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Interventricular Electrical Delay Is Predictive of Response to Cardiac Resynchronization Therapy

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ABSTRACT

OBJECTIVES This study was conceived to evaluate the relationship between interventricular electrical delay, as measured by the right ventricle-left ventricle (RV-LV) interval, and outcomes in a prospectively designed substudy of the SMART-AV (SMARTDELAY determined AV Optimization) trial.

BACKGROUND Despite the well-documented benefit of cardiac resynchronization therapy (CRT), the nonresponder rate remains an important clinical problem. Implanting LV leads by traditional anatomic criteria has limited impact on outcomes. However, pacing at sites with late electrical activation improves CRT response rates. Thus, we hypothesized that interventricular electrical delay is associated with improved CRT outcomes.

METHODS This was a multicenter study of patients with advanced heart failure undergoing CRT implantation. In 419 subjects, the unpaced RV-LV interval was measured in sinus rhythm. LV volumes and ejection fraction were measured by echocardiography at baseline and after 6 months of CRT by a blinded core laboratory. Quality of life (QOL) was assessed by a standardized questionnaire.

RESULTS When separated by quartiles based on interventricular delay, the magnitudes of LV volumes, ejection fraction and the QOL measure increased significantly with prolongation of RV-LV delay ($p < 0.05$). The LV end-systolic volume response rate increased progressively from 30% to 75% ($p < 0.001$), and the QOL response rate increased from 50% to 65% ($p = 0.08$). Patients in the highest quartile of RV-LV had a 5.98-fold increase ($p < 0.001$) in their odds of a reverse remodeling response, with female sex, ischemic etiology, and baseline LV end-systolic volume being the other independent predictors of response.

CONCLUSIONS Baseline interventricular delay is a potent independent predictor of remodeling and QOL responses with CRT. (J Am Coll Cardiol EP 2016;2:438–47) © 2016 by the American College of Cardiology Foundation.

Multiple prospective, randomized trials have established the role of cardiac resynchronization therapy (CRT) for the treatment of selected patients with heart failure (HF), left ventricular (LV) systolic dysfunction, and QRS prolongation. These studies demonstrated improvements in quality of life (QOL), exercise capacity, LV systolic function, decreased hospitalizations

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for HF, and improved survival (1-6). Despite the benefit of CRT, a significant number of patients are classified as "nonresponders" (2-7), the proportion being dependent on the endpoint chosen (8) or may be partial responders (9).

Traditionally, LV leads were placed preferentially on the lateral wall based on small acute hemodynamic studies (10). However, post-hoc analyses from the large pivotal clinical trials of CRT showed a relative lack of effect of LV lead anatomic position on outcomes, with the exception of worse response in apical positions (11–13). In contrast, lead position guided by physiologic parameters rather than anatomic location has shown a much better predictive value for a variety of outcome measures including remodeling endpoints, QOL, and clinical events. Specifically, leads placed in areas of late electrical or mechanical activation are associated with better response (14–17). The most common studied measure of electrical delay is the QLV interval, which is the time from the onset of the QRS complex on the surfaced electrocardiogram to the local LV activation at the site of the LV lead. Right ventricular (RV) lead activation time may be a good surrogate of the time of initiation of ventricular activation, particularly in the presence of left bundle branch block (LBBB). Moreover, with simultaneous biventricular pacing, the most common modality used with CRT, the time from RV to LV activation represents a measure of the electrical resynchronization that will be achieved with pacing. To investigate the predictive value of RV-LV time, we evaluated the relationship between this measure of electrical delay and reverse remodeling in a prospectively designed substudy of the SMART-AV (SMARTDELAY determined AV Optimization) trial (18,19).

METHODS

Details of the design and primary results of the SMART-AV study have been published previously (18,19). Briefly, this was a multicenter, randomized trial of atrioventricular (AV) optimization/programming methods among patients with advanced HF undergoing CRT defibrillator implantation. The major inclusion criteria for the study were New York Heart Association functional class (NYHA) III or IV despite optimal medical therapy, an LV ejection fraction (LVEF) ≤35%, and QRS duration ≥120 ms. Patients were required to be in sinus rhythm and those who were in complete heart block were excluded. CRT implantation was performed using standard techniques, with no requirements regarding lead positions. The location of the LV lead was at the discretion of the implanting physician without guidance by RV-LV timing.

