Impact of QRS Duration and Ventricular Pacing on Clinical and Arrhythmic Outcomes in Continuous Flow Left Ventricular Assist Device Recipients: A Multicenter Study

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ABSTRACT

Objectives: Wide QRS duration and ventricular pacing are common in recipients of continuous-flow left ventricular assist devices (CF-LVADs) but their impact on outcomes remains unclear. We assessed the clinical and arrhythmic outcomes of CF-LVAD patients with wide QRS or right ventricular (RV) pacing at baseline, compared with those with narrow QRS and those with continued cardiac resynchronization therapy (CRT).

Methods and Results: A total of 520 patients (57 ± 13 years) with an implantable cardioverter-defibrillator (ICD) (n = 240) or CRT-defibrillator (n = 280) who underwent CF-LVAD implantation at 5 centers in 2007−2015 were studied. Patients were divided into 3 groups: ICD-N (QRS ≤120 ms; n = 134), ICD-W (QRS >120 ms; n = 106), and CRT (n = 280). Mortality, hospitalization, and ventricular arrhythmia (VA) incidence were compared among the groups. Baseline QRS duration was different among the groups (100 ± 13 [ICD-N] vs 155 ± 26 [ICD-W] vs 159 ± 29 ms [CRT]; $P < .0001$). In the ICD-W group, 37 (35%) had >80% RV pacing at baseline. Median biventricular pacing in the CRT group was 96%. Over 523 days of CF-LVAD support, Kaplan-Meier analysis showed no difference in survival among groups (log rank $P = .9$). According to multivariate Cox regression, wide QRS duration and RV pacing were not associated with survival. QRS narrowed during CF-LVAD support in the ICD-W and CRT groups but was not associated with improved survival ($P = .9$). No differences were noted among the groups in hospitalizations ($P = .9$), VA ($P = .2$), or ICD shocks ($P = .06$).

Conclusions: In this large CF-LVAD cohort, a wide QRS duration, high percentage of RV pacing at baseline, and changes in QRS duration after LVAD implantation were not associated with survival. Continued CRT after CF-LVAD implantation also was not associated with improved survival or HF hospitalizations. (*J Cardiac Fail 2019;25:355−363*)

Key Words: Left ventricular assist device, wide QRS, right ventricular pacing, cardiac resynchronization therapy, hospitalization, heart failure, ventricular arrhythmias.

Cardiac electrical conduction abnormalities, such as left bundle branch block (LBBB), right bundle branch block (RBBB), or nonspecific intraventricular conduction delay, can be seen in up to 50% of patients with advanced heart failure (HF).[1−3] Conduction abnormalities, especially when QRS duration is >120 ms, can result in intra- and interventricular dyssynchrony and have been associated with worsening HF symptoms, decline in left ventricular ejection fraction (LVEF), and increased risk of mortality in HF patients.[3−6] Similarly, high percentage of right ventricular (RV) pacing can result in cardiomyopathy and worsening HF.[7] Cardiac resynchronization therapy (CRT), by improving electromechanical synchrony, has been shown to improve mortality, left ventricular (LV) dimensions, functional status, and quality of life in patients with LVEF ≤35%, HF, and a wide QRS.[8−11] CRT can result in

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electrical synchrony and consequent narrowing of QRS duration, and this has been associated with favorable clinical outcomes in HF patients with wide QRS.[12,13]

Continuous-flow left ventricular assist devices (CF-LVADs) have been increasingly used in patients with advanced HF as bridge-to-transplantation as well as destination therapy, and have been shown to improve survival, morbidity, and functional status.[14−16] Although early studies suggested that LVAD implantation was associated with narrowing of QRS duration and reduction in nonsustained ventricular arrhythmias (VAs), they were limited by very small sample size and lack of long-term follow-up to assess hard clinical end points.[17−19] Many patients on LVAD support continue to exhibit electrical conduction delays, either from RV pacing or due to residual intrinsic conduction abnormalities. The role of baseline QRS duration and changes in QRS duration after LVAD implantation on clinical outcomes is not known. Moreover, whether high-percentage RV pacing is associated with adverse outcomes remain unclear. Several patients who receive an LVAD have preexisting CRT devices in place, with CRT continued in many after LVAD implantation. Although available small observational studies show no impact on survival,[20,21] the role of CRT as well its impact on QRS duration after LVAD implantion also are not well elucidated.

In the present large multicenter study, we sought to assess the clinical and arrhythmic outcomes of CF-LVAD patients with wide QRS or RV pacing at baseline, compared with those narrow QRS and those with continued CRT. A second objective was to understand the progression of QRS changes after CF-LVAD implantation and their impact on survival.

