Heart Rate Variability and Dispersion of QT Interval in Patients With Vulnerability to Ventricular Tachycardia and Ventricular Fibrillation After Previous Myocardial Infarction

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Objectives. This study was designed to compare QT dispersion measured from the standard 12-lead electrocardiogram and 24-h heart rate variability in patients with vulnerability to either ventricular tachycardia or ventricular fibrillation after a previous myocardial infarction.

Background. Increased QT interval dispersion and reduced heart rate variability have been shown to be associated with vulnerability to ventricular tachyarrhythmias, but the data have mainly been pooled from patients with presentation of stable ventricular tachycardia and ventricular fibrillation.

Methods. QT dispersion and time domain and two-dimensional vector analysis of heart rate variability were studied in 30 survivors of ventricular fibrillation with a previous myocardial infarction and with inducible unstable ventricular tachyarrhythmia by programmed electrical stimulation and in 30 postinfarction patients with clinical and inducible stable monomorphic sustained ventricular tachycardia. Both of these patient groups were matched, with respect to age, gender and left ventricular ejection fraction, with an equal number of postinfarction control subjects without a history of arrhythmic events or inducible ventricular tachyarrhythmia and arrhythmia-free survival during a follow-up period of 2 years. Forty-five age-matched healthy subjects served as normal control subjects.

Results. Standard deviation of all sinus intervals and long-term continuous RR interval variability analyzed from Poincaré plots were reduced in patients with vulnerability to ventricular fibrillation (p < 0.001 for both), but not in patients with ventricular tachycardia (p = NS for both), compared with postinfarction control subjects. Corrected QT (QTc) dispersion was significantly broader both in patients with ventricular fibrillation (p < 0.001) and in those with ventricular tachycardia (p < 0.05) than in matched postinfarction control subjects. Heart rate variability performed better than QTc dispersion in predicting vulnerability to ventricular fibrillation.

Conclusions. Increased QT dispersion is associated with vulnerability to both ventricular tachycardia and ventricular fibrillation. Low heart rate variability is specifically related to susceptibility to ventricular fibrillation but not to stable monomorphic ventricular tachycardia, suggesting that the autonomic nervous system modifies the presentation of life-threatening ventricular arrhythmias.

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Broad QT dispersion (i.e., increased variability in the QT interval length between the leads of a 12-lead surface electrocardiogram [ECG]) reflects differences in the local myocardial repolarization/recovery times (1–6) and hence the electrophysiologic environment (substrate) that favors reentry (7–10). Low heart rate variability, an indicator of abnormal cardiac autonomic regulation, may condition the heart to a spontaneous onset of ventricular tachyarrhythmias but is not a specific marker of an arrhythmic substrate (11). Both increased QT dispersion and reduced heart rate variability have been shown (10,12–14) to be associated with vulnerability to life-threatening ventricular arrhythmias in patients with a previous myocardial infarction. However, the data have mainly been pooled from patients with presentation of stable ventricular tachycardia and ventricular fibrillation, without regard for possible differences in the underlying pathophysiologic mechanisms of the two arrhythmias. In the present work, we compared QT dispersion and heart rate variability between groups with different clinical and electrophysiologic presentations of ventricular tachyarrhythmia after a previous myocardial infarction.

Methods

Patients. The study included 94 consecutive patients with coronary artery disease admitted to the Oulu University Hospital (n = 88) or the Miami University Medical Center (n = 6)
because of ventricular tachycardia or ventricular fibrillation and 70 consecutive patients with a previous myocardial infarction referred to the Oulu University Hospital for coronary angiography but with no history of ventricular tachyarrhythmia (postinfarction control subjects). Of the 94 patients with a history of arrhythmic events, 59 underwent resuscitation for ventricular fibrillation, and of these 59 patients ventricular fibrillation (n = 8) or hemodynamically unstable ventricular tachycardia (polymorphic ventricular tachycardia in 11, ventricular flutter in 11) was induced during programmed electrical stimulation in 30. Thirty-five of these 94 patients presented with hemodynamically stable ventricular tachycardia, and stable monomorphic ventricular tachycardia during programmed electrical stimulation was induced in 30 of these 35 patients.

