

The Diagnostic Value of QT Dispersion for Acute Coronary Syndrome in Patients Presenting with Chest Pain and Nondiagnostic Initial Electrocardiograms

MURAT PEKDEMIR, M.D.¹, ILGIN KARACA, M.D.², YUNSUR CEVIK, M.D.¹, SEDAT YANTURALI, M.D.³,
AND ERDOGAN ILKAY, M.D.²

Abstract

BACKGROUND: Patients presenting with chest pain and nondiagnostic electrocardiograms (ECG) in the emergency department (ED) often pose a challenge to physicians. QT dispersion (QTD) is an electrocardiographic marker of myocardial ischemia due to nonhomogeneous ventricular repolarization. We hypothesized that QTD could accurately identify patients with acute coronary syndrome (ACS) who presented with chest pain and nondiagnostic initial ECGs.

METHODS: All patients admitted to the ED with chest pain and nondiagnostic initial ECGs were included in the study prospectively. QTD and QTc dispersion (QTcD) were measured at the initial ECGs and compared for ACS patients vs. non-ACS patients. A receiver operating characteristic curve was drawn to evaluate the diagnostic value of QTD and QTcD for ACS.

RESULTS: Of the 137 patients with an initially nondiagnostic ECG, 51 were finally diagnosed with ACS (37%). Mean QTD and QTcD of patients with ACS were significantly greater than those of patients without ACS (39.61 ± 12.9 vs. 32.56 ± 15.1 , $p=0.004$; 46.12 ± 16.3 vs. 38.10 ± 18.2 , $p=0.009$, respectively). The area under the curve was 0.624, $p=0.015$ for QTD, and 0.603 and $p=0.049$ for QTcD. When various cut-off points were evaluated, potentially useful values were determined between 30 and 50 ms for QTD (sensitivity 86% and 10%, specificity 35% and 97%, respectively). These values were 40.5 and 49.5 ms for QTcD (sensitivity was 96% and 32%, specificity was 12% and 77%, respectively).

CONCLUSION: For patients with chest pain and nondiagnostic initial ECG, ACS risk is high if QTD and QTcD values are greater than 40 ms. Therefore, QTD and QTcD can help identify patients with acute coronary syndrome who present with chest pain and a nondiagnostic initial ECG. However, poor operator characteristics of QT dispersion could limit its value as a diagnostic test in the clinical setting.

Key Words: Chest pain, QT dispersion, emergency department, nondiagnostic electrocardiogram, acute coronary syndrome.

Background

CHEST PAIN is a frequent cause for admission to the emergency department. It can be a sign of various conditions, from a minor disorder to a life-threatening disease such as acute myocardial infarction (AMI) (1). It is crucial for the physician to diagnose acute coronary syndrome correctly for the patient admitted to the ED with chest pain. (Patients with chest pain comprise 5–20% of all ED presentations [2, 3]). A majority of the patients presenting with chest pain are usually admitted to the hospital for further evaluation and management, but studies in-

dicating that some 60% are discharged with a diagnosis other than ACS. Despite the availability of modern-day tools for diagnosis of AMI, about 5% of patients with AMI are missed in the ED, with subsequent associated morbidity and mortality, as well as legal consequences. So, patients with low AMI risk must be observed in the ED for a period of time and discharged if clinical features and cardiac markers warrant it, in order to decrease the cost and duration of hospitalization (4).

Since the beginning of the 20th century, the electrocardiogram has been used widely for diagnosis and patient follow-up. Of the patients with classical ECG findings, such as new Q wave development or ST segment changes, 75–86% have been diagnosed with AMI, while only 40–65% of the AMI patients and 10% of unstable angina pectoris (UAP) patients have displayed these classical findings in their initial ECG (5, 6).

The QT interval represents the total duration of ventricular depolarization and repolarization. In

Departments of ¹Emergency Medicine and ²Cardiology, Firat University, Elazığ, Turkey; and ³Department of Emergency Medicine, Dokuz Eylül University, Izmir, Turkey.

