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PR Prolongation Predicts Inadequate Resynchronization with Biventricular Pacing in Left Bundle Branch Block

Short title: PR Predicts Inadequate CRT in LBBB

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Abstract:

Background: PR interval prolongation is associated with poor outcome after cardiac resynchronization therapy (CRT) among patients with left bundle branch block (LBBB) but the mechanisms are unknown. We investigated clinical outcomes, electrocardiogram (ECG) and echocardiogram changes after CRT by PR interval.

Methods: This is a retrospective study of CRT recipients with a baseline ejection fraction ≤35% and ECG showing sinus rhythm and LBBB. Patients were stratified by baseline PR interval quartile and the primary combined endpoint was time to heart transplantation, left ventricular assist device (LVAD) implantation or death. ECG, echocardiogram and clinical variables were compared to identify mechanisms for observed differences in outcomes.

Results: Of 291 eligible patients, the mean age was 65 years, 60% were male, and 19% had prior atrial fibrillation. Patients with PR prolongation (quartile 4, PR >200ms) more frequently had a history of atrial fibrillation, coronary artery bypass graft surgery, prior implantable cardioverter defibrillator implantation, and use of amiodarone than patients in PR quartiles 1-3. A PR >200ms was associated with an adjusted hazard ratio of 1.7 (95% CI 1.1-2.5) for the primary endpoint. Patients with PR >200ms had less reduction in QRS duration and QRS area after CRT while having more increase in QT and QTc intervals than patients with PR ≤200 ms. No major differences were observed in echocardiography by baseline PR interval quartiles.

Conclusions: PR prolongation predicts shorter survival free of heart transplantation or LVAD implantation in patients with LBBB. This may be due to inadequate ventricular resynchronization.

Keywords
Electrocardiology; PR interval; Cardiac Resynchronization Therapy; Electrophysiology; Echocardiography; Mortality/Survival

Introduction:

Prolongation of the electrocardiogram (ECG) PR interval > 200 ms is associated with increased adjusted risks of atrial fibrillation and all-cause mortality(1-4). Prior studies on the association

between baseline PR interval and outcomes after cardiac resynchronization therapy (CRT) are conflicting, patients with left bundle branch block (LBBB) and prolonged baseline PR interval have increased likelihood of heart failure related hospitalization or death after CRT compared to patients with LBBB normal baseline PR interval while patients with non-LBBB conduction abnormalities and PR prolongation may have lower likelihood of adverse events after CRT compared to patients with non-LBBB conduction abnormalities and normal PR interval (5-7). Whether the poorer outcomes after CRT among patients with LBBB and PR prolongation are related to a higher burden of medical comorbidity or if different implantation, programming or follow-up techniques may be needed to optimize outcomes remains unclear. Little information is available comparing the ECG and echocardiographic response to CRT among patients with normal and prolonged baseline PR interval and LBBB and prior studies are limited by lack of data regarding device programming and biventricular pacing percentage.(4) To better understand possible mechanisms for poor CRT outcomes, we performed a retrospective single center analysis to compare the clinical, ECG, and echocardiographic response to CRT among patients with LBBB and prolonged PR interval and those with normal PR interval.

Methods:

Study population:

This is a retrospective analysis of patients who received a *de novo* implantation of a CRT-defibrillator at Duke University Medical Center between April 2006 and September 2015. Patients were identified using an institutional dataset created for submission to the National Cardiovascular Data Registry. For this study patients were required to have an echocardiogram performed within 365 days of CRT-D implantation demonstrating a left ventricular ejection fraction (LVEF) of ≤ 35% and a digital ECG at baseline (≤ 180 days prior to CRT implantation) demonstrating a QRS ≥ 120ms with left bundle branch block morphology and follow up ECG ≤ 90 days after the index procedure

demonstrating CRT pacing. Patients were excluded if they died prior to discharge, if they were not in normal sinus rhythm (NSR) on the baseline ECG or if they had evidence of 2nd or 3rd degree atrioventricular (AV) block. If multiple ECGs were available in the allowable pre- and/or post-CRT time frame the ECG closest to the procedure date was utilized. The study was approved by the Duke Institutional Review Board.

