






RESEARCH LETTER

Utility of Echocardiography in Patients With Suspected Acute Myocardial Infarction and Left Bundle-Branch Block

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Patients with suspected acute myocardial infarction (AMI) in the setting of left bundle-branch block (LBBB) present an important diagnostic and therapeutic challenge to clinicians, as altered ventricular depolarization might mask changes in ventricular repolarization associated with AMI.^{1,2} We hypothesized that the use of early echocardiography may provide value in the differentiation of AMI from other causes of acute chest pain.^{1–4} This hypothesis is based on the assumption that patients with LBBB and AMI would exhibit relevant wall motion abnormalities (WMA), particularly in the anterior wall, while patients with other causes of acute chest pain would not exhibit these WMA. Unfortunately, this assumption has never been verified in an appropriate diagnostic study.³

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The aim of our study was to evaluate the diagnostic accuracy of echocardiography among patients presenting with suspected AMI and LBBB to 26 emergency departments (EDs) in 3 international, prospective, diagnostic studies.⁵ Ethics approval was obtained by local ethics committee and patients provided

written informed consent. The data that support the findings of this study are available from the corresponding author upon reasonable request. Final diagnoses were centrally adjudicated by 2 independent cardiologists according to the fourth universal definition of AMI based on all available information including the ECG, serial measurements of cardiac troponin, echocardiography, magnetic resonance imaging, and coronary angiography performed both after as well as before the index event to verify that abnormalities were causally related to the chest pain episode leading to ED presentation (eg, if in a patient with LBBB the acute chest pain episode did not lead to a rise and/or fall in cardiac troponin, during serial sampling, AMI was ruled out). Patients underwent echocardiography if considered clinically indicated by the treating physician. Echocardiography was performed by specifically trained cardiologists or echocardiographic sonographers following current echocardiographic guidelines. A WMA was reported only if imaging quality was good enough and if it was clearly distinguishable from paradoxical septum motion. For this analysis, patients were only eligible for this analysis if echocardiography was performed in the ED before revascularization to exclude the possible confounding of revascularization on

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WMA. Unfortunately, data on preexisting LBBB and/or WMA were not available in most patients.

Among 10 959 patients presenting with acute chest pain to the ED, LBBB was recorded in 286 (2.6%) patients. Transthoracic echocardiography had been performed in 35% (100/286) of patients with LBBB in the ED. AMI was the final diagnosis in 41% (41/100) of these patients. Among 59 patients without AMI, there were 29 with noncardiac causes of chest pain, 23 with cardiac but noncoronary causes, and 7 with unstable angina. WMAs were documented in 77 (77%) patients, with a similar prevalence in patients

with versus patients without AMI (33 [80%] and 44 [75%], $P=0.49$, Figure). The same finding emerged when specifically evaluating WMA of the anterior wall. In patients with LBBB, the prevalence of WMA of the anterior wall (54% versus 54%, $P=0.95$) and WMA of the septum (66% versus 58%, $P=0.41$) was comparable in patients with adjudicated AMI versus patients with other final diagnosis. Furthermore, other structural and/or functional abnormalities assessed did not differ for patients with versus without adjudicated AMI (eg, left atrium dilation 67% versus 66%, $P=0.885$, left ventricular hypertrophy 56% versus

