QRS-T angle as a predictor of sudden cardiac death in a middle-aged general population

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Aims Spatial QRS-T angle measured from a 12-lead electrocardiogram (ECG) has been shown to predict cardiac mortality. However, there is a paucity of studies on the prognostic significance of frontal QRS-T angle, which is more readily available from the standard 12-lead ECG. The purpose of the present study was to investigate the importance of wide frontal QRS-T angle, QRS-axis, and T-wave axis as cardiac risk predictors in general population.

Methods We evaluated the 12-lead ECGs of 10,957 Finnish middle-aged subjects from the general population recorded between 1966 and 1972, and followed them for 30 ± 11 years. QRS-T angle 0 to 90°, QRS-axis — 30 to 90°, and T-wave axis 0 to 90° were considered normal. The primary endpoint was death from arrhythmia, and the secondary endpoints were all-cause mortality and non-arrhythmic cardiac mortality. QRS-T angle ≥100° was present in 2.0% of the subjects, and it was associated with an increased risk of sudden arrhythmic death [relative risk (RR) 2.26; 95% confidence interval (CI) 1.59–3.21; P < 0.001] and all-cause mortality (RR 1.57; CI 1.34–1.84; P < 0.001), but not with non-arrhythmic cardiac mortality (RR 1.34; CI 0.93–1.92; P = 0.13). The prognostic significance of wide QRS-T angle was mainly due to abnormal T-wave axis, which predicted death from arrhythmia (RR 2.13; CI 1.63–2.79; P < 0.001), all-cause mortality (RR 1.39; 1.24–1.55; P < 0.001), and non-arrhythmic cardiac death (RR 1.87; CI 1.50–2.34; P < 0.001).

Conclusion Frontal QRS-T angle ≥100° increases the risk of arrhythmic death, this being mainly the result of an altered T-wave axis.

Keywords QRS-T angle • T-wave axis • Electrocardiography • Sudden cardiac death • Mortality • Population

Introduction

Abnormalities of ventricular depolarization and changes during the vulnerable repolarization phase in particular can predict future cardiovascular mortality. The spatial QRS-T angle defined as the angle between the directions of ventricular depolarization and repolarization combines both phenomena, and it has indeed been shown to predict cardiac death in various studies.1–4 However, measurement of the spatial QRS-T angle is not familiar to most clinicians and it is not routinely available from the computerized electrocardiographic analysis software currently in use.5 In contrast, frontal plane QRS-axis and T-wave axis are readily available from a standard 12-lead electrocardiogram (ECG) and are also usually included in the reports of automated ECG machines. QRS-T angle can be easily calculated from them, and it has been demonstrated to have a good correlation with the spatial QRS-T angle for risk prediction.6

There are few studies that have examined the long-term prognosis associated with the frontal QRS-T angle in general population samples. Therefore, we set out to investigate the prognostic significance of QRS-T angle in a large middle-aged population-based cohort with a mean follow-up of 30 years, and assessed separately how QRS-T angle, T-wave axis, and QRS-axis contribute to the risk of arrhythmic death in both genders.

Methods

Study population

The study population consists of subjects in the Finnish Social Insurance Institution’s Coronary Heart Disease Study (CHD Study) who had undergone clinical baseline examinations between 1966 and 1972, and included 35 population groups from four different areas of
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Finland representing the middle-aged Finnish population. The population groups included either the whole population of an area or randomly selected samples of larger population with known varying morbidity and mortality rates. The study cohort comprises a total of 10,957 subjects between the ages of 30 and 59 years (males 52.3%). Electrocardiograms presenting bundle branch block (N = 64) or pre-excitation pattern (N = 3) were excluded together with those having missing data or being otherwise unreadable (N = 58). Electrocardiograms with unreadable axis of QRS-complex or T-wave were excluded from respective analysis. Consequently, QRS-axis could be recorded from 10,778 subjects, T-axis from 10,750 subjects, and QRS-T angle from 10,713 subjects. A detailed account of the study rationale and procedures performed at the baseline examination has been described previously. Briefly, a standard 12-lead ECG was taken and blood pressure, body mass index, and serum cholesterol were measured. The subjects also completed a questionnaire regarding their health habits, medication, and known diseases. A specially trained nurse checked the questionnaire making sure that all the questions were answered appropriately. The use of beta-blockers or other medications potentially causing changes during cardiac repolarization was extremely rare at the time when baseline examinations were performed. Any symptoms of cardiovascular disease were documented during the examination using the Rose angina questionnaire.