ECG Analyses:

Clinically obtained ECGs were reanalyzed using the GE MUSE Cardiology Information System version 8.0.2.0132 with analysis software version 241 (GE Healthcare, Chicago Il, USA) and exported in .XML format. QRS morphology was designated by two readers (DF and KE) blinded to outcome. Left bundle branch block (LBBB) morphology was defined according to previously accepted criteria including QRS duration ≥ 120 ms, QS or rS in lead V_1, broad R waves in leads I, aVL, V_5, or V_6, and absent Q waves in leads V_5 and V_6 (8). LBBB was further divided into strict and non-strict LBBB using the Strauss criteria(9). P wave, QRS, and QT onset and offset and thereby P wave duration, PR interval, QRS duration, and QT interval as detected by the software were over read and manually corrected if needed. The QT interval was corrected (QTc) using the Freiderica formula. P wave dispersion was calculated as the maximum P wave duration minus the minimum P wave duration on a 10 second ECG. Vectorcardiograms were derived from the XML files using customized MATLAB software (MathWorks, Inc., Natick, MA, USA) using the Kors matrix.(10)

Device Follow-Up Data:

Patients were longitudinally followed using remote patient monitoring or in-clinic device interrogation and reports were retrospectively reviewed in the electronic medical record. To be included in analyses of device follow-up, data must have been acquired at least 30 days after implantation. If multiple follow-up reports were available in the electronic medical record, device data obtained as close as possible to 180 days after implantation was used.

End Points:

The primary clinical study endpoint was incident left ventricular assist device (LVAD), cardiac transplant, or all-cause death. Endpoint occurrence was determined via a May 24, 2017 query of the Duke Enterprise Data Unified Content Explorer, which incorporates data from billing claims, hospital records, and the Social Security Death Index.(11) The echocardiographic imaging study endpoints were % change in LV end systolic volume (LVESV), % change in LV end diastolic volume (LVEDV) and absolute % change in LVEF. The ECG endpoints were % change in PR interval, % change in QRS duration, % change in QRS area, % change in QT interval, and % change in corrected QT interval. Because prior studies have shown that the relationship between baseline PR interval and CRT outcomes is non-linear, the primary clinical analysis compared outcomes by baseline PR interval quartile. To further explore the results of the primary clinical endpoint, all further analyses compared PR interval quartile 4 (PR interval > 200 ms) to PR interval quartiles 1-3 (PR ≤ 200ms).

Statistical Analyses:

Baseline characteristics of the study population were compared using frequencies with percentages for categorical variables and means with standard deviations or medians with interquartile range for continuous variables. Differences between groups were compared using the chi-square tests for categorical variables and Wilcoxon rank-sum tests or student's T-tests for continuous variables. Because prior studies (4)have shown that the relationship between baseline PR interval and CRT outcomes is non-linear, the primary clinical analysis compared outcomes by baseline PR interval quartile. The unadjusted association between baseline PR interval quartile and time to LVAD, transplant or death was depicted using a Kaplan Meier plot and differences were assessed using the Log Rank test. To further explore the results of the primary clinical endpoint, all further analyses compared PR interval quartile 4 to PR interval quartiles 1-3. The adjusted long term association between baseline PR interval quartile (quartile 4 vs. quartiles 1-3) and time to LVAD, transplant, or

death was assessed using Cox proportional hazards models. All variables that differed between patients in quartile 4 and quartiles 1-3 were included in the adjusted analysis, including QRS duration, QRS area, prior CABG, prior ICD, prior cardiac arrest, ICD indication, prior atrial fibrillation, and prior or current amiodarone use. Statistical analyses were performed in JMP Pro Version 13.1 (SAS, Cary, NC). A $P < 0.05$ was considered statistically significant for all tests.