Methods

A retrospective analysis of data collected on 520 consecutive patients with preexisting ICD or CRT-D devices undergoing durable CF-LVAD implant (2007−2015) at 5 high-volume LVAD centers in the United States (University of Louisville, Louisville, Kentucky, University of Minnesota, Minneapolis, Advocate Christ Medical Center, Oak Lawn, Illinois, University of Florida, Gainesville, and Saint Vincent's Heart Center, Indianapolis, Indiana) was conducted. The University of Louisville served as the data coordinating center. The study protocol was approved by the Institutional Review Boards at all of the centers.

All patients had CF-LVADs implanted either as a bridge-to-transplantation or as destination therapy. Implanted CF-LVADs included Heartmate II (Abbott Medical, Chicago, Illinois) in 417 patients and Heartware (Heartware International, Framingham, Massachusetts) in 103 patients. Patients with an existing CRT device who had their LV lead deactivated during the first 60 days after LVAD implantation as well as those who underwent ICD or CRT-D implantation after LVAD implantation were included. We excluded patients who died during their index hospitalization for CF-LVAD implantation.

The LVAD study population was divided into 3 groups based on QRS duration and the presence of continued CRT: ICD-N group with narrow QRS (QRS <120 ms; n = 134), ICD-W group with >80% RV pacing or native QRS duration >120 ms (n = 106), and CRT group (n = 280).

In addition to baseline demographics and clinical data, electrocardiograms (ECGs) obtained before surgery and 6 and 12 months after LVAD implantation were reviewed. QRS duration was measured manually from the limb leads on a standard 12-lead ECG (25 mm/s). We also evaluated the change in mean QRS duration in each patient group after LVAD implantation. Furthermore, we sought to assess the impact of the changes in QRS duration during CF-LVAD support on survival. Based on prior data on the impact of QRS shortening on clinical outcomes in HF patients with CRT[13] as well as the differences in mean QRS duration in the ICD-N, ICD-W, and CRT groups before and after LVAD implantation, we chose a difference of ≥10 ms from baseline (QRS narrowing or widening) to be a significant.

Mortality, all-cause and HF hospitalization, incidence of heart transplantation, VA, and ICD therapies were compared among the 3 groups. Device interrogation reports and ECGs were reviewed for incidence of atrial arrhythmias (AAs), VA, ICD therapies, and percentage of biventricular pacing. Reported incidence for AA, VA, and ICD shocks during CF-LVAD support were assessed during the 6−12-month period after LVAD implantation. In those patients who had <6 months of follow-up, the latest available device interrogation was used.

Cardiac resynchronization therapy devices were kept in DDD(R) mode (VVIR in patients with permanent atrial fibrillation) with AV delay settings to allow consistent biventricular pacing. CRT programming was left to the discretion of the patient's electrophysiologist. No specific programming protocol was used.

VA was defined as sustained ventricular tachyarrhythmias lasting >30 s or requiring ICD therapy (antitachycardia pacing or shocks). AA was defined as atrial tachycardia, atrial flutter, or atrial fibrillation lasting either >6 hours or ≥1% burden on device interrogation or requiring pharmacologic or electrical therapy for termination.[22] HF hospitalization was defined as any hospitalization due to clinical signs and symptoms of congestive HF (dyspnea, fatigue, or volume overload, as well as use of intravenous diuretics or inotropes for volume). The day of CF-LVAD implantation marked the start date for follow-up. The last day of follow-up was August 31, 2016, date of heart transplantation, CF-LVAD explantation, or date of death, whichever came first.

Statistical Analysis

Baseline characteristics between the ICD-N, ICD-W, and CRT-D groups were evaluated by means of nonparametric (Kruskal Wallis) test for continuous variables and chi-square test for categoric variables. Continuous variables were reported with the use of median (interquartile range) and categoric variables were reported with the use of

percentage. Changes in the QRS duration before and after LVAD implantation were evaluated between the groups by means of paired *t* tests and reported as mean ± SD.

Kaplan-Meier estimated survivals were computed for patients based on QRS grouping, and the log-rank test was used to compare survival differences between groups. Patients were censored at the time of transplantation, explantation for recovery, or study end. Multivariate Cox regression modeling was used to identify independent predictors of survival as a post hoc analysis. Regression candidate variables included previously established and clinically relevant correlates of survival after LVAD and other baseline variables (Table 1) with a *P* value of ≤.05 on univariate analysis. Device type and QRS duration (one model using QRS >120 ms and one model using QRS >150 ms) were forced into the survival analyses. A *P* value of <0.05 was considered to be statistically significant. All statistical analyses were performed with the use of the SAS 9.3 (SAS Institute, Cary, North Carolina).

