior fascicles. Left bundle branch block (LBBB) resulting from an incident myocardial infarction requires a lesion just distal to the bundle of His **(1)** or extensive myocardial damage involving a large portion of the distal conduction system, including both fascicles **(2 and 3)**.

do not specifically include this application of the criteria in their recommendations.

Epidemiology and Clinical Trial Results

Individuals with LBBB represent approximately 2% of all patients who seek treatment with suspected ACS (Table 1). They are more likely to be older, to be female, and to have a history of pre-existing cardiovascular disease, hypertension, and congestive heart failure than non-BBB patients with ACS (1,16). Patients with LBBB also have a greater likelihood of major adverse cardiac events, including death, AMI, stroke, and revascularization over long-term follow-up compared with patients without BBB (1). However, these observations may be explained, in large part, by underlying ischemic and structural heart disease that is the substrate for the development of LBBB, rather than by the LBBB itself. Because LBBB is strongly related to advancing age, which, in turn, is associated with many chronic disease states and the development of cardiac conduction disease, LBBB may be an integrative marker of overall cardiac risk, rather than an independent contributor to morbidity and mortality (16).

The excess mortality risk associated with LBBB in AMI compared with normal conduction is unclear. Early observations of high mortality rates may have been confounded by comorbid conditions or delays in diagnosis and treatment because ECG criteria to diagnose AMI in LBBB were not available. More contemporary studies from the reperfusion era reported that patients with BBB were less likely to receive immediate reperfusion therapy (including fibrinolysis or PCI), had longer delays between hospital arrival and initiation of reperfusion therapies, were less likely to receive evidence-based medical therapy, and had a 34% to 64% increased risk of in-hospital death, even after adjustment for potential confounders (2). However, right BBB was observed to have a greater risk for mortality than LBBB, and other investigators have not been able to confirm an independent mortality risk of LBBB (16–18).

Initial clinical trials investigating the efficacy of fibrinolytic therapy included a broad range of patients, including those with ST-segment elevation, ST-segment depression, and BBB. For example, the ISIS-2 (Second International Study of Infarct Survival) trial (19) randomized 17,187 subjects within 24 h after the onset of suspected AMI to streptokinase alone, aspirin alone, streptokinase plus aspirin, or placebo in addition to usual care. BBB (left or right) was present in 1,032 (6%) of subjects at randomization; those with BBB had numerically lower rates of death with each intervention versus placebo (83 vs. 102, 74 vs. 111, and 29 vs. 57 in the streptokinase, aspirin, and streptokinase plus

Table 1	Prevalence of LBBB and AMI in Studies of Patients With Suspected ACS				
First Author (Ref. #)		**Year**	**Total No. of Patients**	**No. of Patients With LBBB (%)**	**No. of LBBB Patients With AMI (%)**
Randomized trials or registries enrolling patients with high suspicion or documentation of AMI, STEMI, or new LBBB					
Sgarbossa et al. (13)		1996	26,003	145 (0.6)	131 (90)
Cannon et al. (3)		1997	1,416	127 (9)	40 (31)
Wong et al. (22)		2005	17,073	300 (1.8)	242 (81)
Al-Faleh et al. (23)		2006	22,839	267 (1.2)	158 (63)
Lopes et al. (36)		2011	5,742	98 (1.7)	85 (87)
Jain et al. (42)		2011	892	36 (4)	12 (33)
Subtotal (n = 6)			73,965	973 (1.3)	668 (67)
More broadly representative studies of patients with suspected AMI presenting to ED					
Rude et al. (52)		1983	3,697	178 (4.8)	82 (46)
Fesmire et al. (53)		1989	440	24 (5.5)	3 (13)
Otto and Aufderheide (54)		1994	428	18 (4.2)	5 (28)
Kudenchuk et al. (55)		1998	3,027	57 (1.9)	20 (35)
Edhouse et al. (56)		1999	797	50 (6)	26 (52)
Shlipak et al. (39)		1999	n/a	83 (100)	26 (31)
Li et al. (15)		2000	n/a	190 (100)	25 (13)
Kontos et al. (14)		2001	7,725	182 (2.4)	24 (13)
Gunnarsson et al. (43)		2001	n/a	158 (100)	76 (48)
Maynard et al. (57)		2003	n/a	56 (100)	18 (32)
Chang et al. (31)		2009	7,937	191 (2.4)	11 (6)
Bansilal et al. (1)		2011	2,271	102 (4.5)	5 (5)
Kontos et al. (34)		2011	n/a	401 (100)	116 (29)
Subtotal (n = 13)			26,322	802 (3.0)*	437 (26)†
Total (n = 19)			100,287	1,775 (1.8)*	1,105 (42)‡

*Does not include studies of patients with LBBB only. †Includes patients in all studies (n = 1,690). ‡Includes patients in all studies (n = 2,663).

