Original Investigation

QRS Duration, Bundle-Branch Block Morphology, and Outcomes Among Older Patients With Heart Failure Receiving Cardiac Resynchronization Therapy

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IMPORTANCE The benefits of cardiac resynchronization therapy (CRT) in clinical trials were greater among patients with left bundle-branch block (LBBB) or longer QRS duration.

OBJECTIVE To measure associations between QRS duration and morphology and outcomes among patients receiving a CRT defibrillator (CRT-D) in clinical practice.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study of Medicare beneficiaries in the National Cardiovascular Data Registry's ICD Registry between 2006 and 2009 who underwent CRT-D implantation. Patients were stratified according to whether they were admitted for CRT-D implantation or for another reason, then categorized as having either LBBB or no LBBB and QRS duration of either 150 ms or greater or 120 to 149 ms.

MAIN OUTCOMES AND MEASURES All-cause mortality; all-cause, cardiovascular, and heart failure readmission; and complications. Patients underwent follow-up for up to 3 years, with follow-up through December 2011.

RESULTS Among 24 169 patients admitted for CRT-D implantation, 1-year and 3-year mortality rates were 9.2% and 25.9%, respectively. All-cause readmission rates were 10.2% at 30 days and 43.3% at 1 year. The unadjusted rate and adjusted risk of both 3-year mortality and of 1-year all-cause readmission were lowest among patients with LBBB and QRS duration of 150 ms or greater. There were no observed associations with complications.

	LBBB		No LBBB	
Outcome	QRS ≥150 ms	QRS 120-149 ms	QRS ≥150 ms	QRS 120-149 ms
No.	9889	6259	3306	4715
3-y Mortality, No. (%)	1859 (20.9)	1511 (26.5)	929 (30.7)	1380 (32.3)
Adjusted HR (99% CI)	1 [Reference]	1.30 (1.18-1.42)	1.34 (1.20-1.49)	1.52 (1.38-1.67)
1-y All-cause re-admission, No. (%)	3752 (38.6)	2760 (44.8)	1489 (45.7)	2301 (49.6)
Adjusted HR (99% CI)	1 [Reference]	1.18 (1.10-1.26)	1.16 (1.08-1.26)	1.31 (1.23-1.40
1-y Cardiovascular readmission, No. (%)	1927 (19.8)	1552 (25.1)	873 (26.8)	1372 (29.5)
Adjusted HR (99% CI)	1 [Reference]	1.27 (1.17-1.38)	1.29 (1.17-1.44)	1.47 (1.34-1.62)
1-y Heart failure re-admission, No. (%)	845 (8.7)	794 (12.9)	491 (15.1)	793 (17.1)
Adjusted HR (99% CI)	1 [Reference]	1.47 (1.30-1.67)	1.62 (1.40-1.87)	1.92 (1.68-2.20)

CONCLUSIONS AND RELEVANCE Among fee-for-service Medicare beneficiaries undergoing CRT-D implantation in clinical practice, LBBB and QRS duration of 150 ms or greater, compared with LBBB and QRS duration less than 150 ms or no LBBB regardless of QRS duration, was associated with lower risk of all-cause mortality and of all-cause, cardiovascular, and heart failure readmissions.

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Clinical trials have shown that cardiac resynchronization therapy (CRT) improves symptoms and reduces mortality and readmission among selected patients with heart failure and left ventricular systolic dysfunction. Following broad implementation of CRT, it was recognized that one-third to one-half of patients receiving the therapy for heart failure do not improve.[1] Identification of patients likely to benefit from CRT is particularly important, because CRT defibrillator (CRT-D) implantation is expensive, invasive, and associated with important procedural risks.

A primary question regarding optimal patient selection for CRT is whether patients with longer QRS duration or left bundle-branch block (LBBB) morphology derive greater benefit than others. Current guidelines recommend selection of patients primarily on the basis of QRS duration and morphology based predominantly on meta-analyses and subgroup analyses of clinical trials evaluating either QRS duration or morphology. Only 1 study specifically evaluated the combination of QRS duration and morphology but did not assess meaningful patient outcomes.[2] Thus, the role of QRS duration and morphology in the selection of patients for CRT in contemporary clinical practice remains unclear.

CABG *coronary artery bypass graft*

CRT-D *cardiac resynchronization therapy defibrillator*

LBBB *left bundle-branch block*

NYHA *New York Heart Association*

PCI *percutaneous coronary intervention*

The objectives of this study were to determine the long-term outcomes of unselected patients undergoing CRT-D implantation in real-world settings and associations between combinations of QRS duration and presence of LBBB and longitudinal outcomes, including mortality, readmission, and complications following CRT-D implantation in a large population of Medicare beneficiaries who received CRT-Ds.

Methods

Data Sources

The institutional review board of the Duke University Health System approved the study. Data were from the National Cardiovascular Data Registry's ICD (implantable cardioverter-defibrillator) Registry. The registry data include demographic characteristics, medical history, clinical information, and laboratory test results obtained before or during the implantation procedure, as well as physician and site identifiers. Standardized data elements and definitions are used. Participating hospitals submit the data using certified software. Data quality is examined through a formal data quality program to ensure completeness and consistency, and accuracy is examined through yearly audits.[3,4]

Longitudinal outcomes were obtained by linking the registry data to Medicare claims using indirect identifiers—hospital, admission date, discharge date, patient sex, and birth date.[5] Combinations of these identifiers are almost completely unique, enabling identification of registry implantations in the Medicare claims data. Medicare inpatient claims and denominator files were used for follow-up through December 31, 2011. The inpatient files contain hospital claims for reimbursement under Medicare Part A. The denominator files contain death dates.

