QRS Duration as a Predictor of Left Ventricular Outflow Tract Velocity Time Integral in Patient with Cardiac Resynchronization Therapy

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Abstract

Background: Cardiac resynchronization therapy (CRT) has a morbidity and mortality benefits in moderate to severe heart failure. It reduces mortality and hospitalization and improves cardiac function. It can be used according to the European guidelines in severely depressed left ventricular ejection fraction (i.e., ≤35%) and complete left bundle branch block. However, 30% of patients may show no benefit from CRT therapy. Therefore, prediction of CRT response seems to be an important subject for study in the current researches. We aimed to study the correlation between Surface ECG QRS complex duration (QRS) duration and cardiac output measured by ventricular outflow tract velocity time integral (LVOT VTI) as a predictor of response in patients with CRT implantation.

Methods: We studied 100 consecutive patients prospectively with biventricular pacing system. Each patient was subjected to a focused transthoracic echocardiographic examination in which a parasternal long axis view was obtained to measure the diameter of the LVOT in mid-systole. The LVOT VTI was measured by pulsed-wave Doppler in the LVOT using a 2-mm sample volume positioned just proximal to the aortic valve in the apical five chamber view.

Results: We found a statistically significant difference between CRT responders and nonresponders as regards age, body surface area (BSA), time since CRT implantation and smoking status (P = 0.018, 0.039, 0.002, <0.001). There was negative significant correlation between QRS duration and LVOT VTI and stroke volume index. The optimal cut off values for optimal response to CRT using receiver operating characteristics curves were 13 ms for postimplant QRS duration and 17.1 cm for LVOT VTI. We also found a significant difference between responders and nonresponders as regard CO. It was higher in responders (5.97 vs. 3.34, P < 0.001).

Conclusion: CRT response is more in patients with lower BSA, and without previous history of ischemic heart disease or smoking. There is a significant negative correlation between QRS duration and LVOT VTI.

Keywords: Cardiac resynchronization therapy, left ventricular outflow tract velocity time integral, prediction, response, resynchronization

Introduction

Heart failure (HF) remains one of the prevalent and costly cardiovascular disease to treat in the health care system.[1]

Electrocardiogram (ECG) and echocardiography are widely used tests to investigate HF, QRS prolongation is an important criteria used for selection of HF patients for cardiac resynchronization therapy (CRT) insertion.[2,3]

Echocardiography is the most widely used test to investigate HF providing information on ejection fraction (EF), left ventricular (LV) volume, diastolic function, right ventricular (RV) function, hemodynamics, and valvular regurgitation.[4] Using Doppler we can estimate left ventricular outflow tract velocity time integral (LVOT VTI) which is a measure of the distance traveled by midstream blood through the LVOT in a single cardiac cycle (i.e., stroke distance). In European Society of Cardiology (ESC) guidelines, LVOT VTI <15 cm is defined as an abnormality suggesting reduced LV stroke volume (SV).[5]

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CRT improves cardiac performance, patients symptoms and reduces morbidity and mortality in appropriately selected patients\(^6\) by producing reverse remodeling, improving EF and reducing mitral regurgitation and in LV volumes.\(^6\)

For patients with moderate-to-severe HF (New York Heart Association [NYHA] Class III–IV), CRT has been shown in multiple trials (MUSTIC SR, MIRACLE, CONTAK-CD, MIRACLEICO) to provide very consistent improvements in NYHA functional class ranking, exercise capacity, peak oxygen consumption, and quality of life.\(^7\)

According to the latest ESC guidelines, CRT is recommended in symptomatic patients with reduced EF (35% with sinus rhythm and QRS duration >130 with left bundle branch block (LBBB), and to be considered in patients with non-LBBB and QRS >130.\(^8\)

CRT effect on mortality mentioned above is most probably related to the reverse remodeling or anti-remodeling property of the device.\(^9\) The reported long-term data from REVERSE confirm the long lasting beneficial effect of CRT.