Results:

A total of 1001 patients underwent CRT-D implant during the study period; 162 patients were excluded for a missing or low quality baseline ECG, 335 patients were excluded for non-LBBB QRS morphology, 59 patients were excluded for atrial fibrillation or flutter on the baseline ECG, and 14 patients were excluded for 2nd or 3rd degree AV block on the baseline ECG. A total of 126 patients were excluded for lack of baseline echocardiogram and 13 patients were excluded because baseline echo images were low quality and uninterpretable. One patient was excluded because of failure to place an LV lead leaving a total of 291 patients available for analysis.

Baseline Patient Characteristics by PR Interval Quartile:

Patient characteristics at the time of CRT implantation are shown in **Table 1.** The range of PR interval in each quartile were: quartile 1= 86 - 164ms, quartile 2= 165 - 180ms, quartile 3= 181 - 200ms and quartile 4= 201 - 380ms. Patients in PR interval quartile 4 more frequently had a history of coronary artery bypass surgery, a secondary prevention indication for ICD implantation, prior ICD implantation, cardiac arrest, atrial fibrillation or flutter, and were more likely to be treated with amiodarone. Patients in PR interval quartile 4 also had more P wave dispersion, slower ventricular rate, longer QRS duration and QT interval, and smaller QRS area than patients in PR interval quartiles 1-3 (**Table 2**). They also had more prolonged isovolumic contraction time (ICT) on tissue Doppler echocardiography, but similar baseline LVEF, LV size, and diastolic filling time.

Clinical End Points:

Over a median follow-up of 3.1 years (1.7 - 5.9 years), 120 (41%) patients reached the primary combined endpoint. The study end point was death in 99 (34%) patients, LVAD implantation in 12 (4%) patients, and heart transplantation in 9 (3%) patients. The combined clinical endpoint occurred in 22/72 (31%) patients in PR interval quartile 1, 29/73 (40%) patients in quartile 2, 26/73 (36%) patients in quartile 3, and 43/73 (59%) patients in quartile 4 (**Figure 1**). Baseline PR interval in quartile 4 was associated with an unadjusted HR of 2.7 (95% CI 1.6-4.6, $P < 0.0001$) compared to PR quartile 1, HR 1.9 (95% CI 1.2-3.1, $P = 0.007$) compared to PR quartile 2, and HR 2.7 (95% CI 1.7-4.5, $P < 0.0001$) compared to PR quartile 3 for reaching the combined clinical endpoint. Because PR interval quartile 4 differed from PR interval quartiles 1-3 but PR quartiles 1-3 had no significant differences with each other in survival, all further analyses were performed comparing PR interval quartile 4 to the combined PR interval quartiles 1-3. After combining PR interval quartiles 1-3, baseline PR interval in quartile 4 was associated with an unadjusted HR of 2.4 for reaching the combined clinical endpoint (95% CI 1.6-3.5, $P < 0.0001$). Baseline PR interval in quartile 4 remained predictive of time to combined clinical endpoint after adjustment for differences in baseline covariates with a HR of 1.7 (95% CI 1.1-2.5, $P = 0.02$). Median survival free of heart transplant or LVAD after CRT implantation was 3.3 (IQR 1.5-6.9) years for patients in PR quartile 4 versus 9.6 (IQR 3.1->10) years for patients in PR interval quartiles 1-3.

Device Programming and Follow-up Device Data by Baseline PR Interval Quartile:

Follow-up device data were available in 253 (87%) patients. The median time from implant to follow-up device interrogation was 202 days (134 - 296 days). There was no difference in the time from implant to device follow-up between PR interval quartile 4 and PR interval quartiles 1-3 (**Table**

