

The left bundle-branch block puzzle in the 2013 ST-elevation myocardial infarction guideline: From falsely declaring emergency to denying reperfusion in a high-risk population. Are the Sgarbossa Criteria ready for prime time?

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Prompt and accurate identification of ST-elevation myocardial infarction (STEMI) in the presence of left bundle-branch block (LBBB) remains difficult. The 2004 STEMI guideline recommended emergent reperfusion therapy to patients with suspected ischemia and new or presumably new LBBB. These recommendations have led to frequent false catheterization laboratory activation and inappropriate fibrinolytic therapy because most patients with suspected ischemia and new or presumably new LBBB do not have acute coronary artery occlusion on angiography. The new 2013 STEMI guideline makes a drastic change by removing previous recommendations. Therefore, patients with suspected ischemia and new or presumably new LBBB would no longer be treated as STEMI equivalent. The new guideline fails to recognize that some patients with suspected ischemia and LBBB do have STEMI, and denying reperfusion therapy could be fatal. The Sgarbossa electrocardiography criteria are the most validated tool to aid in the diagnosis of STEMI in the presence of LBBB. A Sgarbossa score of ≥ 3 has a superb specificity (98%) and positive predictive value for acute myocardial infarction and angiography-confirmed acute coronary occlusion. Thus, we propose a diagnosis and triage algorithm incorporating the Sgarbossa criteria to quickly and accurately identify, among patients presenting with chest pain and new or presumably new LBBB, those with acute coronary artery occlusion. This is a high-risk population in which reperfusion therapy would be denied by the 2013 STEMI guideline. Our algorithm will also significantly reduce false catheterization laboratory activation and inappropriate fibrinolytic therapy, the inevitable consequence of the 2004 STEMI guideline. (Am Heart J 2013;166:409-13.)

In patients presenting with ischemic symptoms, prompt and accurate identification of acute coronary artery occlusion is critical for the timely use of reperfusion therapy.^{1,2} The triage of these patients relies on the standard 12-lead electrocardiogram (ECG), with ST-segment elevation criteria the primary indication for emergent reperfusion therapy.³ However, recognition of

ST-segment elevation myocardial infarction (STEMI) in the presence of left bundle-branch block (LBBB) remains difficult.⁴ Repolarization in LBBB is characterized by ST-segment deviation away from the direction of the terminal QRS waveforms.⁵ Therefore, the ECG manifestations of STEMI may be either obscured or mimicked by the baseline "secondary" ST-segment deviations of LBBB.

While acknowledging the formidable challenge and diagnostic uncertainty from LBBB, the 1996 and 2004 American College of Cardiology and American Heart Association (ACC/AHA) STEMI guidelines recommended emergent reperfusion therapy including fibrinolytics or primary percutaneous coronary intervention (PCI) to patients with symptoms compatible with STEMI and new or presumably new LBBB if these symptoms arose within the prior 12 hours (class I indication).^{6,7} The recently published 2012 European Society of Cardiology STEMI guideline also recommended early mechanical (PCI) or pharmacological reperfusion as early as possible for

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patients with clinical presentation of STEMI and new or presumed new LBBB (class IA recommendation).⁸ These guideline recommendations stemmed from the Fibrinolytic Therapy Trialists' review of 9 major randomized trials in the fibrinolytics era, which suggested that patients with a bundle-branch block on the initial ECG had higher baseline mortality and had the greatest incremental improvement in survival when given fibrinolytics.^{1,9}

