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Improvement of Reverse Remodeling Using Electrocardiogram Fusion-Optimized Intervals in Cardiac Resynchronization Therapy

A Randomized Study

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ABSTRACT

OBJECTIVES The aim of this study was to compare patient response to cardiac resynchronization therapy (CRT) using fusion-optimized atrioventricular (AV) and interventricular (VV) intervals versus nominal settings.

BACKGROUND The additional benefit obtained by AV- and VV-interval optimization in patients undergoing CRT remains controversial. Previous studies show short-term benefit in hemodynamic parameters; however, midterm randomized comparison between electrocardiogram optimization and nominal parameters is lacking.

METHODS A group of 180 consecutive patients with left bundle branch block treated with CRT were randomized to fusion-optimized intervals (FOI) or nominal settings. In the FOI group, AV and VV intervals were optimized according to the narrowest QRS, using fusion with intrinsic conduction. Clinical response was defined as an increase >10% in the 6-min walk test or an increment of 1 step in New York Heart Association functional class. The left ventricular (LV) remodeling was defined as >15% decrease in left ventricular end-systolic volume (LVESV) at 12-month follow-up. Additionally, patients with LVESV reduction >30% relative to baseline were considered super-responders; by contrast, negative responders had increased LVESV relative to baseline.

RESULTS Participant characteristics included a mean age of 65 $\pm$ 10 years, 68% male, 37% with ischemic cardiomyopathy, LV ejection fraction 26 $\pm$ 7%, and QRS 180 $\pm$ 22 ms. Baseline QRS was shortened significantly more by FOI, compared with nominal settings (-56.55 ± 17.65 ms vs. -37.81 ± 22.07 ms, respectively; $p = 0.025$). At 12 months, LV reverse remodeling was achieved in a larger proportion of the FOI group (74% vs. 53% [odds ratio: 2.02 (95% confidence interval: 1.08 to 3.76)], respectively; $p = 0.026$). No significant differences were observed in clinical response (61% vs. 53% [odds ratio: 1.43 (95% confidence interval: 0.79 to 2.59)], respectively; $p = 0.24$).

CONCLUSIONS Device optimization based on FOI achieves greater LV remodeling, compared with nominal settings. (ECG Optimization of CRT: Evaluation of Mid-Term Response [BEST]; NCT01439529) (J Am Coll Cardiol EP 2018;■:■–■) © 2018 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AP = atrial pacing

AS = atrial sensing

AV = atrioventricular

CI = confidence interval

CRT = cardiac resynchronization therapy

ECG = electrocardiogram

FOI = fusion-optimized intervals

HF = heart failure

IEGM = intrinsic electrogram

LBBB = left bundle branch block

LV = left ventricular

LVEF = left ventricular ejection fraction

LVESV = left ventricular end-systolic volume

NYHA = New York Heart Association

OR = odds ratio

RV = right ventricular

VV = interventricular

Cardiac resynchronization therapy (CRT) reduces mortality and heart failure (HF) hospitalizations in selected patients with left ventricular (LV) systolic dysfunction and prolonged QRS duration. This therapy aims to resynchronize the electrical ventricular activation, improving cardiac function and functional status (1,2).

However, not all patients respond to CRT; up to 30% of CRT-implanted patients are currently considered clinical nonresponders (3,4), and up to 50% do not achieve LV reverse remodeling (5). Optimization of CRT pacing intervals may improve results (6–8), increasing the number of responders and the magnitude of the response. The short-term benefit obtained by echocardiographic optimization suggests that atrioventricular (AV) delay and interventricular (VV) interval optimization may further improve response, compared with nominal settings (9,10).

Echocardiography, considered the reference method for AV and VV intervals optimization (11), is complex and time-consuming. Due to its limited feasibility and large interobserver and intraobserver variability, a minority of clinicians perform CRT optimization in routine clinical practice (12). Moreover, despite several studies showing short-term benefits of AV and VV optimization, only limited data exist to suggest that systematic interval optimization results in long-term improvement (5,13,14), and previous randomized studies failed to show superiority of echocardiographic optimization over default parameters during follow-up. QRS-based optimization may be a simpler and more effective way to optimize CRT. A previous randomized study obtained the best short-term hemodynamic response by selecting a VV interval guided by narrowest QRS (15). These results were confirmed by a higher response rate at 6-month follow-up, compared with echocardiographic optimization (16). Furthermore, adding fusion with intrinsic conduction may increase CRT benefit, compared with only LV and right ventricular (RV) pacing (17).

A previous study described a simple new method to optimize AV and VV intervals in CRT, based on obtaining the narrowest QRS using fusion with intrinsic conduction (fusion-optimized intervals [FOI]) (18); short-term hemodynamic results were improved, compared with nominal settings (19). The aim of our study was to compare the clinical response and echocardiographic LV reverse remodeling of CRT using FOI versus the device's nominal settings programming.

METHODS

POPULATION. A cohort of 180 consecutive patients who received a CRT were included in the study. The inclusion criteria were: patients with HF, in sinus rhythm, with New York Heart Association (NYHA) functional class II to IV despite optimal medical treatment, LV ejection fraction (LVEF) ≤35%, and QRS width ≥120 ms with left bundle branch block (LBBB) and successful CRT implantation. Patients with treatable cardiomyopathies, life expectancy <1 year, conduction disturbances (AV interval ≥250 ms or complete AV block), or atrial fibrillation were excluded. Patients received a CRT device with or without a defibrillator, based on comorbidities and clinical indication.

Clinical response was defined as an increase >10% at the 6-min walking test (6MWT) or an increment of 1 step in NYHA functional class. The LV remodeling was defined as a decrease exceeding 15% in left ventricular end-systolic volume (LVESV) at 12-month follow-up. Additionally, patients with LVESV reduction >30% relative to baseline were considered super-responders, and negative responders had increased LVESV relative to baseline (20).

The study protocol was approved by our hospital's ethics committee, and written informed consent was obtained for all patients. The study design is published at clinicaltrials.gov (NCT01439529).

FOLLOW-UP. All patients underwent a 12-lead electrocardiogram (ECG), echocardiogram, and clinical evaluation before implantation and at 6- and 12-month follow-up. Symptoms of HF, functional capacity, and quality of life were assessed with NYHA functional class, the 6MWT (21), and the Minnesota Living With Heart Failure test (22), respectively. All pharmacological treatment was recorded. Readers blinded to randomization assessed response. Deaths were categorized as cardiac, noncardiac, or unknown. Cardiac deaths were classified as sudden (not preceded by HF or ischemic symptoms) or due to HF per Epstein et al. (23). When the cause of death could not be determined, it was classified as unknown.

ELECTROCARDIOGRAPHIC MEASUREMENTS AND FOI. The day after CRT implantation, in the absence of complications and with confirmation of a stable position of the LV electrode with appropriate capture, QRS measurements were performed (E.A., E.T.) in 3 different configurations: during spontaneous sinus rhythm, while using the device's nominal settings, and after optimization of the AV and VV intervals. Interobserver variability was negligible (0.97 (95% confidence interval [CI]: 0.92 to 0.99) at a screen