Study Population

We included patients 65 years or older who had a registry record for a CRT-D implantation between April 1, 2006, and December 31, 2009; were enrolled in fee-for-service Medicare at the time of the procedure; and could be linked to Medicare claims data. If multiple implantation records were linked for a single patient, we used the earliest record for the analysis. We excluded patients who had undergone epicardial lead implantation, previous placement of an ICD or pacemaker, implantation for secondary prevention, or coronary artery bypass graft (CABG) surgery or percutaneous coronary intervention (PCI) during the implantation hospitalization or who were missing documentation for any of the exclusion criteria.

We hypothesized that patients admitted for CRT-D implantation would have different characteristics and outcomes than patients admitted for other reasons (eg, heart failure, acute coronary syndrome). Therefore, patients were categorized as either admitted for CRT-D implantation or admitted for other reasons. The primary analyses included patients admitted for CRT-D implantation; secondary analyses included patients admitted for other reasons.

Exposures

Predictor variables of interest included QRS duration and LBBB. QRS duration was recorded as a continuous variable in the registry. For consistency with guidelines for CRT-D available during the study, we limited the analysis to patients with QRS duration of 120 ms or greater.[6] Intraventricular conduction from electrocardiogram findings was recorded as a categorical variable in the registry with 9 possible values, including LBBB. Based on current literature, we focused on LBBB morphology and QRS duration categories of 120 to 140 ms and 150 ms or greater. We combined QRS duration and the presence or absence of LBBB and assigned patients to 1 of 4 categories: LBBB and QRS duration of 120 to 149 ms, no LBBB and QRS duration of 120 to 149 ms, LBBB and QRS duration of 150 ms or greater, and no LBBB and QRS duration of 150 ms or greater.

Outcomes

The outcomes of interest were all-cause mortality, all-cause readmission, cardiovascular readmission, heart failure readmission, and complications. Patients underwent follow-up for up to 3 years after CRT-D implantation, and the number of days to each outcome was calculated using the implantation date recorded in the registry. The relevant periods for each outcome were selected on the basis of clinical judgment. Mortality was assessed at 30 days, 1 year, and 3 years. Readmission was assessed at 30 days and 1 year. Complications included (1) pneumothorax, hemothorax, hematoma, cardiac tamponade, and a composite end point of these complications at 30 days; and (2) infection and mechanical complications at 90 days, 1 year, and 3 years, and a composite end point of these outcomes at 90 days.

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All-cause mortality was determined from death dates in the Medicare denominator files. Readmission outcomes were based on subsequent inpatient claims, excluding claims for the index procedure, interhospital transfers, and admissions for rehabilitation. Readmission outcomes included all-cause readmission, cardiovascular readmission (diagnosis related groups [DRGs] 104-112, 115-118, 121-145, 479, 514-518, 525-527, 535, 536, and 547-558 before October 1, 2007, and DRGs 215-238, 242-254, 258-262, and 280-316 on or after October 1, 2007), and heart failure readmission (DRG 127 before October 1, 2007, and DRGs 291-293 on or after October 1, 2007).

For complications, we searched for the relevant *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis and procedure codes in any position on an inpatient claim. Complications included pneumothorax or hemothorax (*ICD-9-CM* diagnosis codes 512.1, 511.8, or 511.89), hematoma (diagnosis codes 998.1x), cardiac tamponade or pericardiocentesis (diagnosis codes 420.x, 423.0, 423.3, or 423.9 or procedure codes 37.0 or 37.12), infection (diagnosis code 996.61), and mechanical complications of ICD with system revision (diagnosis codes 996.04 or 996.01 combined with procedure codes 37.75, 37.79, 37.97, 37.99, or 00.52). We also created 2 composite end points for (1) pneumothorax, hemothorax, hematoma, or cardiac tamponade and (2) infection or mechanical complications.

Patient Characteristics

Baseline characteristics were obtained from the registry and included demographic characteristics, medical history, and clinical measures. Data for the demographic variables were complete, and the other variables had low rates of missingness (ie, <5% of records). Missing continuous variables were imputed to the overall median value, and missing dichotomous variables were imputed to "no."[7]

Statistical Analysis

For baseline characteristics, categorical variables are presented as frequencies with percentages and continuous variables as means with SDs. Patients were grouped by reason for admission, and differences in baseline characteristics were tested for using χ^2 tests for categorical variables and Kruskal-Wallis tests for continuous variables. The primary analysis included patients admitted for CRT-D implantation; secondary analyses included patients admitted for other reasons.

Kaplan-Meier methods were used to estimate mortality and log-rank tests to assess differences in mortality among strata of QRS duration and LBBB categories. For other outcomes, we used the cumulative incidence function, which accounts for the competing risk of death, and we used Gray tests to assess differences in outcomes between the groups.

Cox proportional hazards models were used to examine univariate and multivariable associations between QRS duration and LBBB category and outcomes after CRT-D implantation. In multivariable analyses, each outcome was modeled as a function of QRS duration and LBBB category, age, sex, race, renal failure, hypertension, diabetes, atrial fibrillation, chronic lung disease, cerebrovascular disease, ischemic heart disease, prior myocardial infarction, prior CABG surgery, prior PCI, congestive heart failure duration, history of syncope, history of ventricular tachycardia, prior congestive heart failure hospitalization, New York Heart Association (NYHA) class, ejection fraction, systolic blood pressure, serum sodium level, serum creatinine level, blood urea nitrogen level, year of procedure, quartile of annualized implanting clinician ICD volume, and quartile of annualized site-level ICD volume. Robust standard errors were used to account for clustering of patients within hospitals. The censoring date was the earliest of the end of the period for which data were available (December 31, 2011) or the date on which the patient's data were no longer available because the patient enrolled in a Medicare managed care plan. For outcomes other than mortality, patients were censored at the time of death. In all analyses, the proportionality assumption was tested for the QRS duration and LBBB category of interest.

A significance level of $P < .01$ was used for all hypotheses to correct for multiple comparisons. All tests were 2-sided. We used SAS version 9.2 (SAS Institute Inc) for all analyses.