CRT response rates varied significantly and are highly dependent on the criteria used to define the response.\(^12\) Lack of response to CRT may be attributed to inappropriate patient selection.\(^13\)

However, a variable proportion of CRT patients do not benefit from treatment (termed “non-responders”). The problem of nonresponse to CRT might become increasingly important. The effort to improve patient selection in order to maximize human and financial resource utilization has fallen short so far.

QRS prolongation is an independent stable criteria used for long time for selection of patients for CRT insertion, an inverse correlation exists between QRS prolongation measured by surface ECG and left ventricular ejection fraction (LVEF).\(^2\) Barold et al. found a stepwise increase in the prevalence of systolic LV dysfunction as QRS complex duration increased progressively above 120 ms.\(^3\)

There are several echocardiographic techniques used to improve response to CRT by optimizing atrioventricular delay, the most widely employed being Ritter’s and iterative techniques. Both of them aim to maximize atrial emptying and LV filling, thus maximizing the diastolic transmural flow.\(^14\)

A wide QRS has traditionally been used as a marker of patients with mechanical dyssynchrony. Nawar et al. showed a significant correlation between VV programming based on the shortest QRS interval at 12-lead ECG pacing and that based on highest LVOT VTI by echocardiography. A combined ECG and echocardiographic approaches although time consuming technique, however could be more convenient solution in performing CRT device optimization.\(^15\)

**Aim of study**

To study the correlation between QRS duration and cardiac output (CO) measured by LVOT VTI in patients with CRT implanted.

**Methods**

Over a period of 15 months from May 2018 to August 2019, we studied 100 patients with sequential activation capability biventricular pacing system. They included 60 males and 40 females. The patients were studied at the pacemaker follow-up clinic. The following patients were excluded from the study: those not on optimal medical treatment, patients with nonfunctioning CRT, uncooperative patients. Each patient was subjected to: Full medical history with special emphasis on: age and gender, indication for implantation, date of implantation, medical treatment and duration from onset of symptoms till implantation. General and local examination including heart rate (HR), blood pressure and body mass index (BMI) and body surface area (BSA) is calculated from the following equation:

\[
\text{BSA} = \sqrt{\frac{\text{weight} \times \text{height}}{3600}}
\]

**Electrocardiographic measurements**

A 12 lead ECG was at a paper speed of 25 mm/s and 10-mm/mV gain, and QRS duration in ms was measured from the first deflection of the QRS complex to its terminal isoelectric component.

**Echocardiography study**

All patients were subjected to transthoracic echocardiographic examination using vivid 7 echocardiographic machine using a 3.5 MHz transducer. A parasternal long axis view was obtained; measuring the caliper of the LVOT diameter was made in mid-systole. An apical five chamber view was obtained, the LVOT VTI was measured by pulsed-wave Doppler in the LVOT using a 2 mm sample volume positioned just proximal to the aortic valve. The LVOT VTI is considered as a surrogate of SV according to the following equation:

\[
\text{Flow rate} = \text{cross sectional area (CSA)} \times \text{flow velocity}
\]

\[
\text{SV} = \text{CSA} \times \text{VTI}
\]

\[
\text{Stroke volume index (SVi)} = \text{SV/BSA}
\]

\[
\text{CO} = \text{SV} \times \text{HR}
\]

**Definition of response**

Patients were considered responders if they had a one class or more improvement in NYHA classification and they didn’t hospitalize for acute HF decompensation.\(^12\)

**Statistical analysis**

Recorded data were analyzed using the Statistical Package for Social Sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation. Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples *t*-test, one-way analysis of variance when comparing between more than two means, Chi-square test of significance was used in order to compare proportions between two qualitative parameters
- Pearson’s correlation coefficient test was used to assess
the degree of association between two sets of variables

• Receiver operating characteristic (ROC curve) analysis was used to find out the overall predictivity of parameter in and to find out the best cut-off value with detection of sensitivity and specificity at this cut-off value

• Sensitivity = (true +ve)/[(true +ve) + (false –ve)]

• Specificity = (true –ve)/[(true –ve) + (false +ve)]

• Positive predictive value (PPV) = (true +ve)/[(true +ve) + (false +ve)]

• Negative predictive value (NPV) = (true –ve)/[(true –ve) + (false –ve)].

