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Time interval from left ventricular stimulation to QRS onset is a novel predictor of nonresponse to cardiac resynchronization therapy

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BACKGROUND Left ventricular (LV) lead placement at the late activation site (LAS) has been proposed as an optimal LV pacing site (ie, Q-LV interval). However, LAS may be relevant to local electrical conduction, measured as an interval from LV pacing stimulation to QRS onset (S-QRS interval).

OBJECTIVE The purpose of this study was to evaluate the prognostic value of S-QRS for reverse remodeling and the impact of S-QRS on pacing QRS configuration in patients undergoing cardiac resynchronization therapy (CRT).

METHODS Sixty consecutive heart failure patients with a wide QRS complex underwent CRT. A site with Q-LV $\geq$95 ms was targeted for LV lead placement. A responder was defined as one with $>$15% reduction in LV end-systolic volume 6 months after CRT.

RESULTS LV lead placement with Q-LV $\geq$95 ms was achieved in 52 of 60 patients (86.7%). Thirty-two of 52 patients (61.5%) were responders. S-QRS was significantly shorter in responders than nonresponders ($P < .01$), whereas Q-LV was not significantly different. A cutoff value of 37 ms for S-QRS had sensitivity and specificity of 81% and 90%, respectively. Shorter S-QRS ($<$37 ms) showed significantly narrower LV pacing QRS width and biventricular pacing QRS width compared to longer S-QRS. After multivariate analysis, PQ interval (odds ratio 0.97; $P = .01$) and long S-QRS $\geq$ 37ms (odds ratio 0.014; $P < .01$) were independent predictors of response to CRT.

CONCLUSION In addition to a sufficient Q-LV, S-QRS can be a useful indicator of optimal LV lead position to achieve reverse remodeling. S-QRS contributes to the pacing QRS configuration associated with CRT response.

KEYWORDS Cardiac resynchronization therapy; Electrocardiogram; Heart failure; Left ventricular lead; Prognosis; Scar

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Introduction

Cardiac resynchronization therapy (CRT) is an established treatment for patients with heart failure due to left ventricular (LV) dysfunction and QRS prolongation.[1–4] However, some candidates fail to achieve clinical or echocardiographic benefit from CRT, which has been attributed in part to a suboptimal LV lead position.[5]

LV lead placement at the latest electrical activation site has been proposed as an important factor for a superior CRT response compared with a conventional anatomic approach. The time interval from QRS onset to local LV activation at the LV lead (Q-LV) is a common indicator determining optimal LV pacing site and is associated with acute hemodynamic improvement, LV reverse remodeling, and clinical outcome.[6–9]

LV late activation site (LAS) may be due to scarring or fibrosis within the viable myocardium where anatomic or functional conduction block can occur. Therefore, LV pacing within those areas may be less effective for CRT.[10–13]

Local conduction disturbance during LV pacing (ie, stimulus to QRS interval [S-QRS]) may indicate that the LV lead has been placed on a scar or fibrotic region. Furthermore, S-QRS may influence the QRS configuration during LV pacing or biventricular pacing, which are predictors of CRT response.[14–16]

Therefore, we hypothesized that long S-QRS would also predict CRT nonresponse. The present study aimed to (1) evaluate the prognostic value of S-QRS on LV reverse remodeling and (2) elucidate the relevance of S-QRS on QRS configurations during LV and biventricular pacing in CRT patients with optimal LV lead position at the LAS.

Methods

Ethics statement

This study was a retrospective study approved by the Ethics Committee of the Tokyo Women's Medical University and conducted in accordance with the principles of the

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Declaration of Helsinki. Written informed consent was obtained from all patients or their guardians.

Study population

All heart failure patients who underwent CRT implantation between January 2012 and February 2016 at our hospital were reviewed for study eligibility. Inclusion criteria were based on our country's guidelines, specifically for sinus rhythm, New York Heart Association (NYHA) functional class II to IV heart failure on optimal pharmacologic therapy, QRS duration (QRSd) ≥120 ms, and left ventricular ejection fraction (LVEF) ≤35%. Exclusion criteria were age ≤18 years, chronic atrial tachycardia/fibrillation, and complete atrioventricular block. Patients with Q-LV <95 ms at the LV pacing site were excluded because recent reports indicate this was an inadequate LV pacing site.[6,7]

CRT implantation procedure

CRT devices were implanted in the standard fashion, and LV leads were transvenously implanted in a coronary vein branch. During the procedure, simultaneous recording of 12-lead electrocardiograms (ECGs) and intracardiac electrograms were continuously obtained using a digital recording system (Prucka CardioLab System, GE Healthcare, Waukesha, WI). The recorded intracardiac electrograms were bandpass filtered between 0.5 and 500 Hz. Q-LV mapping was performed with a decapolar catheter or LV lead electrodes, and the latest LV activation site was targeted as the optimal pacing site in all patients.

