Duration of QRS Complex in Resting Electrocardiogram Is a Predictor of Sudden Cardiac Death in Men

Sudhir Kurl, MD; Timo H. Mäikikallio, MD, PhD; Pentti Rautaharju, MD, PhD; Vesa Kiviniemi, LicPhil; Jari A. Laukkanen, MD, PhD

Background—Previous studies indicate that increased QRS duration in ECG is related to the risk of all-cause death. However, the association of QRS duration with the risk of sudden cardiac death (SCD) is not well documented in large population-based studies. Our aim was to examine the relation of QRS duration with SCD in a population-based sample of men.

Methods and Results—This prospective study was based on a cohort of 2049 men aged 42 to 60 years at baseline with a 19-year follow-up, during which a total of 156 SCDs occurred. As a continuous variable, each 10-ms increase in QRS duration was associated with a 27% higher risk for SCD (relative risk, 1.27; 95% confidence interval, 1.14–1.40; P<0.001). Subjects with QRS duration of >110 ms (highest quintile) had a 2.50-fold risk for SCD (relative risk, 2.50; 95% confidence interval, 1.38–4.55; P=0.002) compared with those with QRS duration of <96 ms (lowest quintile), after adjustment for established key demographic and clinical risk factors (age, alcohol consumption, previous myocardial infarction, smoking, serum low- and high-density lipoprotein cholesterol, C-reactive protein, type 2 diabetes mellitus, body mass index, systolic blood pressure, and cardiorespiratory fitness). In addition to QRS duration, smoking, previous myocardial infarction, type 2 diabetes mellitus, cardiorespiratory fitness, body mass index, systolic blood pressure, and C-reactive protein were independently associated with the risk of SCD.

Conclusions—QRS duration is an independent predictor of the risk of SCD and may have utility in estimating SCD risk in the general population. (Circulation. 2012;125:2588-2594.)

Key Words: cardiovascular risk factors ■ ECG ■ population ■ primary care ■ sudden cardiac death

Sudden cardiac arrest accounts for one half of all deaths related to coronary heart disease (CHD) and presents as the first manifestation of CHD in ≈20% to 30% of the deaths. A large majority of sudden cardiac deaths (SCDs) occur among more general segments of the population. However, most of the studies on risk markers of arrhythmic events have focused on patients with a specific heart disease.1 Large epidemiological surveys have not been able to identify specific risk markers for SCD in the general population, although general risk markers for atherosclerosis identify the risk of SCD nonspecifically.2,3 Little is known about the relationship between the duration of QRS in ECG and the risk of SCD among the general population.4 One study has shown that QRS duration is an independent predictor of SCD in patients with coronary artery disease.4

Clinical Perspective on p 2594

The relations of QRS duration and specific QRS morphologies such as bundle branch block to the risk for SCD are not clear. In previous studies in patients with congestive heart failure, prolonged QRS duration has been associated with a higher incidence of SCD and decrease in overall survival.5,6 Some studies have shown that patients with left bundle branch block have an elevated risk for SCD and overall mortality compared with those with right bundle branch block.5,7 However, the association of QRS duration and the risk of SCD is not well documented in population studies. The present study was conducted to investigate the predictive value of QRS duration with respect to the risk of SCD in a population-based random sample of men and to explore prospects for identification of subgroups of men in the general population at increased risk of SCD.

Methods

Study Population

This study was designed to investigate risk predictors for atherosclerotic cardiovascular outcomes in a population-based sample of men. The study group is a randomly selected sample of 3433 men aged 42 to 60 years who resided in the town of Kuopio, Finland, or its surrounding rural communities. Of those invited, 2682 (83%) participated in the study, and those with complete data on ECG,
covariates, and outcomes (n=2049 men) were included in the final analyses. Baseline examinations were conducted between March 1984 and December 1989. The study was approved by the research ethics committee of the University of Kuopio, Kuopio, Finland. Each participant gave written informed consent.

ECG Method
Standard resting 12-lead ECG was recorded in all subjects at baseline. Paper speed was 50 mm/s. Duration of QRS was measured from the beginning of the earliest to the end of the last QRS deflection.