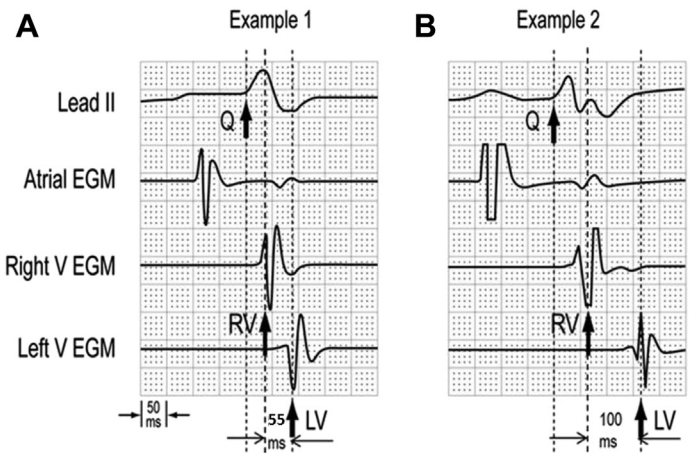
A subset of 419 patients enrolled in the SMART-AV trial was included in the RV-LV substudy. This represents all patients from participating centers in whom stable electrogram data were available. At the final lead positions, surface lead II, right RV, and LV electrograms (EGMs) were recorded simultaneously on paper strips at a sweep speed of 100 mm/s. RV-LV and QLV delays were measured by a blinded core lab with no knowledge of lead position or clinical outcomes. The RV-LV interval was measured in sinus rhythm and in the absence of pacing as the interval of the first large positive or negative peaks of RV and LV electrograms during a cardiac cycle with the resolution of 5 ms (**Figure 1**). The amplitude of the first large peak needed to be >50% of the amplitude of the largest peak in the same cardiac cycle if more than 1 peak was present. Otherwise, the largest peak was chosen (17). Core lab measurements were performed independently by 2 reviewers, and a sample of 15 EGMs were reviewed by both to assess reproducibility of the results. The QLV interval was measured as the time from the onset of the QRS complex in lead II to the same peak in the LV electrogram as used for RV-LV measurements. Lead location was classified by investigators by fluoroscopic imaging as apical or nonapical in the right anterior oblique projection, as well as anterior, posterior, or lateral in the left anterior oblique projection.

The primary endpoint of the SMART-AV trial was left ventricular end-systolic volume (LVESV). Secondary endpoints included left ventricular end-diastolic volume (LVEDV), LVEF, and QOL score as assessed by the Minnesota Living With Heart Failure Questionnaire as defined previously (18,19). The echocardiographic endpoints were analyzed blindly by a single echocardiography core laboratory blinded to group assignment and RV-LV delay measurements. The echocardiographic measurements were described in details previously (18,19). Briefly, off-line software (Pro-Solv version 3.0 [Fujifilm Corporation, Tokyo, Japan] or GE Echo Pac version 6.0 [GE Medical Systems, Inc., Milwaukee, Wisconsin]) was used for measurements, with 2-dimensionally derived LV volumes determined in the apical 4- and 2-chamber views by the biplane method of discs. All echocardiographic measures were performed at baseline and after 6 months of CRT. QOL was self-assessed by patients.

ABBREVIATIONS AND ACRONYMS

AV = atrioventricular
CRT = cardiac resynchronization therapy
HF = heart failure
LBBB = left bundle branch block
LV = left ventricle
LVEDV = left ventricular end-diastolic volume
LVEF = left ventricular ejection fraction
LVESV = left ventricular end-systolic volume
NYHA = New York Heart Association functional class
QOL = quality of life
RBBB = right bundle branch block
RV = right ventricle

FIGURE 1 Two Examples of RV-LV Measurements



The calipers are aligned with the peaks of the RV and LV electrograms. The RV-LV was calculated as 55 ms for the patient in **A** and 100 ms for the patient in **B**. LV = left ventricle; RV = right ventricle.

STATISTICAL ANALYSIS. Patients in SMART-AV were randomized to 1 of 3 AV optimization algorithms, nominal settings, echocardiographic optimization of mitral inflow by the iterative technique, and electrogram based optimization using the SmartDelay algorithm. Because there were no differences in primary or secondary outcomes between these groups (19), data were pooled for the present analyses. The CRT responses were compared among subgroups based on RV-LV quartiles. Multivariate logistic regression models were used to analyze the association between RV-LV and CRT response, adjusting for baseline covariates including age, sex, ischemia, LBBB, QRS duration, NYHA functional class, LVEF, and LVESV. In addition, RV-LV (dichotomized at the median) was analyzed as a predictor of response in univariate logistic regression models separately for subgroups of patients by conduction disorder type (LBBB vs. non-LBBB), ischemic etiology, QRS duration (>150 ms vs. 120 to 150 ms), sex, and lead location. Heterogeneity of the effect of RV-LV on CRT response by subgroup was formally tested by fitting an interaction term in logistic regression models with RV-LV and the covariate of interest (QRS morphology, QRS duration, etiology of HF, sex, age, and lead location) assessed as predictors of response. The CRT response rate was defined for both reverse remodeling (LVESV) and QOL measures. The response for LVESV was defined prospectively as a >15-ml reduction in LVESV from implantation to 6 months (17–19). The response for QOL was defined as >10 points reduction from implantation to 6 months (17,18). Youden's J statistic was used to identify the best cutpoint to optimize the sensitivity and specificity of response rates. Continuous variables were compared with F tests. Discrete variables were compared with Fisher exact and Pearson chi-square tests. A $p < 0.05$ was considered statistically significant. Data are presented as mean ± SD unless noted otherwise. SAS version 9.3 (SAS Institute, Cary, North Carolina) was used for statistical analysis.