ECG measurements

The ECG measurements were retrospectively performed by 2 independent reviewers blinded to the outcome. Q-LV was defined as the time interval from the earliest QRS onset to the first major peak of the local bipolar electrogram. The % Q-LV was calculated as the percentage of Q-LV in native QRSd. S-QRS was defined as the time from the LV pacing to the earliest onset of QRS. LV pacing QRSd (LVp-QRSd) was measured from the pacing to the offset of QRS, whereas subtraction of S-QRS from LVp-QRSd was termed as the actual LV pacing QRSd (actual LVp-QRSd). Similarly, simultaneous biventricular pacing QRSd (BiV-QRSd) was measured from the pacing to the offset of QRS (Figure 1). Finally, the difference between native QRSd and BiV-QRSd (Delta-QRSd) was calculated. These parameters were measured with a caliper in the recording system at a sweep speed of 200 mm/s. LV pacing was performed with output at pacing threshold (1.1 ± 0.6V at 0.4 ms), and pacing rate was programmed at 10 bpm faster than the sinus rhythm.

Echocardiographic assessment

All patients had a comprehensive echocardiographic assessment using commercially available echocardiographic systems, and data at baseline and 6 months after CRT implantation were stored digitally. Standard LV volumetric measurements were performed using the recommended Simpson biplane method. Intraventricular dyssynchrony was assessed by radial speckle tracking analysis of the anteroseptal and posterolateral mid-LV segments.[17] A CRT responder was defined as one who had a >15% reduction in left ventricular end-systolic volume (LVESV) at 6 months compared with baseline.

Optimization of CRT device programming

VVD optimization was performed to minimize BiV-QRSd during the procedure; thereafter, echocardiography was performed to maximize pulsed-wave LV outflow tract velocity–time integral. AVD optimization was performed by Doppler echocardiography to provide the maximum LV filling time without interference of atrial wave and diastolic mitral regurgitation. After AVD optimization, BiV-QRSd and QRS morphology were confirmed again.

Statistical analysis

All statistical analyses were performed using JMP version 13.0 (SAS Institute, Cary, NC). Continuous variables are given as mean ± SD, whereas categorical variables are given as frequency and percentage. A linear regression analysis was applied to study the correlation between percent reduction in LVESV and S-QRS or Q-LV. For univariate analysis, the Fisher exact test and Wilcoxon exact test were used. Receiver operating characteristic curve analysis was performed to determine the optimal cutoff value of S-QRS for predicting CRT nonresponders. A multivariate logistic regression model was constructed to assess the association of clinical variables to predict the response to CRT. $P < .05$ was used to select variables from the univariate analysis. All statistical tests were 2-tailed, and $P < .05$ was considered significant.

Results

Baseline patient characteristics

Sixty consecutive CRT patients were enrolled in the present study. Of these patients, 8 were excluded because of suboptimal LV lead position without sufficient electrical latency. The final study population consisted of 52 patients (79% male) with mean age 62.6 ± 13.9 years (Table 1). Mean native QRSd was 159.5 ± 34.0 ms, and mean LVEF was 26.0% ± 6.2%. In the QRS morphologic features, 36 patients (69%) had left bundle branch block (LBBB), whereas 16 patients (31%) had non-LBBB. Nonischemic etiology and ischemic disease were present in 75% and 25% of patients, respectively. Eighteen patients were classified as NYHA III and IV, and all patients were receiving optimal medical therapy before CRT implantation. According to LV volumetric evaluation results before and 6 months after CRT implantation, 32 patients (61.5%) were responders. Patients were divided into responder and nonresponder groups to compare their characteristics. Baseline characteristics were not significantly different except for defibrillator device indication.

