Recoordination Rather than Resynchronization Predicts Reverse Remodeling after Cardiac Resynchronization Therapy

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Background: Mechanical discoordination as studied by magnetic resonance imaging has been shown to be a better predictor of left ventricular (LV) reverse remodeling after cardiac resynchronization therapy (CRT) compared with mechanical dyssynchrony.

Materials and Methods: This study assessed the value of acute recoordination derived from speckle-tracking echocardiography for predicting response to CRT compared with acute resynchronization. Thirty patients with heart failure scheduled for CRT were studied at baseline, immediately after CRT, and after 6 months of CRT. Acute recoordination after CRT was indexed by an acute reduction in radial discoordination index (RDI), defined as the ratio of average myocardial thinning to thickening during the ejection phase.

Results: CRT responders were defined as those patients whose LV end-systolic volume decreased by ≥ 15% at the 6-month follow-up. Immediately after CRT, the responders (n = 18) demonstrated a significant reduction in RDI ($P < .001$), which was sustained at the 6-month follow-up ($P < .001$). The nonresponders, however, did not show a significant change in RDI after CRT. LV reverse remodeling at the 6-month follow-up was significantly correlated with acute recoordination ($r = 0.75$, $P < .001$) but weakly correlated with acute resynchronization ($r = 0.43$; $P = .02$).

Conclusions: Receiver operating characteristic analysis revealed that acute recoordination provided the best separation for prediction of CRT responders compared with acute resynchronization, baseline dyssynchrony, or baseline discoordination. LV recoordination after CRT is an acute phenomenon and predicts response to CRT at 6-month follow-up better than resynchronization. (J Am Soc Echocardiogr 2010;23:611-20.)

Keywords: Cardiac resynchronization therapy, Discoordination, Dyssynchrony, Echocardiography, Speckle tracking

Cardiac resynchronization therapy (CRT) has proven helpful in patients with heart failure and a wide QRS complex.[1] Despite its efficacy, 30% to 40% of patients do not benefit from CRT.[2] Several studies suggested that mechanical dyssynchrony is a potential tool to identify CRT responders.[3-7] In addition, immediate reduction in left ventricular (LV) dyssynchrony after CRT was thought to predict LV reverse remodeling at 6-month follow-up.[8] However, the Predictors of Response to CRT (PROSPECT) study showed disappointing results on the use of mechanical dyssynchrony in predicting response to CRT.[9]

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In a recent study using circumferential strain by magnetic resonance imaging, Kirn et al[10] demonstrated that mechanical discoordination (opposite strain within the LV wall) predicted reverse remodeling after CRT better than mechanical dyssynchrony. In the present study, we hypothesize that LV recoordination rather than resynchronization is a better approach to predict response to CRT. A novel approach to detect LV recoordination with speckle-tracking echocardiography was evaluated for predicting CRT response compared with resynchronization derived from classic dyssynchrony metrics. Immediate LV recoordination after CRT was indexed by an acute reduction in radial discoordination index (RDI), defined as the ratio of average myocardial thinning to thickening during the ejection phase.

MATERIALS AND METHODS

Patients

Consecutive patients with heart failure scheduled for CRT implantation were enrolled. The selection criteria for CRT included moderate to severe heart failure (New York Heart Association functional class III and IV) despite optimal medical therapy, LV ejection

Abbreviations

AS-P delay = Time difference between the anteroseptal and posterior segments

CRT = Cardiac resynchronization therapy

EF = Ejection fraction

LV = Left ventricular

MD-6 = Time difference between the earliest and latest segments of 6 segments

PROSPECT = Predictors of Response to CRT study

RDI = Radial discoordination index

RDI-B = 6 basal LV segments

RDI-M = 6 mid-LV segments

RDI-12 = 12 LV segments

RS-SD = Standard deviation of times to peak strain for 6 segments

fraction (EF) ≤ 35%, and QRS duration > 120 ms. Two age-matched groups with narrow QRS (duration < 120 ms) served as controls: 1) patients without structural heart disease and with a normal echocardiogram (normal group) and 2) patients with LV EF < 35% (low EF group). Patients' clinical status, LV volumes, and EF were assessed before CRT implantation and after 6 months of CRT. LV dyssynchrony and discoordination were assessed at baseline, immediately after CRT, and at a 6-month follow-up. Each parameter was measured from 3 consecutive beats and averaged for purpose of analysis.