Address all correspondence to Dr. Murat Pekdemir, Kocaeli University School of Medicine, Department of Emergency Medicine, Izmit/Kocaeli, Turkey; email: mpekdemir@yahoo.com

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1990, Day et al. (7) named the difference in the QT intervals between the derivations from ECG leads as "QT dispersion" (QTD) and noted that it represents the degree of the repolarization heterogeneity. "QTD" is defined as the difference between the maximum and minimum QT intervals, occurring in any of the 12 leads. Prolonged QTD is associated with an increased risk of serious ventricular arrhythmias in patients with long QT syndrome, hypertrophic cardiomyopathy, chronic heart failure or myocardial infarction (8). Experimental work has shown that increased dispersion of electrical recovery after activation is a key factor in the development of serious and fatal arrhythmias associated with ischemia (9).

In the United States each year, more than 5.3 million individuals present to emergency departments with chest discomfort and related symptoms. Ultimately, more than 1.4 million people are hospitalized for unstable angina and non-ST-segment elevation myocardial infarction. For emergency physicians and cardiologists alike, these patients represent an enormous challenge to accurately diagnose and appropriately treat. Identifying patients with ACS presenting to the ED is vital, and so it is critical to perform risk stratification early in the course of a patient's evaluation. The history, including risk factors for coronary artery disease development, as well as the physical examination, helps the clinician to screen patients for ACS. The 12-lead ECG and cardiac biomarkers serve as the major ancillary testing tools for risk stratification in the emergency setting (10). Yet despite all efforts to identify ACS, missed diagnosis is a continuing challenge. Discharging patients with acute myocardial infarction or unstable angina from the ED because of missed diagnoses can have dire consequences.

It has been suggested that QTD is a useful indicator for ischemic heart disease diagnosis and that it will reach the highest level in the first hours following AMI but may still be high when compared with healthy controls (11). The aim of this study was to assess the use of QTD and QTc dispersion (QTcD) to predict the likelihood of ACS in patients who present to the ED with chest pain and nondiagnostic initial ECG.

Material and Methods

The study was conducted at Firat University, Department of Emergency Medicine, between June and November 2002. Included in the study were patients with chest pain and without diagnostic initial ECG findings indicating ACS on ED presentation. Each patient was placed on a cardiac

monitor and a standard 12-lead ECG with a paper speed of 25 mm/s was taken. Patients' age, gender and time of pain onset were recorded. One copy of all initial ECGs of patients with chest pain was collected for the study. A single attending emergency physician and a cardiologist interpreted the initial ECGs without knowing the clinical presentation. All patients with nondiagnostic ECGs were included in the study.

Diagnosis of ACS

All study patients were examined and treated according to the usual practice. Diagnosis was based on final hospital discharge. Diagnosis of ACS (as per our institution's protocol) was based on ACS-specific special ECG changes in typical clinical features. In addition, serum markers were evaluated for indications of cardiac damage: specifically, initial cardiac troponin-T (cTn-T), creatine kinase myocardial band (CK-MB), and myoglobin levels were measured initially and repeated after the 6th hour. If the result was positive, samples were taken at six-hour intervals for 48–72 hours.

Determination of Myocardial Necrosis

1. Serial increase in plasma CK-MB level (more than 25% increase between two measurements).
2. CK-MB to total CK rate over 5%.
3. After 12 hours, cTn-T value over 0.1 ng/mL.

Evaluation of Serum Samples

Quantitative serum CK-MB and myoglobin level measurements were made with Cobas Integra-800 autoanalyzer (Roche Laboratory Systems, Mannheim, Germany) in the biochemistry laboratory. cTn-T levels were measured with Cardiac Reader (Roche Laboratory Systems) at bedside. Normal levels were 0–25 mg/dL for CK-MB, 7–76 mg/dL for myoglobin, and 0–0.10 ng/mL for cTn-T.

