

Race and Sex Differences in QRS Interval and Associated Outcome Among Patients with Left Ventricular Systolic Dysfunction

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Background—Prolonged QRS duration is associated with increased mortality among heart failure patients, but race or sex differences in QRS duration and associated effect on outcomes are unknown.

Methods and Results—We investigated QRS duration and morphology among 2463 black and white patients with heart failure and left ventricular ejection fraction $\leq 35\%$ who underwent coronary angiography and 12-lead electrocardiography at Duke University Hospital from 1995 through 2011. We used multivariable Cox regression models to assess the relationship between QRS duration and all-cause mortality and investigate race-QRS and sex-QRS duration interaction. Median QRS duration was 105 ms (interquartile range [IQR], 92–132) with variation by race and sex ($P < 0.001$). QRS duration was longest in white men (111 ms; IQR, 98–139) followed by white women (108 ms; IQR, 92–140), black men (100 ms; IQR, 91–120), and black women (94 ms; IQR, 86–118). Left bundle branch block was more common in women than men (24% vs 14%) and in white (21%) versus black individuals (12%). In black patients, there was a 16% increase in risk of mortality for every 10 ms increase in QRS duration up to 112 ms (hazard ratio, 1.16; 95% CI, 1.07, 1.25) that was not present among white patients (interaction, $P = 0.06$).

Conclusions—Black individuals with heart failure had a shorter QRS duration and more often had non-left bundle branch block morphology than white patients. Women had left bundle branch block more commonly than men. Among black patients, modest QRS prolongation was associated with increased mortality. (*J Am Heart Assoc.* 2017;6:e004381. DOI: 10.1161/JAHA.116.004381.)

Key Words: heart failure • mortality • QRS • race • sex

Prolonged QRS duration (>120 ms) may be associated with an increased risk of sudden cardiac death and all-cause mortality.^{1,2} More than 20% of individuals with reduced left ventricular ejection fraction (LVEF) have a QRS duration ≥ 120 ms.^{2,3} QRS duration is longer in healthy men than women^{4–6} and longer in healthy white individuals than black.^{5,7,8} However, among patients with reduced LVEF, less is known about race and sex differences in QRS duration and morphology and associated outcomes.²

Cardiac resynchronization therapy (CRT) has been shown to improve functional status, decrease hospitalizations, and improve survival in appropriately selected patients with heart failure (HF).^{9,10} Predictors of a favorable response to CRT include female sex, nonischemic etiology of systolic HF, left bundle branch block (LBBB) morphology, and prolonged QRS duration.¹¹ However, CRT is underutilized in the overall HF population,^{12,13} and black individuals are less likely to have CRT devices implanted than their white counterparts, despite being disproportionately affected by HF and having a higher prevalence of some factors predicting a favorable CRT response.^{12,14,15} Although black women are more likely than black men to have CRT devices implanted, the data are conflicting as to whether women overall have an equal likelihood of receiving a CRT device as their male counterparts.^{12,16} Whether race and sex differences in CRT are attributable, in part, to differences in QRS duration and morphology is currently not well understood.

The purpose of this study is to assess race and sex differences in QRS duration and morphology among patients with reduced LVEF and investigate the association of QRS duration with mortality as a function of race and sex.

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Methods

Data Sources

Data for this analysis were abstracted and merged from 3 sources: the Duke Databank for Cardiovascular Disease (DDCD), Duke Heart Station, and Duke Echocardiography Database. The DDCCD and its data elements have been previously described.¹⁷ Briefly, the DDCCD is a single-center database established in the 1960s that collects clinical characteristics of all patients who undergo cardiac catheterization at Duke University Medical Center (DUMC; Durham, NC) and continues to follow these patients for assessment of outcomes. The Duke Heart Station and Duke Echocardiography Database store electrocardiogram (ECG) and echocardiogram (echo) variables, respectively, on each patient who has an ECG or echo at DUMC. The Duke University Hospital Internal Review Board approved use of these data for the purposes of this study and waived the requirement for informed consent.

Patient Population

We examined 92 135 cardiac catheterization procedures that occurred at the DUMC between January 1, 1995 and December 31, 2011. Index catheterization was determined by taking the earliest qualifying catheterization for a given

patient. The 12-lead ECG data include computer-generated measurements of the relevant electrocardiographic intervals (PR, QRS, QT, and RR) as analyzed using Philips TraceMaster ECG software (Andover, MA).^{4,18,19} We included ECGs within 1 month of the index cardiac catheterization, and, in the case of multiple ECGs, we selected the one closest to the index procedure. LVEF was determined primarily from Duke Echocardiography Database quantification. In the case where LVEF was not available at the time of the index catheterization, LVEF data were obtained from the closest source within 3 months preceding and 1 month following the index catheterization. The sources of additional LVEF data included nuclear imaging, magnetic resonance imaging, or left ventriculography. Patients without LVEF assessment or QRS interval documentation were excluded.