Results

Between April 2006 and December 2009, 96 380 Medicare beneficiaries 65 years or older were admitted for CRT-D implantation and could be linked to Medicare claims data. Exclusions were based on receipt of an epicardial lead (n = 4287), previous ICD placement (n = 34 133), previous pacemaker placement (n = 19 370), CRT for secondary prevention (n = 14 870), CABG surgery (n = 689) or PCI during the hospitalization (n = 1403), and QRS duration of less than 120 ms (n = 4688). After these exclusions, 35 248 patients met the inclusion criteria. Of those excluded, 540 (0.6%) were excluded because of missing documentation of exclusion criteria. Among patients meeting the inclusion criteria, 11 079 were admitted for other reasons, resulting in a primary study cohort of 24 169 patients admitted for CRT-D implantation. eFigure 1 (Supplement) shows the derivation of the study population.

Among fee-for-service Medicare beneficiaries admitted for CRT-D implantation, the mean age was 75 years; 68% of the patients were men and 90% were white (**Table 1**). Common coexisting conditions included hypertension (78%), ischemic heart disease (65%), diabetes mellitus (38%), atrial fibrillation or flutter (32%), and chronic lung disease (23%). The majority of patients had NYHA class III heart failure symptoms (83%), 67% had LBBB, and 55% had a QRS duration of 150 ms or greater. Among patients without LBBB, 29% had a nonspecific intraventricular conduction delay, 29% had right bundle-branch block, 20% had normal conduction, 10% had right bundle-branch block with left anterior or posterior fascicular block, 6% were paced, and 6% had either left anterior or posterior fascicular block alone.

Mortality rates in the primary overall study cohort were 0.8% at 30 days, 9.2% at 1 year, and 25.9% at 3 years. Rates of all-cause readmission were 10.2% at 30 days and 43.3% at 1 year. Rates of heart failure readmission were 2.2% at 30 days and

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Table 1. Baseline Characteristics of the Study Population

Characteristic	No. (%)					P Value[a]
		LBBB		No LBBB		
	All Patients (N = 24 169)	QRS ≥150 ms (n = 9889)	QRS 120-149 ms (n = 6259	QRS ≥150 ms (n = 3306)	QRS 120-149 ms (n = 4715)	
Age, mean (SD), y	74.9 (6.1)	74.8 (6.0)	75.0 (6.0)	75.3 (6.1)	74.7 (6.1)	<.001
Men	16 496 (68.3)	6171 (62.4)	3881 (62.0)	2733 (82.7)	3711 (78.7)	<.001
Race						
Black	1608 (6.7)	632 (6.4)	419 (6.7)	206 (6.2)	351 (7.4)	.24
White	21 743 (90.0)	8935 (90.4)	5625 (89.9)	2980 (90.1)	4203 (89.1)	
Other/unknown	818 (3.4)	322 (3.3)	215 (3.4)	120 (3.6)	161 (3.4)	
Medical history						
Atrial fibrillation	7607 (31.5)	2559 (25.9)	1996 (31.9)	1280 (38.7)	1772 (37.6)	<.001
Cerebrovascular disease	3557 (14.7)	1316 (13.3)	923 (14.7)	515 (15.6)	803 (17.0)	<.001
Chronic lung disease	5609 (23.2)	2119 (21.4)	1478 (23.6)	788 (23.8)	1224 (26.0)	<.001
CABG surgery						
No	14 722 (60.9)	6707 (67.8)	3909 (62.5)	1730 (52.3)	2376 (50.4)	<.001
≤3 mo	101 (0.4)	43 (0.4)	25 (0.4)	17 (0.5)	16 (0.3)	
>3 mo	9346 (38.7)	3139 (31.7)	2325 (37.1)	1559 (47.2)	2323 (49.3)	
Diabetes mellitus	9102 (37.7)	3594 (36.3)	2277 (36.4)	1313 (39.7)	1918 (40.7)	<.001
Heart failure duration						
3 mo	2596 (10.7)	985 (10.0)	663 (10.6)	383 (11.6)	565 (12.0)	<.001
>3 to 9 mo	3654 (15.1)	1543 (15.6)	981 (15.7)	447 (13.5)	683 (14.5)	
>9 mo	17 919 (74.1)	7361 (74.4)	4615 (73.7)	2476 (74.9)	3467 (73.5)	
Heart failure hospitalization	12 250 (50.7)	4911 (49.7)	3356 (53.6)	1618 (48.9)	2365 (50.2)	<.001
Hypertension	18 864 (78.1)	7665 (77.5)	4888 (78.1)	2602 (78.7)	3709 (78.7)	.31
Ischemic heart disease	15 739 (65.1)	5691 (57.5)	3993 (63.8)	2458 (74.3)	3597 (76.3)	<.001
Nonischemic dilated cardiomyopathy	8859 (36.7)	4464 (45.1)	2408 (38.5)	845 (25.6)	1142 (24.2)	<.001
Percutaneous coronary intervention						
No	16 698 (69.1)	7140 (72.2)	4383 (70.0)	2193 (66.3)	2982 (63.2)	<.001
≤3 mo	929 (3.8)	344 (3.5)	236 (3.8)	109 (3.3)	240 (5.1)	
>3 mo	6542 (27.1)	2405 (24.3)	1640 (26.2)	1004 (30.4)	1493 (31.7)	
Previous myocardial infarction[b]						
No	12 095 (50.0)	5619 (56.8)	3220 (51.4)	1410 (42.6)	1846 (39.2)	<.001
≤40 d, or ≤40 d and >40 d	1098 (4.5)	376 (3.8)	291 (4.6)	180 (5.4)	251 (5.3)	
>40 d	10 976 (45.4)	3894 (39.4)	2748 (43.9)	1716 (51.9)	2618 (55.5)	<.001
Renal failure with dialysis	693 (2.9)	239 (2.4)	182 (2.9)	125 (3.8)	147 (3.1)	<.001
Syncope	2123 (8.8)	843 (8.5)	567 (9.1)	295 (8.9)	418 (8.9)	.67
Ventricular tachycardia						
No	20 505 (84.8)	8597 (86.9)	5276 (84.3)	2752 (83.2)	3880 (82.3)	<.001
Not sustained	3371 (13.9)	1204 (12.2)	901 (14.4)	508 (15.4)	758 (16.1)	
Clinical measures						
Ejection fraction						
Mean (SD), %	24.6 (6.6)	24.0 (6.5)	24.7 (6.4)	25.1 (6.7)	25.4 (6.5)	<.001
Normal or slightly impaired (>40%)	102 (0.4)	30 (0.3)	28 (0.4)	21 (0.6)	23 (0.5)	
Moderately impaired (26%-40%)	9064 (37.5)	3356 (33.9)	2361 (37.7)	1323 (40.0)	2024 (42.9)	
Severely impaired (≤25%)	15 003 (62.1)	6503 (65.8)	3870 (61.8)	1962 (59.3)	2668 (56.6)	
NYHA class						
I	341 (1.4)	124 (1.3)	78 (1.2)	58 (1.8)	81 (1.7)	.004
II	2864 (11.8)	1166 (11.8)	717 (11.5)	432 (13.1)	549 (11.6)	
III	20 065 (83.0)	8261 (83.5)	5237 (83.7)	2670 (80.8)	3897 (82.7)	
IV	899 (3.7)	338 (3.4)	227 (3.6)	146 (4.4)	188 (4.0)	
Serum sodium, mean (SD), mEq/L	138.9 (3.4)	138.9 (3.5)	139.0 (3.3)	139.0 (3.4)	138.8 (3.6)	.11
Serum creatinine, mean (SD), mg/dL	1.4 (0.9)	1.3 (0.8)	1.4 (1.0)	1.5 (1.1)	1.4 (0.9)	<.001
Systolic blood pressure, mean (SD), mm Hg	133.2 (22.4)	133.9 (22.2)	133.1 (22.3)	132.1 (22.5)	132.9 (22.7)	<.001
Blood urea nitrogen, mean (SD), mg/dL	26.4 (13.7)	26.2 (13.4)	25.9 (13.6)	27.9 (14.8)	26.5 (13.7)	<.001

