

# QT Dispersion and Mental Stress Testing

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**Introduction:** Ventricular arrhythmias are often responsible for sudden cardiac death and acute mental stress is reported that introduce dangerous ventricular arrhythmias. The aim of this study is to investigate the influence of acute mental stress on the QT-dispersion (QT-d) in patients with coronary artery disease (CAD).

**Methods:** We studied 46 patients (pts) with coronary artery disease documented with cardiac catheterization (33 male, 13 female, mean age:  $59.1 \pm 7.1$  years), who where admitted to our department with angina and without acute myocardial infarction (AMI) or unstable angina (UA). Twenty-eight of these patients (21 male, 7 female, mean age:  $61.3 \pm 6.1$  years) had severe CAD (2–3 vessels disease) with a positive exercise test and intervention (angioplasty or surgery) had recommended to them (Group A). The remaining 18 patients (12 male, 6 female, mean age:  $63.5 \pm 5.9$  years) had less severe CAD (one vessel disease) under medical treatment with a negative previous exercise test (Group B). After the fourth day of hospitalization and clinical condition stabilization (absence of angina symptoms and improvement of ECG changes), the patients underwent a mental arithmetic stress test. The control group (Group C) was composed of 20 patients (13 male, 7 female, mean age:  $59.9 \pm 7.1$  years) with atypical angina symptoms and normal coronary arteries in coronary angiography. The dispersion of QT (normal values  $< 70$  msec) was measured in all participants using a continuous ECG before and during the mental testing.

**Results:** There were no differences in QT-dispersion among the three groups at baseline. At the end of the trial, mental stress was confirmed in 22 patients of Group A, 14 of Group B, and 15 patients of Group C. The patients of both Groups A and B had a major increase in QT-dispersion ( $p < 0.001$ ) compared to their initial values while the patients of the control group had no increase. Ten patients (10/22-45,4%) of Group A and 2 patients (2/14-14,3%) of Group B, who reported mental stress, had a major increase in QT-dispersion ( $> 70$  msec) while none of the 15 patients of Group C, who reported mental stress, had QT-dispersion  $> 70$  msec.

**Conclusion:** Acute mental stress seems to increase QT dispersion significantly.

**T**he increase in QT interval dispersion after acute myocardial infarction is a risk indicator for ventricular tachycardia, but not for cardiac mortality although the increased QT dispersion and the prolonged QT interval are considered independent prognostic risk factors for fatal or non-fatal myocardial infarction<sup>1-4</sup>. Ventricular arrhythmias are often responsible for sudden death<sup>5-7</sup>. It has been reported that an acute psychological or mental stress in coronary artery disease patients, may cause malignant ventricular arrhythmias<sup>8</sup>.

Aim of our study was to quantify acute psychological stress effect on the QT interval in patients with known coronary artery disease.

## Methods

We studied forty-six patients (male:33, female: 13, mean age:  $59.1 \pm 7.1$  years), who where admitted to our department (between April 1999 and September 2002) with angina symptoms and ischaemic electrocardiographic (ECG) alterations wi-

thout acute myocardial infarction (AMI) or unstable angina (UA). These patients had coronary artery disease (CAD) under medication that was proved with cardiac catheterization within the last 6 months.

Twenty-eight of these patients (male: 21, female: 7, mean age:  $61.3 \pm 6.1$  years) had severe CAD (2–3 vessels disease) with a positive exercise test and intervention (angioplasty or surgery) had recommended to them (Group A).

The remaining 18 patients (male:12, female:6, mean age:  $63.5 \pm 5.9$  years) had less severe CAD (one vessel disease) under medical treatment with a negative previous exercise test (Group B).

After the fourth day of hospitalization and clinical condition stabilization (absence of angina symptoms and improvement of ECG changes), the patients underwent a mental arithmetic stress test.

The test was the following: patients were required to remember 6 digit numbers and repeat them backwards for five minutes; afterwards, the patients were subtracted sequentially the number 17 from 1,000 for five minutes; the degree of mental stress was evaluated by themselves with a proportional method using a scale from 1-10. The acute stress disorder scale (ASDS) was used as a guideline. ASDS is a scale based on criteria of Diagnostic and Statistical Manual of Mental Disorders, which is composed of 19 divisions and complemented by the patients themselves who classify and report their reactions during stress. This test has good sensitivity (95%) and specificity (83%) for ASD classification<sup>9</sup>.

The control group (Group C) was composed of 20 patients (male: 13, female:7, mean age:  $59.9 \pm 7.1$  years) with atypical symptoms and normal coronary arteries in coronary angiography.

The QT dispersion (normal values < 70 msec) was measured in all participants using a continuous ECG before and during the mental testing (12 lead Schiller Cardiovit CS 200). The test took place the same time (11–12 a.m.). Two cardiologists evaluated the QT-dispersion. Whenever it was necessary there was a combination of automatic and manual evaluation of the T wave ending.

In this system of QT-dispersion analysis, the various QT intervals are estimated, in each of the 12 leads, based on the mean values of a 10 seconds resting ECG. The end of T wave has to be quantified in at least 8 leads and by a certain algorithm (Figure 1 shows an example of QT-dispersion analysis)<sup>10</sup>.