RESULTS

PATIENT POPULATION. A summary of the baseline clinical characteristics of the 419 patients in this study is shown in **Table 1**. They were typical of the general HF population receiving CRT, with primarily late middle aged men with advanced HF and LBBB. A majority of patients had underlying ischemic heart disease and the mean unpaced QRS duration was 150 ms. The cohort was well treated medically for a population of largely NYHA functional class III patients with 92% receiving a beta blocker and 85% receiving either an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker. This substudy included 43% of the subjects randomized in the SMART AV trial. The baseline characteristics in the susbstudy patients did not differ significantly from the full trial cohort.

LV LEAD POSITION. As noted above, recent studies have indicated that apical LV lead position is associated with worse clinical outcomes (12,13). In the present study, LV lead position was classified by the implanter according to standard criteria (18,19). Only 11% of patients had apically placed leads, whereas 97% were in traditional lateral or posterior locations.

INTERVENTRICULAR DELAY. The mean RV-LV delay was 68 ± 41 ms. The median delay was 70 ms with interquartile ranges of 40 to 100 ms. The RV-LV duration did not differ by randomization group in the SMART-AV study. The values for the fixed, echocardiogram-, and electrogram-based optimization arms of the main trial were 69 ± 40 ms, 68 ± 42 ms, and 68 ± 41 ms, respectively ($p = 0.95$). Examples of short and long RV-LV delays from 2 different patients are shown in **Figure 1**. The RV activation preceded LV activation in 93% of subjects as expected in the presence of LV dilation and predominately LBBB. In this cohort, the mean QLV was 93 ± 36 ms and was strongly correlated to the RV-LV delay (Pearson correlation coefficient = 0.84, $R^2 = 0.71$).

The baseline characteristics of the patient population grouped by interventricular (RV-LV) delay are

TABLE 1 Baseline Characteristics for All Patients and Patients in the 4 RV-LV Quartiles

	All Patients (N = 419)	Baseline RV-LV (ms) Q1 (≤40 ms) (n = 109)	Q2 (45–65 ms) (n = 91)	Q3 (70–100 ms) (n = 116)	Q4 (≥105 ms) (n = 103)	p Value
Age (yrs)	66 ± 11	64 ± 10	68 ± 12	65 ± 11	67 ± 10	0.055
Male	66.1	75.2	72.5	59.5	58.3	0.013
Ischemic heart disease (% yes)	59.4	70.6	64.8	54.3	48.5	0.004
NYHA functional class II	2.9	4.7	0.0	4.3	1.9	
NYHA functional class III	94.5	90.7	97.8	93.1	97.1	0.199
NYHA functional class IV	2.6	4.7	2.2	2.6	1.0	
ACE/ARB (% yes)	84.5	85.3	76.9	87.1	87.4	0.177
Beta-blocker (% yes)	92.4	91.7	90.1	91.4	96.1	0.365
Diuretic (% yes)	81.9	78.0	85.7	85.3	78.6	0.300
Digoxin (% yes)	22.0	20.2	28.6	22.4	17.5	0.300
QRS (ms)	150 ± 25	140 ± 23	138 ± 23	152 ± 21	167 ± 22	<.001
LBBB (% yes)	75.2	52.3	61.5	89.7	95.1	<.001
RBBB (% yes)	13.6	33.9	17.6	2.6	1.0	<.001
IVCD (% yes)	13.1	16.5	20.9	11.2	4.9	0.004
LVESV (ml)	129 ± 63	116 ± 50	131 ± 60	137 ± 65	132 ± 72	0.076
LVEDV (ml)	174 ± 68	161 ± 53	178 ± 66	181 ± 72	177 ± 80	0.118
LVEF (%)	28.0 ± 8.7	29.6 ± 9.2	28.3 ± 8.2	26.4 ± 8.8	27.9 ± 8.3	0.056
Lead position, apical	11.4	8.0	11.2	14.0	11.8	0.586
Lead position - posterior/ posterolateral/anterolateral	96.8	94.1	95.5	98.2	99.0	0.164
Programmed AV delay (ms)	126 ± 33	131 ± 35	136 ± 37	118 ± 23	120 ± 33	<.001

Values are mean ± SD or %.