(continued)

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Table 1. Baseline Characteristics of the Study Population (continued)

Characteristic	No. (%)					P Value[a]
		LBBB		No LBBB		
	All Patients (N = 24 169)	QRS ≥150 ms (n = 9889)	QRS 120-149 ms (n = 6259	QRS ≥150 ms (n = 3306)	QRS 120-149 ms (n = 4715)	
Year of procedure						
2006	4978 (20.6)	2087 (21.1)	1312 (21.0)	683 (20.7)	896 (19.0)	.02
2007	6650 (27.5)	2696 (27.3)	1756 (28.1)	872 (26.4)	1326 (28.1)	
2008	6154 (25.5)	2482 (25.1)	1594 (25.5)	893 (27.0)	1185 (25.1)	
2009	6387 (26.4)	2624 (26.5)	1597 (25.5)	858 (26.0)	1308 (27.7)	
Length of stay, d						
Mean (SD)	1.7 (2.1)	1.6 (1.9)	1.7 (2.1)	1.7 (2.2)	1.8 (2.4)	.001
Median (IQR)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)	

Abbreviations: CABG, coronary artery bypass graft; IQR, interquartile range; LBBB, left bundle-branch block; NYHA, New York Heart Association.

SI conversion factors: To convert creatinine values to μmol/L, multiply by 88.4; blood urea nitrogen values to mmol/L, multiply by 0.357.

[a] For comparison across all categories.

[b] Categories include patients who have experienced multiple myocardial infarctions.

Table 2. Unadjusted Cumulative Incidence of Outcomes Among Patients Admitted for Implantation of a Cardiac Resynchronization Therapy Defibrillator

Outcome	No. of Patients (Cumulative Incidence)				P Value
	LBBB		No LBBB		
	QRS ≥150 ms (n = 9889)	QRS 120-149 ms (n = 6259)	QRS ≥150 ms (n = 3306)	QRS 120-149 ms (n = 4715)	
Mortality					
30 d	59 (0.6)	60 (1.0)[a]	33 (1.0)	42 (0.9)	.03
1 y	630 (6.5)	595 (9.7)[b]	385 (11.9)[b]	555 (12.0)[b]	<.001
3 y	1859 (20.9)	1511 (26.5)[b]	929 (30.7)[b]	1380 (32.3)[b]	<.001
All-cause readmission					
30 d	907 (9.2)	658 (10.5)[a]	364 (11.0)[a]	521 (11.1)[b]	<.001
1 y	3752 (38.6)	2760 (44.8)[b]	1489 (45.7)[b]	2301 (49.6)[b]	<.001
Cardiovascular readmission					
30 d	527 (5.3)	404 (6.5)[a]	221 (6.7)[a]	307 (6.5)[a]	.002
1 y	1927 (19.8)	1552 (25.1)[b]	873 (26.8)[b]	1372 (29.5)[b]	<.001
Heart failure readmission					
30 d	141 (1.4)	150 (2.4)[b]	97 (2.9)[b]	147 (3.1)[b]	<.001
1 y	845 (8.7)	794 (12.9)[b]	491 (15.1)[b]	793 (17.1)[b]	<.001
Complications at 30 d					
Pneumothorax or hemothorax	94 (1.0)	82 (1.3)	23 (0.7)	39 (0.8)	.01
Hematoma	181 (1.8)	122 (1.9)	57 (1.7)	107 (2.3)	.25
Cardiac tamponade	85 (0.9)	50 (0.8)	16 (0.5)	33 (0.7)	.17
Any of the above	346 (3.5)	244 (3.9)	96 (2.9)	171 (3.6)	.09
Complications at 90 d					
Infection	70 (0.7)	45 (0.7)	28 (0.9)	48 (1.0)	.21
Mechanical complications	243 (2.5)	151 (2.4)	55 (1.7)[a]	104 (2.2)	.06
Either of the above	308 (3.1)	193 (3.1)	82 (2.5)	152 (3.2)	.23
Complications at 3 y					
Infection	148 (1.6)	98 (1.7)	59 (1.9)	96 (2.1)	.09
Mechanical complications	385 (4.0)	241 (4.0)	89 (2.8)[a]	159 (3.5)	.007

Abbreviation: LBBB, left bundle-branch block.

