

## SIGNIFICANCE OF QT DISPERSION TO IMPROVE THE DIAGNOSTIC ACCURACY OF EXERCISE STRESS TESTS FOR MYOCARDIAL ISCHAEMIA

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### ABSTRACT

**Background:** This study consisted of 60 randomly selected patients (49 men and 11 women) who had undergone both symptom-limited treadmill exercise tests and coronary angiography, within one month, for clinical indications. This was a prospective study done during the period of December 1998 to July 1999 in NICVD, Dhaka Bangladesh. The ECG is generally considered to provide a summation of the electrical activity of the heart and to be insensitive to local electrophysiological events. Recent studies suggest that important local electrophysiological differences can be detected from a standard 12-lead ECG, allowing new insights into the electrical behavior of patient's hearts. The QT dispersion recorded as the difference between maximum and minimum QT intervals on a 12-lead ECG, is sensitive to myocardial ischaemia and may improve the accuracy of exercise testing.

**Methods and Results:** Exercise ECGs were analyzed in 60 patients who had undergone exercise ECG and coronary angiography for clinical indications:

1) The true-positive (TP) group consisted of 22 patients with mean  $\pm$ SD age of  $52 \pm 9$  years. These patients had a positive treadmill test result with  $\geq 1$  mm horizontal ST-segment depression and an abnormal coronary angiogram, defined as  $\geq 50\%$  diameter stenosis of a major epicardial coronary artery. Two patients were female in this group.

2) The true negative (TN) group consisted of 20 patients who had a negative exercise test and non significant CAD based on coronary angiography. The mean  $\pm$  SD age of the group was  $44 \pm 8$  years. Five patients were female in this group.

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3) Eight patients with positive treadmill test result with abnormal exercise ECGs and non significant coronary artery disease (False positive [FP] group). This group had a mean age of  $43 \pm 10$  years. Three patients were female in this group.

4) The false negative (FN) group consisted of 10 patients with mean  $\pm$ SD age of  $48 \pm 7$  years. These patients had negative exercise ECG and an abnormal coronary angiogram. This group had one female patient.

The exercise QTD Was  $41 \pm 14$ ms in TN,  $78 \pm 22$ ms in TP ( $P < 0.001$  versus TP) and  $47 \pm 16$ ms in FP ( $P = \text{NS}$  versus TN and  $P < 0.001$  versus TP) groups. The exercise QTD was  $84 \pm 17$ ms in FN ( $P = \text{NS}$  versus TP) group.

A stress QTD of  $>60$ ms had a sensitivity of 88% and specificity of 93% for the diagnosis of significant CAD compared with 68% ( $P < 0.05$ ) and 71% ( $P < 0.01$ ) respectively, for  $\geq 1$ mm ST-segment depression during stress. When QTD of  $>60$ ms was added to ST-segment depression as a condition for positive test, the specificity increased to 100%.

**Conclusion:** Exercise QTD is an easily measurable ECG variable that significantly increases the accuracy of exercise testing.

**Key Words:** *QT dispersion . coronary disease . electrocardiography . exercise.*

## INTRODUCTION

For much of this Century, the electrocardiogram (ECG) has been used widely in the diagnosis and management of patients. It is indispensable in the diagnosis of acute ischaemia<sup>1</sup> and myocardial infarction, and in the identification of serious and potentially fatal arrhythmias. The ECG, is generally considered to provide a summation of the electrical activity of the heart and to be insensitive to local electrophysiological events. Recent studies suggest that important local electrophysiological differences can be detected from a standard 12 lead ECG, allowing new insights into the electrical behavior of patient's hearts.<sup>2,3,4</sup>

The conventional criteria for designating an abnormal exercise test is the demonstration of  $\geq 1.0$  mm of horizontal or downsloping ST - segment depression.<sup>5</sup>

Using above criteria Meta-analysis of 147 consecutive published reports involving 24,074 patients who underwent both coronary angiography (CAG) and exercise testing revealed mean ( $\pm$  SD) sensitivity  $68 \pm 16$  percent and mean ( $\pm$  SD) specificity  $77 \pm 17$  percent for the diagnosis of coronary artery disease.<sup>6</sup>

The ECG QT interval is a measure of the duration of ventricular repolarization and is sensitive to myocardial ischaemia. The interlead variation of QT interval in the 12-lead ECG is referred to as QT dispersion. The QT or QTc dispersion is a noninvasive measure of regional variation in ventricular recovery time. Increased dispersion of ventricular recovery time has been associated with increased risk of serious arrhythmias that may trigger sudden cardiac death,<sup>7</sup> particularly in conditions in which QT is prolonged, including

congenital long QT syndrome,<sup>3</sup> drug toxicity, hypertrophic cardiomyopathy<sup>8</sup> and post-myocardial infarction arrhythmias.<sup>9</sup>

Considering low sensitivity and specificity and high false positivity of ST segment criteria<sup>10</sup> QT dispersion criteria have been proposed<sup>11</sup> to exclude false positive cases and to avoid unnecessary CAG. By correlating exercise QT dispersion values with CAG findings, this study attempted to see, how sensitivity and specificity of treadmill test can be increased, particularly in sub groups of population. To test this concept, we made a hypothesis that **"QT dispersion improves the diagnostic accuracy of thread mill stress test"**.

