QRS Duration and QT Interval Predict Mortality in Hypertensive Patients With Left Ventricular Hypertrophy

The Losartan Intervention for Endpoint Reduction in Hypertension Study

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Abstract—Left ventricular hypertrophy is a risk factor for cardiovascular mortality, including sudden cardiac death. Experimentally, left ventricular hypertrophy delays ventricular conduction and prolongs action potential duration. Electrocardiographic QRS duration and QT interval measures reflect these changes, but whether these measures can further stratify risk in patients with electrocardiographic left ventricular hypertrophy is unknown. We measured the QRS duration and QT intervals from the baseline 12-lead electrocardiograms in the Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) study, which included hypertensive patients with electrocardiographic evidence of left ventricular hypertrophy randomized to either losartan-based or atenolol-based treatment to lower blood pressure. In the present study, we related study baseline electrocardiographic measures to cardiovascular and all-cause mortality. There were 5429 patients (male 45.8%; mean age 66±7 years) included in the present analyses. After a mean follow-up of 4.9±0.8 years, there were 417 deaths from all causes, including 214 cardiovascular deaths. In separate univariate Cox regression analyses, QRS duration and several QT measures were significant predictors of cardiovascular mortality and all-cause mortality. However, in multivariate Cox analyses including all electrocardiographic measures and adjusting for other risk factors as well as treatment strategy, only QRS duration and maximum rate-adjusted QT apex interval remained as significant independent predictors of cardiovascular (P=0.022 and P=0.037, respectively) and all-cause mortality (P=0.038 and P=0.002, respectively). In conclusion, in a hypertensive risk population identified by electrocardiographic left ventricular hypertrophy, increased QRS duration and maximum QT apex interval can further stratify mortality risk even in the setting of effective blood pressure-lowering treatment. (Hypertension. 2004;43:1029-1034.)

Key Words: electrocardiography ■ hypertension ■ mortality ■ hypertrophy

Left ventricular hypertrophy (LVH) is an important indicator of target organ damage in chronic arterial hypertension. Electrocardiographically and echocardiographically detected LVH independently predict increased morbidity and mortality,1,2 including sudden cardiac death,3,4 and the relative risk of these events increases with increasing LV mass. The impact of LVH on outcome may in part be mediated by adverse changes in LV mechanical function. However, LVH also induces potentially arrhythmogenic changes in LV electrophysiology. Experimental evidence shows that LVH alters ventricular conduction and repolarization.5–14 In the 12-lead ECG, these changes may prolong the QRS and QT interval duration, respectively, and affect T-wave morphology.15–17 In hypertensive patients with ECG LVH, increase in LV mass was associated with prolonged QRS and QT interval duration and measures of QT dispersion.18 However, it is unknown if these ECG measures can further stratify risk in patients with LVH. Therefore, we investigated, in a large longitudinal study of hypertensive patients with ECG evidence of LVH, the value of QRS duration, QT interval duration, and QT dispersion as predictors of cardiovascular and all-cause mortality.

Methods

Study Population

The present study population originated from The Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) study. The study design, inclusion and exclusion criteria, baseline characteristics of the LIFE study population, and the main results of the LIFE study have been previously published.19–21 ECG evidence of LVH was an inclusion criterion in the LIFE study.19,20 The study was approved by institutional review committees, and all subjects gave informed consent. After randomization, target blood pressure was <140/90 mm Hg and patients were followed-up for at least 4 years. All 9193 patients included in the LIFE study were considered eligible for the present study, in which 5429 patients were included.

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The QT substudy center excluded the ECGs from 3764 patients from the present study before any knowledge of the outcome data because of the following reasons: (1) missing data (n = 236) or low quality of the received ECG (n = 130); (2) ECG recording not suitable for QT dispersion analysis (< 2 simultaneously recorded leads, amplitude calibration other than 10 mm/mV, or only 1 signal-averaged QRS-T complex in the ECG; n = 1570); (3) generally accepted exclusion criteria from QT measurements (atrial fibrillation, bundle branch block, heart rate <40 or >120 bpm; n = 889); and (4) QT dispersion measurement not technically feasible according to predefined criteria (wandering signal baselines, <6 leads with 2 measurable consecutive QRS-T complexes [<3 precordial leads], or drugs possibly affecting QT intervals: n = 939).

