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Predictors of super-responders to cardiac resynchronization therapy for congestive heart failure in Bangladeshi population

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Abstract

Background: *Super-responders (SRs) are patients who improve critical cardiac function following cardiac resynchronization therapy (CRT). Cardiac resynchronization therapy (CRT) is the standard of care for patients with heart failure (HF) who have left ventricular (LV) systolic dysfunction and signs of electrical dyssynchrony.*

Aim of the study: *The aim of our study was to identify predictors of being a super-responder to CRT in Bangladeshi population.*

Methods: *The current study is a prospective study in which thirty-five (35) consecutive patients underwent CRT for a period of one year were studied. Before and 3 months after CRT implantation clinical, electrocardiographic and echocardiographic evaluations were performed. At the 3 months follow-up, patients were classified as super-responders. All collected data was entered into a Microsoft Excel Work Sheet and analyzed in SPSS 11.5 using descriptive statistics.*

Results: *In this study, 28 patients were male (80.0%) and 7 were female (20.0%). The mean age was 58.1± 9.3 years. Nine patients were in NYHA class IV (25.7%), 26 in class III (62.9%), and 4 patients were in class II (11.4%). The cause of heart failure was ischemic in 15 (42.9%) patients and dilated cardiomyopathy (DCM) in 20 (57.1%) patients. The mean QRS duration was 156.3±13.2 ms. Severe dilation of the LV was observed in most patients [mean LV end-diastolic diameter (LVEDD) of 67.9±5.2 mm, mean LV end-systolic diameter (LVESD) of 56.4±6.5 mm, associated with a mean LVEF of 27.5±4.3%. Here, 12% of patients treated with CRT for refractory heart failure are recognised as super-responders.*

Conclusion: *Patients in the early stages of cardiomyopathy, with less advanced left-sided structural involvement of the heart, appear to be more likely to become super-responders and independent predictors of reverse remodeling.*

Keywords: *Cardiac resynchronization therapy, Heart failure, Super-responders, Predictors.*

I. INTRODUCTION

Cardiac resynchronization therapy (CRT) is a common treatment for heart failure (HF) patients who have ventricular desynchrony. Patients' reactions to CRT, on the other hand, vary greatly. Even though they met the guidelines' inclusion criteria, approximately one-third of the patients had disappointing results [1, 2]. About 20%-30% of patients' cardiac anatomy and function could return to normal after CRT; these patients are known as super-responders (SRs) to CRT implantation. Heart failure (HF) is a major public health issue, affecting over 23 million people worldwide [1]. Trials of cardiac resynchronization therapy (CRT) have consistently shown improvements in HF morbidity, quality of life, and survival in patients with low LVEF, advanced HF symptoms, and increased QRS duration [2,3]. CRT implantation is recommended in symptomatic HF patients with sinus

rhythm, low LVEF, and a prolonged QRS duration [4, 5]. Recent guidelines expanded the indications for CRT to include patients with less severe symptoms (NYHA classes I and II), as well as patients with non-LBBB and a QRS P150 ms [6–9]. Despite the fact that the majority of patients benefit from CRT, approximately two-thirds of patients who meet the current guidelines criteria for this therapy respond to the therapy. It is estimated that 30-35% of patients will not respond to CRT [9–11]. The extent of LV remodeling and improvement in LVEF with CRT varies greatly [12]. The current selection criteria, which include only functional class, LVEF, QRS duration, and QRS morphology, may explain the lack of response to CRT [9]. Because a significant proportion of eligible patients continue to fail to benefit from this treatment, identifying potential responders to CRT is an important goal in order to recommend this therapy to patients who are most likely to benefit [13]. Although the fact that several studies have presented various factors predicting super-response to CRT, there are still unknown factors that could contribute to greater cardiac function recovery. As a result, we conducted the following study to look for potential predictors of CRT super-response.

