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Original Article

Assessment of right ventriclular systolic function prior to cardiac resynchronization therapy: Does it make any difference?

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ABSTRACT

Background: Cardiac resynchronization therapy (CRT) is an effective treatment for patients with advanced heart failure (HF). Nearly 30% of candidates are inadequate responders. The benefit of patients with right sided heart failure from CRT is still a matter of debate. We examined the effect of CRT on right ventricular (RV) dimensions and overall systolic function and whether RV function prior to CRT could have an impact on CRT response.

Methods: 94 patients with a mean age of 53.7 ± 14.6 years including 19 (20%) females, with advanced HF (EF < 35%, LBBB > 120 ms, or non-LBBB > 150 ms, with NYHA –III or ambulatory class IV) were enrolled and underwent CRT implantation. Standard two dimensional (2D) echocardiography, tissue Doppler imaging, for assessment of Left ventricular (LV) end-diastolic (LVEDV), and end-systolic volumes (LVESV), ejection fraction, RV maximum basal (RVD basal), maximum mid (RVD mid) transverse, maximum longitudinal (RVD long) diameters, TAPSE, fractional area change (FAC), and tricuspid lateral annular systolic velocity (S′), in addition to RV global longitudinal strain (RVGLS) measured by speckle tracking echocardiography, were done before CRT implantation and at the end of the follow up period (5.9 ± 1.2 months). Patients presenting with reductions of LVESV of >15% were termed volumetric responders for further statistical analysis.

Results: 63 (67%) cases were volumetric responders. Both groups were matched regarding demographic, clinical, ECG, and echocardiographic criteria apart from the RV significantly smaller transverse diameters and significantly better systolic function parameters in the responders group prior to CRT compared to non-responders (NR) group. At the end of the follow up, only the responders group had further significant reduction in RV basal, mid and longitudinal diameters (33.6 ± 7.1 vs 40.7 ± 8.6, 21.4 ± 4.9 vs 27 ± 6.1, 68.3 ± 10.8 vs 81.2 ± 15, respectively), $p < 0.01$, together with significant improvement in RV systolic performance: FAC (47.7 ± 7.3 vs 40.9 ± 6.4), TAPSE (25.2 ± 4.6 vs 22.1 ± 4.9), S′ (15.3 ± 2.3 vs 12.8 ± 2.3), and GLS (26.1 ± 2.1 vs 18.5 ± 1.6), $P < 0.01$, compared to baseline readings. S' and GLS were the only independent predictors of CRT response by multivariate analysis. S′ >9 cm/s, and GLS >12.45% had 100% sensitivity and 70%, 99.7% specificity, respectively for prediction of response to CRT.

Conclusions: CRT induces RV reverse remodeling and improves RV systolic function particularly in cardiac volumetric responders. RV systolic dysfunction before CRT implantation could identify patients that might not benefit from CRT thus helping proper patient selection and optimizing CRT response.

1. Introduction

Heart failure (HF) prevalence is rising throughout the world. Approximately 1–2% of the adult population in developed countries has HF, with the prevalence rising to ≥10% among persons 70 years of age or older.[1]

Cardiac resynchronization therapy (CRT) is an established treatment of drug-refractory heart failure and left ventricular (LV) mechanical dys-synchrony. In addition to the clinical benefits, improvement of LV systolic function and associated LV reverse remodeling had been reported, however nearly 30% of potential CRT candidates are inadequate responders.[2,3]

The right ventricle (RV) plays an important role in the morbidity and mortality of patients presenting with signs and symptoms of heart failure. The benefit of patients with right sided heart failure from CRT is a matter of debate. However, the systematic assessment of right heart function prior to CRT is not uniformly carried out, partly due to the attention given to the evaluation of the left heart, non-familiar ultrasound techniques used in imaging

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the right heart, and rarity of ultrasound studies providing reference values of right heart size and function.[3,4] RV global longitudinal strain (RVGLS) measured by 2D speckle tracking echocardiography being less angle and load dependent than traditional RV function indices, could offer additional value for RV function assessment.[4]

We examined the effect of CRT on RV dimensions and overall systolic function and whether RV function prior to CRT could have an impact on CRT response.

2. Methods

2.1. Study population

94 consecutive patients representing a convenient sample from the pool of patients presenting to the heart failure clinic at Ain Shams University hospitals, during the period from march 2015 to march 2016, and meeting inclusion criteria (symptomatic heart failure despite optimal medical therapy, NYHA class III or ambulatory class IV, ejection fraction $\leq 35\%$, sinus rhythm, LBBB with QRS ≥ 120 ms, or non LBBB with QRS ≥ 150 ms) were enrolled in the current study. Poorly echogenic patients, and those with decompensated NYHA class IV, rheumatic or congenital heart diseases, and sustained atrial arrhythmias, were excluded.

