International Journal of Research in Medical Sciences
Roy B et al. Int J Res Med Sci. 2023 Oct;11(10):3667-3671
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20233016

Original Research Article

Respondent or non-respondent comparison post cardiac resynchronisation therapy implantation in patients with dilated cardiomyopathy

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Received: 05 September 2023
Revised: 19 September 2023
Accepted: 20 September 2023

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ABSTRACT

Background: Dilated cardiomyopathy can be treated using cardiac resynchronisation therapy (CRT) effectively. In our study, we compared the clinical and biochemical profile of responders and non-responders to CRT device (CRTD) implantation suffering from DCM.
Methods: A cross-sectional observational study was performed in 47 patients with dilated cardiomyopathy for CRTD implantation for a period of 18 months. The tools used for the study include electrocardiography 12 lead, echocardiography: 2D, M mode, Doppler, strain echo, Holter monitoring, coronary angiography and CRTD implantation. Statistical analysis was performed using Epi Info (TM) 7.2.2.2.
Results: The proportion of responders (68.1%) was significantly higher than non-responder (31.9%). Almost 60% of patients in non-responder group had smoking as a risk factor. Around 60% were suffering from hypertension and 33% from T2DM in non-respondent group. Parameters of dyssynchrony has significantly improved in responder group than in non-responder group. LVEDV, LVESV has shown an increase and EF has decreased considerably in DCM patients. Many patients in non-responder category have shown mitral and tricuspid regurgitation. Strain echocardiography parameters-GLS, GRS and GCS were significantly decreased. Post CRTD echocardiographic parameter has improved considerably and LVESV was reduced in more than 15% of responders.
Conclusions: The CRTD implantation improves patients' clinical and Echocardiographic data which can help in better patient management, improving quality of life and decreased healthcare cost. By this study we can improve patients' selection and predict accordingly for CRT responders and non-responders and can take necessary measures for better patient's management.

Keywords: Respondent, Non-respondent, Post CRT, Dilated cardiomyopathy

INTRODUCTION

Cardiomyopathies are among the important causes of heart failure (HF) and dilated cardiomyopathy (DCM) characterized by dilatation and impaired contraction, or systolic dysfunction of the left and sometimes right ventricle is the most common type responsible for more 10,000 deaths every year.[1] The typical symptoms are ventricular (LV) heart failure (i.e., dyspnoea on exertion, impaired exercise tolerance, orthopnoea, paroxysmal nocturnal dyspnoea, and peripheral oedema) accompanied by swelling of ankles and abdominal bloating.[2-4]

DCM can be effectively treated using CRT where the suitable patient selection is aided by echocardiography.

dysfunction, and mechanical dyssynchrony, routinely identified by electrocardiography (ECG) as abnormal electrical activation.[5,6] CRT devices can modify the electrical activation patterns of the ventricles and result in improvements in both intra-ventricular and inter-ventricular synchrony, in turn leading to an improvement in overall hemodynamic function.[7]

The major mechanism of action of CRT is believed to be reversal of the abnormal ventricular activation pattern seen in patients with LBBB conduction delay. Biventricular pacing results in the generation of two ventricular activation wavefronts, which result in a more normal pattern of ventricular activation.[8] However more than one-third of the patients with CRT implantation fail to achieve the expected results.[7] In this study, we have tried to compare the clinical and biochemical profile of responders and non-responders to crtd implantation suffering from DCM.

METHODS

A cross-sectional observational study was performed at IPGMER and SSKM Hospital Kolkata in patients (n=47) admitted with DCM for CRTD implantation for a period of 18 months from 1 January 2019 to 31 June 2020. The study population included adults (>18 years) diagnosed with DCM and fulfilled the criteria for and CRTD implantation. Individuals suffering from DCM but not a candidate for CRTD implantation and those unwilling to participate or give medical records for use of research purposes were excluded from the study. The tools used for the study include ECG 12 lead, echocardiography: 2D, M mode, Doppler, strain echo, Holter monitoring (24 hours monitoring), coronary angiography and CRTD implantation.

Statistical analysis

Statistical analysis was performed with help of Epi Info (TM) 7.2.2.2 EPI INFO is a trademark of the Centre for Disease Control and Prevention (CDC). Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (SD). Test of proportion was used to find the standard normal deviate (Z) to compare the difference proportions and Chi-square

CRT has had a major favourable impact on the care of patients with heart failure, left ventricular (LV) systolic

test was performed to find the associations. T-test was used to compare two means. P<0.05 was taken to be statistically significant.