Only patients with LVEF $\leq 35\%$ were included in the analysis. Patients were excluded for missing data on race, key baseline characteristics, myocardial infarction (MI) within 30 days preceding the index catheterization, or revascularization within the previous 3 months. Patients with ventricular pacing, an uninterpretable ECG, and those taking flecainide or propafenone were excluded. To exclude potentially erroneous QRS estimates, ECGs with QRS interval missing or considered to be outside the range of feasible physiological values >200 ms were excluded (Figure 1). Our

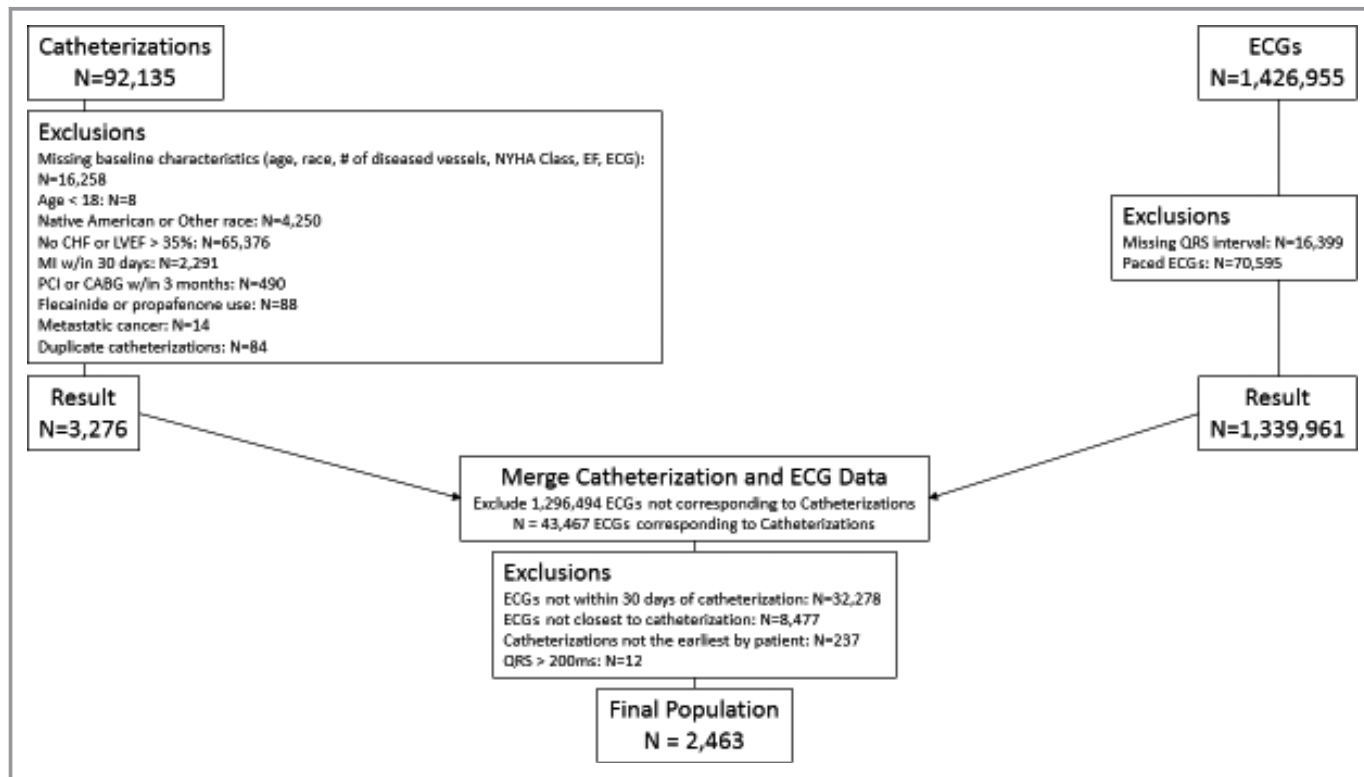


Figure 1. Flow diagram for final study population. CABG indicates coronary artery bypass graft; CHF, congestive heart failure; ECG, electrocardiogram; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

analysis population consisted of 2463 patients. Patient-reported race was classified at the time of data collection as black or white. Patients with racial classifications other than black or white were excluded. We repeated the primary analysis among patients who met all the primary exclusion criteria with the addition of those patients who had ventricular pacing in order to account for the subset of patients with CRT (N=2678).