Assessment of Risk Factors
The lifelong exposure to smoking (cigarette pack-years) was estimated as the product of the number of years smoked and the number of tobacco products smoked daily at the time of examination. Resting blood pressure was measured between 8 and 10 AM with a random-zero sphygmomanometer. Information on use of medications and diagnosis of diseases was collected at baseline examination by an internist.

Echocardiographic studies were performed with an ATL Ultramark IV system (2-dimensional guided M-mode measurements with a 3.0- or 3.5-MHz transducer). Echocardiographic images were obtained from the parasternal window and a perpendicular projection across the heart, with participants lying in a modified left lateral decubitus position. Left ventricular systolic function was among the measures collected. Alcohol consumption was assessed with the use of the Nordic Alcohol Consumption Inventory. Cardiorespiratory fitness (VO2max) was measured with the use of a respiratory gas exchange on a bicycle ergometer. Eight, nine

Classification of SCD
All deaths that occurred by the end of 2008 were checked from hospital documents, wards of health centers, and death certificates. The sources of information were interviews with family members, hospital documents, death certificates, autopsy reports, and medical reports. There were no losses to follow-up. Deaths were coded with the use of the International Classification of Diseases, Ninth Revision or International Classification of Diseases, Tenth Revision codes.

A death was defined as SCD when it occurred either within 1 hour after the onset of an abrupt change in symptoms or within 24 hours after onset of symptoms when autopsy data did not reveal a noncardiac cause of sudden death or after successful resuscitation from ventricular tachycardia and/or ventricular fibrillation. The deaths due to aortic aneurysm rupture, cardiac rupture or tamponade, pulmonary embolism, cancer, or other noncardiac comorbidities were not included as SCD. Diagnostic classification of events was based on symptoms, ECG findings, cardiac enzyme elevations, autopsy findings (80% of SCDs), and history of CHD together with clinical and ECG findings. Other cardiac-related deaths were defined as non-SCD. All death-related documents were cross-checked in detail by 2 physicians. An independent Events Committee blinded to clinical data classified all deaths.

Statistical Analysis
Descriptive data are presented as means and percentages. Risk factors for main outcomes were analyzed with a multivariate Cox model. QRS duration was entered into forced SPSS Cox proportional hazards models. Cox models were adjusted for age and other demographic and clinical factors previously reported to be predictive of SCD by considering their clinical relevance.

Relative risks (RRs) with 95% confidence intervals (CIs), adjusted for clinical risk factors, were estimated as antilogarithms of the coefficients from multivariable models. The fit of the proportional hazards models was examined by plotting the hazard functions in different categories of risk factors over time. The proportional hazards assumption was verified for all variables by inspection of the plots of Schoenfeld residuals for covariates. The linearity assumption was satisfied for all continuous variables, and it was assessed with Martingale residuals for each continuous variable against survival time. A P value of <0.05 was considered statistically significant. These statistical analyses were performed with the use of SPSS 17.0 for Windows.

The incremental value of QRS duration added to other risk predictors was evaluated with the use of C statistics. The C index was calculated to assess the model discrimination, which is the ability of the model to correctly identify subjects with respect to SCD. The Harrell C index was used as the primary measure of discrimination. Additionally, we calculated the integrated discrimination improvement and binary R² value for the model with and without QRS duration.

We assessed risk reclassification by sorting the predicted risk for the model into 3 categories (<6%, 6-20%, and >20%) according to previous findings. We then computed the net reclassification index, which compares the shifts in reclassified categories by observed outcome. This measure determines net percentages of those men who did and did not have SCD over the follow-up period and were correctly reclassified with the new function. Previously mentioned predicted probabilities of SCD were calculated on the basis of a 19-year follow-up period.

Results
Baseline Characteristics
The distributions of baseline demographic, ECG, and echocardiographic characteristics by quintiles of QRS duration are shown in Table 1. The mean of QRS duration was 104 ms (SD=10.9 ms). Previous history of myocardial infarction was more prevalent among men with a long duration of QRS complex (13.4% versus 4.9%). Similarly, diastolic blood pressure and serum high-density lipoprotein cholesterol levels were higher and serum triglycerides levels were lower in this group of men, although the absolute differences were small.