Measurement of QT and QTc

Excluded from the study were patients with any of the following: ECGs with diagnostic features for ACS, unclear QT interval in at least seven ECG leads, bigeminal ventricular systole, atrial fibrillation, a pacemaker, or current drug use affecting QT interval. QT interval was calculated from the onset of the QRS complex to the point of return of the T wave to the isoelectric line. Three sequential complexes were measured and the mean

value was used for QT interval calculation. For the patients with biphasic T waves, the intersection point of downstroking maximum T wave curve and the line tangential to isoelectric line was accepted as the end point. If there was a U wave, the lowest point between the two waves was accepted as the end point of the T wave (1). The difference between the maximum and minimum QT intervals, occurring in any of the 12 leads, was measured as QTD. QTc max and QTc min were determined with the Bazett formula ($QTc = QT / \sqrt{RR}$), and the difference between QTc max and QTc min was calculated as QTcD (12).

Quantitative data were reported as mean \pm standard deviation and qualitative data were reported as percentages. Differences in continuous variables (QTD and QTcD) were assessed using a 2-tailed Student's t test. Additionally, differences in the covariates of interest (gender and history of myocardial infarction) were assessed using the Mann-Whitney U test and chi square test, where appropriate for the patients with and without ACS. A p value <0.05 was considered to indicate statistical significance. Agreement between observers was verified using the Bland-Altman method (13). To evaluate the diagnostic value of QTD and QTcD for ACS, a receiver-operating characteristic (ROC) curve was created and the area under the curve (AUC) was calculated. The data were analyzed in the SPSS 11.0 program (SPSS Inc., Chicago, IL).

Results

During the study period, 232 patients with chest pain were admitted to the ED. A total of 95 patients were excluded (41%) from the study; 21 of the patients (9%) were excluded because QT measurements were not obtained or QT interval

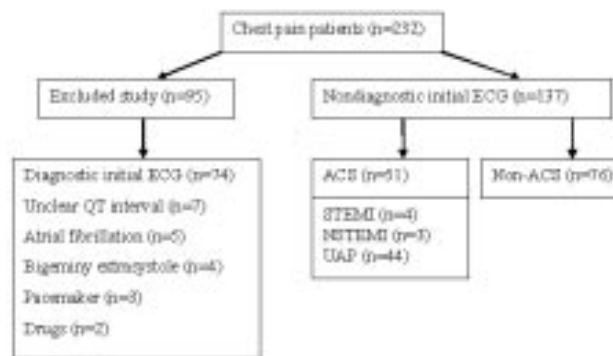


Fig. 1. Inclusion and exclusion criteria.

ACS = acute coronary syndrome; ECG = electrocardiogram; UAP = unstable angina pectoris; STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-STEMI.

was affected by drugs or pacemaker. Of the 137 studied patients, 51 had ACS (37%). ST-segment elevation myocardial infarction (STEMI), non-STEMI, and UAP were diagnosed in the ACS group during follow-up period ($n=4, 3,$ and $44,$ respectively; Fig. 1). Demographic features of the groups are shown in the Table. The mean difference between observers in the measurement of QTD and QTcD ($n=30$) was 0 ± 5 ms and 0 ± 4 ms; 95% CI was between -1 and 1 ms respectively.

Mean QTD of patients with ACS was significantly greater than that of patients without ACS (39.61 ± 12.9 vs. 32.56 ± 15.1 , $p=0.004$). Similarly, mean QTcD of patients with ACS was significantly greater than that of non-ACS patients (46.12 ± 16.3 versus 38.10 ± 18.2 , $p=0.009$). An ROC curve was created, to determine the diagnostic value for ACS of the QTD and QTcD of the initial ECGs (Fig. 2), and the AUC was calculated. AUC was 0.624 , $p=0.015$ for QTD, and 0.603 and $p=0.049$ for QTcD. When various cut-off points were evaluated, potentially useful values for predicting ACS