Outcomes

We examined the distribution of QRS duration, the prevalence of LBBB, right bundle branch block (RBBB), and intraventricular conduction delay (IVCD), and the association between QRS duration and all-cause mortality by race and sex. Sensitivity analyses were performed including patients with paced rhythms, in order to assess the distribution of QRS duration and morphology and the association between

Table 1. Baseline Characteristics by Race and Sex

Characteristics	Black			White		
	Overall (N=932)	Male (N=542)	Female (N=390)	Overall (N=1531)	Male (N=1073)	Female (N=458)
Age, y	56 (47, 66)	55 (47, 64)	58 (47, 69)	65 (56, 73)	64 (55, 73)	66 (57, 75)
Medical history						
Hypertension	77.0	75.5	79.2	64.9	66.5	61.1
Diabetes mellitus	33.4	27.7	41.3	31.8	32.6	29.9
Hyperlipidemia	37.9	38.0	37.7	51.8	55.1	44.1
Atrial fibrillation	4.2	6.1	1.5	11.7	13.1	8.3
Ejection fraction	23 (16, 30)	20 (15, 30)	25 (20, 30)	25 (20, 30)	25 (20, 30)	25 (20, 30)
NYHA class						
I	4.4	4.8	3.8	6.3	6.0	7.2
II	21.0	23.1	18.2	22.8	23.7	20.7
III	39.6	37.6	42.3	42.9	43.5	41.5
IV	35.0	34.5	35.6	28.0	26.8	30.6
Ischemic heart disease						
MI	15.8	16.6	14.6	31.2	35.6	21.0
PCI	9.7	10.9	7.9	18.2	19.7	14.6
CABG	10.5	12.9	7.2	30.7	35.5	19.4
PVD	7.2	6.6	7.9	11.4	12.2	9.6
Cerebrovascular disease	9.7	7.7	12.3	13.6	14.4	11.8
COPD	6.2	7.6	4.4	10.0	10.6	8.5
Systolic blood pressure	135 (119, 151)	133 (118, 149)	138 (121, 155)	130 (114, 146)	129 (114, 144)	131 (115, 150)
DBP	83 (72, 94)	84 (73, 96)	81 (70, 93)	76 (66, 86)	77 (68, 87)	73 (64, 82)
Heart rate	81 (70, 94)	81 (69, 93)	83 (71, 96)	80 (68, 94)	79 (67, 92)	84 (72, 98)
BMI	28.7 (24.1, 34.3)	28.1 (24.0, 33.3)	29.4 (24.2, 35.6)	27.4 (23.9, 31.6)	27.7 (24.5, 31.7)	26.2 (22.4, 31.2)
GFR	71.2 (52.2, 88.7)	74.5 (55.2, 90.3)	68.2 (48.1, 86.1)	64.9 (48.8, 81.8)	66.2 (50.1, 83.2)	62.6 (45.6, 78.6)
Valvular heart disease	17.1	14.0	21.3	21.1	18.8	26.4
Left ventricular hypertrophy	57.7	63.2	50.3	44.8	47.7	38.3
Medications						
Beta-blockers	80.2	82.8	76.4	77.7	78.0	76.9
ACE-I	82.9	84.5	80.8	77.6	78.0	76.6
ARB	15.3	15.5	15.1	18.6	17.1	22.3
ICD placement during follow-up	28.2	30.1	25.6	28.2	30.6	22.7

All values are reported as median (interquartile range) or percent. ACE-I indicates angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; GFR, glomerular filtration rate; ICD, implantable cardioverter defibrillator; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease.

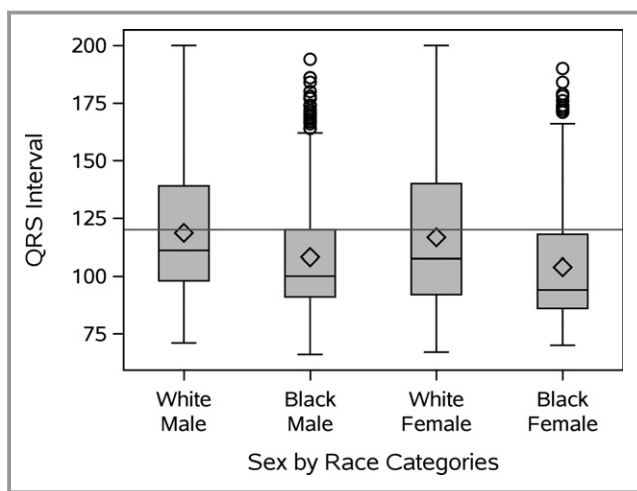


Figure 2. Box plots of QRS interval by race and sex. The horizontal line marks a QRS duration of 120 ms. In the figure, diamonds indicate the mean QRS, horizontal lines within the box indicates the median. The box extends from the 25th to the 75th percentile, and the vertical whiskers extend to the minimum and maximum values, or to the 75th percentile plus 1.5 times the distance between the 75th and 25th percentile. Open circles indicate individual data values beyond the whiskers.

QRS duration and mortality by race. Follow-up data were obtained by self-administered questionnaires and telephone contact at 6 months post-index catheterization and every year thereafter on the anniversary of the initial presentation. The National Death Index was used to determine vital status for nonresponders.^{20–22} Eighty-six percent of patients had complete follow-up for at least 1.6 years, and median follow-up for those who survived was 6.3 years.