[a] $P < .01$ for comparison with LBBB and QRS duration of 150 ms or greater.

[b] $P < .001$ for comparison with LBBB and QRS duration of 150 ms or greater.

12.3% at 1 year. Unadjusted rates of mortality and readmission at each time point stratified by QRS duration and LBBB category are presented in **Table 2**. By 1 year, unadjusted rates of all outcomes were significantly lower among patients with LBBB and QRS duration of 150 ms or greater. The 1-year cumulative incidence of mortality and readmission among patients admitted for CRT-D implantation was lowest among those with LBBB and QRS duration of 150 ms or greater (6.5% for mortality, 38.6% for readmission), followed by patients with LBBB and QRS duration of 120 to 149 ms (9.7%, 44.8%), pa-

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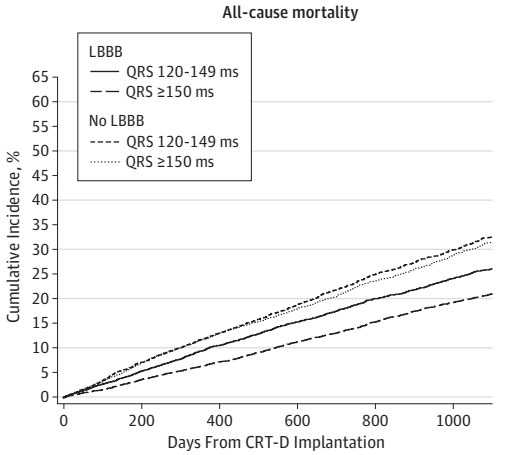
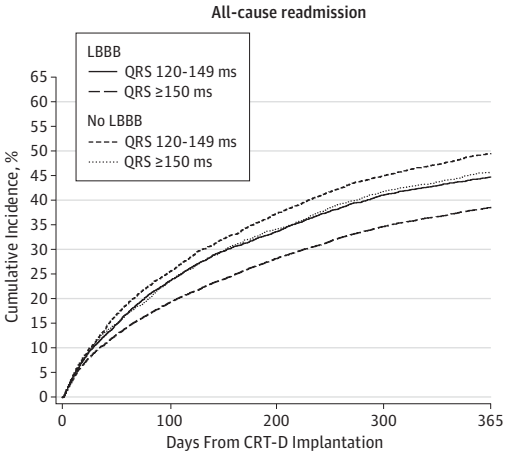
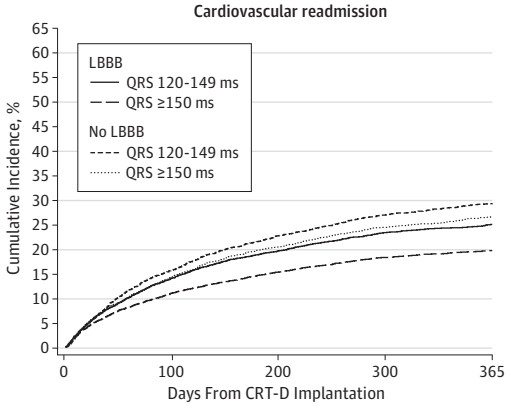
Figure. Cumulative Incidence of All-Cause Mortality, All-Cause Readmission, Cardiovascular Readmission, and Heart Failure Readmission Among Patients Admitted for Implantation of Cardiac Resynchronization Therapy Defibrillator



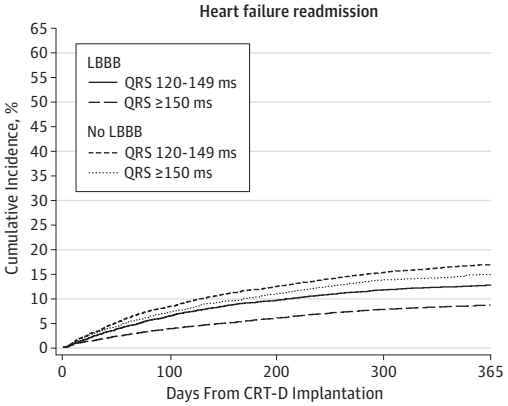
No. at risk						
LBBB						
QRS 120-149 ms	6259	5780	5332	4962	4400	3486
QRS ≥150 ms	9889	9268	8726	8211	7332	5757
No LBBB						
QRS 120-149 ms	4715	4265	3889	3574	3118	2366
QRS ≥150 ms	3306	2998	2745	2531	2228	1729



No. at risk					
LBBB					
QRS 120-149 ms	6259	4688	3991	3475	3230
QRS ≥150 ms	9889	7837	6825	6108	5694
No LBBB					
QRS 120-149 ms	4715	3423	2820	2427	2203
QRS ≥150 ms	3306	2469	2082	1805	1659



No. at risk					
LBBB					
QRS 120-149 ms	6259	5219	4738	4380	4204
QRS ≥150 ms	9889	8581	7932	7474	7236
No LBBB					
QRS 120-149 ms	4715	3831	3375	3085	2930
QRS ≥150 ms	3306	2737	2442	2254	2147



No. at risk					
LBBB					
QRS 120-149 ms	6259	5667	5302	5018	4856
QRS ≥150 ms	9889	9262	8770	8383	8172
No LBBB					
QRS 120-149 ms	4715	4148	3796	3535	3398
QRS ≥150 ms	3306	2952	2711	2539	2453

CRT-D indicates cardiac resynchronization therapy defibrillator; LBBB, left bundle-branch block.

tients with no LBBB and QRS duration of 150 ms or greater (11.9%, 45.7%), and patients with no LBBB and QRS duration of 120 to 149 ms (12.0%, 49.6%) (**Figure**).

