ORIGINAL ARTICLE

Adjusting the QRS Duration by Body Mass Index for Prediction of Response to Cardiac Resynchronization Therapy: Does One QRS Size Fit All?

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Background: QRS duration (QRSd) is known to be affected by body weight and length. We tested the hypothesis that adjusting the QRSd by body mass index (BMI) may provide individualization for patient selection and improve prediction of cardiac resynchronization therapy (CRT) response.

Methods: A total of 125 CRT recipients was analyzed to assess functional (≥1 grade reduction in NYHA class) and echocardiographic (≥15% reduction in LVESV) response to CRT at 6 months of implantation. Baseline QRSd was adjusted by BMI to create a QRS index (QRSd/BMI) and tested for prediction of CRT response in comparison to QRSd.

Results: Overall, 81 patients (65%) responded to CRT volumetrically. The mean QRS index was higher in CRT responders compared to nonresponders (6.2 ± 1.1 vs 5.2 ± 0.8 ms.m^2/kg, $P < 0.001$). There was a positive linear correlation between the QRS index and the change in LVESV ($r = 0.487$, $P < 0.001$). Patients with a high QRS index (≥5.5 ms.m^2/kg, derived from the ROC analysis, AUC = 0.787) compared to those with a prolonged QRSd (≥150 ms, AUC = 0.729) had a greater functional (72% vs 28%, $P < 0.001$) and echocardiographic (80% vs 44%, $P < 0.001$) improvement at 6 months. QRS index predicted CRT response at regression analysis.

Conclusions: Indexing the QRSd by BMI improves patient selection for CRT by eliminating the influence of body weight and length on QRSd. QRS index is a novel indicator that provides promising results for prediction of CRT response.

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QRS duration; QRS index; cardiac resynchronization therapy; CRT response

Since the preliminary studies[1,2] that proved the beneficial effects of biventricular pacing in heart failure, the major concern has been targeted to identification of responders to cardiac resynchronization therapy (CRT) based on the baseline clinical features. Several ECG predictors have been tested previously to designate a parameter to correlate with outcomes after CRT.[3–5] However, a significant intraventricular conduction delay reflected by a prolonged QRS duration (QRSd ≥150 ms) with left bundle branch block (LBBB) morphology remained as the main CRT indication for patients with symptomatic heart failure and reduced ejection fraction as recommended by the current guidelines.[6]

Eligibility for CRT based on the QRSd on the surface ECG may be prone to selection errors derived from individual differences in left ventricular dimensions, gender, and body size leading to a misdiagnosis of patients that would benefit from CRT, especially for those within the gray zone for QRSd (between 120 and 150 ms). In this study, we hypothesized that eliminating the effect of body weight and length on QRSd would improve patient selection for CRT and provide a better prediction of CRT response compared to QRSd.

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MATERIAL AND METHODS

Patient Selection and Study Design

A total of 151 patients that received a biventricular device with or without a defibrillator (CRT-D or CRT-P) was retrospectively analyzed in the study. Compatible with these guidelines,[6] all patients had a left ventricular ejection fraction (LVEF) ≤35%, an increased QRSd (≥120 ms), and symptomatic heart failure (NYHA II–IV) despite optimal medical therapy. Patients with right ventricular pacing upgraded to CRT (n = 8) were excluded. Patients with inadequate image quality to calculate left ventricular (LV) volumes and ejection fraction (n = 12) were excluded from the study. Patients who failed to continue follow-up visits (n = 6) were also excluded and the final study population consisted of 125 CRT recipients. The study protocol was approved by the local ethics committee and written informed consent was obtained from all participants.

ECG Recordings and Calculation of QRS Index

Baseline and postimplantation (paced) 12-lead ECG tracings were recorded on a chart paper at a speed of 50 mm/sec with a gain setting of 10 mm/mV. QRSd was defined as the widest interval in any of the 12 leads. QRSd was manually measured and double-checked with the computer output. Baseline QRS morphologies were recorded as either LBBB or non-LBBB based on the well-defined criteria.[7] Paced QRS interval was calculated after echocardiographic optimization during the hospital stay.

Body mass index (BMI) was calculated for all patients according to body weight and length based on the existing formula (BMI = kg/m^2). Baseline QRSds were adjusted by BMI to obtain a QRS index (QRSd/BMI) for evaluating its effect on CRT response.