## MATERIALS AND METHODS

### Study population, place and period

The study population consisted of 72 randomly selected patients who underwent exercise tolerance test and coronary angiography for clinical indications. The study was conducted in the cardiology department of National institute of cardiovascular diseases, Dhaka, during the period of december 1998 to july 1999.

### Exercise stress test protocol

All patients underwent symptom-limited treadmill stress tests with Bruce or modified Bruce protocols. All the medications that patients were receiving were discontinued through the treadmill testing. Patients symptoms, peak heart rate, blood pressure and any ECG changes were noted. The exercise test was considered positive if there was  $\geq 1$ - mm ST depression at 80 ms after the J point on the exercise ECG.

### QT interval and QTD measurements

The QT interval was measured in as many limb and precordial leads as possible (minimum of 9 and mean of 10.5 leads) in the 12 -lead ECG (from

the onset of Q wave to the end of T wave) at baseline and peak exercise. When the T wave was fused with the U or P wave, a straight line was drawn tangential to the downstroke of the T wave, and the intersection of the latter with the baseline was taken as the end of the T wave. The PR segment was taken as baseline to obviate the difficulty in identifying the end of the T wave in the presence of ST-segment depression. The QT interval was corrected for heart rate using Bazett's equation<sup>10</sup> ( $QT_c = QT / \text{square root of RR interval in seconds}$ ).

QTc dispersion was measured as the difference between the maximum and the minimum QTc dispersion for a given heart rate. The QT interval measurements were performed while blinded to clinical and angiographic data.

### Coronary arteriography

Within one month of treadmill stress testing , all the patients had to undergo selective coronary arteriography and left ventriculography. The patients were hospitalized on the day before procedure. Coronary angiography was done using Judkins technique in multiple projections. Fifty percent or greater stenosis of the lumen of a major coronary artery was defined as significant

## RESULTS

### Clinical Characteristics

Based on the results of exercise testing and coronary angiographic findings, the patients were divided into the following four groups.

- 1) The true-positive (TP) group consisted of 22 patients with mean  $\pm$  SD age of  $52 \pm 9$  years. These patients had a positive treadmill test result with  $\geq 1$  mm horizontal ST - segment depression and an abnormal coronary

positive [FP] group). This group had a mean age of 43 ± 10 years. Three patients were female in this group.

- Table I shows all the baseline clinical characteristics of patients. Smoking was the commonest risk factor (58%).

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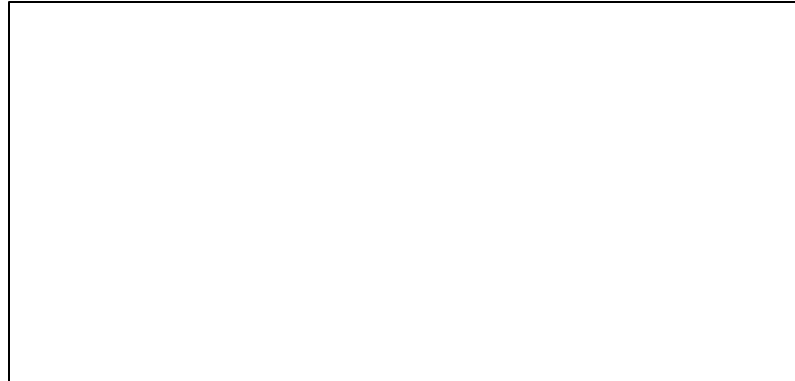
*LM* = Left main

There was a significant difference between the TP and FP groups ( $p < 0.01$ ). There also was a significant difference between the TP and TN groups ( $P < 0.001$ ). There were no significant difference between FP and TN groups, TP and FN groups.


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**Table -VII**  
**Diagnostic accuracy of ST-segment depression and peak exercise QTD and QTcD**



**PPV = Positive Predictive value**

**NPV = Negative Predictive value**

An exercise QTcD of 70 ms has sensitivity of 94%, specificity of 75%, positive predictive value of 81% and negative predictive value of 92%.