After adjustment for demographic and clinical factors, compared with patients with LBBB and QRS duration of 150 ms or greater, the other 3 groups had significantly higher risks of mortality and all-cause, cardiovascular, and heart failure readmission (Figure, **Table 3**). The adjusted risk of 3-year mortality was lowest among patients with LBBB and QRS duration of 150 ms or greater (20.9%), compared with LBBB and QRS duration of 120 to 149 ms (26.5%; hazard ratio [HR], 1.30 [99% CI, 1.18-1.42]), no LBBB and QRS duration of 150 ms or greater (30.7%; HR, 1.34 [99% CI, 1.20-1.49]), and no LBBB and QRS duration of 120 to 149 ms (32.3%; HR, 1.52 [99% CI, 1.38-1.67]). The adjusted risk of 1-year all-cause readmission were also lowest among patients with LBBB and QRS duration of 150 ms or greater (38.6%), compared with LBBB and QRS duration of 120 to 149 ms (44.8%; HR, 1.18 [99% CI, 1.10-1.26]), no LBBB and QRS duration of 150 ms or greater (45.7%; HR, 1.16 [99% CI, 1.08-1.26]), and no LBBB and QRS duration of 120 to 149 ms (49.6%; HR, 1.31 [99% CI, 1.23-1.40]). The only association observed between QRS duration and morphology and risk of complications was a greater risk of 3-year infection among those with no LBBB and QRS duration of 120 to 149 ms compared with those with LBBB and QRS duration of 150 ms or greater (HR, 1.40 [99% CI, 1.01-1.94]).

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Table 3. Unadjusted and Adjusted Associations Between Left Bundle-Branch Block or QRS Duration and Outcomes Among Patients Admitted for Implantation of a Cardiac Resynchronization Therapy Defibrillator

	HR (99% CI)						
	LBBB			No LBBB			
Outcome	QRS ≥150 ms (n = 9889)	QRS 120-149 ms (n = 6259)	*P* Value	QRS ≥150 ms (n = 3306)	*P* Value	QRS 120-149 ms (n = 4715)	*P* Value
Unadjusted Analysis							
Mortality at 3 y	1 [Reference]	1.33 (1.21-1.46)	<.001	1.59 (1.44-1.77)	<.001	1.68 (1.53-1.85)	<.001
All-cause readmission at 1 y	1 [Reference]	1.23 (1.15-1.31)	<.001	1.26 (1.17-1.36)	<.001	1.41 (1.32-1.50)	<.001
Cardiovascular readmission at 1 y	1 [Reference]	1.32 (1.21-1.44)	<.001	1.42 (1.28-1.57)	<.001	1.59 (1.45-1.75)	<.001
Heart failure readmission at 1 y	1 [Reference]	1.53 (1.35-1.74)	<.001	1.83 (1.59-2.10)	<.001	2.10 (1.84-2.39)	<.001
Complications within 30 d							
Pneumothorax or hemothorax	1 [Reference]	1.38 (0.94-2.02)	.03	0.73 (0.39-1.38)	.21	0.87 (0.53-1.43)	.47
Hematoma	1 [Reference]	1.07 (0.79-1.44)	.59	0.94 (0.65-1.37)	.68	1.24 (0.92-1.67)	.06
Cardiac tamponade	1 [Reference]	0.93 (0.60-1.44)	.67	0.56 (0.28-1.13)	.03	0.81 (0.49-1.36)	.30
Any of the above	1 [Reference]	1.12 (0.90-1.38)	.19	0.83 (0.61-1.12)	.11	1.04 (0.81-1.32)	.70
Complications within 90 d							
Infection	1 [Reference]	1.02 (0.64-1.62)	.92	1.20 (0.70-2.08)	.38	1.45 (0.90-2.34)	.05
Mechanical complications	1 [Reference]	0.98 (0.75-1.29)	.87	0.68 (0.45-1.01)	.01	0.90 (0.66-1.22)	.38
Any of the above	1 [Reference]	0.99 (0.78-1.26)	.93	0.80 (0.57-1.11)	.08	1.04 (0.80-1.35)	.71
Complications within 3 y							
Infection	1 [Reference]	1.07 (0.77-1.48)	.62	1.24 (0.83-1.85)	.17	1.42 (1.02-1.98)	.006
Mechanical complications	1 [Reference]	1.00 (0.81-1.24)	.99	0.70 (0.52-0.96)	.003	0.89 (0.69-1.14)	.22
Adjusted Analysis[a]							
Mortality at 3 y	1 [Reference]	1.30 (1.18-1.42)	<.001	1.34 (1.20-1.49)	<.001	1.52 (1.38-1.67)	<.001
All-cause readmission at 1 y	1 [Reference]	1.18 (1.10-1.26)	<.001	1.16 (1.08-1.26)	<.001	1.31 (1.23-1.40)	<.001
Cardiovascular readmission at 1 y	1 [Reference]	1.27 (1.17-1.38)	<.001	1.29 (1.17-1.44)	<.001	1.47 (1.34-1.62)	<.001
Heart failure readmission at 1 y	1 [Reference]	1.47 (1.30-1.67)	<.001	1.62 (1.40-1.87)	<.001	1.92 (1.68-2.20)	<.001
Complications within 30 d							
Pneumothorax or hemothorax	1 [Reference]	1.39 (0.95-2.03)	.02	0.99 (0.51-1.91)	.96	1.13 (0.67-1.89)	.55
Hematoma	1 [Reference]	1.02 (0.75-1.38)	.88	0.82 (0.56-1.21)	.19	1.10 (0.80-1.50)	.44
Cardiac tamponade	1 [Reference]	0.99 (0.64-1.54)	.98	0.91 (0.46-1.81)	.72	1.28 (0.74-2.21)	.25
Any of the above	1 [Reference]	1.11 (0.89-1.38)	.21	0.90 (0.66-1.23)	.40	1.12 (0.87-1.45)	.24
Complications within 90 d							
Infection	1 [Reference]	1.01 (0.63-1.61)	.96	1.25 (0.70-2.23)	.32	1.55 (0.95-2.53)	.02
Mechanical complications	1 [Reference]	0.99 (0.75-1.29)	.91	0.74 (0.49-1.10)	.05	0.96 (0.69-1.32)	.72
Any of the above	1 [Reference]	0.99 (0.78-1.26)	.93	0.86 (0.61-1.20)	.24	1.11 (0.85-1.45)	.33
Complications within 3 y							
Infection	1 [Reference]	1.05 (0.75-1.45)	.73	1.20 (0.79-1.81)	.25	1.40 (1.01-1.94)	.009
Mechanical complications	1 [Reference]	1.01 (0.81-1.26)	.92	0.78 (0.57-1.07)	.04	0.97 (0.75-1.25)	.75