RESULTS

A total of 47 individuals with mean age between 44 and 60 years were included in the study. Male to female ratio was 1:6 and all individuals experienced the symptom of dyspnoea on exertion (Table 1). Table 1 presents the baseline characteristics and symptoms of the study individuals. The proportion of responders (68.1%) was significantly higher than non-responder (31.9%).

Table 1: Baseline characteristics and clinical parameters of patients included in the study.

Demographics	Total
N	47
Age, in years (mean±SD)	52.3±8.8
Gender	
Male	29 (61.7)
Female	18 (38.3)
NYHA classification, N (%)	
Grade-II	11 (23.4)
Grade-III	36 (76.6)
Symptoms, N (%)	
Dyspnoea on exertion	47 (100)
Chest pain	6 (12.8)
Palpitations	32 (68.1)
Syncope	17 (36.2)
Anasarca	7 (14.9)
Pulse rate, mean±SD, in beats/minute	80.98±8.37
SBP, mean±SD, in mm Hg	112.94±13.20
DBP, mean±SD, in mm Hg	72.51±5.66
Chest examination-normal	47 (100)
CVD examination, presence of S3	6 (12.8)
Hepatomegaly	6 (12.8)
CNS findings, normal	47 (100)
Presence of pallor	21 (44.7)
Oedema	7 (14.9)

Table 2: Comparison between responders and non-responders of CRT.

Parameters	Responders (n=32)	Non-responders (n=15)	P value
Risk factors			
Smoking			
Present	14 (43.8)	9 (60.0)	0.299
Absent	18 (56.3)	6 (40.0)	
Hypertension			0.055
Present	9 (28.1)	9 (60.0)	

Continued.

Parameters	Responders (n=32)	Non-responders (n=15)	P value
Absent	23 (71.9)	6 (40.0)	
Type 2 diabetes mellitus			
Present	12 (37.5)	5 (33.3)	0.285
Absent	20 (62.5)	10 (66.7)	
ECG			
Rate	67.19±6.582	68.93±5.849	0.385
QRS duration	142.44±5.180	140.93±3.555	0.315
Echocardiography			
IVSD	7.34±0.602	7.07±0.458	0.121
LVPWD	7.56±0.504	7.47±0.516	0.550
LVIDD	53.81±1.908	58.60±2.849	<0.001S
LVIDS	42.78±2.324	48.73±3.494	<0.001S
LVEDV	190.41±7.991	200.53±16.634	0.007
LVESV	142.22±7.409	166.87±15.170	<0.001S
EF	25.19±1.768	17.53±1.407	<0.001S
MRVCW			
Absent	32	2	<0.001S
Mild	0	13	
Moderate	0	0	
MV A velocity	0.610±0.0886	0.640±0.1220	0.344
E wave DT	186.59±16.244	195.13±17.574	0.109
Diastolic dysfunction			
Absent	25 (78.1)	9 (60.0)	0.295
Grade I	7 (21.9)	6 (40.0)	
TR			
Absent	9 (28.1)	2 (13.3)	0.461
Present	23 (71.9)	13 (86.7)	
TAPSE	20.22±1.099	17.07±1.280	<0.001S
LA	32.50±2.476	38.20±2.210	<0.001S
ARD	26.69±2.442	28.40±2.324	0.028
LVEMD	131.69±3.306	150.47±4.357	<0.001S
IVD	33.53±3.282	48.73±3.918	<0.001S
GLS	-11.250±1.0749	-6.467±1.0293	<0.001S
GCS	-11.003±0.7381	-6.727±1.0532	<0.001S
GRS	15.608±1.7236	10.354±1.185	<0.001S
SPWMD	32.97±15.079	145.13±3.523	<0.001S

Table 3: Comparison between treatment interventions in respondents and non-respondents.

Treatment	Total	Responders	Non-responders	P value
	N (%)	N (%)	N (%)	
Salt restriction+water restriction	46 (97.9)	31(96.9)	15(100.0)	0.489
Diuretics		32(100.0)	15(100.0)	-
ACEI/ARB	23 (48.9)	13(40.6)	10(66.7)	0.096
ARNI	24 (51.1)	19(59.4)	5(33.3)	0.096
Aldosterone antagonist		32(100.0)	15(100.0)	-
Beta blockers	41 (87.2)	29(90.6)	12(80.0)	0.309
SGLT2 inhibitors (gliflozins)	13 (27.7)	12(37.5)	1(6.7)	0.028
Oral hypoglycaemic agents	16 (34)	12(37.5)	4(26.7)	0.465
Insulin	6 (12.8)	6(18.8)	0(0.0)	0.157
IV Iron therapy	20 (42.6)	15(46.9)	5(33.3)	0.529

In our study, the non-responder group have 60% of the patients had smoking as a risk factor. Around 60% were suffering from hypertension and 33% from T2DM in non-respondent group.