Patients with clinical presentation of ventricular fibrillation and inducible unstable ventricular tachyarrhythmia and those with clinical and inducible monomorphic sustained ventricular tachycardia were matched with respect to age, left ventricular ejection fraction and gender with corresponding control postinfarction patients without inducible nonsustained or sustained ventricular tachycardia during programmed electrical stimulation and without death or an occurrence of ventricular tachyarrhythmia during the follow-up period of 2 years. The matched variables were scaled as follows: 1) age between 45 and 50 years, 50 and 55 years, 55 and 60 years, 60 and 65 years, 65 and 70 years and >70 years; 2) left ventricular ejection fraction <20%, 20% to 25%, 25% to 30%, 30% to 35%, 35% to 40%, 40% to 45%, 45% to 50% or >50%; and 3) male or female gender. Each patient in both arrhythmia groups was matched 1:1 with a control postinfarction patient according to these criteria. Forty-five age- and gender-matched healthy subjects (mean [±SD] age 60 ± 12 years; 40 men, 5 women) served as normal control subjects and were selected from among subjects who were participating in a larger trial comparing the characteristics of hypertensive and normotensive subjects, the latter group having been randomly selected from the general population of Oulu on the basis of their social security numbers. They had all undergone a complete physical examination and had a medical history that revealed no cardiovascular disease or medication. They also had normal blood pressure levels; normal 12-lead ECG and M-mode, two-dimensional and doppler echocardiographic results; and none had evidence of ischemic ST segment depression on exercise electrocardiography. Patients and healthy control subjects gave their informed consent, and the tests were approved by the ethics committee of the University of Oulu.

All patients with and without arrhythmias were examined by cardiac catheterization, coronary angiography and programmed electrical stimulation. A 12-lead surface ECG was recorded in each patient at a 50-mm/s paper speed. The clinical and angiographic characteristics of the postinfarction patients are presented in Table 1.

Electrophysiologic and angiographic studies. Electrophysiologic testing included incremental ventricular pacing and programmed ventricular stimulation using up to three extra-stimuli and two basic drive cycle lengths (600 and 400 ms) from the right ventricular apex and the outflow tract. The protocol of the electrophysiologic testing and the definitions of induc-

### Table 1. Clinical and Angiographic Characteristics of Study Patients*

<table>
<thead>
<tr>
<th></th>
<th>VF Group (n = 30)</th>
<th>VF Control Group (n = 30)</th>
<th>VT Group (n = 30)</th>
<th>VT Control Group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yr)</strong></td>
<td>64 ± 6</td>
<td>61 ± 6</td>
<td>64 ± 7</td>
<td>61 ± 5</td>
</tr>
<tr>
<td><strong>Men/women</strong></td>
<td>26/4</td>
<td>26/4</td>
<td>27/3</td>
<td>27/3</td>
</tr>
<tr>
<td><strong>Time since prior MI (mo)</strong></td>
<td>22 ± 30</td>
<td>35 ± 44</td>
<td>39 ± 46</td>
<td>37 ± 42</td>
</tr>
<tr>
<td><strong>Medication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Ca blocker</td>
<td>4</td>
<td>9</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>17</td>
<td>21</td>
<td>11†</td>
<td>20</td>
</tr>
<tr>
<td>Digitalis</td>
<td>15</td>
<td>10</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Diuretic drugs</td>
<td>14</td>
<td>16</td>
<td>7†</td>
<td>15</td>
</tr>
<tr>
<td><strong>NYHA functional class</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
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<td>II</td>
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<td>IV</td>
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<td><strong>Coronary angiography</strong></td>
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<tr>
<td>1 VD</td>
<td>3</td>
<td>4</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>2 VD</td>
<td>11</td>
<td>7</td>
<td>13†</td>
<td>6</td>
</tr>
<tr>
<td>3 VD</td>
<td>15</td>
<td>19</td>
<td>8†</td>
<td>18</td>
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<tr>
<td><strong>LVEF (%)</strong></td>
<td>40 ± 9</td>
<td>42 ± 6</td>
<td>42 ± 11</td>
<td>41 ± 6</td>
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<td><strong>Location of MI</strong></td>
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<tr>
<td>Ant</td>
<td>15</td>
<td>15</td>
<td>16</td>
<td>13</td>
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<td>Inf</td>
<td>6</td>
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<td>Multiple</td>
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<td>9</td>
</tr>
<tr>
<td><strong>VPD class</strong></td>
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</tr>
<tr>
<td>1 (&lt;10 VPDs/h)</td>
<td>13</td>
<td>18</td>
<td>20</td>
<td>16</td>
</tr>
<tr>
<td>2 (10–30 VPDs/h)</td>
<td>7</td>
<td>6</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>3 (&gt;30 VPDs/h)</td>
<td>10</td>
<td>6</td>
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<td>6</td>
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<tr>
<td><strong>NSVT on Holter</strong></td>
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<td></td>
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<tr>
<td></td>
<td>6</td>
<td>6</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

