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Cross-Sectional Relations of Electrocardiographic QRS Duration to Left Ventricular Dimensions

The Framingham Heart Study

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OBJECTIVES The goal of this study was to assess the relations of electrocardiographic QRS duration to left ventricular (LV) measurements in individuals without heart failure (HF) or prior myocardial infarction (MI).

BACKGROUND Increased electrocardiographic QRS duration (≥120 ms) is a marker of ventricular dyssynchrony.

METHODS We evaluated the relations of maximal electrocardiographic QRS duration to echocardiographic LV dimensions in 4,534 Framingham Heart study participants (mean age 54 years, 57% women) without prior HF or MI. QRS duration was analyzed as a continuous variable and as categories (<100, 100 to 119, and ≥120 ms).

RESULTS In linear regression models, LV mass, end-diastolic dimension, and septal and posterior wall thicknesses were positively related to log-QRS duration, whereas fractional shortening (FS) was inversely related ($p < 0.001$). There was a significant trend for increasing LV mass and dimensions, and decreasing FS across categories of QRS duration ($p < 0.001$). Left bundle branch block was associated with higher LV mass and lower FS compared with a normal QRS duration ($p < 0.001$).

CONCLUSIONS In our community-based sample of individuals free of HF and MI, increasing electrocardiographic QRS duration was positively related to LV mass and dimensions, and inversely associated with LV FS. Additional investigations are warranted to elucidate the mechanisms underlying the observed associations. (J Am Coll Cardiol 2005;45:685–9) © 2005 by the American College of Cardiology Foundation

A prolonged electrocardiographic QRS duration (≥120 ms) may be a marker of inter- or intraventricular mechanical dyssynchrony, and has been associated with adverse prognosis in systolic heart failure (HF) (1). Cardiac resynchronization therapy has been demonstrated to favorably influence clinical outcomes in systolic HF patients with QRS duration ≥150 ms (2). Others have reported associations of left bundle branch block (LBBB) (3) and interventricular conduction delay (4) with left ventricular (LV) systolic and diastolic dysfunction in patients without clinical HF.

The aforementioned reports linking increased QRS duration to LV dysfunction are paralleled by reports emphasizing associations of prolonged QRS duration with LV structural changes (5,6). Experimental investigations suggest that asynchronous LV contraction (indicated by prolonged electrocardiographic QRS duration) may promote LV remodeling, manifested by increases in wall thickness of late-activated LV segments (6). We hypothesized that increased electrocardiographic QRS duration is associated with greater LV mass and dimensions, and lower systolic function in people without prior myocardial infarction (MI) or HF.

METHODS

The designs of the Framingham Heart study (7) and the Framingham Offspring study (8) have been described previously. Participants who attended either the 16th (n = 2,351) or the 17th (n = 2,180) biennial examination of the original cohort (1979 to 1984), or the 2nd Offspring study (1979 to 1983) examination (n = 3,867), and who had electrocardiographic and echocardiographic measurements available, were eligible. Observations from two sequential original cohort examinations were used because 1,215 attendees at the 16th examination and 866 individuals at the 17th examination underwent computerized electrocardiography. Attendees underwent complete medical history, physical examination, and assessment of cardiovascular risk factors.

Participants were excluded for the following reasons: prevalent HF (Framingham criteria; n = 51); previous MI (n = 146); digoxin or quinidine use (n = 206); and a history of permanent pacemaker implantation (n = 3). After

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Abbreviations and Acronyms

BBB = bundle branch block
FS = fractional shortening
HF = heart failure
IVS = interventricular septum at end-diastole
LA = left atrial size at end-systole
LBBB = left bundle branch block
LV = left ventricle/ventricular
LVDD = left ventricular internal dimensions in diastole
LVDS = left ventricular internal dimensions in systole
MI = myocardial infarction
PW = posterior wall
RBBB = right bundle branch block

exclusions, 1,805 participants (1,132 women) from the original cohort and 2,729 offspring cohort participants (1,451 women) remained eligible. All participants gave written informed consent, and the study was approved by the institutional review board at the Boston Medical Center.