Electrocardiographic measurements

At baseline, a standard 12-lead ECG was recorded with the subject at rest in supine position using a paper speed of 50 mm per second and a calibration of 1 mV per 10 mm. Measurements were carried out by nine-trained readers at the time of baseline examinations, and the results were transferred to an electrical database for further use. ST segment abnormalities were classified according to the Minnesota code, but this information was not used in the current study. QRS-axis and T-axis were determined manually at 10° intervals. QRS-axis was measured by examining the areas of positive and negative deflections using the hexaxial reference system. T-axis was determined by analysing in which frontal leads the highest T-waves were seen. The frontal QRS-T angle was calculated as the absolute value of difference between QRS- and T-axis yielding values between 0 and 180°, and it was categorized as normal (≤90°) or abnormal (≥100°). In addition, the QT-interval was measured and corrected according to Bazett’s formula, and the presence or absence of left ventricular hypertrophy was assessed using the Sokolow–Lyon criteria. To ensure the accuracy of electrocardiographic measurements, all readers were repeatedly evaluated using standard ECG material that was not part of the present study. When compared with the reference values, intraclass correlation coefficient (R-coefficient) between all readers and the test material was 0.97 for measuring QRS-axis and 0.98 for measuring T-wave axis. R-coefficient for intraserver correlation was 0.98 for measuring QRS-axis and 0.96 for measuring T-axis.

Follow-up

From the baseline examination between 1966 and 1972, the subjects were followed up for a mean of 30 ± 11 years until the end of 2007. The primary endpoint was sudden arrhythmic death, and secondary endpoints were all-cause mortality and non-arrhythmic cardiac death. The mortality data were determined from the Causes of Death Register maintained by Statistics Finland. Less than 2% of subjects were lost to follow-up as a result of moving abroad, but for the majority of subjects the survival status could still be determined even in this group. Because of the extensive administrative registers in Finland every death in the country is recorded, and the quality and reliability of these registers have been well validated previously. Death from cardiac causes was determined according to the relevant International Classification of Diseases (ICD) codes. All deaths from cardiac causes were reviewed by two experienced cardiologists (O.A., H.V.H.) to identify the arrhythmic deaths. After reviewing data available from death certificates and hospital records, the cardiac deaths were classified as probable arrhythmic deaths and deaths that were not likely associated with arrhythmia, based on the definitions presented in the Cardiac Arrhythmia Pilot Study. Death from arrhythmia was defined as spontaneous cessation of respiration and blood circulation with loss of consciousness in one of the following situations: witnessed and instantaneous without new or accelerating symptoms; witnessed and preceded or accompanied by symptoms attributable to myocardial ischaemia in the absence of heart failure; witnessed and preceded by symptoms attributable to cardiac arrhythmia (e.g. syncope); and unwitnessed but with no other identifiable cause of death. In the presence of severe congestive heart failure, arrhythmia was considered as the immediate cause of death only if it was judged that the patient would probably have survived at least 4 months had the arrhythmia not occurred.

Statistical analysis

All continuous data are presented as means ± SD. The general linear model was used to compare the age- and sex-adjusted mean values for continuous variables and the prevalence of categorical variables between the groups. The hazard ratios and 95% confidence intervals (CIs) for death was calculated using Cox proportional hazards model. The primary adjustments to these models were for age and sex, with further adjustments for covariates that differed between the groups or are known to predict cardiovascular mortality. Age, heart rate, and QRS duration were added as continuous variables and sex, smoking, chronotropic medication, and presence or absence of electrocardiographic signs of coronary artery disease or infarction were added as categorical variables. Kaplan–Meier survival curves were plotted for the QRS-T angle and T-wave axis. The statistical analyses were performed with SAS software, version 9.1.3 (SAS Institute) and with the Statistical Package for Social Studies, version 14.0 (SPSS). P value of <0.05 was considered to indicate statistical significance.