*All with a previous myocardial infarction (MI). †p < 0.05, arrhythmic group versus corresponding control group. Data presented are mean value ± SD or number of patients. ACE = angiotensin-converting enzyme; Ant = anterior; Ca = calcium; Inf = inferior; LVEF = left ventricular ejection fraction; NSVT = nonsustained ventricular tachycardia; NYHA = New York Heart Association; VD = vessel disease; VF Control Group = matched control subjects for the VF Group (ventricular fibrillation [VF]); VT Control Group = matched control subjects for the VT Group (clinical and inducible stable monomorphic ventricular tachycardia).
ible arrhythmias have been described previously (15). If ven-
tricular tachyarrhythmia was inducible with three extrastimuli
and the shortest coupling interval was <200 ms, the arrhythmia
was classified as nonclinical. Left-sided cardiac catheterization
was performed using the Judkins technique. Selective coronary
ertery angiograms were obtained in multiple projections, in-
cluding caudal and cranial views, and a lumen narrowing
>50% was considered significant stenosis.

Measurement of QT interval and dispersion. The QT and
QT apex (QTa) intervals and the QRS complex duration were
measured at each lead of the 12-lead surface ECG for two
consecutive cycles. The details of the method of measuring the
dispersion of intervals have been previously described (10).
The QTa intervals were measured from the onset of the QRS
complex to the apex of the T wave. QRS duration was
measured from the beginning of the QRS complex to its end.
The T end (Te) interval (from the apex of the T wave to its
end) was calculated from the equation Te = QT – QTa and
the JT interval (from the J point to the end of the T wave) from
the equation JT = QT – QRS. The measurements were
performed manually by an experienced observer (J.S.P.) who
had no knowledge of the clinical data of the patients. The QT,
QTa, Te and JT dispersions were defined as the differences
between the maximal and minimal QT, QTa, Te and JT values,
respectively, and the mean value of two consecutive cycles was
calculated. The Bazett formula was used to obtain heart
rate-corrected values of the QT intervals and the QTc, Te
and JT dispersions. An ECG was recorded 2 to 7 days after the
arrhythmic event, before the electrophysiologic studies. Pa-
patients were excluded from the QT dispersion analysis if no
technically relevant ECG had been recorded during that
period. ECGs were excluded if the rhythm was paced, atrial
fibrillation or atrial flutter occurred, or if the QT interval could
not be accurately measured on at least six leads.

Analysis of heart rate variability. The patients were exam-
ined with an ambulatory ECG recorder for a 24-h period
(Dynacord Holter Recorder, model 420, DM Scientific). The
ECG data were transferred from the Del Mar Avionics scanner
(model 500) to a microcomputer for analysis of heart rate
variability by a method described in detail previously (16,17).
Premature beats and noise were excluded both automatically
and manually, and the gaps were then refilled with an average
value. Patients with segments with <85% qualified beats were
excluded from the analysis.