Device Implantation and Programming

Transvenous approach via the left subclavian vein was used to implant CRT-D or CRT-P devices under local anesthesia in the vast majority of patients. The right atrial lead was located in the right atrial free wall (in patients with sinus rhythm) and the right ventricular lead was located in the right ventricular apex or the outflow tract according to the operator's choice. Following a coronary sinus angiography, the LV lead was inserted preferably in the posterolateral vein as recommended.[8] In case of anatomic difficulties for implanting the LV lead in the optimal position (in 12 patients), minimal invasive surgical approach was preferred to implant an epicardial LV lead. Use of a defibrillator lead depended on the clinical indication or the operator's choice. Initial device programming was performed by setting default values of 100 ms for the sensed AV interval, 130 ms for the paced AV interval, and 20 ms for the VV interval (LV preceding RV). Both AV and VV intervals were checked before patient discharge and optimized with a previously described echocardiographic method in case of necessity.[9] The ECG obtained after optimization was used to calculate the paced QRSd.

Echocardiographic Analyses

Baseline and 6-month follow-up echocardiography were performed with a commercially available system (Vivid E9, General Electric, Milwaukee, WI, USA) using a 3.5 MHz transducer. The cine-loops for measurements of LV volumes and LVEF were recorded in the left lateral decubitus position. Offline analysis was performed by two expert sonographers who were blinded to the study data.

LV Measures

Apical two- and four-chamber views were used to calculate LV volumes both in end-systole (LVESV) and end-diastole (LVEDV); once obtained, the results were used to calculate the LVEF using the biplane Simpson's method.[10]

Follow-Up and Definition of CRT Response

The end points of the study were defined as functional and echocardiographic response to CRT at 6 months. Improvement in functional status (functional response) was defined as ≥1 grade decrease in NYHA class at 6 months of follow-up. Echocardiographic response was defined as a reduction in LVESV ≥15% at 6 months. The study population (n = 125) was divided into groups based on the cutoff values for both baseline QRSd (150 ms) and for QRS index (5.5 $ms.m^2/kg$) to evaluate and compare the functional and echocardiographic CRT response at 6 months.

Table 1. Baseline Demographic, Clinical, and Electrocardiographic Features of the Study Population and Comparison According to the Status of Echocardiographic Response to CRT at 6 Months

	Overall(n = 125)	CRT-R(n = 81)	CRT-NR(n = 44)	P Value
Age (years)	63.5 ± 11.7	62.5 ± 12.2	65.3 ± 10.8	0.224
Female gender % (n)	36% (45)	38% (31)	32% (14)	0.477
Length (cm)	164.2 ± 18.4	162.5 ± 20.8	167.3 ± 22.1	0.116
Weight (kg)	72.7 ± 11.2	72.3 ± 10.6	73.3 ± 12.3	0.455
BSA (/m^2)	1.86 ± 0.20	1.84 ± 0.23	1.89 ± 0.15	0.239
BMI (kg/m^2)	27.07 ± 4.10	27.49 ± 4.02	26.2 ± 4.07	0.131
Nonischemic etiology % (n)	54% (68)	52% (42)	59% (26)	0.442
Hypertension % (n)	72% (90)	70% (57)	75% (33)	0.585
Diabetes % (n)	34% (43)	38% (31)	27% (12)	0.220
Hyperlipidemia % (n)	45% (56)	47% (38)	41% (18)	0.523
Atrial fibrillation[a] % (n)	37% (46)	39% (32)	32% (14)	0.205
Baseline NYHA class	2.8 ± 0.7	2.8 ± 1.1	2.7 ± 0.4	0.124
CRT-D % (n)	88% (110)	86% (70)	91% (40)	0.232
LBBB morphology % (n)	82% (102)	79% (64)	86% (38)	0.345
Baseline QRSd (ms)	156.7 ± 21.9	163.2 ± 22.1	144.8 ± 16.1	0.012
Paced QRSd (ms)	146.1 ± 25.7	139.6 ± 24.3	158.1 ± 24.1	< 0.001
QRS index (ms.m^2/kg)	5.89 ± 1.14	6.26 ± 1.11	5.22 ± 0.83	< 0.001
Baseline LVESV (mL)	156.7 ± 50.5	151.7 ± 45.9	166.1 ± 57.5	0.130
Baseline LVEDV (mL)	211.8 ± 57.7	206.5 ± 51.6	221.4 ± 67.1	0.169
Baseline LVEF (%)	26.3 ± 5.6	26.9 ± 5,4	25.3 ± 6.1	0.142
Hb (g/dL)	12.5 ± 1.7	12.7 ± 1.6	12.1 ± 1.8	0.245
Cr (mg/dL)	1.08 ± 0.40	1.09 ± 0.4	1.07 ± 0.3	0.856
Medication % (n)				
Beta-blocker	94% (118)	95% (77)	93% (41)	0.477
ACE-I/ARB	95% (119)	95% (77)	95% (42)	0.921
Spironolactone	77% (96)	74% (60)	82% (36)	0.331
Furosemide	91% (114)	90% (73)	93% (41)	0.664
Digoxine	42% (53)	40% (32)	48% (21)	0.232
Nitrate	30% (38)	28% (23)	34% (15)	0.345
Amiodarone	38% (48)	36% (29)	43% (19)	0.122
Oral anticoagulation[b]	44% (55)	41% (33)	50% (22)	0.132