Outcome Events During Follow-Up
The average follow-up period for the cohort was 19.1 years. Among men with SCD, the average follow-up time from baseline to SCD was 4235 days (11.6 years). There were 156 SCDs including subjects with successfully resuscitated ventricular tachycardia/ventricular fibrillation. A total of 120 SCDs (77.9%) occurred in out-of-hospital conditions, and 103 (66.3%) of these outcomes were due to documented ventricular tachycardia, ventricular fibrillation, or death, with autopsy revealing no other reason for death. The number of those with implantable cardioverter-defibrillator implantation was 7 (Table 2). Usually, an implantable cardioverter-defibrillator was implanted after successful resuscitation, as recommended, and a total of 10 men were successfully resuscitated. The numbers of all-cause death and nonsudden death from CHD were 357 and 185, respectively. Cumulative survival curves for SCD according to the quintiles of QRS duration are shown in the Figure. Table 2 shows other resting ECG characteristics.

Risk Factors for SCD
Significant risk factors for SCD are shown in Tables 3 and 4, including the subgroup of men with echocardiographic data available (Table 4). QRS duration, smoking, cardiorespiratory fitness, previous myocardial infarction, type 2 diabetes mellitus, systolic blood pressure, body mass index, and C-reactive protein were entered into forced SPSS Cox proportional hazards models. Cox models were adjusted for age and other demographic and clinical factors previously reported to be predictive of SCD.
were risk factors for SCD in the multivariable model. The C index for the total model discrimination was 0.784 (95% CI, 0.750–0.815). After QRS duration was added into the multivariable model, the C index increased from 0.776 (95% CI, 0.744–0.811) to 0.784, showing the significant incremental value of QRS duration in predicting SCD. The integrated discrimination improvement was 0.013 (95% CI, 0.005–0.021), and relative integrated discrimination improvement was 0.13, showing the significant level of discrimination between men classified with and without the use of QRS duration in addition to other risk factors. Consistently, binary $R^2$ increased from 0.124 to 0.134 after QRS duration was added into the multivariable model. The Hosmer-Lemeshow statistics for models with and without QRS duration were 8.60 ($P=0.377$) and 6.00 ($P=0.647$), respectively, suggesting an excellent fit.

### QRS Duration and SCD

QRS duration, as a continuous variable, was significantly related to the risk of SCD. Each 10-ms increase in QRS duration was associated with 27% higher adjusted risk (RR=1.27; 95% CI, 1.20–1.35). 