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; AV = atrioventricular; IVCD = intraventricular conduction delay; LBBB = left bundle branch block; LV = left ventricular; LVEG = left ventricular ejection fraction; NYHA = New York Heart Association functional class; Q = quartile; RBBB = right bundle branch block; RV = right ventricular.

shown in Table 1. There were some significant differences among subgroups, most notably male sex and ischemic etiology of HF decreased as RV-LV delay prolonged, whereas QRS duration and proportion of LBBB increased. A multivariate analysis, however, showed that only QRS duration and morphology were independent predictors of RV-LV duration (Table 2). It is noteworthy that apical lead position was not a predictor of this measure.

CRT RESPONSES. To assess the impact of interventricular delay on outcomes, subjects were again grouped based on quartiles of the RV-LV duration. All 3 echocardiographic remodeling measures, LVESV, LVEDV and EF, as well as QOL were significantly increased as RV-LV times increased. These results are shown in Figure 2, with progressive large responses clearly noted as interventricular delay increases.

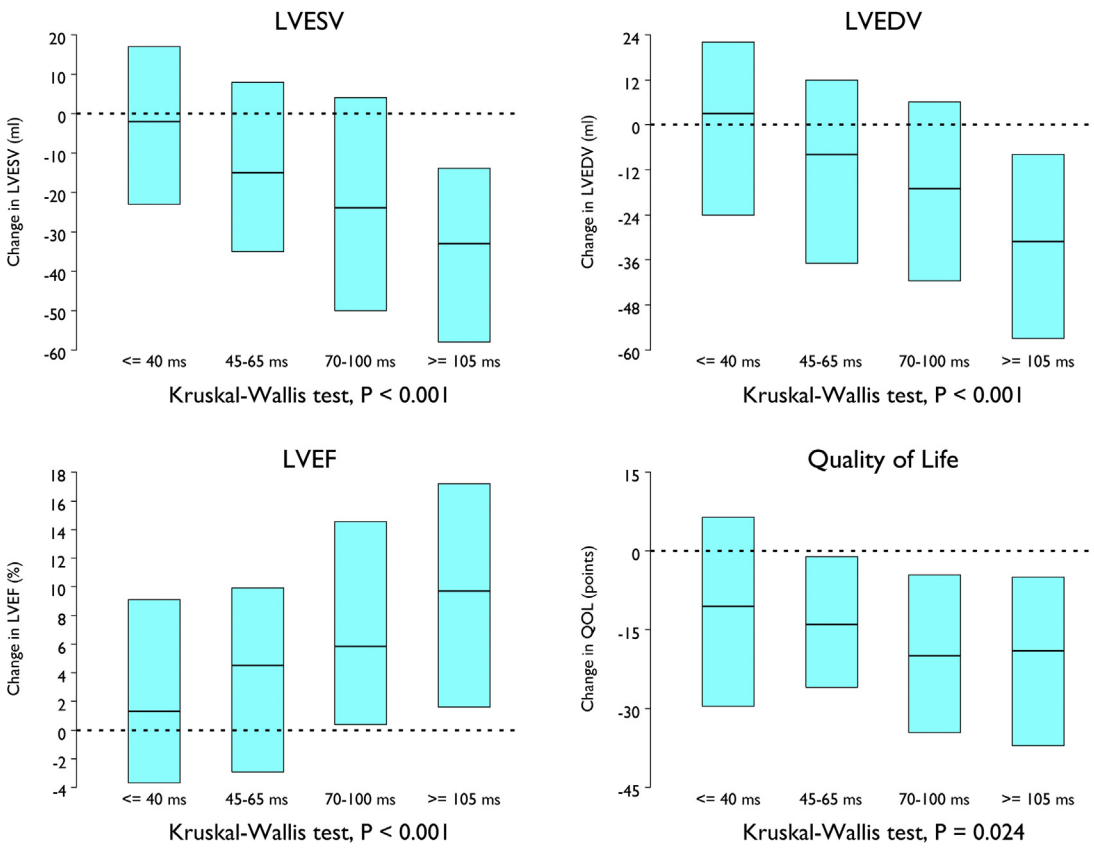
CRT RESPONSE RATE. The overall response rates were 53% for LVESV and 60% for QOL in this population, which are typical response rates for these parameters with CRT (8). The response rates for each RV-LV quartile are shown in Table 3. The response rates increased progressively from the shortest quartile to the longest quartile for both LVESV (30% to 75%) and QOL (50% to 65%) criteria. The best cutpoint for optimizing sensitivity and specificity was 80 ms. Given the imbalances in several important clinical parameters between interventricular delay groups, a multivariate analysis was performed. These results are shown in Figure 3. For the LVESV endpoint, RV-LV delay was a strong independent predictor with an almost 6-fold greater response rate for the largest quartile compared with the shortest quartile. Female sex, nonischemic etiology of HF, and baseline LVESV were the other predictors of response (Figure 3A).