CRT-R = responders to CRT; CRT-NR = nonresponders to CRT; BSA = body surface area; BMI = body mass index; NYHA = New York Heart Association; CRT-D = biventricular device combined with a defibrillator; LBBB = left bundle branch block; LVESV = left ventricular end-systolic volume; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; Hb = hemoglobin; Cr = creatinine; ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker.
[a]Chronic or paroxysmal atrial fibrillation; [b]warfarin or novel agents (dabigatran, apixaban, or rivaroxaban).

Statistical Analyses

Statistical analyses were conducted using SPSS (version 17.0, SPSS Inc., Chicago, IL, USA). Data were expressed as mean ± SD for continuous variables and percentage for categorical variables. Shapiro-Wilk test was used to test normality and a P value >0.05 was defined as normally distributed data. Continuous variables were compared using Student's *t*-test for independent samples that showed normal distribution, while the Mann-Whitney U test was used for nonnormally distributed samples based on QRSd and QRS index. Associations of the categorical variables between groups were tested using chi-square test.

Pearson's correlation analysis was used to test the association between the baseline QRSd and the QRS index as a continuous variable with the change in LVESV (ΔLVESV). The results of the correlation were shown on separate scatted-dot graphs with the corresponding r and P values. The difference between the coefficients of the correlations was compared by the Fisher r-to-z transformation method. Receiver operating characteristic (ROC) analyses were also performed for defining cutoff levels for both QRSd and QRS index to detect CRT response. Results of the ROC analyses were expressed as area under the curve, SD, P value, and 95% confidence intervals (CI) along with a graphical demonstration. Based on the cutoff value,