### Table 1: Baseline Characteristics According to Quintiles of QRS Duration

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Men</th>
<th>Quintile 1</th>
<th>Quintile 2</th>
<th>Quintile 3</th>
<th>Quintile 4</th>
<th>Quintile 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>52.7 (5.1)</td>
<td>52.6 (5.7)</td>
<td>52.9 (5.1)</td>
<td>52.7 (4.9)</td>
<td>52.7 (4.8)</td>
<td>52.5 (4.9)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.9 (3.6)</td>
<td>26.9 (3.6)</td>
<td>26.8 (3.5)</td>
<td>27.0 (3.6)</td>
<td>26.8 (3.6)</td>
<td>27.0 (3.8)</td>
</tr>
<tr>
<td>Smokers, %</td>
<td>31.0</td>
<td>29.4</td>
<td>34.2</td>
<td>30.5</td>
<td>28.8</td>
<td>29.5</td>
</tr>
<tr>
<td>Cigarette smoking, pack-years**</td>
<td>8.5 (16.7)</td>
<td>8.6 (16.4)</td>
<td>9.8 (18.2)</td>
<td>8.4 (15.9)</td>
<td>8.1 (17.6)</td>
<td>7.6 (15.1)</td>
</tr>
<tr>
<td>Alcohol consumption, g/wk</td>
<td>76.3 (140.7)</td>
<td>82.1 (132.4)</td>
<td>74.0 (106.1)</td>
<td>71.4 (149.2)</td>
<td>78.9 (124.2)</td>
<td>76.1 (182.1)</td>
</tr>
<tr>
<td>Serum total cholesterol, mmol/L</td>
<td>5.92 (1.08)</td>
<td>5.83 (1.03)</td>
<td>5.98 (1.02)</td>
<td>5.90 (1.09)</td>
<td>5.94 (1.14)</td>
<td>5.92 (1.11)</td>
</tr>
<tr>
<td>Serum LDL cholesterol, mmol/L</td>
<td>4.06 (1.02)</td>
<td>3.99 (0.97)</td>
<td>4.12 (0.97)</td>
<td>4.04 (1.03)</td>
<td>4.08 (1.08)</td>
<td>4.04 (105)</td>
</tr>
<tr>
<td>Serum HDL cholesterol, mmol/L</td>
<td>1.28 (0.30)</td>
<td>1.25 (0.29)</td>
<td>1.29 (0.30)</td>
<td>1.27 (0.29)</td>
<td>1.29 (0.30)</td>
<td>1.30 (0.30)</td>
</tr>
<tr>
<td>Serum triglycerides, mmol/L</td>
<td>1.29 (0.81)</td>
<td>1.41 (0.80)</td>
<td>1.31 (0.89)</td>
<td>1.29 (0.83)</td>
<td>1.22 (0.69)</td>
<td>1.23 (0.81)</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>134.3 (16.8)</td>
<td>131.4 (14.9)</td>
<td>134.0 (16.4)</td>
<td>135.5 (17.1)</td>
<td>135.4 (17.0)</td>
<td>135.0 (18.4)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>89.2 (10.5)</td>
<td>87.5 (10.0)</td>
<td>89.0 (10.4)</td>
<td>90.0 (10.9)</td>
<td>90.2 (10.7)</td>
<td>89.0 (10.5)</td>
</tr>
<tr>
<td>Blood glucose, mmol/L</td>
<td>4.78 (1.15)</td>
<td>4.71 (0.95)</td>
<td>4.79 (1.07)</td>
<td>4.74 (1.11)</td>
<td>4.74 (1.02)</td>
<td>4.95 (1.51)</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>2.38 (4.22)</td>
<td>2.19 (2.65)</td>
<td>2.61 (5.92)</td>
<td>2.31 (3.42)</td>
<td>2.15 (3.88)</td>
<td>2.59 (4.47)</td>
</tr>
<tr>
<td>Coronary heart disease, %</td>
<td>24.0</td>
<td>22.7</td>
<td>26.2</td>
<td>22.5</td>
<td>21.6</td>
<td>28.9</td>
</tr>
<tr>
<td>History of myocardial infarction, %</td>
<td>8.0</td>
<td>4.9</td>
<td>8.9</td>
<td>5.0</td>
<td>5.6</td>
<td>13.4</td>
</tr>
<tr>
<td>Family history of coronary heart disease, %</td>
<td>48.0</td>
<td>50.5</td>
<td>48.2</td>
<td>49.3</td>
<td>46.3</td>
<td>47.8</td>
</tr>
<tr>
<td>History of hypertension, %</td>
<td>31.0</td>
<td>28.7</td>
<td>30.6</td>
<td>29.6</td>
<td>30.2</td>
<td>34.1</td>
</tr>
<tr>
<td>Family history of hypertension, %</td>
<td>48.0</td>
<td>44.6</td>
<td>46.8</td>
<td>48.7</td>
<td>48.1</td>
<td>49.3</td>
</tr>
<tr>
<td>Cardiac insufficiency, %</td>
<td>7.0</td>
<td>7.0</td>
<td>6.3</td>
<td>6.1</td>
<td>7.7</td>
<td>8.5</td>
</tr>
<tr>
<td>Cardiomyopathy, %</td>
<td>2.0</td>
<td>0.8</td>
<td>2.3</td>
<td>1.8</td>
<td>1.6</td>
<td>3.9</td>
</tr>
<tr>
<td>Cerebrovascular disease, %</td>
<td>2.0</td>
<td>2.0</td>
<td>1.6</td>
<td>1.9</td>
<td>2.1</td>
<td>3.1</td>
</tr>
<tr>
<td>Claudication, %</td>
<td>4.0</td>
<td>3.9</td>
<td>4.9</td>
<td>4.4</td>
<td>3.1</td>
<td>3.9</td>
</tr>
<tr>
<td>Arrhythmias, %†</td>
<td>15.0</td>
<td>14.4</td>
<td>14.3</td>
<td>14.6</td>
<td>15.5</td>
<td>18.8</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus, %</td>
<td>5.0</td>
<td>4.1</td>
<td>4.9</td>
<td>5.2</td>
<td>4.1</td>
<td>7.7</td>
</tr>
<tr>
<td>Coronary artery bypass surgery</td>
<td>1.0</td>
<td>1.1</td>
<td>0.9</td>
<td>1.2</td>
<td>0.0</td>
<td>1.6</td>
</tr>
</tbody>
</table>