TABLE 2 Multivariate Analysis of Predictors of RV-LV Delay

	Comparison	Effect	(95% CI)	p Value
Intercept		33.7	(23.2 to 44.3)	<0.001
Age (yrs)	≥65 vs. <65	4.4	(−2.5 to 11.3)	0.214
Sex	Female vs. male	2.9	(−4.6 to 10.3)	0.449
Ischemic etiology	Ischemic vs. nonischemic	−4.3	(−11.7 to 3.1)	0.257
Bundle branch block	LBBB vs. Non-LBBB	35.7	(27.6 to 43.7)	<0.001
QRS duration (ms)	>150 vs. ≤150	25.1	(18.3 to 31.9)	<0.001
Lead position	Apical vs. nonapical	−4.9	(−15.9 to 6.0)	0.375
Lead position	Anterior/anterolateral/anteroseptal vs. posterior/lateral/posterolateral	−8.9	(−16.5 to −1.4)	0.021

CI = confidence interval; other abbreviations as in Table 1.

FIGURE 2 Comparisons of the Changes in LVESV, LVEDV, EF and QOL From Implant Baseline to 6 Months for the 4 RV-LV Quartiles



The data was presented as median ± interquartile range. EF = ejection fraction; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; QOL = quality of life.

Female sex was the sole independent predictor of QOL response (Figure 3B). As noted above, the QLV duration was previously shown to predict the same outcomes in the SMART-AV study (17). To assess the relative contributions of this measure of LV delay on the response, multivariate models of the primary endpoint (LVESV change) with either RV-LV or QLV were performed. In both the odds ratio of LV electrical delay to predict response was very similar, 1.14 for RV-LV and 1.13 for QLV. However, when both RV-LV and QLV were included in a multivariate analysis, the resulting model excluded QLV and retained RV-LV, indicating that RV-LV is the better predictor of LVESV change.

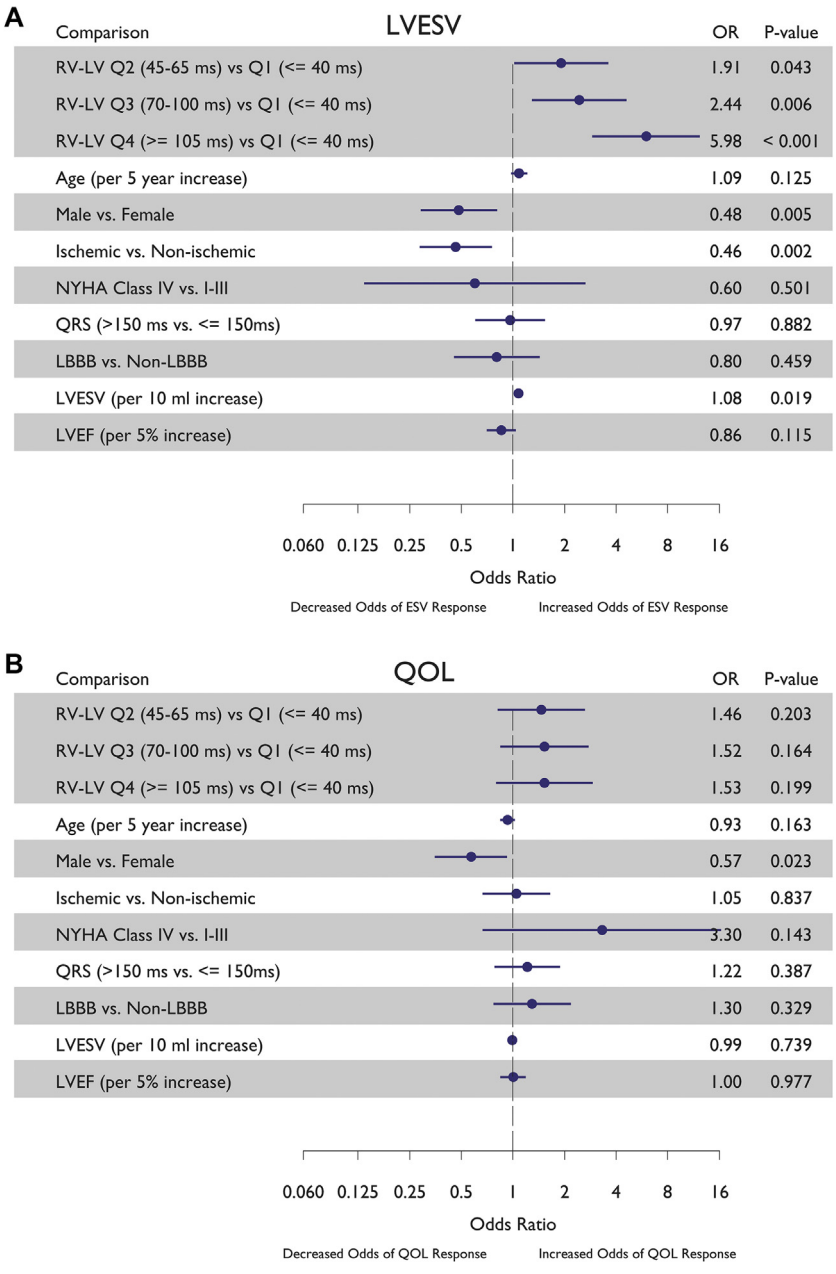
TABLE 3 The LVESV and QOL Response Rates for the RV-LV Quartiles

