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Correlation of QT Dispersion after Exercise Stress-Test with Coronary Artery Disease

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Introduction

Within the last decade, QT dispersion (QTD) has been proposed as a descriptor of ventricular repolarization inhomogenity and, as such as potential prognostic tool in the detection of future ventricular tachyarrhythmic events and death [1, 2]. More recent studies showed that QTD values correlate with the parameters of vectorcardiographic T loop morphology [3]. Based on these results, it has been proposed that the different projections of the T wave vector into the different electrocardiogram (ECG) leads are essential and that an increase of QTD merely could mean an unusual projection of a more complicated T wave loop. To date, it remains unsettled whether QTD at rest bears any prognostic value for the cardiovascular mortality, because the results of various prognostic studies have been conflicting [1, 2, 4]. QTD has been shown to increase in response to transient myocardial ischemia and a significant positive correlation has been demonstrated between QTD and the degree of ischemia [5, 6]. There are some results, showing that QTD on maximal exercise or psychological stress is related to coronary artery disease (CAD). But the usefulness of heart rate corrected QT dispersion (QTcD) comparing to QTD in predicting arrhythmic events or detecting CAD in exercise test remain contradictory [7]. The aims of our study were to determine if QTD and QTcD on maximal exercise are more evident in cases of CAD, if an exercise-induced increase in QTD is a useful indicator for detecting significant coronary stenosis in patients who do not have exercise-induced significant ST-segment depression, and if QTcD has any advantages comparing to QTD in indicating CAD in exercise test.

Methods

Patients: The study population consisted of 94 unselected patients consecutively referred for coronary angiography due to chest pain, dyspnoea or abnormal exercise stress test. Patients on antiaarhythmic drugs except beta-blockers or patients unable to perform physical exercise were excluded from the study.

Stress Test: Prior to coronary angiography symptom limited bicycle stress test was performed using twelve-leads of ECG. The ECG was recorded minutely during the test and until 6 minutes after the end of test. The ST-segment level was measured 60 ms after J point in all 12 leads. Exercise induced ST-segment depression was defined as follows: horizontal or downsloping ST-segment depression $\geq$ 1,0 mm, or upsloping ST-segment depression $\geq$ 2,0 mm in any lead, present within the first 3 minutes of the recovery period. QT intervals were prospectively assessed from ECG recordings (12 leads, paper speed 100 mm/s) at rest and immediately after bicycle stress- test in all patients referred to our cardiological outpatient service due to suspected CAD or for preoperative risk stratification due to variety of diseases. The QT interval for each lead was assessed by two experienced cardiologists unaware of the results of coronary angiography. QT duration was measured from the beginning of the QRS complex to the visual return of the T wave to the baseline. When a T wave was interrupted by a U wave, the end of the T wave was defined as the nadir between the T and the U waves. Whenever such a distinction was not possible, the lead was discharded from analysis. Flat T waves, T waves with unidentifiable patterns were excluded from T-wave offset determinations as well. QTD was calculated as the difference between the maximum and the minimum QT intervals in any of the 12 leads and QTcD as the difference between the maximum and the minimum QTc intervals according to Bazett's formula (QTc = QT/square root of the RR interval) in any of the 12 leads.

Coronary angiography: Coronary angiography was performed by Judkins technique with multiple projections. Coronary stenoses were quantified visually and with the help of callipers. A luminal narrowing $\geq$ 50% of the cross-section was considered to represent as a hemodynamically significant coronary artery lesion.

Statistics: Continuous data are expressed as mean ± SD or as median with interquartile range where appropriate. Group comparisons of continuous variables were calculated using Mann Whitney statistics for non-normally distributed data and Student's t test in normally distributed data. Chi-square test was used for categorical variables. A two-tailed p value < 0.05 was considered as statistically significant. The results of the exercise ECG's were compared to angiographic data to calculate sensitivity

and specificity of exercise electrocardiographic parameters. Receiver operating (ROC) plots were generated for QTD, QTcD and ST depression ($\geq$ 1mm) on ECG during exercise test for all study patients.

