Original Article

Response to Cardiac Resynchronization Therapy in Cardiomyopathy Patients with Right Bundle Branch Block

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Received 22 August 2022; Accepted 14 December 2023

Abstract

Background: *The use of cardiac resynchronization therapy (CRT) in heart failure patients with right bundle branch block (RBBB) is under debate. We present early and late echocardiographic characteristics of a series of heart failure patients with RBBB who underwent CRT.*

Methods: *In this retrospective descriptive study, 18 patients with RBBB in the surface electrocardiogram underwent CRT between 2005 and 2015. All the patients had the New York Heart Association functional class III/IV, a left ventricular ejection fraction (LVEF) ≤35%, and a QRS duration ≥120 milliseconds. The median follow-up duration was 19 months. The echocardiographic response was based on a ≥5% increase in LVEF.*

Results: *Within 48 hours after CRT implantation, LVEF increased from 24.58%±7.08% before to 28.46±8.91% after CRT (P=0.005) and to 30.00±9.44% at follow-up (P=0.008). Among the 18 patients, 12 (66.7%) were responders within 48 hours after CRT. The following baseline echocardiographic parameters were higher in the responders than in those without an increased LVEF, although the difference did not reach statistical significance: septal-to-lateral wall delay (48.33±33.53 vs 43.33±38.82 ms), anteroseptal-to-posterior wall delay (41.7±1.75 vs 38.33±18.35 ms), and interventricular mechanical delay (48.50±21.13 vs 31.17±19.93 ms). The mean QRS duration was higher in the responders than in the non-responders (183.58±40.69 vs 169.00±27.36 ms). Death was reported in 3 out of the 18 patients (16.7%) at follow-up. The 3 deceased patients had a higher baseline interventricular mechanical delay than those who survived.*

Conclusion: *Our results indicated that patients with RBBB might benefit from CRT. Further, patients with higher intra and interventricular dyssynchrony and a wider QRS may show better responses.*

J Teh Univ Heart Ctr 2023;18(2):109-114

This paper should be cited as: Zand S, Sadeghian H, Kazemisaid A, Lotfi-Tokaldany M, Jalali A, Sardari A. Response to Cardiac Resynchronization Therapy in Cardiomyopathy Patients with Right Bundle Branch Block. J Teh Univ Heart Ctr 2023;18(2):109-114.

Keywords: *Cardiac resynchronization therapy; Right bundle branch block; Cardiomyopathies*

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Introduction

Introduction

Cardiac resynchronization therapy (CRT) device implantation in heart failure patients with right bundle branch block (RBBB) is controversial. According to the guidelines of the European Society of Cardiology in 2013, the use of CRT in heart failure patients with a left ventricular ejection fraction (LVEF) ≤35% and the New York Heart Association (NYHA) functional class II, III, and IV but without left bundle branch block (non-LBBB) is class IIa in patients with a QRS >150 milliseconds and class IIb in patients with a QRS between 120 and 150 milliseconds. Nonetheless, the use of CRT in heart failure patients with RBBB should be individualized based on other imaging or clinical criteria.[1] According to the guidelines of the American Heart Association, the use of CRT for non-LBBB heart failure patients with the NYHA functional classes III and IV and an LVEF ≤35% is class IIa if QRS is ≥150 milliseconds and class IIb if QRS ranges between 120 and 149 milliseconds, while there is no benefit for CRT in RBBB heart failure patients with a QRS <150 milliseconds.[2] Moreover, the results from the RAFT trial showed a weak interaction between QRS morphology and the benefit of CRT.[3]

The rate of CRT use in heart failure patients with RBBB is between 5% and 26% in large studies.[4] Some investigations have shown no clinical benefits of CRT in patients with RBBB and even worse survival and higher mortality compared with LBBB patients receiving CRT.[5, 6]

In this report, we present the clinical and echocardiographic characteristics of a series of heart failure patients with RBBB who underwent CRT. We also describe early and late responses to CRT concerning the baseline echocardiographic markers of dyssynchrony.

Methods

The present investigation is a retrospective descriptive study. Between January 2005 and March 2015, a total of 179 patients with heart failure symptoms underwent CRT in our catheterization laboratory. The patients were candidates for CRT according to the following criteria: an LVEF ≤35%, the NYHA functional class III or IV, and a QRS duration >120 milliseconds.