3). At follow-up, there were no significant differences in the frequency of DDD, DDDR, VVI, or VVIR programming modes, or the frequency of use of adaptive LV only pacing or programmed AV intervals across the baseline PR interval quartiles. Patients in PR interval quartile 4 had a higher mean programmed lower rate limit, (57 ± 8 beats per minute vs. 55 ± 7 beats per minute, $P = 0.03$). Despite differences in the frequency of history atrial fibrillation or flutter at CRT implant, there were no differences in the mean atrial fibrillation burden or mean percentage of biventricular pacing between PR interval quartiles 1-3 and PR interval quartile 4 on follow-up device interrogation. Patients in PR interval quartile 4 received more ICD shocks per patient than patients in the combined PR interval quartiles 1-3, 17 shocks occurred in 57 patients with device follow up data in PR interval quartile 4 (0.3 shocks per patient) vs. 17 shocks in 187 patients (0.09 shocks per patient) in PR interval quartiles 1-3. These differences were not significant after adjusting for time of follow-up, patients in PR interval quartile 4 received 0.5 ± 3 shocks per life year of follow-up while patients in PR interval quartiles 1-3 received 0.2 ± 1.4 shocks per life year of follow-up ($P = 0.27$ for difference).

ECG Endpoints:

A total of 211 (72%) patients had follow-up CRT paced ECGs available for analysis. There were no differences in the CRT paced PR interval or heart rate between patients in baseline PR interval quartile 4 and quartiles 1-3. Patients in baseline PR interval quartile 4 had more prolonged CRT paced QRS duration (146 ± 21 ms vs. 163 ± 22 ms, $P < 0.01$), QT interval (463 ± 47 ms vs. 494 ± 43 ms, $P < 0.01$), and QTc (512 ± 39 ms vs. 541 ms ± 42 ms, $P < 0.01$) interval than patients in PR interval quartiles 1-3. Patients in PR interval quartile 4 also had significantly larger CRT paced QRS area than patients in PR interval quartile 1-3, 76 ± 35 μVs vs. 65 ± 31 μVs ($P = 0.04$). Patients in baseline PR interval quartile 4 had significantly less reduction in QRS duration and QRS area while having significantly more increase in QT and QTc intervals than patients in PR interval quartiles 1-3

(**Figure 2**). After CRT, patients in baseline PR quartile 4 (PR > 200 ms) had less reduction in QRS duration and QRS area than patients in PR quartiles 1-3, (0 ± 22 ms vs. -9 ± 23 ms, $P = 0.01$) and (-21 ± 37 μVs vs. -43 ± 44 μVs, $P < 0.01$), respectively. Patients in baseline PR quartile 4 also had more QT and QTc prolongation after CRT pacing than patients in PR quartiles 1-3 (29 ± 45 ms vs. 13 ± 40 ms, $P<0.01$) and (41 ± 44 ms vs. 15 ± 38 ms, $P < 0.01$) respectively.

Echocardiographic Endpoints:

A total of 123 (42%) patients had follow-up echocardiograms available for analysis. There were no significant differences between baseline PR interval quartiles 1-3 and quartile 4 for changes in LVEF, LVESV, LVEDV, global longitudinal strain, or longitudinal strain pattern after CRT pacing. (**Table 3**)

Discussion

In this single center study we used detailed ECG and echocardiographic data to explore mechanisms that may explain the poor outcomes observed after CRT implantation among patients with prolonged baseline PR interval. Specifically, we sought to compare the burden of medical comorbidity, presence or absence of ECG and echocardiographically identifiable dyssynchrony, and the degree of correction of that dyssynchrony during CRT pacing across PR interval quartiles. First, we confirmed that patients with baseline PR interval prolongation (> 200 ms, PR interval quartile 4) experienced increased risk of death, LVAD implantation, or heart transplantation after CRT implantation. We also confirmed findings from other studies that patients undergoing CRT implantation with baseline PR interval > 200 ms (quartile 4) more frequently had a prior history of atrial fibrillation, ischemic heart disease, coronary artery bypass grafting surgery and prior ICD implantation. After adjustment for these differences, patients with prolonged baseline PR interval continued to demonstrate shorter survival free of LVAD or heart transplant, confirming prior findings

that differences in baseline characteristics do not fully explain the observed differences in outcomes after CRT implantation.(5)