Additionally, sensitivity and specificity of QTD and QTcD assessed immediately after exercise test in respect to predict CAD were calculated after the assessment of a cutoff point of QTcD ex. $\geq$ 40 ms.

Results

Out of 94 consecutive patients referred for angiography due to chest pain, dyspnoea or abnormal exercise stress test 67 patients (71%) had relevant CAD on angiography whereas 27 (29%) patients showed normal coronary arteries. Baseline clinical characteristics of these patients are presented in table 1.

Table 1. Baseline clinical characteristics of patients with and without significant coronary stenosis

		CAD n = 67	No CAD n =27	P
Age	years	62.1 $\pm$ 11.7	61.1 $\pm$ 10.2	0.706
Sex	m/f	59/8	10/17	< 0.0001
Beta-blocker	number (%)	58 (87%)	16 (59%)	0.003
Ejection fraction	%	61.7 $\pm$ 10.3	66.0 $\pm$ 10.3	0.07

Interestingly, we found no significant difference with respect to the percentage of age predicted exercise capacity between patients with and without CAD (74 % (IQR 63-94.5) vs. 80% (IQR 63-103.5) p = 0.401), although the use of beta-receptor blockers was significantly more frequent in patients with CAD (87% vs. 59%; p = 0.003).

Table 2. Stress exercise test and electrocardiographic findings of study patients with and without significant coronary stenosis
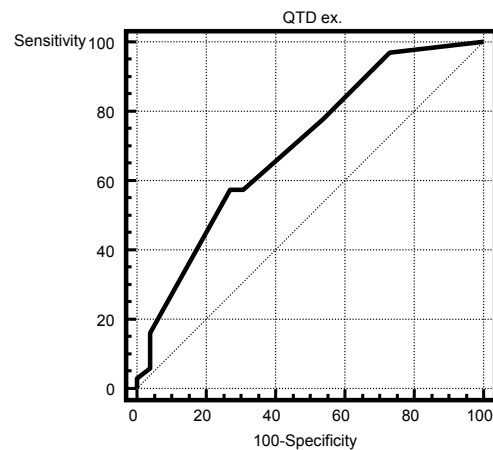
		CAD n = 67	No CAD n = 27	P value
Predicted exercise capacity	%	74 (63-94.5)	80 (63-103.5)	0.401
ST-segment depression $\geq$ 1mm	number (%)	26 (38.8)	2 (7.4)	0.003
QTD	ms	30 (20-40)	20 (10-40)	0.655
QTcD	ms	27 (18.5-38)	23 (10-44)	0.779
QTD ex.	ms	30 (20-40)	20 (5-30)	0.006
QTcD ex.	ms	40 (23.5-52)	29 (6.5-38)	0.006

ex. denotes QT dispersion assessed immediately after exercise test
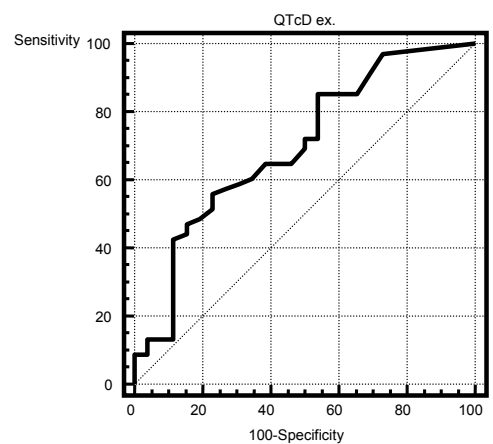
QTD and QTcD at rest did not differ between both groups (table 2). However, patients with CAD had a significantly higher QTD immediately after exercise (QTD ex.) as compared to the patients without significant changes in coronary arteries (30ms (IQR 20-40) vs. 20 ms (IQR 5-30); p=0.006). The same differences could be demonstrated for QTcD ex. (40 ms (IQR 23.5-51.5) vs. 29 ms (IQR 6.5-38); p = 0.006).

