Prognostic Significance of Corrected QT and Corrected JT Interval for Incident Coronary Heart Disease in a General Population Sample Stratified by Presence or Absence of Wide QRS Complex

The ARIC Study With 13 Years of Follow-Up

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Background—Heart rate–corrected QT interval (QTc) is the traditional method of assessing the duration of repolarization. Prolonged heart rate–corrected QT interval is associated with higher risk of mortality in patients with coronary heart disease (CHD) and in the general population. However, the QTc is typically not evaluated when QRS duration is ≥120 ms, because increased QRS duration (QRSd) contributes to QT interval prolongation. In these circumstances, the JT interval has been proposed as a more valid way to assess ventricular repolarization.

Methods and Results—To allow for variation in heart rate, corrected JT interval (JTc) was defined as QTc/QRSd. Using data from the Atherosclerosis Risk in Communities Study, JTc and QTc were compared for their prognostic associations with incident CHD events among 14,696 men and women who were CHD-free at baseline, having either normal conduction or wide QRS complex. Among individuals with normal QRS duration, logistic regression adjusted for age, hypertensive status, diabetes, race, systolic blood pressure, smoking, HDL and LDL cholesterol, R-R interval, and menopausal status in women showed QTc and JTc were nonpredictive of future coronary events in men but significant in women. In individuals with wide QRS complex (QRSd ≥120 ms), similar analyses showed JTc had a significant prognostic advantage compared with QTc in men but not in women, among whom only 11 events occurred.

Conclusions—The JTc is a simple measurement that is a significant independent predictor of incident CHD events in men with wide QRS complex. (Circulation. 2003;108:1985-1989.)

Key Words: electrocardiography ■ prognosis ■ bundle-branch block

The heart rate–corrected QT (QTc) interval from a 12-lead ECG is the traditional measurement for assessing the duration of ventricular repolarization. A prolonged QTc is a risk factor in patients with the long-QT syndrome,1 in patients with myocardial infarction, 2,3 and in healthy men and women.4,5 The QT interval represents the time from the beginning of ventricular depolarization to completion of repolarization. However, because the QT interval encompasses ventricular depolarization, its value is limited when increased QRS duration (QRSd) contributes to QT prolongation. Thus, clinicians usually do not assess the QT interval in patients with bundle-branch block or nonspecific ventricular conduction delay with QRSd ≥120 ms.

The JT interval has been proposed as a more appropriate measure of ventricular repolarization than the QT. This seems justified, because in normal conduction, the QT interval is largely determined by the duration of repolarization, and that corresponds to the JT interval.6 Additionally, several investigators have reported that JT is independent of QRSd and suggest that the JT interval better represents the specific repolarization time than does the QT interval.6,7 Other researchers have found that the JT interval is not independent of the QRS duration, with the relationship varying according to the conduction abnormality.8

In view of the practical importance of these issues, we examined the prognostic value of QT and JT in normal conduction and in wide QRS complex. Our primary goal was to derive a simple, clinically useful tool for determining abnormally long repolarization in the face of ventricular conduction delay and to validate it against future coronary heart disease (CHD).

Methods

Subjects
The source of the data was the Atherosclerosis Risk in Communities (ARIC) study, a population-based, prospective cohort study investigating the natural history and determinants of atherosclerotic disease.9 From 1987 to 1989, probability sampling was used to recruit...
Follow-Up Methods and Documentation of New CHD Events

The methods of follow-up have been previously reported.12 Trained interviewers contacted participants annually by telephone to identify hospitalizations (and deaths). Death certificates and discharge lists from hospitals were surveyed by ARIC staff to detect additional deaths and cardiovascular events. For hospitalized patients with potential acute CHD events, trained abstractors recorded the presenting signs and symptoms, including chest pain, cardiac enzymes, and related clinical information. Up to 3 12-lead ECGs were visually coded using the Minnesota Code criteria for significant change.10 Out-of-hospital deaths were investigated using death certificate information and, in most cases, an interview with next of kin, as well as questionnaires completed by the patient’s physician. Coroner and autopsy reports, when available, were used in the validation process. Sudden cardiac death was defined as definite fatal MI, definite fatal CHD, or possible fatal CHD within 1 hour from the time of onset of acute symptoms or from the time when decedent was last known to be alive and free of acute symptoms. All potential in-hospital and out-of-hospital CHD events were reviewed and adjudicated by the ARIC Morbidity and Mortality Classification Committee using established criteria.12 Follow-up information on incident CHD events was available through 1999. The documented CHD events used as outcome measures for this study were definite or probable acute myocardial infarction and definite fatal CHD. Excluded were silent (ECG) MI between ARIC examinations and coronary artery revascularization procedures.

