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Left ventricular scar impact on left ventricular synchronization parameters and outcomes of cardiac resynchronization therapy

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A B S T R A C T

Background: Left ventricular scar, including global scar and lateral wall, plays an important role in predicting response to cardiac resynchronization therapy (CRT).
Materials and methods: Thirty patients underwent CRT implantation. Assessment of left ventricular (LV) dyssynchrony was done through Gated SPECT LV phase analysis. Pre-implantation cardiac magnetic resonance (CMR) with late gadolinium enhancement technique to examine LV scar burden. Echocardiographic examination of LV end-systolic volume (LVES) prior to CRT and 6 months later.
Results: Thirty patients received CRT (mean age 58.7±9.0, 24 males). Reverse LV remodeling (decline ≥15% from baseline VES) was documented in 19 patients. Temporal changes in LV dyssynchrony parameters were correlated to LV reverse remodeling. Applying ROC for predicting CRT non-response showed a cutoff 36.5% of global LV scar burden had a sensitivity of 81.8% and specificity of 68.4%. A cutoff for lateral wall scar burden 40.5% of whole lateral wall had a sensitivity of 72.7% and specificity of 68.4%.
Conclusion: Reverse LV remodeling is associated with temporal improvements in LV dyssynchrony parameters. LV scar had an unfavorable impact on CRT response. Both global and lateral wall scar burden could predict CRT nonresponse status.

1. Introduction

Several studies have demonstrated benefits of cardiac resynchronization therapy in patients with end-stage HF, provided by the multisite pacing of the right and left ventricles and improving intraventricular and interventricular dyssynchrony [1–4].

Accordingly, ACCF/AHA guidelines have incorporated CRT implantation in managing drug-refractory HF patients with prolonged QRS duration [5]. However, applying conventional criteria, 20% to 40% of patients fail to respond to CRT [6–11]. It was suggested that the extent of the viable or infarcted myocardium and mechanical dyssynchrony could be related to the success of CRT [8–10,12–16].

Cardiac magnetic resonance and Gated SPECT offer the ability to assess cardiac perfusion and viability. Besides, LV phase analysis by Gated SPECT could provide an assessment of LV dyssynchrony [11].

In our institution, we examined the ability of Gated SPECT and CMR examination to reveal the impact of LV scar substrate on CRT response and provide predictors of CRT outcome. Also, LV dyssynchrony was examined and temporal changes in phase parameters were recorded.

2. Methods

2.1. Patient population

Thirty patients participated in this study. Patients were eligible for CRT implantation according to ACCF/AHA guidelines for managing heart failure [5]. All patients consented written consent forms for participation.

2.2. Exclusion criteria

Patients with recent myocardial infarction of less than 3 month duration or dysrhythmias that could result in gating artifacts.

2.3. Echocardiographic examination

Each patient was examined using Phillips ATL-HDI 5000 colored echocardiograph machine, with a 2.5–3 MHz transducer. Two-dimensional and M-mode echocardiography was performed to document volumetric LV measurements. Left ventricle contractility was assessed using Simpson's method.

2.3.1. Rest myocardial perfusion imaging (Gated SPECT)

Patients were intravenously injected with 20-25 mCi Tc-99m SestaMIBI. Acquisition of SPECT images was performed within 1 h of the injection of the Tc-99m SestaMIBI

Abbreviation: CMR, cardiac magnetic resonance; CRT, cardiac resynchronization therapy; LV, left ventricle; HF, heart failure; H., histogram; BW, bandwidth; SD, standard deviation; SRS, summed rest score; DCM, dilated cardiomyopathy; ICM, ischemic cardiomyopathy; ICC, intraclass correlation; No., number; LVES, left ventricular end-systolic volume; ACCF/AHA, American College of Cardiology/American Heart Association.

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using dual head Siemens gamma camera (Symbia E) utilizing Cedars-Sinai software 1994-2009. Analysis of Gated SPECT images was performed using Syngo MI VA60A workstation (QGS, QPS, and phase analysis).