• Binary logistic regression: was used to predict the outcome of categorical variable based on one or more predictor variables

• The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the P value was considered significant as the following:

  - Probability (P value)
  - P < 0.05 was considered significant
  - P < 0.001 was considered as highly significant
  - P > 0.05 was considered insignificant.

### Results

There were 60 men and 40 women (ranged age 24–81 with mean 58.25 ± 11.78, BMI 19–40 [27.49 ± 3.79], BSA 1.5–2.3 [1.86 ± 0.16]). The indication for CRT was chronic HF (13%), dilated cardiomyopathy (DCM) (46%) and ischemic cardiomyopathy (ICM) (41%) [Table 1].

The mean QRS duration was 127.10 ± 28.54, with 64 patients <130 ms, 15 patient 130–150 ms, and 21 patient >150 ms. The LVOT diameter (cm) ranged 1–3 with a mean 2.23±0.36, LVOT VTI (cm²) 5–27.5 (15.92 ± 5.32), SV (cm³) 15.7–138.74 (63.42 ± 24.98), CO (L/min) 1.2–8.7 (4.60 ± 1.79) and Svi (ml/m²) 8.63–64 (33.53 ± 13.00) [Table 2].

According to the clinical response of the patients, they were divided into responders, if they had an improvement in NYHA class ≥1 and didn’t admitted in hospital for HF decompensation post-CRT implantation, and nonresponders.

We found a statistically significant difference between responders and nonresponders in age, BSA and time since CRT implantation. There was also a statistically significant difference between both groups according to smoking status, these differences are illustrated in Table 3.

According to the ECG and echocardiographic findings, we find that responders had narrower QRS complex and smaller LVOT diameter, but larger LVOT VTI, SV, CO and Svi. All these differences were statistically significant [Table 4].

We studied the correlation between the postimplant QRS duration and echocardiographic measures of CO. We found a statistically significant positive correlation between QRS duration and LVOT diameter, also we found a negative significant correlation between QRS duration with LVOT VTI [Figure 1] and Svi [Table 5].

Furthermore, ROC curve was used to define the best cut off value [Table 6] of:

• LVOT VTI was >17.1, with sensitivity of 63.5% specificity of 59.2% PPV of 61.1%, NPV of 58.7% with diagnostic accuracy of 68.3%

• QRS duration was <130, with sensitivity of 52.7% specificity of 48.7% PPV of 49.9%, NPV of 50.7% with diagnostic accuracy of 51.1%.

Based on the results of Univariate regression analysis [Table 7] to detect which parameter would help to detect the response to CRT we found a positive significant correlation between LVOT diameter and a negative significant correlation between LVOT VTI with P value <0.001 and P value <0.001 respectively:

$$P = \frac{e^{0.164(LVOT\ VTI)-2.31}}{1 + e^{0.164(LVOT\ VTI)-2.31}}$$
Using patient’s specific LVOT VTI, if the value of $P > 0.66$ (the estimated cut-off value for the deduced equation), the patient is more likely to benefit from CRT (CRT-on). If the calculated $P < 0.66$, the patient is less likely to benefit from CRT (CRT-off).