All patients were receiving b-blockers. Patients with conductance and rate disorders (permanent or pe-

riodical), heart failure (ejection fraction < 50%), old MI and under anti-arrhythmic treatment were excluded.

The demographic and other characteristics of the patients who participated in the study are shown in table 1. The statistic analysis was performed using SPSS.10 (Student's t-test).

## Results

At the end of the trial, mental stress was confirmed in 22 patients of Group A, 14 of Group B, and 15 of Group C (Table 1). The patients of both Groups A and B had a major increase in QT-dispersion ( $p < 0.001$ ) compared to their initial values while the patients of the control group had no increase (Table 2).

Ten patients (10/22-45,4%) of Group A and 2 patients (2/14-14,3%) of Group B, who reported mental stress, had a major increase in QT-dispersion (>70 msec) whilst none of the 15 patients of Group C, who reported mental stress, had QT-dispersion >70 msec (Table 3).

There were no differences in QT-dispersion between the three groups at baseline (Table 1). Ventricular arrhythmias, conductivity disorders, or angina symptoms were not reported. Ischaemic ECG changes (ST depression  $\geq 1$ mm, ST elevation  $\geq 1$ mm, T and P wave alteration) were observed in two patients, one from each group. There were no differences ( $p > 0.05$ ) in blood pressure and heart rate before and during the mental testing.

There were no differences ( $p > 0.05$ ) in the QT-dispersion estimation between the two cardiologists (stand. error 4.5%).

## Discussion

There are quite many tests used for the evaluation of mental or psychological stress and their effect on neural-hormonal function. The variations of mental arithmetic testing are the most commonly used. Public speech, stroop color test, word color test, movies, videos and interviews are also often used. These tests seem to have solved the major problem of reproducibility, although there is a definite differentiation between tests done in a lab and those done during daily routine activity<sup>11-13</sup>.

The blood pressure levels and the heart rate are directly affected by psychological stress during his\her daily routine activity. The mental-psychological stress seems to greatly reduce the variations in heart rate in the general population<sup>14-17</sup>.



Figure 1. An example of QT-dispersion analysis.

The increased mortality in patients with left ventricular hypertrophy is correlated with mental stress. The increased mass of the left ventricle is an independent prognostic factor for cardiac mortality or morbidity. The ambulatory or random detection of arterial hypertension has been referred as a prognostic index for left ventricular hypertrophy. The correspondence

of systolic blood pressure to mental stress is strongly correlated with left ventricular hypertrophy<sup>18</sup>.

The activity of platelets is also altered during mental tests resulting in complications from the cardiovascular system<sup>19</sup>.

The prognostic value of psychological testing in coronary artery disease is considered important.

**Table 1.** Demographic and other characteristics of the study population.

	<b>Group A</b> <b>28</b> <b>(m: 21, f: 7,</b> <b>mean age: 61.3±6.1)</b>	<b>Group B</b> <b>18</b> <b>(m: 12, f: 6,</b> <b>mean age: 63.5±5.9)</b>	<b>Total</b> <b>46</b> <b>(m: 33, f: 13,</b> <b>mean age: 59.1±7.1)</b>	<b>Control Group C</b> <b>20</b> <b>(m: 13, f: 7,</b> <b>mean age: 65.9±7.1)</b>
Two-Three vessels disease	28	–	28	–
One vessel disease	–	18	18	–
AH	16	15	31	13
DM	5	3	8	1
EF	57%	56%	57%	59%
BMI≥90 <sup>th</sup>	5	7	12	8
Medications				
• β-B	28	18	36	20
• ACE	11	9	18	5
• Ca <sup>++</sup>	6	8	14	1
• Nitrates	22	16	38	4

AH=arterial hypertension, DM= diabetes mellitus, EF=mean value of ejection fraction, BMI=body mass index (age adjusted), β-B=β blockers, ACE=angiotensin converting enzyme inhibitor, Ca<sup>++</sup>= Ca<sup>++</sup> channels antagonists.

**Table 2.** Correlation of mental stress (MS) to QT-dispersion (QTd).

	<b>Initial QTd values (msec)</b>	<b>Patients with (+) MS</b>	<b>Initial QTd values in patients with (+) MS (msec)</b>	<b>QTd values after a (+) MS (msec)</b>
Group A n=28	33 (22-48)	22	35 (27-48)*	56 (25-91)*
Group B n=18	31 (24-45)	14	32 (26-43)**	51 (30-77)**
Control Group C n=20	33 (20-44)	15	34 (24-41)***	40 (23-47)***

\*p<0,05, \*\* p<0,05, \*\*\* Non statistical significant.