Heart rate variability was analyzed by a measurement of the
standard deviation of all sinus intervals from the 24-h period
and by measuring separately the instantaneous and continuous
RR interval variability by using a two-dimensional vector
analysis technique recently described in detail (18). Briefly, the
Poincaré plot is a diagram in which each RR interval of a
tachogram is plotted as a function of the previous RR interval
for a predetermined segment length. The program used in
these experiments provides a graphic display of the plots and a
quantitative analysis of the shape of the scattergrams. The
scattergrams of successive RR intervals were plotted for the
24-h period throughout the 24-h recording period. The stan-
dard deviation of instantaneous RR interval variability and the
standard deviation of long-term continuous RR interval vari-
ability were then analyzed (18). The standard deviation of all
sinus intervals and the standard deviation of long-term contin-
uous RR interval variability were calculated as absolute values
and in normalized units obtained by dividing the absolute value
by the average RR interval and multiplying by 1,000.

Statistical methods. A nonparametric independent sample
t test (Mann-Whitney) was used to estimate the differences in
the QT and heart rate variability values between the patient
groups and the matched postinfarction control group, and the
Kruskal-Wallis test was used to compare patients with different
clinical presentations of arrhythmia. Analysis of covariance
was used for comparison of corrected QT (QTc) dispersion
and heart rate variability between the ventricular tachycardia
group and the matched postinfarction control group adjusting
for baseline differences in clinical and angiographic variables.
When analyzing the sensitivity, specificity and accuracy of the
different measures of heart rate variability and QTc dispersion
in identifying the patients with vulnerability to ventricular
fibrillation or ventricular tachycardia, the 95% percentiles of
the heart rate variability values and QTc dispersion obtained
from the healthy subjects were used as cutoff points for
abnormal heart rate variability and QTc dispersion, respec-
tively. p < 0.05 was considered significant. Receiver operating
characteristic curves, which show sensitivity as a function of the
complement of specificity, were calculated using GraphROC
software (19).

Results

Clinical and angiographic data. Clinical and angiographic
data for the study patients are presented in Table 1. Age,
gender, time from previous myocardial infarction, left ventric-
ular ejection fraction and infarct location did not differ signif-
icantly between the arrhythmia groups and the corresponding
matched postinfarction control group. The patients in the
ventricular tachycardia group used beta-adrenergic blocking
agents and diuretic drugs less often than the matched postin-
farction control group. Otherwise, medication did not differ
significantly between the arrhythmia groups and the corre-
sponding control group. The frequency of ventricular prema-
ture depolarizations or the occurrence of nonsustained ven-
tricular tachycardia on the Holter recordings did not differ
significantly between the arrhythmia groups and the corre-
sponding postinfarction control group.

Heart rate variability. In the group of 45 healthy subjects,
the standard deviation of all sinus intervals was (mean ± SD)
150 ± 40 ms (range 79 to 228, cutoff point 94), and the
standard deviation of long-term continuous RR interval vari-
ability was 125 ± 38 ms (range 62 to 223, cutoff point 70). The
standard deviations of all sinus intervals and long-term contin-
uous RR interval variability were significantly lower in the
ventricular fibrillation group than in the postinfarction control
group (Table 2). The 24-h mean RR interval was also shorter
in the ventricular fibrillation group than in the postinfarction
control group, but the differences in the standard deviation of all sinus intervals and the standard deviation of long-term continuous RR interval variability remained significant after normalization of the values with the average heart rate. None of the measures of heart rate variability differed between the patients with stable ventricular tachycardia and the postinfarction control subjects (Table 2), even after adjusting for beta-blocker and diuretic medication and angiographic severity of coronary artery disease. The standard deviations of all sinus intervals and long-term continuous RR interval variabilities for the original study cohort according to the presenting clinical arrhythmia are shown in Table 3.

QT dispersion and QT intervals. In the group of 45 healthy subjects, the QTc dispersion was 56 ± 19 ms (range 25 to 101, cutoff point 94). All the measures of QTc dispersion were significantly broader in the patients with ventricular fibrillation than in the postinfarction control subjects. The QTc maximal and minimal intervals were longer and the RR interval shorter in the ventricular fibrillation group than in the postinfarction control group (Table 4).