## DISCUSSION

The presence or absence of CAD based on ST-segment deviation is a traditional qualitative interpretation for the diagnosis of CAD. Many other variables of the exercise test responses are now analyzed to detect patients with CAD and is a new direction in treadmill testing.<sup>12</sup> QT dispersion criteria is one of them.<sup>10,11</sup>

### QTD and QTCD during exercise

The results of this study indicate that QTD and QTcD are increased during exercise - induced myocardial ischaemia in patients with significant coronary artery disease. The TP group had a wider baseline QTD, Which increased further with exercise. The baseline and exercise QTD and QTcD were similar in TN and FP groups. QTD has been reported to be increased during acute myocardial infarction.<sup>13</sup> These results are consistent with the reported findings during acute myocardial infarction and dobutamine stress

echocardiography.<sup>14,15</sup> Lee et al. found an increased QTD and QTc dispersion on the surface 12-lead ECG in association with regional ischaemia and wall motion abnormalities induced with dobutamine, dipyridamole, or exercise.

Moreno et al. demonstrated that successful thrombolysis is associated with a reduction in QT dispersion in patients with acute myocardial infarction. These findings provide some support to the hypothesis that QT dispersion on the surface ECG may reflect regional differences in ventricular recovery time or repolarization, which is increased during myocardial ischaemia.

### Diagnostic value of exercise QTD and QTc dispersion

The values of QTD and QTcD were assessed in terms of their potential to improve the accuracy of interpretation of stress ECG. The diagnostic accuracy of ST-segment depression of  $\geq 1$ mm alone has a sensitivity of 68% compared with 88% for QTD of  $>60$  ms and 94% for QTcD of  $>70$  ms. When either ST depression or QTD of  $>60$  ms was found, abnormal sensitivity rose to 95% with a drop of specificity to 60%.

When both ST-segment depression and QTD prolongation were needed for the test to be called positive, the specificity increased to 100%. These results are comparable to the diagnostic accuracy of the exercise test combined with an imaging modality.

Exercise- induced QTD  $>60$  ms had a positive predictive value of 94% for the prediction of significant CAD. The QTD  $\leq 60$  ms had a negative predictive value of 87% for the prediction of absence of coronary disease and identified 7 of the 8 patients with FP treadmill results.

Again QTcD of  $>70$  ms had a specificity of 75% for the detection of CAD with a sensitivity of 94%. Based on these results, it may be stated that if the goal of exercise testing in a study population is to detect the presence of any CAD, then one should use any abnormality in ST-segment deviation or an increase in QTD or QTcD as a potential marker of CAD. If the goal is to reduce false-positive results, then QTD or QTcD should be used as an additional condition for a positive test. These results indicate that measurement QTD or QTcD may be a useful adjunct in the interpretation of stress ECGs.

#### Study Limitations

One of the limitation of this study was the limited size of the study population, especially the one with false-positive exercise ECGs. It is also possible that the measured QT interval in a given lead may depend on the T-wave vector, especially the terminal forces.

However, we did not measure QT intervals in leads in which the T wave was flat or its termination was unclear. In addition, the same errors in QT interval measurements would have affected QTD calculations in all four groups. Although the QTD

measurement was made with the observer blinded to angiographic data, it was not possible to blind the observer to ST-segment depression, and this factor can potentially introduce a bias in its measurement. Our study population was predominantly male and hence these results may not be extrapolated to women.

#### CONCLUSION

It is evident from this study that QT dispersion criteria (exercise QTD $>60$  ms) can predict presence or absence of significant CAD with high sensitivity and specificity and positive predictive value may be as high as 94% as this study observed.

QT dispersion criteria is more sensitive (88%) and more specific (93%) for the diagnosis of significant CAD compared with 68% and 71%, respectively, for  $\geq 1$ mm ST-segment depression during stress.

When exercise QTD of  $\geq 60$ ms was added to ST-segment depression as a condition for positive test, the specificity increased to 100%. This criteria is extremely useful to exclude false positivity.

Exercise QTD  $\geq 60$ ms in female population has sensitivity of 67% and specificity of 88% for the diagnosis of significant CAD compared with 66% and 62%, respectively, for  $\geq 1$ mm ST-segment depression. Sensitivity and specificity of QTD  $\geq 60$ ms in female population are comparable with results of combined population of this study.

This preliminary study indicates that the measurement of QTD or QTcD is a useful adjunct in the interpretation of exercise ECG and may markedly improve the accuracy of exercise ECG. But this theory must be confirmed in a larger study population comparing the value of QTD or QTc dispersion to concomitant stress imaging studies.

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