Results

Demographic and Clinical Characteristics

Of the 520 patients included in the analysis, 240 patients had an ICD and 280 a CRT-D. Fifteen patients in the ICD group and 1 in the CRT group had their device implanted shortly after CF-LVAD implantation. Among the ICD group, 134 (56%) had a baseline QRS duration ≤120 ms (ICD-N group) whereas 106 (44%) had a baseline QRS duration >120 ms (ICD-W). Among the ICD-W group patients, 37 (35%) had >80% right ventricular pacing at baseline, 14 (14%) had LBBB, 12 (12%) had RBBB, and the rest had a nonspecific interventricular conduction delay. Baseline demographic and clinical characteristics are presented in Table 1. At baseline, the ICD-N group was younger (51 ± 13 vs 60 ± 13 vs 60 ± 12 years for ICD-N, ICD-W, and CRT groups respectively; *P* = .0001) and had fewer white patients (58% vs 69% vs 69%; *P* = .01), less AA (29% vs 39% vs 52%; *P* < .0001), a lower frequency of preoperative amiodarone use (23% vs 34% vs 40%; *P* = .008), and a higher proportion of patients with nonischemic cardiomyopathy (60% vs 38% vs 46%; *P* = .01). Other comorbidities, including CF-LVAD indication (bridge-to-transplantation vs destination therapy), use of HF medications, and incidence of preoperative VA and ICD shocks, were similar among the 3 groups. In the CRT group, 18 patients had their LV lead deactivated within the first 60 days after CF-LVAD implantation. The reasons for deactivation of the LV included high LV lead capture thresholds (n = 7), LV lead cut during LVAD implantation (n = 4), suspected proarrhythmia from LV lead (n = 3), phrenic nerve stimulation (n = 1), and unknown (n = 3)

Baseline ECG Parameters

Mean baseline (pre-LVAD) QRS durations in the ICD-N, ICD-W, and CRT groups were 100 ± 12.5, 155 ± 26, and 159 ± 29 ms, respectively (*P* < .0001). PR intervals

Table 1. Differences in Demographic and Clinical Characteristics Between the Narrow QRS, Wide QRS and CRT-D groups

Characteristic	ICD-N (n = 134)	ICD-W (n = 106)	CRT (n = 280)	*P* Value
Age (y; mean ± SD)	51 ± 13	60 ± 13	60 ± 12	.0001*
Male sex (%)	76	81	83	.2
White (%)	58	69	69	.01*
BMI (kg/m^2; mean ± SD)	30 ± 7	29 ± 6	29 ± 8	.1
Nonischemic cardiomyopathy (%)	60	38	46	.01*
Diabetes mellitus (%)	40	44	44	.6
Hypertension (%)	61	74	66	.1
Coronary artery disease (%)	44	63	61	.002*
Chronic kidney disease (%)	38	42	45	.4
Smoking (%)	53	58	56	.7
LVAD as destination therapy (%)	48	50	55	.4
Angiotensin-converting enzyme inhibitor use (%)	38	40	39	.5
Beta-blocker use (%)	85	86	82	.6
Amiodarone use (%)	23	34	40	.003*
PR interval (ms; mean ± SD)	172 ± 36	180 ± 41	145 ± 46	<.0001*
QRS duration (ms; mean ± SD)	100 ± 13	155 ± 26	159 ± 29	<.0001*
QTc interval (ms; mean ± SD)	477 ± 40	520 ± 73	537 ± 60	<.0001*
Pre-LVAD LVEF (%; mean ± SD)	16 ± 6	16 ± 6	16 ± 6	.9
Pre-LVAD LVEDD (cm; mean ± SD)	7 ± 1	7 ± 1	7 ± 1	.13
Pre-LVAD LVESD (cm; mean ± SD)	6.3 ± 1	6.3 ± 0.9	6.5 ± 1.1	.4
Biventricular pacing percentage (mean ± SD)	NA	NA	96 ± 5	
Atrial arrhythmias (%)	29	39	52	<.0001*
Ventricular ARRHYTHMIA (%)	53	69	63	.08
ICD shocks (%)	30	44	37	.1
LVAD SUPPORT (median days)	600	444	525	.3

ICD-N: ICD group with narrow QRS (≤120 ms); ICD-W: ICD group with wide QRS (>120 ms); CRT-D: group with continued biventricular pacing during LVAD support. LVAD, left ventricular assist device; BMI, body mass index; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter-defibrillator.

(172 ± 36 vs 180 ± 41 vs 145 ± 46 ms; $P < .0001$) and QTc intervals (477 ± 40 vs 520 ± 73 vs 537 ± 60 ms; $P < .0001$) were also significantly different among the 3 groups.

Clinical Outcomes

Overall mean and median follow-ups for the whole CF-LVAD cohort were, respectively, 651 ± 528 days and 523 days (9065 patient-months). Median follow-up duration was not significantly different among the ICD-N, ICD-W, and CRT groups (600 vs 444 vs 525 days; $P = .3$). During follow-up, 42 patients (32%) died in the ICD-N group, 32 (30%) in the ICD-W group, and 88 (32%) in the CRT group. Kaplan-Meier analysis showed no significant difference in survival among the 3 groups at the end of follow-up (log rank $P = .9$; Fig. 1). In a separate analysis, we examined survival in the ICD-W group with the use of a more stringent cutoff of >150 ms. Even with a higher QRS cutoff, no significant survival differences were noted among the groups (log rank $P = .7$; Fig. 2).