ROC plot analyses were performed with respect to prediction of coronary artery stenoses > 50% on angiography for QTD ex., QTcD ex., and ST-segment depression ($\geq$ 1mm) during or after exercise stress test (figures 1-3). Interestingly, ROC plots for QTcD ex. showed better results in predicting relevant CAD compared to the assessment of ST-segment depression during or after stress test alone.
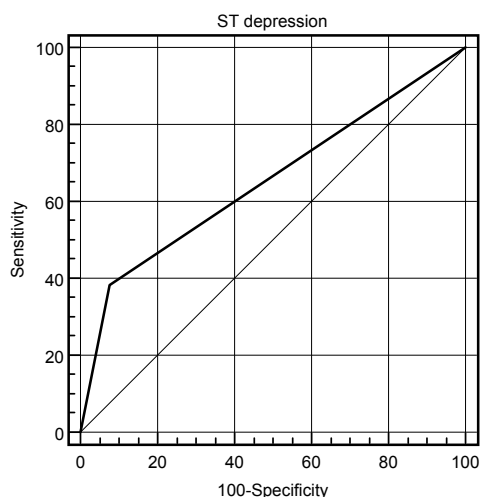
On the basis of our data we assessed a cutoff of $\geq$ 40 ms for QTD ex. and QTcD ex. (figure 1,2,4) and calculated the corresponding sensitivity and specificity for this cutoff in predicting significant CAD. A cutoff QTcD ex. $\geq$ 40 ms showed a better sensitivity to predict significant CAD as compared to the ST-depression during or after the stress test (50.7% vs. 38.8%) or QTD ex. $\geq$ 40 ms (37.7%).

Fig. 1. ROC Plot of all QTD ex measurements in respect to predict coronary artery disease (stenoses > 50%) ex. Area under the ROC curve = 0.698; standard error = 0.057; 95% confidence interval = 0.595 to 0.789

Fig. 2. ROC Plot of all QTcD ex. measurements in respect to predict coronary artery disease (stenoses > 50%). Area under the ROC curve = 0.696; standard error = 0.057; 95% confidence interval = 0.593 to 0.787
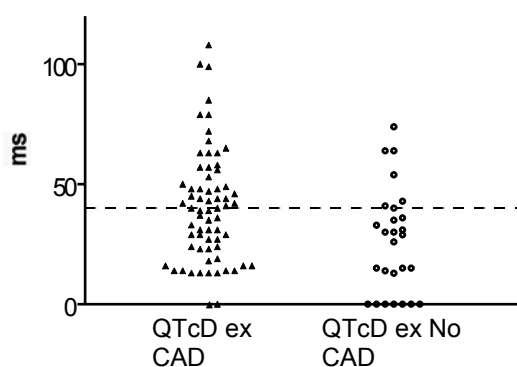
Fig. 3. ROC Plot of all ST-segment depressions (≥ 1mm) during or after exercise stress test in respect to predict coronary artery disease (stenoses > 50%) Area under the ROC curve = 0.653; standard error = 0.066; 95% confidence interval = 0.548 to 0.748

However, specificity for CAD was lower using the 40 ms cutoff of QTcD ex. (74.1%) as compared to the ST-depression during the stress test (92.6%) (table 3) or QTD ex. ≥40 ms (85.2%).

Table 3. Sensitivity and Specificity of ST-depression, assessment of QTcD during exercise or a combination of both parameters with respect to predict CAD

Study population n=94		Sensitivity for CAD	Specificity for CAD
ST-depression ≥ 1mm	%	38.8	92.6
QTcD ex. ≥ 40 ms	%	50.7	74.1
ST depression ≥ 1 mm or QTcD ex. ≥ 40 ms	%	64.2	74.1

ex. denotes QT dispersion assessed immediately after exercise test

Fig. 4. Corrected QTD assessed immediately after exercise stress test in patients with coronary artery disease (CAD) compared to patients without CAD. The dotted line indicates the 40 ms cutoff point for specific calculations of sensitivity and specificity of QTcD ex. (see results)

Additionally we have analyzed the 41 patients with CAD, which showed no ST-depression during or after the exercise test. 18 (43.9%) of them had a QTcD ex. ≥ 40 ms and 15 (36.6%) QTD ex. ≥ 40 ms (figure 4).