Since its publication, this guideline recommendation has elicited continued debate. Firstly, data from randomized clinical trials establishing a clear benefit of urgent reperfusion therapy exclusively in patients with LBBB are lacking because relatively few patients seeking evaluation for suspected acute myocardial infarction (AMI) have LBBB, accounting for only 1% to 9% of patients in clinical trials and registries.^{4,5,10-15} Earlier clinical trials analyzed for this guideline recommendation did not even separate LBBB from other bundle-branch block.¹ In addition, the timely availability of a previous ECG for comparison is the exception rather than the rule. Physicians can promptly determine whether a LBBB is new or old only if a recent previous ECG is available or if the LBBB develops after a first ECG has been recorded during the index episode of chest pain. Therefore, the categorization of the LBBB is subjective and may explain the wide variation in the reported percentage of new (compared with old) LBBB in AMI patients, ranging from 29% to 61% from different studies.^{5,16} Furthermore, although the proven new appearance of LBBB in a patient with acute chest pain could be suggestive of AMI, it is more often a preexisting marker of underlying structural heart disease such as degenerative conduction disease, chronic ischemic heart disease, cardiomyopathy, or valvular heart disease.^{9,17,18} Patients with these cardiac conditions may present with symptoms that can be easily misinterpreted as "STEMI equivalent." Patients with newly developed LBBB from AMI would most probably be hemodynamically unstable because very proximal coronary occlusion is required to involve the septal perforating arteries that supply the proximal left bundle branch.¹⁹

The 1996 and 2004 STEMI guideline recommendations on LBBB with suspected AMI were based on early fibrinolytic trials where the diagnosis of AMI typically was not confirmed angiographically, but rather biochemically.^{20,21} Cardiac biomarkers can also be elevated by nonischemic cardiac disorders and by noncardiac conditions such as renal failure, pulmonary embolism, and sepsis.^{22,23} Relying on cardiac biomarkers in the presence of LBBB may overestimate the prevalence of AMI.

The diagnostic approach and management strategy for STEMI have evolved in the last decade with primary PCI currently the preferred reperfusion therapy.²⁴ This has produced abundant angiographic evidence, which would challenge the validity of these guideline recommendations. Larson et al¹⁴ recently reported angiographic findings in 36 patients who presented with a new or

presumably new LBBB from a regional STEMI registry. They found that 44% of these patients did not have culprit coronary occlusion on emergent angiography, suggesting false catheterization laboratory activation. The rate of false activation in patients with STEMI but without LBBB was only 14% in the same registry. Chang et al⁵ analyzed a cohort of patients who presented to emergency departments with suspected acute coronary syndromes. They found no difference in the rate of clinical AMI between patients with a new or presumably new LBBB, old LBBB, or without an LBBB (7.3% vs 5.2% vs 6.1%, $P = .75$). At 30 days of follow-up, among those with a new or presumably new LBBB, only 19.2% had documented coronary disease by angiography, and 7.8% underwent coronary revascularization. Most recently, Jain et al⁴ reported in a single-center STEMI registry only 14% (5/36) of those who presented with new or presumably new LBBB and suspected AMI had culprit coronary occlusion on emergent angiography. These angiographic studies suggest that new or presumably new LBBB provides limited diagnostic value in identifying patients with acute coronary occlusion and should not be considered a reliable indicator for STEMI. It is logical to postulate that a significant proportion of those patients with LBBB and suspected AMI in the early fibrinolytic trials did not have an occluded culprit artery and thus received inappropriate fibrinolysis. Adverse effects are potentially serious because patients with LBBB have a higher risk of bleeding including intracranial bleeding as they are more likely to be female, older, and have both hypertension and cardiovascular disease.¹⁸ With increased pressure to reduce door-to-balloon time, LBBB with suspected ischemic symptoms has emerged as a frequent reason for false activation of the cardiac catheterization laboratory for primary PCI.²⁵ Such false activation exposes patients to unnecessary procedure-related risks, prolongs hospital stay, increases health care expenses, and imposes a burden on limited resources.²⁵