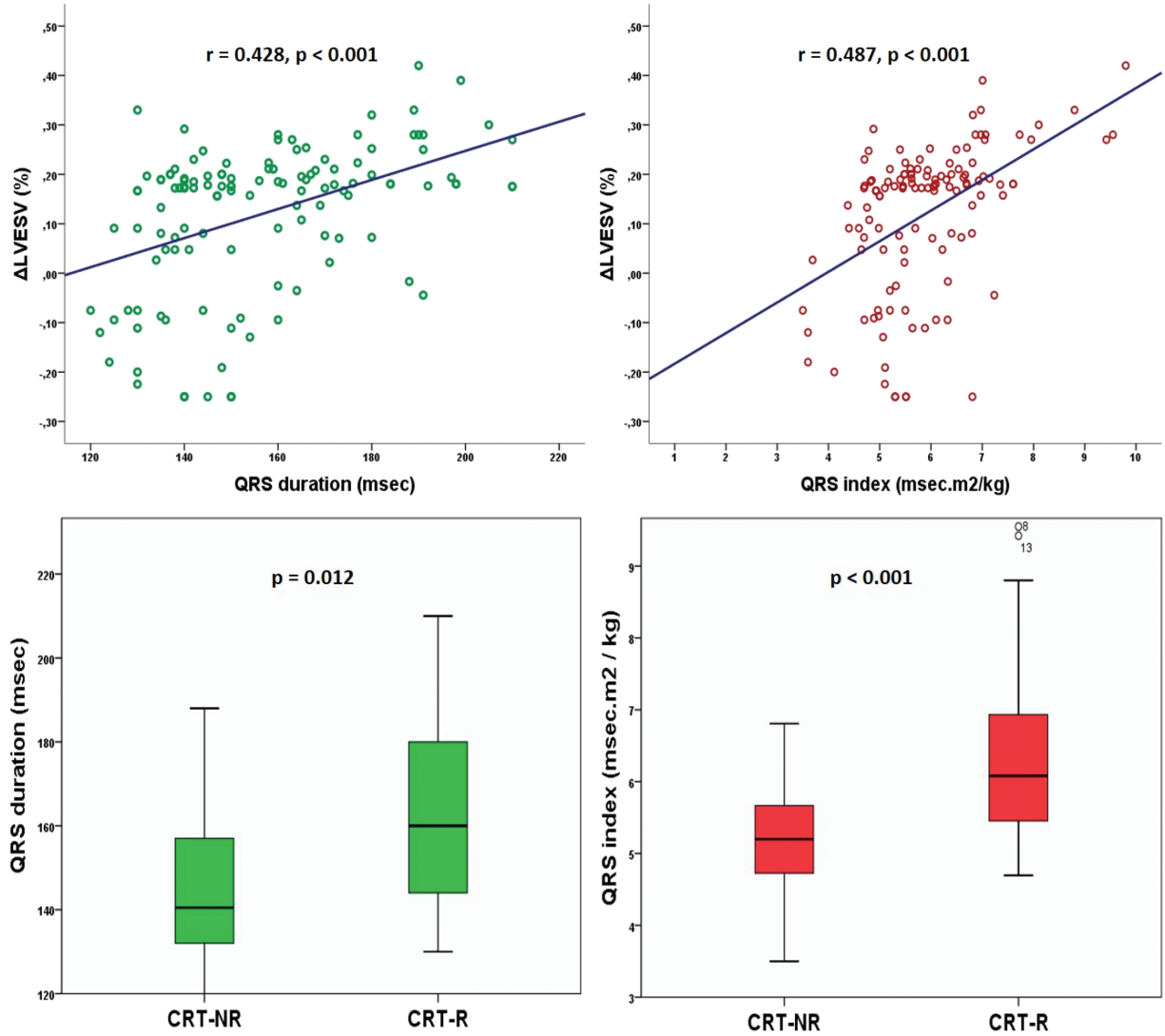

Figure 1. Demonstration of the association of the baseline QRSd and QRS index with the change in LVESV (ΔLVESV) and CRT response at 6 months. The correlation of QRS index with ΔLVESV (upper right panel, r = 0.487, P < 0.001) was stronger than the correlation of QRSd with ΔLVESV (upper left panel, r = 0.428, P < 0.001). Both the mean QRSd (P = 0.012) and the mean QRS index (P < 0.001) were significantly higher in patients with CRT-R (lower right and left panel, respectively).

the relation of QRS index with functional and volumetric CRT response were analyzed with chi-square tests and the results were expressed as odds ratio, Pearson chi-square, and P values and shown with separate clustered bar charts. CRT response parameters were compared based on the cutoff values for QRSd and QRS index by independent samples t-test and the results were shown with a table. Statistical significance was defined as a P value <0.05 for all comparisons.

Univariate and multivariate logistic regression analyses were performed in order to evaluate the predictive values of QRSd and QRS index for CRT response. Age, female gender, LBBB morphology, nonischemic etiology, baseline QRSd, QRSd ≥150 ms, QRS index, and QRS index ≥5.5 ms.m^2/kg were the independent variables whereas functional and volumetric CRT response were defined as the dependent variables of the regression models. Statistical significance was defined as a P

value <0.05 for all analyses. Significant variables in the univariate model were subsequently tested in the multivariate regression model. Results of the analyses were expressed as the P value and hazard ratio (HR) in CI of 95% and demonstrated within a table.

RESULTS

The study population (n = 125) had a mean age of 63.5 ± 11.7 (36% female), mean LVEF of 26.5 ± 5.7%, and mean baseline QRSd of 156.7 ± 21.9 ms. Overall, 81 patients (65%) responded to CRT at 6 months. Comparison of the baseline features of the study population based on CRT response was shown in Table 1. Patients with CRT response (CRT-R) had significantly longer baseline QRSd (163.2 ± 22.1 ms vs 144.8 ± 16.1 ms, P = 0.012), shorter-paced QRSd (139.6 ± 24.3 ms vs 158.1 ± 24.1 ms, P < 0.001) and higher QRS indices (6.26 ± 1.11 ms.m^2/kg vs 5.22 ± 0.83 ms.m^2/kg, P < 0.001) compared to patients with nonresponse to CRT (CRT-NR). Other baseline characteristics were comparable in two groups (P > 0.05).

Figure 1 demonstrates the association of the baseline QRSd and QRS index with the change in LVESV (ΔLVESV) and CRT response at 6 months. The correlation analysis of QRS index with ΔLVESV (upper right panel) revealed an r value of 0.487 and a P value <0.001, whereas the correlation analysis of QRSd with ΔLVESV (upper left panel) revealed an r value of 0.428 and a P value <0.001. Although numerically a higher correlation coefficient was obtained with the QRS index, the difference was not significant by the Fisher r-to-z transformation (P = 0.281). Both the mean QRSd (P = 0.012) and the mean QRS index (P < 0.001) were significantly higher in patients with CRT-R (lower right and left panel, respectively).

The Cutoff Values to Detect CRT Response

Based on the ROC analyses, the cutoff value of 5.5 ms.m^2/kg for QRS index had a numerically greater AUC value compared to the cutoff value of 150 ms of QRSd to identify CRT response (AUC = 0.787, 95% CI = 0.705–0.868, P < 0.001 vs AUC = 0.729, 95% CI = 0.638–0.819, P < 0.001). ROC curves were merged in a single graphic to differentiate the predictive performance of each parameter for CRT response in Figure 2.