QTc and corrected QTa (QTc) dispersion were signifi-

Table 2. Heart Rate Variability

<table>
<thead>
<tr>
<th></th>
<th>VF Group (n = 29)</th>
<th>VT Group (n = 29)</th>
<th>VT Control Group (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg RRi (ms)</td>
<td>734 ± 20‡</td>
<td>745 ± 146</td>
<td>955 ± 146</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>68 ± 26</td>
<td>110 ± 27</td>
<td>108 ± 37</td>
</tr>
<tr>
<td>SDNNn (ms)</td>
<td>115 ± 26</td>
<td>106 ± 33</td>
<td>107 ± 18</td>
</tr>
<tr>
<td>SD1 (ms)</td>
<td>17 ± 10</td>
<td>23 ± 14</td>
<td>22 ± 11</td>
</tr>
<tr>
<td>SD2 (ms)</td>
<td>55 ± 22</td>
<td>99 ± 28</td>
<td>96 ± 35</td>
</tr>
<tr>
<td>SD2n (ms)</td>
<td>66 ± 23</td>
<td>102 ± 20</td>
<td>95 ± 32</td>
</tr>
</tbody>
</table>

*p < 0.01, †p < 0.001, ‡p < 0.05, arrhythmic group versus corresponding control group. Data presented are mean value ± SD. Avg RRi = average RR interval; SDNN = standard deviation of sinus RR intervals analyzed from 24-h Holter recordings; SDNNn = SDNN divided by the average RR interval and multiplied by 1,000; SD1 = standard deviation of instantaneous RR interval variability; SD2 = standard deviation of long-term continuous RR interval variability (see Methods for details); SD2n = SD2 divided by the average RR interval and multiplied by 1,000; other abbreviations as in Table 1.

Table 3. Heart Rate Variability and QTc Dispersion for the Original Study Cohort According to Presenting Clinical Arrhythmia

<table>
<thead>
<tr>
<th></th>
<th>VF</th>
<th>VT</th>
<th>No VT</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD2 (ms)</td>
<td>74 ± 20‡</td>
<td>91 ± 36</td>
<td>100 ± 32</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(n = 56)</td>
<td>(n = 58)</td>
<td>(n = 58)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>86 ± 33§</td>
<td>104 ± 37</td>
<td>108 ± 30</td>
<td>0.001</td>
</tr>
<tr>
<td>(n = 59)</td>
<td>(n = 60)</td>
<td>(n = 60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>QTc dis (ms)</td>
<td>98 ± 40§</td>
<td>98 ± 40</td>
<td>70 ± 32</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(n = 47)</td>
<td>(n = 49)</td>
<td>(n = 49)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*See Methods. †Kruskal-Wallis test. §p < 0.001, ‡p < 0.01, patients with clinical presentation of ventricular fibrillation (VF) versus those with no ventricular tachyarrhythmias (Bonferroni post hoc test). †p < 0.01, patients with clinical presentation of sustained stable ventricular tachycardia (VT) versus those with no ventricular tachyarrhythmias (Bonferroni post hoc test). Data presented are mean value ± SD. QTc dis = corrected QT interval dispersion; other abbreviations as in Tables 1 and 2.

Table 4. RR Interval, QT Intervals and QT Dispersion

<table>
<thead>
<tr>
<th></th>
<th>VF Group (n = 23)</th>
<th>VT Group (n = 27)</th>
<th>VT Control Group (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RRi (ms)</td>
<td>833 ± 115</td>
<td>967 ± 210</td>
<td>1022 ± 210</td>
</tr>
<tr>
<td>QTc max (ms)</td>
<td>520 ± 51†</td>
<td>454 ± 27</td>
<td>487 ± 48§</td>
</tr>
<tr>
<td>QTc min (ms)</td>
<td>406 ± 34†</td>
<td>386 ± 27</td>
<td>388 ± 32</td>
</tr>
<tr>
<td>QTc dis (ms)</td>
<td>113 ± 42‡</td>
<td>68 ± 32</td>
<td>99 ± 43‡</td>
</tr>
<tr>
<td>QT dis (ms)</td>
<td>103 ± 37§</td>
<td>67 ± 32</td>
<td>98 ± 43‡</td>
</tr>
<tr>
<td>QTc dis (ms)</td>
<td>95 ± 39‡</td>
<td>62 ± 34</td>
<td>79 ± 32‡</td>
</tr>
<tr>
<td>QTa dis (ms)</td>
<td>86 ± 35‡</td>
<td>61 ± 33</td>
<td>79 ± 32‡</td>
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<tr>
<td>Tec dis (ms)</td>
<td>68 ± 35‡</td>
<td>44 ± 19</td>
<td>53 ± 22</td>
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<tr>
<td>Te dis (ms)</td>
<td>62 ± 32</td>
<td>43 ± 19</td>
<td>54 ± 24</td>
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<tr>
<td>JTc dis (ms)</td>
<td>117 ± 38†</td>
<td>73 ± 31</td>
<td>104 ± 44</td>
</tr>
<tr>
<td>JT dis (ms)</td>
<td>106 ± 35†</td>
<td>71 ± 32</td>
<td>104 ± 45</td>
</tr>
</tbody>
</table>