**ECG**

- QT interval, ms: 412 (32) – 418 (33)
- PQ interval, ms: 160 (27) – 160 (31)
- LVH, %: 2.0 – 1.8
- Data on echocardiography (fractional shortening)
  - % (in a subpopulation of 802 men): 33.6 (5.6) – 33.1 (149)

### Regular use of medications

- Antihypertensive medication, %: 21.0 – 26.1
- Medication for dyslipidemia, %: 7.0 – 2.6
- β-blocker, %: 18.0 – 20.7
- Acetylsalicylic acid, %: 6.0 – 5.2

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Table 2. Resting ECG Characteristics

<table>
<thead>
<tr>
<th>ECG Findings</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus rhythm</td>
<td>2037 (99.3)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>275 (13.4)‡</td>
</tr>
<tr>
<td>Sinus node dysfunction</td>
<td>22 (1.0)</td>
</tr>
<tr>
<td>Atrioventricular conduction delay*</td>
<td>28 (1.3)</td>
</tr>
<tr>
<td>Extrasystoles†</td>
<td>29 (1.4)</td>
</tr>
<tr>
<td>Left anterior or posterior fascicular block</td>
<td>3 (0.1)</td>
</tr>
<tr>
<td>Nodal rhythm</td>
<td>1 (0.0)</td>
</tr>
<tr>
<td>Pacemaker implantation</td>
<td>25 (1.2)</td>
</tr>
<tr>
<td>Implantable cardioverter-defibrillator</td>
<td>7 (0.3)</td>
</tr>
</tbody>
</table>

*First- or second-degree atrioventricular conduction block; there were no cases of third-degree block.
†Includes supraventricular, ventricular, and aberrant extrasystoles at rest.
‡The numbers of cases of chronic or paroxysmal atrial fibrillation diagnosed at the time of baseline examination or during follow-up were 240 (12.7%) for those without sudden cardiac death and 22 (14.7%) among those with sudden cardiac death.

1.14–1.40; P<0.001) when men with bundle branch block were included. The results were similar among men without bundle branch block. The prevalence of bundle branch blocks (QRS duration ≥120 ms) was rare (3.2%) in this population. Subjects with QRS duration of >110 ms (highest quintile) had a 2.50-fold risk for SCD, after adjustment for demographic and clinical risk factors (Table 5). The results were consistent when previous myocardial infarction and prevalent CHD were included and when they were omitted as covariates in the multivariable model. Additionally, the relationship between QRS duration and risk of SCD did not change when men with a history of myocardial infarction at baseline were excluded. The respective risk of SCD was 2.72-fold (95% CI, 1.53–5.02; P<0.001) among men with QRS duration of >110 ms after additional adjustment for myocardial infarction during the interim period of follow-up.