QRS Duration, QT Interval, and QT Dispersion Measures
A trained technician, unaware of the clinical data or the study design, performed all ECG QRS and QT interval measurements. The measurement procedure and intraobserver variability for measurements have been described in detail previously. QRS duration, QT\(_{\text{apex}}\) (QRS onset to T-wave apex), and QT\(_{\text{end}}\) (QRS onset to T-wave end) interval measurements were performed from ECGs recorded at the randomization visit. All included ECGs had an ECG paper speed of either 25 or 50 mm/s. For each patient, maximum QRS duration (referred to later as QRS duration) and maximum QT\(_{\text{apex}}\) and QT\(_{\text{end}}\) intervals in any lead were determined, and the latter were rate-adjusted with the nomogram (Nc) method (referred to later as QT\(_{\text{apex,Nc}}\) and QT\(_{\text{end,Nc}}\), respectively). QT\(_{\text{apex}}\) dispersion was defined as the standard deviation (SD) of all QT\(_{\text{apex}}\) intervals in the 12 leads (QT\(_{\text{apex,SD}}\)). QT\(_{\text{end}}\) SD was calculated in a similar fashion. Visible T-wave abnormalities (typical strain pattern and/or Minnesota codes 5:1 or 5:2) were defined as previously described.23,24

Outcome Measures
For the present study, cardiovascular mortality and all-cause mortality were prespecified as primary endpoints. We also used the LIFE study primary composite endpoint (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke).19,21

Statistical Analysis
The ECG analyses were prespecified as part of the LIFE ECG substudy protocol. Data were analyzed with SPSS version 10.0.7 software (SPSS Inc, Chicago, Ill). All continuous data are presented as mean±SD. Mean values were compared between groups by use of independent samples t test, except for ECG measures, which were compared by use of 2-way ANOVA adjusting for differences in ECG paper speed, because it has an effect on estimates of QT interval measures.19,23,24 Proportions were compared by \( \chi^2 \) tests. Outcome rates were calculated by the product-limit method and were plotted by the Kaplan-Meier method, with comparisons of outcome rates between dichotomized groups performed with the log-rank test. Dichotomized groups were created for QRS duration and each QT measure by the median value of the respective ECG measure in both ECG paper speed categories, because of the effect of ECG paper speed on QT variables, and because of the fact that outcome rates were slightly higher in centers using an ECG paper speed of 25 mm/s.

Outcome analyses for ECG measures were performed by Cox proportional hazard models by studying each ECG variable separately after adjusting for ECG paper speed. To test the independence of each ECG measure as a predictor of outcome, multivariate Cox models were used. Finally, to identify those ECG variables with the strongest predictive power, all ECG variables and covariates were included in the same multivariate Cox model. A 2-tailed \( P < 0.05 \) was considered statistically significant.

Results
Patient Characteristics
During the follow-up (mean follow-up 4.9±0.8 years), 214 (3.9%) patients died from cardiovascular causes, 417 patients (7.7%) died from all causes, and 581 patients (10.7%) experienced the LIFE study composite endpoint. Patients who experienced cardiovascular death compared with those who did not were older, more often men, and had higher baseline systolic blood pressure, Framingham risk score,27 baseline Sokolow-Lyon voltage, Cornell voltage duration product, and a greater decrease in systolic blood pressure (Table 1). There were no differences between these groups in baseline diastolic blood pressure or change in diastolic blood pressure. The results were similar when comparing those who experienced the LIFE study composite endpoint to those who did not (data not shown). Comparing those who died (all-cause mortality) to survivors, similar differences again were detected between groups, except baseline diastolic blood pressure was lower in those who died (Table 1).

QRS Duration, QT Measures, and Cardiovascular Mortality
The relations of QRS duration and QT measures to cardiovascular mortality and all-cause mortality are also shown in Table 1. All such ECG measures were greater in those patients who had cardiovascular death or all-cause death compared with those who did not experience the respective outcome measure. The results were similar comparing those who experienced the LIFE study composite endpoint to those who did not (data not shown).

Visible T-wave abnormalities were present in 1315 patients (24.2%) at study baseline (617 patients [11.4%] showed the typical strain pattern). QT\(_{\text{apex,Nc}}\) was longer in patients with visible T-wave abnormalities than in those without them (365±23 versus 353±22 ms, respectively; \( P < 0.0001 \)). Visible T-wave abnormalities were associated with cardiovascular and all-cause mortality (Table 1).