**Table 2: Postimplantation electrocardiogram and echocardiographic findings**

| Echo and ECG finding | Mean +/− SD |
|----------------------|-------------|
| QRS duration (ms), mean±SD (range) | 127.10±28.54 (80-200) |
| QRS class, n (%)       |             |
| <130                  | 64 (64)     |
| 130-150               | 15 (15)     |
| >150                  | 21 (21)     |
| LVOT diameter (cm), mean±SD (range) | 2.23±0.36 (1-3) |
| LVOT VTI (cm), mean±SD (range) | 15.92±5.32 (5-27.5) |
| SV (cm³), mean±SD (range) | 63.42±24.98 (15.7-138.74) |
| CO (L/min), mean±SD (range) | 4.60±1.79 (1.2-8.7) |
| SVi (ml/m²), mean±SD (range) | 33.53±13.00 (8.63-64) |

LVOT=Left ventricular tract outflow tract, SD=standard deviation, CO=Cardiac output, SV=Stroke volume, SVi=SV index, ECG=Electrocardiogram, VTI=Velocity time integral, QRS=QRS duration

**Figure 1:** Scatter plot between QRS duration and left ventricular outflow tract velocity time integral

**Table 3: Comparison between responder and nonresponder according to demographic and clinical characteristics**

| Patient characteristic | Responder (n=48), n (%) | Nonresponder (n=52), n (%) | t/χ² | P       |
|------------------------|-------------------------|----------------------------|------|---------|
| Gender                 |                         |                            |      |         |
| Male                   | 25 (52.1)               | 35 (67.3)                  | 2.411* | 0.121   |
| Female                 | 23 (47.9)               | 17 (32.7)                  |      |         |
| Age (years)            | 55.38±13.58             | 60.90±9.20                 | 5.762 | 0.018*  |
| BMI (weight/height²)   | 27.17±4.20              | 27.79±3.37                 | 0.671 | 0.415   |
| BSA                    | 1.83±0.16               | 1.89±0.16                  | 4.373 | 0.039*  |
| Time since CRT implantation (years) | 3.90±1.79 | 2.77±1.76 | 10.09 | 0.002*  |
| Indication of CRT      |                         |                            |      |         |
| Chronic HF             | 7 (14.6)                | 6 (11.5)                   | 2.244* | 0.326   |
| DCM                    | 25 (52.1)               | 21 (40.4)                  |      |         |
| ICM                    | 16 (33.3)               | 25 (48.1)                  |      |         |
| Co-morbidities         |                         |                            |      |         |
| DM                     | 20 (41.7)               | 22 (42.3)                  | 0.040 | 0.948   |
| HTN                    | 27 (56.3)               | 25 (48.1)                  | 0.668 | 0.414   |
| IHD                    | 17 (35.4)               | 24 (46.2)                  | 1.190 | 0.275   |
| Smoking                | 8 (16.7)                | 25 (48.1)                  | 11.138 | <0.001** |

P<0.05 NS, *P<0.05 S, **P<0.001 HS. Independent sample t-test. $χ^2$=Chi-square test, NS=Not significant, HS=Highly significant, BMI=Body mass index, BSA=Body surface area, CRT=Cardiac resynchronization therapy, DCM=Dilated cardiomyopathy, ICM=Ischemic cardiomyopathy, DM=Diabetes mellitus, HTN=Hypertension, IHD=Ischemic heart disease, HF=Heart failure

**Table 4: Comparison between responder and nonresponder according to electrocardiogram and echo finding**

| Echo and ECG finding | Responder (n=48) | Nonresponder (n=52) | t-test | P       |
|----------------------|------------------|---------------------|--------|---------|
| QRS duration         | 114.58±20.42     | 136.42±34.44        | 9.820  | 0.007** |
| LVOT diameter (cm)   | 2.12±0.33        | 2.35±0.36           | 10.849 | <0.001**|
| LVOT VTI (cm³)       | 19.15±3.74       | 12.93±4.81          | 51.526 | <0.001**|
| SV (cm³)             | 80.75±13.83      | 47.42±22.16         | 79.842 | <0.001**|
| CO (L/min)           | 5.97±1.25        | 3.34±1.18           | 116.396 | <0.001**|
| SVi (ml/m²)          | 44.63±7.94       | 23.38±6.83          | 208.732 | <0.001**|

*P<0.05 S, **P<0.01 HS. S=Significant, HS=Highly significant, LVOT=Left ventricular tract outflow tract, VTI=Velocity time integral, CO=Cardiac output, SV=Stroke volume, SVi=SV index, ECG=Electrocardiogram, QRS=QRS duration