After the evaluation of QRS morphology, 18 patients (10%) had RBBB, defined as a QRS>120 milliseconds, a prominent and notched R wave recorded by the right precordial leads, and a wide S wave recorded by the left precordial, I, and aVL leads wider than the preceding R waves.[7]

All the patients had an echocardiographic measurement of LVEF before and within 48 hours after CRT implantation. Another measurement of LVEF was taken after 24 to 26 months. Tissue Doppler echocardiography was also performed for all the patients before CRT. Dyssynchrony indices were measured. Improvements in LVEF within 48 hours following CRT and at follow-up were evaluated. The echocardiographic response was defined as a ≥5% increase in LVEF. Moreover, the clinical outcome after a mean follow-up of 24.42±18.7 months was described. This study complies with the Declaration of Helsinki, and all the subjects signed an informed consent form to permit the researchers in the hospital to use their data for research purposes.

Standard 2D and M-mode echocardiographic data were acquired with a commercially available digital ultrasound machine (VIVID 7, Vingmed-General Electric, Horten, Norway) using a 3.5 MHz phased array Transducer. Measurements were performed for left ventricular end-systolic volume (LVESV), LV end-diastolic volume, LV end-systolic diameter, LV end-diastolic diameter, and other parameters according to the published echocardiography guidelines. LVEF was assessed via the biplane Simpson rule. The regurgitation severity of the mitral and tricuspid valves was graded as mild, moderate, and severe using the guidelines of the American Society of Echocardiography.[8] The opening and closing times of the aortic and pulmonic valves were also measured using the systolic blood flow by pulsed Doppler, with the sample volume placed at the level of the aortic and pulmonic annulus. Interventricular mechanical delay (IVMD) was defined as the difference between the aortic and pulmonary pre-ejection times. Septal-to-posterior wall motion delay was also obtained using an M-mode recording from the parasternal long-axis view.[9,10]

The time-to-peak myocardial systolic velocity of 6 basal and 6 middle LV segments was measured using tissue velocity imaging under the guidance of tissue synchronization imaging in 4-, 3-, and 2-chamber apical views. Gain and filters were adjusted whenever needed to eliminate background noise and allow for a clear spectral display. The measurements were recorded at a sweep speed of 100 mm/s and were digitally stored. Three consecutive beats for patients with normal sinus rhythm and 10 cycles for patients with atrial fibrillation were saved and analyzed offline, and the results were averaged. The definitions of all the measured indices by tissue Doppler echocardiography can be found in previous studies.[11,12] The following indices (as LV dyssynchrony markers) were calculated: all segments delay, basal segments delay, all segments standard deviation (SD), basal segments SD, septal-to-lateral delay, and anteroseptal-to-posterior delay. Inter and intraobserver variability of time-to-peak myocardial systolic velocity and LVESV was measured in our previous studies.[9-12]

After the preparation of the patients for the procedure, 3 different access points were used for lead implantation. The right ventricular (RV) lead was implanted first because of transient complete heart block risks during implantation, which may occur during lead manipulation. If the RV apical region showed a high threshold or any instability (electrically or mechanically), the RV septum was chosen as the second position of interest. After complete coronary sinus angiography, a bipolar LV lead was implanted. All the LV leads were placed percutaneously under fluoroscopic guidance through the coronary sinus. Lateral or posterolateral cardiac veins were preferentially targeted, with alternative positions dictated by anatomy. The LV lead was checked several times by different outputs for phrenic nerve stimulation, and if it did happen, the position was changed. Finally, the atrial lead was positioned in the right atrial appendix if the appendix showed a high output or any sign of far-field potential changed to the right atrial free wall. The implanted devices were Medtronic, St Jude, and Boston Scientific.[9]

Empiric "out-of-the-box" atrioventricular (AV) delay device settings of approximately 100 to 130 milliseconds for CRT were used. Additionally, V-V optimization was performed using device-based algorithms, with the LV and RV activated synchronously or the LV activated before the RV up to 40 milliseconds. Echocardiography was performed over 48 hours after CRT implantation, and the echocardiographic-based optimization of AV and V-V delays was undertaken[13] if there were any of the following conditions:

1) the presence of A wave truncation, 2) E and A waves not clearly identified and separated (in normal sinus rhythm patients), 3) IVMD by pulsed-wave Doppler ≥40 milliseconds; 4) any worsening of the functional class, and 5) <5% improvements in LVEF.

Continuous variables are presented as mean±standard deviation (SD) and categorical variables as frequencies and percentages. Before-and-after comparisons for LVEF and LVESV were tested using the Mann–Whitney *U* test. All P values ≤0.05 were considered statistically significant. The analyses were conducted using the statistical software package (SPSS for Windows, version 17, SPSS Inc, Chicago, Illinois, USA).