Electrocardiography. At these examinations computerized electrocardiograms were performed using a three-channel simultaneous system (Marquette Electronics, Milwaukee, Wisconsin). Standard 12-lead configuration and XYZ orthogonal leads were recorded in analog form and digitized and read by the IBM Bonner (V2) program (IBM Corp., Armonk, New York) (9). The program measured the electrocardiographic QRS duration within groups of contiguous leads, and the maximum QRS duration across groups was determined.

For participants with QRS duration ≥120 ms, a physician reviewed electrocardiograms for establishing a definitive diagnosis of left or right bundle branch block (BBB); LBBB was defined as QRS duration ≥120 ms, absence of Q waves, and presence of wide-notched R waves in leads V_5 and V_6, presence of monophasic QS in V_1 and V_2 leads, and absence of secondary R waves in lead V_1 (10). Criteria used for RBBB were QRS duration ≥120 ms, broad, notched R waves (rsr′, rsR′, or rSR′ patterns) in leads V_1 and V_2, and wide, deep, and notched S waves in leads V_5 and V_6 (10). Electrocardiograms with QRS ≥120 ms that did not meet the criteria for LBBB or RBBB were categorized as "indeterminate" BBB. The sum of the R-wave in aVL and the S-wave in lead V_3 was used to assess electrocardiographic LV hypertrophy (Cornell voltage criteria) (11). QRS voltage was used as a covariate in secondary analyses because of its modest correlation with QRS duration (r = 0.23 [men], 0.30 [women]; p = 0.0001).

Echocardiography. All attendees underwent routine transthoracic two-dimensionally guided M-mode echocardiography at the 16th (original cohort) and the 2nd (offspring cohort) examinations. For the 866 attendees selected on the basis of availability of computerized electrocardiographic measurements at examination 17, we used echocardiographic data from examination 16; we excluded participants with an interim MI or HF. Measurements of LV internal dimensions in diastole (LVDD) and systole (LVDS), the thicknesses of the posterior wall (PW) and interventricular septum (IVS) at end-diastole, and left atrial (LA) size at end-systole were obtained by using a "leading edge" technique, averaging measurements in three cardiac cycles according to the American Society of Echocardiography guidelines (12). Left ventricular mass was calculated by using the formula: 0.8 [1.04 (LVDD + IVS + PW)^3 − (LVDD)^3] + 0.6 (13). Left ventricular fractional shortening (FS) was used as an indicator of LV systolic function.

Statistical analyses. QRS duration was modeled as a continuous (with natural logarithmic transformation to normalize the skewed distribution) and as a categorical variable (<100, 100 to 119, and ≥120 ms). Gender-specific multivariable linear regression models were used to assess the relations of QRS duration to LV mass, IVS, PW, LVDD, FS, and LA size. Gender-specific analyses of covariance were used to examine linear trends in mean values of covariate-adjusted echocardiographic measures across categories of QRS duration. Multivariable models adjusted for age, height, weight, systolic blood pressure, use of antihypertensive medications, and diabetes mellitus. In secondary analyses, we also adjusted for QRS voltage (RaVL + SV_3). We compared participants with right, left, and indeterminate BBB with those with QRS duration <100 ms (referent).

We tested for effect modification by age (<55 vs. ≥55 years), body mass index (<30 vs. ≥30 kg/m^2), and hypertension by incorporating appropriate interaction terms. A two-sided p value <0.05 was considered statistically significant.

RESULTS

The baseline characteristics of our sample are shown in Table 1. In multivariable models, log-QRS duration was positively related to LV dimensions but inversely related to FS (Table 2; all $p < 0.001$). These associations noted remained robust after additional adjustment for QRS voltage. Partial R^2 associated with QRS duration in men were 0.06 for LV mass (model $R^2 = 0.27$), 0.02 for IVS (model $R^2 = 0.20$), 0.02 for PW (model $R^2 = 0.21$), 0.05 for LVDD (model $R^2 = 0.20$); and in women 0.06 for LV mass (model $R^2 = 0.40$), 0.02 for IVS (model $R^2 = 0.39$), 0.02 for PW (model $R^2 = 0.41$), and 0.05 for LVDD (model $R^2 = 0.20$). The contribution of QRS duration to LV mass noted above was three times the magnitude of contribution due to systolic BP in men (partial $R^2 = 0.02$) and in women (partial $R^2 = 0.02$). There was a statistically significant trend of increasing LV measurements and decreasing FS across QRS interval categories (Table 2). A stronger relation of QRS duration to LV mass was noted in obese men ($p < 0.05$) and in women who were hypertensive ($p < 0.0001$) or were ≥55 years ($p < 0.02$).