Results

Baseline characteristics

Of the 10,713 subjects with a measurable QRS-T angle, 52.2% were men, and the average age of the study group at baseline was 43.9 ± 8.4 years. The median value for QRS-T angle was 20°, and the median values for QRS-axis and T-axis were 40 and 30°, respectively. QRS-T angle did not differ between genders, with a mean QRS-T angle being 29° in men and women, or in different age groups. In subjects of 30–39 years, 40–49 years, and 50–59 years of age, mean QRS-T angle was 29, 28, and 30°, respectively. A wide QRS-T angle ≥100° was present in 212 (2.0%) of the subjects. The baseline characteristics of the subjects are presented in Table 1. The subjects with a wide QRS-T angle were older and more often male, were more likely to smoke, had higher blood pressure and resting heart rate, and had a longer duration of QRS complex. However, there was no difference in electrocardiographic left ventricular hypertrophy (LVH) or in the history of prior myocardial infarction between the two groups, but angina pectoris was more common in subjects with...
normal QRS-T angle. The mean QRS-axis for men and women was 39 and 36° (P < 0.001), respectively. Of the subjects 2.1% had a QRS-axis ≤ 40° and 1.3% had a QRS-axis ≥ 100°. The mean T-axis for men and women was 33 and 28° (P < 0.001), respectively. A negative T-axis (≤ −10°) was present in 4.4% (N = 509), and T-axis ≥ 100° in 0.7% (N = 46) of the subjects.

### Risk of death associated with wide QRS-T angle

During the follow-up (mean follow-up 30 ± 11 years) 6024 of the 10 713 subjects (56.2%) died. Of these deaths 1931 (32.1%) were from cardiac causes and 779 (40.3%) of these were classified as non-arrhythmic cardiac mortality (RR 1.34, 95% CI 0.93–1.92; significant difference in non-arrhythmic cardiac mortality (RR 1.34; CI 1.17–2.35; P < 0.001). When subjects without any apparent heart disease (N = 9864) and those with a suspected

#### Table 1 Characteristics of the subject at baseline by QRS-T angle classification

<table>
<thead>
<tr>
<th>QRS-T angle</th>
<th>Males (%)</th>
<th>Age (years)</th>
<th>Current smoker (%)</th>
<th>Cholesterol (mmol/L)</th>
<th>BMI (kg/m²)</th>
<th>Heart rate (b.p.m.)</th>
<th>Diastolic blood pressure (mmHg)</th>
<th>Electrocardiographic LVH (%)</th>
<th>QTc duration (ms)</th>
<th>Electrocardiographic LVH (%)</th>
<th>QTc duration (ms)</th>
<th>Electrocardiographic LVH (%)</th>
<th>QTc duration (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–90°</td>
<td>52.0</td>
<td>43.9 ± 8.4</td>
<td>33.8</td>
<td>6.50 ± 1.31</td>
<td>25.9 ± 3.8</td>
<td>75 ± 15</td>
<td>138 ± 21</td>
<td>31.6</td>
<td>87 ± 8</td>
<td>0.7</td>
<td>1.1</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>≥ 100°</td>
<td>59.6</td>
<td>48.7 ± 8.7</td>
<td>40.0</td>
<td>6.60 ± 1.53</td>
<td>25.5 ± 4.7</td>
<td>81 ± 16</td>
<td>144 ± 28</td>
<td>31.7</td>
<td>90 ± 10</td>
<td>20.1</td>
<td>0.1</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>N = 10 501</td>
<td>N = 212</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Plus-minus values are means ± SD. QTc denotes QT corrected for heart rate. To convert the values of cholesterol to milligrams per decilitre, divide by 0.02586.

*Adjusted for age.

*Adjusted for sex.

*Adjusted for age and sex.

*In leads other than V1 and aVR.

#### Table 2 Clinical outcomes associated with wide QRS-T angle

<table>
<thead>
<tr>
<th>QRS-T angle</th>
<th>All-cause mortality</th>
<th>Non-arrhythmic cardiac mortality</th>
<th>Sudden arrhythmic death</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–90°</td>
<td>1 1.34 (0.93–1.92)</td>
<td>1.57 (1.34–1.84)</td>
<td>2.26 (1.59–3.21)</td>
</tr>
<tr>
<td>≥ 100° (N = 10 501)</td>
<td>1.81 (1.55–2.11)</td>
<td>1.66 (1.17–2.35)</td>
<td>2.95 (2.11–4.14)</td>
</tr>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

*Adjusted for age, sex, smoking, heart rate, systolic blood pressure, chronotropic medication, QRS duration, electrocardiogram signs of coronary artery disease.