RV-LV (ms)	N	LVESV Response Rate (%)	QOL Response Rate (%)
≤40	109	30	50
45-65	91	49	58
70-100	116	59	65
≥105	103	75	65
Pearson chi-square		$p < 0.001$	$p = 0.080$

LVESV = left ventricular systolic volume; QOL = quality of life; other abbreviations as in Table 1.

SUBGROUP ANALYSIS. Certain subgroups have been shown to respond better to CRT in SMART-AV, as well as other trials. Most commonly, QRS duration and morphology, sex, age, and etiology of HF are significant predictors. To understand better the effect of interventricular electrical delay in these subgroups, logistic regression analysis was performed. The Forest plots of this analysis are shown in Figure 4. All subgroups showed a greater response to CRT with longer RV-LV delay, with no significant interactions noted. This was observed for both endpoints. To illustrate the relative importance of interventricular electrical delay, a comparison of patients with long and short RV-LV duration grouped by QRS

FIGURE 3 Multivariate Predictors of Response to CRT After Adjusting for Baseline Covariates (Age, Gender, Ischemia, QRS Duration, Bundle Branch Block Type, Baseline LVESV and LVEF)



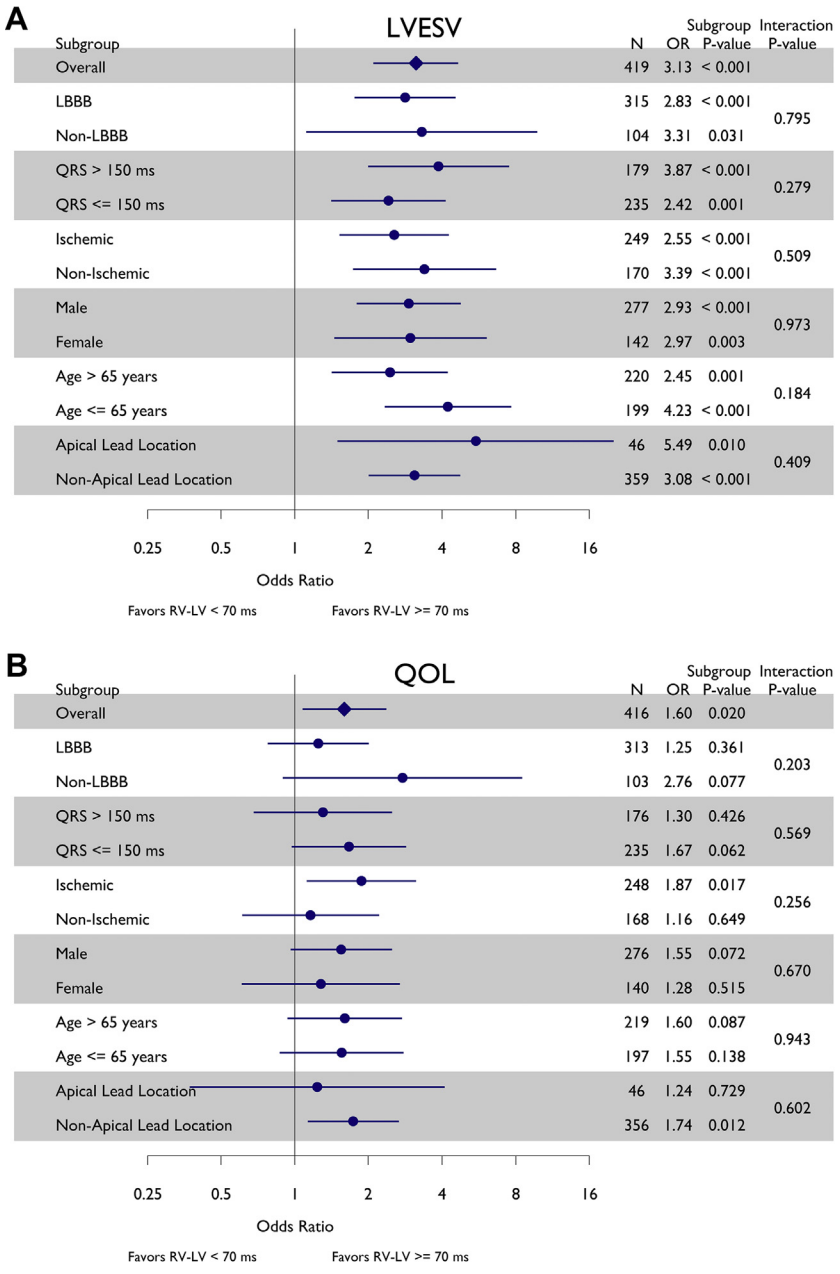
LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association functional class; other abbreviations as in Figures 1 and 2.