Electrocardiography

At the baseline examination, each participant underwent a resting standard supine 12-lead ECG at least 1 hour after smoking or caffeine ingestion. Electrodes were positioned using a standardized protocol, which has been described previously.13 The MAC PC Personal Cardiograph (Marquette Electronics) was used to record ECGs. Each consisted of 10 seconds of the 12 leads recorded simultaneously. The ECGs were sent via phone modem to the ARIC computer ECG Reading Center in Halifax, Nova Scotia, Canada. Computer analysis included measurement of the voltage and duration of ECG waves, ECG classification according to the Minnesota Code, and globally determined PR interval, QRS duration, QT interval, JT interval, and heart rate using the NOVACODE computer-aided classification system.14 The QTc interval was determined using the Bazett’s formula.15 A corrected JT interval (JTc) was derived simply by subtracting the QRS duration from the QTc. Normal QRS duration was defined as a duration <120 ms. Prolonged QRS duration was considered when the duration was ≥120 ms or when the ECG was classified by the Minnesota Code as 7-1-1, 7-2-1, or 7-4, respectively. The following Minnesota Code definitions were used:10 7-1-1 complete left bundle-branch block (LBBB) was defined as QRS duration ≥120 ms in a majority of beats (of the same QRS pattern) in any of leads I, II, III, aVL, or aVF; plus R peak duration ≥60 ms in a majority of beats (of the same QRS pattern) in any of leads I, II, III, aVL, or aVF, plus R’ >R in V1 or QRS mainly upright, plus R peak duration ≥0.06 seconds in V1 or V2 or S duration >R duration in all beats in lead I or II. 7-4 nonspecific intraventricular conduction delay (IVCD) was defined as QRS duration ≥120 ms in a majority of beats in any of leads I, II, III, aVL, or aVF.

Statistical Methods

Characteristics potentially related to incident CHD were examined in strata of normal conduction or wide QRS complex. Use of cardiac medication likely to modify the electrical cardiac cycle (amiodarone, digitalis, β-blockers [nonselective and cardioselective], antiarrhythmics type I-A and type III, and ACE inhibitors) was considered but not significant. Traditional risk factors (age, systolic blood pressure, hypertensive status, current smoking status, LDL cholesterol, HDL cholesterol, and diabetic status) as well as race, R-R interval, and, in women, menopausal status were used as covariate adjustments. The association of QTc and JTc with incident CHD was investigated by logistic regression separately in men and women in strata of normal conduction or wide QRS complex, adjusted for the above covariates. The adequacy of each regression fit was assessed by the Hosmer and Lemeshow statistic.16 Cox proportional hazard regression17 for the prognostic associations of adjusted QTc and JTc with incident CHD showed very similar findings to those reported in Table 3 using logistic regression, but the results are not presented. Numbers at risk, CHD events up to 13 years of follow-up (total, nonfatal, fatal but not sudden, or sudden death), and the rates in men and women were stratified by normal conduction, LBBB, RBBB, and IVCD. Because the rates for incident CHD events among individuals with RBBB showed little or no increased risk compared with individuals having normal conduction, RBBB was combined with normal conduction in additional analyses.

The logistic model (in men) provided covariate adjusted odds ratios for risk of future CHD associated with the wide QRS complex, with hypertensive or diabetic statuses, and with JTc compared with men who were normotensive and nondiabetic, had normal conduction or RBBB, and had an average JTc of 310 ms. Women with wide QRS complex had too few events for reliable estimation. Interactions of QTc and of JTc with hypertensive status and with diabetic status were nonsignificant.

Results

Included in these analyses were 6372 men and 8324 women. Table 1 shows the characteristics of men and women stratified by normal and prolonged QRS interval. Wide QRS complex occurred in 284 men and in 172 women; compared with control subjects, these were older and more likely to be taking cardiac medications and have hypertension, longer QTc, and a higher proportion of new CHD events. Men but not women with wide QRS had a higher prevalence of diabetes.

