



EFFECT OF QRS DURATION ON CARDIAC RESYNCHRONIZATION THERAPY IN PATIENTS WITH HEART FAILURE AND ITS RELATED FACTORS

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ABSTRACT

Background: Cardiac resynchronization therapy (CRT) is effective in reducing the risk of death and hospitalization and clinical events in systolic heart failure patients with a wide QRS. Previous retrospective studies suggest only patients with QRS prolongation due to a left bundle-branch block (LBBB) benefit from CRT.

Objective: The main purpose of this study was to assess the effect of different durations of QRS on the outcome of CRT / CRTD implantation in patients with heart failure and its subgroups.

Methods: A retrospective cohort study was conducted on 151 heart failure patients receiving CRT / CRTD treatment at Xi'an Jiaotong University's First Affiliated Hospital, from January 2016 to December 2018. The inclusion criteria were QRS duration of approximately 130, left bundle branch block (LBBB) and non-left bundle branch block (NLBBB), LVEF≤35%, ischemic and non-ischemic heart disease, N.Y.H.A II-IV. The diagnostic criteria for non-ischemic heart disease include X-ray and echocardiographic tests. The findings of coronary angiography, X-ray, and echocardiography are focused on ischemic heart disease. The observation indexes were ECG's QRS duration before and 12 months after operation. Echocardiography used the Simpson biplane technology to measure the percentage of left ventricular ejection fraction. M-mode was used to measure the changes in left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDd), and left atrial size (LA). Comparison has been made of the response of IHD, NIHD, LBBB, and NLBBB groups to CRT.

Results: The QRS morphology was LBBB in 79 cases (52.31%) and NLBBB in 72 cases (47.68%). Cardiac resynchronization therapy appears to be beneficial in patients with QRSd ≥ 150 ms, compared to 130 ms ≤ QRSd ≤ 149 ms patients. The CRT response of NIHD patients was better

than that of IHD patients. Both LBBB and NLBBB patients responded in $130 \text{ ms} \leq \text{QRSd} \leq 149 \text{ ms}$ and $\text{QRSd} \geq 150 \text{ ms}$. However, LVEF and LVESV of LBBB patients improved more significantly.

Conclusion: The relative benefit of CRT or CRTD therapy increased with the prolongation of the QRS duration.

Keywords: Cardiac resynchronization therapy, LBBB, ECG

INTRODUCTION

A new period of implantable device therapies for heart failure treatment was introduced with the U.S. in the year 2001, Food and Drug Administration (FDA) 1st product approval for heart resynchronization therapy (CRT) [1]. For patients with chronic left ventricular heart failure and a large QRS complex, CRT improves symptoms and decreases mortality. Consequently, the latest guidelines strongly advocate the use of QRS morphology to help pick CRT candidates. An electrocardiogram (ECG) with a QRS length (QRSd) of more than 130ms is a primary criterion for CRT receipt [2-5]. The QRSd values were found to be suboptimal markers in patients receiving CRT to either measure mechanical dyssynchrony or correlate accurate CRT responses [6] and there is evidence that patients experiencing left branch block bundle (LBBB) has a higher CRT response rate [2-5]. CRT is successful almost two-thirds of the time and has shown better results in LBBB patients than in right bundle branch block (RBBB) patients [6-11]. The most likely cause for this ischemic cardiomyopathy 13 leads to a large anteroseptal scar, present in most RBBB patients [12]. Responders to therapy are classified into three groups; the highest, intermediate, and lowest. The best responders are those with large QRS, women, LBBB and non-ischemic heart disease. Males or those with ischemic cardiomyopathy in nature are Moderate Responders, whereas patients with smaller QRS complexes and patients with no LBBB or RBBB are the lowest (non-responders) [13, 14]. CRT is licensed as a substantially effective treatment for patients with moderate to severe heart failure, with lower ejection fraction (EF), who showed poor response to conservative management [15]. Cardiac resynchronization therapy-defibrillator (CRTD) leads are inserted into three settings namely Right Atrium and Ventricle (RA, RV) and Left Ventricle (LV). CRT system aims to imitate the normal heart rhythm by simultaneously transmitting electrical impulses to both ventricles [18]. In addition, CRTD also has the added advantage of being a defibrillator which responds immediately to end any atypical life-threatening rhythm [16-21]. CRT is extremely useful for patients with HF and abnormal cardiac wall movements because of any form of conduction delay that may increase the risk of heart failure [22, 23]. CRT can resynchronize the contraction of heart muscles in such a way that the left ventricle can increase the efficiency of the ejection fraction [27]. With regard to the decrease in mortality, physical exertion capability and the quality of a patient's life (QoL), In the long run, CRT has proved very beneficial [15,24] as it helps to restore structural integrity over time [12,26,27] while progress in survival remains to be determined. Despite the importance of CRT or CRTD for the symptomatic type of moderate and serious heart failure patients and patients with heart blocks, its efficacy is still not standardized and depends on various factors, like careful patient selection, appropriate lead placements and system settings [16]. Ensuring these considerations is essential for maximizing the benefits of CRT or CRTD. There is increasing evidence that patients with LBBB have a higher rate of response to CRT [2-5]. CRT has been shown to be successful almost two-thirds of the time and has shown better results in LBBB patients than in RBBB patients [7-12]. CRT's function remains debatable for Complete Right Bundle Branch Block (CRBBB) until now. It is commonly believed that patients who are non-LBBB will not benefit satisfactorily from CRT. As long as QRS duration is taken into account, patients with QRS duration $\geq 150\text{ms}$ display more positive LV systolic progress with CRT pacing, but patients with $\text{QRS} \leq 150\text{ms}$ display more or less negative systolic changes. Richard J et al indicated that non-LBBB or RBBB Patients with advanced cardiac insufficiency should have more QRS -length baseline on ECG [18]. Non LBBB patients are considered to have less dyssynchrony relative to patients with LBBB [17]. Different studies have shown that pure RBBB