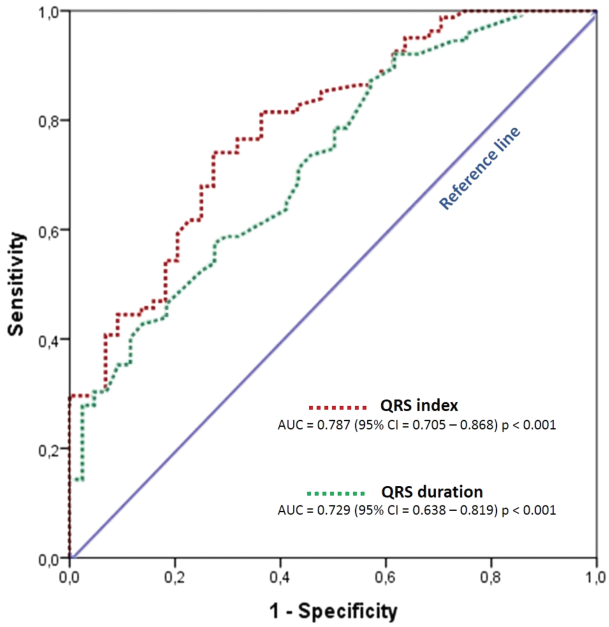

Figure 2. Analyses of the receiver operating characteristics (ROC) curves. Comparison of the cutoff value of 5.5 ms.m^2/kg for QRS index which had a greater area under the curve (AUC) compared to the cutoff value of 150 ms of baseline QRSd to identify CRT response (AUC = 0.787, 95% CI = 0.705–0.868, P < 0.001 vs AUC = 0.729, 95% CI = 0.638–0.819, P < 0.001 for QRS index and QRSd, respectively). ROC curves are merged in a single graphic to differentiate the predictive performance of each parameter for CRT response.

Comparison of the functional and echocardiographic CRT response parameters based on the cutoff values for both QRSd and QRS index was shown in Table 2. The mean baseline NYHA class, LVESV, and LVEF were similar (P > 0.05) in all groups. The comparison based on QRSd revealed that patients with a baseline QRSd ≥150 ms had a significant reduction in follow-up NYHA class (2.4 ± 0.9 vs 2.1 ± 0.8, P = 0.040) and in follow-up LVESV (149.7 ± 55.9 mL vs 127.1 ± 40.9 mL, P = 0.011) and a significant increase in follow-up LVEF (27.8 ± 6.6% vs 31.8 ± 7.2, P = 0.001). Although a high baseline QRSd was associated with a greater volumetric CRT response (51.6% [n = 33] vs 78.7% [n = 48], P = 0.002), functional response did not differ (46.9% [n = 30] vs 59.1% [n = 36], P = 0.174) in groups based on QRSd. In contrast, patients with a high QRS index (QRS index ≥5.5 ms.m^2/kg) showed a significant CRT response based on both functional improvement (71.8% [n = 51] vs 27.8% [n = 15], P < 0.001) and echocardiographic

Table 2. Comparison of the Functional and Echocardiographic Response Parameters Based on the Cutoff Values for QRSd and QRS Index in the Total CRT Cohort of 125 Patients

	QRSd <150 ms	QRSd ≥150 ms	P Value	QRS Index <5.5 ms.m²/s	QRS Index ≥5.5 ms.m²/kg	P Value
Number of patients	64	61		54	71	
Baseline NYHA class	2.9 ± 0.7	2.7 ± 0.7	0.363	2.9 ± 0.6	2.8 ± 0.7	0.350
Follow-up NYHA class	2.4 ± 0.9	2.1 ± 0.8	0.040	2.7 ± 0.9	1.9 ± 0.7	< 0.001
Functional response % (n)	46.9 (30)	59.1 (36)	0.174	27.8 (15)	71.8 (51)	< 0.001
Baseline LVESV (mL)	162.9 ± 60.1	150.3 ± 37.4	0.164	161.2 ± 49.5	153.3 ± 51.4	0.392
Follow-up LVESV (mL)	149.7 ± 55.9	127.1 ± 40.9	0.011	149.8 ± 50.8	130.1 ± 48.5	0.029
Change in LVESV (mL)	13.2 ± 23.7	23.2 ± 15.7	0.007	11.3 ± 22.1	23.2 ± 18.3	< 0.001
Baseline LVEF (%)	25.6 ± 5.7	27.1 ± 5.5	0.140	25.3 ± 6.1	27.1 ± 5.2	0.068
Follow-up LVEF (%)	27.8 ± 6.6	31.8 ± 7.2	0.001	27.3 ± 6.2	31.7 ± 7.3	0.001
Change in LVEF (%)	2.1 ± 4.9	4.7 ± 4.5	0.003	1.9 ± 4.6	4.5 ± 4.8	0.004
Echocardiographic response % (n)	51.6 (33)	78.7 (48)	0.002	44.4 (24)	80.3 (57)	< 0.001