In Cox regression analyses, after adjusting for ECG paper speed, QRS duration and all QT measures separately predicted cardiovascular mortality (Table 2). After adjusting for QRS duration, QT\(_{\text{apex,Nc}}\) \( (P = 0.011) \) remained a predictor of cardiovascular mortality, whereas QT\(_{\text{end,Nc}}\) did not \( (P = 0.434) \). When stratifying the study population by QRS duration above and below the median values in both ECG paper speed categories, those above the median had cardiovascular death more often \( (P = 0.0006 \) by log-rank test; Figure). The results were similar for groups similarly dichotomized by median QT\(_{\text{apex,Nc}}\) \( (P = 0.0017 \) Figure), QT\(_{\text{apex,SD}}\) (hazard ratio [HR] 1.67 [95% CI: 1.27 to 2.20], \( P = 0.0002 \)), and QT\(_{\text{end,SD}}\) (HR 1.49 [95% CI: 1.13 to 1.95], \( P = 0.0042 \), whereas there was no significant difference in QT\(_{\text{end,Nc}}\) \( (P = 0.11) \). In separate multivariate Cox analyses adjusting each ECG measure for covariates (gender, baseline systolic and diastolic blood pressure, treatment arm [losartan or atenolol], baseline Framingham risk score, Sokolow-Lyon voltage and Cornell voltage duration product, ECG paper speed), QRS duration, QT\(_{\text{apex,Nc}}\), and QT\(_{\text{end,Nc}}\) remained significant predictors (Table 2), even after further adjustment for the presence of visible T-wave abnormalities in the ECG. After entering all ECG measures and covariates in the same model, QRS duration (\( \chi^2 = 5.3; P = 0.022 \); HR 1.16 per SD [13 ms] of QRS [95% CI: 1.09 to 1.24]) and QT\(_{\text{apex,Nc}}\) (\( \chi^2 = 4.3; \) \( P = 0.037 \); HR 1.16 per SD [23 ms] of QT\(_{\text{apex,Nc}}\) [95% CI: 1.08...
to 1.24) were independent predictors of cardiovascular mortality. In patients with both QRS duration and QT\textsubscript{apexNc} ≥ median, cardiovascular mortality rate was significantly higher than in patients who had both measures below the median (90/1514 [5.9%] versus 42/1501 [2.8%] patients, respectively; HR 2.14 [95% CI: 1.49 to 3.09], P<0.0001).

### QRS Duration, QT Measures, and All-Cause Mortality

In Cox regression analyses, after adjusting for ECG paper speed, QRS duration and all QT measures separately predicted all-cause mortality (Table 2). After adjusting for QRS duration, QT\textsubscript{apexNc} (P<0.001) and QT\textsubscript{endNc} (P=0.006) re-

### TABLE 1. Clinical and Electrocardiographic Variables in Relation to Cardiovascular and All-Cause Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cardiovascular Mortality</th>
<th>All-Cause Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>Survived (n=5215)</td>
<td>Died (n=214)</td>
</tr>
<tr>
<td>Gender, % male</td>
<td>66±7</td>
<td>71±7</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>174±14</td>
<td>177±14</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>98±9</td>
<td>97±10</td>
</tr>
<tr>
<td>Δ Systolic BP, mm Hg</td>
<td>-29.4±18.5</td>
<td>-32.4±19.4</td>
</tr>
<tr>
<td>Δ Diastolic BP, mm Hg</td>
<td>-16.6±9.7</td>
<td>-16.1±11.0</td>
</tr>
<tr>
<td>Framingham risk score, %</td>
<td>21.7±9.2</td>
<td>27.3±10.6</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage, mm</td>
<td>30.3±10.2</td>
<td>32.2±10.8</td>
</tr>
<tr>
<td>Cornell VP, mm×ms</td>
<td>2645±766</td>
<td>2837±895</td>
</tr>
<tr>
<td>ECG paper speed 50 mm/s, %</td>
<td>65.9</td>
<td>51.4</td>
</tr>
<tr>
<td>T-wave abnormality, %</td>
<td>23.4</td>
<td>45.3</td>
</tr>
<tr>
<td>QRS duration, ms</td>
<td>105±14</td>
<td>109±13</td>
</tr>
<tr>
<td>Maximum QT\textsubscript{endNc}, ms</td>
<td>426±25</td>
<td>430±24</td>
</tr>
<tr>
<td>Maximum QT\textsubscript{apexNc}, ms</td>
<td>357±23</td>
<td>363±22</td>
</tr>
<tr>
<td>QT\textsubscript{endSD}, ms</td>
<td>15.4±6.4</td>
<td>16.5±6.0</td>
</tr>
<tr>
<td>QT\textsubscript{apexSD}, ms</td>
<td>16.4±7.1</td>
<td>18.2±6.7</td>
</tr>
</tbody>
</table>

Values are mean±SD or proportions.