During CF-LVAD support, narrowing of QRS duration was noted in both the ICD-W (155.17 ± 25.6 to 140.2 ± 35.5 ms during LVAD support; $P = .0001$) and CRT (158.8 ± 29.1 to 149.3 ± 29.0 ms; $P < .0001$) groups but not in the ICD-N group (100.0 ± 12.5 to 103.7 ± 27.0 ms; $P = .11$; Table 2). Figure 3 depicts a Kaplan-Meier analysis of overall survival difference among patients with narrowing of QRS duration by ≥10 ms (*i*; n = 241 [45%]), no change in QRS duration (*n*; n = 155 [32%]), or widening of QRS duration by ≥10 ms (*w*; n = 110 [23%]) during follow-up. Changes in QRS duration, or lack thereof, during LVAD support was not associated with any difference in survival (log rank $P = .9$).

During follow-up, no significant differences were noted among the ICD-N, ICD-W, and CRT groups in all-cause hospitalization (0.59 vs 0.58 vs 0.48 median hospitalizations/100 days; $P = .2$) and HF hospitalizations (0.18 vs 0.15 vs 0.15 median hospitalizations/100 days; $P = .9$). We also compared the incidence of HF hospitalizations between the >80% RV pacing subgroup in the ICD-W group versus the CRT group, and did not find any significant differences:

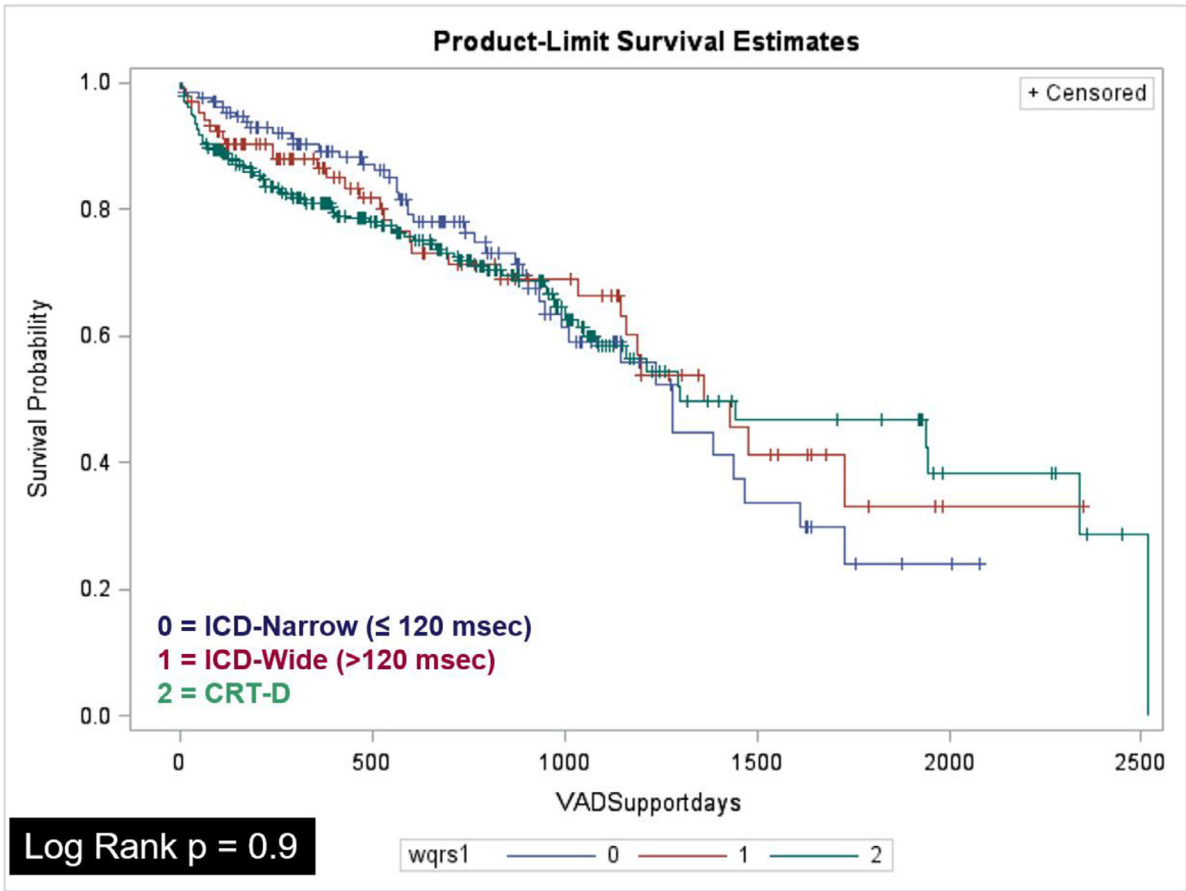

Fig. 1. Kaplan-Meier analysis, showing relationship between baseline QRS duration and survival. There was no significant difference in survival between the ICD-N, ICD-W, and CRT groups. The cutoff for wide QRS in the ICD group for this analysis was >120 ms. The log-rank test was used to compare survival estimates. The mean and median survival times for the ICD-N group were 1162 ± 63 and 1279 (994−1468) days, for ICD-W 1184 ± 75 and 1363 (1146−1480) days, and for CRT 1464 ± 89 and 1302 (1086−2339) days. CRT-D, cardiac resynchronization therapy defibrillator; ICD, implantable cardioverter-defibrillator.