has really shown poor response, whereas few RBBBs have better response and are defined as RBBBs with simultaneous LBBB defect shown on the EKG by the presence of axis deviating to the left with large, unclear and sometimes notched R (R) 'in lateral leads (lead I, avL). In addition, few studies showed that non-LBBB patients with extended EKG PR intervals showed some benefit from CRT compared to those with standard PR intervals [23]. Overall, the benefits of cardiac resynchronization therapy consist of an improvement of tolerance to exercise, a decrease in the loss of myocardial remodeling, and maybe some regain of the normal cardiac shape and form. A decreased mortality and hospital admissions were observed in patients having sinus rhythms using CRT [16, 25].

METHODS

Study Population and Sample

A retrospective cohort study was conducted on 151 Heart Failure (HF) patients who received CRT or CRTD between the time periods of January 2016 to December 2018. In this study 62 Patients with $130 \leq \text{QRSd} \leq 149$ (46 male and 16 female) while 89 patients with $\text{QRS} \geq 150$ msec (64 male and 25 female) from Xi'an Jiaotong University, First Affiliated Hospital. The total included information is gathered from the medical archives at the cardiovascular department with full consent from the patients and was permitted by the Commission on Clinical Research. Diagnostic Criteria for nonischemic heart disease included X-ray findings (showing increased heart size in normal chest X-ray), Electrocardiogram strip and echocardiography results. Coronary intervention including cardiac catheterization and/or interventional therapy was performed for ischemic heart disease. Primary inclusive criterion of this study is $\text{QRS} \geq 130\text{ms}$ ($130 \leq \text{QRSd} \leq 149$ & $\text{QRS} \geq 150$), N.Y.H.A Class II-IV, LBBB along with NLBBB, $\text{LVEF} \leq 35\%$.

Electrocardiography (ECG)

Diagnosis of various arrhythmia types, bundle branch blocks (RBBB / LBBB), and QRS durations before and after CRT or CRTD implantation was made by the 12-electrode ECG (specified as 0.5–150 Hertz, 25 millimeter per second, 10 millimeters per mill volts). Diagnoses of normal and abnormal ECGs were made by my professor and me separately to enhance accuracy. LBBB and RBBB were diagnosed according to conventional criteria (RsR' / RR design in electrode V1-V3 or may present as a wide one phasic R wave or qR pattern in V1 and broad slurred S wave in electrode I, avL, and V5-V6 for NLBBB and LBBB, there must be the existence of a QS or rS complex in electrode V1 also there must be a presence of the notched ('M'-shaped) R wave in electrode V6).

Echocardiography (UCG)

Bleeker et al explained a scheme which is mentioned as follows, echocardiography was accomplished right at the time of diagnosis and post 12 months in follow-up operating a widely accessible scheme (Vivid-7, G-E Health-care, Philips iE33). A 3.5 Mega Hertz sensor is exercised for 16 cm deep para-sternal and top view (standard axis along the length, as well as 2 and 4 chambers pictured). The trigger to QRS compound, and the standard duo dimensional and data from the color Doppler are stored as a movie cycle. LVEF was estimated by using traditional two and four-chamber pictures exercising the dual plane Simpson method.

The diameter of the ventricle at the end of each systole and diastole and the size of the left atrial chamber were measured by M-mode Ultrasound.

CRT/CRT-D Device Implantation:

Auxiliary vein or subclavicular vein was considered as the incision marker point. With the help of Chest radiography and coronary sinus venography, the first electrode lead was inserted and steered all the way from the SVC to the right atrium and then progressed in to the RV. The second electrode lead was directed from the coronary sinus to the left heart ventricle progressing into the lateral vein (mostly). As far as right chamber leads are concerned, the right ventricular electrode was fixated at

the apical region of the RV and the appendage point of the RA was chosen for the right atrium electrode.