#### Figure 1 Kaplan–Meier survival plots for death from arrhythmia in subjects with wide QRS-T angle. Subjects with QRS-T angle ≥ 100° in a standard 12-lead electrocardiogram had an elevated risk of death from arrhythmia as compared with those with QRS-T angle < 100°, with a multivariate adjusted relative risk of 2.26 (95% confidence interval 1.59–3.21; P < 0.001).
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Table 3 Clinical outcomes associated with abnormal T-wave axis

<table>
<thead>
<tr>
<th>T-axis</th>
<th>P value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–90° (N = 10 195)</td>
<td>Other (N = 555)</td>
<td></td>
</tr>
</tbody>
</table>

All-cause mortality
- Number of deaths: 5682, 363
- Age- and sex-adjusted risk: 1.45 (1.31–1.62), <0.001
- Multivariate adjusted risk: 1.39 (1.24–1.55), <0.001

Non-arrhythmic cardiac mortality
- Number of deaths: 1111, 98
- Age- and sex-adjusted risk: 2.01 (1.63–2.47), <0.001
- Multivariate adjusted risk: 1.87 (1.50–2.34), <0.001

Sudden arrhythmic death
- Number of deaths: 713, 69
- Age- and sex-adjusted risk: 2.39 (1.87–3.06), <0.001
- Multivariate adjusted risk: 2.13 (1.63–2.79), <0.001

*Adjusted for age, sex, smoking, heart rate, systolic blood pressure, chronotropic medication, QRS duration, ECG signs of coronary artery disease.

Risk of death associated with abnormal QRS- and T-axis

Abnormal QRS-axis (≤ –40 or ≥ 100°) did not predict adverse outcome. Table 3 presents the risk of death associated with T-wave axis. Subjects with an abnormal T-axis (≤ –10 or ≥ 100°) had an increased risk of arrhythmic death (RR 2.13; CI 1.63–2.79; P < 0.001), an increased risk of death from any cause (RR 1.39; CI 1.24–1.55; P < 0.001), and a higher risk of non-arrhythmic death (RR 1.87; CI 1.50–2.34; P < 0.001). Figure 2 shows the Kaplan–Meier curves for sudden arrhythmic death in subjects with abnormal T-axis. Abnormal T-axis predicted adverse outcome in both genders with a RR for arrhythmic death 2.27 (CI 1.65–3.12, P < 0.001) in men and 1.74 (CI 1.06–2.86, P = 0.04) in women. When subjects with abnormal T-axis ≤ –10 and ≥ 100° were considered separately, the risk of adverse outcome persisted in both groups. Also when subjects with (N = 851) and without (N = 9899) any suspected heart disease were analysed separately, the risk of sudden arrhythmic death associated with abnormal T-axis remained essentially the same (RR 2.22; CI 1.26–3.91; P = 0.008 vs. RR 1.96; CI 1.43–2.68; P < 0.001, respectively).

Discussion

The results of the present study demonstrate that a wide frontal QRS-T angle measured from a standard 12-lead ECG increases the risk of arrhythmic death in excess of two-fold in both genders. The prognostic significance of a wide QRS-T angle was mainly due to an abnormal T-wave axis, while QRS-axis alone had no effect on prognosis.

