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CORRESPONDENCE

Research Correspondence

# Left Bundle Branch Block in Non–ST-Segment Elevation Acute Coronary Syndromes

## Incidence, Angiographic Characteristics, and Clinical Outcomes

**To the Editor:** Acute coronary syndrome (ACS) patients presenting with left bundle branch block (LBBB) have higher mortality rates and worse overall outcomes than patients without LBBB (1,2). We compared clinical characteristics of 29,176 patients with and without LBBB enrolled in non–ST-segment elevation (NSTE) ACS clinical trials of antithrombotic therapy and explored the relationship of LBBB with outcomes.

We used 5 trials: GUSTO IIb (Global Use of Strategies to Open Occluded Arteries in Acute Coronary Syndromes, NSTE cohort) (n = 8,011, 27.5%), PARAGON-A (Platelet IIb/IIIa Antagonist for the Reduction of Acute Coronary Syndrome Events in a Global Organization Network A) (n = 2,282, 7.8%), PARAGON-B (Platelet IIb/IIIa Antagonist for the Reduction of Acute Coronary Syndrome Events in a Global Organization Network B) (n = 5,224, 17.9%), SYNERGY (Superior Yield of the New Strategy of Enoxaparin, Revascularization and Glycoprotein IIb/IIIa Inhibitors) (n = 4,256, 14.6%), and EARLY ACS (Early versus Delayed, Provisional Eptifibatide in Acute Coronary Syndromes) (n = 9,403, 32.2%). LBBB status was identified on the case report form and/or by the electrocardiogram core laboratory. Inclusion of patients with LBBB in these trials was generally by investigator discretion. If LBBB was known to be new or believed to represent an ST-segment elevation MI (STEMI) equivalent, the patient was excluded. Angiographic and echocardiographic data were reported on the case report form or obtained from a core angiography laboratory.

Our primary analysis examined 1-year mortality among survivors to hospital discharge (n = 24,848). We also examined in-hospital mortality (n = 25,934) and death or MI from hospital discharge to 30 days post-discharge among patients who survived event free to hospital discharge (n = 23,044).

Of 29,176 total patients, 27,832 (95.4%) had information on LBBB at baseline; LBBB was present in 490 (1.8%). LBBB patients were older, were more often female, had more comorbidities, and had a higher Killip class. In a subgroup with in-hospital assessment, they also had a lower left ventricular ejection fraction (40% vs. 55%, $p < 0.001$). Among 11,083 patients who had coronary angiographic data available (125 with and 10,958 without LBBB), right coronary artery lesion severity was greater among those with LBBB than without (80% vs. 72%, $p = 0.032$). Lesion severity was similar for the left anterior descending (LAD), left main, and left circumflex coronary arteries. Overall, 29.3% (3,242 of 11,083) had 100% occlusion in ≥1 main coronary vessel. Among patients with LAD lesions, more patients with LBBB than without had total LAD occlusion (26.8%, 19 of 71 vs. 14.9%, 1,265 of 8,467; $p = 0.0055$).

Patients with LBBB had greater in-hospital mortality than those without (4.3% vs. 2.6%), but the difference was not significant after adjustment for baseline characteristics (odds ratio: 0.99, 95% confidence interval [CI]: 0.62 to 1.59). Death or MI at 30 days post-discharge was also similar between groups (1.6% vs. 1.4%; adjusted odds ratio: 0.94, 95% CI: 0.43 to 2.05). Mortality between hospital discharge and 1-year post-discharge was higher among patients with LBBB at discharge (13.6%) than without (4.3%) (Fig. 1). After adjustment, 1-year mortality was nearly 2-fold greater among LBBB patients (hazard ratio: 1.84, 95% CI: 1.4 to 2.4). Results were similar in sensitivity analyses using LBBB at baseline instead of discharge.