morphology is shown in Table 4. Whereas subjects with LBBB have a larger change in LVESV with CRT, the effect of RV-LV duration is much greater. In fact, subjects with a non-LBBB and long RV-LV duration have a more than 2-fold greater reduction in LVESV compared with subjects with LBBB and a short RV-LV.

DISCUSSION

CRT has been shown to promote reverse remodeling, improve clinical outcomes, and reduce mortality among patients with HF with a reduced EF and QRS prolongation. Despite the clear benefit of this

FIGURE 4 Univariate Predictors of Response to CRT



CRT = cardiac resynchronization therapy; Q = quartile; other abbreviations as in Figures 1 and 3.

therapy, the nonresponder rate has remained problematic, despite newer AV optimization algorithms and anatomically guided lead placement (20). This has led to updated guidelines focusing more on patient selection guided by QRS duration and morphology rather than intraoperative parameters (21,22). However, more recent studies of LV lead placement in areas of late electrical or mechanical delay have shown the importance of lead position (14–17). Previous studies in diverse populations using the QLV interval as a measure of LV electrical delay demonstrated the predictive value of this measure for acute hemodynamic changes, reverse remodeling, and clinical outcome with CRT (16,17,23,24). We now show that RV-LV duration is also a strong independent predictor of reverse

remodeling parameters and QOL in a multicenter, blinded clinical trial.

Previously, the impact of RV-LV interval on echocardiographic measures of remodeling was assessed in several relatively small, single-center trials. The results were mixed with regard to predicting the magnitude of changes in LVESV or remodeling endpoints (25–27). For instance, Kristiansen et al. (27) showed that RV-LV interval predicted the magnitude of LV volumetric change but not remodeling response rates. These studies were approximately 5-fold smaller (<100 subjects) than the present study, which may explain some of the inconsistent results. This also precluded more advanced statistical analysis of the data, such as predictors of this measure and evaluation of clinically important subgroups.

The association of RV-LV duration with chronic CRT response was robust and present for remodeling endpoints and QOL. The graded response with increasing RV-LV duration lends further support to the value of this measure. Moreover, this relationship was observed in all major subgroups, indicating that even parameters associated with traditionally lower CRT response rates, such as non-LBBB or QRS duration <150 ms, a longer interventricular delay predicts a better response. QRS morphology and duration were predictive of RV-LV duration as noted above, so it is intriguing to speculate that the higher nonresponder rates observed in the presence of non-LBBB and QRS duration <150 ms is due to an decreased probability of sufficiently long electrical delay at anatomically guided lead positions. In support of this hypothesis, patients with non-LBBB and long RV-LV duration have a more than 2-fold larger change in LVESV compared with LBBB patients with a short RV-LV.

Most HF patients with QRS prolongation have LV conduction delays, most commonly LBBB. One mechanism for the benefit of CRT is to restore electrical synchrony by pre-exciting the delayed LV area to achieve more synchronous interventricular electrical activation. When pacing at sites of late electrical activation, AV optimization designed to achieve fusion with normal conduction will further increase the remodeling response (28). To identify patients with such conduction delays, QRS duration and morphology are commonly used. This confirms the heterogeneity of LV conduction noted previously in subjects with dilated LVs or LBBB (29,30). It is interesting that this and other studies consistently show that some patients with an LBBB morphology will still have short electrical delay and pacing at the apical location with a longer delay can also have good CRT outcomes (31). This observation again emphasizes that the potential importance of direct measurements of the timing of LV activation may be superior to simply using anatomic positions to guide LV lead placement.