The QRS-T angle is defined as the angle between the directions of ventricular depolarization and repolarization. Therefore, a wide QRS-T angle reflects either structural abnormalities affecting the depolarization or regional pathophysiological changes in ionic channels altering the sequence of repolarization. Previously, a few studies have evaluated the prognostic value of the spatial QRS-T angle. In an elderly general population cohort from Rotterdam, the Netherlands, the spatial QRS-T angle was found to be a strong predictor of cardiac mortality. More recently, in the large Women’s Health Initiative Study a wide spatial QRS-T angle was shown to be a significant predictor of incident congestive heart failure, CHD events, and mortality in women. The prognostic significance of the spatial QRS-T angle has also been demonstrated in a large clinical population from California, USA, where it was shown to independently predict cardiovascular mortality. Our results are in accordance with these previous studies. To the best of our knowledge, this is the first study to report on the prognostic value of the frontal QRS-T angle in a middle-aged general population. A wide QRS-T angle seemed to be associated with
arrhythmic mortality, as QRS-T angle did not predict non-
arrhythmic deaths in our study population. Interestingly, this risk
of arrhythmic death associated with a wide QRS-T angle was sub-
stantially greater than with some other well-known electrocardio-
graphic risk markers, such as prolonged QTc interval and LVH in
the same population. 12 This increased risk was mainly due to
changes in the T-wave axis, as an abnormal T-axis was associated
with a two-fold increase in the arrhythmic deaths.

In keeping with our results, T-axis deviation has been demon-
strated to be an independent risk factor for cardiac events in an
elderly population in some previous studies. 13,14 In contrast, left-
ward deviation of the QRS-axis, which is due to left anterior hemi-
block in the majority of cases, is considered to carry a benign
prognosis in the absence of cardiac disease. 15 Therefore, the prog-
nostic significance of an abnormal QRS-T angle is most likely to be
due to an abnormal axis of the T-wave, which reflects an abnormal
sequence of ventricular repolarization. As a result, subjects with a
wide QRS-T angle may be prone to ventricular rhythm disturbances
that may lead to a fatal arrhythmia. In fact, the vulnerability to
ventricular arrhythmias associated with a wide QRS-T angle has been
demonstrated in patients with cardiac disease. In an implantable
cardioverter-defibrillator (ICD) trial with patients having
non-ischaemic cardiomyopathy, a frontal QRS-T angle > 90° was
an independent predictor of a composite endpoint of death, appro-
priate ICD shock, and resuscitated cardiac arrest. 16 In another ICD
trial with primary prevention patients having ischaemic heart
disease, a wide QRS-T angle predicted ventricular arrhythmia. 17

The information about spatial QRS-T angle could be incorpo-
rated into the reports of modern computer-based electrocardio-
graphic machines, but currently this information is not generally
available. 9 In contrast, QRS- and T-axes are readily available
from a standard 12-lead ECG and the frontal QRS-T angle can
be easily calculated from them. Except for the case in which the
QRS- or T-axis is lying exactly in the horizontal plane, any
change in their direction will be projected to the frontal plane as
well, and frontal plane QRS-T angle has indeed been demonstrated
to be a suitable clinical substitute for spatial QRS-T angle for risk
prediction. 6 The frontal QRS-T angle could not be determined in
<2% of subjects in the present study, mainly due to intraventricu-
lar conduction block or indifferent electrical axis of the heart.
Although these changes might represent an abnormality by
themselves, ECG recordings with indifferent QRS- or T-axis were
excluded from the analysis. The thresholds for distinguishing
between a normal and abnormal QRS-T angle has varied in differ-
ent studies, and the optimal cut-off values can also differ between
genders. Based on previous studies and for simplicity, we defined a
QRS-T angle ≥ 100° as abnormal. When subjects with QRS-T
angles between 50 and 90° were considered separately and com-
pared with those having QRS-T angle < 50°, no significant increase
in mortality was observed in either sexes.

A limitation of the present study is that echocardiography
was not available at the time of the baseline study in late 1960s.
Therefore, the presence and prevalence of structural heart
disease in those subjects with an abnormal T-wave axis is not
exactly known. Despite this limitation, the present data suggest
that echocardiography should perhaps be performed to diagnose
the subclinical cardiac disease among those with a wide QRS-T
angle in a standard 12-lead ECG, which is routinely recorded in
a large number of asymptomatic subjects.

In summary, a wide QRS-T angle in a standard 12-lead ECG is a
strong and independent predictor of fatal arrhythmias in both men
and women. The risk associated with a wide QRS-T angle is mostly
due to an abnormal T-wave axis, which can be an early marker
of myocardial damage. Therefore, when interpreting an ECG, a
measurement of T-axis, and QRS-T angle should be included
in the analysis to identify individuals in need of more careful
evaluation and closer monitoring.

**Conflict of interest:** none declared.

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