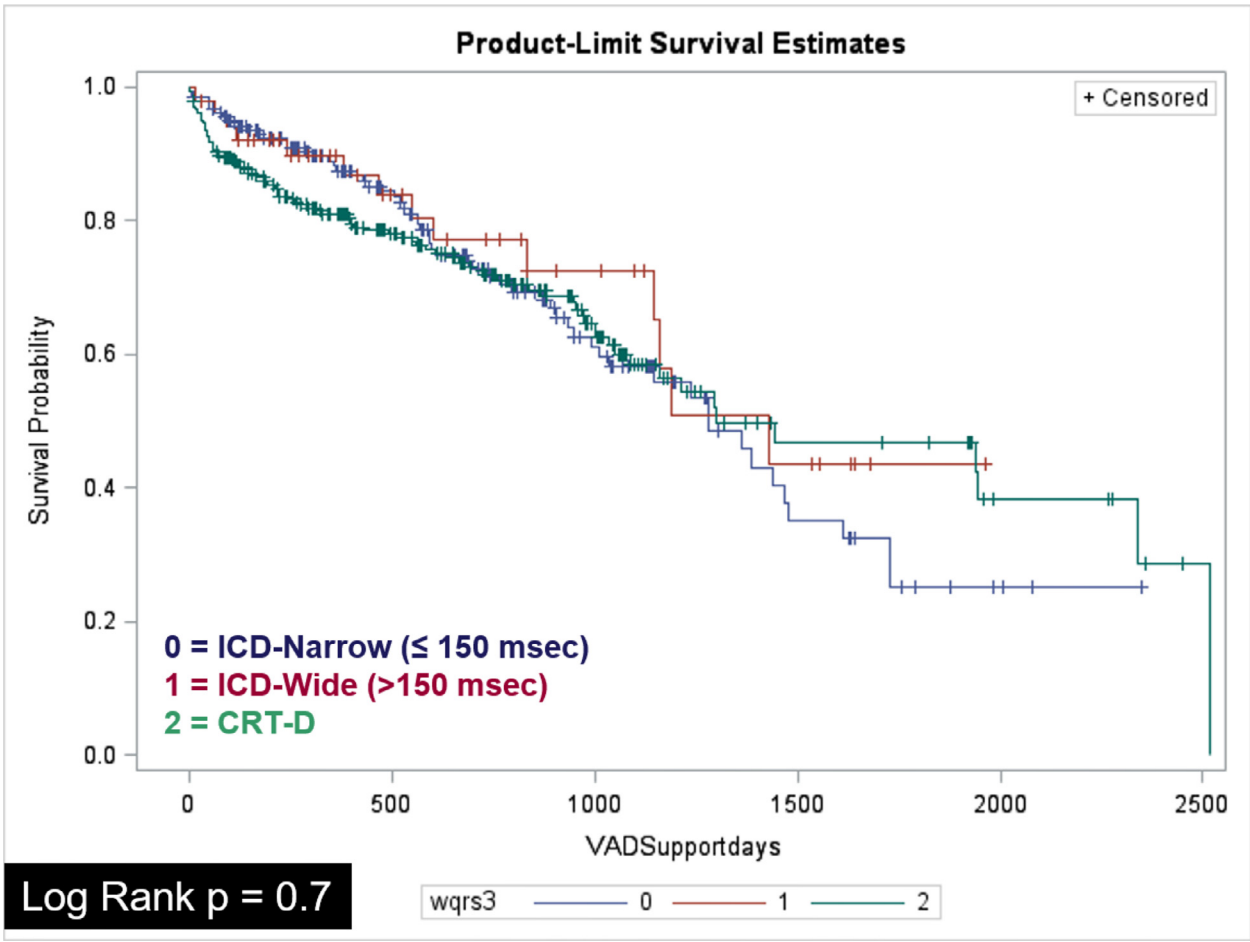

Fig. 2. Kaplan-Meier analysis, showing relationship between baseline QRS duration and survival. The cutoff for wide QRS in the ICD group for this analysis was >150 ms. The mean and median survival times for the ICD-N group were 1150 ± 54 and 1279 (1010−1480) days, for ICD-W 1092 ± 79 and 1430 (1146−1480) days, and for CRT 1364 ± 87 and 1305 (1083−2330) days. Abbreviations as in Fig. 1.

0.14 [0−0.50] vs 0.15 [0−0.45] median hospitalizations/100 days of LVAD support (P = .8).