Prior work suggests that differences in CRT response observed between patients with various conduction abnormalities can largely be explained by differences in underlying intrinsic electrical substrate(12). We used echocardiogram and ECG data to evaluate whether differences in electrical and mechanical intrinsic substrate may explain the differences in survival seen between patients with prolonged PR interval and those with normal PR interval and found that overall patients with baseline PR interval prolongation had similar intrinsic substrates for CRT based on several commonly used metrics. In fact, patients with baseline PR interval in quartile 4 (> 200 ms) had more prolonged baseline QRS duration than patients with normal PR interval with equal likelihood of a strict LBBB QRS configuration. Echocardiography showed that patients with prolonged PR interval had more prolonged ICT than patients with normal baseline PR interval, suggesting that they may have more to gain from improvement of LV filling and dP/dT through CRT than patients with normal PR interval(13). Of interest, although the QRS duration was more prolonged in PR quartile 4 than other quartiles, the QRS area was significantly smaller. QRS area has recently proven to be a powerful predictor of CRT outcomes and may be a better tool than QRS duration for measurement of intrinsic global ventricular dyssynchrony(14,15). Thus, although several commonly used tools suggest similar substrate among patients with a prolonged versus normal PR interval, QRS area assessment suggests that patients with a prolonged PR interval may have less global ventricular dyssynchrony at baseline and thus may have less to gain with resynchronization therapy.

Next, we investigated whether CRT delivery differed among patients with prolonged PR interval and patients with normal PR interval. We found that patients with prolonged PR had similar biventricular pacing %, similar AF burden after CRT implantation, and similar programmed pacing parameters. Despite the similarities in device programming, patients with prolonged baseline PR interval had less reduction in QRS duration and QRS area than patients with normal PR interval,

suggesting inadequate electrical resynchronization of underlying electrical dyssynchrony may be common in patients with prolonged PR interval. Prior studies suggest that patients with LBBB and normal PR interval have intact right bundle branch and septal fascicular conduction that contribute to ventricular depolarization during CRT pacing while little or no contribution is present in patients with PR prolongation.(16) This is the physiological basis for adaptive LV only pacing. The additional contribution of the intact right bundle and septal fascicles to biventricular paced ventricular depolarization among patients with normal PR interval may provide a more synchronous overall LV activation than pure biventricular pacing using an epicardial LV lead and an RV endocardial lead among patients with PR prolongation, explaining the more significant reductions in QRS duration and QRS area among patients with normal baseline PR interval. Future studies exploring alternative CRT pacing strategies such as multipoint pacing, LV endocardial pacing, His bundle pacing, or a combination of His bundle and LV epicardial pacing(17) may provide opportunities to improve outcomes for patients with intrinsic PR prolongation.

Finally, patients with baseline PR prolongation more often experienced VT/VF events requiring ICD shock during follow-up, although in the modest sample size these differences did not reach significance. At baseline they were more likely to have a secondary ICD indication for sudden cardiac death prevention, a history of prior ICD implantation, prior cardiac arrest, use of amiodarone, and QT prolongation, all potentially increasing the likelihood of arrhythmic events. We found that baseline PR prolongation was also associated with more severe prolongation of the QT and QTc intervals after CRT pacing. It is possible that this group experiences a higher likelihood of developing intramyocardial repolarization heterogeneities with CRT pacing, which could be proarrhythmic. Further work examining the role of repolarization on predicting outcomes after CRT pacing is needed.

Limitations:

The major limitations of this study are the retrospective design and the lack of a control group who did not receive CRT. As a result, the treatment effect of CRT implantation in patients with PR

interval prolongation cannot be established. The single center nature of the study limits generalizability of the findings. Cardiac resonance imaging data were unavailable, as a result we were unable to compare differences in ventricular scar burden between patients with normal versus prolonged PR interval. Left ventricular lead position is an important predictor of CRT outcomes and was not available in the dataset; if different across PR interval quartiles this may account for the observed differences in outcomes. The severity of heart failure symptoms was available at baseline but was not available at follow-up, preventing us from assessing this important CRT endpoint. Finally, ECG and echocardiogram data were missing in some patients, limiting our ability to detect differences in ECG and especially echocardiographic response to CRT across PR interval quartiles.