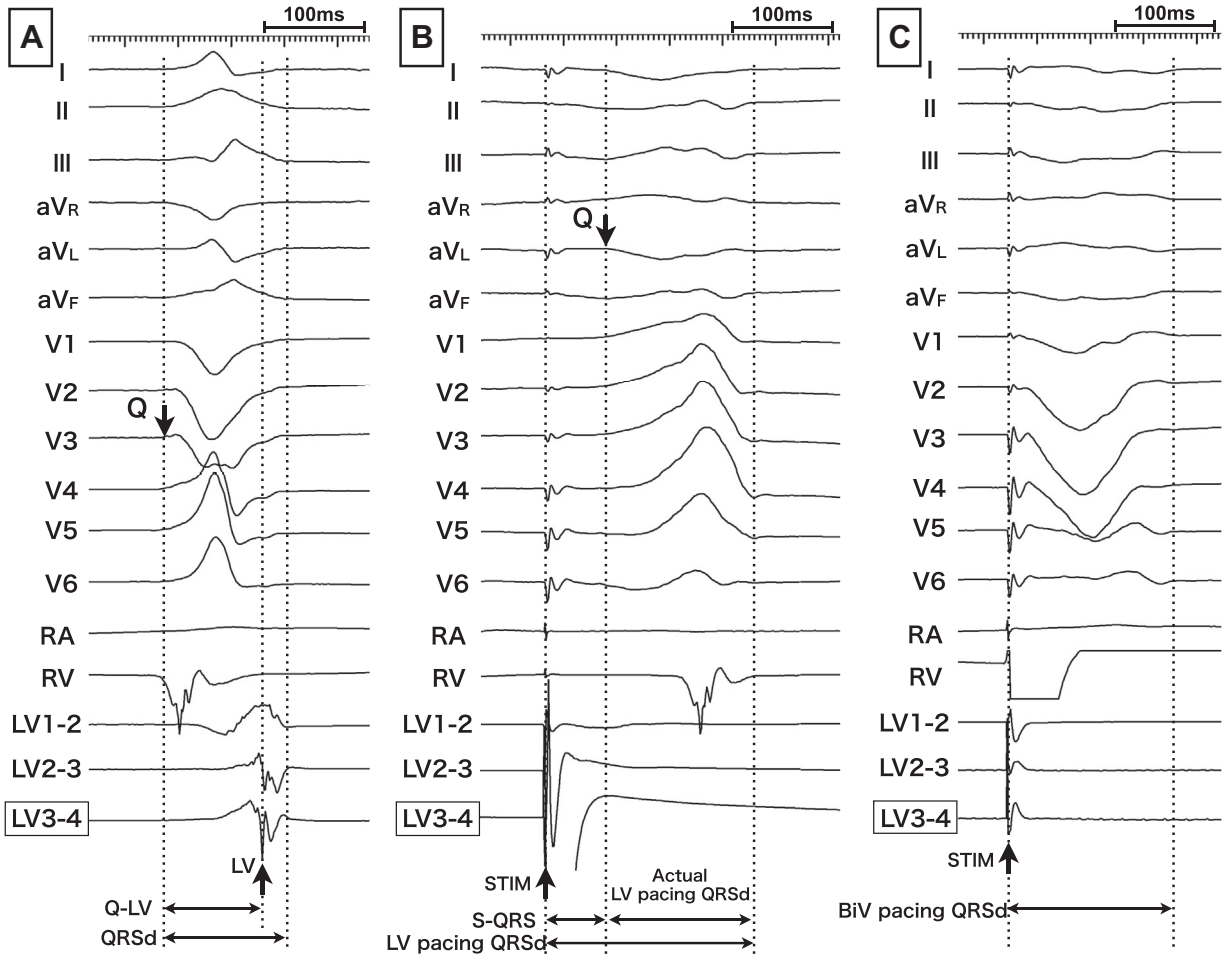

Figure 1 Examples of 12-lead electrocardiograms and intracardiac electrograms during sinus rhythm with native QRS (**A**), during LV pacing (**B**), and during BiV pacing (**C**). The calipers are aligned with the onset of QRS, offset of QRS, peak of the latest LV electrogram, and pacing stimulation signal. BiV = biventricular; LV = left ventricular; Q = onset of QRS; Q-LV = interval from QRS onset to latest LV electrogram; QRSd = QRS duration; S-QRS = interval from stimulus to QRS onset; STIM = stimulation signal.