ACS = acute coronary syndrome; AMI = acute myocardial infarction; ED = emergency department; LBBB = left bundle branch block; n/a = not applicable; STEMI = ST-segment elevation myocardial infarction.

aspirin groups, respectively). The GISSI (Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico) trial (20) randomized 11,802 subjects with suspected AMI to streptokinase or usual care, with BBB observed in 661 (5.6%) subjects. The 21-day mortality was no different between subjects with BBB receiving streptokinase (8%) versus those receiving placebo (8.6%), with a relative risk of 0.92 (95% CI: 0.53 to 1.60).

An analysis of pooled data from 9 fibrinolytic trials including more than 58,000 patients with suspected AMI, including both patients with ST-segment elevation myocardial infarction (STEMI) and those with BBB, provided more statistical power for evaluation of subgroups with BBB (Table 2). Subjects with BBB (n = 2,146) treated with early fibrinolysis had lower mortality (18.7% vs. 23.6%) than those treated with placebo, although the overall benefit was partially offset by an increase in stroke (2.1% vs. 1.1%) and major bleeding (1.3% vs. 0.3%) (21). These data form the basis for the current recommendations to treat new or presumed new LBBB as a STEMI equivalent requiring urgent reperfusion therapy. However, an important limitation not frequently recognized is that the primary analysis on which these recommendations are based did not differentiate between the type or chronicity of BBB and subjects with BBB represented only 3.6% of the total cohort.

Data from more recent fibrinolytic trials, with specific inclusion criteria for patients with presumed new LBBB, provide more direct comparisons of outcomes between STEMI and LBBB. For example, the HERO-2 (Hirulog and Early Reperfusion or Occlusion) trial demonstrated that patients with new or presumed new LBBB had a lower incidence of enzymatically confirmed AMI (80.7% vs. 88.7%, p = 0.006) and lower 30-day mortality (16% vs. 22.7%, p = 0.027) than matched STEMI controls. Differences were observed, however, between LBBB patients with and without Sgarbossa ST-segment concordance criteria: those without concordance had a lower adjusted risk of 30-day mortality compared with those with STEMI (odds ratio: 0.52, 95% CI: 0.33 to 0.80), whereas those meeting concordance criteria had a similar risk (odds ratio: 1.37, 95% CI: 0.78 to 2.47) (22). Similarly, in the ASSENT (Assessment of the Safety and Efficacy of a New Thrombolytic) -2 and -3 trials, 37.5% of LBBB versus 15.6% of STEMI patients (p < 0.001) did not have AMI enzymatically confirmed, and mortality was found to differ between patients with and without Sgarbossa concordance. In this

analysis, the adjusted relative risk of mortality at 1 year among patients with LBBB and Sgarbossa concordance (score ≥3) compared with STEMI was 3.8 (95% CI: 2.17 to 6.78); however, those with LBBB but without ST-segment concordance had a similar risk of 1-year mortality compared with STEMI patients (relative risk: 0.91, 95% CI: 0.47 to 1.77) (23). It should be noted that enrollment in these trials required a high clinical suspicion for AMI, and nevertheless, a substantially higher proportion of LBBB patients did not have AMI confirmed, especially among those without concordant ECG changes. Taken together, these data suggest that (1) patients with LBBB have heterogeneous outcomes with fibrinolytic therapy in part because of the significant variability in AMI incidence among this group and (2) Sgarbossa concordance on ECG may identify a high-risk population with similar (or worse) outcomes compared with STEMI.

More contemporary trials comparing the use of primary PCI with fibrinolysis have not provided much additional information regarding the benefit of urgent reperfusion strategies in patients with LBBB. Although the clinical superiority of primary PCI over fibrinolysis has been established, there are limited randomized trial data comparing the 2 therapies in patients with LBBB. Only 7 of the 23 trials reported in the meta-analysis by Keeley et al. (24) included patients with LBBB; efficacy or safety outcomes in patient subgroups with LBBB have not been reported from these trials, and the largest trial to date specifically excluded such patients (25). Thus, randomized clinical trial data establishing a clear benefit of urgent reperfusion therapy in patients with LBBB in the modern era are lacking.