**Table 3.** Pathological increase of QT dispersion (QTd) in patients who reported mental stress (MS).

	<b>Patients with (+) MS</b>	<b>QTd increase &gt; 70 msec</b>
Group A n=28	22	10/22 (45,4%) patients 77 (70-91) msec
Group B n=18	14	2/14 (14,3%) patients 74 (72-76) msec
Control Group C n=20	15	–

There are strong indications of provoked angina after psychological stress either in the lab or in a daily routine<sup>20-21</sup>. Patients with ischaemic manifestations

during daily routine show a stronger response to mental testing. ST depression during mental or physical testing is a better prognostic indicator of ST depression during daily routine compared to other blood test indicators. Therapeutic interventions may have to focus on patients who present these reactions to mental testing and show improvement of ischemia if the intensity of test is reduced<sup>22</sup>. Transient silent ischemic episodes have been attributed to mental stress, even though some reports confirm that mental or psychological stress are unusual stimulants of silent or symptomatic ischaemia; on the other hand, is reported that the combination of mental and physical stress is an important stimulator for ischaemia<sup>23-26</sup>.

Comparisons have been done between mental and other tests for inducing angina, such as the cold

pressor test, hyperventilation, exercise test according to Master two-step protocol in patients with stable angina, by measuring epinephrine and norepinephrine before and after mental stress. Mental stress seems to be an effective stimulant for angina, which may be a result of neural-hormonal reaction and/or an increase of the left ventricle afterload<sup>27</sup>.

The indications for arrhythmia induction after mental tests are strong but they have not fully been linked to them<sup>7,8</sup>.

The QT-dispersion, as a variation of the QT interval, is a simple method for evaluating the heterogeneity of ventricular myocardium repolarization. The increase in QT-dispersion is considered an important indicator for ventricular arrhythmias. The QT dispersion reflects certain changes in ventricular repolarization<sup>27-37</sup>. Certainly there are studies that dispute the correlation between QT-dispersion and the heterogeneity of ventricular repolarisation. Furthermore, it is greatly supported that the QT-dispersion is a result of the various angles formed by the vector of T wave with the axis of each ECG lead and it is not correlated with the ventricular repolarisation<sup>34, 38-39</sup>.

It is difficult to define boundaries for QT dispersion<sup>1-2</sup>. Remarkable variance of QT-dispersion have been confirmed specially during daily activity. Many contemporary indications are referred to the limit of 50 msec at rest<sup>1-7,33</sup>. However, we accepted a higher limit (70 msec) in order to avoid false positive tests<sup>40</sup>.

Our results support the fact that acute psychological stress causes a significant increase in QT-dispersion in patients with severe or less coronary artery disease ( $p < 0.001$ ) (Table 2). Furthermore, even though the normal limit of QT-dispersion is 70 msec in this study, 45.4% of patients in Group A and 14.3% of Group B, with a positive mental test, exceeded this limit (Table 3). Finally, 12 patients (33.3%) of a total of 36 patients of both groups who reported mental stress after the test, showed a pathologic increase in QT-dispersion. This may be due to changes in repolarisation, which are related to ischaemic alterations of the action potential. There is notable heterogeneity in answers to mental and physical test using ECG, Holter, and scintigraphic criteria for ischaemia<sup>40-46</sup>.

In opposition with other studies, our results do not strongly support a relation between the increased QT-dispersion during mental test and ischaemic ECG changes although ECG ischaemia (two patients) was appeared only in those patients

who mentioned mental stress<sup>41, 43-47</sup>. It is supported that patients with coronary artery disease can be defined from the QT-dispersion in combination with a pharmaceutical exercise test<sup>47</sup>. Also, in our study, patients with confirmed severe coronary artery disease were those who showed a pathologic increase in QT-dispersion during mental test (45.4%) confirming the relation between coronary artery disease and QT-dispersion. Perhaps, a larger sample of patients and a better-organized study may support these results.

It is reported a high percentage of error in QT-dispersion evaluation (20-30%)<sup>32-34</sup>. For this reason, our results could be attributed to variations in QT-dispersion measurement; however, the inexistence of variations (4.5%) in the estimations of the two observers reduces this possibility.

The proportional method for reporting mental stress during mental psychological test using grading scale, usually from 1-10, is the simplest and fastest method for evaluation; however is less reliable compared to other mentioned methods<sup>9</sup>.

The used questionnaire was standardized so that the results could be evaluated, but the small number of patients requires better organized study which may have better reliability in the results.

The hyper-reactivity of the sympathetic nervous system as a response to psychological tests is accompanied by factors that create nervousness in adults and may affect the secretion of growth hormone (GH) and testosterone (TE)<sup>12</sup>.

The therapeutic management may have to focus on these patients who show intense reactions to mental testing and evaluate if by abolishing these reactions, there is any decrease in QT-dispersion or any improvement in myocardial ischaemia<sup>21-22,47-54</sup>.

Therapeutic interventions may have to focus on patients who present these reactions to mental testing and show improvement of ischemia if the intensity of testing is reduce.

The combination of mental and physical tests may improve the diagnosis and the prognosis of myocardial ischaemia; furthermore, the possibility of severe ventricular arrhythmias prevention may be improved effectively<sup>55-56</sup>.

## Conclusion

The acute psychological/mental stress causes a significant increase in QT-dispersion which is a known risk factor for arrhythmogenesis in patients with

coronary artery disease; therefore, the global management of coronary artery disease may need to focus on another factor aside from these already treated such as diabetes mellitus, arterial hypertension and dyslipidaemia.

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