Echocardiographic parameters before and 6 months after CRT implantation

At baseline, patients had severely reduced LV systolic function with enlarged LV, with mean LVESV at 197.0 ± 96.1 mL. Severe radial dyssynchrony was present at 204.5 ± 120.1 ms, and mean global longitudinal strain (GLS) was reduced at 9.0% ± 3.5%. There were no significant differences in LV volumetric evaluation and radial dyssynchrony between responders and nonresponders; however, responders showed significantly greater GLS than nonresponders (9.9% ± 3.8% vs 7.6% ± 2.6%; $P = .02$). LVESV was significantly improved in responders (from 196.5 ± 106.0 mL to 134.8 ± 67.4 mL; $P < .01$) but not in nonresponders (from 197.8 ± 80.4 mL to 200.7 ± 80.8 mL; $P = .74$). Similarly, LVEF was significantly improved in responders but not in nonresponders (from 26.6% ± 6.7% to 34.6% ± 8.9%; $P<0.01$; and from 25.1% ± 5.3% to 26.6% ± 7.3%; $P = .15$, respectively) (Supplemental Table S1). There were no significant differences in sensed/paced AVD and VVD between responders and nonresponders (Supplemental Table S2). In addition, patients who needed an excessively short AVD setting because of short intrinsic atrioventricular conduction were not observed.

Association of ECG parameters with response to CRT

LV lead was placed at an LAS with mean Q-LV of 128.0 ± 31.7 ms and mean %Q-LV of 78.7% ± 13.2%. There were no significant differences in Q-LV and %Q-LV between responders and nonresponders (Table 2 and Figure 2C). In addition, there was no significant correlation between Q-LV and percent reduction in LVESV (Figure 2D). During LV pacing, mean S-QRS of 39.0 ± 17.5 ms was observed. Nonresponders showed a significantly longer S-QRS compared with responders (53.1 ± 17.4 ms vs 30.8 ± 9.5 ms; $P < .01$) (Figure 2A). There was a significant correlation between S-QRS and percent reduction in LVESV (Figure 2B). Nonresponders had significantly longer LVp-QRSd than responders; however, actual LVp-QRSd was similar between the 2 groups. Therefore, the difference in LVp-QRSd arose from a difference in S-QRS. BiVp-QRSd was significantly shorter and Delta-QRSd was significantly greater in responders than in nonresponders (Table 2).

Table 1 Baseline clinical characteristics in the total population and those with and without response to cardiac resynchronization therapy

	Total (N = 52)	Responders (n = 32)	Nonresponders (n = 20)	*P* value
Age (y)	62.6 ± 13.9	62.6 ± 13.7	62.6 ± 14.7	.78
Male gender	41 (79)	24 (75)	17 (85)	.5
Ischemic	13 (25)	9 (28)	4 (20)	.74
Nonischemic	39 (75)	23 (72)	16 (80)	
NYHA				.59
I	0 (0)	0 (0)	0 (0)	
II	34 (65)	21 (66)	13 (65)	
III	10 (19)	5 (16)	5 (25)	
IV	8 (15)	6 (19)	2 (10)	
QRS duration (ms)	159.5 ± 34.0	161.4 ± 28.4	157.0 ± 32.6	.44
QRS block type				.67
RBBB	7 (13)	4 (13)	3 (15)	
LBBB	36 (69)	21 (66)	15 (75)	
IVCD	9 (17)	7 (22)	2 (10)	
Device type				.46
CRT-P	8 (15)	6 (19)	2 (10)	
CRT-D	44 (85)	26 (81)	18 (90)	
Primary prevention	35 (80)	24 (92)	11 (61)	.04
Secondary prevention	9 (20)	2 (8)	7 (39)	

Values are given as mean ± SD or n (%).

CRT = cardiac resynchronization therapy; IVCD = intraventricular conduction delay; LBBB = left bundle branch block; NYHA = New York heart association; RBBB = right bundle branch block.

Long S-QRS interval is associated with nonresponse to CRT

After receiver operating characteristic curve analysis for optimal cutoff value of S-QRS for prediction of CRT response, 37 ms of S-QRS had sensitivity and specificity of 81% and 90%, respectively, with the area under the curve of 0.91. Patients were then divided into a short S-QRS group (<37 ms) and a long S-QRS group (≥37 ms). The responder rate was significantly higher in the short S-QRS group compared with the long S-QRS group (96% vs 32%; P <.01). Both groups had a significant improvement in LVESV and LVEF (Table 3); however, percent reduction in LVESV and change in LVEF were significantly greater in the short S-QRS group (Figure 3). LVp-QRSd was significantly wider in the long S-QRS group, with no significant difference in actual LVp-QRSd compared with the short S-QRS group. BiVp-QRSd was significantly narrower and Delta-QRSd was significantly greater in the short S-QRS group than the long S-QRS group (Table 3). After optimization of device programming, there were no significant differences in AVD and VVD between short S-QRS and long S-QRS (Table 3). The significant predictors in the univariable models for response in LVESV were GLS, PQ interval, long S-QRS (≥37 ms), LVp-QRSd, BiVp-QRSd, and Delta-QRSd. After multivariate analysis, PQ interval and long S-QRS (≥37 ms) were independent predictors of LVESV response (Table 4).