Clinical Controversies

The initial rationale for using ST-segment elevation on ECG as a decision point for early reperfusion therapy in patients with suspected ACS was the high specificity for identifying patients who had complete occlusion of a coronary artery and who were most likely to benefit from treatment with a fibrinolytic agent. In this regard, a new (or presumably new) LBBB was thought to be equivalent to ST-segment elevation. However, recent data have called into question the principle that suspected ACS with a new or presumed new LBBB should be treated as a STEMI equivalent. In the fibrinolytic era, a diagnosis of AMI typically was not confirmed angiographically, but rather biochemically

Table 2	Clinical Outcomes in Patients With BBB in Randomized Controlled Trials of Intravenous Fibrinolytic Therapy Versus Standard Care in AMI*					
	Death		Stroke		Bleeding	
Patient Population	Fibrinolytic	Control	Fibrinolytic	Control	Fibrinolytic	Control
All patients (n = 58,600)	2,820 (9.6)	3,357 (11.5)	340 (1.2)	224 (0.8)	325 (1.1)	111 (0.4)
Patients with BBB (n = 2,146)†	188 (18.7)	242 (23.6)	21 (2.1)	11 (1.1)	13 (1.3)	3 (0.3)

Values are n (%). *Data from the FTT Collaborative Group (21). †Includes patients with both LBBB and RBBB.
BBB = bundle branch block; RBBB = right bundle branch block. Other abbreviations as in Table 1.

with creatine kinase, creatine kinase-myocardial band, or both. As primary PCI became more feasible, a larger number of studies were able to confirm AMI angiographically. Overall, these studies have demonstrated that less than half of all patients with suspected ACS and LBBB ultimately will be diagnosed with an AMI (Table 1). Moreover, a significant proportion of those patients with AMI will not have an occluded culprit artery at catheterization, and thus are classified more appropriately as having a non–ST-segment elevation myocardial infarction (NSTEMI), unstable angina, or non-ACS presentation (Table 3). This has important implications for the treatment of patients with presumed new LBBB who do not have immediate access to coronary angiography. If many of the patients with LBBB do not have AMI, they are unlikely to benefit from early reperfusion therapy. In addition, fibrinolytics have been shown to offer no benefit, and in fact may be harmful, to patients with NSTEMI (26).

The significant variability in the prevalence of AMI complicated by LBBB reported in prior studies may be partially explained by diagnostic criteria with poor specificity for AMI. Because circulating biochemical markers of myocardial necrosis can be associated with structural heart disease, heart failure, kidney disease, and other comorbid conditions (27,28), patients with LBBB may have been misclassified previously as having AMI based solely on biochemical testing. Moreover, because elevated cardiac biomarkers are associated with greater risk in many non-ACS conditions compared with ACS (29), it is likely that some of the excess risk associated with LBBB reflects comorbid conditions not related to incident LBBB.

In addition to the more accurate classification of AMI in the primary PCI era, it is also possible that the distribution of new versus old LBBB has changed. For example, in 2 reports from the 1970s, the proportion of AMI patients with new (compared with old) LBBB ranged from 53% to 61% (7,30). In contrast, a recent study by Chang et al. (31) reported that new LBBB was observed in only 29% of LBBB patients. Because patients hospitalized with myocardial infarction increasingly are older; are more likely to be

female; are more likely to have coexisting conditions such as hypertension, dyslipidemia, and diabetes mellitus; and are more likely to have undergone previous coronary revascularization (32), the prevalence of chronic LBBB likely is increasing, despite a general decline in overall incident STEMI. This phenomenon suggests that chronic LBBB may have become more common, whereas incident LBBB in AMI has decreased, because of longer life expectancy and better survival for patients with heart failure and other coexisting conditions (33). Furthermore, other studies have demonstrated no difference in the prevalence of AMI between patients with chronic LBBB and new or presumed new LBBB (31,34), suggesting that true myocardial infarction-associated LBBB is indeed rare.