**Discussion**

We studied 100 patients with implanted CRT, 60 of them were males and 40 females, their mean age was 58.25 years and most of them had DCM (46%), the remaining are of ischemic heart failure.
type (41%) and undetermined etiology (13%). In our study, patients were considered CRT responders if they had a one or more improvement in NYHA class and they didn‘t hospitalize for acute decompensation since insertion of the CRT.\(^{[12]}\)

There was no significant difference between responders and nonresponders in gender, BMI, indication for CRT implantation and disease comorbidity (diabetes mellitus, hypertension and ischemic heart disease [IHD]). However, there was a significant difference in age, BSA, time since CRT implantation and smoking status.

We found that responders were younger in age, and this was a statistically significant difference \((P = 0.018)\). The mean age of responders were 55.38 years while that of the nonresponder were 60.90 years which could be attributed to the shorter duration of the disease and less progression of cardiac negative remodeling in contrast to the older age patients. This come in agree with the study done by Zoltan \(et\ al.\) which concluded that the responders were younger in age (70 vs. 74 years, \(P = 0.04\)).\(^{[16]}\)

Another statistically significant difference between both groups was the BSA, we found that the responders had less BSA (1.83 vs. 1.89 \(m^2\)). This looks to be accepted theoretically as the obesity is considered to affect multisystem and come in agree with the last ESC HF guidelines which suspect that CRT response is more in female with less BSA.\(^{[9]}\) and also with the study done by Hsu \(et\ al.\) which stated that lower BMI is associated with superior echocardiographic response and improvement of LVEF, which itself was associated with improved clinical outcomes.\(^{[17]}\) On the other hand, many studies concluded that obesity is paradoxically associated with improved outcome after CRT implantation. This was showed by Wand \(et\ al.\) who concluded that higher BMI is strongly associated with improved long-term survival free from transplant or ventricular assist device after cardiac resynchronization therapy with defibrillator.\(^{[18]}\)

In our study the time since CRT implantation was longer in the responder group (3.9 vs. 2.77 year for nonresponders) \((P = 0.002)\). This come in agreement with the study conducted by Burns \(et\ al.\) which showed that the response to CRT increased with time and 43% of the patients who were non responders after 1 year became responders after 3 years.\(^{[19]}\)

As regard smoking, we also found a statistically significant difference in smoking status between both groups, 16.7% of responders had previous smoking history while in nonresponders the percentage was 48.1% with \(P < 0.001\). This come in agreement with the previous mentioned study done by Hsu \(et\ al.\) which found that patients without previous smoking history or IHD were associated with super response to CRT and this was statistically significant.\(^{[17]}\)

According to the electrocardiographic findings, we found that responders had a significantly narrower postimplantation QRS duration than the nonresponders (114.58 vs. 136.42, \(P = 0.007\). This come in agreement with many studies such as that conducted by Molhoek \(et\ al.\) which found a significant reduction in QRS duration immediately (from 179 ± 30 ms to 158 ± 26 ms, \(P < 0.01\)) after CRT implantation and after 6 months (from 179 ± 30 ms to 159 ± 25 ms, \(P < 0.01\)), however non responder did not exhibit a significant shortening.\(^{[20]}\)

As regard echocardiographic findings, we found that responders had a significant higher postimplantation LVOT VTI (19.15 vs. 12.93 cm, \(P < 0.001\)). This come in agreement with Rism \(et\ al.\) study which showed that the LVOT VTI was greater significantly in responders (17.1 cm) than nonresponders (15.4 cm) at 6 months \((P < 0.001)\).\(^{[21]}\)

We also found a significant difference between responders and nonresponders as regard CO. It was higher in responders (5.97 vs. 3.34, \(P < 0.001\)). Most of the studies compare between responders and nonresponders as regard preimplantation QRS, QRS shortening and aortic or LVOT VTI. We didn‘t find studies comparing between both groups as regard echocardiographic measurement of CO.