ECG left ventricular hypertrophy and rate-adjusted QT and PQ intervals were not significant predictors of SCD when added as covariates into the risk models. The risk of SCD among men with QRS duration >110 ms was 2.54-fold after additional adjustment for left ventricular hypertrophy (Table 5). When we further adjusted for atrial fibrillation and kidney function (creatinine clearance), the risk of SCD was 2.50-fold (RR = 2.50; 95% CI, 1.38–4.53; P = 0.003) for those men who had QRS duration >110 ms (highest quintile). The risk of SCD was increased even though QTc interval was taken into account in the multivariable model (RR = 2.52; 95% CI, 1.38–4.60; P = 0.003). The correlation coefficient between QTc interval and SCD survival was low (r = 0.166). Consistently, QRS duration (per 10-ms increase) was also related to the risk of out-of-hospital SCD (RR = 1.21; 95% CI, 1.07–1.38; P = 0.003).

Table 3. Risk Factors for Sudden Cardiac Death Among Men

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Riska</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS duration (10-ms increase)</td>
<td>1.27</td>
<td>1.14–1.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cigarette smoking (per 10-pack-years)†</td>
<td>1.25</td>
<td>1.17–1.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiorespiratory fitness (per 1-MET increase)†</td>
<td>0.63</td>
<td>0.49–0.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous myocardial infarction (yes vs no)</td>
<td>3.21</td>
<td>2.16–4.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus (yes vs no)</td>
<td>2.21</td>
<td>1.37–3.58</td>
<td>0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (per 10-mm Hg increase)</td>
<td>1.11</td>
<td>1.02–1.22</td>
<td>0.012</td>
</tr>
<tr>
<td>Body mass index (per 5-kg/m² increase)</td>
<td>1.26</td>
<td>1.02–1.57</td>
<td>0.033</td>
</tr>
<tr>
<td>C-reactive protein (per 1 mmol/L)</td>
<td>1.03</td>
<td>1.00–1.05</td>
<td>0.044</td>
</tr>
</tbody>
</table>

*Relative risks (confidence interval [CI]) are adjusted for age, alcohol consumption, serum low- and high-density lipoprotein, systolic blood pressure, and all variables shown in the table. Sudden cardiac death was defined when the arrest occurred within 24 hours after onset of any symptoms.
†Pack-years denotes the lifelong exposure to smoking that was estimated as the product of years smoked and the number of tobacco products smoked daily at the time of examination.
‡Exercise capacity was measured directly during exercise test with the use of a respiratory gas analyzer; 1 metabolic equivalent task (MET) = 3.5 mL/kg per minute.

Table 4. Risk Factors for Sudden Cardiac Death Among Subgroup of Men With Data on Echocardiography

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Riska</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS duration (10-ms increase)</td>
<td>1.14</td>
<td>1.05–1.25</td>
<td>0.003</td>
</tr>
<tr>
<td>Cigarette smoking (per 10-pack-years)†</td>
<td>1.24</td>
<td>1.09–1.39</td>
<td>0.001</td>
</tr>
<tr>
<td>Cardiorespiratory fitness (per 1-MET increase)†</td>
<td>0.55</td>
<td>0.35–0.87</td>
<td>0.010</td>
</tr>
<tr>
<td>Previous myocardial infarction (yes vs no)</td>
<td>3.01</td>
<td>1.50–6.00</td>
<td>0.001</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus (yes vs no)</td>
<td>2.21</td>
<td>1.37–3.58</td>
<td>0.001</td>
</tr>
<tr>
<td>Fractional shortening (per 1% decrease)</td>
<td>1.40</td>
<td>1.03–1.90</td>
<td>0.029</td>
</tr>
<tr>
<td>Body mass index (per 5-kg/m² increase)</td>
<td>1.48</td>
<td>1.01–2.18</td>
<td>0.045</td>
</tr>
</tbody>
</table>

*Relative risks (confidence interval [CI]) are adjusted for age, alcohol consumption, serum low- and high-density lipoprotein, systolic blood pressure, and all variables shown in the table. Sudden cardiac death was defined when the arrest occurred within 24 hours after onset of any symptoms.
†Pack-years denotes the lifelong exposure to smoking that was estimated as the product of years smoked and the number of tobacco products smoked daily at the time of examination.
‡Exercise capacity was measured directly during exercise test with the use of a respiratory gas analyzer; 1 metabolic equivalent task (MET) = 3.5 mL/kg per minute.