In additional analyses relating LV dimensions to the type of BBB, LBBB was associated with higher LV mass and LVDD, and with lower FS compared with the referent

Table 1. Baseline Characteristics by QRS Duration

QRS Duration (ms)	Women (n = 2,583)			Men (n = 1,951)		
	<100 (n = 2,262)	100–119 (n = 261)	≥120 (n = 60)	<100 (n = 1,165)	100–119 (n = 666)	≥120 (n = 120)
Clinical						
Age, yrs	55 ± 15	58 ± 15	68 ± 12	54 ± 14	51 ± 14	61 ± 15
≥55 yrs, %	52	60	87	49	42	76
Height, cm	159 ± 7	160 ± 7	158 ± 7	174 ± 7	175 ± 8	173 ± 8
Weight, kg	64 ± 12	69 ± 16	64 ± 12	80 ± 12	83 ± 13	81 ± 12
Obese (BMI ≥ 30 kg/m^2), %	14	23	20	14	20	17
Systolic BP, mm Hg	127 ± 21	133 ± 24	143 ± 22	131 ± 17	131 ± 18	139 ± 21
Diastolic BP, mm Hg	76 ± 9	78 ± 11	78 ± 9	80 ± 10	81 ± 9	81 ± 10
Hypertensives, %	36	53	60	39	41	65
Antihypertensive use, %	20	33	42	16	20	38
Diabetes, %	4	6	3	8	7	15
Electrocardiographic						
QRS duration, ms	86 ± 7	105 ± 5	138 ± 13	90 ± 6	107 ± 5	140 ± 17
QRS voltage,* μV	1,296 ± 559	1,616 ± 781	2,104 ± 1,528	1,525 ± 541	1,766 ± 641	1,898 ± 1,206
Echocardiographic						
LV mass, gm	132 ± 32	154 ± 43	171 ± 52	184 ± 41	201 ± 57	219 ± 64
Septal thickness, cm	0.87 ± 0.14	0.94 ± 0.22	1.04 ± 0.29	0.98 ± 0.15	1.00 ± 0.16	1.06 ± 0.17
Posterior wall thickness, cm	0.86 ± 0.13	0.92 ± 0.16	1.00 ± 0.23	0.98 ± 0.14	1.00 ± 0.15	1.05 ± 0.17
LV diastolic dimension, cm	4.54 ± 0.36	4.69 ± 0.41	4.64 ± 0.60	5.00 ± 0.38	5.17 ± 0.45	5.22 ± 0.52
Left atrial size, cm	3.59 ± 0.48	3.75 ± 0.56	3.91 ± 0.59	3.99 ± 0.44	4.04 ± 0.49	4.14 ± 0.59
Fractional shortening, %	38.4 ± 4	37.8 ± 4	37.8 ± 5	36.1 ± 3	35.3 ± 4	35.4 ± 5

*QRS voltage by Cornell criteria equal to R in lead aVL + S in lead V_3 expressed in μV. All values are shown as mean ± SD or percent.
BMI = body mass index; BP = blood pressure; LV = left ventricular.

group in both genders (Table 3). Right bundle branch block was not related to any LV measurement in men, but was positively associated with LV mass, and wall thickness in women. Statistically significant increases in LV mass and wall thicknesses were noted in both genders with indeterminate BBB (Table 3).

