Echocardiography-guided left ventricular lead placement for cardiac resynchronization therapy in ischemic vs nonischemic cardiomyopathy patients

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BACKGROUND Echocardiography-guided (EG) left ventricular (LV) lead placement at the site of latest mechanical activation improves outcome in heart failure (HF) patients receiving a cardiac resynchronization therapy (CRT)-defibrillator (CRT-D).

OBJECTIVE The purpose of this study was to examine the effect of a strategy of EG LV lead placement in each of ischemic (ICM) vs nonischemic (NICM) cardiomyopathy patients.

METHODS Patients enrolled in the Speckle Tracking Assisted Resynchronization Therapy for Electrode Region (STARTER) prospective, randomized trial who were treated with a CRT-D device (108 EG strategy and 75 routine strategy) were followed to the endpoints of death, appropriate CRT-D therapy, or HF hospitalization.

RESULTS Of the patients enrolled in STARTER, 115 had ICM and 68 had NICM. Over mean follow-up of 3.7 ± 2.1 years, 62 patients died, 40 received appropriate CRT-D therapy, and 67 had HF hospitalizations. Compared to NICM patients, patients with ICM had worse survival ($P = .0003$), worse survival free from implantable cardioverter-defibrillator therapy ($P = .004$), and survival free from HF hospitalization ($P = .0001$). A strategy of EG LV lead placement improved the outcome of CRT-D therapy-free survival primarily in ICM patients and the outcome of HF hospitalization-free survival in both ICM and NICM patients. Achieving LV resynchronization was most critical in ICM patients in whom arrhythmic and HF outcomes improve with resynchronization to levels comparable to those of NICM patients.

CONCLUSION A strategy of EG LV lead placement improves HF-free survival equally in ICM and NICM patients and CRT-D therapy-free survival more favorably in ICM patients to levels comparable to those of NICM patients.

KEYWORDS Cardiac resynchronization therapy; Targeted lead placement; Death; Defibrillator therapy; Cardiomyopathy

ABBREVIATIONS **CI** = confidence interval; **CRT** = cardiac resynchronization therapy; **CRT-D** = cardiac resynchronization therapy-defibrillator; **EG** = echocardiography guided; **HF** = heart failure; **HR** = hazard ratio; **ICD** = implantable cardioverter-defibrillator; **ICM** = ischemic cardiomyopathy; **LV** = left ventricle; **NICM** = nonischemic cardiomyopathy; **STARTER** = Speckle Tracking Assisted Resynchronization Therapy for Electrode Region

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Introduction

Cardiac resynchronization therapy (CRT) improves clinical and echocardiographic outcomes in heart failure (HF) patients with severe cardiomyopathy (ejection fraction ≤35%) and wide QRS complex (≥120 ms).[1–4] The Speckle Tracking Assisted Resynchronization Therapy for Electrode Region (STARTER) was a randomized, controlled, prospective trial that demonstrated the superiority of a strategy of speckle tracking echocardiography-guided (EG) left ventricular (LV) lead placement during CRT device implantation over the routine approach for the primary outcome of time to death or first HF hospitalization.[5]

Previous studies demonstrated worse outcome after CRT in patients with ischemic cardiomyopathy (ICM) vs nonischemic cardiomyopathy (NICM),[6–8] but the causes of this difference are not fully elucidated. In addition, strategies to mitigate this problem and improve outcome in ICM patients are lacking. Because ICM is often related to heterogeneous regions of scar that is deleterious to LV lead location, we

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examined the effect of a strategy of EG LV lead placement in each of ICM vs NICM patients.

Methods

STARTER was a prospective, single-center, double-blinded, randomized trial comparing speckle tracking EG LV lead positioning through the transvenous approach during CRT implantation to a routine approach without imaging guidance.[5] A total of 187 patients were enrolled in STARTER and implanted at the University of Pittsburgh Medical Center between June 2005 and March 2011: 110 in the EG arm and 77 in the routine arm. Details of the study were reported elsewhere.[5] In brief, STARTER-enrolled patients were at least 18 years of age, had New York Heart Association HF class II, III, or IV symptoms on optimal medical therapy, left ventricular ejection fraction $\leq$35%, and QRS width $\geq$120 ms. All patients received a CRT-defibrillator (CRT-D), except for 4 patients (2 in each study arm) who received a CRT-pacemaker. Therefore, the current analysis is based on the 183 patients with a CRT–implantable cardioverter-defibrillator (CRT-ICD): 108 in the EG arm and 75 in the routine arm.