Images were gated to the R-wave of the ECG, and image acquisition was interrupted for one beat if the R-R interval varied by 15% of the preceding R-R interval. Thirty-two views with 20 seconds each, over 180° arc, with the patient in the supine position head-in. Processing and filtering of the SPECT images were done using back- projection technique.

The seventeen segment model was used for quantitative analysis of radioactive tracer uptake. Segments were scored visually according to tracer uptake defect percentage into five categories (**0**: No tracer uptake defect; **1**: 0-25% tracer uptake defect; **2**: 25-50% tracer uptake defect; **3**: 50-75% tracer uptake defect; **4**: 75-100% tracer uptake defect). The highest attainable score is 68. **SPECT scar burden** was calculated by summing all segment scores; SRS and dividing SRS by 68. All images were interpreted by a consensus of 2 nuclear cardiology readers and controversial issues were judged by a senior nuclear cardiologist.

2.3.2. Phase analysis of Gated SPECT

Throughout the cardiac cycle, amplitude and phase of systolic wall thickening were extracted from the regional LV count changes. The analysis used first-harmonic fast Fourier transform to approximate the wall thickening data to calculate a phase angle for each region [15]. Histograms of the calculated phase arrays were obtained and the following quantitative indices were calculated from each phase array: ***histogram bandwidth***: includes 95% of the elements of the phase distribution in degrees and ***histogram standard deviation***: is the SD of the phase distribution in degrees.

2.4. Cardiac magnetic resonance

A Philips Achieva (1.5 T) superconducting magnet (Netherlands) was used in the Radiology Department, Kasr Al Ainy Hospitals. Patients were positioned in a supine position, and images were acquired during breath-holds of approximately 15 seconds. The heart was imaged in the 4 chambers, 2 chambers, LVOT and short-axis views using a sensitivity encoding, balanced, fast-field echo sequence. Contrast-enhanced images were acquired 17 to 19 min after bolus injection of gadolinium diethylenetriamine penta-acetetic acid (Magnevist, Shering/Berlex, Berlin, Germany; 0.15 mmol/kg) with an inversion-recovery gradient sequence; inversion time was determined using a lock locker scan plan. The following parameters were applied: 300 ∗ 300 mm^2 field of view, 8-mm slice thickness, slice gap of -5 mm, 15° flip angle, echo time of 1.36 ms, and 4.53-ms repetition time. Contrast-enhancement images were scored visually, using the 17-segment model. Analysis of CMR images was performed using extended MR WorkSpace eXplore release workstation. Determination of the presence of late gadolinium enhancement was done by visually reviewing all contrast-enhanced images. Segments were scored visually according to whole wall scar percentage in five categories (**0**: no scar; **1**: 0-25% scar; **2**: 25-50% scar; **3**: 50-75% scar; **4**: 75-100% scar). ***CMR scar burden*** was calculated by summing CMR scar score and dividing CMR scar score by 68. ***CMR lateral wall scar burden*** was calculated by summing CMR scar score of 5 segments, comprising lateral wall (lateral, mid anterolateral, mid inferolateral, basal anterolateral, basal inferolateral segments), and dividing by 20. All images were interpreted by a consensus of 2 cardiac MRI readers and controversial issues were judged by a senior CMR reader.

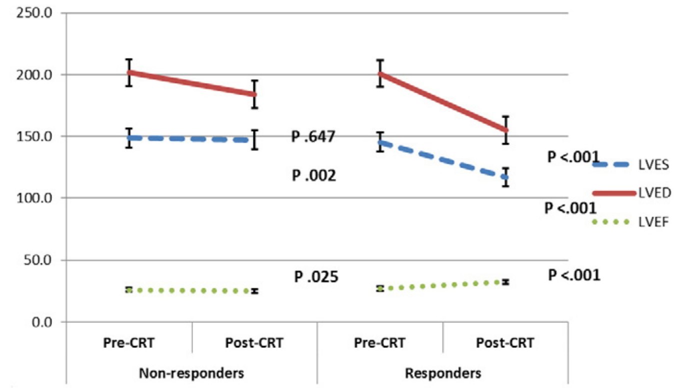

Fig. 1. Temporal changes in LV volumes & contractility in both responders and non-responders (pre- and post-CRT implantation by TTE). The solid line represents LVED, the dashed line represents LVES and the dotted line represents LVEF.