TABLE 4 The LVESV Response as a Function of Interventricular Delay and QRS Morphology

		Change in LVESV From Baseline to 6 Months					
RV-LV (ms)	QRS Morphology	N	Mean	SD	Median	25th Percentile	75th Percentile
<70	Non-LBBB	87	−6.67	35.36	−2	−23	17
<70	LBBB	113	−10.40	37.85	−11	−34	11
≥70	Non-LBBB	17	−24.65	37.04	−29	−50	5
≥70	LBBB	203	−31.23	44.74	−27	−56	−5

Abbreviations as in Tables 1 and 3.

There is a paucity of data comparing different measures of electrical and mechanical delay. However, in our study the RV-LV time was approximately 25 ms shorter, but well correlated with the QLV interval which has been shown to be a strong predictor of CRT response (16,17,23,24). This suggests that these 2 measures may be comparable for guiding lead placement, but the cutoff values for accepting or repositioning leads would differ. The multivariate analyses performed suggested that RV-LV duration may be a better predictor of the remodeling response. However, the results were very similar for these 2 measures, suggesting that further prospective comparison of measures of electrical delay to predict CRT response is needed.

CLINICAL IMPLICATIONS. Reducing the nonresponder rate continues to be an important goal for CRT. Analyses of large pivotal CRT studies suggest that a purely anatomic approach to lead position will be of limited value to reduce nonresponder rates. However, the RV-LV interval is strongly associated with remodeling responses and HF hospitalization with CRT and is easily measured during lead placement. Thus, it seems reasonable to evaluate this parameter at the time of LV lead implantation and consider repositioning or using a different electrode with longer electrical delay for pacing when short intervals are observed. An RV-LV interval >80 ms is a reasonable goal in this regard based on the statistical analysis of these data. This is likely of increased importance in subgroups with lower response rates, such as non-LBBB or ischemic cardiomyopathy. These are groups where the LV activation sequence would likely be less predictable because of sequence of His-Purkinje activation or scar patterns.

The RV-LV time has the benefit of simplicity of not requiring echocardiography or surface

electrocardiographic measurements. Moreover, it has the potential to be measured automatically by devices which would further simplify lead optimization.

Whereas the emphasis on CRT lead placement has been focused on the LV lead, RV-LV time can also be altered by repositioning the RV lead. The importance of anatomic RV lead position could not be assessed in this study because a vast majority of such leads were placed in the apex. However, further study is warranted to assess if a strategy of placing RV leads to maximize interventricular delay would improve outcomes.

STUDY LIMITATIONS. This study should be interpreted in light of several methodologic limitations. The cohort studied had advanced HF, so it is unknown if these observations apply to milder HF which is also indicated for CRT. The primary endpoint of this study was a change in LVESV. Although remodeling endpoints are predictive of "harder" endpoints such as HF hospitalization and death (32), this has not been shown for measures of LV electrical delay such as RV-LV time. The echocardiograms were performed during biventricular pacing at follow-up which may have affected the magnitude of response. However, previous randomized studies have shown that a similar magnitude of LV volumetric changes and thus remodeling occurs with CRT despite temporarily suspending pacing (5). As noted above, the effect of RV lead position on RV-LV duration could not be assessed as almost all patients had RV leads placed in the apex. A previous randomized study of RV lead position showed no effect on interventricular delay (25). This measure can only be performed in patients with intact AV conduction, so this approach is not relevant to guide lead position in patients with heart block or with chronic RV pacing. Finally, this was an observational study of interventricular delay among patients with traditionally placed LV leads. A randomized study will be needed to assess if a strategy of guided lead positioning by interventricular delay reduces the nonresponder rate.

CONCLUSIONS

The RV-LV interval is a strong and independent predictor of remodeling with CRT. This parameter predicted reverse remodeling even in subgroups traditionally associated with low response rates. Based on these results, measuring RV-LV time at implantation may help to identify optimal pacing sites.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE 1: CRT has been shown to improve exercise capacity, promote reverse remodeling, and decrease HF hospitalizations and death. However, approximately 30% of patients who are eligible for CRT are nonresponders.

COMPETENCY IN MEDICAL KNOWLEDGE 2: Anatomic guidance for LV lead position with CRT has little impact on outcomes, but placing leads in areas of late electrical or mechanical activation is associated with better response.

TRANSLATIONAL OUTLOOK: Interventricular electrical delay can potentially be measured simply and automatically by CRT devices, but a prospective trial is needed to demonstrate if using this approach to guide lead position will result in improved response rates.

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