Statistical Analysis

We identified baseline characteristics of study subjects in each of 4 race-sex groups (black men, white men, black women, and white women). Median, 25th, and 75th percentiles (interquartile range; IQR) were reported for continuous variables and percentages were reported for categorical variables. We used a Kruskal–Wallis test to compare the distribution of the QRS duration across the 4 race-sex groups. We then assessed differences in the QRS duration distribution between pair-wise comparisons for each of the 4 race-sex groups using Wilcoxon rank-sum tests. We also identified the distribution of black and white subjects in 3 clinically relevant QRS duration distributions: QRS <120 ms, QRS 120 to 149 ms, and QRS ≥150 ms.²

We used multivariable Cox regression modeling to assess the relationship between the QRS duration and the time from index catheterization to all-cause mortality. One analysis of the relationship used the QRS duration as a continuous variable and another used QRS prolongation as a categorical variable. QRS prolongation was defined as QRS interval >120 ms, given that previous studies have demonstrated worse outcomes in HF patients with QRS ≥120 ms.^{23–26} Covariates were prespecified based on a minimum of 10 events per variable. Based on previous research, as well as statistical and clinical judgment, the model was adjusted for age at catheterization, baseline glomerular filtrate rate (GFR), New York Heart Association (NYHA) class, LVEF, Duke coronary artery severity index,^{25,27} heart rate, diabetes mellitus, peripheral vascular disease (PVD), chronic obstructive lung disease, coronary artery bypass grafting (CABG),

Table 2. Distribution of QRS Duration and Morphology in Primary Cohort

Characteristics	Black			White			P Value*
	Overall (N=932)	Male (N=542)	Female (N=390)	Overall (N=1531)	Male (N=1073)	Female (N=458)	
QRS interval, ms							
Median (Q1, Q3)	98.0 (88.0, 119.5)	100.0 (91.0, 120.0)	94.0 (86.0, 118.0)	111.0 (97.0, 139.0)	111.0 (98.0, 139.0)	107.5 (92.0, 140.0)	<0.001
QRS morphology (%)							
LBBB	115 (12.3)	50 (9.2)	65 (16.7)	319 (20.8)	177 (16.5)	142 (31.0)	0.012
RBBB	14 (1.5)	13 (2.4)	1 (0.3)	48 (3.1)	42 (3.9)	6 (1.3)	0.002
IVCD	128 (13.7)	94 (17.3)	34 (8.7)	284 (18.5)	231 (21.5)	53 (11.6)	<0.001
QRS category, ms (%)							
<120	699 (75.0)	403 (74.4)	296 (75.9)	906 (59.2)	644 (60.0)	262 (57.2)	
120 to 149	142 (15.2)	83 (15.3)	59 (15.1)	370 (24.2)	253 (23.6)	117 (25.6)	
≥150	91 (9.8)	56 (10.3)	35 (9.0)	255 (16.7)	176 (16.4)	79 (17.3)	

*Comparison between races. RBBB indicates right bundle branch block; IVCD, intraventricular conduction delay; LBBB, left bundle branch block.

Table 3. Distribution of QRS Duration and Morphology Including Patients With Paced Rhythms

Characteristics	Black			White			P Value*
	Overall (N=970)	Male (N=563)	Female (N=407)	Overall (N=1708)	Male (N=1216)	Female (N=492)	
QRS interval, ms							
Median (Q1, Q3)	99.0 (89.0, 123.0)	101.0 (91.0, 124.0)	94.0 (86.0, 122.0)	115.0 (98.0, 146.0)	116.0 (99.0, 146.0)	112.0 (94.5, 146.0)	<0.001
QRS category, ms (%)							
<120	702 (72.4)	401 (71.2)	301 (74.0)	916 (53.6)	652 (53.6)	264 (53.7)	
120 to 149	150 (15.5)	88 (15.6)	62 (15.2)	406 (23.8)	284 (23.4)	122 (24.8)	
≥150	118 (12.2)	74 (13.1)	44 (10.8)	386 (22.6)	280 (23.0)	106 (21.5)	

*Comparison between races.

diastolic blood pressure (DBP), year of ECG, and body mass index (BMI).

As part of the multivariable Cox regression modeling process, linearity assumptions for the model were checked by examining the results of cubic polynomial spline plots of the log hazard ratio (HR) of a death against the continuous QRS duration and each of the continuous or categorical adjustment variables.²⁸ Transformations were then determined for each of the adjustment variables that had a significant nonlinear relationship.

Multivariable Cox regression modeling was also used to determine whether the relationship between QRS duration and all-cause mortality depended on race or sex. Given the lack of significance of interaction between the QRS interval with sex, we did not further explore differences in the relationship between QRS interval and mortality by sex.

Kaplan–Meier plots were created for all-cause mortality stratified by race and prolonged QRS duration to illustrate the difference in event rates across these strata. We also created adjusted spline curves of the predicted 3-year risk of mortality across the QRS duration for the overall population and for each race.

All statistical tests were 2-sided, and a *P* value of <0.05 was considered statistically significant. Statistical analyses were conducted at the Duke Clinical Research Institute using SAS software (version 9.4; SAS Institute Inc., Cary, NC). The authors had full access to the data in the study and take responsibility for the data analysis and its integrity.