The QTc correlated modestly with the QRSd in normal conduction in both men (0.16) and women (0.20); the JTc had a small negative correlation with QRSd (men, −0.24; women, −0.19). In participants with a wide QRS complex, the QTc was strongly correlated with QTc (men, 0.60; women, 0.53), whereas the JTc was only modestly correlated with the QTc (men, −0.12; women, −0.26). Table 2 displays the types of ventricular conduction and the number with an incident CHD event by gender. Of 284 men with wide QRS complex, 8% had LBBB, 28% had RBBB, and 64% had IVCD. The risk of incident CHD for men was elevated only for those with LBBB and IVCD. Of the 172 women with wide QRS complex, 20% had LBBB, 23% had RBBB, and 57% had IVCD. The risk of incident CHD for women was elevated for those with LBBB, RBBB, and IVCD but was based on 11 events total. Table 2

null
additionally classifies events into nonfatal, fatal but not sudden, or sudden death (within 1 hour). In these sparse data, the main point of interest is the 5 men with IVCD who suffered sudden cardiac death. We defined normal conduction or RBBB as low-risk findings based on the literature, the evidence in the men, and the small numbers of events (n=3) in women with RBBB. Thus, in Table 2, we compare CHD risk in those with LBBB or IVCD against those with normal conduction or RBBB. The unadjusted relative risks from LBBB or IVCD compared with normal conduction (RBBB): in men, 5 of 205 (2.44%) vs 40 of 6167 (0.65%), RR=0.39; in women, 0 of 133 vs 28 of 8191 (0.34%), RR=0.11.

Table 3 presents the adjusted prognostic associations of QTc and JTc with incident CHD event in 13 years of follow-up stratified by gender and wide QRS complex using logistic regression analysis. In men with normal conduction, covariate-adjusted QTc was weakly (P=0.15) associated with incident CHD, whereas adjusted JTc was less predictive (P=0.29). For men with wide QRS complex, adjusted QTc showed no significant association with incident CHD event (P=0.49). On the other hand, adjusted JTc was positively associated with incident CHD event (P=0.04). In women with normal conduction, adjusted QTc was positively and significantly associated with incident CHD (P=0.006), and again adjusted JTc was weaker (P=0.054). Neither QTc nor JTc intervals were independently predictive among women with wide QRS complex. Hosmer and Lemeshow statistics

Table 2. Gender-Specific Categories of QRS Interval Duration and Incident CHD Event, Including the Breakdown Into Nonfatal Events, Fatal But Not Sudden Events, and Sudden Death

<table>
<thead>
<tr>
<th>Conduction Type</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Total Incident CHD, n (%)</td>
</tr>
<tr>
<td>Normal conduction</td>
<td>6088</td>
<td>485 (8.0)</td>
</tr>
<tr>
<td>LBBB</td>
<td>24</td>
<td>3 (12.5)</td>
</tr>
<tr>
<td>RBBB</td>
<td>79</td>
<td>4 (5.1)</td>
</tr>
<tr>
<td>IVCD</td>
<td>181</td>
<td>29 (16.0)</td>
</tr>
<tr>
<td>Normal + RBBB</td>
<td>6167</td>
<td>489 (7.9)</td>
</tr>
<tr>
<td>LBBB + IVCD</td>
<td>205</td>
<td>32 (15.6)</td>
</tr>
</tbody>
</table>

N indicates number at risk; n, number of CHD events; and n1, n2, and n3 partition n into non-fatal, fatal non-sudden, and sudden death, respectively.

*Rates of sudden death in wide QRS complex (LBBB + IVCD) compared with normal conduction (+RBBB): in men, 5 of 205 (2.4%) vs 40 of 6167 (0.65%), RR=3.8; in women, 0 of 133 vs 28 of 8191 (0.34%), RR=0.11.

†Relative risk of CHD for LBBB + IVCD compared with normal + RBBB.
TABLE 3. Summary of the Adjusted* Predictive Power of QTc and JTc for Incident MI/Fatal CHD Over 13 Years, Stratified by Absence or Presence of Wide QRS Complex: The ARIC Study by Gender

<table>
<thead>
<tr>
<th></th>
<th>Normal Conduction</th>
<th>Wide QRS Complex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Events/No. at Risk</td>
<td>Odds Ratio (10 ms)</td>
</tr>
<tr>
<td>Men</td>
<td>479/6031</td>
<td>...</td>
</tr>
<tr>
<td>QTc</td>
<td>...</td>
<td>1.04</td>
</tr>
<tr>
<td>JTc</td>
<td>...</td>
<td>1.03</td>
</tr>
<tr>
<td>Women</td>
<td>287/8042</td>
<td>...</td>
</tr>
<tr>
<td>QTc</td>
<td>...</td>
<td>1.09</td>
</tr>
<tr>
<td>JTc</td>
<td>...</td>
<td>1.06</td>
</tr>
</tbody>
</table>

*Adjusted for hypertension, diabetes, age, race, systolic blood pressure, HDL cholesterol, LDL cholesterol, current smoking, R-R interval, and menopausal stage in women.

†In men with wide QRS complex, this logistic model provides positive predictive value of 32% at a negative predictive value of 95%.

for lack-of-fit showed that adjusted logistic regressions fit the data adequately except for the model of QTc in men with wide QRS complex (P = 0.01). The proportional hazard model of Cox gave very similar results (not reported).