Abbreviations: HR, hazard ratio; LBBB, left bundle-branch block.

[a] In multivariable analyses, each outcome was modeled as a function of QRS duration and LBBB category, age, sex, race, renal failure, hypertension, diabetes, atrial fibrillation, chronic lung disease, cerebrovascular disease, ischemic heart disease, prior myocardial infarction, prior coronary artery bypass graft surgery, prior percutaneous coronary intervention, congestive heart failure duration, history of syncope, history of ventricular tachycardia, prior congestive heart failure hospitalization, New York Heart Association class, ejection fraction, systolic blood pressure, serum sodium level, serum creatinine level, blood urea nitrogen level, year of procedure, quartile of annualized implanting clinician implantable cardioverter-defibrillator volume, and quartile of annualized site-level implantable cardioverter-defibrillator volume.

The adjusted pairwise comparisons of groups are presented in **Table 4**. Among patients with no LBBB, those with QRS duration of 120 to 149 ms had greater risks of mortality and readmission, compared with those with QRS duration of 150 ms or greater. Among patients with QRS duration of 120 to 149 ms, those without LBBB had greater risks of mortality and readmission compared with those with LBBB. No significant differences in outcomes were observed between patients with no LBBB and QRS duration of 150 ms or greater and patients with LBBB and QRS duration of 120 to 149 ms.

Patients admitted for a reason other than CRT-D implantation were older and had greater comorbidity than patients admitted for CRT-D implantation (eTable 1 [Supplement]). All outcomes, other than infection and mechanical complications, were more common among patients admitted for a reason other than CRT implantation (eTable 2 [Supplement]). De-

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Table 4. Adjusted Relationships Between Categories of QRS Duration and Left Bundle-Branch Block and Outcomes Among Patients Admitted for Implantation of a Cardiac Resynchronization Therapy Defibrillator[a]

	Pairwise Group Comparison					
	No LBBB and QRS Duration ≥150 ms vs LBBB and QRS Duration 120-149 ms		No LBBB and QRS Duration 120-149 ms vs No LBBB and QRS Duration ≥150 ms		No LBBB and QRS Duration 120-149 ms vs LBBB and QRS 120-149 ms	
Outcome	Adjusted HR (99% CI)	*P* Value	Adjusted HR (99% CI)	*P* Value	Adjusted HR (99% CI)	*P* Value
Mortality at 3 y	1.03 (0.93-1.15)	.46	1.14 (1.02-1.27)	.003	1.17 (1.06-1.30)	<.001
All-cause readmission at 1 y	0.99 (0.91-1.07)	.66	1.13 (1.03-1.23)	<.001	1.11 (1.03-1.20)	<.001
Cardiovascular readmission at 1 y	1.02 (0.91-1.14)	.67	1.14 (1.02-1.27)	.003	1.16 (1.05-1.28)	<.001
Heart failure readmission at 1 y	1.10 (0.95-1.27)	.10	1.19 (1.02-1.38)	.003	1.30 (1.14-1.50)	<.001
Mechanical complications at 1 y	0.77 (0.56-1.07)	.04	1.24 (0.88-1.76)	.11	0.96 (0.74-1.25)	.70

Abbreviations: HR, hazard ratio; LBBB, left bundle-branch block.

[a] In multivariable analyses, each outcome was modeled as a function of QRS duration and LBBB category, age, sex, race, renal failure, hypertension, diabetes, atrial fibrillation, chronic lung disease, cerebrovascular disease, ischemic heart disease, prior myocardial infarction, prior coronary artery bypass graft surgery, prior percutaneous coronary intervention, congestive heart failure duration, history of syncope, history of ventricular tachycardia, prior congestive heart failure hospitalization, New York Heart Association class, ejection fraction, systolic blood pressure, serum sodium level, serum creatinine level, blood urea nitrogen level, year of procedure, quartile of annualized provider-level implantable cardioverter-defibrillator volume, and quartile of annualized site-level implantable cardioverter-defibrillator volume.

spite these differences, the outcomes were consistent with the findings among patients admitted for CRT-D implantation; patients with LBBB and QRS duration of 150 ms or greater had the lowest incidence of all outcomes (eTable 3 and eFigure 2 [Supplement]). After adjustment, patients with no LBBB and QRS duration of 120 to 149 ms had the greatest risks of mortality and readmission (eTable 4 [Supplement]).

The proportionality assumption was met for the QRS duration and LBBB categorical variable in all models except 1-year cardiovascular readmission ($P < .01$). There was an increase over time in the hazard of cardiovascular readmission for patients with no LBBB and QRS duration of 120 to 140 ms, compared with patients with LBBB and QRS duration of 150 ms or greater (HR, 1.34 at 30 days and 1.63 at 1 year in the full cohort model).