Table 4. Association Between QRS Duration and Mortality

	Overall (N=2463)	Black (N=932)	White (N=1531)
Mortality association with continuous QRS duration, HR (95% CI)	1.10 (1.04, 1.15)	1.16 (1.07, 1.25)	1.05 (0.98, 1.12)
Mortality association with prolonged QRS duration, HR (95% CI)	1.08 (0.96, 1.22)	1.25 (1.01, 1.54)	1.02 (0.88, 1.17)

Association between 10-ms increments in QRS duration up to 112 ms and mortality. Hazard ratio (HR) estimates are adjusted for age at catheterization, baseline glomerular filtrate rate, New York Heart Association class, left ventricular ejection fraction, Duke coronary artery severity index,²⁷ heart rate, diabetes mellitus, peripheral vascular disease, chronic obstructive lung disease, coronary artery bypass grafting, diastolic blood pressure, year of electrocardiogram, and body mass index.

Results

Baseline Patient Characteristics

Table 1 summarizes baseline characteristics across race and sex groups. Median age varied across groups with black individuals younger; black men 55 (interquartile range [IQR], 47–64), white men 64 (IQR, 55–73), black women 58 (IQR, 47–69), and white women 66 (IQR, 57–75). Black patients had more hypertension (77.0% vs 64.9%) and left ventricular hypertrophy (57.7% vs 44.8%) than white patients. Relative to black patients, white patients had a higher incidence of previous MI (31.2% vs 15.8%), percutaneous coronary intervention (PCI; 18.2% vs 9.7%), and coronary artery bypass grafting (CABG; 30.7% vs 10.5%). Black (25.6%) and white women (22.7%) were less likely to have an implantable cardioverter defibrillator (ICD) than black (30.1%) and white men (30.6%).

Differences in QRS Duration and Morphology by Race and Sex

Median QRS duration was 105 ms (IQR, 92–132), and the distribution of the QRS interval varied significantly by race and sex (*P*<0.001). The median QRS interval was shortest among black females (94.0 ms) followed by black males (100.0 ms), white females (107.5 ms), and white males (111.0 ms; Figure 2; Table 2). The distribution of QRS interval was similar when including patients with paced rhythms (Table 3). Comparisons between each group demonstrated distributional

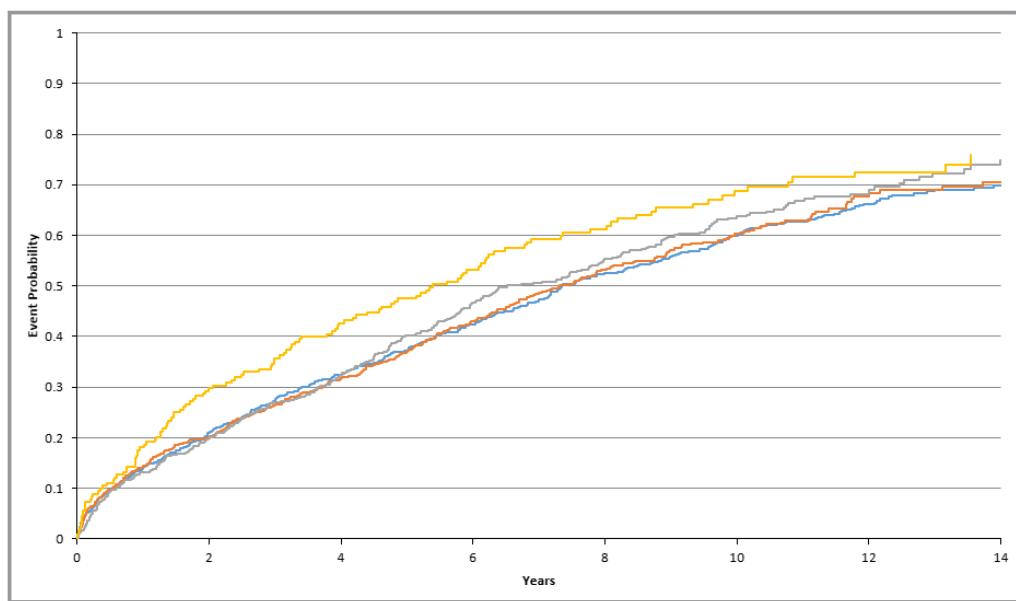


Figure 3. Adjusted mortality rates by QRS variation and race. Yellow, black individuals QRS >120 ms; gray, black individuals QRS ≤120 ms; orange, white individuals QRS >120 ms; blue, white individuals QRS ≤120 ms. $P=0.003$. P -value represents comparison across the four subgroups.

differences in the QRS interval for each pair ($P<0.001$), with the exception of white males versus white females ($P=0.092$). Evaluation of QRS duration across clinical cutoffs of <120, 120 to 149, and ≥150 ms showed that black HF patients were less likely to have QRS prolongation at each interval (Table 2).