LBBB has been associated with higher long-term mortality among acute MI patients; yet it is less certain whether LBBB independently predicts mortality (2). LBBB has not been studied in solely NSTE ACS populations. In mixed STEMI and NSTE ACS populations, there has been no clear association between LBBB and 1-year mortality (3). We demonstrated that LBBB at discharge was independently associated with nearly 2-fold higher 1-year mortality among NSTE ACS patients, but found no significant association with in-hospital or short-term outcomes. This contrasts with STEMI, in which LBBB patients had higher short-term mortality and in-hospital complications (1).

Lower left ventricular ejection fraction in the LBBB population could help to explain worse 1-year mortality. No data were available on use of implantable cardiac defibrillator devices or resynchronization therapy, which could additionally have affected this observed association.

Nearly twice as many LBBB patients had total LAD occlusion versus those without LBBB (26.8% vs. 14.9%). We could not distinguish between those with chronic occlusion (with collateral flow) versus acute (i.e., misdiagnosed STEMI), beyond presuming previous coronary artery bypass graft (52.6% [10 of 19] with LBBB vs. 46.2% [584 of 1,265] without) represented revascularized LAD. Electrocardiograms were not available to determine Sgarbossa criteria; thus, we could not determine based on these criteria whether some LBBB patients represented patients with possible STEMI (4). Further, there is not consensus that LBBB is a marker of acute MI or coronary disease severity among patients presenting with potentially ischemic symptoms (5). However, the more frequent total LAD occlusion and more severe coronary lesions we observed illustrate the importance of coronary angiography in NSTE ACS patients with LBBB.

In this retrospective study, we could not account for unmeasured confounders, and cause–effect relationships cannot be established. LBBB was classified by individual investigators, and protocols varied by trial – potentially introducing selection bias or misclassification of some STEMI patients as having NSTE ACS. We were unable to adjust for severity of coronary disease (particularly in LAD), which could contribute to differences in mortality.

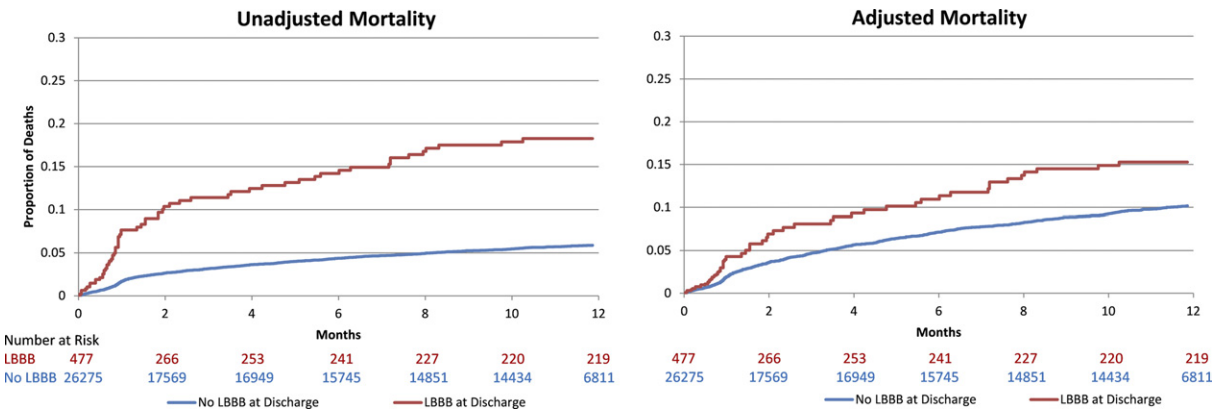


**Figure 1** **1-Year Cumulative Kaplan-Meier Death Rate by LBBB at Discharge**

**(Left)** Unadjusted curve; hazard ratio (HR): 3.51, log rank p value <0.0001. **(Right)** Adjusted curve; HR: 1.84, Cox Model p value <0.0001. LBBB = left bundle branch block.

There were few patients with LBBB and relatively few events, limiting power to detect differences between those with and without LBBB.

LBBB patients were older and had more comorbidities than those without LBBB. Short-term and in-hospital ischemic outcomes were similar, but LBBB patients had nearly 2-fold higher 1-year mortality after adjustment for other factors. Thus, it may be reasonable to consider LBBB in addition to other factors to identify NSTE ACS patients at higher longer-term risk.