Response Echocardiographic criterion 12-month post-CRT/CRTD Implantation: Post 12 months follow-up; patients were divided into the following response groups. 1) Responders→ Stroke Volume improvement, Decrease of LVESV \geq 15%, Increase in LVEF \geq 10%. 2) Non-Responders→ Patients without any Echocardiographic improvement Post-CRT/CRTD response will be observed in both $130 \leq \text{QRSd} \leq 149$ & ≥ 150 patients. After that subgroups will be compared to find which subgroup has shown better response.

Statistical Analysis

Analysis of statistics was executed operating SPSS for Microsoft Windows v. 18 and V20 (SPSS) for Microsoft Windows 10. The data was compared using multiple categories of response markers for CRT which was collected one year post-implant. Statistical analysis was performed by using Paired sample T-test was exercised for the purpose of evaluation. $P < 0.05$ was noted as statistically substantial.

RESULTS

Step 1 : Comparison of $130 \text{ msec} \leq \text{QRSd} \leq 149 \text{ msec}$ and $\text{QRS} \geq 150 \text{ms}$ CRT / CRT-D responses: Echocardiographic comparison of $130 \leq \text{QRSd} \leq 149$ & ≥ 150 patients with Pre and Post CRTD implantation are shown in **Table 1**. The study population of 151 heart failure patients integrated with this study has an average age of 61.94 ± 9.18 years. Out of 151 patients, the percentage of male patients is 72.80 % and female patients constitute 27.20 %. All heart failure patients are included in the table. The reason behind HF is either Ischemic or Non-ischemic Cardiomyopathy. 31 (20.50%) patients are of IHD while 120 (79.50%) patients are of NIHD origin. As far as NYHA class is concerned, a total of 2 patients are of NYHA class I (1.32 %), 41 patients are of NYHA class II (27.15 %), 66 patients are of NYHA class III (43.70 %) and 42 patients belong to NYHA class IV (27.81 %). ECG findings of Pre and Post CRT/CRTD implantation are also mentioned, which includes mean and standard deviation of QRS duration pre and post CRT/CRTD implantation, which shows a significant ($P < 0.05$) decrease in QRS duration after CRT/CRTD in all groups. QRS morphology is LBBB and NLBBB in 79(52.31%) and 72(47.68%) patients, respectively. All of these patients received appropriate Heart Failure medications which were beta-blockers, Diuretics, CCBs (Calcium Channel blockers) and ACEI or ARBs.

In **Table 1**, the preoperative and postoperative values are shown for comparison according to QRS Duration, i.e. $130 \leq \text{QRSd} \leq 149$ & $\text{QRS} \geq 150$. The variables compared are EF, LVEDV, LVESV and Mitral Regurgitation (MR). In this comparison, all parameters show significantly good response under all categories except Mitral Regurgitation which only showed significant improvement postoperatively in $\text{QRS} \geq 150 \text{ msec}$ patients ($P < 0.05$).

Table 1 Echocardiography Response in two main groups after CRT-D.

| ECHO | $130 \leq \text{QRSd} \leq 149$ | | P. value | $\text{QRSd} \geq 150$ | | P. value |
|-------|---------------------------------|--------------|----------|------------------------|--------------|----------|
| | Pre | Post | | Pre | Post | |
| EF | 28.50+5.90 | 37.60+9.21 | .00 | 28.38+5.54 | 38.21+9.59 | .00 |
| LVEDD | 72.23+9.10 | 67.62+10.78 | .01 | 73.51+10.44 | 68.29+12.16 | .00 |
| LVESD | 61.77+9.39 | 56.00+11.15 | .00 | 62.91+12.28 | 56.57+12.93 | .00 |
| LVEDV | 293.02+92.09 | 242.53+75.66 | .00 | 302.75+93.28 | 238.21+78.85 | .00 |
| LVESV | 212.52+82.21 | 150.72+70.12 | .00 | 219.57+78.85 | 144.92+71.62 | .00 |
| MR | 8.867+10.28 | 6.06+4.48 | .13 | 7.87+5.83 | 5.08+4.56 | .00 |

The **Table 1** shows the comparison of Ejection Fraction before and after CRT/CRTD implant in two main groups. In almost all patients, the preoperative EF in group 1 (28.50 \pm 5.90)% and group2

(28.38±5.54)% increased significantly after CRTD implant with a postoperative EF of (37.60±9.21)% in group 1 and (38.21±9.59)% in group two with a *P value* < 0.05.

Among most of the CRT patients, the preoperative levels of LVESV in groups one and two (212.52±82.21 & 219.57±78.85) ml are higher as compared to post-operative LVESV (150.72±70.12 & 144.92±71.62) ml, which shows the post-operative LVESV is significantly lower (*P* < 0.05). The preoperative levels of LVEDV (293.02±92.09 & 302.75±93.28) ml are higher as compared to post-operative LVEDV (242.53±75.66 & 238.21±78.85) ml, which shows the post-operative LVEDV is significantly lower (*P* < 0.05).