Interventricular conduction abnormalities were more common among white patients than black patients (Table 2). LBBB was present in 20.8% of white patients and 12.3% of black patients. Both white and black women were approximately twice as likely to have LBBB as their male counterparts. However, RBBB and nonspecific IVCD were more common in men than women.

Association Between QRS Duration and Mortality by Race and Sex

One hundred fifty patients (6.1%) were excluded from the mortality assessment because of missing data. Of the remaining 2313 patients, 1301 died during follow-up. Median follow-up of patients who survived throughout the analysis was 6.3 years for both black and white patients. The unadjusted Kaplan–Meier mortality rate for the overall population at 14 years was 74.7%. After adjustment, black patients with a QRS >120 ms had a 25% higher risk of mortality than black patients with a QRS <120 ms. White patients with a QRS >120 ms had a 2% higher risk of mortality than white patients with a QRS duration <120 ms (Table 4; Figure 3).

In the overall population, the relationship between QRS duration and mortality was nonlinear, in that the mortality risk

increased as the QRS duration increased until 112 ms. After 112 ms, the risk of mortality did not appear to change as the QRS duration increased. After adjusting for baseline covariates, every 10 ms increase in QRS duration below 112 ms was associated with a 10% increase in risk of mortality over the follow-up period (HR, 1.10; 95% CI, 1.04, 1.15; Table 4). There was a nonsignificant trend in race-based, but no sex-based, differences in the association between QRS duration and mortality. Accounting for the race-based differences, it was estimated that among black patients, a 10 ms increase in the QRS duration below 112 ms was associated with a 16% increase in risk of mortality (interaction of QRS <112 ms and race, $P=0.06$). The association between progressive QRS prolongation below 112 ms and mortality was not significant among white patients. When analyzing the black population in our cohort, increases in QRS duration were associated with higher 3-year predicted mortality rates. A similar trend in predicted mortality rates was not observed in white patients (Figure 4B and 4C).

As a sensitivity analysis, the association between QRS duration and mortality by race was tested in a population of patients that included paced rhythms. The results of this analysis did not differ significantly from the primary analysis (Table 5).

Discussion

There are 3 important findings in our study. First, QRS prolongation and LBBB morphology were less common

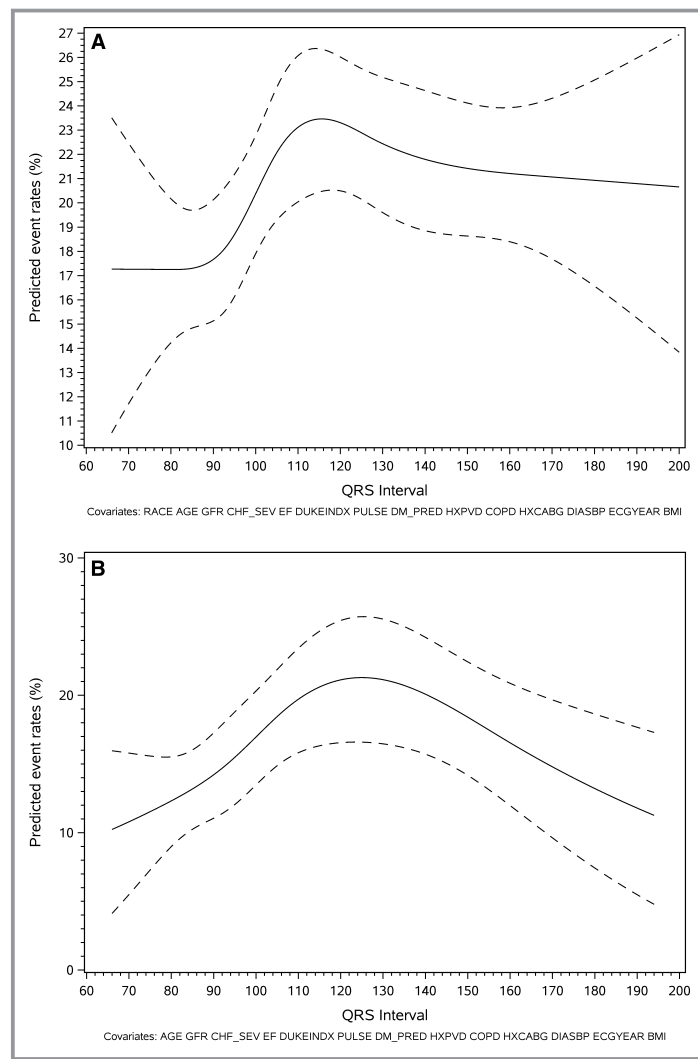


Figure 4. A, Adjusted expected 3-year mortality rates for the overall population by QRS interval. B, Adjusted expected 3-year mortality rates for the black population by QRS interval. C, Adjusted expected 3-year mortality rates for the white population by QRS interval. BMI indicates body mass index; CHF_SEV, congestive heart failure severity; COPD, chronic obstructive pulmonary disease; DIASBP, diastolic blood pressure; DM_PRED, diabetes mellitus and prediabetes; DUKEINDEX PULSE, Duke coronary artery severity index; ECGYEAR, year of electrocardiogram; EF, ejection fraction; GFR, glomerular filtration rate; HXCABG, history of coronary artery bypass graft; HXPVD, history of peripheral vascular disease.

among black HF patients than their white counterparts. Second, LBBB was more common among women than men independent of race. Finally, among black HF patients, modest QRS prolongation was associated with an increase in mortality after adjustment, whereas there was no significant association between QRS duration and mortality among white patients. Similarly, there were no significant sex differences in the relationship between QRS duration and mortality.