NYHA = New York Heart Association; LVESV = left ventricular end-systolic volume; LVEF = left ventricular ejection fraction.

improvement (80.3% [n = 57] vs 44.4% [n = 24], P < 0.001) at 6 months. The mean follow-up NYHA class (1.9 ± 0.7 vs 2.7 ± 0.9, P < 0.001) and the mean follow-up LVESV (130.1 ± 48.5 mL vs 149.8 ± 50.8 mL, P = 0.029) were also significantly lower and the mean follow-up LVEF (31.7 ± 7.3% vs 27.3 ± 6.2, P = 0.001) was significantly higher in patients with a high QRS index.

Figure 3 demonstrates the strong association of the QRS index with the incidence of functional response (Fig. 3A) and the change in NYHA class compared to baseline (Fig. 3B). The relation of QRS index with echocardiographic CRT response was shown in Figure 4. Patients with a high QRS index were more likely to be CRT responders (Fig. 4A) and were associated with a significant reduction in LVESV (Fig. 4B) and significant increase in LVEF (Fig. 4C) at 6 months.

We also evaluated the impact of QRS index on CRT response in a subgroup analysis based on gender. The mean QRS index of females (6.14 ± 1.06 ms.m²/kg, n = 45) was higher than the mean QRS index of males (5.75 ± 1.16 ms.m²/kg, n = 80). The correlation between QRS index and ΔLVESV at 6 months was stronger in women compared to men (r = 0.642, P < 0.001 vs r = 0.384, P = 0.024). Moreover, the females with a QRS index ≥ms.m²/kg were more likely to be CRT responders compared to males with a high QRS index. Corresponding Pearson chi-square, P values, and the odds ratios (OR) in 95% CI were 12.411, P < 0.001, OR = 5.84 (2.09–16.26) vs 4.409, P = 0.012, OR = 4.16 (1.05–16.4) for females and males, respectively.

QRS Index for Prediction of CRT Response

Using a cutoff value of 5.5 ms.m²/kg for QRS index identified CRT responders with an odds ratio of 5.12 (95% CI = 2.37–10.97, P < 0.001) for functional improvement, and with an odds ratio of 5.08 (95% CI = 2.30–11.25, P < 0.001) for volumetric improvement. Univariate logistic regression analysis revealed that both QRSd (as a continuous variable) and QRSd ≥150 ms (as a dichotomous variable) predicted echocardiographic response (P = 0.024 and P = 0.002, respectively) but not functional response (P = 0.121 and P = 0.232, respectively). However, QRS index was a significant predictor of both echocardiographic response (HR = 3.399, 95% CI = 1.980–5.836, P < 0.001) and functional response (HR = 2.326, 95% CI = 1.515–3.712, P < 0.001). As a nominal variable, QRS index ≥5.5 ms.m²/kg was also a significant predictor of both echocardiographic response (HR = 1.662, 95% CI = 0.935–1.007, P = 0.021) and functional response (HR = 2.071, 95% CI = 0.808–5.010, P = 0.013). Multivariate predictors of functional CRT response were nonischemic etiology (HR = 1.242, 95% CI = 1.019–1.465, P = 0.046) and QRS index (HR = 1.662, 95% CI = 1.462–1.862, P = 0.012). Multivariate predictors of echocardiographic CRT response were QRSd ≥150 ms (HR = 0.701, 95% CI = 0.237–2.071, P = 0.031) and QRS index (HR = 2.011, 95% CI = 1.268–2.754, P = 0.005). The results are shown in Table 3.