We obtained a Super Response in patients with QRSd ≥ 150 while the patients in group one showed a super response only with LVESV. Group 1 (130 ≤ QRSd ≤ 149) patient's CRT response rate was 81%, and group 2 (QRS ≥ 150) patient's CRT response rate was 80%. The overall Response Rate of 151 patients was 80% while patients in group one had 81 % and in group two 80%.

As far as NYHA class is concerned, a total of 2 patients are of NYHA class I (1.32 %), 41 patients are of NYHA class II (27.15 %), 66 patients are of NYHA class III (43.70 %) and 42 patients belong to NYHA class IV (27.81 %).

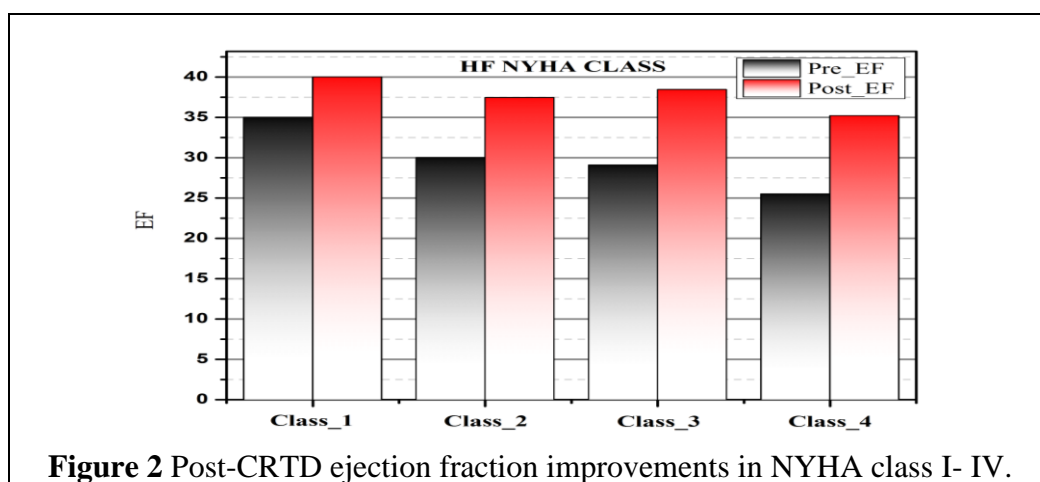


Figure 2 Post-CRTD ejection fraction improvements in NYHA class I- IV.

Figure 1 demonstrated that all patients responded significantly but the outcome is becoming better as the NYHA class increases from I to IV, in class I the average increase of EF from 35 to 40, class II increment of EF is from 30.01 to 37.46, and class III from 29.09 to 38.45 and class IV 25.52 to 35.21 with *P value* < 0.05.

STEP 2 → 130 ≤ QRSd ≤ 149 and QRS ≥150 subgroups (IHD vs NIHD, LBBB vs NLBBB,) comparison:

1) Different etiology

Table 2 Comparison of ECHO parameters with IHD and NIHD in two major groups

| Diagnose | ECHO | 130 ≤ QRSd ≤ 149 | | P.value | QRSd ≥150 | | P.value |
|----------|-------|------------------|--------------|---------|--------------|--------------|---------|
| | | Pre | Post | | Pre | Post | |
| IHD | EF | 30.53±4.40 | 39.18±7.57 | .00 | 31.14±4.62 | 37.29±11.36 | .07 |
| | LVEDD | 69.18±7.99 | 62.94±8.84 | .03 | 72.50±10.09 | 66.64±9.88 | .13 |
| | LVESD | 58.53±7.12 | 50.35±9.86 | .00 | 62.57±9.56 | 55.86±9.52 | .07 |
| | LVEDV | 270.82±82.27 | 203.23±51.59 | .00 | 277.77±74.19 | 232.35±82.09 | .13 |
| | LVESV | 190.58±66.25 | 119.58±42.58 | .00 | 195.12±61.12 | 145.14±67.63 | .05 |
| | MR | 5.59±3.44 | 3.58±3.27 | .13 | 6.04±3.32 | 5.61±3.61 | .79 |
| NIHD | EF | 27.73±6.24 | 37.00±9.77 | .00 | 27.86±5.57 | 38.387±9.30 | .00 |
| | LVEDD | 73.38±9.30 | 69.43±11.00 | .07 | 73.69±10.56 | 68.60±12.57 | .00 |
| | LVESD | 63.00±9.90 | 58.34±10.92 | .04 | 62.97±12.77 | 56.71±13.52 | .00 |
| | LVEDV | 301.40±95.04 | 257.37±78.40 | .01 | 307.41±96.12 | 239.31±98.86 | .00 |
| | LVESV | 220.80±86.70 | 162.48±75.10 | .00 | 224.13±81.26 | 144.88±72.77 | .00 |
| | MR | 10.26±11.84 | 7.28±4.57 | .27 | 8.14±6.08 | 4.99±4.73 | .00 |