The cumulative incidence of VA (35% vs 44% vs 43%, -P = .2) and ICD shocks (28% vs 37% vs 41%; P = .06) were similar among the groups during follow-up, whereas AA incidence during follow-up was higher in the CRT group. There was no statistically significant difference among the 3 groups in the proportion of patients undergoing heart transplantation (16% vs 18% vs 7%; P = .7). Beta-blocker and amiodarone use also were similar among the 3 groups during follow-up (Table 3).

Adjusted survival outcomes based on Cox-regression modeling showed that wide QRS duration was not significantly associated with survival, when using a cutoff of either >120 ms or >150 ms (Table 4). The type of cardiac implantable electronic device (ICD vs CRT-D), INTERMACS profile, and >80% RV pacing at baseline (hazard ratio 0.928; P = .92) also were not significantly associated with survival.

Table 2. Changes in QRS Duration (ms) in the 3 Groups During Follow-Up

Group	Before	After	P Value
ICD-N	100.0 ± 12.5	103.7 ± 27.0	.11
ICD-W	155.17 ± 25.6	140.2 ± 35.5	.0001*
CRT	158.8 ± 29.1	149.3 ± 29.0	<.0001*

Abbreviations as in Table 1.

Discussion

In this multicenter study of more than 500 patients on CF-LVAD support, we found no association between wide QRS duration nor high percentage of RV pacing and overall survival, even after adjusting for known correlates of risk. Moreover, QRS duration was not associated with hospitalization or the development of VA after CF-LVAD implantation. Although some patients exhibited a change in QRS duration after CF-LVAD implantation, such changes (QRS prolongation or QRS decrement) did not affect survival. Finally, in line with an earlier analysis, the type of cardiac implantable electronic device (ICD vs CRT-D) also as not significantly associated with survival.[20]

Conduction abnormalities are common in advanced HF patients, with 14%−47% patients having a wide QRS (>120 ms) and LBBB being more common than RBBB.[2] Wide QRS, especially LBBB, and the resultant inter- and