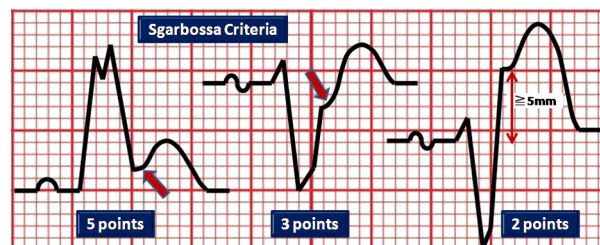
The newly published 2013 STEMI guideline recognizes both the diagnostic uncertainty of LBBB and some of the new angiographic evidence.²⁴ It acknowledges that most cases of LBBB at presentation are "not known to be old" when no ECG is available for comparison. It explicitly states that new or presumably new LBBB at presentation occurs infrequently, may interfere with ST-elevation analysis, and should not be considered diagnostic of AMI by itself. It concludes that urgent catheterization for such patients may increase the risk of complications from the invasive procedure, resulting in prolonged hospital stays, higher costs, and decreased quality of life. The new guideline has removed previous recommendations that new or presumably new LBBB should be treated as STEMI equivalent and considered for emergent reperfusion therapy. This drastic conceptual change from "all comers" to none will significantly reduce the incidences

of false catheterization laboratory activation and inappropriate fibrinolytic therapy. However, it fails to recognize that some patients with chronic LBBB do have STEMI, and delaying reperfusion therapy in this population could be fatal. Although these patients represent a relatively small proportion, it was estimated that they account for approximately 5,000 to 10,000 patients per year in the United States.⁴

There is a pressing need for readily available noninvasive diagnostic tools to accurately identify the patients presenting with LBBB and chest pain who do have an acute coronary occlusion. The Sgarbossa ECG criteria are the most validated tool. In 1996, Sgarbossa et al²⁶ published an analysis from the GUSTO-1 trial evaluating different ECG criteria to diagnose AMI in the presence of LBBB. They evaluated >26,000 patients and found that 0.6% had LBBB. The ECG from patients with LBBB and AMI confirmed by cardiac enzymes were compared with those of control patients who had chronic coronary artery disease and LBBB. Three independent ECG predictors of AMI were identified: (1) ST-segment elevation ≥ 1 mm concordant with the QRS complex in any lead (5 points); (2) ST-segment depression ≥ 1 mm in lead V₁, V₂, or V₃ (3 points); and (3) ST-segment elevation ≥ 5 mm discordant with the QRS complex in any lead (2 points) (Figure 1).²⁶ A total score ≥ 3 (concordance) was found to be highly specific (>95%) for the diagnosis of AMI; its sensitivity, however, was only 20%. The HERO-2 trial and the ASSENT 2 and 3 trial showed that patients meeting Sgarbossa concordance criteria had similar or higher mortality rates compared with STEMI patients, whereas, in patients without concordance, the mortality was lower than in patients with STEMI.^{27,28}

The clinical performance of the Sgarbossa criteria has been examined in contemporary practice. Tabas et al²⁹ published a meta-analysis including 11 studies with 2,100 patients that met at least 1 component of the Sgarbossa criteria in the fibrinolytic era. For 10 studies with 1,614 patients who had a Sgarbossa ECG score ≥ 3 , they reported a summary sensitivity of 20%, specificity of 98%, a positive likelihood ratio of 7.9, and a negative likelihood ratio of 0.8. For 7 studies with 1,213 patients who had a Sgarbossa ECG score of ≥ 2 , the sensitivities ranged from 20% to 79%, and the specificities ranged from 61% to 100%. The positive likelihood ratios ranged from 0.7 to 6.6, and negative likelihood ratios ranged from 0.2 to 1.1. They concluded that a Sgarbossa ECG score of ≥ 3 is useful for diagnosing AMI confirmed by cardiac biomarkers in patients with LBBB. However, a Sgarbossa ECG score of 2 only demonstrated modest value. The Sgarbossa criteria were further tested in patients undergoing primary PCI. Lopes et al¹⁰ analyzed the APEX-AMI trial and reported that, in patients with new LBBB and ≥ 1 mm concordant ST-segment elevation, 71.4% had occluded coronary artery on emergent angiography. However, in patients with new LBBB but without