As pressures to reduce reperfusion times have increased, and acute cardiac care—both in the emergency department and in the ambulance—is increasingly driven by protocol, LBBB of unknown duration has emerged as a frequent reason for false activation of the cardiac catheterization laboratory for primary PCI. In this setting, a false activation is defined as an activation in which the coronary angiogram does not identify a culprit artery consistent with STEMI. Because only a minority of patients with LBBB ultimately are diagnosed with AMI, false-positive cardiac catheterization laboratory activation is frequent. In a single-center study of 1,335 patients, Larson et al. (35) reported that the prevalence, of false-positive catheterization laboratory activation was 14% overall, but among patients with LBBB at presentation, the rate of false activation was 44%. These findings have been confirmed in a recent PCI study demonstrating that 39% of the 98 patients with new LBBB, most of whom even had concordant ST-segment changes on ECG, did not have an occluded culprit coronary artery on angiography (36). In our experience, it is not uncommon for catheterization laboratory activation to occur in patients with atypical chest pain or evidence of new onset heart failure in whom LBBB is present but cannot be confirmed to be old.

Urgent catheterization for all-comers can lead to an increased risk of complications related to the invasive procedure, resulting in prolonged hospital length of stay and higher costs and decreased quality of life for providers (37). In centers where primary PCI is not readily available, these issues obviously are more concerning given the risks of bleeding, particularly intracranial hemorrhage, with fibrinolytic therapy; the risks of fibrinolytic therapy may be magnified in patients with LBBB who generally are older and have higher rates of hypertension. Alternatively, given that patients with LBBB are less likely to receive reperfusion therapy (because of comorbid conditions or lack of diagnostic accuracy of the ECG procedure), there is appropriate concern that delays in diagnosis and therapy may lead to missed opportunities to reduce morbidity and mortality in patients with LBBB and true AMI (38). For example, a decision analysis found that routine administration of fibrinolytic therapy to all patients with LBBB and possible

Table 3	Prevalence of STEMI-Equivalent AMI in Angiographic Studies of Patients With Suspected ACS and LBBB		
		No. of Patients With Occluded Culprit Artery/Total With LBBB (%)	
First Author (Ref. #)	Year	New or Presumed New LBBB	Old LBBB
Larson et al. (35)	2007	20/36 (56)	n/a
Chang et al. (31)	2009	4/55 (7)	7/136 (5)
Lopes et al. (36)	2011	60/98 (61)	n/a
Jain et al. (42)	2011	5/36 (14)	n/a
Total (n = 4)		89/225 (40)	7/136 (5)

Values are n/N (%).
Abbreviations as in Table 1.

	Assigned Point Value	Sensitivity (%)	Specificity (%)	Positive Likelihood Ratio	Negative Likelihood Ratio
ST-segment elevation ≥1 mm and concordant with QRS complex	5				
ST-segment depression ≥1 mm in lead V$_1$, V$_2$, or V$_3$	3	20 (18–23)	98 (97–99)	7.9 (4.5–13.8)	0.81 (0.78–0.85)
ST-segment elevation ≥5 mm and discordant with QRS complex	2	41 (37–45)	85 (82–88)	2.0 (1.1–3.8)	0.81 (0.67–0.99)

Table 4   **Sgarbossa Electrocardiogram Criteria for the Diagnosis of Evolving AMI in the Presence of LBBB***

*Data from Tabas et al. (41). Sensitivity, specificity, and positive and negative likelihood ratios are presented as summary statistics (95% confidence intervals) for scores of ≥ 3 and ≥ 2. †ST-segment deviation is measured at the J point. Concordance and discordance of ST segments are determined by comparison with the main direction of the QRS complex.

ECG = electrocardiography; other abbreviations as in Table 1.

AMI would result in a small but significant mortality reduction; however, this approach may lead to unnecessary administration of fibrinolytic therapy to most patients who do not have AMI (39). It should be noted that this analysis was performed more than 10 years ago, based on epidemiological data suggesting a higher proportion of STEMI-equivalent AMI in patients with LBBB than seems to be the case today. In the modern era, the risk-to-benefit ratio may be even less favorable. Therefore, as systems of care improve and delays in transfer for primary PCI decrease, applying a routine transfer strategy for patients with suspected AMI and LBBB may preserve the benefit of reperfusion therapy for the highest-risk patients while minimizing potential harm associated with administering fibrinolytic therapy to patients without occluded arteries.

Do the Sgarbossa Criteria Help?