II. METHODOLOGY

The current study is a prospective study in which thirty-five (35) consecutive patients underwent CRT for a period of one year were studied. Before and 3 months after CRT implantation clinical, electrocardiographic and echocardiographic evaluations were performed. They all met the criteria for CRT: HF classified as New York Heart Association (NYHA) class II, III, or IV despite optimal pharmacological therapy, LVEF $) \leq 0.35$, and QRS duration $\geq$ 120 ms with left bundle branch block (LBBB) or QRS duration $\geq$ 150 ms with non-LBBB. The recruited patients provided baseline data, preoperative and postoperative markers, and follow-up data. The severity of mitral regurgitation was graded from 0 to 4; grades 3 and 4 were regarded to have severe functional mitral regurgitation (FMR). Clinical, demographic, and echocardiographic characteristics were all evaluated before and after CRT. During the 3 months follow-up, patients were classified as SRs to CRT with a reduction of one or more NYHA functional classes, a decrease in the LVESV $\geq$ 15% and a LVEF absolute value $\geq$ 45%. Non-responders were defined with a decrease in the LVESV $\leq$ 15% or who had been re-hospitalized for the reason of heart failure or died during follow-up. Continuous variables were reported as mean ± standard deviation and were compared using Student's t test. Categorical variables were given in terms of number and percentage of total, and they were compared using the Fisher exact test or the Chi-square test. The potential predictors of super-response were identified using logistic regression analysis. P values less than 0.05 were considered statistically significant. All statistical analyses were conducted with SPSS 20.0 (SPSS, Chicago, IL, USA). At the 3 months follow-up, patients were classified as super-responders. All collected data was entered into a Microsoft Excel Work Sheet and analyzed in SPSS 11.5 using descriptive statistics.

III. RESULT

In this study, 28 patients were male (80.0%) and 7 were female (20.0%). The mean age was 58.1± 9.3 years. Nine patients were in NYHA class IV (25.7%), 26 in class III (62.9%), and 4 patients were in class II (11.4%). The cause of heart failure was ischemic in 15 (42.9%) patients and dilated cardiomyopathy (DCM) in 20 (57.1%) patients. The mean QRS duration was 156.3±13.2 ms. Severe dilation of the LV was observed in most patients [mean LV end-diastolic diameter (LVEDD) of 67.9±5.2 mm, mean LV end-systolic diameter (LVESD) of 56.4±6.5 mm, associated with a mean LVEF of 27.5±4.3% (Table 1). There were no statistically significant differences in baseline characteristics between super-responders and the other patients, except that super-responders had significantly less mitral regurgitation, smaller LV diastolic diameters (LVDDs), and shorter duration of heart failure symptoms (Table 2). Among the 35 patients with DCM, 4 (12%) demonstrated a reduction of one or more NYHA functional class, an increase in the LVEF to two-fold or more the baseline LVEF or to an absolute value >45%, and a decrease in the LVESV >15%, 3 months after CRT. These patients, who had no re-hospitalizations for the management of congestive heart failure, were considered super-responders to CRT. After CRT, we observed a significant improvement of NYHA functional class, LVEF, LV diameters, mitral regurgitation JA, intraventricular dyssynchrony, and IVD in both groups. Left ventricular end-systolic volume showed a significant decrease in both groups; however, LVEDV reduced significantly only in the super-responder group (Table 3). Figure 1 shows that the distribution of the study patients according to response where super-responders is the most.

Table -1: Baseline demographics of the study patients (N=35)

Parameters	Before CRT (mean± SD)
Age, yrs	58.1±9.3
Male	80% (n=28)
Female	20% (n=7)
NYHA, % class II	11.4% (n=4)

NYHA, % class III	62.9% (n=22)
NYHA, % class IV	25.7% (n=9)
QRS duration, ms	156.3±13.2
ICM	42.9% (n=15)
NICM	57.1% (n=20)
LVEDV mm	67.9±5.2
LVESV mm	56.4±6.5
LVEF %	27.5±4.3
MR, grade-No MR	5.7% (n=2)
I	42.9% (n=15)
II	48.6% (n=17)
III	2.9% (n=1)
Systolic BP, mm Hg	95.0±15.0
Diastolic BP, mm Hg	73.0±18.7
No. of hospitalization	2.51±1.44

Table-2: Comparison of baseline characteristics of super-responders and the other patients (N=35)

Characteristics	**Super-responders (n=4)**	**Other patients (n =31)**	**P-value**
Female gender (%)	67	10	0.53
DCM (%)	100	57.1	0.32
Age (years)	60±8	62±11	0.41
NYHA class	3.0±0.7	3.1±0.6	0.66
Duration of symptoms (months)	15.1+17.8	33.9+35.7	0.001
QRS duration (ms)	153.5±30.8	143.5±31.6	0.30
LA (mm)	42.8±4.6	50.0±6.5	0.04
MR grade	1.9±.9	2.6±.8	0.06
LVEDD (mm)	65.4±6.4	73.4±9.3	0.04
LVESD (mm)	57.3±7.5	63.6±10.2	0.06
LVEF (%)	25±5	22±4	0.43

Table-3: Three-month follow-up results in super-responders and the other patients (N=35)