Discussion

To evaluate the additional impact of S-QRS on CRT response, this study focused on CRT patients with an LV lead placed at the LAS. Our major findings are as follows: (1) mapping of LAS enabled successful LV lead placement at a site with Q-LV ≥95 ms in 86.7% of patients; (2) there was nearly 40% of nonresponders in our study population; (3) the optimal cutoff point of S-QRS for nonresponse prediction was 37 ms, and patients with short S-QRS (<37 ms) showed a considerably

Table 2 Comparison of electrocardiographic assessment during the procedure in responders vs nonresponders

	Total (N = 52)	Responders (n = 32)	Nonresponders (n = 20)	*P* value
Native QRSd (ms)	159.5 ± 34.0	161.4 ± 28.4	157.0 ± 32.6	.44
PQ interval (ms)	223.2 ± 57.1	209.2 ± 42.5	250.4 ± 55.4	<.01
Q-LV interval (ms)	128.0 ± 31.7	130.8 ± 28.0	126.1 ± 29.6	.46
%Q-LV (%)	78.7 ± 13.2	81.1 ± 9.9	80.5 ± 9.2	.76
LV pacing QRSd (ms)	245.5 ± 46.9	238.5 ± 29.1	264.0 ± 40.5	.016
S-QRS interval (ms)	39.0 ± 17.5	30.8 ± 9.5	53.1 ± 17.4	<.01
Actual LV pacing QRSd (ms)	206.6 ± 39.4	207.7 ± 28.6	210.9 ± 33.6	.41
Biventricular pacing QRSd (ms)	152.1 ± 28.6	146.3 ± 18.5	165.6 ± 21.8	<.01
Delta-QRS (ms)	−6.7 ± 29.9	−15.2 ± 26.0	+8.6 ± 30.0	<.01

Values are given as mean ± SD.

LV = left ventricular; QRSd = QRS duration.