The Sgarbossa criteria (13), as proposed in 1996, are listed in Table 4 and include ST-segment elevation of 1 mm or more concordant with the QRS complex in any lead; ST-segment depression of 1 mm or more in lead V$_1$, V$_2$, or V$_3$; and ST-segment elevation of 5 mm or more discordant with the QRS complex in any lead (Fig. 2). These criteria are weighted differently to reflect their varied estimated probability for AMI diagnosis. The original study by Sgarbossa et al. (13) reported that the ST-segment concordance criteria (score ≥3) were the most accurate for AMI diagnosis. The authors found that ST-segment discordance (score of 2) was of limited value because of poor specificity and suggested that patients with ST-segment discordance
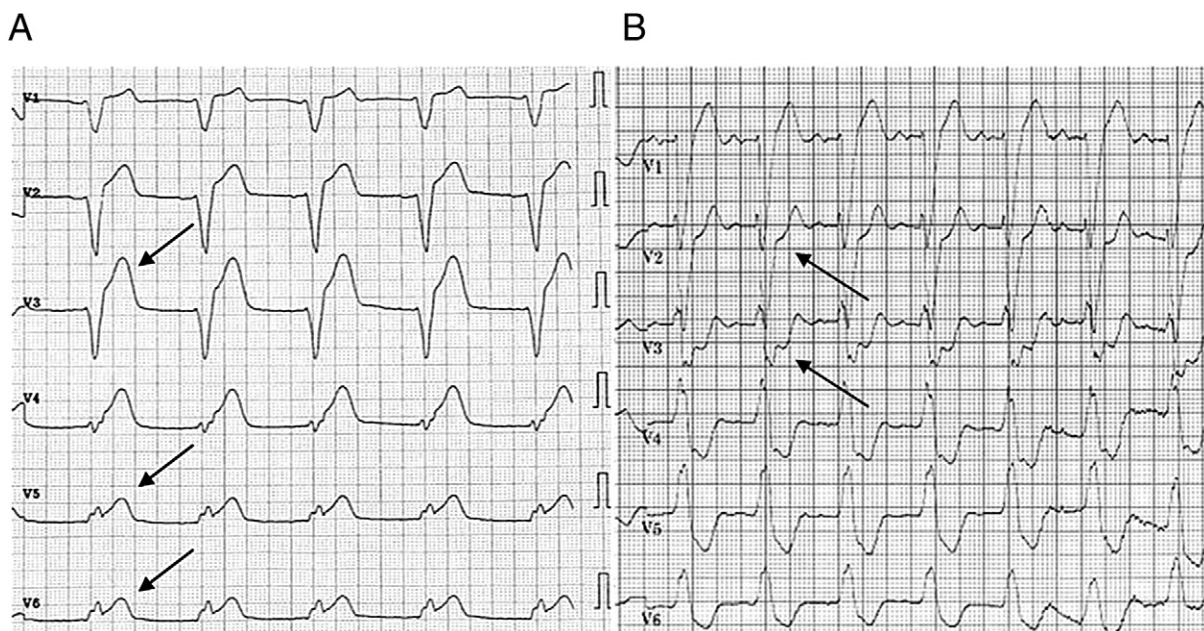
Figure 2   **Electrocardiograms Demonstrating the 3 Sgarbossa Criteria for the Diagnosis of Acute Myocardial Infarction in a Patient With LBBB**

(A) Electrocardiography (ECG) image showing ST-segment elevation of at least 1 mm that is concordant with the QRS complex (**arrows**, leads V$_5$ and V$_6$) and ST-segment elevation of at least 5 mm that is discordant with the QRS complex (**arrow**, lead V$_3$). **(B)** ECG image showing ST-segment depression of at least 1 mm in leads V$_2$ and V$_3$ (**arrows**). ECG images reprinted with permission courtesy of ECGpedia.org. Abbreviation as in Figure 1.