Conclusion:

CRT recipients with prolonged baseline PR interval have shorter survival free of heart transplant or LVAD therapy after CRT than patients with normal PR interval. While comorbidities may play a role in this association, it also appears that patients with prolonged baseline PR interval experience less resynchronizing effect of CRT than patients with normal PR interval despite generally similar intrinsic substrates for resynchronization at baseline.

Author Contributions:

Dr. Atwater designed the project, performed data analysis and drafted the manuscript. Drs. Emerek, Sorensen, Hansen, Loring, Graff, Polcwiartek, and Friedman performed data collection, critically revised the manuscript, and approved the manuscript. Drs Kisslo and Søgaard secured funding, critically revised the manuscript, and approved the manuscript**.**

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Figure 1 (central figure): Kaplan-Meier survival plots by baseline PR interval quartile. Log-Rank test $P < 0.0001$. Red line = baseline PR interval quartile 1, Green line = baseline PR interval quartile 2, Blue line = baseline PR interval quartile 3, Orange Line = baseline PR interval quartile 4.

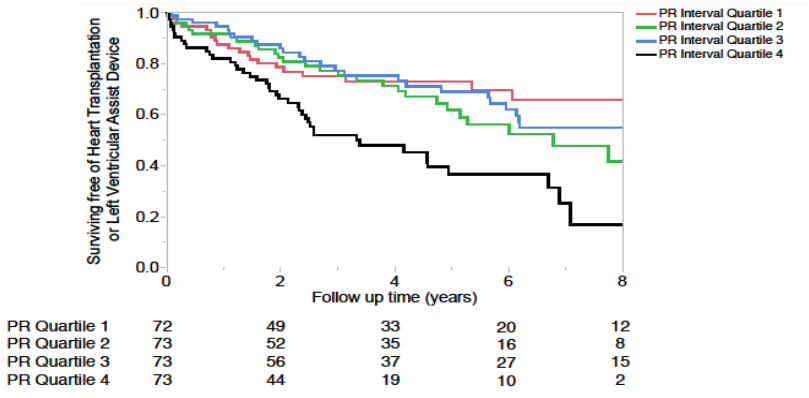

Figure 2: Change in QRS duration (Panel A), QRS area by Kors transformation method (Panel B), QT interval (Panel C) and corrected QT interval (Panel D) stratified by baseline PR interval quartile 1-3 versus 4.

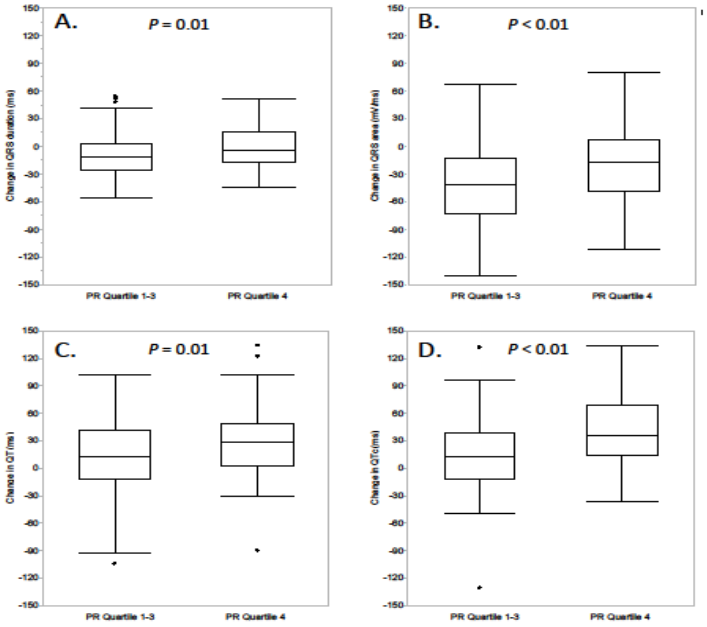

Table 1: Baseline patient clinical characteristics.

