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Impaired Recovery of Left Ventricular Function in Patients With Cardiomyopathy and Left Bundle Branch Block

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ABSTRACT

BACKGROUND Patients with left bundle branch block (LBBB) often respond to cardiac resynchronization therapy (CRT) with left ventricular ejection fraction (LVEF) improvement. Guideline-directed medical therapy (GDMT), not CRT, is first-line therapy for patients with reduced LVEF with LBBB. However, there are little data on how patients with reduced LVEF and LBBB respond to GDMT.

OBJECTIVES This study examined patients with cardiomyopathy and sought to assess rates of LVEF improvement for patients with LBBB compared to other QRS morphologies.

METHODS Using data from the Duke Echocardiography Laboratory Database, the study identified patients with baseline electrocardiography and LVEF ≤35% who had a follow-up LVEF 3 to 6 months later. The study excluded patients with severe valve disease, a cardiac device, left ventricular assist device, or heart transplant. QRS morphology was classified as LBBB, QRS duration <120 ms (narrow QRS duration), or a wide QRS duration ≥120 ms but not LBBB. Analysis of variance testing compared mean change in LVEF among the 3 groups with adjustment for significant comorbidities and GDMT.

RESULTS There were 659 patients that met the criteria: 111 LBBB (17%), 59 wide QRS duration ≥120 ms but not LBBB (9%), and 489 narrow QRS duration (74%). Adjusted mean increase in LVEF over 3 to 6 months in the 3 groups was 2.03%, 5.28%, and 8.00%, respectively ($p < 0.0001$). Results were similar when adjusted for interim revascularization and myocardial infarction. Comparison of mean LVEF improvement between patients with LBBB on GDMT and those not on GDMT showed virtually no difference (3.50% vs. 3.44%). The combined endpoint of heart failure hospitalization or mortality was highest for patients with LBBB.

CONCLUSIONS LBBB is associated with a smaller degree of LVEF improvement compared with other QRS morphologies, even with GDMT. Some patients with LBBB may benefit from CRT earlier than guidelines currently recommend.
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In patients with cardiomyopathy, traditional interventions to improve left ventricular ejection fraction (LVEF) include medical modulation of the renin-angiotensin-aldosterone axis or direct intervention on a reversible cardiac pathology, such as coronary artery disease, valvular heart disease, or arrhythmia-induced tachycardia (among others) (1–3). More recently, cardiac resynchronization therapy (CRT) has introduced correction of electromechanical dyssynchrony as a powerful new mechanism to induce left ventricular (LV) functional recovery (4–8).

Most clinical trials that have studied CRT have found that it is only efficacious in patients with left bundle branch block (LBBB) (5,9–12). This implicitly suggests that LBBB may represent a previously unrecognized cause of LV dysfunction. Although LBBB has long been identified as a comorbid factor carrying an adverse prognosis, there is now evidence that LBBB not only leads to adverse patient outcomes in otherwise healthy patients, but as seen in dog models, and small retrospective series, may also be a potential cause of nonischemic cardiomyopathy itself (13–17).

Although CRT is considered the definitive treatment for patients with LBBB and symptomatic cardiomyopathy, it remains unclear how LBBB affects rates of LV functional recovery in patients without a cardiac device. For example, current guidelines recommend at least 3 months of guideline-directed medical therapy (GDMT) before implantation of CRT, in the hopes that medical therapy alone will lead to improvement in LVEF (8). However, it is worth emphasizing that none of the major trials supporting medical therapy stratified outcome analyses by the presence or absence of LBBB or reported QRS morphology as a baseline clinical characteristic (18–25).

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This study sought to examine how LBBB affects rates of LV functional recovery in patients with cardiomyopathy. We made use of the Duke Echocardiography Laboratory Database and Duke Electrocardiography database to identify patients with a diagnosis of cardiomyopathy, an electrocardiogram (ECG), and a follow-up echocardiogram in 3 to 6 months. We hypothesized that in the "real world," LBBB would be a significant predictor for decreased rates of LV functional recovery, and that many patients with LBBB would not improve their LVEF by >35%. This would suggest that some patients might benefit from receiving CRT earlier than current guidelines recommend.

METHODS

DATA SOURCES. The study cohort was selected from the Duke Echocardiography Laboratory Database. It includes all clinical echocardiograms performed at Duke University Health System since 1995, and its setup has been described previously (26). Basic demographic information is available, and patient clinical data are imported from the Duke Decision Support Repository and Duke Databank for Cardiovascular Disease. For the purposes of this study, the Duke Echocardiography Laboratory Database was linked to the ECG reporting database to identify patients with both a baseline echocardiogram and ECG.

Direct chart review was conducted to determine medication use. The occurrences of the following nonbaseline events were identified from the Duke Databank: 1) intercurrent percutaneous coronary intervention; 2) intercurrent bypass surgery; and 3) intercurrent myocardial infarction. The time period for intercurrent revascularization procedures was pre-specified to include dates from 2 weeks before baseline echocardiogram to the time of follow-up echocardiogram. Intercurrent myocardial infarction was pre-specified to be any myocardial infarction that occurred between baseline and follow-up echocardiogram. Heart failure hospitalizations after follow-up echocardiogram could be obtained for any admission at a Duke-affiliated hospital through the electronic medical record. All-cause mortality was obtained through the medical record and National Death Index.

DEFINITIONS. The diagnosis of cardiomyopathy reflected an LVEF ≤35%, assessed visually by an attending cardiologist with level 3 training in echocardiography. The designation of LBBB in the Duke Electrocardiography database matches the clinical diagnosis of attending cardiologists at Duke University Hospital responsible for reading patient ECGs. Patients without a clinical read of LBBB were stratified by QRS duration. Patients without LBBB who had a wide QRS duration ≥120 ms (WQRS) were placed into one group, whereas patients with a narrow QRS duration <120 ms (NQRS) were placed into a second comparator group. For the purpose of a sensitivity analysis, a physician trained in the Strauss criteria provided an additional over-read of all LBBB ECGs and placed these patients either into a strict LBBB group or back into the WQRS group (27). Use of GDMT was defined as use of a beta-blocker (BB) plus an

ABBREVIATIONS AND ACRONYMS

ACE = angiotensin-converting enzyme

ARB = angiotensin receptor blocker

BB = beta-blocker

CRT = cardiac resynchronization therapy

ECG = electrocardiogram

GDMT = guideline-directed medical therapy

LBBB = left bundle branch block

LV = left ventricular

LVEF = left ventricular ejection fraction

NQRS = narrow QRS duration

NYHA = New York Heart Association

WQRS = non-left bundle branch block with wide QRS duration