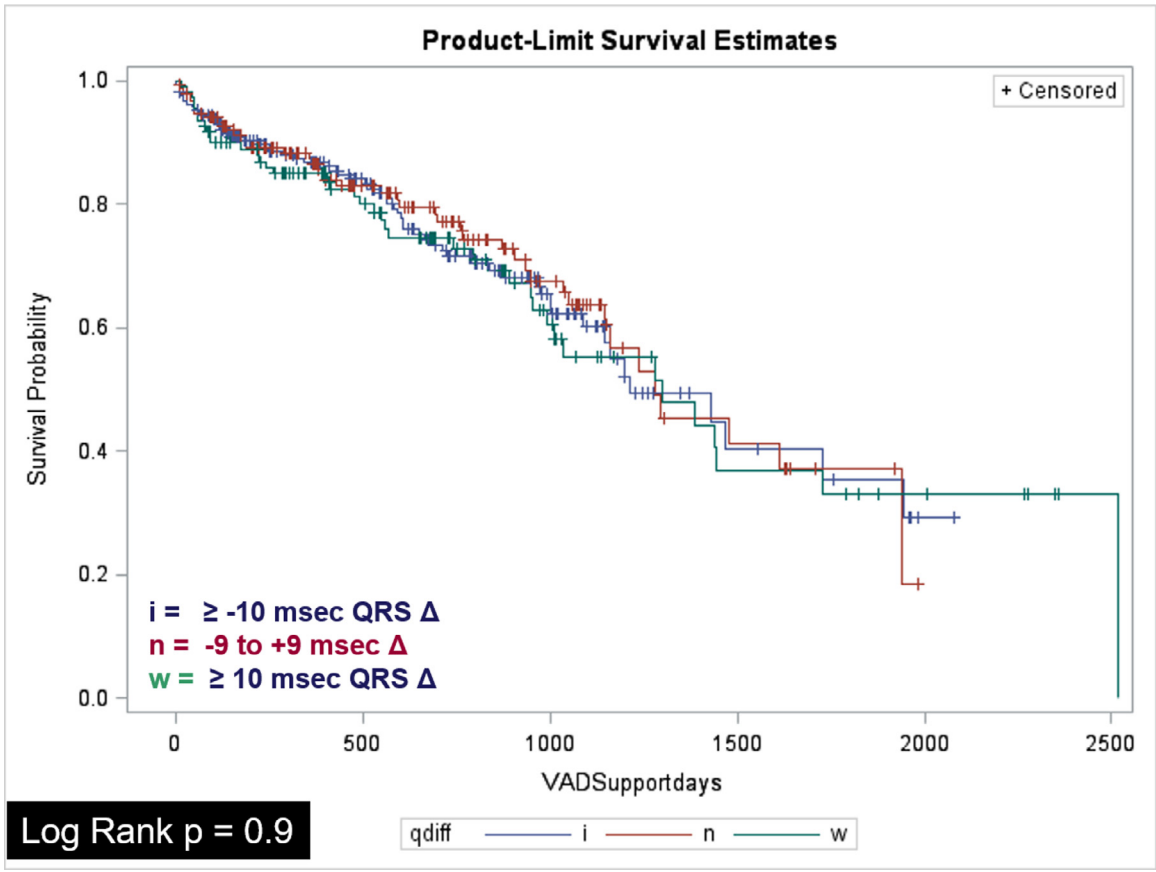

Fig. 3. Kaplan-Meier analysis, showing overall survival difference between patients with improved QRS duration (*i*), no change in QRS duration (*n*), or widening of QRS duration (*w*) during follow-up. The mean and median survival times for the *i* group were 1246 ± 69 and 1211 (1086−1945) days; for *n* 1267 ± 77 and 1279 (1148−1940) days, and for *w* 1398 ± 123 and 1302 (994-1728) days.

intraventricular electrical dyssynchrony has been associated with worse outcomes in the HF population with low EF.[2,4] However, the impact of wide QRS, whether native, RV paced, or biventricularly paced, on outcomes after CF-LVAD implantation remains unclear. Previous studies evaluating improvement in QRS duration after LVAD implantation have had conflicting results. Harding et al, in 2001, evaluated 23 patients who underwent LVAD implantation and reviewed changes in QRS from baseline (before LVAD), immediately after LVAD implantation and then >1 week after LVAD implantation and found that there was immediate improvement in QRS duration (117 ± 6 to 103 ± 6 ms; $P < .01$) after LVAD implantation but it was not sustained during follow-up. However, only 4 out of 23 patients had wide QRS (2 with RBBB and 2 with LBBB), none had CRT, and none of the patients were supported with contemporary CF-LVADs.[17] In contrast, a study of 12 patients who underwent LVAD implantation noted progressive shortening of QRS and QTc duration at both 1 week and 6 months after LVAD implantation, accompanied by a reduction in the burden of premature ventricular beats, suggesting favorable electrical remodeling.[18] However, data on long-term outcomes in that small sample were not provided.

Table 3. Differences in Clinical Outcomes Between the ICD-N, ICD-W, and CRT Groups During Follow-Up

Outcome	ICD-N (n = 134)	ICD-W (n = 106)	CRT (n = 280)	*P* Value
Deaths, n (%)	42 (32%)	32 (30%)	88 (32%)	.9
Transplantation, n (%)	21 (16%)	19 (18%)	18 (7%)	.7
All-cause hospitalizations, n/100 days	0.59	0.58	0.48	.2
HF hospitalizations, n/100 days	0.18	0.15	0.15	.9
Post-LVAD AA (%)	45%	55%	61%	.01*
Post-LVAD VA (%)	35%	44%	43%	.2
Post-LVAD ICD shocks (%)	28%	37%	41%	.06
Beta-blocker use (%)	71%	66%	64%	.4
Amiodarone use (%)	42%	54%	49%	.2

AA, atrial arrhythmias; HF, heart failure; VA, ventricular arrhythmias; other abbreviations as in Table 1.

The results from the present analysis support previous findings that there is a variable response to LVAD therapy in terms of electrical conduction, with 45% of patients having a decrease in QRS duration, 32% an increase in QRS duration, and 23% no change in QRS duration. However, we did not find an adverse association between wide QRS duration before or after LVAD implantation and survival, readmission, or arrhythmias. This analysis differs from the aforementioned studies in its large sample size, long duration of follow-up, and a dedicated CRT group with

Table 4. Adjusted Survival Outcomes Based on Multivariate Cox Regression Model Using QRS Cutoffs of 120 ms and 150 ms

	QRS >120 ms		QRS >150 ms	
Parameter	Hazard Ratio	*P* Value	Hazard Ratio	*P* Value
Age at LVAD implantation	1.02 (0.97−1.08)	.54	1.02 (0.97−1.08)	.54
Sex	0.92 (0.15−5.7)	.93	0.83 (0.15−4.5)	.82
BMI at LVAD implantation	1.01 (0.92−1.13)	.74	0.97 (0.88−1.1)	.61
Caucasian race	0.18 (0.02−1.3)	.09	0.21 (0.04−1.22)	.08
INTERMACS profile	0.87 (0.55−1.4)	.55	1.1 (0.7−1.7)	.73
PR interval	1.01 (0.99−1.03)	.11	1.02 (0.99−1.04)	.09
QTc interval	0.99 (0.98−1.03)	.19	0.99 (0.98−1.01)	.35
Pre-LVAD LVEDD	0.85 (0.36−1.96)	.7	1.78 (0.78−4.0)	.17
Pre-LVAD AA	1.05 (0.31−3.55)	.94	0.89 (0.23−3.45)	.86
LVAD indication	1.22 (0.35−4.23)	.75	1.01 (0.30−3.32)	.98
Cardiomyopathy type	0.9 (0.2−4.0)	.38	1.29 (0.27−6.2)	.74
RV pacing >80% at baseline	1.4 (0.30−6.4)	.67	1.3 (0.30−6.4)	.74
QRS >120 ms	1.96 (0.49−7.9)	.34	0.23 (0.03−2.1)	.19
Amidarone use	0.98 (0.3−3.56)	.97	1.15 (0.3−3.97)	.82

Abbreviations as Tables 1 and 3.

continued biventricular pacing at a very high percentage (96%), helping to clearly identify the impact of CRT and QRS narrowing on outcomes in this CF-LVAD cohort.

