JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2015 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER INC.

VOL. 66, NO. 6, 2015
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2015.06.020

Identification of Typical Left Bundle Branch Block Contraction by Strain Echocardiography Is Additive to Electrocardiography in Prediction of Long-Term Outcome After Cardiac Resynchronization Therapy

Niels Risum, MD, PhD,* Bhupendar Tayal, MD,†‡ Thomas F. Hansen, MD,§ Niels E. Bruun, MD, DMSc,†§ Magnus T. Jensen, MD, PhD,‖ Trine K. Lauridsen, MD,§ Samir Saba, MD,† Joseph Kisslo, MD,¶ John Gorcsan III, MD,† Peter Sogaard, MD, DMSc‡

ABSTRACT

BACKGROUND Current guidelines suggest that patients with left bundle branch block (LBBB) be treated with cardiac resynchronization therapy (CRT); however, one-third do not have a significant activation delay, which can result in nonresponse. By identifying characteristic opposing wall contraction, 2-dimensional strain echocardiography (2DSE) may detect true LBBB activation.

OBJECTIVES This study sought to investigate whether the absence of a typical LBBB mechanical activation pattern by 2DSE was associated with unfavorable long-term outcome and if this is additive to electrocardiographic (ECG) morphology and duration.

METHODS From 2 centers, 208 CRT candidates (New York Heart Association classes II to IV, ejection fraction ≤35%, QRS duration ≥120 ms) with LBBB by ECG were prospectively included. Before CRT implantation, longitudinal strain in the apical 4-chamber view determined whether typical LBBB contraction was present. The pre-defined outcome was freedom from death, left ventricular assist device, or heart transplantation over 4 years.

RESULTS Two-thirds of patients (63%) had a typical LBBB contraction pattern. During 4 years, 48 patients (23%) reached the primary endpoint. Absence of a typical LBBB contraction was independently associated with increased risk of adverse outcome after adjustment for ischemic heart disease and QRS width (hazard ratio [HR]: 3.1; 95% CI: 1.64 to 5.88; $p < 0.005$). Adding pattern assessment to a risk prediction model including QRS duration and ischemic heart disease significantly improved the net reclassification index to 0.14 ($p = 0.04$) and improved the C-statistics (0.63 [95% CI: 0.54 to 0.72] vs. 0.71 [95% CI: 0.63 to 0.80]; $p = 0.02$). Use of strict LBBB ECG criteria was not independently associated with outcome in the multivariate model (HR: 1.72; 95% CI: 0.89 to 3.33; $p = 0.11$. Assessment of LBBB contraction pattern was superior to time-to-peak indexes of dyssynchrony ($p < 0.01$ for all).

CONCLUSIONS Contraction pattern assessment to identify true LBBB activation provided important prognostic information in CRT candidates. (J Am Coll Cardiol 2015;66:631–41) © 2015 by the American College of Cardiology Foundation.

From the *Department of Cardiology, Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark; †Division of Cardiology, University of Pittsburgh, Pittsburgh, Pennsylvania; ‡Department of Cardiology and Clinical Medicine, Aalborg University Hospital, Aalborg, Denmark; §Department of Cardiology, Gentofte University Hospital, Hellerup, Denmark; ‖Department of Cardiology, Holbæk Hospital, Holbæk, Denmark; and the ¶Division of Cardiovascular Medicine, Duke University Medical Center, Durham, North Carolina. Dr. Saba has received research grants from Medtronic, St. Jude, and Boston Scientific. Dr. Kisslo has

ABBREVIATIONS AND ACRONYMS

2DSE = 2-dimensional strain echocardiography

CRT = cardiac resynchronization therapy

ECG = electrocardiography/electrocardiographic

LBBB = left bundle branch block

LV = left ventricle/ventricular

LVAD = left ventricular assist device

LVEF = left ventricular ejection fraction

TDI = tissue Doppler imaging

Striking improvement in the prognosis for patients with symptomatic heart failure and left bundle branch block (LBBB) has been obtained in some patients treated with cardiac resynchronization therapy (CRT) (1,2). Current guidelines recommend LBBB with QRS duration of ≥150 ms by electrocardiography (ECG) alone, whereas the role for CRT in patients with intermediate QRS duration and LBBB or non-LBBB QRS morphology is less well established (3). However, approximately one-third of patients do not benefit, and some may even experience worsening after CRT (4). The relationship between LBBB electrical activation and the consequent mechanical dysfunction that results in heart failure is therefore not fully understood.