*p < 0.05, †p < 0.001, ‡p < 0.01, arrhythmic group versus corresponding control group. Data presented are mean value ± SD (ms). dis = dispersion; JTc = corrected JT interval; QTc max = maximal corrected QT interval; QTc min = minimal corrected QT interval; QTa = QT apex interval; QTc = corrected QT apex interval; Te = T end interval; Tec = corrected T end interval; other abbreviations as in Tables 1 and 2.

There was no significant correlation between QTc dispersion and the standard deviation of long-term continuous RR interval variability (r = 0.11, p = NS) or QTc dispersion and the standard deviation of all sinus intervals (r = 0.13, p = NS). The values of QTc dispersion for the original study cohort according to the presenting clinical arrhythmia are shown in Table 3.

Accuracy of QTc dispersion and heart rate variability in predicting susceptibility to ventricular tachyarrhythmias. The sensitivity, specificity and positive and negative predictive accuracy of QTc dispersion, the standard deviation of long-term continuous RR interval variability and the standard deviation of all sinus intervals in predicting vulnerability to ventricular fibrillation and ventricular tachycardia are shown in Table 5. The specificity of the standard deviation of long-term continuous RR interval variability was higher than that of QTc dispersion in identifying the patients with vulnerability to ventricular fibrillation, but QTc dispersion was more accurate than the standard deviation of long-term continuous RR interval variability or the standard deviation of all sinus intervals in identifying vulnerability to ventricular tachycardia (Table 5). The standard deviation of long-term continuous RR interval variability was more specific than the standard devia-
tion of all sinus intervals in predicting vulnerability to ventricular fibrillation (Table 5) because of complex Poincaré plots of some arrhythmic patients, resulting in high standard deviation of all sinus intervals but not of long-term continuous RR interval variability analyzed from the Poincaré plots. The receiver operating characteristic curves also show that the standard deviation of long-term continuous RR interval variability performed better than QTc dispersion in predicting vulnerability to ventricular fibrillation (Fig. 1), but QTc dispersion was better than the standard deviation of long-term continuous RR interval variability in predicting vulnerability to ventricular tachycardia at all sensitivity and specificity levels (Fig. 2).