Figure. Cumulative survival curves for sudden cardiac death according to the quintiles of QRS duration.
The impact of adding QRS duration in the risk model was assessed by evaluating the number of subjects reclassified into a higher or lower level of predicted SCD risk categorized into ranges <6%, 6–20%, and >20% (Table 6). Of the 156 cases with SCD, 14 (9.0%) were reclassified into a higher risk category and 7 of 156 (4.5%) into a lower risk category. When the same model was applied to evaluate reclassification of subjects without SCD (noncases), a nearly equal proportion was reclassified into a higher risk category (3.7%) and a lower risk category (4.0%). This reclassification method appears useful in assessment of the stability of risk classification when the impact of added predictors into a SCD risk model is evaluated.

### QRS Duration, Non-SCD, and Competing Risk

We tested competing risks between QRS duration and non-SCD. QRS duration, as a continuous variable, was not related to the risk of non-SCD. Each 10-ms increase in QRS duration was not statistically significantly associated with the risk of non-SCD (RR=1.15; 95% CI, 0.96–1.39; P=0.118). Subjects with QRS duration of >110 ms (highest quintile) did not have a significantly elevated risk of non-SCD (RR=1.78; 95% CI, 0.73–4.38; P=0.206) compared with subjects with QRS duration of <96 ms (lowest quintile) after adjustment for demographic and clinical risk factors. The association between QRS duration and non-SCD was not statistically significant. Significant risk factors for non-SCD were age, type 2 diabetes mellitus, previous myocardial infarction, and cardiorespiratory fitness (C index 0.784). Similarly, age, alcohol consumption, systolic blood pressure, type 2 diabetes mellitus, smoking, previous myocardial infarction, and cardiorespiratory fitness were statistically significant risk factors for cardiovascular death (C index 0.755).

### QRS Duration and SCD in Different Risk Groups

Among men without history of CHD (n=1540; n=81 deaths), a 10-ms increment in QRS duration was associated with a 1.23-fold increase in SCD risk (RR=1.23; 95% CI, 1.07–1.42; P=0.004) after adjustment for clinical risk factors. Similarly, among men with known CHD (n=509; n=75 deaths), the adjusted risk for a 10-ms increment in QRS duration was increased significantly (RR=1.37; 95% CI, 1.16–1.62; P<0.001).

QRS duration was related to the risk of SCD among hypertensive men (n=1188; n=124 deaths); prolonged QRS duration (10-ms increment) was associated with the risk of SCD (RR=1.47; 95% CI, 1.28–1.69; P<0.001) when other risk factors were taken into account. The respective risk of SCD was not significant among normotensive men.

Among subjects with the assessment of echocardiography (n=802), we found that left ventricular systolic function (per 1% decrement in fractional shortening) was significantly associated with SCD (RR=1.40; 95% CI, 1.03–1.90; P=0.029) after adjustment for other risk factors. In this subanalysis, QRS duration (per 10-ms increase) also remained a significant predictor for SCD (RR=1.14; 95% CI, 1.05–1.25; P=0.003) when left ventricular...
systolic function and other risk factors were taken into account. Men with fractional shortening of $<$33% (median) had 25 SCDs, and men with fractional shortening of $\geq$33% had 32 SCDs. The interaction between left ventricular systolic function and QRS duration was significant ($P=0.024$). QRS duration as a continuous variable (for a 10-ms increase) was related to an increased risk of SCD (RR=1.53; 95% CI, 1.21–1.95; $P<0.001$) among men with left ventricular systolic function below median (fractional shortening 33%), whereas the respective association was not statistically significant among men with left ventricular systolic function above median. Because of the limited number of outcomes, more detailed or graded analyses were not feasible.

Discussion

An important novel finding from the present investigation in our representative population-based cohort of men was that QRS duration is a significant independent predictor for SCD. QRS duration >110 ms was associated with a 2.5-fold increase in SCD risk models adjusted for clinically relevant risk factors. The risk for SCD was increased by 27% for each 10-ms increase in QRS duration. In a subgroup of men with echocardiographic measurement of systolic function (fractional shortening) available, a 10-ms increase in QRS duration was a significant predictor of SCD in men with fractional shortening below the median value (33%). On the other hand, QRS duration was not a significant predictor of non-SCD.