Discussion

Although bicycle and treadmill stress test are the most common noninvasive diagnostic methods to detect CAD, overall sensitivity is reported to be low and vary between 40-90% dependent on several factors such as 1-vessel or 3-vessel disease, medication and left ventricular hypertrophy. A considerable number of false-negative and false positive results have been reported in exercise stress test. Therefore exercise stress test is not always accurate in indicating significant coronary stenosis and much effort has been undertaken in recent years to improve sensitivity and specificity of noninvasive exercise tests. Exercise echocardiography has been reported to increase the sensitivity for detecting CAD to 71-97% with greater sensitivities in multivessel disease and a specificity ranging from 64-100%. The overall sensitivity and specificity in nuclear imaging (SPECT) have been measured at 84% and 83% [8]. However these investigations are expensive and time consuming. Therefore the main purpose of the present study was to determine if non-expensive assessment of QTD ex. or QTcD ex. immediately after stress exercise test can improve the sensitivity of a bicycle exercise test in predicting relevant CAD.

QTD has been shown to increase during exercise and transient myocardial ischemia [7]. The results of the present study demonstrates that in contrary to QTD and QTcD at rest, QTD and QTcD assessed immediately after exercise, were significantly associated with CAD as compared to patients without CAD. Our data are in line with a study from Koide et al [7] who found that QTD ≥ 60 ms immediately after exercise had a sensitivity of 74% and specificity of 85% for the diagnosis of significant coronary stenosis. It has been reported that significant interlead differences in QT interval duration at rest occurs in patients with myocardial infarction and that these patients were at higher risk for malignant ventricular arrhythmias and all-cause mortality [9]. However, there are other studies, which suggested that QTD only correlates with T loop morphology [3] and not with arrhythmic events or as a predictor for mortality in CAD [1].

Until now there are contradictory data whether QTD should be corrected on heart rate values [7]. Our results could demonstrate a small advantage in predicting CAD using QTcD ex. as compared to the assessment of QTD after exercise alone. Using a cutoff point of QTcD ex. ≥ 40 ms we found a higher sensitivity to predict relevant CAD as compared to QTD ex. ≥ 40 ms or ST-depression alone. It is noteworthy that specificity to predict relevant CAD was lower using the 40 ms cutoff point of QTcD ex. (74.1%) compared to ST-depression during exercise stress test (92.6%) or non corrected QTD ex. ≥ 40 (85.2%). Our results demonstrate that QTcD assessed immediately after exercise stress test is an inexpensive and useful method to improve the sensitivity of a bicycle stress test in predicting CAD, even in the absence of ST-segment depressions or in patients taking beta-blockers.

Study limitations. Although great care was taken to use consistent criteria to define the end of the QT interval by two experienced observers who were unaware of angiographic data, the lack of uniformity accepted definition of the end of the QT interval remains a limitation of QT interval dispersion measurements. The limitation for the manual measurement of QTD is reported to be less important than for QTcD. If the end of the T wave cannot be determined reliably, QT interval measurements should not be performed in these leads.

Conclusions

QTD ex. and QTcD ex. assessed immediately after exercise is significantly higher in patients with coronary stenoses > 50% as compared to patients without CAD.
In our study patients assessment of QTcD ex. ≥ 40 ms has a higher sensitivity (50.7%) for CAD as compared to ST-depression assessment during or after stress test (38.8%). 43.9% of patients with significant CAD but without significant ST-depression during or after bicycle exercise test, show a QTcD ex. ≥ 40 ms but only 36.6% of them a QTD ex. ≥ 40 ms.