**Discussion**

The results of the present study, which was specifically designed to differentiate between patients with clinical and electrophysiologic presentation of stable monomorphic ventricular tachycardia or ventricular fibrillation and carefully matched postmyocardial infarction patients without arrhythmic propensity, showed that QT interval dispersion is increased in patients with vulnerability to both stable and unstable arrhythmia, but low heart rate variability is observed only in patients with ventricular fibrillation versus matched postinfarction patients. In previous studies (10,13,14,20–23), measurements of QT interval dispersion from surface ECGs and heart rate variability from Holter recordings have provided important prognostic information after myocardial infarction. However, significant overlapping in the measures of QT dispersion and heart rate variability has been observed between patients with and without susceptibility to ventricular tachyarrhythmias, and the positive predictive accuracy of these noninvasive measures in predicting arrhythmic events has been relatively low (10–14,23). Both cross-sectional and follow-up studies have used mixed patient populations and definitions of arrhythmic events by including pooled data from patients with presentation of stable monomorphic ventricular tachycardia and ventricular fibrillation. However, there is evidence to suggest that the mechanisms of initiation and perpetuation of these arrhythmias may differ significantly, and the data support the assumption that the electrophysiologic substrate differs between patients with ventricular tachycardia and ventricular fibrillation (24,25). There is also evidence to suggest that patients presenting with stable sustained ventricular tachycardia are less likely to experience a lethal recurrence of arrhythmia than are patients presenting with ventricular fibrillation (24,25). There is also evidence to suggest that the mechanisms of initiation and perpetuation of these arrhythmias may differ significantly, and the data support the assumption that the electrophysiologic substrate differs between patients with ventricular tachycardia and ventricular fibrillation (24,25). There is also evidence to suggest that patients presenting with stable sustained ventricular tachycardia are less likely to experience a lethal recurrence of arrhythmia than are patients presenting with ventricular fibrillation (24,25). There is also evidence to suggest that patients presenting with stable sustained ventricular tachycardia are less likely to experience a lethal recurrence of arrhythmia than are patients presenting with ventricular fibrillation (24,25). There is also evidence to suggest that patients presenting with stable sustained ventricular tachycardia are less likely to experience a lethal recurrence of arrhythmia than are patients presenting with ventricular fibrillation (24,25). There is also evidence to suggest that patients presenting with stable sustained ventricular tachycardia are less likely to experience a lethal recurrence of arrhythmia than are patients presenting with ventricular fibrillation (24,25).

Heart rate variability and vulnerability to ventricular tachyarrhythmias. In contrast to the patients with vulnerability to ventricular fibrillation, the patients presenting with stable monomorphic ventricular tachycardia did not show reduced heart rate variability compared with the postinfarction patients without arrhythmic propensity. Farrell et al. (29) reported that patients with inducible monomorphic ventricular tachycardia after an acute myocardial infarction have reduced baroreflex sensitivity and heart rate variability. These results are not comparable to the present findings because the substrate and the triggers of ventricular tachyarrhythmias may be different in patients with subacute and remote myocardial infarction. The present data suggest that neurohumoral or other factors

**Table 5.** Sensitivity, Specificity and Positive and Negative Predictive Accuracy of QTc Dispersion and Heart Rate Variability in Predicting Vulnerability to Ventricular Tachyarrhythmias

<table>
<thead>
<tr>
<th></th>
<th>QTc Dis</th>
<th>SD2</th>
<th>SDNN</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT Sens (%)</td>
<td>65 (49)</td>
<td>83 (52)</td>
<td>90 (64)</td>
</tr>
<tr>
<td>Spec (%)</td>
<td>81 (84)</td>
<td>93 (90)</td>
<td>60 (58)</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>75 (74)</td>
<td>92 (83)</td>
<td>69 (60)</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>73 (63)</td>
<td>85 (66)</td>
<td>86 (62)</td>
</tr>
<tr>
<td>VT Sens (%)</td>
<td>46 (45)</td>
<td>29 (39)</td>
<td>31 (41)</td>
</tr>
<tr>
<td>Spec (%)</td>
<td>77 (84)</td>
<td>90 (90)</td>
<td>52 (58)</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>67 (62)</td>
<td>73 (67)</td>
<td>39 (34)</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>59 (72)</td>
<td>57 (74)</td>
<td>43 (65)</td>
</tr>
</tbody>
</table>