Table 2 shows that out of 151 patients who received CRT, 17 IHD and 45 NIHD patients in group 1 ($130 \leq \text{QRSd} \leq 149$) and 14 IHD and 75 NIHD in group 2 ($\text{QRS} \geq 150$) have preoperative EF in group 1 is (30.53 ± 4.40 and 27.73 ± 6.24) % which significantly increased post-operatively to (39.18 ± 7.57 and 37.00 ± 9.77) %. Preoperative EF in the group 2 is (31.14 ± 4.62 and 27.86 ± 5.57) % with significant improvement postoperatively to (37.29 ± 11.36 and 38.38 ± 9.30) %, it shows that significant changes were made in post-operative EF ($P < 0.00$) except IHD group 2 in which P value is 0.07.

LVESV: In group 1 and group 2 IHD patient's preoperative levels of LVESV (190.58 ± 66.25 & 195.12 ± 61.12) ml are higher as compared to post-operative LVESV (119.58 ± 42.58 & 145.14 ± 67.63) ml, which shows the post-operative LVESV is significantly lower ($P < 0.05$) in group one but not significant in group two. In NIHD patients pre-CRT levels of LVESV in group 1 and group 2 were (220.80 ± 86.70 and 224.13 ± 81.26) ml while post-operative LVESV (162.48 ± 75.10 & 144.88 ± 72.77) ml, which decreased significantly with P value < 0.05 . We obtained Super Response in NIHD patients. Group 1 ($130 \leq \text{QRSd} \leq 149$) IHD patient's CRT response rate was 88%, and group 2 ($\text{QRS} \geq 150$) IHD patient's CRT response rate was 71%. An overall Response rate of 31 IHD patients was 81% while patients in group one had 88 % and in group two 71%.

Group 1 ($130 \leq \text{QRSd} \leq 149$) NIHD patient's CRT response rate was 80%, and group 2 ($\text{QRS} \geq 150$) NIHD patient's CRT response rate was 80%. The overall Response rate in NIHD patients was 80%. Response in Ischemic Heart Disease between group one is better than group two which shows significant improvement in the echocardiography report. While response in Non Ischemic Heart Disease patients is better in group two than group one.

The primary outcome is based on Ejection Fraction and LVESV. For almost all patients, the ejection fraction showed statistically significant improvement as a P value < 0.05 except IHD group 2. However, these effects are more pronounced among the NIHD group 2 patients receiving CRT/CRTD and more so in those with IHD group 1.

2) LBBB and NLBBB

Table 3 Comparison of ECHO parameters with LBBB and NLBBB in two major groups

| Diagnose | ECHO | $130 \leq \text{QRSd} \leq 149$ | | P.value | $\text{QRSd} \geq 150$ | | P.value |
|----------|-------|---------------------------------|--------------|---------|------------------------|---------------|---------|
| | | Pre | Post | | Pre | Post | |
| LBBB | EF | 28.75±4.79 | 40.83±10.56 | .00 | 27.57±5.13 | 38.74±10.20 | .00 |
| | LVEDD | 72.21±8.29 | 66.38±11.93 | .05 | 73.85±10.75 | 67.40±13.68 | .00 |
| | LVEDS | 61.25±8.58 | 53.92±12.26 | .02 | 62.75±12.40 | 55.85±14.51 | .00 |
| | LVEDV | 282.59±63.32 | 228.73±69.39 | .00 | 308.11±97.18 | 226.95±104.63 | .00 |
| | LVESV | 201.17±48.12 | 135.98±62.33 | .00 | 225.85±81.05 | 135.05±72.61 | .00 |
| | MR | 9.82±15.51 | 3.56±2.42 | .21 | 7.64±4.70 | 5.37±5.14 | .03 |
| NLBBB | EF | 28.34±6.56 | 35.55±7.72 | .00 | 29.68±5.99 | 37.35±7.95 | .00 |
| | LVEDD | 72.24±9.68 | 68.43±10.05 | .09 | 72.94±10.05 | 69.74±9.20 | .17 |
| | LVEDS | 62.11±9.96 | 57.47±10.24 | .05 | 63.18±12.25 | 57.74±9.95 | .04 |
| | LVEDV | 299.60±106.65 | 251.23±79.01 | .02 | 294.07±87.29 | 256.44±78.23 | .06 |
| | LVESV | 219.68±97.80 | 160.02±73.90 | .00 | 209.42±75.23 | 160.88±68.01 | .00 |
| | MR | 8.27±4.95 | 7.12±4.80 | .39 | 8.30±7.55 | 4.49±3.14 | .04 |