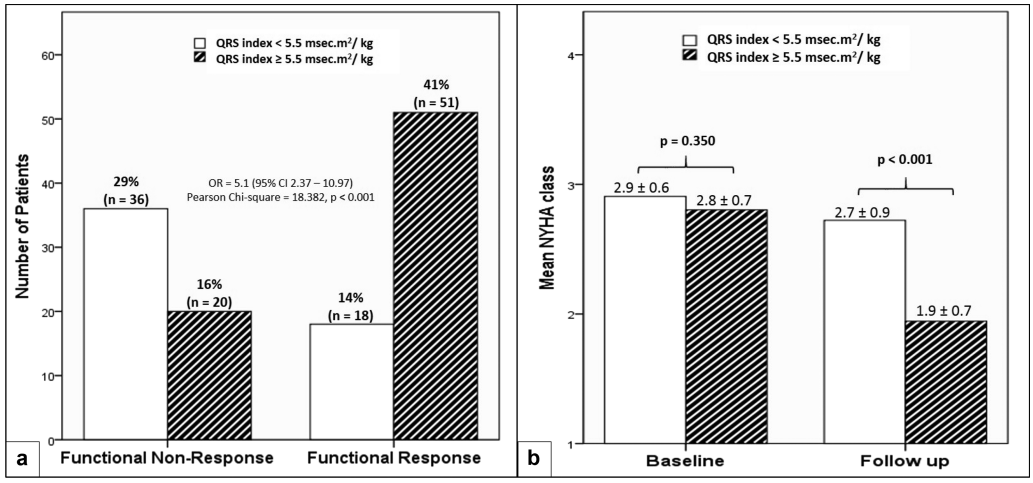

Figure 3. Demonstration of the association of the QRS index with the incidence of functional response (A) and the change in NYHA class compared to baseline **(**B**)**.

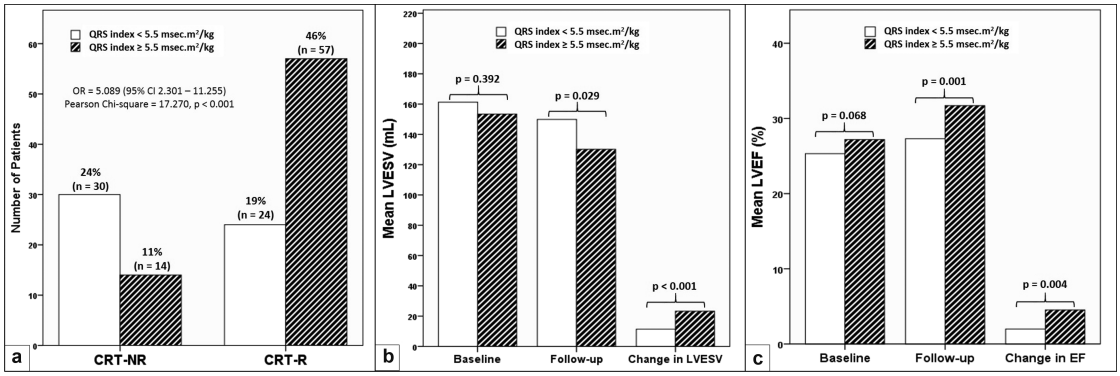

Figure 4. The relation of QRS index with echocardiographic CRT response. Patients with a high QRS index are more likely to be CRT responders (A) and are associated with a significant reduction in LVESV (B) and significant increase in LVEF (4C) at 6 months.

DISCUSSION

This study investigated the predictive value of the QRS index for CRT response compared to the conventional assessment with QRSd. Patients with CRT response had significantly higher QRS indices compared to nonresponders. QRS index was found to have a significant correlation with LV reverse remodeling (ΔLVESV at 6 months) with a correlation coefficient numerically higher than that of the QRSd. Besides, the cutoff value of 5.5 ms.m^2/kg for QRS index clearly distinguished CRT responders with an AUC greater than the cutoff value of 150 ms for QRSd. Finally, the regression analysis revealed that the QRS index was a predictor of both functional and echocardiographic CRT response at 6 months.

The Rationale for Indexing QRSd by BMI

Baseline electrical dyssynchrony, clinically reflected by a prolonged QRSd on the surface ECG, is an essential criterion for CRT implantation which aims to improve systolic function by restoring the synchronous contractions of the opposing myocardial walls.[11] However, as a surrogate of intraventricular conduction delay, baseline QRSd may involve possible limitations to quantify electrical dyssynchrony. Individual differences in body size that correlate with LV dimensions may influence baseline QRSd suggesting that a larger ventricle would exhibit a more pronounced intraventricular conduction delay.[12] Accordingly, patients presenting with the same QRSd on the surface ECG might possibly have variations on

Table 3. Univariate and Multivariate Predictors of CRT Response Based on Functional and Echocardiographic Improvement at 6 Months of Implantation Analyzed by Logistic Regression Analyses