DISCUSSION

Principal findings. In our study increasing electrocardiographic QRS duration was positively related to LV mass, wall thickness, and LVDD, and inversely associated with FS. These associations were observed across the spectrum of

Table 2. Relations of QRS Duration and Echocardiographic Variables

Echocardiographic Variables	Log QRS Duration		Categories of QRS Duration, ms					
			Men					
	β*	P	Category 1 (<100)	Category 2 (100–119)	Category 3 (≥120)	p Value (Category 2 vs. 1)	p Value (Category 3 vs. 1)	p for Trend
LV mass, g	10.4 (1.2)	0.0001	186 (1.4)	198 (1.8)	212 (4.7)	0.0001	0.0001	0.0001
LV diastolic dimension, cm	0.09 (0.01)	0.0001	5.02 (0.01)	5.14 (0.02)	5.24 (0.04)	0.0001	0.0001	0.0001
Septal wall thickness, cm	0.02 (0.004)	0.0001	0.99 (0.005)	1.00 (0.006)	1.03 (0.02)	0.05	0.009	0.003
Posterior wall thickness, cm	0.02 (0.004)	0.0001	0.98 (0.004)	1.00 (0.006)	1.02 (0.01)	0.03	0.01	0.002
Fractional shortening, %	−0.33 (0.10)	0.0001	36.0 (0.12)	35.5 (0.15)	35.0 (0.39)	0.006	0.02	0.0008
Left atrial size, cm	0.03 (0.01)	0.007	4.00 (0.01)	4.03 (0.02)	4.07 (0.04)	0.18	0.09	0.05
			Women					
			Category 1 (<100)	Category 2 (100–119)	Category 3 (≥120)	p Value (Category 2 vs. 1)	p Value (Category 3 vs. 1)	p for Trend
LV mass, g	5.8 (0.6)	0.0001	133 (0.6)	146 (1.9)	159 (4.2)	0.0001	0.0001	0.0001
LV diastolic dimension, cm	0.06 (0.008)	0.0001	4.54 (0.008)	4.66 (0.02)	4.67 (0.05)	0.0001	0.005	0.0001
Septal wall thickness, cm	0.01 (0.003)	0.0001	0.87 (0.003)	0.91 (0.009)	0.96 (0.02)	0.0002	0.0001	0.0001
Posterior wall thickness, cm	0.01 (0.002)	0.0001	0.87 (0.002)	0.89 (0.007)	0.94 (0.02)	0.03	0.0001	0.0001
Fractional shortening, %	−0.43 (0.09)	0.0001	38.5 (0.09)	37.6 (0.26)	36.9 (0.60)	0.002	0.009	0.0001
Left atrial size, cm	0.03 (0.008)	0.0002	3.61 (0.008)	3.64 (0.03)	3.73 (0.05)	0.23	0.03	0.02

All values are least square means and standard errors (inside parentheses) adjusted for age, weight, height, systolic and diastolic blood pressure, use of antihypertensive medications, and diabetes mellitus. *Regression coefficient (β) is the increase in echocardiographic variable per SD increment in log QRS duration adjusting for covariates. Standard deviation for log QRS in men = 0.136, and women = 0.120.
LV = left ventricular.

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Table 3. Echocardiographic Measurements According to Type of Bundle Branch Block

Echocardiographic Variables	Bundle Branch Block Pattern						
	Men						
	Referent (QRS <100 ms)	LBBB (n = 16)	p* Value	RBBB (n = 59)	p* Value	Indeterminate (n = 45)	p* Value
LV mass, g	186 (1.4)	251 (13)	0.0001	186 (7)	0.96	228 (7)	0.0001
LV diastolic dimension, cm	5.02 (0.01)	5.58 (0.11)	0.0001	5.12 (0.06)	0.16	5.28 (0.06)	0.0001
Septal wall thickness, cm	0.99 (0.005)	1.09 (0.04)	0.009	0.97 (0.02)	0.33	1.08 (0.02)	0.0002
Posterior wall thickness, cm	0.98 (0.004)	1.06 (0.04)	0.06	0.96 (0.02)	0.30	1.07 (0.02)	0.0001
Fractional shortening, %	36.0 (0.12)	30.6 (1.04)	0.0001	36.0 (0.58)	0.96	35.4 (0.59)	0.33
Left atrial size, cm	4.00 (0.01)	4.09 (0.11)	0.43	4.05 (0.06)	0.39	4.09 (0.06)	0.16
	Women						
	Referent (QRS <100 ms)	LBBB (n = 16)	p* Value	RBBB (n = 33)	p* Value	Indeterminate (n = 11)	p* Value
LV mass, g	133 (0.6)	180 (10)	0.0001	145 (5)	0.02	182 (10)	0.0001
LV diastolic dimension, cm	4.54 (0.008)	5.16 (0.12)	0.0001	4.52 (0.07)	0.78	4.76 (0.12)	0.06
Septal wall thickness, cm	0.87 (0.003)	0.92 (0.04)	0.24	0.93 (0.02)	0.01	1.10 (0.04)	0.0001
Posterior wall thickness, cm	0.87 (0.002)	0.91 (0.04)	0.26	0.94 (0.02)	0.001	0.97 (0.04)	0.007
Fractional shortening, %	38.5 (0.09)	33.3 (1.35)	0.0001	39.1 (0.75)	0.37	33.1 (1.35)	0.0001
Left atrial size, cm	3.61 (0.008)	3.80 (0.11)	0.08	3.70 (0.07)	0.20	3.71 (0.12)	0.41