The parameters of dyssynchrony have significantly improved in responder group than in non-responder group. There are significant changes in the echocardiographic parameter in dilated cardiomyopathy patients with dilatation of left ventricle, severe left ventricular systolic dysfunction, and diastolic dysfunction. LVEDV, LVESV has shown an increase and EF has decreased considerably. Many patients in the non-responder category have shown mitral and tricuspid regurgitation. Strain echocardiography parameter like GLS, GRS and GCS has all significantly decreased. Post CRTD echocardiographic parameter has improved considerably and LVESV has reduced in more than 15% in responders according to existing guidelines.

DISCUSSION

In our study, we found that the clinical and biochemical parameters of the responders of the CRTD implantation have improved significantly. In a study conducted by Naik et al in India, it was found that CRT treatment shows a significant improvement in the clinical conditions of the patients compared to other pharmacological interventions.[9] Particularly, the dyssynchrony parameters including SPWMD, LVEMD and IVD significantly improved after CRTD implantation.

LV longitudinal strain is predictor of reverse remodeling. The MADIT-CRT COHORT also supported that decreased average longitudinal strain predicts less beneficial effects of CRT, especially in the setting of LBBB.[10] Several studies reported baseline global longitudinal strain predicts LV reverse remodeling after CRT in patients with both ischemic and non-ischemic cardiomyopathy.[11-13] In our study strain parameters have also significantly improved.

A recent studies showed depressed longitudinal strain was strongly associated with total scar burden assessed by cardiovascular magnetic resonance imaging in ischemic heart failure patients, and it may be a sensitive parameter of LV contractile reserve and the presence of viable myocardium.[14-16] Another report showed longitudinal strain improvement after CRT implantation also indicated better clinical outcome and reverse remodelling, suggesting contractile reserve is associated with reverse remodelling.[17] Since responders showed significant improvement of longitudinal strain in the present study, our findings suggested that underlying myocardial deformation could be the determinant of reverse remodelling after CRT implantation in patients with non-ischemic cardiomyopathy and LBBB.

The baseline left ventricular volumes and ejection fraction were not significantly different between responders and non-responders. However, after a mean follow-up duration of 9±5 months, responders showed a slight improvement in LVEDV and LVESV compared to non-responders.

Before CRT, global along at end systole and early post-systole were lower in the non-responder group. After follow-up, in addition to end-systole and early post-systole along, non-responders showed lower global midsystole along. In responders, global end systolic and early post-systolic along showed an improvement after CRT implantation, whereas there was no significant improvement in non-responder group.

There is significant improvement in diastolic function in responder group than non-responder group. Parameters of dyssynchrony (SPWMD, LVEMD and IVD) significantly improved in responder group than non-responder group.

Limitations

It was a single centre cross sectional observational study from a small group of patients. Echocardiography to diagnose dilated cardiomyopathy was performed by different operator at different times, so there may be observer bias. Strain imaging require excellent image quality for adequate tracking and tracking affected by out of plane cardiac motion. Inter-vendor-related software differences remain a challenge for strain imaging. The main limitation remains that strain values vary among methods, modalities and software version. Therefore, method and software specific cut-off values need currently to be used. Lack of proper validation of most methods vs. absolute and objective reference standard. Contrast echocardiography would be of great importance in improving the visualization of the LV endocardial border. In this study, the contrast was not used mainly because of the costs and lack of reimbursement for contrast echocardiography. The most reliable method for EF measurement is 3D-echocardiography due to a lack of geometric assumptions and should always be used, when possible, especially in remodeled ventricles. There was no control group in this study. Speckle tracking relies on the ability of the ultrasound system to track specific acoustic markers in the myocardium over time, and is thus dependent on achieving high frame rates. Increasing depth and increasing sector width (among other variables related to the transducer) will decrease the frame rate. Frame rates less than 40 frames per second (Hz), result in large frame-to-frame changes, resulting in poor tracking of acoustic speckles. Study carried in a tertiary care hospital so hospital bias can't be ruled out.

CONCLUSION

The CRTD implantation improves patients' clinical and Echocardiographic data. This could lead to better patient management, improve quality of life and decreased

healthcare cost. By this study we can improve patients' selection and predict accordingly for CRT responder and Non responder and can take necessary measures for better patient's management.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Roy B, Haque MA, Paul K, Mandal SC. Respondent/non-respondent comparison post cardiac resynchronisation therapy implantation in patients with dilated cardiomyopathy. Int J Res Med Sci 2023;11:3667-71.