Results in Comparison With Previous Investigations

Most of the studies on risk markers of arrhythmic events have focused on clinical study groups with a specific heart disease. Previous epidemiological studies have not been able to identify specific risk markers for SCD in the general population. QRS duration has been shown to be associated with adverse outcomes in patients with heart failure, and decreased survival is more likely after myocardial infarction associated with impaired left ventricular function or heart failure. QRS duration is a readily available “front-line” clinical indicator of increased risk of SCD, suggesting consideration of cardiac function assessment or evaluation of coronary artery disease in patients with suspected heart failure in particular.

However, no relationship was observed between QRS duration and ventricular tachyarrhythmias as well as the incidence of appropriate defibrillator therapy among patients with cardiomyopathy. Furthermore, it has been shown that intraventricular conduction delay predicts mortality after myocardial infarction and revascularization, although QRS duration was not predictive of SCD or serious arrhythmic events.

Possible Mechanisms of Increased SCD Risk With Prolonged QRS

Although the present investigation was not designed to address the question of why QRS duration is a predictor of SCD, some potential mechanisms may be postulated. Tachyarrhythmias that occur in patients with prolonged QRS duration have been reported to be more complex, to be more likely to degenerate, and to have a higher rate of SCD. It is known that intraventricular conduction delay is related to left ventricular dysfunction, and the relationship between depressed left ventricular systolic function and SCD has been well established. The link between this ECG pattern and malignant arrhythmias is supported by accentuated repolarization abnormalities before the onset of arrhythmia. The prolonged QRS with the perturbed depolarization may play a direct role in SCD via the facilitation of reentrant tachyarrhythmias.

Prolonged QRS duration in patients with hypertension and left ventricular hypertrophy may be due to a number of factors that predispose to such reentry. Previous studies have demonstrated that delayed conduction within the ventricular myocardium may cause monomorphic ventricular tachycardia among patients with structural heart disease. It has also been suggested that complex ventricular ectopy, couplets, or nonsustained ventricular tachyarrhythmias are associated with an increased risk of sudden death among patients with a history of myocardial infarction, and nonischemic dilated cardiomyopathy.

Clinical Implications

Depressed left ventricular function is a well-documented predictor of mortality. Our results show that even a moderate QRS duration $>$110 ms, including incomplete bundle branch blocks, is associated with a significant independent risk of SCD, and the association remains significant after accounting for left ventricular function. New integrative research to further evaluate relationships between SCD predictors may lead to strategies for both improved risk stratification and new therapeutic options.

This study population is a representative sample of the general community-based male population, and the results need to be validated in female populations. Another limitation of our study was that formal competing risk analysis was not performed. However, the associations between QRS duration, non-SCD, and cardiovascular death were not statistically significant in a comparison of the risks with the use of the Cox models. An additional limitation includes the availability of echocardiography for only a small subgroup of men.

Conclusions

Our results suggest that prolonged QRS duration is a potentially important predictor of SCD and as a commonly available ECG variable may have practical utility for SCD risk stratification. Further research is needed to study the mechanism of QRS duration as a SCD predictor.

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Disclosures

References


CLINICAL PERSPECTIVE

Sudden cardiac arrest accounts for one half of all deaths related to coronary heart disease and presents as the first manifestation of coronary heart disease in ≈20% to 30% of the deaths. Large epidemiological studies have not been able to identify specific ECG markers for sudden cardiac death (SCD), and little is known about the relationship between the duration of the QRS complex and the risk of SCD among the general population. Our study shows that prolonged QRS duration is an independent predictor of SCD, with risk levels comparable to those for established clinical risk factors such as smoking, lipids, hypertension, history of myocardial infarction or coronary heart disease, and type 2 diabetes mellitus. Each 10-ms increment in QRS duration was associated with a 27% higher SCD risk. Thus, the measurement of QRS duration may have utility in evaluation of SCD risk in the general population.
Duration of QRS Complex in Resting Electrocardiogram Is a Predictor of Sudden Cardiac Death in Men
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