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ORIGINAL ARTICLE

Reverse electric remodeling after cardiac resynchronization therapy and relation to clinical and echocardiographic outcomes

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Abstract *Background:* In heart failure, there are structural and electric changes that affect the long term prognosis. While structural remodeling could be reversed by cardiac resynchronization therapy (CRT), little is known regarding reverse electric remodeling and its relation to the response to CRT.

Objectives: To study the electric changes following CRT and their relation to patients' response.

Methods: Thirty patients with implanted CRT device were included. Echocardiograms and surface electrocardiograms (ECGs) done before CRT were retrospectively analyzed. At the time of enrollment, echocardiography and ECG (during setting the CRT to off mode) were done. QRS duration (QRSD), QT interval, QTc interval, QT dispersion (QTd), and T wave peak to end (TPE) interval were measured.

Results: Mean time since implantation was 15.26 ± 6 months. QRSD decreased from 146.33 ± 16.29 to 134.33 ± 17.15 ms ($p < 0.001$). QT interval decreased from 420.33 ± 28.46 to 398.66 ± 21.29 ms ($p < 0.001$). QTc interval decreased from 505.66 ± 45.53 to 475.23 ± 31.08 ms

Abbreviations: HF, heart failure; CRT, cardiac resynchronization therapy; LV, left ventricle; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume; DCM, dilated cardiomyopathy; ICM, ischemic cardiomyopathy; QRSD, QRS duration; QTc, corrected QT; QTd, QT dispersion; TPE, T wave peak to end interval; VT, ventricular tachycardia; LBBB, left bundle branch block; SCD, sudden cardiac death.

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($p < 0.001$). QTd decreased from 58 ± 13.23 to 34.66 ± 13.82 ms ($p < 0.001$). TPE interval decreased from 124 ± 24.3 to 102 ± 22.5 ms ($p < 0.001$). Responders to CRT (19 patients, 63.3%) had larger ΔQRSD, ΔQTd, and ΔTPE than non responders ($p = 0.002$, 0.002, and 0.004, respectively). Cutoff values of −20 ms for each of ΔQRSD, ΔQTd, and ΔTPE could predict response to CRT with odds ratio (95% CI) of 4.05 (1.12–14.6), 2.75 (1.25–6), and 4.43 (1.21–15.5), respectively. *Conclusions:* CRT induced reverse electric remodeling affecting both depolarization and repolarization parameters on surface ECG. Reverse electric remodeling was associated with favorable clinical and echocardiographic outcomes.

1. Introduction

Heart failure (HF) is associated with hemodynamic and neurohormonal abnormalities that result in structural and electric remodeling. Structural remodeling has been reversed by cardiac resynchronization therapy (CRT) in association with a decrease in NYHA class and increase in the left ventricular ejection fraction (LVEF). Reduction in LVESV by ⩾15% after CRT has been considered the most powerful parameter that predicts long term mortality and morbidity.[1–3]

In association with structural remodeling in HF, there is interventricular or intraventricular conduction delay that leads to mechanical dyssynchrony and more worsening of HF. There are also several changes in ion channel dynamics that result in spatial and transmural prolongation and heterogeneity of repolarization, which provide substrate for ventricular arrhythmias and sudden cardiac death.[4,5] Since structural remodeling was reversed by CRT, electric remodeling might be also reversed in concordance with the favorable clinical course of HF patients following CRT. There are little data available regarding the post-CRT recovery of the adverse electric changes affecting ventricular conduction and repolarization, and its relation to clinical and echocardiographic outcomes.

2. Methods

Thirty patients with implanted CRT device were enrolled in the study during routine hospital visits for device programming in the Ain Shams University and Kobri-ElKobba Military hospital clinics. All patients had CRT-P devices (St. Jude) and were assessed at least 6 months after implantation. Indications of CRT were LVEF ⩽35% with NYHA class III or IV while on optimal medical therapy, and QRS complex duration of ⩾120 ms. All patients were in sinus rhythm. Transthoracic echocardiograms and surface ECGs done before CRT were retrospectively analyzed. At the time of enrollment, new transthoracic echocardiogram and 12-lead surface ECG were done. The post-CRT ECGs were done during device programming while setting CRT to off mode to acquire unpaced electrocardiograms. Device programming was done to assess lead impedances, pacing and sensing thresholds. Patients with no intrinsic rhythm, device malfunction, or receiving antiarrhythmic drugs were not included in the study.

2.1. Echocardiography

Left ventricular dimensions were measured by the M-mode in short axis parasternal view. LVEF was calculated by the M-mode in case of dilated cardiomyopathy and by 2D (modified Simpson's equation) in case of ischemic cardiomyopathy. LV end-diastolic and end-systolic volumes were calculated.

2.2. Definition of CRT response

Response to CRT was defined as both clinical response (improvement of NYHA class by ⩾1) and echocardiographic response (defined as an absolute increase in LVEF by ⩾10% and/or decrease in LV end systolic volume by ⩾15%).[1–3]

2.3. ECG acquisition and analysis

Standard 12-lead surface ECGs with a paper speed of 25 mm/s and 10 mm/mV gain were analyzed prior to and at least 6 months after implantation while setting the device to CRT-off mode. Biventricular pacing was restored after acquiring the ECGs. Measurements were assessed manually and taken from the average of 2 measurements made by 2 cardiologists who were blinded to each other's measurements and to patients' data. The following measurements were taken:

- RR interval.
- Intrinsic QRS duration (QRSD).
- QT interval measured from the beginning of QRS to the end of the T wave defined as the point of return to the isoelectric line. QTc interval was calculated by Bazett's formula[6] (QTc = QT/square root of RR interval in seconds). Intervals were measured in the lead with the highest T wave amplitude among leads II, V5, or V6, using the same lead in pre and post-CRT measurements.
- QT dispersion (QTd), defined as the difference between the longest and shortest QT interval among all ECG leads.
- T wave peak to end (TPE) interval, defined as the duration from the peak to the end of the T wave in II, V5, or V6 according to the highest T wave amplitude, using the same lead in pre and post-CRT measurements.
- ΔQRSD, ΔQT, ΔQTc, ΔQTd, and ΔTPE are the differences between baseline values and post-CRT values.

2.4. Statistical analysis

Statistical Package for Social Sciences (SPSS version 15.0) was used. Categorical data were expressed as frequencies and percentages, while continuous data were expressed as mean ± SD or median according to data distribution. D'Agostino-Pearson test for normal distribution was done and accordingly, non parametric test was used when distribution was non-normal.