Δ indicates change (from baseline); BP, blood pressure; VP, voltage product; SD, standard deviation of the respective QT intervals; Nc, nomogram-corrected for heart rate.

### TABLE 2. Cox Proportional Hazards Models for Prediction of the Cardiovascular and All-Cause Mortality Examining ECG Measures as Continuous Variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Comparison, ms†</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>(\chi^2)</th>
<th>P</th>
<th>(\chi^2)‡</th>
<th>Pt‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prediction of cardiovascular mortality</td>
<td>QRS duration</td>
<td>13</td>
<td>1.28</td>
<td>1.21–1.36</td>
<td>19.2</td>
<td>&lt;0.0001</td>
<td>9.5</td>
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<tr>
<td></td>
<td>QT\textsubscript{endNc}</td>
<td>25</td>
<td>1.17</td>
<td>1.09–1.25</td>
<td>5.1</td>
<td>0.024</td>
<td>0.8</td>
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<tr>
<td></td>
<td>QT\textsubscript{apexNc}</td>
<td>23</td>
<td>1.27</td>
<td>1.19–1.36</td>
<td>13.1</td>
<td>0.0003</td>
<td>8.2</td>
</tr>
<tr>
<td></td>
<td>QT\textsubscript{endSD}</td>
<td>6.3</td>
<td>1.18</td>
<td>1.10–1.26</td>
<td>6.3</td>
<td>0.012</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>QT\textsubscript{apexSD}</td>
<td>7.1</td>
<td>1.27</td>
<td>1.19–1.36</td>
<td>13.5</td>
<td>0.0002</td>
<td>5.1</td>
</tr>
<tr>
<td>Prediction of all-cause mortality</td>
<td>QRS duration</td>
<td>13</td>
<td>1.21</td>
<td>1.16–1.27</td>
<td>20.0</td>
<td>&lt;0.0001</td>
<td>11.7</td>
</tr>
<tr>
<td></td>
<td>QT\textsubscript{endNc}</td>
<td>25</td>
<td>1.22</td>
<td>1.17–1.28</td>
<td>17.3</td>
<td>&lt;0.0001</td>
<td>11.2</td>
</tr>
<tr>
<td></td>
<td>QT\textsubscript{apexNc}</td>
<td>23</td>
<td>1.25</td>
<td>1.19–1.31</td>
<td>20.9</td>
<td>&lt;0.0001</td>
<td>14.8</td>
</tr>
<tr>
<td></td>
<td>QT\textsubscript{endSD}</td>
<td>6.3</td>
<td>1.12</td>
<td>1.06–1.17</td>
<td>5.2</td>
<td>0.023</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>QT\textsubscript{apexSD}</td>
<td>7.1</td>
<td>1.15</td>
<td>1.09–1.21</td>
<td>8.0</td>
<td>0.005</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Nc indicates nomogram-corrected for heart rate; SD, standard deviation of the respective QT intervals.

*All analyses adjusted for ECG paper speed.

†Relative risks calculated for a 1–SD (in the column) increase in the mean.

‡After adjusting for covariates (gender, baseline systolic and diastolic blood pressure, treatment arm [losartan or atenolol], Framingham risk score, baseline Sokolow-Lyon voltage, Cornell voltage duration product).
mained as significant predictors of all-cause mortality. When stratifying the study population by QRS duration above and below median values in both ECG paper speed categories, those above the median died more often (HR 1.10 per SD [13 ms] of QRS [95% CI: 1.05 to 1.16], P = 0.0009). In separate multivariate Cox analyses adjusting each ECG variable for covariates, QRS duration, QT apex Nc, and QT end Nc remained significant predictors (Table 2), even after further adjustment for the presence of visible T-wave abnormalities in the ECG. After entering all ECG measures and covariates in the same model, QT apex Nc (HR 1.17 per SD [23 ms] of QT apex Nc [95% CI: 1.11 to 1.23]) and QT end SD (HR 1.10 per SD [6.3 ms] of QT end SD [95% CI: 1.06 to 1.15]) were independent predictors of the LIFE study composite endpoint.