Results

Among 179 patients who underwent CRT, 18 (10%) had RBBB. Table 1 demonstrates the characteristics of the 18 patients with RBBB. The mean age of the patients was 59.11±8.53 years, ranging between 38 and 72 years. Ischemia was the underlying cause of cardiomyopathy in 9 patients (50%), with 22.2% having a history of coronary artery bypass graft surgery. The remaining half of the participants had dilated cardiomyopathy. QRS duration was ≥150 milliseconds in 14 patients (77.78%) and <150 milliseconds in 4.

Table 1. Baseline demographic, clinical, and echocardiographic characteristics of the study population

	Patients (n=18)
Age (y)	59.11±8.53
Sex	
Male	11(61.7)
Female	7(38.9)
Type of Cardiomyopathy	
Ischemic	9 (50)
Dilated	9 (50)
Risk Factors	
Diabetes mellitus	5 (27.8)
Hypertension	2 (11.1)
Hyperlipidemia	3 (16.7)
Smoking	3 (16.7)
History of CABG	4 (22.2)
Atrial fibrillation	2 (11.1)
QRS duration, ms	178.72± 36.62
QRS≥ 150 ms	14(77.8)
Echocardiographic Findings	
Global EF	24.58±7.08
LVESV	146.17±68.75
LVEDV	194.94±72.12
Right ventricular diameter, mm	34.24±9.82
Left atrial diameter, mm	45.94±6.63
Mitral Regurgitation Grade	
Mild/Trivial	9 (50)
Moderate	5 (27.8)
Moderate to severe	2 (11.1)
Severe	1 (5.6)
Tricuspid Regurgitation Grade	
Mild/Trivial	11 (61.1)
Moderate	4 (22.2)
Moderate to severe	1 (5.6)
Severe	1 (5.6)
Right Ventricular Dysfunction	
Mild	6 (33.3)
Moderate	0
Severe	2 (11.1)

CABG, Coronary artery bypass graft; LVESV, Left ventricular end-systolic volume; LVEDV, Left ventricular end-diastolic volume

Within 48 hours after CRT implantation, global EF increased from 24.58%±7.08% to 28.46±8.91% (P=0.005). Among the 18 patients, 12 (66.7%) were responders (increased EF≥5%). Moderate or severe mitral regurgitation before CRT was reported in 8 patients, of whom 5 (62.5%) had at least a 1-grade improvement in the severity of mitral regurgitation. The different baseline dyssynchrony indices in RBBB patients with and without improvement in LVEF within 48 hours after CRT are presented in Table 2. Although nonsignificant, the responders showed higher values of septal-to-lateral wall delay, anteroseptal-to-posterior wall delay, and IVMD at baseline compared with

Table 2. Different baseline dyssynchrony indices in RBBB patients with and without improvement in LVEF within 48 hours after CRT

Dyssynchrony Marker, ms	Increased LVEF (n=12)	No Change in LVEF (n=6)	*P*
QRS duration	183.58±40.69	169.00±27.36	0.574
Dyssynchrony of all segments	106.67±36.52	123.33±99.73	0.738
Dyssynchrony of basal segment	85.00±34.25	101.67±73.05	0.814
SD-all,	36.76±12.58	38.22±27.76	0.851
SD-basal	33.25±12.53	37.32±25.12	0.779
Septal-to-lateral wall delay	48.33±33.53	43.33±38.82	0.571
Anteroseptal-to-posterior wall delay	49.17±31.75	38.33±18.35	0.478
Interventricular mechanical delay	48.50±21.13	31.17±19.93	0.133

RBBB, Right bundle branch block; LVEF, Left ventricular ejection fraction; CRT, Cardiac resynchronization therapy; SD-all, Standard deviation of the time-to-peak systolic velocity of all segments; SD-basal, Standard deviation of the time-to-peak systolic velocity of basal segments
P values were obtained using the Mann–Whitney U test.

Table 3. Baseline dyssynchrony indices in RBBB patients regarding the clinical outcome

Dyssynchrony Marker, ms	Mortality (n=3)	Surviving Patients (n=15)
QRS duration- before CRT	150.00±8.66	184.47±37.50
Dyssynchrony all segments	80.00±20.00	118.67±65.99
Dyssynchrony basal segments	63.33±23.09	96.00±51.38
SD-all	27.74±12.12	39.15±18.87
SD-basal	26.92±12.08	36.15±17.81
Septal-to-lateral wall delay	40.00±26.46	48.00±36.29
Anteroseptal-to-posterior wall delay	36.67±30.55	47.33±28.15
Interventricular mechanical delay	50.33±11.72	41.20±23.32

Values are reported in milliseconds.
RBBB, Right bundle branch block; CRT, Cardiac resynchronization therapy; SD-all, Standard deviation of the time-to-peak systolic velocity of all segments; SD-basal, Standard deviation of the time-to-peak systolic velocity of basal segments

the other patients. The mean QRS duration was longer in the responders than in the non-responders (187.55± 40.18 vs 163± 25.77 ms, respectively).