Differences in QRS Duration and Morphology by Race

Our analysis found that QRS prolongation, IVCD, and LBBB were more common among white patients than black patients with systolic HF. These findings are consistent with previous studies among patients with^{3,29} and without HF.^{5,7,8} One study with 936 black, white, and Hispanic patients demonstrated that black patients with HF were less likely to have a

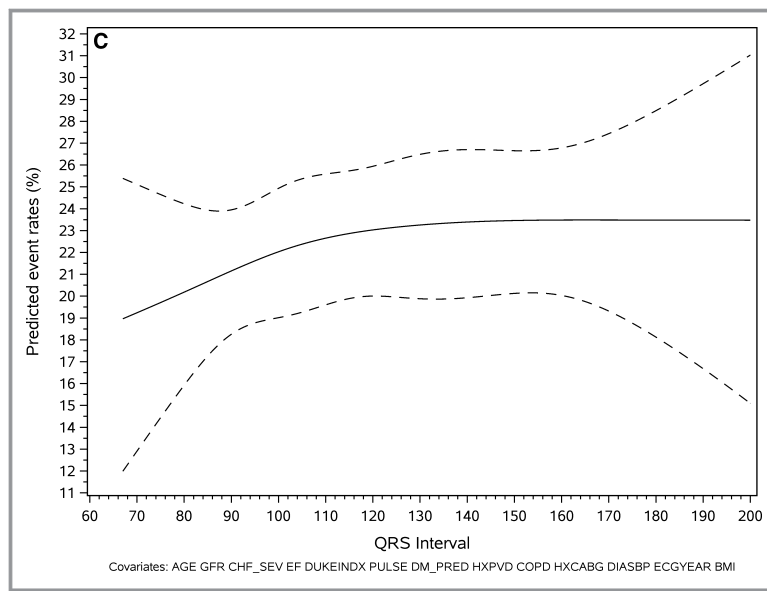


Figure 4. Continued

QRS >120 seconds (15.8% black, 26% white, and 25.3% Hispanic; $P=0.01$).³ Hebert et al also found that LBBB morphology was most common among Hispanic patients (14.3%) followed by white individuals (8.8%) and black individuals (5.8%; $P=0.002$). This study did not assess the association between QRS morphology and clinical outcomes. A retrospective analysis of the Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan (EVEREST) trial found that QRS prolongation in a cohort of hospitalized HF patients was more common among white patients than black patients ($P<0.01$).²⁹

Given that QRS duration >150 ms and LBBB morphology are important in determining the eligibility for implantation of CRT devices, differences in prevalence of conduction abnormality between races may partially explain the differences in use of CRT by race. Piccini et al found significantly lower odds of CRT use among black patients than white patients in the GWTG-HF registry; however, this analysis was limited by the inability to adjust for NYHA class, QRS duration, or morphology.¹² The failure of black HF patients to meet criteria for CRT implantation is not likely to completely explain the underutilization of CRT devices in black relative to white individuals. The following year, Farmer et al used the National Cardiovascular Data Registry (NCDR) to assess ICD and CRT defibrillator (CRT-D) use by race and found that eligible black patients had 26% lower odds of receiving CRT-D than white patients.¹⁴ The NCDR registry captures QRS duration, morphology, NYHA class, and duration of HF symptoms, thus increasing the likelihood that patients included in the analysis were eligible to receive CRT.

The presence of racial differences in QRS duration and morphology that are evident in both healthy subjects and

patients with systolic HF indicates that these differences may be, in part, determined through the interaction of genetic variants, comorbidities, and environmental exposures. Several studies have sought to identify genetic variants underlying these racial differences. Genome-wide association studies have identified an association between a nonsynonymous single-nucleotide polymorphism (SNP) of the *SCN10A* gene and prolonged QRS duration.³⁰ This gene encodes a voltage-gated sodium channel expressed in cardiac tissue. Similarly, the *SCN5A* gene encodes the most common voltage-gated sodium channel in the human heart. Investigators studied the *SCN5A* gene among 4558 black patients from Jackson, Mississippi, and found 4 SNPs associated with decreased QRS duration and 1 SNP associated with longer QRS duration.³¹ Jeff et al discovered similar findings using 455 patients in the Vanderbilt Genome-Electronic Records Project and Northwestern University NUgene Project.³² These studies support the concept that there may be a genetic component to QRS duration that varies by self-reported race. These findings warrant further investigation. Last, the higher prevalence of nonischemic etiology of systolic HF in black individuals may lend itself to lower scar burden and thus less interventricular electrical delay relative to their white counterparts, who exhibit a higher burden of ischemic etiology of systolic HF.