Echocardiography

As previously detailed, all echocardiographic studies (GE Vivid 7 system, Horten, Norway) were analyzed by the core lab at UPMC Presbyterian.[5] LV volumes were assessed by biplane Simpson rule using manual tracing of digital images.[9] For speckle tracking radial strain,[10] digital gray-scale 2-dimensional cine loop images were acquired at end-expiratory apnea from basal and mid-LV short-axis views with frame rates of 60 to 90 Hz for offline analysis (GE EchoPac BT08-BT11).[10–12] The times to peak strain from 8 free-wall segments (4 from each view) were determined from a minimum of 3 consecutive beats and averaged. The site of latest activation was determined as the segment with latest peak strain. Dyssynchrony was determined as the time difference between peak strain in the anteroseptal segment to peak strain in the posterior wall, as previously described.[12–14]

Follow-up

LV volumes and ejection fractions were determined from follow-up echocardiography obtained 6 to 12 months after CRT. Dyssynchrony after CRT was determined by speckle tracking as before CRT. Resynchronization was defined as a 50% decrease in radial dyssynchrony (difference in time to peak anteroseptal to posterior wall strain) from before to after CRT, providing they had at least 95-ms dyssynchrony measure at baseline. Clinically, the patients were followed up to the primary end-point of death from any cause or first CRT-D therapy (shock or antitachycardia pacing) for ventricular arrhythmia as well as to the end-point of death or HF hospitalization. Deaths and device therapy events were examined in October 2013 and HF hospitalizations in December 2013 using the institutional electronic medical records.

Statistical analysis

All continuous variables are expressed as mean $\pm$ SD and were compared using the Student t test or analysis of variance, as appropriate. Discrete variables are expressed as number of events and percentages and compared using the χ^2 test. Time to events (death, ventricular arrhythmia or ICD therapy, HF hospitalization) were calculated according the Kaplan-Meier method and compared using the log-rank test. Multivariate analysis of time-dependent events was performed using the Cox proportional hazard method. All analyses were conducted using IBM PASW software version 19 (IBM Corp, Armonk, NY). $P \leq .05$ were considered significant.

Results

Baseline characteristics and outcome of ischemic vs nonischemic cardiomyopathy patients

Of the patients enrolled in STARTER[5] and implanted with a CRT-D device, 115 had ICM and 68 had NICM. Baseline

Table 1 Baseline characteristics of ischemic vs nonischemic cardiomyopathy patients enrolled in STARTER

	Ischemic (n = 115)	Nonischemic (n = 68)	*P* value
Age (years)	69 ± 10	61 ± 12	<.001
Gender (male)	84%	55%	<.001
New York Heart Association class (II/III/IV)	11%/66%/23%	16%/68%/16%	.71
Atrial fibrillation	28%	17%	.55
Ejection fraction (%)	26 ± 6	26 ± 7	.79
QRS width (ms)	156 ± 28	164 ± 26	.08
QRS ≥150 ms	57%	72%	.041
QRS morphology			.42
LBBB*	67%	71%	
Right ventricular pacing	26%	26%	
Non-LBBB	7%	3%	
Left ventricular end-systolic volume (mL)	142 ± 63	142 ± 72	.97
Left ventricular end-diastolic volume (mL)	189 ± 63	187 ± 81	.88
Plasma creatinine (mg/dL)	1.3 ± 0.5	1.2 ± 0.6	.028

LBBB = left bundle branch block; STARTER = Speckle Tracking Assisted Resynchronization Therapy for Electrode Region.

*Non-LBBB group includes patients with right bundle branch block or intraventricular conduction delay.