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# Single Exhaled Breath Metabolomic Analysis Identifies Unique Breathprint in Patients With Acute Decompensated Heart Failure

**To the Editor:** Acute decompensated heart failure (ADHF) is the most common indication for hospital admission, particularly in the elderly, yet the identification of those with impending decompensation using conventional clinical methods is unreliable and frequently leaves insufficient lag time for therapeutic interventions (1). Exhaled breath constitutes a complex mixture of hundreds of volatile organic compounds (VOCs) that could potentially be used as a safe and noninvasive method of diagnostic and therapeutic monitoring (2). Previous research studies have identified elevated acetone, pentane, and nitric oxide levels in exhaled breath in the setting of HF correlated with disease severity (3–5). Selected ion-flow tube mass-spectrometry (SIFT-MS) combines a fast flow tube technique with quantitative mass spectrometry that is ideally suited for exhaled breath analysis because it allows for the analysis of small and humid samples without the need for cumbersome sample preparation or calibration (6). Scan times are relatively brief, thus facilitating high throughput and serial comparisons. Using this technology, we conducted a prospective, single-center cohort study to assess the feasibility of exhaled breath analysis to identify patients admitted for ADHF. The study protocol was approved by the Cleveland Clinic Institutional Review Board. We recruited 25 consecutive patients admitted with ADHF as their primary diagnosis (mean left ventricular ejection fraction 27 ± 13%, median N-terminal pro–B-type natriuretic peptide level 954 pg/ml) and a control group of 16 subjects admitted with non-ADHF cardiovascular diagnoses and who had no clinical evidence of systemic or venous congestion at the time of enrollment. Indications for hospitalization in the control group included unstable angina or non–ST-segment elevation myocardial infarction (6 of 16), conduction disorders (3 of 16), hypertensive emergency (3 of 16), atrial tachyarrhythmia (2 of 16), or stable angina (2 of 16). All analyses were performed using JMP Pro 9.0 (SAS Institute, Cary, North Carolina). As expected, there were significant ($p < 0.01$) baseline differences in the frequency of hypertension (54%

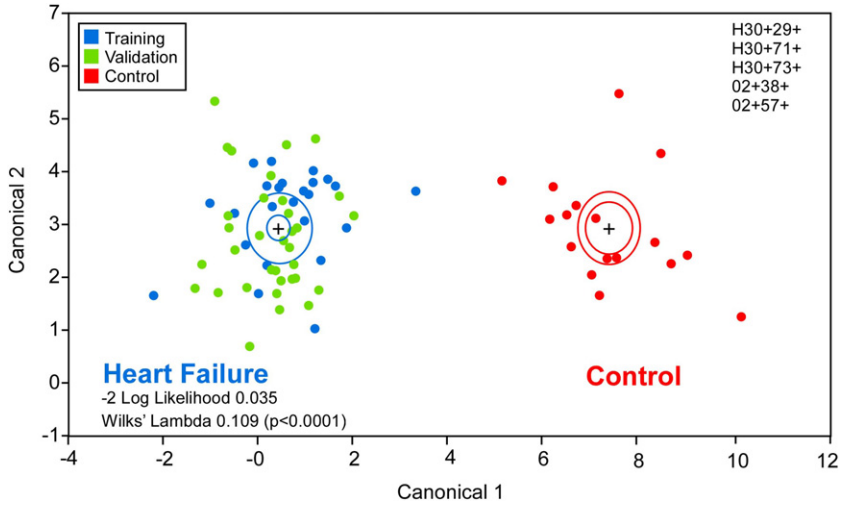


**Figure 1** **Canonical Discriminant Analysis: ADHF Versus Non-HF Controls**

Canonical discriminant analysis using 5 selected mass scanning ion peaks was performed in a training cohort of 25 acute decompensated heart failure (ADHF) subjects **(blue)** and 16 controls **(red)**. This ADHF "breathprint" was then used to classify an independent validation cohort of 36 ADHF subjects **(green)** with no misclassifications.