Variable	**Total**	**Quartile 1-3, PR=86-200ms**	**Quartile 4, PR=201-380ms**	***P*-value**
N	291	218	73	
Age (years), mean (SD)	65 (11.5)	64 (12)	67 (11)	0.13
Sex (female)	117 (40)	91 (42)	26 (36)	0.47
Race				0.34
Black	68 (23)	54 (25)	14 (19)	
White	132 (45)	100 (46)	32 (44)	
Other	9 (2)	5 (2)	4 (5)	
Missing	82 (28)	59 (27)	23 (32)	
Ischemic	133 (46)	93 (43)	40 (55)	0.08

Cardiomyopathy				
CABG	73 (25)	46 (21)	27 (37)	<0.01
NYHA Class				0.92
I	10 (3)	7 (3)	3 (4)	
II	48 (16)	36 (17)	12 (16)	
III	224 (77)	169 (78)	55 (75)	
IV	9 (3)	6 (3)	3 (4)	
Duration of Heart Failure				0.06
< 3 months	10 (3)	9 (4)	1 (1)	
3-9 months	43 (15)	37 (17)	6 (8)	
> 9 months	233 (81)	168 (79)	65 (90)	
ICD Indication				0.01
Primary Prevention	262 (90)	202 (93)	60 (82)	
Secondary Prevention	29 (10)	16 (7)	13 (18)	
Prior ICD	45 (15)	23 (11)	22 (30)	<0.01
Cardiac Arrest	17 (6)	8 (4)	9 (12)	0.01
Diabetes	88 (30)	60 (28)	28 (38)	0.09
Hypertension	200 (69)	145 (67)	55 (75)	0.15
Atrial Fibrillation or Flutter	55 (19)	29 (13)	26 (36)	<0.01
Chronic Lung Disease	55 (19)	41 (19)	14 (19)	0.94
Cerebrovascular Disease	29 (10)	19 (9)	10 (14)	0.23
Creatinine (mg/dL)	1.5 (1.5)	1.4 (1.4)	1.8 (1.7)	0.06
Amiodarone	41 (14)	19 (8.8)	22 (30)	<0.01
Beta Blocker	263 (91)	200 (93)	63 (86)	0.12
ACE or ARB	236 (82)	182 (84)	54 (74)	0.06

ACE = angiotensin converting enzyme, ARB = angiotensin receptor blocker, CABG = coronary artery bypass graft surgery, ICD = implantable cardioverter-defibrillator, NYHA = New York Heart Association.

Table 2: Baseline ECG and echocardiographic patient characteristics.

Variable	**Total**	**Quartile 1-3, PR=86-200ms**	**Quartile 4, PR=201-380ms**	***P*-value**
N	291	218	73	
QRS Morphology				
Strict LBBB (%)	235 (81)	175 (80)	60 (82)	0.71
ECG Intervals				
PR Interval (ms)	185 (36)	171 (20)	231 (36)	<0.01
P Duration (ms)	114 (18)	112 (15)	118 (23)	0.05
P Dispersion (ms)	76 (20)	74 (20)	82 (22)	0.02
Ventricular Rate (BPM)	74 (14)	75 (14)	71 (13)	0.02
QRS Duration (ms)	157 (21)	155 (20)	162 (23)	0.04
QT Interval (ms)	454 (40)	451 (38)	465 (45)	0.02
QT Corrected (ms)	498 (38)	498 (37)	499 (39)	0.82
QRS Area (μVs)	104 (42)	108 (43)	93 (36)	<0.01
LVEF (%)	24 (9)	24 (9)	23 (9)	0.59
LVEDV (mL)	220 (84)	218 (86)	230 (80)	0.29
LVESV (mL)	172 (79)	169 (80)	180 (76)	0.32
Isovolumic Contraction Time (ms)	130 (34)	127 (33)	139 (37)	0.04
Ejection Time (ms)	264 (38)	263 (39)	268 (37)	0.37
Isovolumic Relaxation Time (ms)	141 (37)	143 (35)	136 [115. 165]	0.26
Diastolic Filling Time (ms)	320 (136)	312 (134)	308 (142)	0.87
Diastolic Filling Time (% RR)	35 (9)	36 (9)	35 (10)	0.64
Myocardial Performance Index	1.05 (0.27)	1.05 (0.26)	1.04 (0.29)	0.86