QTcD ex. ≥ 40 ms showed a higher sensitivity (50.7%) to predict significant coronary artery disease as compared to uncorrected QTD ≥ 40 ms (37.7%).

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Aprašomi metodai, kuriais buvo nustatyti QTd ir QTcd ryšį su vainikinių arterijų susiaurėjimais. Įvertinta QT intervalą ramybės EKG metu ir tuoj po veloergometrinio tyrimo 94 pacientams. 67 ligoniams (amžius 62,1± 11,7 m.) koronarografijos metu buvo nustatyti vainikinių arterijų susiaurėjimai > 50 proc. 27 ligoniams (amžius 61,1±10,2 m.) vainikinių arterijų susiaurėjimų nebuvo nustatyta. Atliktas šių parametrų sulyginimas abiejų grupių ligoniams. Įvertinus ramybės EKG, QTd ir QTcd skirtumų nebuvo nustatyta. Tačiau QTd (atitinkamai 30 ms ir 20 ms; p=0,006) ir QTcd (atitinkamai 40 ms ir 29 ms; p=0,006) reikšmės, įvertintos tuoj po veloergometrinio tyrimo, buvo patikimai ilgesnės ligoniams, kurių vainikinės arterijos buvo susiaurėjusios >50 proc. Il. 4, bibl. 9 (anglų kalba; santraukos lietuvių, anglų ir rusų k.).

P. Ammann, I. Bluzaitė, H. Roelli, W. Korte, H. Rickli, J. Brazdzionytė, G. Urbonaviciene, R. Zaliunas. Correlation of QT Dispersion after Exercise Stress-Test with Coronary Artery Disease // Electronics and Electrical Engineering. – Kaunas: Technologija, 2004. – No. 2(51). –P. 78-81.
The aim of this study was to determine if QTD and heart rate corrected QT dispersion (QTcD) are related to coronary artery disease (CAD). We prospectively assessed QT intervals from electrocardiograms (ECG) at rest and immediately after bicycle stress-test, in 94 patients. In 67 patients (age 62.1 ± 11.7y; 59m/8f) relevant CAD (stenoses > 50%) was assessed. 27 patients (age 61.1 ± 10.2 y; 10m/17f) showed normal coronary arteries. There were no significant differences between patients with or without CAD in QTD at rest. However, QTD (30ms(20-40) vs. 20 ms (5-30); p=0.006) and QTcD (40 ms (23.5-51.5) vs. 29 ms (6.5-38); p = 0.006) assessed immediately after stress-test were significantly longer in CAD. Sensitivity of QTcD to predict CAD (cut off of QTcD $\geq$ 40 ms) was higher (50.7%) as compared to ST-depression on ECG (38.8%), whereas specificity was lower (74.1% vs. 92.6%). Ill. 4, bibl. 9 (in English; summaries in Lithuanian, English and Russian).

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Описываются результаты определения кореляции между дисперсией интервала QT (QTd), дисперсией корригированного интервала QT (QTcd) и степенью поражения коронарных артерий. В обследование были включены 94 больных, которым был измерен QT интервал в состоянии покоя и сразу после велоэргометрической пробы. У 67 больных в возрасте 62,1±11,7 года были установлены сужения коронарных артерий >50 %. У 27 больных в возрасте 61,1±10,2 года, сужений коронарных артерий не было установлено. Мы не нашли различий QTd и QTcd между группами на поверхностной ЭКГ в покое. Значения QTd и QTcd измеренные сразу после велоэргометрической пробы были достоверно больше у больных, которым были установлены сужения коронарных артерий >50 % (соответственно QTd 30 мс и 20 мс; p=0,006 и QTcd 40 мс и 29 мс; p=0,006). Ил. 4, библ. 9 (на английском языке; рефераты на литовском, английском и русском яз.).