alone at presentation should undergo further diagnostic testing. Several prospective studies and a recent meta-analysis generally have concluded that the Sgarbossa criteria, with the exception of discordant ST-segment elevation, are highly specific for the diagnosis of AMI in the setting of LBBB, have good interobserver agreement ($\kappa = 0.81$), and have similar usefulness whether the LBBB is new or old (40). Recent validation studies have confirmed that a Sgarbossa score of 3 or more (requiring either concordant ST-segment elevation of 1 mm or more or ST-segment depression of 1 mm or more in lead V_1, V_2, or V_3) has specificity for AMI of more than 95% and is associated with higher 30-day mortality compared with LBBB patients with discordant ST-segment elevation alone (22,23,41). For example, Kontos et al. (34) studied 401 patients in the emergency department with suspected AMI and found that ST-segment concordant elevation or depression was an independent predictor of AMI (odds ratio: 17.0, 95% CI: 3.4 to 81, p < 0.001) and 30-day mortality (odds ratio: 4.3, 95% CI: 1.3 to 15, p = 0.02). Other studies have concluded that ST-segment elevation concordance is the single most specific criterion for the diagnosis of AMI and improves identification of individuals who will have positive cardiac biomarkers or who have an occluded culprit artery on angiography (i.e., STEMI equivalent) (36,42). However, although use of these ECG criteria improves diagnostic specificity and may decrease false positive AMI diagnoses, concern appropriately exists over a lack of sensitivity (15), because the sensitivity of a Sgarbossa score of 3 or more is only approximately 20% (41). Moreover, other studies suggest that there may be no improvement over clinical judgment alone (43), and some investigators have even advocated for additional ECG criteria to improve sensitivity. For example, Smith and Dodd (44) found "excessive discordance" on ECG, defined as a ratio of ST-segment elevation to S-wave amplitude of −0.20 or less to be 84% sensitive and 99% specific for left anterior descending coronary artery occlusion in 148 patients with LBBB and suspected AMI.

Future Strategies

Given the substantial gap between recent evidence and current recommendations, new diagnostic strategies are needed to guide the selection of appropriate patients with suspected AMI and LBBB for urgent reperfusion therapy. The clinical need is greater in centers without on-site primary PCI, because the implications of false catheterization laboratory activation are not as significant as unnecessary administration of fibrinolytic therapy. Potential strategies include differential algorithms for transfer to primary PCI centers for patients with LBBB compared with those who have ST-segment elevation and normal conduction; use of more specific ECG criteria; increased use of cardiac biomarkers, including sensitive assays for cardiac troponins;

and bedside echocardiography to improve diagnostic accuracy and timely intervention.

Transfer for primary PCI in patients with STEMI at presentation is equivalent or superior to fibrinolytic therapy as long as the overall first medical contact-to-balloon time is within 120 minutes (45,46). In general, if the anticipated time to reperfusion will exceed this threshold, on-site fibrinolytic therapy is recommended. However, because a substantial proportion of patients with LBBB do not have a STEMI-equivalent AMI, and patients with LBBB have an overall higher risk of bleeding (more likely female, older, and with pre-existing cardiovascular disease, hypertension, and congestive heart failure), transfer for primary PCI may be the preferred strategy, with judicious use of on-site fibrinolysis reserved for patients highly likely to have a STEMI-equivalent AMI when PCI is not available. This approach seems particularly attractive for most LBBB patients, because the risk-to-benefit calculation in such patients may favor primary PCI even when the delay associated with transfer for primary PCI exceeds 90 min (47). Additionally, as prehospital triage of chest pain patients by emergency medical services evolves, patients with LBBB may be recognized immediately and routed preferentially to a PCI-capable hospital, as long as delays are within acceptable time limits.

The use of cardiac biomarkers, specifically the cardiac troponins I and T, holds additional promise in the diagnosis of AMI with LBBB. In recent years, the analytic sensitivity for detection of cardiac troponins has improved 100-fold (48). Newer assays have improved precision as well, which enables 2 cardiac troponin values with a difference as small as a few picograms per milliliter to be reliably differentiated. This is important because although small cardiac troponin elevations can be measured in many chronic cardiac and noncardiac conditions, and thus lack specificity for AMI, a rise in absolute levels of troponin strongly supports the diagnosis of an evolving AMI (49). A rapid rise in troponin on serial measurement in a patient with LBBB, especially in the setting of ongoing chest discomfort, could represent a masked STEMI and may prompt additional diagnostic testing such as bedside echocardiography (see below), an invasive angiographic approach, or administration of fibrinolytic therapy if PCI is not available. In contrast, a more gradual rise and lower peak in troponin levels may signal an NSTEMI (in which case, transfer to a PCI-capable facility still would be recommended typically), whereas a static troponin level would suggest a non-ACS cause. Although few data are available, it is becoming increasingly more feasible to accelerate the timing of serial biomarker assessment, such that measurements are performed every 15 min, rather than every 60 to 90 min, in patients with LBBB and suspected AMI. Such an approach would minimize reperfusion delays in those ultimately determined to have STEMI equivalents. Assessment of rapid biomarker measurements, ideally performed at the point of care, should be the focus of additional study in patients with suspected AMI and LBBB.