**Discussion**

**Main Findings**

The present results show that in hypertensive patients with ECG evidence of LVH, prolonged QRS duration, and maximum rate-adjusted QT apex interval (QT apex Nc; right panels) for cardiovascular mortality (upper panels) and all-cause mortality (lower panels). Median values were 106 ms (ECG paper speed 25 mm/s) and 100 ms (50 mm/s) for QRS duration, and 360 ms and 351 ms for QT apex Nc, respectively. See text for the rationale of equal proportions of patients from both paper speed categories in the 2 groups. The probability value is from the log-rank test. Hazard ratios (HR) with 95% confidence intervals (CI) are also shown.

QRS Duration, QT Intervals, and Mortality in Patients With LVH

The LIFE study included only patients with ECG evidence of LVH. In previous studies it has been shown that patients with ECG LVH, compared with those without ECG LVH, are at higher risk for cardiovascular mortality, including sudden cardiac death.1,3 Within the group of patients with LVH, the relative risk of these events increases as LV mass increases.2,4,28 Previously, we showed in a subgroup from the LIFE study that QRS duration and QT interval measures prolong as LV mass increases,18 suggesting that these ECG measures might identify LVH patients at even higher risk.

Our present results show that prolonged QRS duration is, independently of several baseline prognostic variables, associated with increased cardiovascular and all-cause mortality. An increased QRS duration was associated with a 28% higher

### Kaplan-Meier event–probability curves in patients above and below median values for QRS duration (left panels) and maximum rate-adjusted QT apex interval (QT apex Nc; right panels) for cardiovascular mortality (upper panels) and all-cause mortality (lower panels). Median values were 106 ms (ECG paper speed 25 mm/s) and 100 ms (50 mm/s) for QRS duration, and 360 ms and 351 ms for QT apex Nc, respectively. See text for the rationale of equal proportions of patients from both paper speed categories in the 2 groups. The probability value is from the log-rank test. Hazard ratios (HR) with 95% confidence intervals (CI) are also shown.
rate of cardiovascular mortality and a 21% higher rate of all-cause mortality for every SD of the mean increase in value within the range of studied values. Furthermore, QRS duration retained its independent predictive value when all QT interval variables were included in the model. In experimental studies, chronic LVH delays ventricular conduction, \(^5\) which seems to be related to an increase in intracellular resistivity caused by increased gap junctional resistance between adjacent cells, and to loss of conduction anisotropy. \(^6-7\) In the ECG, QRS duration is a measure of differences in activation times. \(^29\) The observed prognostic value of QRS duration in the present study may be related in part to the fact that delayed conduction per se is one of the factors increasing susceptibility to reentrant ventricular arrhythmias. In addition, prolonged QRS duration may be a marker of cellular uncoupling, and even small changes in cellular coupling may have profound effects on repolarization gradients at the myocardial level. \(^17,30\)

We also observed that prolongation of maximum rate-adjusted QT intervals were predictors of all outcome measures. An increased QT\(_{\text{apex}}\)Nc was associated with a 27% higher rate of cardiovascular mortality and a 25% higher rate of all-cause mortality for every SD of the mean increase in value within the range of studied values. QT\(_{\text{apex}}\)Nc was a predictor of all-cause and cardiovascular mortality independently of QRS duration, the other QT measures, and the studied covariates. Even when adjusting for the presence of visible T-wave abnormalities, QT\(_{\text{apex}}\)Nc remained a significant predictor of all-cause and cardiovascular mortality.

In experimental studies, LVH has been consistently associated with prolongation of action potential duration (APD), \(^8-13\) which may occur in a spatially heterogenous fashion, possibly increasing the arrhythmic vulnerability. \(^10-12,31,32\) In LVH, the changes in epicardial versus endocardial APDs have been disparate, with some studies showing prolongation of APD in the epicardium only, \(^13,33\) preferentially in the epicardium \(^12\) or preferentially in the endocardium. \(^34\) The mechanisms of these changes in LVH may be related, in part, to downregulation of the slow component of the delayed rectifier potassium current (I\(_{\text{Ks}}\)), \(^17,35,36\) as well as to prolongation of epicardial repolarization time (sum of activation time and APD), because of prolonged transmural activation time and loss of the inverse relation between activation time and APD as a consequence of reduced cell-to-cell coupling induced by fibrosis characteristic of pathological hypertrophy. \(^29,37\) In the electrogram, QT\(_{\text{apex}}\) interval reflects epicardial or endocardial APD depending on T-wave polarity. \(^16,17,29\) In the present study, visible T-wave abnormalities were more frequent in those patients who experienced cardiovascular and all-cause mortality, and QT\(_{\text{apex}}\)Nc was longer in patients with these abnormalities. Importantly, however, the predictive value of QT\(_{\text{apex}}\)Nc remained significant even after taking the presence of visible T-wave abnormalities into account, suggesting that QT\(_{\text{apex}}\)Nc is not just another way of characterizing T-wave inversions. In a population at high coronary risk, QT\(_{\text{apex}}\)Nc was a strong predictor of sudden cardiac death, but not of fatal myocardial infarction, \(^38\) possibly linking QT\(_{\text{apex}}\)Nc to arrhythmic vulnerability. In a subgroup of the LIFE study population, we observed regression of both ECG indices of LVH and echocardiographic LVH to be associated with a significant shortening of QT\(_{\text{apex}}\)Nc after 1 year of blood-pressure-lowering treatment, \(^24\) suggesting that effective treatment may partially reverse this adverse repolarization phenotype.