Discussion

In a large population of fee-for-service Medicare beneficiaries who underwent CRT-D implantation in clinical practice, patients with LBBB and a QRS duration of 150 ms or greater had the lowest risks of mortality and all-cause, cardiovascular, and heart failure readmission. After adjustment, no statistically significant differences in outcomes were observed between patients with LBBB and QRS duration of 120 to 149 ms and those without LBBB and QRS duration of 150 ms or greater. Patients with no LBBB and QRS duration of 120 to 149 ms consistently had the greatest risks of adverse outcomes. The observed outcomes of patients with LBBB and a wide QRS duration are particularly notable, given that both LBBB and prolonged QRS duration have been shown to be independent predictors of mortality among patients with left ventricular systolic dysfunction without CRT.[8,9] Because CRT addresses dyssynchrony, it is not surprising that LBBB and wide QRS duration in CRT recipients were associated with a lower risk of mortality.

Although prior data regarding the effects of CRT as a function of QRS duration are largely limited to meta-analyses of clinical trials, this study provides an important perspective on the role of QRS duration in outcomes after CRT implantation in clinical practice. Although all of the clinical trials demonstrating the efficacy of CRT included patients with QRS duration of 120 ms or greater, the mean QRS duration in these trials ranged widely, from 155 to 209 ms.[10] Subgroup analyses in several trials suggested better outcomes among patients with a wider QRS duration, but small numbers may have resulted in insufficient power to identify statistically significant interactions.[11-13] Although the majority of patients in the present analysis had NYHA class III heart failure symptoms, the results are also consistent with clinical trials including asymptomatic and mildly symptomatic patients that demonstrated the efficacy of CRT in patients with a QRS duration greater than 150 ms.[14-16] We found that patients with a QRS duration of 120 to 149 ms and LBBB had greater benefit than those with a QRS duration of 120 to 149 ms without LBBB. This finding highlights the combined importance of QRS duration and morphology.

The majority of patients enrolled in the clinical trials of CRT had LBBB, which limits the capacity to understand outcomes after CRT in this population. Single-center observational studies have generally found that patients with LBBB experienced greater improvements in symptoms and echocardiographic findings with CRT, but these studies were inconclusive with regard to long-term survival.[17-19] A large observational study found that right bundle-branch block was associated with higher mortality among Medicare beneficiaries receiving CRT in clinical practice; however, this study did not incorporate QRS duration, which is also central to current guideline recommendations for CRT, nor did it characterize the risks of hospitalization, an important end point in randomized trials of CRT.[20] Moreover, subgroup analysis of the MADIT-CRT (Multicenter Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy) trial found no better outcomes of CRT among mildly symptomatic or asymptomatic patients without LBBB. We observed that patients with LBBB and longer QRS duration fared best among those undergoing CRT-D implantation in clinical practice. We also found that, among patients un-

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dergoing CRT-D implantation and with QRS duration of 120 to 149 ms, there was significantly lower mortality and lower rates of readmission among patients with LBBB than among patients without LBBB. Our real-world data add to the increasing body of evidence that patients with LBBB have better outcomes after CRT.

The American College of Cardiology/American Heart Association/Heart Rhythm Society Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities, recently updated based on new clinical trials and additional analyses from previous clinical trials, emphasize the importance of QRS duration and morphology on patient selection for CRT therapy.[21] The revised class I recommendation for CRT is for patients with NYHA class II-IV symptoms, LBBB, and QRS duration of 150 ms or greater. Class IIa recommendations include CRT in patients with NYHA class II-IV symptoms and either LBBB and QRS duration of 120 to 149 ms or no LBBB and QRS duration of 150 ms or greater. The use of CRT in patients with no LBBB and QRS duration of 120 to 149 ms and NYHA class III or IV symptoms is a class IIb recommendation. These guidelines, based on data from clinical trials, have important implications for the selection of the most appropriate patients for CRT in clinical practice. Our findings in this large cohort of patients receiving CRT-D in clinical practice are concordant with the guidelines, which provide stronger recommendations for patients with LBBB compared with those without and for patients with more prolonged QRS duration.

Notably, however, our study does not include a control group of patients who did not undergo CRT to assess the comparative effectiveness of CRT. Therefore, our results should not lead to conclusions regarding the benefit of CRT, or the lack thereof, in patients with QRS duration of 120 to 149 ms and without LBBB. Our findings support the conclusion that the benefits of CRT are likely greater among patients with wider QRS duration and LBBB. However, the findings that patients with LBBB and QRS duration of 150 ms or greater had the best outcomes after accounting for differences in other measured patient characteristics are concordant with current guideline recommendation classifications.

Other issues should be considered in the interpretation of these findings. First, this was an observational study, and observed differences in outcomes among the groups categorized by QRS duration and LBBB may have resulted from residual and unmeasured confounding. However, we were able to adjust for a number of robust baseline demographic and clinical characteristics. Some potential confounders, such as echocardiographic data, lead location, and follow-up strategies, were not available. Second, findings depend on the quality and accuracy of medical record documentation and chart abstraction. However, the ICD Registry has a robust data quality program that enhances data fidelity.[4] Third, the study population consisted of fee-for-service Medicare beneficiaries. Whether the findings would be similar or different in other populations requires further study. Last, we were unable to determine outcomes among patients receiving CRT pacing alone (without defibrillator function) because these patients were not included.

In conclusion, in a population of fee-for-service Medicare beneficiaries undergoing CRT-D implantation in routine clinical practice, LBBB and QRS duration of 150 ms or greater, compared with LBBB and QRS duration less than 150 ms or no LBBB regardless of QRS duration, was associated with lower risk of all-cause mortality and of all-cause, cardiovascular, and heart failure readmissions. These findings support the use of QRS morphology and duration to help identify patients who will have the greatest benefit from CRT-D implantation.

ARTICLE INFORMATION

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