Table 3 presented that out of 151 patients who received CRT, Among the 79 LBBB, 24 had $130 \leq \text{QRSd} \leq 149$, The preoperative EF value (28.75 ± 4.79) % increased significantly postoperatively with EF value (40.83 ± 10.56) % and a P -value < 0.00 ; 55 LBBB patients had $\text{QRS} \geq 150$, and the preoperative EF value (27.57 ± 5.13) % increased significantly postoperatively with an EF value (38.74 ± 10.20), ($P < 0.00$). Among the 72 NLBBB, 38 had $130 \leq \text{QRSd} \leq 149$, and the preoperative EF value (28.34 ± 6.56) % increased significantly postoperatively with EF value (35.55 ± 7.72)% and a P -value < 0.00 ; 34 NLBBB patients had $\text{QRS} \geq 150$, and the preoperative EF value (29.68 ± 5.99)% increased significantly postoperatively with an EF value (37.35 ± 7.95)%, ($P < 0.00$).

LVESV: In group 1 and group 2 LBBB patient's preoperative levels of LVESV (201.17 ± 48.12 & 225.85 ± 81.05) ml are higher as compared to post-operative LVESV (135.98 ± 62.33 & 135.05 ± 72.61) ml, which shows the post-operative LVESV is significantly lower ($P < 0.05$). In NLBBB patients pre-CRT levels of LVESV in group 1 and group 2 were (219.68 ± 97.80 and 209.42 ± 75.23) ml while post-operative LVESV (160.02 ± 73.90 & 160.88 ± 68.01) ml, which decreased significantly with P value < 0.05 .

We obtained Super Response in LBBB patients. Group 1 ($130 \leq \text{QRSd} \leq 149$) LBBB patient's CRT response rate was 79%, and group 2 ($\text{QRS} \geq 150$) LBBB patient's CRT response rate was 84%. An overall Response rate of 79 LBBB patients was 82% while patients in group one had 79 % and in group two 84%.

Group 1 ($130 \leq \text{QRSd} \leq 149$) NLBBB patient's CRT response rate was 71%, and groups 2 ($\text{QRS} \geq 150$) NLBBB patient's CRT response rate was 74%. The overall Response rate in 72 NLBBB patients was 72% while patients in group one had 71 % and in group two 74%.

The primary outcome is based on Ejection Fraction and LVESV. For almost all patients, the ejection fraction showed statistically significant improvement as a P value < 0.05 . However, this effect is more pronounced among the LBBB patients receiving CRT/CRTD. The response among group 1 LBBB is better than that of NLBBB and it's the same for the group 2 as well. If we compare the whole response between LBBB and NLBBB, the patient having LBBB improved well.

In comparison of P value with and without equality of variances, Ejection Fraction P values 0.05 and 0.05 in the group 1 while 0.05 and 0.05 in group 2 respectively. All other parameters have shown a good response as well. P value < 0.05 without equality of variance is considered as most statistically significant for this study.

5) QRS Duration before and after CRT/CRTD implantation

Table 4 Comparison of ECG's in all subgroups with two major groups

| Parameters | $130 \leq \text{QRSd} \leq 149$ | | <i>P</i> .value | $\text{QRSd} \geq 150$ | | <i>P</i> .value |
|------------|---------------------------------|-------------|-----------------|------------------------|--------------|-----------------|
| | <i>Pre</i> | <i>Post</i> | | <i>Pre</i> | <i>Post</i> | |
| Over All | 140.89±5.63 | 121.73±7.75 | .00 | 171.58±13.22 | 145.36±14.39 | .00 |
| IHD | 141.00±5.29 | 121.35±8.34 | .00 | 169.93±12.51 | 143.07±11.05 | .00 |
| NIHD | 140.84±5.81 | 121.87±7.61 | .00 | 171.89±13.41 | 144.79±15.53 | .00 |
| LBBB | 142.58±5.24 | 124.42±6.78 | .00 | 172.65±13.14 | 146.00±14.15 | .00 |
| NLBBB | 139.82±5.68 | 120.03±7.93 | .00 | 169.85±13.36 | 144.32±16.18 | .00 |

Table 4 shows QRS Duration-specific response in group 1 ($130 \leq \text{QRSd} \leq 149$) and group 2 ($\text{QRS} \geq 150$) respectively. Overall all response was significant among the two groups, Group one pre CRT/CRT-D QRSd 140.89 ± 5.63 ms decreased to 121.73 ± 7.75 ms post implant while group two preoperational QRSd 171.58 ± 13.22 ms decreased to 145.36 ± 14.39 ms after operation.