2.2. Methodology

Detailed history (illness duration, NYHA class, hospital admissions, previous revascularization, latest medical therapy, Minnesota living with heart failure questionnaire: MLHFQ), clinical examination, 12 lead ECG (QRs morphology and duration), and six minute walk test[5] (the distance in meters an individual was able to walk on a hard, flat surface with self-pacing and rest as needed), were done in all cases.

MLHFQ was translated into Arabic and included 21 questions. Scoring of the questionnaire was done by summating the responses to all 21 questions where each question was scaled from 0 (no effect on quality of life [QOL]), to 5 (highest impact on QOL) where higher scores reflected poorer QOL.[6]

2.3. Echocardiography

Baseline echocardiographic examination was performed using a standard commercial ultrasound machine with a 2.5 MHz transducer and repeated after 6 months. Examinations were made by the same operator to minimize inter-observer variability.

2.4. LV assessment

Standard M-mode, 2D echocardiographic views, and Doppler examination were used to assess LV end-diastolic diameter (EDD), end-systolic diameter (ESD), 2D ejection fraction (EF) by modified Simpson's method, end-diastolic volume (EDV), end-systolic volume (ESV), mitral E and A velocities (diastolic function).

Patients presenting with reductions of LVESV >15% at the end of the follow up period were termed volumetric responders for further statistical analysis.

2.5. RV assessment

Maximum transverse diameter at the RV base and mid-level (2 cm below the tricuspid valve), and maximum longitudinal dimension were measured at the end-diastole in RV focused apical 4 chamber view. Values >42, 35, 86 mm respectively indicated RV dilatation.[4]

In apical 4 chamber view, RV systolic function was assessed by measuring the distance of systolic excursion of the RV annular segment along its longitudinal plane (TAPSE) and RV fractional area change (FAC) which is calculated as (end-diastolic area – end-systolic area)/end-diastolic area X 100). TAPSE <16 mm and FAC $<35\%$ indicated RV dysfunction. In addition, tricuspid lateral annular systolic velocity (S′), was obtained by tissue Doppler imaging where measurements <10 cm/s indicated RV dysfunction. Finally, RV systolic pressure (RVSP) was calculated using the simplified Bernoulli equation.[4]

RV 2D global longitudinal strain (RVGLS): RV endocardial border was manually traced by a point and click approach in 4 chamber view. An epicardial surface tracing was automatically generated by the system creating a region of interest. The software divided the RV endocardium into 7 segments (basal RV free wall, mid RV free wall, apical RV free wall, apex, apical septum, mid septum, and basal septum) and calculated average for 7 RV segments. The images taken for 2D strain were digitized and analyzed offline using EchoPAC-PC version BT12, application SW 112 (GE Healthcare, Milwaukee, WI).

2.6. CRT implantation

All implantations were done via percutaneous transvenous (subclavian) approach. The LV pacing lead was inserted targeting the lateral or postero-lateral cardiac vein, achieving a stable LV lead position in mid LV segment with suitable threshold and absence of diaphragmatic stimulation.

All patients gave a written informed consent and the study was approved by the Research and Ethics Committee of the cardiology department, faculty of medicine, Ain Shams University.

2.7. Statistics

Data were collected, coded, tabulated, and then analyzed using SPSS version 19 for Windows (SPSS Inc, Chicago, IL, USA). Data were presented as mean (standard deviation) and frequency (%) for numerical variables and categorical variables respectively. Comparisons were performed using Paired T test and Mann-Whitney test for paired data and comparing the percentage of changes. Categorical variables were compared using Chi square test. Multivariate stepwise logistic regression analysis was used to identify predictors of CRT response (reverse remodeling). Receiver operating characteristics (ROC) curve analysis was done to find the impact of different echocardiographic parameters on response to CRT. Cutoff values were selected if area under the curve (AUC) was significantly different from 0.5. A P value <0.05 was considered statistically significant.

3. Results

The current study included 94 cases: 75 males, 19 females (20%) with a mean age of 53.7 ± 14.6 years. All patients had successful CRT implantation via transvenous left subclavian access targeting postero-lateral vein in 66 (70.2%) cases, lateral vein in 18 (19%) cases, and posterior vein in the remaining 10 cases. The RV lead tip was placed in the apex and the RA lead in RA appendage.

CRT resulted in significant improvement in NYHA class, QRS duration, MLHHQ, LVESV and EF, together with significant reduction in RV basal and longitudinal diameters and significant improvement in RV systolic function, compared to baseline irrespective of HF etiology whether dilated 59 (62.7%), or ischemic (Table 1).

At the end of the follow up period, 63 (67%) cases of the study population were termed volumetric responders according to pre-specified criteria, while the remaining 31 cases were termed non-responders (NR) for further statistical analysis. Both groups were matched regarding demographic, clinical, ECG, and

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