SEE PAGE 642

CRT, an electrical intervention aimed at resolving the LBBB-related abnormal activation of the left ventricle (LV) associated with dyssynchronous heart failure, may alleviate the mechanical dysfunction caused by this electrical delay (5). In contrast, if heart failure is caused by underlying myocardial disease, such as scar, CRT is unlikely to benefit the patient (5). Thus, methods that reliably reflect a significant activation delay of the LV are thought to be of potential value in selection of candidates for CRT (6). Unfortunately, current modalities have generally proven suboptimal in this regard. Indeed, not all LBBBs by ECG reflect a true LV activation delay (7). Studies using LV endocardial mapping have reported that up to one-third of patients thought to have LBBB are misdiagnosed (8,9). Progressive evidence suggests that an LBBB activation delay can be identified from LV mechanical deformation patterns (6,10–16). True LBBB activation leads to a unique contraction pattern of opposing wall motion (12) with apical rocking motion (15). We recently demonstrated the use of 2-dimensional strain echocardiography (2DSE) to specifically identify LBBB-related wall deformation (6,14), which can be reversed by CRT and is highly predictive of LV remodeling response (14). It is, however, unknown whether such patterns are associated with long-term outcome after CRT.

Using a larger, 2-center group of patients with LBBB undergoing CRT, we hypothesized that: 1) the absence of a typical LBBB contraction pattern identified by 2DSE would be associated with unfavorable long-term outcome in comparison with those with evidence of typical LBBB contraction; 2) risk prediction of adverse outcome would be improved beyond conventional ECG criteria, QRS duration, and LBBB morphology by identification of a typical LBBB contraction pattern; and 3) risk prediction of adverse outcome would be improved beyond traditional time-to-peak indexes of mechanical dyssynchrony.

METHODS

STUDY POPULATION. Inclusion criteria. The study design was prospective, with analysis of the typical LBBB pattern applied to a consecutive patient series meeting the inclusion and exclusion criteria. The population included patients eligible for CRT at 2 centers. Patients had native LBBB by conventional ECG criteria (left ventricular ejection fraction [LVEF] ≤35%, QRS duration ≥120 ms, and New York Heart Association class II to IV, despite optimal pharmacological therapy) (17). Overall, 234 patients with LBBB were included (139 from the University of Pittsburgh Medical Center and 95 from Gentofte University Hospital, Denmark). The decision to implant a CRT device was on the basis of routine ECG criteria. Pre-implant dyssynchrony was not among the selection criteria.

Exclusion criteria. Patients were excluded if they had significant primary valve disease, atrial fibrillation, acute coronary syndrome, or revascularization within 3 months of the baseline echocardiography or if baseline echocardiographic images were not of suitable quality for quantitative strain analysis. All patients were implanted with a CRT device with defibrillator capacity, according to standard clinical practice, with 1 lead in the high right atrium, a right ventricular apical or septal lead, and an LV lead positioned through the coronary sinus in an epicardial vein targeting posterolateral or lateral branches. Data collection included pre-implant ECG, echocardiography, routine laboratory work, and demographic and clinical data. The study protocol was approved by the Institutional Review Boards at both centers and complied with the Declaration of Helsinki.

served as a speaker and consultant for GE Healthcare and Phillips. Dr. Gorcsan III has received research grants from Medtronic, Biotronik, Toshiba, and GE Healthcare. Dr. Sogaard has received research grants from Biotronik and GE Healthcare. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.
Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

Manuscript received January 27, 2015; revised manuscript received May 7, 2015, accepted June 2, 2015.