3 month follow-up results		Super-responders (n=6)		Other patients (n =29)
NYHA class		3.0±0.6	2.9±0.6	1.7±0.5*
Baseline	Follow-up			2.0±0.8*
LVEF (%)		25±.05		41.2±3.2*
Baseline		22±.04		29.6±8.1*
Follow-up				
LVEDD (mm)		65.4±6.4	73.4±9.3	59.1±3.7*
Baseline				68.7±6.9*
Follow-up				
LVESD (mm)		57.3±7.5		46.4+9.1*
Baseline		61.4±10.2		53.7±11.3*
Follow-up				
MR grade		1.9±0.9	2.6±0.8	0.9±0.4
Baseline				1.4±0.7
Follow-up				
QRSd (ms)		153.5±30.8	143.5±31.6	116.9±18.9

Baseline	122.9±16.8
Follow-up	

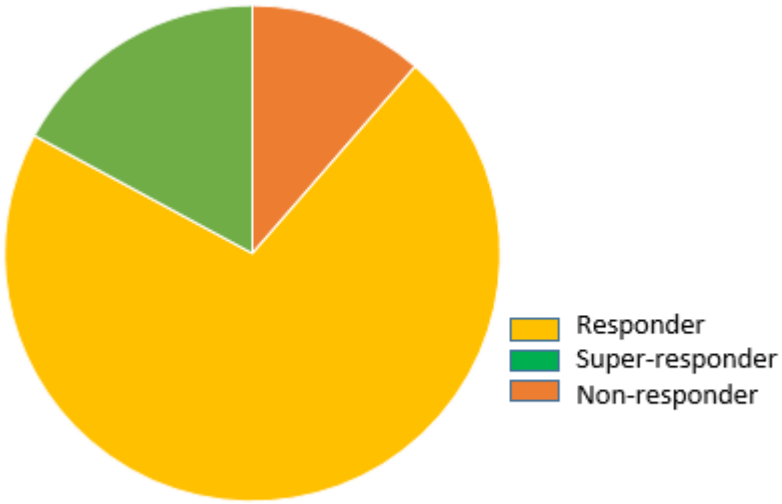

Figure 1: Distribution of the study patients according to response (N=35)

IV. DISCUSSION

Despite the optimistic outcomes of recent trials, patient responses to CRT may vary greatly. Some people may do worse or do not improve at all following CRT, while others may have a super-response to CRT. In our group, 12% of patients treated with CRT for refractory heart failure are recognized as super-responders. This proportion is comparable to previously reported figures, which ranged from 13 to 16% [14, 15]. This optimum response was more likely to occur in those with less changed ventricular shape. In fact, patients with smaller LV diameters and mild-to-moderate mitral regurgitation appear to have a higher chance of undergoing complete reverse remodeling and becoming super-responders after CRT than those with drastically changed ventricular geometry. However, neither LVEDD nor mitral regurgitation JA were independent predictors of super-response to CRT. Similarly, despite the fact that super-responders had more dilated idiopathic cardiomyopathy, a larger QRS, and were more desynchronized at baseline, these parameters did not differ substantially between groups and were not independent predictors of such remarkable response to CRT. In our study, the progression of heart failure symptoms over 12 months was an independent predictor of CRT super-response, implying that resynchronization may be more effective in the early stages of the disease. The current study indicated, for the first time to our knowledge, that even in individuals with AF, this prospective normalization of LV systolic function and morphology can be achieved. This is consistent with previous findings describing a comparable CRT effect in terms of functional capacity and LV function in the sinus rhythm and AF groups [16]. Similarly, short QRS duration or NYHA class II do not appear to impede complete reverse remodeling. Recent research has shown that CRT improves LV function, reversal remodeling, and survival in patients with NYHA class II as well as those with NYHA class III or IV [17, 18]. These findings support CRT's favorable influence on disease progression in individuals with mild heart failure and may justify the possibility of having super-responders with lower baseline NYHA class. Our findings extend existing findings by demonstrating that patients with a history of <12 months of symptoms benefit the most after CRT. To the best of our knowledge, the possibility of having super-responders even if they lack the traditional signs for CRT has never been described. Our findings show that super-responders to CRT are not uncommon in the actual world. Furthermore, these findings show that patients with less changed LV geometry are more likely to be super-responders. This could have significant therapeutic consequences. If verified by large, long-term, multi-center investigations, these findings could lead to CRT in the early stages of cardiomyopathy, when the likelihood of complete reverse remodeling is greatest. Finally, this is the first report of super-responders in CRT indications that are not on the label.

Limitation of the study:

This study had a single focal point and small sample sizes. Additionally, the study was completed in a very condensed amount of time. Therefore, it's possible that the study's findings don't accurately capture the overall situation in the nation.

V. CONCLUSION & RECOMMENDATION

According to the study, patients in the early stages of cardiomyopathy, with less advanced left-sided structural involvement of the heart, appear to be more likely to become super-responders and independent predictors of reverse remodeling.

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