Among the 31 IHD patients, 17 had $130 \leq \text{QRSd} \leq 149$, the preoperative QRSd value (141.00 ± 5.29) ms decreased significantly postoperatively with QRSd value (121.35 ± 8.34) ms and P -value < 0.00 ; 14 IHD patients had $\text{QRS} \geq 150$, preoperative QRSd value (169.93 ± 12.51) ms decreased significantly postoperatively with QRSd value (143.07 ± 11.05) ms, ($P < 0.00$). Among the 120 NIHD, 45 had $130 \leq \text{QRSd} \leq 149$, and the preoperative QRS duration value (140.84 ± 5.81) ms decreased significantly postoperatively with QRS duration (121.87 ± 7.61) ms and a P -value < 0.00 ; 75 NIHD patients had $\text{QRS} \geq 150$, and the preoperative QRS duration (171.89 ± 13.41) ms decreased significantly postoperatively with a QRS duration (144.79 ± 15.53) ms, ($P < 0.00$). Patients with ischemic heart disease responded better in group one than of group two while those having Non ischemic heart disease shown better outcomes in group two than in group one.

Among the 79 LBBB patients, 24 had $130 \leq \text{QRSd} \leq 149$, the preoperative QRSd value (142.58 ± 5.24) ms decreased significantly postoperatively with QRSd value (124.42 ± 6.78) ms and P -value < 0.00 ; 55 LBBB patients had $\text{QRS} \geq 150$, preoperative QRSd value (172.65 ± 13.14) ms decreased significantly postoperatively with QRSd value (146.00 ± 14.15) ms, ($P < 0.00$). Among the

72 NLBBB, 38 had $130 \leq \text{QRSd} \leq 149$, and the preoperative QRS duration value (139.82 ± 5.68) ms decreased significantly postoperatively with QRS duration (120.03 ± 7.93) ms and a P -value < 0.00 ; 34 NLBBB patients had $\text{QRS} \geq 150$, and the preoperative QRS duration (169.85 ± 13.36) ms decreased significantly postoperatively with an QRS duration (144.32 ± 16.18) ms, ($P < 0.00$). Among LBBB and NLBBB patients LBBB patients responded better in decrement of QRSd than NLBBB patients.

The primary outcome is based on EF and LVESV. For all patients, the P value showed statistically significant improvement. However, this effect is more pronounced among the NIHD, Urban and female patients receiving CRTD of either LBBB or NLBBB QRS morphology, and more so in those with LBBB.

DISCUSSION

Our analysis consists of 41.05 percent of $130 \leq \text{QRSd} \leq 149$ and 58.94 percent $\text{QRS} \geq 150$ patients who were implanted with CRT or CRTD. In general, We also observed a good response in CRT with a tendency to prioritize NIHD, LBBB and patients in our study, although it is still not universal among physicians worldwide. Numerous features may predict morbidity and mortality rate change, and the degree of reverse remodeling is definitely one of CRT's highest significant mechanisms. Due to the existence of cardiac scar tissue, improving left-ventricular function in patients having ischemic pathology in nature will be limited, and beneficial remodeling of myocardial scar tissue is impossible [28].

Post-CRT, if patients have improved heart functions then it is assumed that these subjects have improved prognosis [29], However, this mechanism is a comparatively small fraction of the effect of CRT on long-term death rates at the same time as most studies showed some or close to no benefit of CRT in NLBBB subjects [15, 30].

Improvement of cardiac function is a welcome sign after implant of CRT devices, but an untrustworthy response marker for long-term responses [31]. In addition, in a randomized controlled study trial in subjects with HF and $\text{QRS} < 130$ ms, CRT also failed to benefit quality of life (QoL), operative and Echocardiographic parameters [32]. According to the Heart Failure Cardiac-Resynchronization (CARE-HF) study, different criteria were used to determine the improvement if there was a 5-6 percent improvement in the reduction of N.Y.H.A class or a 5-6 percent improvement in the quality of life, then a positive response is considered [33]. While other research concentrates on the result of echocardiography. A contrary association between QRS duration and LVEF endures [34]. The degree of QRS post-CRT reduction projected a positive response [35].

In our study, in all subgroups, 62 patients with $130 \leq \text{QRSd} \leq 149$ and 89 patients with $\text{QRS} \geq 150$ ms had significantly increased LVEF. The difference in the length of QRS was an indicator of improvement in the clinically fused ranking, in the evaluation PROSPECT-ECG [36]. Iler et al have demonstrated increased mortality and increased cardiac transplantation in patients with a broader QRS post-implantation [37]. Rickard et al. demonstrated the worst aggravation of Left ventricular activity with QRS extension brought by CRT [38]. LVESV Post-CRT implantation has also witnessed a major decline in several studies [28,29,31,33,35,36,38], this change becomes apparent as quickly as 1 month after implantation [32] and is sustained for up to 29 months [39] as a predictor of good response.

According to White H D et al, the LV (LVESV) sinks into the end-systolic volume as the most important gage of reverse LV remodeling [34]. With a drop of at least 15 percent in LVESV that is rare in NLBBB patients [40] because they have fewer LV dyssynchrony before implantation.