In our study, we aimed to correlate between the QRS duration and echocardiographic measures of CO postimplantation as parameters for prediction of response to CRT. We found a negative significant correlation between QRS duration with LVOT VTI \((P = 0.003)\) and SVI \((P = 0.041)\). This come in agreement with Derval \(et\ al.\) who found that postimplantation QRS duration (during LV pacing) is inversely correlated

| Table 5: Correlation between QRS duration and cardiac output, using Pearson correlation coefficient of the study group |
|-----------------|------|------|
|                  | \(r\) | \(P\) |
| LVOT diameter (cm) | 0.381 | 0.027* |
| LVOT VTI (cm)      | −0.494 | 0.003* |
| SV (cm³)           | 0.003 | 0.975  |
| CO (L/min)         | −0.088 | 0.384  |
| Svi (ml/m²)        | −0.317 | 0.041* |
| Pulse rate (beat/min) | −0.033 | 0.748  |

\(P<0.05\) NS; \(*P<0.05\) S, \(r\)=Pearson correlation coefficient, S=Significant, HS=Highly significant, LVOT=Left ventricular tract outflow tract, VTI=Velocity time integral, CO=Cardiac output, SV=Stroke volume, Svi=SV index, QRS=QRS duration

| Table 6: Defining optimal cut off values for optimal response to cardiac resynchronization therapy |
|-----------------|-------|------|------|------|------|------|
|                  | Cut-off | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
| LVOT VTI (cm)    | 17.1   | 63.5  | 59.2  | 61.1  | 58.7  | 68.3  |
| QRS duration (ms)| 130    | 52.7  | 48.7  | 49.9  | 50.7  | 51.1  |

LVOT=Left ventricular tract outflow tract, VTI=Velocity time integral, PPV=Positive predictive value, NPV=Negative predictive value, QRS=QRS duration
to hemodynamic response ($P < 0.001$).\cite{22} It also comes in agreement with Horwich et al. who found that upgrading the patient from RV pacing to CRT would associated with significant reduction in QRS duration and comparable improvement in indices of systolic function.\cite{23}

However, it disagrees with Sassone et al. who demonstrated in the subgroup analysis that there was a significant linear inverse relation between LV dyssynchrony and QRS duration in patients with nonischemic origin because septal-to-lateral wall delay shortens as the QRS duration lengthens ($P = 0.006$); conversely, this was not demonstrated in ischemic patients.\cite{24} however, the QRS discussed in this study was the baseline preimplantation QRS.

From the above mentioned correlation, we can say that prediction of response to CRT could be assessed simply during or postimplantation by either surface ECG QRS duration or echocardiographic LVOT diameter and LVOT VTI, and our results pointed to that the shorter QRS duration post-CRT implantation could be a target per say and encourage operators to do every effort during and postimplantation to reach the shorter QRS complex. Multi-electrodes CS lead with different polarities, multisite CS lead and his bundle pacing all might help in reaching narrower QRS duration and improving CRT response and needs further researches. Our results comes in agreement with the study performed by Nawar et al. who found a significant concordance during ventricular pacing between V–V programming based on the shortest QRS interval at 12-lead ECG pacing and echocardiographic-guided V–V interval optimization using LVOT VTI and recommended that a combined ECG-and echocardiographic approach could be a more convenient solution in performing V–V optimization.\cite{15}

Moreover, intraoperative selection of coronary sinus tributary which will lead to more QRS shortening is preferable. This come in agree with Bomb et al. who concluded that postimplant QRS duration prolongation is associated with a worse clinical outcome and these patients have poorer LV function and size.