The small number of patients precluded sufficient comparisons to detect significant differences. Nevertheless, the baseline values of dyssynchrony markers for the responders and non-responders are presented in Table 2. A QRS duration≥ 150 milliseconds was seen in 10 responders (83.3%) and 4 non-responders (66.7%).

The median follow-up duration was 19 (25%, 75% percentile: 5.5, 43) months. Death was reported in 3 out of the18 patients (16.7%). Two of the deceased patients were in the responder group after CRT, and 1 of them did not have echocardiographic assessments before death. Therefore, compared with the baseline, LVEF increased from 24.71±7.28% before CRT to 30.00±9.44% at follow-up among 17 patients (P=0.008). All 11 patients who had an increased EF (≥5%) within 48 hours after CRT still had an increased LVEF at follow-up. Left ventricular end-systolic volume decreased from 146.20±68.70 mL before CRT to 142.80±84.10 mL at follow-up (P=0.937). In 4 out of the 5 patients who had improved mitral regurgitation severity early after CRT, this improvement remained the same at follow-up. The 3 deceased patients had an increased LVEF (≥5%) within 48 hours after CRT. Two had a QRS duration ≥150 milliseconds, and 1 had a QRS of 140 milliseconds. Table 3 demonstrates the baseline echocardiographic dyssynchrony markers in the dead and surviving patients.

Discussion

Among our study population, 66.7% had a ≥5% increase in LVEF early after CRT and had higher values of septal-to-lateral wall delay, anteroseptal-to-posterior wall delay, and IVMD at baseline compared with those without an increased LVEF. At follow-up, death was reported in 3 out of the 18 patients (16.7%); and in the group with an increased LVEF, values for the mean baseline QRS duration, anteroseptal-to-posterior wall delay, and IVMD were greater.

In line with previous investigations, our study yielded evidence supporting the notion that RBBB patients with a wider QRS and higher intra- and interventricular dyssynchrony have better outcomes after CRT implantation. Workhlu et al[5] reported that the NYHA functional class and LV functional improvement were less in patients with RBBB, and intraventricular conduction delay was shorter than in those with LBBB. They also observed that in a median follow-up of 2.6 years, patients with RBBB survived significantly less, and RBBB independently predicted death with a hazard ratio of 3.5 (P<0.001). Adelstein et al[6] showed that heart transplantation-free survival and symptomatic responses were best in LBBB and worst in RBBB patients, and echocardiographic responses also showed a similar trend. In the studies by Bilchick et al,[14, 15] RBBB and ischemic cardiomyopathy were the strongest predictors of early and late mortality, and a QRS ≥150 milliseconds had a favorable effect on the outcome of LBBB but not on RBBB patients.

Some studies have supported CRT in a subset of patients with RBBB. Garrigue et al16 reported the usefulness of CRT in reducing LV end-diastolic diameter, improving mitral regurgitation, and increasing the aortic velocity time integral in RBBB patients with LV mechanical dyssynchrony. In their study, 9 out of 12 patients with RBBB were responders and had longer septal-to-lateral wall delay according to tissue Doppler echocardiography.[16] Hara et al[17] concluded that patients with RBBB and greater LV mechanical dyssynchrony determined by radial strain showed a more favorable response to CRT.

The principal limitation of the present study is that it is a single-center experience, and data presented in this study were derived from a small number of RBBB patients, precluding an adequately powered statistical analysis for changes in the echocardiographic parameters and comparisons. Our study was performed during a considerable time interval (2005–2015), during which the criteria for CRT implantation changed.

Conclusion

According to this study, patients with RBBB who received CRT had improved LVEF and mitral regurgitation severity. Following CRT, we had some evidence that RBBB patients with greater intra- and interventricular dyssynchrony and a wider QRS duration might show a favorable response. Further studies with more RBBB patients are needed to determine the subgroup of RBBB patients who may benefit from CRT.

Acknowledgments

The authors appreciate the indefatigable staff in the Echocardiography Clinic of Tehran Heart Center for their kind assistance during data collection. This study was approved and supported by the Cardiovascular Diseases Research Institute at Tehran Heart Center, affiliated with Tehran University of Medical Sciences.

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