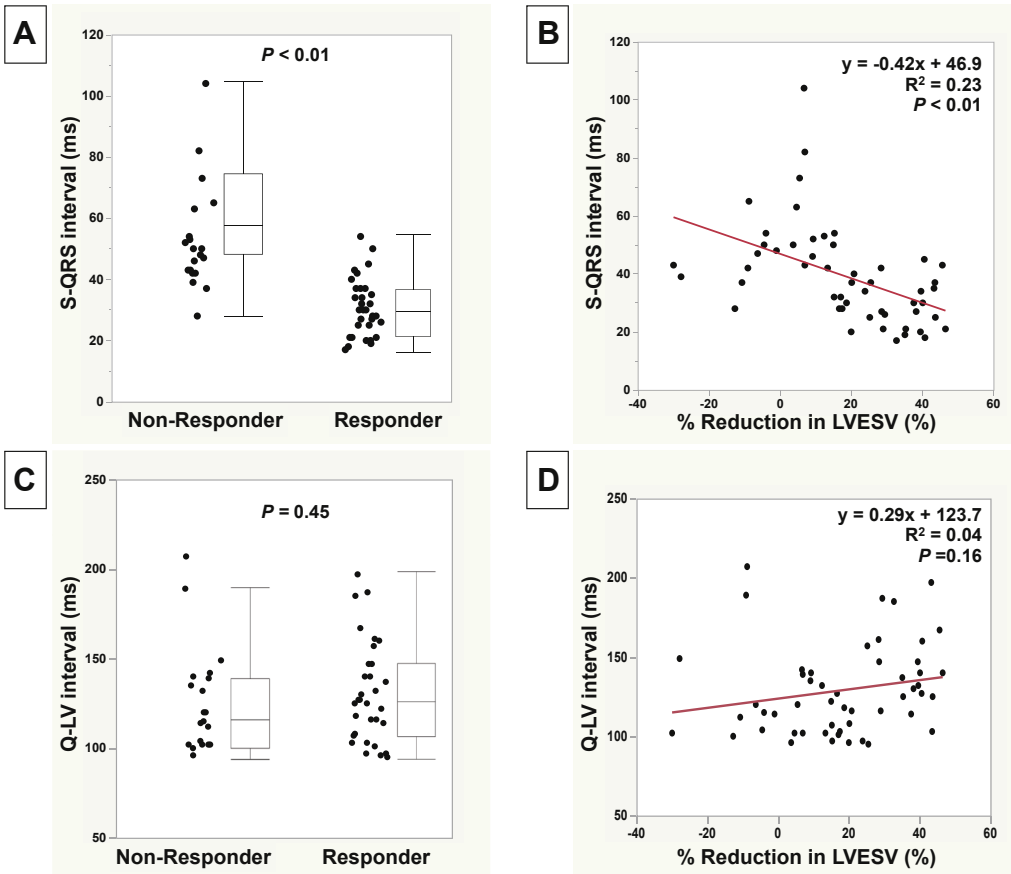

Figure 2 Distribution and comparison of S-QRS interval (**A**) and Q-LV interval (**C**) in nonresponders and responders, and the correlation between percent reduction in LVESV and S-QRS interval (**B**) and Q-LV interval (**D**). LVESV = left ventricular end-systolic volume.

Table 3 Comparison of clinical characteristics between short S-QRS group (<37 ms) and long S-QRS group (≥37 ms)

	Short S-QRS (<37 ms) (n = 24)	Long S-QRS (≥37 ms) (n = 28)	*P* value
Age (y)	64.5 ± 13.3	60.9 ± 14.4	.51
Male gender	17 (71)	24 (86)	.31
Ischemic etiology	9 (37)	4 (14)	.11
LVESV at baseline (mL)	174.3 ± 80.0	216.5 ± 105.5	.06
LVEF at baseline (%)	27.8 ± 6.3	24.5 ± 5.8	.03
LVESV after 6 months (mL)	123.6 ± 61.3*	191.4 ± 79.9*	<.01
LVEF after 6 months (%)	35.4 ± 9.6*	28.2 ± 7.4*	<.01
% reduction in LVESV	13.3 ± 2.7	−8.5 ± 18.3	<.01
Radial dyssynchrony (ms)	215.2 ± 134.6	195.4 ± 107.9	.67
LVGLS (%)	10.5 ± 3.6	7.7 ± 3.0	<.01
Native QRSd (ms)	163.1 ± 26.6	156.9 ± 32.6	.3
Q-LV interval (ms)	132.8 ± 28.7	125.6 ± 28.3	.33
S-QRS interval (ms)	26.2 ± 5.5	50.6 ± 15.1	<.01
LV pacing QRSd (ms)	234.9 ± 31.9	259.8 ± 35.4	<.01
Actual LV pacing QRSd (ms)	208.8 ± 31.8	209.1 ± 29.7	.49
Biventricular pacing QRSd (ms)	145.0 ± 18.0	161.1 ± 22.3	<.01
Delta-QRS (ms)	−18.0 ± 26.7	+4.2 ± 28.6	<.01
Sensed AVD (ms)	114.6 ± 25.4	122.9 ± 31.3	.5
Paced AVD (ms)	153.3 ± 29.7	162.5 ± 35.0	.55
VVD (ms)	−12.3 ± 17.3	−11.8 ± 18.1	.83
Responder rate	23 (96)	9 (32)	<.01

Values are given as mean ± SD or n (%).

AVD = atrioventricular delay; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; LVGLS = left ventricular global longitudinal strain; QRSd = QRS duration, VVD = interventricular delay.

*P <.01 vs baseline.