	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	P Value	HR	95% CI	P Value
Functional Response[a]						
Age	0.970	0.951–0.990	0.246			
Female gender	1.103	1.007–1.208	0.023	0.996	0.985–1.007	0.162
LBBB	1.003	0.990–1.016	0.135			
Nonischemic etiology	1.916	1.228–2.290	0.012	1.242	1.019–1.465	0.046
QRSd	1.005	0.989–1.021	0.121			
QRSd ≥150 ms	0.842	0.416–1.706	0.232			
QRS index	2.326	1.515–3.712	< 0.001	1.662	1.462–1.862	0.012
QRS index ≥5.5 ms.m^2/kg	2.071	0.808–5.310	0.013	1.916	1.228–2.290	0.081
Echocardiographic Response[b]						
Age	1.040	1.23–1.057	0.445			
Female gender	0.725	0.270–1.949	0.132			
LBBB	1.009	0.991–1.028	0.321			
Nonischemic etiology	1.044	0.977–1.117	0.096			
QRSd	1.051	1.021–1.076	0.024	1.012	0.990–1.034	0.121
QRSd ≥150 ms	0.288	0.132–0.632	0.002	0.701	0.237–2.071	0.031
QRS index	3.399	1.980–5.836	< 0.001	2.011	1.268–2.754	0.005
QRS index ≥5.5 ms.m^2/kg	1.662	0.935–1.007	0.021	1.242	1.019–1.465	0.088

HR = hazard ratio; CI = confidence interval.
[a]≥1 degree improvement in NYHA class at 6 months; [b]≥15% increase in LVESV at 6 months.

the extent of electrical dyssynchrony due to the discrepancies in body weight and length. In this study, we aimed to personalize the assessment of baseline electrical dyssynchrony in CRT recipients. We adjusted the QRSd by BMI to eliminate the discrepancies in body size and investigated the impact of QRS indexing on detection of CRT responders.

Gender-Related Differences in CRT Response

More favorable response to CRT in women compared to men[13,14] may be explained by the gender-related differences in body size that concomitantly affects LV dimensions and intraventricular conduction time. Female patients may have more conduction disturbance and more prominent electrical dyssynchrony for the same entry criteria of QRSd.[15] Another possible explanation by Zusterzeel et al.[16] is that male patients with larger ventricles are more likely to have a false-positive LBBB diagnosis at the lower end of the QRSd prolongation spectrum. Our results suggest that, when indexed by BMI, the same QRSd on the surface ECG may reflect a higher baseline electrical dyssynchrony due to the lower BMI of women leading to higher levels of QRS indices.

Previous reports clearly established that increasing BMI results in higher LV mass and dimensions that positively relates to electrocardiographic QRSd regardless of gender differences.[12] In this study, due to a subgroup analysis on gender, we found that the association of QRS index with CRT response is more prominent in women by correlation and chi-square analyses. The predictive power of QRS index to detect CRT responders might be mainly attributed to female participants that represented with higher QRS index values for a given QRSd due to the naturally lower BMI values. However, our findings need to be confirmed in future studies that are specifically aimed at this topic.

Electrocardiographic Predictors of CRT Outcome

Prolonged QRSd (> 150 ms) with a LBBB morphology has been proved in numerous studies as the gold standard ECG criteria for both patient selection and for prediction of outcomes after CRT.[17–19] Although several ECG parameters have been previously studied for prediction of CRT response,[3–5,20] none of them gained acceptance by the current guidelines.[6] In this study, we investigated and proved the usefulness of a novel

index to predict CRT response by comparing its predictive value with the widely-accepted marker of duration in CRT recipients. Simple clinical variables (QRSd, body weight, and height) that are required for calculation of the QRS index allows implications of the index in daily practice. Our preliminary results should be tested in future prospective trials with follow-up data apart from the echocardiographic and functional CRT response.

LIMITATIONS

Our study has typical limitations of a single-center study with a relatively small sample size. Although the correlation and the ROC curve analyses regarding the association of QRS index revealed better results than that of the QRSd, the mild difference might not be assumed to approve superiority for CRT response. There are also a few limitations derived from the retrospective nature of the study. First, patient selection was performed based on the guideline recommendations (QRSd $\geq$120 ms and LBBB morphology) rather than the QRS index. Second, the gender related differences of QRS index and CRT outcome were not tested in detail, although we found that female gender was associated with higher QRS indices and CRT response rates attributed to the lower BMI values. Finally, lack of strong clinical end points such as death or hospitalization is the main shortcoming that impairs the evaluation of QRS indexing on long-term CRT outcome. However, as a preliminary study, the promising results on echocardiographic and functional CRT response may lead to future prospective studies that would evaluate beneficial effects of QRS indexing on determining prognosis after CRT.

CONCLUSION

Adjustment of QRSd by BMI is a novel and simple method to evaluate baseline electrical dyssynchrony that eliminates the individual discrepancies of body weight and length on QRSd. QRS index provides a CRT response prediction at least comparable to QRSd that might be a promising parameter in the future for selection of CRT candidates.

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