2.5. Pacemaker implantation

CRT-P/D devices were implanted in the left infraclavicular region. The left ventricular lead was inserted via the coronary sinus, targeting lateral wall pacing, discerned by the operator. Operators were blinded to cardiac MRI and Gated SPECT data, regarding LV scar assessment.

2.6. Follow-up period

After 6 months, all patients were subjected to transthoracic echocardiography (TTE) to document delta change in LVES. Also Gated SPECT was done to document temporal changes in phase parameters. The response was stated as a change of at least 15% decrease of LVES from initial baseline measurements i.e. reverse LV remodeling.

3. Statistical analysis

Numerical variables were described as mean ± SD. Categorical variables were described as percentages. Comparisons were done using Student "t" test for numerical variables, paired "t" test for paired comparisons and Chi-square test for categorical variables. For correlations, P values and r values (correlation coefficients) were stated. ROC curves were plotted to determine cutoff values of LV scar to predict CRT outcome. Bland-Altman analysis was done for comparing Gated SPECT & CMR for LV scar examination. P was considered significant if

Table 1
Comparison of demographic data between responders and non-responders.

All patients	Responders	Non-responders	P
Age	55.3 ± 10.6	57.7 ± 9.8	NS[a]
Gender (female)	5 (26.3%)	1 (9.1%)	NS
Diabetes	5 (26.3%)	6 (54.5%)	NS
Smoking	11(57.9%)	7 (63.6%)	NS
Hypertension	8 (42.1%)	9 (81.8%)	NS
ICM	12 (63.2%)	9 (81.8%)	NS
LBBB pattern	6 (31.6%)	-	-
Pre-CRT QRS duration	144.2 ± 12.6	147.3 ± 11.9	NS
Post-CRT QRS duration	131.1 ± 18.2	145.5 ± 16.3	**.039**
Baseline LVES	145.4 ± 18.2	148.6 ± 21.1	NS
Follow-up LVES	116.9 ± 16.4	147.3 ± 22.1	<**.001**
LVES delta change	19.7 ± 3.5%	0.8 ± 6.3%	<**.001**
QRS duration delta change	9.3 ± 8.1%	1.2 ± 7.9%	**.013**
Histogram BW delta change	31.7 ± 4.8%	23.6 ± 3.9%	<**.001**
Histogram SD delta change	29.8 ± 6.1%	18.2 ± 6.3%	<**.001**

[a] NS: non-significant.

Table 2
Paired comparison for LVES in both responders and non-responders.

LVES	Pre-CRT	Post-CRT	P
Non-responders	148.6 ± 21.1	147.3 ± 22.1	NS
Responders	145.4 ± 18.2	116.9 ± 16.4	<**.001**

Table 3
Comparison between pre- and post-implantation cardiac imaging.

Gated SPECT		Responders	Non-responders	P
Pre-implantation	Histogram BW	150.7 ± 24.8	174.1 ± 32.2	**.034**
	Histogram SD	53.8 ± 9.1	61.9 ± 10.0	**.033**
Post-implantation	Histogram BW	102.8 ± 18.1	132.6 ± 22.7	<**.001**
	Histogram SD	37.6 ± 6.0	50.6 ± 9.1	**.001**

Table 4
Paired comparison between pre- and post-implantation cardiac imaging.

Gated SPECT		Pre-CRT	Post-CRT	P
All patients	Histogram BW	159.3 ± 29.5	113.7 ± 24.4	<**.001**
	Histogram SD	56.8 ± 10.1	42.4 ± 9.6	<**.001**
Non-responders	Histogram BW	174.1 ± 32.2	132.6 ± 22.7	<**.001**
	Histogram SD	61.9 ± 10.0	50.6 ± 9.1	<**.001**
Responders	Histogram BW	150.7 ± 24.8	102.8 ± 18.1	<**.001**
	Histogram SD	53.8 ± 9.1	37.6 ± 6.0	<**.001**