However, focusing on obtaining a shorter QRS duration, may improve outcomes in patients undergoing CRT.\cite{25}

From the above comparison between the responders and nonresponders and from the ROC curve we concluded that the postimplantation optimal cut off values for prediction of response to CRT for postimplant LVOT VTI and QRS duration were 17.1 cm and 130 ms respectively with an accuracy of 68.3 and 51.1% respectively, although this is modest results, however this may reflects prediction of response and could be a target in CRT implantation or optimization to improve the response to CRT. Bonakdar et al. identified that preimplantation QRS width $>145$ ms, QRS shortening $>20$ ms, and early postimplantation aortic VTI $>14$ cm are optimal cut off values to predict responders.\cite{26} however this cut off values need to be emphasized with large scale studies.

Finally, and based on the results of multivariate regression analysis, we can conclude an equation for prediction of CRT response using the early postimplantation patient specific LVOT VTI. Based on this equation, if the value of $P > 0.66$, the patient is more likely to benefit from CRT (CRT-on). If the calculated $P < 0.66$, the patient is less likely to benefit from CRT (CRT-off).

However, some limitations in our study should be noted. First we focused on specific ECG and echocardiographic parameters which is the core of our study with less data available on other echocardiographic findings in these patients. Second we collected and analyzed the data from our patients only after cardiac device implantation in the pacemaker clinic, however we did not address echocardiographic data before device implantation in our study. We also were specified to our aiming target which is correlating the QRS width with the LV outflow VTI regardless the position or the characteristic of the coronary sinus lead. Also the sensitivity and specificity of our results are somewhat modest and further studies with larger number of patients could be conducted.

**Conclusion**

Based on the results of the current study it can be concluded that: CRT response is more in patients with lower BSA, and without previous history of IHD or smoking. CRT response increase with increase of the time since CRT implantation. There is significant negative correlation between QRS duration and LVOT VTI. Postimplantation cut off value of QRS duration ($<130$) predict higher LVOT VTI and also the postimplantation benefit for the patient with CRT implanted.