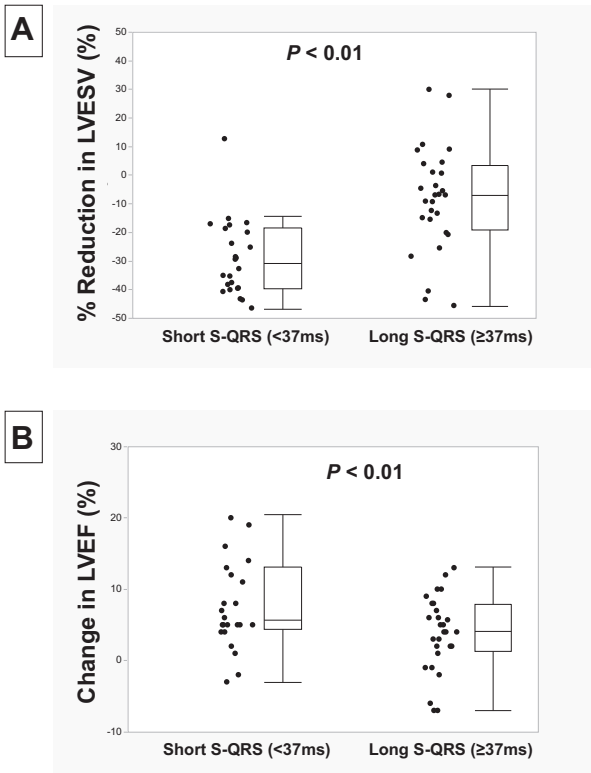

Figure 3 Comparison of percent reduction in LVESV (**A**) and change in LVEF (**B**) between the short S-QRS group and the long S-QRS group. LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume.

higher response rate at 96%; (4) shorter LVp-QRSd was associated with CRT response and mainly contributed by S-QRS; (5) significant shortening in BiVp-QRSd resulting in greater Delta-QRSd was observed in patients with shorter S-QRS; and (6) PQ interval and long S-QRS (≥37 ms) were independent predictors of CRT response.

LV pacing at the LAS and CRT response

CRT has been shown to promote reverse remodeling and improve clinical outcome by restoring electrical and mechanical dyssynchrony. LV pacing at the LAS is essential to decrease the nonresponse rate. However, LV lead placement by a conventional anatomic approach is limited for optimal lead placement on the LAS, and a suboptimal LV lead position may contribute to nonresponses. Q-LV or % Q-LV has been proposed as a simple intraprocedural evaluation of LAS. Singh et al[9] reported that CRT patients with % Q-LV ≥50% showed significant improvement in hemodynamic response and mortality. Similarly, Kandala et al[8] reported that %Q-LV ≥50% was a predictor of better clinical outcome in CRT patients. In these studies, however, successful LV lead implantation on the LAS by a conventional anatomic approach was only 62% and 76%, respectively. Furthermore, Q-LV ≥95 ms also showed a remarkable predictive value for improved reverse remodeling and better clinical outcome[7]; however, successful LV lead placement on the LAS was achieved in <50% of patients. In the present study, Q-LV mapping during the procedure enabled successful LV lead placement on the LAS in 87% of patients. Despite an optimal LV lead position, Gold et al[7] reported that the responder rate of CRT patients with Q-LV ≥95 ms was 62.7%, which was similarly observed in our study population. Importantly, there were nearly 40% nonresponders even in our selected CRT patients, suggesting other reasons for suboptimal LV lead position. Particularly, the LAS may represent a longer S-QRS due to localized scar or fibrotic legion, which should be avoided in a suitable LV pacing site.

Long S-QRS interval is associated with nonresponse to CRT

LV lead implantation away from the scar area using cardiac imaging modalities has been shown to benefit CRT response and mortality.[10–13] However, an intraprocedural ECG predictor may be more ideal to locate the scar area. Therefore, this study focused on S-QRS, which may indicate localized tissue property. A longer S-QRS has been frequently observed during pace mapping for ventricular tachycardia ablation. Bogun et al[18] reported that pacing at the scar area with delayed potential showed a longer

Table 4 Multivariate analysis for prediction of response to cardiac resynchronization therapy

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
LVEDV (mL)	1	0.99–1.01	.91			
LVESV (mL)	1	0.99–1.01	.96			
LVEF (%)	1.04	0.95–1.14	.41			
Radial dyssynchrony (ms)	1	1.00–1.01	.24			
LVGLS (%)	1.24	1.04–1.52	.023	1.14	0.85–1.51	0.39
Native QRSd (ms)	1.01	0.99–1.03	.6			
PQ interval (ms)	0.98	0.96–0.99	.012	0.97	0.94–1.0	.01
Long S-QRS interval (≥37 ms)	0.02	0.002–0.18	<.01	0.014	0.001–0.26	<.01
LV pacing QRSd (ms)	0.98	0.96–1.0	.02			
Actual LV pacing QRSd (ms)	1	0.98–1.02	.71			
Biventricular pacing QRSd (ms)	0.95	0.92–0.98	<.01	0.97	0.92–1.02	.17
Delta-QRS (ms)	0.97	0.94–0.99	<.01	0.99	0.95–1.02	.44

CI = confidence interval; LVEDV = left ventricular end-diastolic volume; other abbreviations as in Tables 2 and 3.