All values are least square means and standard errors (inside parentheses) adjusted for age, weight, height, systolic and diastolic blood pressure, use of antihypertensive medications, and diabetes mellitus. *P values are comparisons of bundle branch block to the referent group (QRS <100 ms).

LBBB = left bundle branch block; LV = left ventricular; RBBB = right bundle branch block.

QRS duration and were consistent in both genders. The absolute effect sizes were modest—a trend for a 10 to 12 g increment in LV mass across the QRS interval categories. A stronger association of LV mass with QRS duration was seen in obese men, in older women, and in hypertensive women, likely because obesity, age, and blood pressure are key determinants of LV mass.

We had limited statistical power to analyze the relations of BBB type to LV measurements; LBBB was associated with higher LV mass and LVDD, and lower FS in both genders, an observation consistent with the published literature (3). Right BBB was associated with increased LV mass, PW, and IVS in women only. The latter observation is new and intriguing, but needs to be interpreted with caution given our small sample size.

Possible mechanisms underlying the observed associations. Given the cross-sectional design of our study, it is not possible to determine if prolonged QRS duration preceded or followed the increased LV dimensions. We postulate three possible mechanisms to explain our findings. First, it is possible that increased QRS duration and higher LV mass and measurements both may be the result of another disease process, such as hypertension or MI. We do not think this is the case because we excluded individuals with prior MI and adjusted for blood pressure. Second, prolongation of QRS may be the result of LV dilation, with concomitant increases in conduction time of the cardiac impulse (4); LV dilation and fibrosis have been reported to reduce conduction velocity due to alterations in the intracellular T-tubular system. Third, it is possible that the prolongation of the QRS complex is a marker of dyssynchronous LV contraction. Such noncoordinated mechanical contraction of the ventricle results in a redistribution of mechanical load and differential hypertrophy of the late-activated segments (6). Prolongation of the QRS complex may result in a lower ejection fraction also because opposing walls do not contract synchronously (14). In our study we did not observe asymmetric hypertrophy of wall thickness (septum vs. PW) in individuals with BBB, which may make dyssynchrony a less likely explanation for the observed associations.

It is important to note that the QRS duration is a crude marker of inter- and intraventricular synchrony. Mechanical dyssynchrony has been reported in individuals with QRS duration <120 ms (15). The true effect of ventricular dyssynchrony on LV remodeling would require more sensitive and specific indicators of dyssynchrony (such as tissue Doppler imaging) and the demonstration of a temporal sequence between presence of dyssynchrony and the development of alterations in LV structure and function via well-designed prospective studies.

Study limitations. Limitations of our investigation include the single occasion assessment of QRS duration and the limited power to analyze relations of BBB type to LV measurements. The predominantly Caucasian sample limits the generalizability of our results.

Conclusions. In our large cross-sectional community-based study of individuals free of prior HF and MI, we observed a positive association between electrocardiographic QRS duration and LV mass, dimensions and wall thickness, and an inverse relation to systolic function. Additional investigations are warranted to confirm our findings.

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