In our analysis, we found that post-CRT decrease in QRS duration appears to have more patients with a substantial reduction in LVESV than those with post-CRT increases in QRS duration ($P < 0.05$) And a greater postoperative LVEF percentage than post-CRT rises in QRSd ($P < 0.05$).

All of the above reaction markers appear to benefit LBBB patients. In a research carried out by Auricchio et al., it was decided that direct implantation of C.R.T in subjects with NLBBB should be discouraged [41].

Gender correlation in the utility of CRTD in HF Patients with NLBBB and LBBB. Roman Nevzorov et.al confirmed that no gender-based dissimilarities were found in the patient's primary outcome, 1-year mortality risk and complications of post-procedure were considered primary outcomes. They observed that the level of implantation of devices in men was more than female and the rate of complication in females was higher [42].

In another study, it was reported that when it comes to selecting the CRTD implantation women vary a lot from men. But, in the result, that does not translate similarly. They suggested that they do not see any difference in results [43]. Ramezan et.al also indicated the same finding, noting that the CRTD answer does not appear to be linked to gender or age [44].

Statistical analysis of Gender Comparison between group 1 ($130 \leq \text{QRSd} \leq 149$) and group 2 ($\text{QRS} \geq 150$) heart failure patients generated the results discussed below.

In our study among most of the CRT patients, the preoperative levels of LVESV (61.77 ± 9.39 & 62.91 ± 12.28) are higher as compared to post-operative LVESV (56.00 ± 11.15 & 56.57 ± 12.93) ml, which shows the post-operative LVESV is significantly lower ($P < 0.05$).

Our Study carried out in LBBB and NLBBB patients delivers an improved result, whereas for LBBB it is more noticeable. For all Echocardiographic factors in the primary outcome, there were noticeable results in the EF and LVEDV, All the above response markers tend to favor patients with LBBB morphology. In a research carried out by Auricchio et al., it was determined that direct implantation of C.R.T in subjects with RBBB should be discouraged [41].

Gender relationship in the usefulness of CRTD in HF patients with RBBB and LBBB. Roman Nevzorov et.al stated that no gender-based dissimilarities were found in the patient primary outcome, 1-year death rate and complications after the procedure were considered primary outcomes. They noticed that the level of implantation of devices in men was more than female and the rate of complication in females was higher [42].

Statistical analysis of group 1 ($130 \leq \text{QRSd} \leq 149$) and group 2 ($\text{QRS} \geq 150$) Comparison between LBBB and NLBBB heart failure patients generated the results discussed below.

LBBB and NLBBB responses in group 1 ($130 \leq \text{QRSd} \leq 149$) and group 2 ($\text{QRS} \geq 150$) respectively. Among the 79 LBBB, 24 had $130 \leq \text{QRSd} \leq 149$, and the preoperative EF value (28.75 ± 4.79) % increased significantly postoperatively with EF value (41.04 ± 10.08) % and a $P\text{-value} < 0.00$; 55 LBBB patients had $\text{QRS} \geq 150$, and the preoperative EF value (27.57 ± 5.13) % increased significantly postoperatively with an EF value (37.69 ± 11.91) %, ($P < 0.00$).

Among the 72 NLBBB, 38 had $130 \leq \text{QRSd} \leq 149$, and the preoperative EF value (28.34 ± 6.56) increased significantly postoperatively with EF value (34.79 ± 8.70) % and a $P\text{-value} < 0.00$; 34 NLBBB patients had $\text{QRS} \geq 150$, and the preoperative EF value (29.68 ± 5.99) % increased significantly postoperatively with an EF value (36.85 ± 7.69) %, ($P < 0.00$).

Our Study carried out in LBBB and NLBBB patients delivers an improved result, whereas for LBBB it is more noticeable. For all Echocardiographic factors in the primary outcome, there were noticeable results in the EF and LVESV.

CONCLUSION

As a conclusion, The relative benefit of CRT or CRTD therapy increased with the prolongation of the QRS duration. Patients with $\text{QRSd} \geq 150$ ms had better CRT response, compared to $130 \text{ ms} \leq \text{QRSd} \leq 149 \text{ ms}$ patients and patients with $\text{QRSd} \leq 129$ ms should not be considered for CRT implantation as it may be potentially harmful in terms of clinical adverse events. While CRT was very effective in reducing clinical events in patients with LBBB, Both LBBB and NLBBB patients responded in $130 \text{ ms} \leq \text{QRSd} \leq 149 \text{ ms}$ and $\text{QRSd} \geq 150 \text{ ms}$. However, LVEF and LVESV of LBBB patients improved more significantly. These findings have important clinical implications for the selection of patients for this important treatment modality. The CRT response of NIHD patients was better than that of IHD patients. Together with the consistent data from other large-scale randomized trials, these findings may have important implications for further guidance regarding the optimal QRS duration cut-off for CRT.

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