Finally, bedside echocardiography may be used as an adjunctive measure in clinically complex situations to gain additional insight as to whether a new or presumed new LBBB is the result of a STEMI-equivalent ACS presentation. Point-of-care pocket-size echocardiographic devices can be used by emergency medicine physicians and cardiologists and have been shown to have high feasibility and reliability in the assessment of cardiac structure and function (50). The presence of significant cardiac chamber dilatation, wall thinning, or chronic valvular dysfunction in the absence of an acute anterior wall motion abnormality suggests that the LBBB is more likely secondary to chronic cardiac disease than AMI. Alternatively, evidence of a hypokinetic or akinetic segmental wall motion abnormality in the anterior wall, in the absence of evidence of a prior infarction (wall thinning, chamber dilatation), may represent a STEMI-equivalent AMI and should prompt emergent coronary angiography. In fact, the use of portable echocardiography to clarify the diagnosis of STEMI, especially if confounded by LBBB, has a class IIa indication in the most recent American College of Cardiology/American Heart Association guidelines (51). Thus, rapid beside echocardiography represents another potential strategy for improved clinical decision making in patients with suspected AMI and LBBB and may be used in conjunction with the other methods described above.

Investigators have recently proposed changes to the current American College of Cardiology/American Heart Association guidelines for the management of patients with suspected ACS and LBBB, based on the limited randomized trial data demonstrating efficacy of reperfusion therapy in this subgroup. These include demotion of the Class I, Level of Evidence: A recommendation that new or presumed new LBBB be treated as a STEMI equivalent and a proposal that most patients with LBBB be evaluated for ST-segment concordance on ECG and positive cardiac biomarkers to determine the need for urgent reperfusion therapy (37). We also propose an algorithm for the diagnosis and management of these patients (Fig. 3) that includes a rapid clinical and ECG assessment. Clinically or hemodynamically unstable patients with possible AMI and LBBB should be considered for immediate reperfusion therapy. Among stable patients, ECG assessment should be performed to determine the presence or absence of ST-segment concordance criteria in both new and chronic LBBB. Patients meeting ST-segment concordance criteria should be treated as having STEMI-equivalent disease and should receive urgent reperfusion therapy. If concordance criteria are absent, rapid serial cardiac biomarker testing, bedside echocardiography, or both should be considered. If biomarkers increase in the presence of ongoing symptoms or a large wall motion abnormality in the anterior wall is seen, emergent angiography should be performed, recognizing that many of these individuals will still have NSTEMI—rather than STEMI—equivalents, because our current clinical tools are insufficient to distinguish between the 2 entities when evidence of infarction is present. Given the
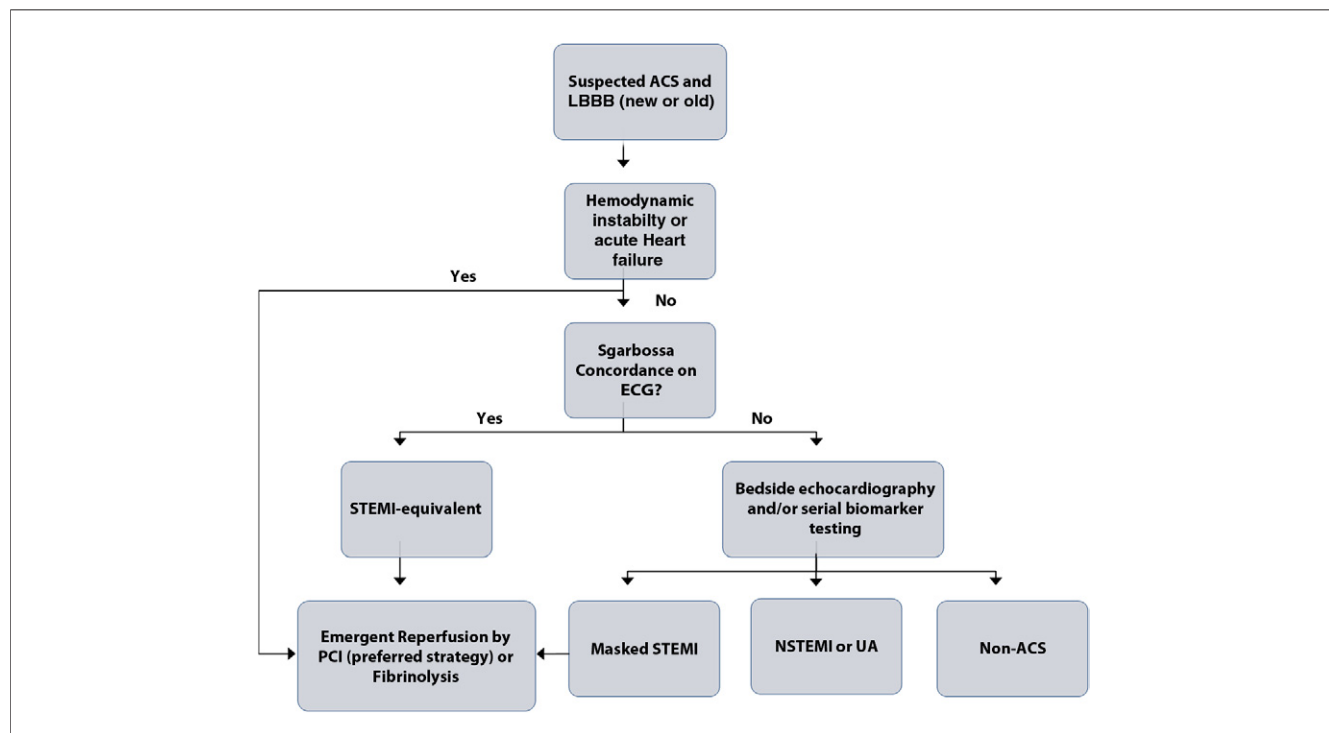
Figure 3   Proposed Diagnostic Algorithm for Suspected Myocardial Infarction and LBBB