Values ≥94, ≤70 and ≤94 ms were considered abnormal for QTc dispersion, SD2 and SDNN, respectively. Data presented are values calculated for study groups (original study cohort according to the presenting clinical arrhythmia). NPV = negative predictive value; PPV = positive predictive value; Sens = sensitivity; Spec = specificity; other abbreviations as in Tables 1 to 3.
Various methods of analyzing heart rate variability have been used in previous cross-sectional and follow-up studies (12–14) to predict propensity for ventricular tachyarrhythmias. Two-dimensional vector analyses of Poincaré plots can separately quantify the instantaneous and continuous long-term RR interval variabilities. Recently, reduced long-term continuous RR interval variability was observed (18) to precede the spontaneous onset of ventricular tachyarrhythmia and was also the most specific noninvasive marker for vulnerability to ventricular fibrillation in the present study. Quantitative analysis of long-term RR interval variability from the Poincaré plots is a more specific assessment of arrhythmic risk because some patients with vulnerability to life-threatening arrhythmias present with complex plots with relatively higher values for standard deviation of all sinus intervals than for standard deviation of long-term continuous RR interval variability. Similar complex plots have recently been observed (30) to predict sudden death in patients with heart failure. Concurrent with previous observations (31), the average heart rate was faster in the ventricular fibrillation group than in the control group. However, the difference in heart rate variability remained significant after correction for heart rate, confirming that an analysis of heart rate variability gives more specific information on the risk for fatal arrhythmia than does the average 24-h heart rate. There were some differences in medication between the ventricular tachycardia group and the matched control group (i.e., in beta-blockers, which may potentially influence heart rate variability). However, previous data (32) suggest that beta-blockers increase (not reduce) heart rate variability in patients with coronary artery disease. Thus, the results of the present study concerning the reduced heart rate variability in the ventricular fibrillation group but not in the ventricular tachycardia group cannot be explained by the differences in beta-blocker medication.

**QT dispersion and vulnerability to ventricular tachyarrhythmias.** The mechanism of ventricular tachycardia originating in chronic myocardial infarction has been shown to be reentry (33–37). The role of increased dispersion of repolarization in the genesis of ventricular fibrillation has also been generally recognized (7,38–40), and infarct scar and reentrant circuits serve as fixed substrates in the pathogenesis of sustained monomorphic ventricular tachycardia (41). Strong evidence supports the hypothesis that dispersion of refractoriness and repolarization provides a pathophysiologic basis for reentry (7–9,42,43). Furthermore, QT dispersion has been demonstrated (1–6) to reflect the dispersion of recovery times and repolarization. Thus, increased QT dispersion indicates the presence of a substrate for ventricular tachyarrhythmias, most obviously by a reentry mechanism. In accordance with these observations, the present cross-sectional study showed that among patients with a previous myocardial infarction, the patient groups with different presentations of ventricular tachyarrhythmia had broader QT dispersion than those without arrhythmic propensity, indicating the presence of a fixed arrhythmic substrate for ventricular tachyarrhythmias. In the present study, heart rate was faster in the ventricular fibrillation group than in the matched control group. However, QT dispersion was significantly broader in the ventricular fibrillation group than in the corresponding control group, even without correction for heart rate.

**Accuracy of QT dispersion and heart rate variability in predicting vulnerability to ventricular tachyarrhythmias.** Previous follow-up studies (13,14,20,22,23) evaluating the accuracy of heart rate variability and QT dispersion as predictors of arrhythmic death have used different definitions, such as death within 1 h after the onset of symptoms or a combination of sudden death and the occurrence of ventricular tachycardia. However, recent data (44,45) suggest that these definitions lack specificity in terms of tachyarrhythmic death. Although complete matching of all variables is difficult in case-control studies, the present data suggest that analysis of long-term continuous RR interval variability alone has a high positive predictive accuracy for detecting vulnerability to unstable ventricular tachyarrhythmia. QTc dispersion seems to be less

![Figure 2. Receiver operating characteristic curves for SD2 (standard deviation of long-term continuous heart rate variability) and QTc dispersion in differentiating between postinfarction patients with a clinical presentation of hemodynamically stable sustained ventricular tachycardia and with inducible stable sustained monomorphic ventricular tachycardia during programmed electrical stimulation and the postinfarction patients without history of ventricular tachyarrhythmia during programmed electrical stimulation. AUC = area under the curve.](image-url)
specific because of a notable overlap in individual values between patients with and without a propensity to ventricular fibrillation. However, no correlation was observed between the measures of heart rate variability and QT dispersion. It would be important to assess the value of combining these two easily obtained noninvasive methods in an attempt to identify the postmyocardial infarction patients at highest risk for ventricular fibrillation and sudden arrhythmic death and those who are candidates for prophylactic automatic implantable cardioverter-defibrillator therapy in future prospective studies.

References