Figure 1

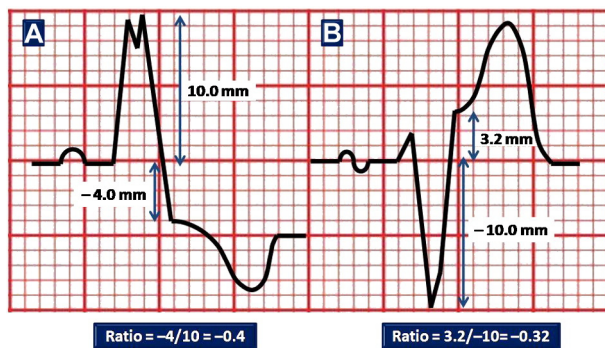


Sgarbossa electrocardiography criteria.

concordant ST-segment elevation, only 44.1% had an occluded coronary artery. Jain et al⁴ reported that, in 5 patients who had LBBB and acutely occluded culprit arteries, a Sgarbossa score ≥ 5 had low sensitivity (14%) but 100% specificity for identifying these patients, with a negative predictive value of 65% and a positive predictive value of 100%. These validating studies demonstrated that the value of Sgarbossa criteria lies in their high specificity and positive predictive value. Thus, systematically using the Sgarbossa criteria should significantly reduce false catheterization laboratory activation and inappropriate fibrinolytic therapy. Although the ACC/AHA STEMI guidelines discussed the Sgarbossa ECG algorithm, they did not include recommendations for its use in treatment decisions for patients with LBBB.^{7,24}

Diagnostic tests for potentially life-threatening conditions such as AMI need to be highly sensitive. The low sensitivity of the Sgarbossa criteria has limited their use in clinical practice. This could be remedied by using additional ECG criteria. Smith et al³⁰ compared ECGs from 33 patients presenting with an acutely occluded coronary artery and LBBB with 129 emergency department patients with suspected ischemia and LBBB but without coronary occlusion. They calculated the ST/S ratio, defined as the ratio of ST-segment elevation measured at the J point to the R or S wave, whichever was most prominent (Figure 2). They found that absolute discordant ST-segment elevation of ≥ 5 mm was present in 30% patients with confirmed coronary occlusion versus 9% of the control group, whereas excessive relative discordant ST-segment elevation with ST/S ratio -0.25 or less was present in 58% versus 8%. Substituting the absolute ST-elevation measurement of ≥ 5 mm in the third component of the Sgarbossa criteria with an ST/S ratio -0.25 or less greatly improved the diagnostic sensitivity from 52% to 91% in identifying angiographically proven STEMI. The specificity of the revised criteria (90%) remains similar to the Sgarbossa criteria (98%). Positive and negative likelihood ratios for the revised criteria were 9.0 and 0.1, respectively. If validated in an independent study, the new criteria would provide a more sensitive tool to guide the decision for reperfusion therapy.

Figure 2



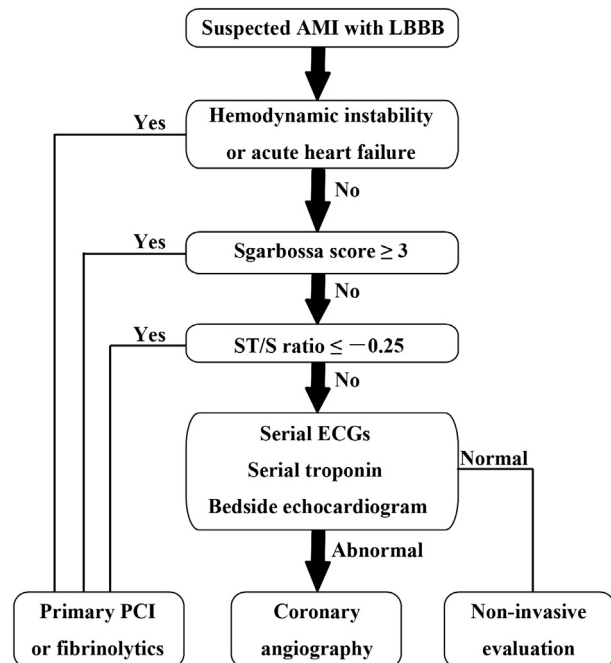
Calculation of ST/S ratio in the presence of excessive relative discordance of the ST segment in the opposite direction from QRS. ST segment is measured at the J point.