**Recommendations**

1. We recommend use of postimplantation QRS duration as a simple method for CRT optimization
2. Prediction of response to CRT could be assessed by either postimplantation QRS duration or LVOT VTI
3. Postimplantation cut off values can be used for identification of patients with optimum response to CRT
4. Postimplantation cut off value of QRS duration ($<130$) predict higher LVOT VTI and also the postimplantation benefit for the patient with CRT implanted
5. Our results raise the importance of using tools to reduce QRS duration e.g., either quadrupolar leads or his bundle pacing in optimizing the response to CRT as both of them achieve a shorter QRS duration
6. CRT response is more in female with non-ICM, lower BSA and longer time since CRT implantation
7. Further studies are needed to verify the similarity with our cut off values for CRT response prediction.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart disease and stroke statistics – 2017 update: A report from the American heart association. Circulation 2017;135:e146-603.
2. Mant J, Doust J, Roalfe A, Barton P, Cowie MR, Glasziou P, et al. Systematic review and individual patient data meta-analysis of diagnosis of heart failure, with modelling of implications of different diagnostic strategies in primary care. Health Technol Assess 2009;13:1-207.
3. Kashani A, Barold SS. Significance of QRS complex duration in patients with heart failure. J Am Coll Cardiol 2005;46:2138-2142.
4. Tan C, Rubenson D, Srivastava A, Mohan R, Smith MR, Billick K, et al. Left ventricular outflow tract velocity time integral correlates with low cardiac output syndrome in patients with acute decompensated heart failure. Cardiovasc Ultrasound 2017;15:18.
5. Owen JS, Khatib S, Morin DP. Cardiac resynchronization therapy. Ochsner J 2009;9:248-56.
6. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med 2002;346:1845-53.
7. Linde C, Ellenbogen K, McAlister FA. Cardiac resynchronization therapy (CRT): Clinical trials, guidelines, and target populations. Heart Rhythm 2012;9:S3-13.
8. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur J Heart Fail 2016;18:891-975.
9. Waring AA, Litwin SE. Redefining reverse remodeling: Can echocardiography refine our ability to assess response to heart failure treatments? J Am Coll Cardiol 2016;68:1277-80.
10. Breithardt OA. Reversing heart failure by CRT: How long do the effects last? Eur Heart J 2013;34:2582-4.
11. Linde C, Gold MR, Abraham WT, St John Sutton M, Ghio S, Cerkenvik J, et al. Long-term impact of cardiac resynchronization therapy in mild heart failure: 5-year results from the resynchronization reverses remodeling in systolic left ventricular dysfunction (reverse) study. Eur Heart J 2013;34:2592-9.
12. Tomassoni G. How to define cardiac resynchronization therapy response. J Innov Card Rhythm Manag 2016;7:S1-7.
13. Russell SD, Saval MA, Robbins JL, Ellestad MH, Gottlieb SS, Handberg EM, et al. New York Heart Association functional class predicts exercise parameters in the current era. Am Heart J 2009;158:S24-30.
14. Brabham W, Gold M. The role of AV and VV delay optimization in CRT. J Arrhythmia 2013;29:153-61.
15. Nawar A, Hoseiny RE, Ragab D, Al-Aziz AA. V–V delay interval optimization in CRT using echocardiography compared to QRS width in surface ECG. Egyptian Heart J 2011;64:127-33.
16. Zoltan B, Christian R, Uzma C, Anna WE, Anders R, Lingwei W, et al. Positive response to cardiac resynchronization therapy – The role of NT-proBNP. Int J Cardiovas Res 2016;5:2.
17. Hsu JC, Solomon SD, Bourgoun M, McNitt S, Goldenberg I, Klein H, et al. Predictors of super-response to cardiac resynchronization therapy and associated improvement in clinical outcome: The MADIT-CRT (multicenter automatic defibrillator implantation trial with cardiac resynchronization therapy) study. J Am Coll Cardiol 2012;59:2366-73.
18. Wand AL, Grandin EW, Zamani P, Rame JE, Verdino RJ. Obese patients have improved ten-year survival after CRT-D implantation. J Cardiac Failure 2015;21 Suppl 8:S11-2.
19. Burns KV, Gage RM, Curtin AE, Bank AJ. Longterm echocardiographic response to cardiac resynchronization therapy in initial nonresponders. JACC: Heart Fail 2015;3:990-7.
20. Molhoek SG, VAN Erven L, Bootma M, Steendijk P, Van Der Wall EE, Schalij MJ. QRS duration and shortening to predict clinical response to cardiac resynchronization therapy in patients with end-stage heart failure. Pacing Clin Electrophysiol 2004;27:308-13.
21. Rism N, Sogaard P, Hansen TF, Bruun NE, Hoffmann S, Kisslo J, et al. Comparison of dyssynchrony parameters for VV-optimization in CRT patients. Pacing Clin Electrophysiol 2013;36:1382-90.
22. Derval N, Bordachar P, Lim HS, Sacher F, Ploux S, Laborde J, et al. Impact of pacing site on QRS duration and its relationship to hemodynamic response in cardiac resynchronization therapy for congestive heart failure. J Cardiovasc Electrophysiol 2014;25:1012-20.
23. Horwich TB, Foster E, De Marco T, Tseng Z, Saxon L. Effects of resynchronization therapy on cardiac function in pacemaker patients “upgraded” to biventricular devices. J Cardiakos Electrophysiol 2004;15:1284-9.
24. Sassone B, Bertini M, Beltrami M, Malagù M, Papanisi G, Kusworn HA, et al. Relation of QRS duration to response to cardiac resynchronization therapy in patients with left bundle branch block. Am J Cardiol 2017;119:1803-8.
25. Bomb R, Logan J, Madsen R, Sullivan R, Weachter R, Flake G. QRS prolongation following cardiac resynchronization: Incidence, predictors, and outcomes. J Innov Cardiac Rhythm Manag 2013;4:1346-54.
26. Bonakdar HR, Jorat MV, Fazelifar AF, Alizadeh A, Givtaj N, Samei N, et al. Prediction of response to cardiac resynchronization therapy using simple electrocardiographic and echocardiographic tools. Europace 2009;11:1330-7.