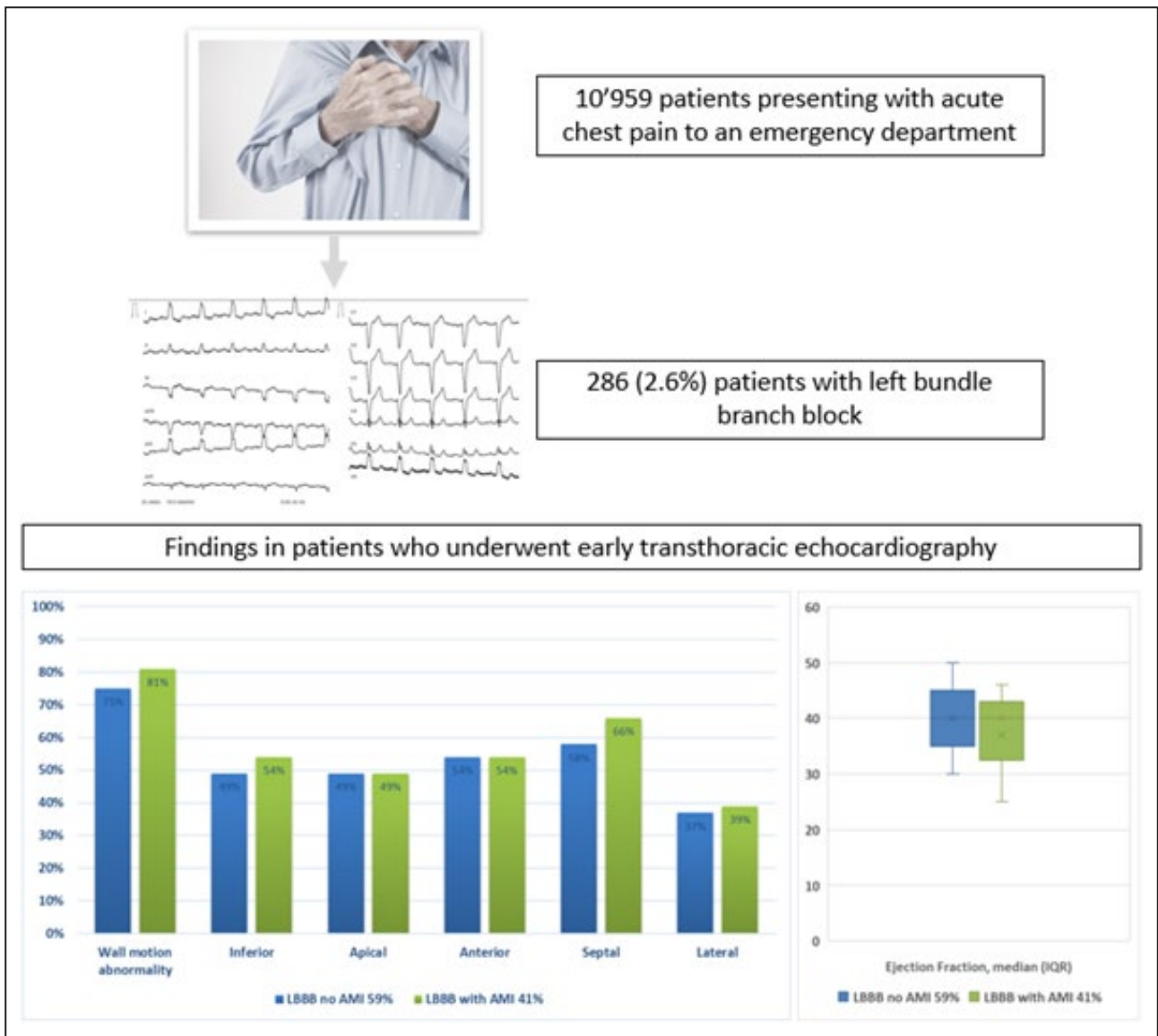


Figure 1. Patient flow chart and echocardiographic findings.

Flow chart of patients presenting with acute chest pain to an emergency department and LBBB. Bar charts and box plot for ejection fraction (with IQR) represent echocardiographic findings in patients with LBBB and adjudicated diagnosis of AMI vs patients with LBBB with an adjudicated diagnosis of no AMI. All P values for comparison are not statistically significant. Data are expressed as medians and IQR for continuous variables, and as numbers and percentages (%) for categorical variables. All variables between T1MI and T2MI were compared by the Mann–Whitney U test for continuous variables or the Pearson χ^2 or Fisher exact test for categorical variables, as appropriate. AMI indicates acute myocardial infarction; IQR, interquartile range; and LBBB, left bundle-branch block.

54, $P=0.822$, and left ventricular dilation 37% versus 44%, $P=0.507$).

These findings have important and immediate clinical consequences, as they falsified the assumption underlying our hypothesis regarding the utility of echocardiography in patients with suspected AMI and LBBB as recommended in current guidelines.^{1,2} As these data were derived from large international diagnostic studies using central adjudication by independent cardiologists, their validity and generalizability seem high. These surprising findings seem well explained by 3 aspects. First, in most patients presenting with LBBB and AMI, LBBB is pre-existing (known or unknown) and not the consequence of the current AMI.² Second, many patients with LBBB have prior AMIs resulting in persistent WMA, which often cannot be reliably differentiated from new WMA related to a new AMI. Third, most AMIs in patients with LBBB are small to moderate in size, and not the catastrophic very large AMI phenotype resulting in LBBB as a consequence of the very large ischemic territory. As only a subgroup of patients with LBBB underwent transthoracic echocardiography in the ED, it is important to highlight that selection bias would be expected to have favored a positive finding.

Accordingly, an integrated triage algorithm including specific ECG criteria (Sgarbossa or modified Sgarbossa criteria) with high specificity, as well as high sensitivity cardiac troponin/I concentrations at presentation and their 0/1-hour or 0/2-hour changes should be used in the selection of patients for immediate and/or early coronary angiography.⁵ It is important to highlight that these findings only apply to patients stable enough to provide written informed consent, which was required for this study. They should not be extrapolated to patients after cardiac arrest or in cardiogenic shock, for which immediate echocardiography should definitely remain the standard of care.¹

In conclusion, in hemodynamically stable patients with suspected AMI and LBBB, standard echocardiographic assessment provides only limited diagnostic value regarding the presence or absence of AMI.

APPENDIX

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REFERENCES

1. O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin B, 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. *J Am Coll Cardiol*. 2013;61:e78–e140.
2. Collet J-P, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, Dendale P, Dorobantu M, Edvardsen T, Folliguet T, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2021;42:1289–1367. doi: 10.1093/eurheartj/ehaa575
3. Neeland IJ, Kontos MC, de Lemos JA. Evolving considerations in the management of patients with left bundle branch block and suspected myocardial infarction. *J Am Coll Cardiol*. 2012;60:96–105. doi: 10.1016/j.jacc.2012.02.054
4. Manfredonia L, Lanza GA, Crudo F, Lamendola P, Graziani F, Villano A, Locorotondo G, Melita V, Mencarelli E, Pennestrì F, et al. Diagnostic role of echocardiography in patients admitted to the emergency room with suspect no-ST-segment elevation acute myocardial infarction. *Eur Rev Med Pharmacol Sci*. 2019;23:826–832. doi: 10.26355/eurrev_201901_16897
5. Nestelberger T, Cullen L, Lindahl B, Reichlin T, Greenslade JH, Giannitsis E, Christ M, Morawiec B, Miro O, Martín-Sánchez FJ, et al. Diagnosis of acute myocardial infarction in the presence of left bundle branch block. *Heart*. 2019;105:1559–1567. doi: 10.1136/heartjnl-2018-314673