Global Longitudinal Strain (%)	-8.1 (3.6)	-8.3 (3.8)	-7.6 (3.3)	0.18
Longitudinal Strain Pattern				0.92
Classical	186 (64)	139 (64)	47 (64)	
Other	105 (36)	79 (36)	26 (36)	

LVEF = left ventricular ejection fraction, LVEDV = left ventricular end diastolic volume, LVESV = left ventricular end systolic volume.

Table 3: Follow up device programming, ECG and echocardiographic data.

Variable	**Total**	**Quartile 1-3, PR=86-200ms**	**Quartile 4, PR=201-380ms**	***P*-value**
Device Programming and Pacing Characteristics at Follow-up, N	**251**	**192**	**59**	
Time from implant to follow-up (days), median, (IQR)	202 (134-296)	202 (139-305)	204 (110-288)	0.81
Pacing Mode				0.10
DDD, n (%)	178 (71)	141 (73)	37 (63)	
DDDR, n (%)	70 (28)	48 (25)	22 (37)	
VVI, n (%)	3 (1)	3 (2)	0 (0)	
Adaptive CRT, n (%)	43 (17)	29 (15)	14 (24)	0.33
Lower Rate Limit (BPM)	55 (8)	55 (7)	57 (8)	0.03
Paced AV Delay (ms)	146 (32)	143 (31)	152 (35)	0.09
Sensed AV Delay (ms)	111 (32)	110 (30)	115 (38)	0.33
LV to RV Delay (ms)*	-11 (17)	-14 (18)	-4 (13)	<0.01
CRT (BIV or LV only) Pacing (%)	95 (13)	96 (13)	94 (14)	0.55
AF Burden (%)	2.4 (13)	1.9 (13)	3.7 (14)	0.40
VT/VF Therapies (n/person years follow-up)	0.3 (1.9)	0.2 (1.4)	0.5 (3)	0.27
Follow-Up ECG Characteristics, N	**211**	**153**	**58**	

Atrial Rhythm				0.05
Sinus	173 (82)	132 (85)	41 (71)	
Atrial Paced	37 (17)	21 (14)	16 (28)	
Atrial Fibrillation	2 (1)	1 (1)	1 (1)	
PR Interval (ms)	140 (32)	138 (33)	143 (33)	0.42
Ventricular Rate (BPM)	75 (14)	75 (15)	74 (14)	0.44
QRS Duration (ms)	151 (23)	146 (21)	163 (22)	<0.01
QRS Area (μVs)	68 (32)	65 (31)	76 (35)	0.04
QT Interval (ms)	472 (48)	463 (47)	494 (43)	<0.01
QT Corrected (ms)	520 (42)	512 (39)	541 (42)	<0.01
Echo Characteristics for Patients with Baseline and Follow-up Studies, N	**123**	**97**	**26**	
Change in LVEF (%)	9 (10)	8 (11)	10 (8)	0.36
Change in LVEDV (mL)	-29 (54)	-33 (54)	-13 (53)	0.09
Change in LVESV (mL)	-37 (53)	-38 (54)	-30 (51)	0.48
Change in Global Longitudinal Strain (%)	-2.7 (4.2)	-2.7 (4.3)	-2.7 (4.2)	0.98
Follow up Longitudinal Strain Pattern				0.55
Classical	19 (15)	14 (14)	5 (19)	
Other	104 (85)	83 (86)	21 (81)	

AF = atrial fibrillation, AV = atrio-ventricular, BIV = biventricular, CRT = cardiac resynchronization therapy, IQR = interquartile range, LV = left ventricular, LVEF = left ventricular ejection fraction, LVEDV = left ventricular end diastolic volume, LVESV = left ventricular end systolic volume.

*Among patients programmed to standard Biventricular (non-Adaptive LV only) CRT pacing.