We have the challenge to quickly and accurately identify, among patients presenting with chest pain and new or presumably new LBBB, those with acute coronary artery occlusion. As stated above, the ACC/AHA STEMI guideline recommendations have radically changed from advising that all patients undergo reperfusion to advising that none does. It seems that recent evidence needs to be considered in the guideline recommendations. We propose a diagnosis and triage algorithm (Figure 3). If patients present with hemodynamic instability or acute heart failure, ischemia should be strongly suspected, and primary PCI should be considered. The Sgarbossa criteria are particularly helpful in this setting, due to their high specificity and positive predictive value. Clinicians can confidently treat for STEMI when a Sgarbossa score of 3 is reached. In those with a Sgarbossa score of ≤ 2 , an ST/S ratio -0.25 or less might further identify those likely to benefit from emergent reperfusion therapy. If none of these criteria are met, a diagnosis of AMI cannot be established, and such patients should be further evaluated with serial ECGs, serial specific biomarker assays (such as high sensitivity troponin), and bedside echocardiography (the use of portable echocardiography to clarify the diagnosis of STEMI in the presence of LBBB had a class IIa indication in the 2004 ACC/AHA STEMI guidelines). Subsequent ECG findings, rapid uptrend of cardiac biomarkers and regional wall motion abnormalities, especially involving the anterior wall, or impaired left ventricular ejection fraction should prompt immediate catheterization laboratory activation for a conclusive diagnosis and possible urgent reperfusion.

Disclosures

No extramural funding was used to support this work.

Figure 3



Diagnosis and triage algorithm for patients with suspected AMI and LBBB.

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

References

1. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet* 1994; 343(8893):311-22.
2. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;361(9351):13-20.
3. Zimetbaum PJ, Josephson ME. Use of the electrocardiogram in acute myocardial infarction. *N Engl J Med* 2003;348(10):933-40.
4. Jain S, Ting HT, Bell M, et al. Utility of left bundle branch block as a diagnostic criterion for acute myocardial infarction. *Am J Cardiol* 2011;107(8):1111-6.
5. Chang AM, Shofer FS, Tabas JA, et al. Lack of association between left bundle-branch block and acute myocardial infarction in symptomatic ED patients. *Am J Emerg Med* 2009;27(8):916-21.
6. Ryan TJ, Anderson JL, Antman EM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1996;28(5):1328-428.

7. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). *J Am Coll Cardiol* 2004;44(3):E1-E211.
8. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012;33(20):2569-619.
9. Bansilal S, Aneja A, Mathew V, et al. Long-term cardiovascular outcomes in patients with angina pectoris presenting with bundle branch block. *Am J Cardiol* 2011;107(11):1565-70.
10. Lopes RD, Siha H, Fu Y, et al. Diagnosing acute myocardial infarction in patients with left bundle branch block. *Am J Cardiol* 2011;108(6):782-8.
11. The I.S.A.M. Study Group. A prospective trial of intravenous streptokinase in acute myocardial infarction (I.S.A.M.). Mortality, morbidity, and infarct size at 21 days. *N Engl J Med* 1986;314(23):1465-71.
12. ISIS-3 (Third International Study of Infarct Survival) Collaborative Group. ISIS-3: a randomised comparison of streptokinase vs tissue plasminogen activator vs anistreplase and of aspirin plus heparin vs aspirin alone among 41,299 cases of suspected acute myocardial infarction. *Lancet* 1992;339(8796):753-70.
13. Stenestrand U, Tabrizi F, Lindback J, et al. Comorbidity and myocardial dysfunction are the main explanations for the higher 1-year mortality in acute myocardial infarction with left bundle-branch block. *Circulation* 2004;110(14):1896-902.
14. Larson DM, Menssen KM, Sharkey SW, et al. "False-positive" cardiac catheterization laboratory activation among patients with suspected ST-segment elevation myocardial infarction. *JAMA* 2007;298(23):2754-60.
15. Sgarbossa EB, Pinski SL, Topol EJ, et al. Acute myocardial infarction and complete bundle branch block at hospital admission: clinical characteristics and outcome in the thrombolytic era. GUSTO-I Investigators. Global Utilization of Streptokinase and t-PA [tissue-type plasminogen activator] for Occluded Coronary Arteries. *J Am Coll Cardiol* 1998;31(1):105-10.
16. Gann D, Balachandran PK, Sherif NE, et al. Prognostic significance of chronic versus acute bundle branch block in acute myocardial infarction. *Chest* 1975;67(3):298-303.
17. Kumar V, Venkataraman R, Aljaroudi W, et al. Implications of left bundle branch block in patient treatment. *Am J Cardiol* 2013;111(2):291-300.
18. Imanishi R, Seto S, Ichimaru S, et al. Prognostic significance of incident complete left bundle branch block observed over a 40-year period. *Am J Cardiol* 2006;98(5):644-8.
19. Hackel DB, Wagner G, Ratliff NB, et al. Anatomic studies of the cardiac conducting system in acute myocardial infarction. *Am Heart J* 1972;83(1):77-81.
20. AIMS Trial Study Group. Effect of intravenous APSAC on mortality after acute myocardial infarction: preliminary report of a placebo-controlled clinical trial. *Lancet* 1988;1(8585):545-9.
21. Wilcox RG, von der Lippe G, Olsson CG, et al. Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. Anglo-Scandinavian Study of Early Thrombolysis (ASSET). *Lancet* 1988;2(8610):525-30.
22. Newby LK, Jesse RL, Babb JD, et al. ACCF 2012 expert consensus document on practical clinical considerations in the interpretation of troponin elevations: a report of the American College of Cardiology Foundation task force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2012;60(23):2427-63.
23. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *Circulation* 2012;126(16):2020-35.
24. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;127(4):e362-425.
25. Barbagelata A, Ware DL. Denying reperfusion or falsely declaring emergency: the dilemma posed by ST-segment elevation. *J Electrocardiol* 2006;39(4 Suppl):S73-4.
26. Sgarbossa EB, Pinski SL, Barbagelata A, et al. Electrocardiographic diagnosis of evolving acute myocardial infarction in the presence of left bundle-branch block. GUSTO-1 (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) Investigators. *N Engl J Med* 1996;334(8):481-7.
27. Wong CK, French JK, Aylward PE, et al. Patients with prolonged ischemic chest pain and presumed-new left bundle branch block have heterogeneous outcomes depending on the presence of ST-segment changes. *J Am Coll Cardiol* 2005;46(1):29-38.
28. Al-Faleh H, Fu Y, Wagner G, et al. Unraveling the spectrum of left bundle branch block in acute myocardial infarction: insights from the Assessment of the Safety and Efficacy of a New Thrombolytic (ASSENT 2 and 3) trials. *Am Heart J* 2006;151(1):10-5.
29. Tabas JA, Rodriguez RM, Seligman HK, et al. Electrocardiographic criteria for detecting acute myocardial infarction in patients with left bundle branch block: a meta-analysis. *Ann Emerg Med* 2008;52(4):329-36.
30. Smith SW, Dodd KW, Henry TD, et al. Diagnosis of ST-elevation myocardial infarction in the presence of left bundle branch block with the ST-elevation to S-wave ratio in a modified Sgarbossa rule. *Ann Emerg Med* 2012;60(6):766-76.