Interestingly, in the present study, patients with both prolonged QRS duration and QT\(_{\text{apex}}\)Nc seemed to be at substantially higher risk for mortality. In the normal myocardium, reduction in I\(_{\text{Ks}}\) prolongs APD in the epicardium and endocardium, but not in the M-cell region, prolonging the QT\(_{\text{apex}}\) interval in the ECG. \(^17\) The reduced repolarization reserve caused by decreased I\(_{\text{Ks}}\) activity may become arrhythmogenic in the presence of cellular uncoupling, a condition possibly reflected by prolonged QRS duration. \(^39,40\)

### QT Dispersion and Mortality in Patients With LVH

In univariate analysis QT\(_{\text{apex}}\) dispersion predicted all-cause and cardiovascular mortality. When controlling for several covariates of prognostic importance, QT\(_{\text{apex}}\)SD remained a predictor of cardiovascular mortality only, but not independently of maximum QT\(_{\text{apex}}\) interval. QT\(_{\text{end}}\) dispersion predicted all-cause and cardiovascular mortality only in univariate analysis, whereas it did predict the LIFE study composite endpoint even in multivariate analysis. Thus, QT\(_{\text{end}}\)SD does not independently further stratify risk of cardiovascular or all-cause mortality in patients with ECG LVH.

### Study Limitations

The LIFE study ECG recording procedure was not standardized; therefore, we excluded a significant proportion of ECGs because of technical reasons. However, the exclusion of ECGs was done before any knowledge of the outcome measures, and the present study population seems to be representative of the complete LIFE study population. Because the LIFE study included only patients with ECG-evidence of LVH, it affects the generalizability of the present results; therefore, the prognostic value of all these ECG variables should also be studied in an unselected population of hypertensive patients.

### Perspectives

The present results suggest that in hypertensive patients identified as being at high risk by the presence of ECG LVH, baseline QRS duration and QT\(_{\text{apex}}\)Nc interval can further stratify the risk of mortality despite an intervention to effectively lower blood pressure. It needs to be studied if these ECG parameters indeed are related to arrhythmogenesis, either directly or by preconditioning the myocardium in conjunction with, for example, sympathetic stimulation, ischemic episodes, or drugs affecting I\(_{\text{Ks}}\). Furthermore, the possible differential effects of the various classes of blood-pressure-lowering drugs on these ECG markers of risk need to be addressed.

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References

1. Kannel WB, Gordon T, Offutt D. Left ventricular hypertrophy by elec-


3. Kreger BE, Cupples LA, Kannel WB. The electrocardiogram in pre-


5. Winterton SJ, Turner MA, O’Gorman DJ, Flores NA, Sheridan DJ. Hy-

physiol. 1997;8:887–894.


8. Aronson RS. Characteristics of action potentials of hypertrophied myo-

9. Aronson RS. Afterpotentials and triggered activity in hypertrophied myo-


14. Kozhevinikov DO, Yamamoto K, Robotis D, Restivo M, El-Shereif N. Electrophysiological mechanism of enhanced susceptibility of hyper-


16. Yan GX, Antzelevitch C. Cellular basis for the normal T wave and the electrocardiographic manifestations of the long-QT syndrome. Cir-


25. Xu X, Rials SJ, Wu Y, Salafia JJ, Liu T, Bharucha DB, Marinchak RA, Kowey PR. Left ventricular hypertrophy decreases slowly but not rapidly activating delayed rectifier potassium currents of epicardial and endo-


28. Kimmel TB, Antzelevitch C. Prominent I Kr in epicardium and endo-
cardium contributes to development of transmural dispersion of repolar-

29. Norderman JM, Guo W. Heterogeneous expression of voltage-gated potassium channels in the heart: roles in normal excitation and arrhyth-
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