Differences in QRS Duration and Morphology by Race and Sex

Among healthy study participants, QRS duration is longer in men than in women.^{4–6} In our analysis, QRS prolongation was more common in black men than black women, but there was no difference between white men and women. Differences in

Table 5. Association Between QRS Duration and Mortality Including Patients With Paced Rhythms

	Overall (N=2678)	Black (N=970)	White (N=1708)
Mortality association with continuous QRS duration, HR (95% CI)	1.08 (1.03, 1.13)	1.15 (1.06, 1.24)	1.03 (0.97, 1.10)
Mortality association with prolonged QRS duration, HR (95% CI)	1.04 (0.93, 1.16)	1.22 (1.00, 1.49)	0.97 (0.85, 1.10)

Association between 10-ms increments in QRS duration up to 108 ms and mortality. Hazard ratio (HR) estimates are adjusted for age at catheterization, baseline glomerular filtrate rate, New York Heart Association class, left ventricular ejection fraction, Duke coronary artery severity index,²⁷ heart rate, diabetes mellitus, peripheral vascular disease, chronic obstructive lung disease, coronary artery bypass grafting, diastolic blood pressure, year of electrocardiogram, and body mass index.

QRS duration by both race and sex are infrequently reported. In one of the few analyses focused on this subject, Hebert et al found no differences in QRS duration between black men and black women or white men and white women, though the QRS duration was shorter in black individuals than white individuals.³ Additionally, this analysis found no differences in QRS duration between men and women. This cohort consisted of patients with reduced LVEF, although the small sample size limited the power to detect differences across subgroups. The inadequate reporting of QRS duration by race and sex along with the divergent findings of the available data suggest the need for more race- and sex-balanced inclusion to determine the true differences between populations.

Our study found that LBBB was more common for women than men of either race. This finding is consistent with an analysis of the Swedish Heart Failure Registry. Despite finding that QRS duration >120 ms was more common in men than women, Linde et al found that LBBB was more common in women (27%) than men (24%).¹³ LBBB carries both therapeutic and prognostic implications for HF patients, given that those with LVEF ≤35% and LBBB morphology meet either class I or IIa indications for CRT implantation depending on the degree of QRS prolongation.³³ A higher incidence of LBBB morphology was also identified in women enrolled in the SMART-AV trial³⁴ and other observational studies.³

Association Between QRS Duration and Mortality

Among black HF patients, we found an association between progressive QRS prolongation and mortality. However, this association was only present up to a QRS duration of 112 ms and was not present in white patients. Mentz et al analyzed a population of black study participants in Jackson, Mississippi, and found that QRS prolongation was associated with an increased risk of mortality across all spectrums of QRS duration.³⁵ Similarly, progressive QRS duration is typically associated with worse outcomes among HF patients.^{24,25,28} Conversely, an observational study of 3471 HF patients (56% black, 41% white, and 3% other) found that mortality was lowest in participants with QRS duration ≥150 ms compared with <120 or 120 to 149 ms.² Similarly, Linde et al found no difference in mortality among women with LBBB compared

with women whose QRS was <120 ms.¹³ These inconsistencies in the data highlight the complexity of the relationship between QRS duration and mortality.

Limitations

The results of this analysis may not be representative of the overall HF population, given that the cohort was identified by patients undergoing cardiac catheterization. However, this cohort is comparable with registry data of acute HF, where over 60% of patients have an ischemic etiology of disease.³⁶ We were unable to screen for ICD or CRT at the time of initial cardiac catheterization and could not reliably determine which patients received an implantable device after the index catheterization. Follow-up data on medication use was also limited and unreliable, and therefore, neither implantable device nor medication data were used in multivariable modeling. In order to assess the true association of QRS duration on mortality, we excluded patients with paced rhythms. This may have excluded patients with CRT devices that could have impacted mortality. We performed a sensitivity analysis including individuals with paced rhythms and RBBB and found similar results. This analysis is subject to the limitations of retrospective cohort studies. Although we used a multivariable model to adjust for potential confounders, residual measured and unmeasured confounding may impact our findings. Finally, over 65% of patients in this data set had a QRS duration <120 ms and 14% had a QRS duration ≥150 ms. It is possible that there is an association between QRS prolongation and mortality; however, because of low event rates among those with wide QRS, we may be underpowered to detect this difference.

Conclusions

In this cohort of HF patients with LVEF <35%, QRS prolongation and LBBB was more common among white patients than black patients and LBBB was more common among black and white women than their male counterparts. A higher prevalence of LBBB has important clinical implications among black and white female HF patients who may preferentially benefit from CRT

compared with men who have systolic HF. Finally, we found that QRS duration was not associated with mortality among white patients, but modest QRS prolongation was associated with increased mortality among black HF patients.

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Race and Sex Differences in QRS Interval and Associated Outcome Among Patients with Left Ventricular Systolic Dysfunction

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