ACS = acute coronary syndrome; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; UA = unstable angina; other abbreviations as in Figures 1 and 2.

low positive predictive value of LBBB, we recommend that patients with LBBB and possible ACS be transferred routinely to a PCI-capable hospital; fibrinolytic therapy should be considered only if the diagnosis is highly likely (i.e., meeting Sgarbossa criteria) or the patient is hemodynamically unstable and transfer to a PCI-capable facility would result in marked treatment delay. This algorithm would ensure that urgent reperfusion is delivered to the highest-risk patients with the greatest likelihood of acute thrombotic coronary occlusion while taking a more deliberate approach to diagnosis among individuals in whom the clinical picture is less clear. Ideally, such a strategy would result in only small treatment delays in patients with STEMI equivalents and would be balanced by less exposure to risk for the larger proportion of patients with non–ST-segment elevation ACS or non-ACS diagnoses.

Given the significant advancements in efficacy and safety of AMI treatments and the lack of contemporary evidence for the existing approach to LBBB, more research encompassing additional diagnostic and therapeutic strategies is needed. Because of the difficulty of diagnosing AMI resulting from acute coronary vessel occlusion, inclusion of LBBB in overall STEMI quality reporting (e.g., door-to-balloon times and other metrics) also should be reconsidered in light of the low specificity and positive predictive value of LBBB for STEMI-equivalent AMI. Removal of LBBB as an automatic STEMI equivalent would provide more specific and accurate evaluation of systems of care and quality of outcomes in STEMI. Therefore, as we evolve toward improved quality of care and better outcomes for patients, management of patients with LBBB and suspected AMI should evolve as well to reflect changing epidemiology, new observational and clinical trial data, advances in technology, and continued high-quality evidence-based research.

Conclusions

Patients with a suspected ACS in the setting of LBBB represent a much more heterogeneous population than STEMI without BBB and present unique diagnostic and therapeutic challenges to the clinician. Most patients will not have an AMI regardless of LBBB chronicity and likely would not benefit from urgent reperfusion therapy. Current guideline recommendations and performance measures do not account for the evolving epidemiology and complexity of LBBB among patients with possible ACS. We recommend a slightly more judicious approach to diagnosis among hemodynamically and clinically stable patients with LBBB who do not have ECG findings highly specific for STEMI. Moreover, we recommend a higher threshold for pharmacological reperfusion than primary PCI, given the lower probability of an occluded culprit artery and the bleeding risks of fibrinolytic therapy. The full impact of this approach, with regard to appropriateness and timeliness of therapy, as well as outcomes, requires prospective study.

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