S-QRS with good paced QRS configuration. In addition, Stevenson et al[19,20] reported that pacing at the scar area with fractionated potential showed S-QRS >40 ms. Therefore, the optimal cutoff point of 37 ms for CRT nonresponse is reasonable to distinguish the scar or fibrotic region. In this study, LVGLS, which is a surrogate marker of scar burden,[21,22] was significantly smaller in the long S-QRS group. Patients with lower GLS may be more likely to have an LV lead on the scar area as a result of larger scar burden. However, GLS, which reflects whole LV scar burden, is fundamentally different from S-QRS, reflecting local conduction property. Furthermore, the final AVD and VVD were not significantly different between the short and long S-QRS groups, whereas the responder rate was significantly higher in the short S-QRS group. Therefore, S-QRS rather than Q-LV or GLS is more useful for evaluation of local conduction property. In addition, Q-LV, which is insensitive to tissue impedance, does not reflect where the activation delay is occurring. However, S-QRS, a measurement during pacing, is clearly affected by localized tissue property.

Scar distribution and scar properties may vary between individuals; therefore, S-QRS mapping may help to avoid pacing at scar lesion. Responders showed a shorter S-QRS and a significant correlation was observed between S-QRS and reduction in LVESV, and similar Q-LV and %Q-LV were observed. These findings might suggest that S-QRS mapping should be used instead of longer Q-LV, rather than in addition to longer Q-LV, if a sufficient LAS (QLV ≥95 ms) was obtained. Moreover, mapping of both shorter S-QRS and longer Q-LV should be feasible; however, whether patients exhibiting a long S-QRS have an alternative LV pacing site with short S-QRS in addition to sufficient Q-LV is still unknown. Electrophysiological study might be useful for optimal patient selection before CRT implantation. Furthermore, high-output pacing or multiple sites/points pacing might resolve the influence of long S-QRS as recently reported.[23,24] However, these concepts require further validation.

Impact of S-QRS interval on QRS configurations during LV and biventricular pacing

LVp-QRSd has been reported as an independent predictor of CRT response.[14] Wider LVp-QRSd is also an indicator of LV pacing proximity to the scar region, with conduction delay leading to insufficient resynchronization. In this study, nonresponders showed significantly wider LVp-QRSd, longer S-QRS, lower LVGLS, and similar actual LVp-QRSd compared with responders. Thus, actual LVp-QRSd may represent total ventricular conduction rather than local conduction. Although BiV-QRSd and Delta-QRSd are still controversial predictors of CRT response,[15,16] our study population showed significantly shorter BiV-QRSd and greater Delta-QRSd in responders as well as in the short S-QRS group. However, both BiV-QRSd and Delta-QRSd were not significant predictors in the multivariate model. Lecoq et al[16] reported the prognostic value of BiV-QRSd and Delta-QRSd on CRT response, but their definition of CRT responder was NYHA improvement and peak VO_2 >10% increase, which is considered as a clinical responder. From the perspective of mechanical response to CRT, longer S-QRS may reflect larger scar burden and produce ineffective CRT pacing; therefore, S-QRS could be a stronger predictor than BiV-QRSd or Delta-QRSd. Although BiV-QRSd represents electrical resynchronization after CRT, longer BiV-QRSd may also imply insufficient electrical resynchronization due to longer S-QRS.

Study limitations

This study has several limitations. First, this was a single-center retrospective cohort study and was not sufficiently sized to evaluate clinical outcomes. Second, this study included more patients with nonischemic etiology and non-LBBB QRS configuration. In addition, patients with relatively narrow QRSd were indicated for CRT according to our country's guideline. Third, LV scar assessment using cardiac imaging modalities was not performed. Therefore, S-QRS does not prove histopathologic scar or fibrosis at the LV pacing site. Finally, in this study, most of the right ventricular (RV) leads were placed on the RV mid-septum; therefore, Q-LV was preferable rather than RV–LV interval.[25]

Conclusion

S-QRS ≥ 37ms at LV pacing site can be a novel independent predictor of CRT nonresponse. S-QRS also contributes to QRS configuration during LV and biventricular pacing and is associated with CRT response. Both Q-LV and S-QRS guided LV lead placement may benefit CRT outcome. Further studies are warranted to establish our concept.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2018.08.035.

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