Cardiac Resynchronization Therapy Procedure

The pacing leads were positioned at the right ventricular apex or mid-septum, at the right atrial appendage, and in the posterior or posterolateral branch of coronary vein. The atrioventricular interval was optimized using the established method to ensure adequate LV filling.[11] No adjustments were made to the interventricular interval before the 6-month follow-up. The local ethics committee approved the study protocol, and all subjects gave informed consent.

Echocardiography

Subjects were imaged in the left lateral decubitus position with a commercially available system (Vivid 7, General Electric Vingmed Ultrasound, Horten, Norway). Standard 2-dimensional and color Doppler data triggered to the QRS complex were saved in cine-loop format. The LV volumes and EF were measured from the conventional apical 2- and 4-chamber images using the biplane Simpson method. The severity of mitral regurgitation was evaluated by color jet area and as percent jet area relative to left atrial size. Patients with a reduction of ≥ 15% in LV end-systolic volume at the 6-month follow-up were considered CRT responders.

LV dyssynchrony and discoordination were evaluated by speckle-tracking echocardiography from the parasternal short-axis views at the level of papillary muscles and mitral valve. Gain settings and imaging width were adjusted to optimize the gray scale (frame rate of 50-80 hertz) and not to compromise the image resolution. Each time, we analyzed a single beat and the gating was set to begin with the onset of the QRS complex. End systole was chosen as the single frame for marking the region of interest to include the maximal wall thickness for strain analysis. The inner marker was traced to the endocardial-cavity interface at end systole, and the outer marker was traced to the LV epicardium to obtain reproducible time–strain curves.[12,13] The software (EchoPac 6.1, General Electric Vingmed Ultrasound) automatically tracked the image speckle and produced 6 regional radial strain and strain rate curves. The region of interest was redrawn if tracking quality was poor or the curves were viewed to be inadequate.

Table 1 Clinical characteristics

	Narrow QRS control groups			
	Normal (n = 20)	Low EF (n = 40)	CRT group (n = 30)	*P*
Age (y)	65 ± 9	67 ± 8	69 ± 10	.22
Female, n (%)	9 (45)	19 (48)	18 (60)	.48
Ischemic cause, n (%)	0 (0)	20 (50)*	12 (40)*	.001
LV EF (%)	64 ± 9	26 ± 6*	23 ± 8*	<.001
LV EDV (mL)	79 ± 19	163 ± 60*	172 ± 65*	<.001
QRS duration (ms)	91 ± 8	95 ± 11	166 ± 23*,†	<.001

EF, Ejection fraction; *CRT*, cardiac resynchronization therapy; *LV*, left ventricular; *EDV*, end-diastolic volume.
*P < .001 vs normal group.
†P < .001 vs low EF group.

Table 2 Clinical characteristics at baseline and 6 months after cardiac resynchronization therapy

	Nonresponders (n = 12)	Responders (n = 18)	*P*
Age (y)	67 ± 11	71 ± 8	.24
Female, n (%)	6 (50)	12 (67)	.36
Ischemic cause, n (%)	8 (67)	4 (22)	.02
QRS duration (ms)	170 ± 29	164 ± 20	.47
Medication, n (%)			
ACE inhibitors/ARB	11 (92)	17 (94)	1.0
B-blockers	10 (83)	16 (89)	1.0
Diuretics	9 (75)	12 (57)	.70
NYHA class			
Baseline	3.2 ± 0.3	3.1 ± 0.3	.65
6 months	2.6 ± 0.7†	1.5 ± 0.5*	<.001
LV EDV (mL)			
Baseline	194 ± 75	158 ± 55	.14
6 months	209 ± 90	101 ± 33*	.002
LV ESV (mL)			
Baseline	156 ± 72	121 ± 48	.12
6 months	171 ± 83	56 ± 24*	.001
LV EF (%)			
Baseline	21 ± 8	24 ± 7	.37
6 months	21 ± 8	46 ± 8*	<.001
Mitral regurgitation (%)			
Baseline	22 ± 10	24 ± 12	.68
6 months	20 ± 10	8 ± 5*	.003

ACE, Angiotensin-converting enzyme; *ARB*, angiotensin receptor blockers; *NYHA*, New York Heart Association; *LV*, left ventricular; *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *EF*, ejection fraction.
Values are mean ± standard deviation or number (percentage).
*P < .001 vs baseline.
†P = .008 vs baseline.

Radial Dyssynchrony and Discoordination Analysis

The data of radial strain and strain rate were exported to a spreadsheet program (Microsoft Excel, Microsoft Corp, Seattle, WA) to calculate dyssynchrony and discoordination. The time to peak strain