Our results also suggest that a high percentage of RV pacing may not have as deleterious an impact in CF-LVAD patients as it does in advanced HF patients. CRT, by improving electrical synchrony, and consequently mechanical synchrony, has been shown to improve survival and functional status in non-LVAD patients with LVEF ≤35%, HF, and a QRS duration >120 ms.[8−11] However, more recent studies have shown an even wider QRS duration and the absence of RBBB morphology being better predictors of CRT benefit, leading the latest American College of Cardiology/American Heart Association/Heart Rhythm Society guidelines to list a QRS duration >150 ms with LBBB as a class I indication.[23] One of the main reasons why CRT improves outcomes in HF patients is by narrowing QRS by causing electrical fusion, thus improving electrical synchrony.[12,13] A meta-analysis of available studies showed that QRS shortening after CRT implantation is associated with a favorable clinical and echocardiographic response in HF patients with reduced LVEF.[12] In the present study, although the QRS duration improved in the CRT group after CF-LVAD implantation, no improvement in survival was seen. This finding corroborates previously published data from Gopinathannair et al.[20,22] Although some degree of electrical remodeling did result from CF-LVAD implantation, and perhaps more from continued CRT, as evidenced by improvement in mean QRS in the ICD-W and CRT groups, it was not enough to affect outcomes in the present durations of LVAD support. In the non-CRT patient population, we performed both survival analysis and Cox regression modeling with the use of baseline wide QRS cutoffs of both 120 ms and 150 ms to see if there was a QRS duration threshold that affects outcome. However, a wider QRS, using either cutoff, did not predict survival. We also stratified patients based on the change in QRS during LVAD support (QRS shortening vs none vs widening) and QRS duration change, or lack thereof, was also not associated with improved survival. Overall, our findings show, in contrast to patients with advanced HF, that wide QRS, either native or paced, was not associated with hard clinical end points following CF-LVAD support.

It is probable that the significant LV decompression from the CF-LVAD supersedes any potential electrical remodeling benefit associated with favorable QRS changes or CRT. Anatomic changes in LV after LVAD implantation can alter conduction patterns and efficient mechanical dynamics. Compared with earlier reports of reduction in premature ventricular contractions and nonsustained ventricular tachycardia, we did not find any significant differences in the incidence of VA and ICD shocks among the ICD-N, ICD-W, and CRT groups. Although the ICD-N group had a lower incidence of ICD shocks than the other groups, that did not reach statistical significance. CRT or RV pacing did not appear to be more proarrhythmic compared with narrow QRS or bundle branch block. Overall, this suggests that changes in QRS duration in a CF-LVAD patient may not represent severity of underlying substrate.

The present cohort is very representative of a real-world CF-LVAD population, with very similar proportion of patients receiving CF-LVAD as bridge-to-transplant or as destination therapy. The LV dimensions and LVEF were also similar across the 3 groups, The ICD-N group, however, was younger, had more patients with nonischemic cardiomyopathy, and had an overall lower arrhythmic burden at baseline. Any baseline differences were adjusted with the use of multivariate analyses when evaluating outcomes. Mortality rates during follow-up were similar to published data from previous studies.[14,24−26] All these factors contribute to the strength of our results.

Study Limitations

This study is limited by its retrospective design. However, the multicenter experience and large sample size, allowing robust multivariate analyses, strengthens the results. CRT group patients were continued on their pre-

LVAD biventricular programming with any programming changes made on a case-by-case basis. Whether a standard CRT programming protocol would have made a difference in outcomes needs further study. We also did not assess RV function and any impact of baseline QRS duration and changes after CF-LVAD implantation on RV function. Finally, we did not have accurate information on mortality during index hospitalization, so we could not include that group in our analysis.

Conclusion

In this large multicenter CF-LVAD cohort, a wide QRS duration and high percentage of RV pacing at baseline, as well as changes in QRS duration after LVAD implantation were not associated with survival. Continued CRT after CF-LVAD implantation also was not associated with improved survival or HF hospitalizations. Our results are hypothesis generating and randomized studies to further understand the relationship between electrical and mechanical activation and their significance in influencing clinical outcomes in CF-LVAD patients are warranted.

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Disclosures

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Supplementary Data

Supplementary data related to this article can be found at doi:10.1016/j.cardfail.2019.02.013.

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