Table 4 was prepared for clinical purposes to estimate the adjusted odds ratios for incident CHD arising from wide QRS complex, hypertension, diabetes, and JTc duration. It applies only to men with wide QRS complex. To illustrate the use of the table, consider a nondiabetic hypertensive man who presents with heart rate 70 bpm, QT 426 ms, and QRSd 125 ms. Then QTc = 426/(10/60) = 460 ms and JTc = 335 ms (= 460–125). The wide QRS contributes an odds ratio of 2, the hypertension contributes an odds ratio of 1.6, and the JTc contributes an odds ratio of approximately 1.7. The overall approximate odds ratio is the product of these component odds ratios and is approximately 5.4 compared with a nondiabetic, normotensive man with normal QRS duration.

Discussion

The purpose of this study was to derive a simple, clinically useful method to measure prolonged repolarization among individuals with wide QRS complex and to validate it against future coronary heart disease. We evaluated the JTc (QTc–QRSd) in the ARIC study and compared it against the QTc using future CHD event in up to 13 years of follow-up as the validation standard.

The QT interval includes 2 components, depolarization and repolarization, and an increase in either or both may result in QT prolongation. As Das suggests, individuals with wide QRS complex and prolonged QTc form a heterogeneous group, those with prolonged repolarization and those with normal repolarization times. The former group is presumably at higher risk of CHD events than the latter. Thus, in wide QRS complex, the contributions of depolarization and repolarization to risk should be investigated separately.

In an editorial report, Spodick commented on the need for replacing the QT with the JT interval for measuring ventricular repolarization from 12-lead ECGs. He suggested that subtraction of the QRS from the QTc or other heart rate correction formulae would provide a more precise measure of repolarization, particularly in patients with wide QRS complex. The study by Pelliccia et al on dilated cardiomyopathy found that individuals who died suddenly had significantly longer QTc–QRS intervals than individuals who died from congestive heart failure. Both Spodick and Pelliccia et al suggest future studies are needed to clarify the role of JT in the assessment of abnormal repolarization, especially in the presence of wide QRS complex.

There have been many excellent reviews on the prognostic importance of prolonged QTc in clinical situations, but QTc evaluation in wide QRS complex has been conspicuously absent because the increased contribution of the QRS duration to the QTc interval presumably confounds the issue of whether ventricular repolarization is actually prolonged or merely increased by virtue of the wide QRS. The relative independence of the JTc in wide QRS complex is in agreement with the study by Salim et al, who evaluated the JT interval preablation and postablation in patients with Wolff-Parkinson-White. These investigators found that both the QT and QTC intervals shortened significantly after ablation compared with before ablation but the JTc did not change after ablation compared with before ablation. The authors conclude JTc is an independent measure of repolarization.
The prognostic significance of wide QRS has been investigated in several studies. Among individuals with existing CHD, bundle-branch block has been shown as a significant independent predictor of mortality. Other studies have found that individuals with bundle-branch block have no excess mortality. We found that both LBBB and IVCD were important risk predictors (unadjusted odds ratios, 2 in men and 1.7 in women). In agreement with other studies, we found no increased mortality risk for RBBB. Men with IVCD and 1.7 in women). In agreement with other studies, we found important risk predictors (unadjusted odds ratios, 2 in men and 1.7 in women). In agreement with other studies, we found no increased mortality risk for RBBB. Men with IVCD seem to carry increased risk of sudden death; there were insufficient events in women to make any statement.

We used the heart rate correction formula developed by Bazett, although concern has often been expressed about its validity.

**Study Limitations**

Although this is a large study, the number of CHD events among women with wide QRS was quite small (n = 11) and significantly affected our ability to determine risk associations. We arbitrarily defined wide QRS complex as QRSd ≥120 ms and did not investigate whether CHD risk was related to QRS duration expressed as a continuous variable. Heart rate correction used Bazett’s formula, which is known to have limitations for heart rates below 60 or above 100 bpm. Finally, we do not know the generalizability of these findings to other populations, especially in those with existing CHD.

**Conclusions**

To our knowledge, this is the only large study that compared the prognostic importance of QTc against JTc in those with normal or wide QRS complex. These results confirm that JT is an index of repolarization largely independent of ventricular depolarization. In men, the JTc provides prognostic information about future CHD events in wide QRS complex. However, the QTc is more useful than the JTc in normal conduction. We have developed a simple procedure to determine estimated risk of incident CHD event for men with wide QRS complex.

**Acknowledgment**

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**References**

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