TABLE
Patient Characteristics and Final Diagnosis

	ACS (n=51)	Non-ACS (n=86)	p value
Patient Characteristics			
Gender (Female/Male) (n)	20/31	36/50	0.901
Age (mean \pm SD)	61.61 \pm 11.8	46.49 \pm 14.8	<0.001
Duration of pain / minute (median, IQR)	120, IQR 180	60, IQR 101	<0.001
History of myocardial infarction (n, %)	14 (27.5)	12 (14)	0.085
Outcome Measures			
QT dispersion (ms)	39.61 \pm 12.9	32.56 \pm 15.1	0.004
QTc dispersion (ms)	46.12 \pm 16.3	38.10 \pm 18.2	0.009

SD=standard deviation, IQR=interquartile range.

were between 30 and 50 ms for QTD (sensitivity 86% and 10%, specificity 35% and 97%, respectively). These values were 40.5 and 49.5 ms for QTcD (sensitivity was 96% and 32%, specificity was 12% and 77%, respectively).

Discussion

One study found that in 30–40% of the admissions with chest discomfort, the diagnosis was ACS (14). It is very important to evaluate patients with chest pain and normal initial ECG in ED. The common feature of the ACS group is that morbidity and mortality decrease significantly if the diagnosis is rapid and the therapy is specific. Therefore, in the emergency setting, it is critical to make appropriate decisions on whether to admit or discharge patients with chest pain of ischemic cause and nondiagnostic ECGs. For these patients, diagnostic cardiac indicators in the serum need time to reach a significant level, and waiting for the results leads to the loss of the crucial period known as the golden hour. In this study, we found that for patients with chest pain and nondiagnostic ECGs who were admitted to the ED, the QTD and QTcD means were different for the ACS and the non-ACS patients. The QTD and QTcD values that were found to be useful in ACS diagnosis, were 40 ms.

Manual QTD measurement is criticized as being operator-dependent (15). It has been reported that automatic and manual QTD measurements differ, but in good-quality ECGs, the difference between the normal and abnormal groups can be determined (16). We excluded the unclear ECG

determinations, to decrease the problem. Generally manual paper speed is 50 mm/s but in ED this is 25 mm/s. In order to make a rapid and practical evaluation of the initial ECG, we calculated the QTD and QTcD with a 25 mm/s speed, as recommended by Calder et al. (1).

Both animal and patient data have shown that during ischemia, repolarization time in the hypoperfused areas tends to shorten. In contrast, infarcted areas are associated with prolonged recovery times, which may result in increased dispersion of repolarization compared with the baseline state (17). Many studies have shown that QTD appears with coronary ischemia. The presence of QTD is also an indicator of myocardial electrical instability and increased arrhythmic mortality. In addition, QTD increase is seen as a response to temporary myocardial ischemia during an exercise test and there is a significant correlation between the QTD and degree of ischemia (18). In a study by Suzuki et al. (8) comparing atypical chest pain and vasospastic angina patients, it was found that QTcD is significantly longer for the vasospastic angina group and that QTD decreases after isosorbide dinitrate application in this group. When compared with healthy controls, QTD was longer in UAP patients and also in survivors when compared with the patients who died during follow-up (19). Independent of severity and localization of coronary artery disease, QTD is seen in myocardial ischemia (20). One study reports that combining automatic QTD measurement with other diagnostic methods has a potential clinical role in identifying AMI and acute cardiac ischemia (21). In this study we found that QTD and QTcD values are higher for ACS patients than for patients without ACS.

For patients who were admitted to the ED with chest pain and nondiagnostic initial ECG but later diagnosed as having AMI, QTD was longer than for the healthy controls, and found to be 44.6 ms (11). It has been suggested that initial QTD level has a low predictive power for new cardiac events, but that QTD can be more helpful for low-risk patient group, and that there is a significant correlation between QTD and mortality. The median QTD value has been determined to be 40 ms (15). As with earlier reports, the present study showed that if QTD and QTcD are over 40 ms, development of ACS is very probable despite the normal initial ECG.

The present study showed that the QT dispersion was greater for those patients who had a final diagnosis of ACS. However, QT dispersion appears to have poor ROC (0.624 or 0.603 for QT and QTc, respectively). This makes the test only slightly better than chance and not particularly

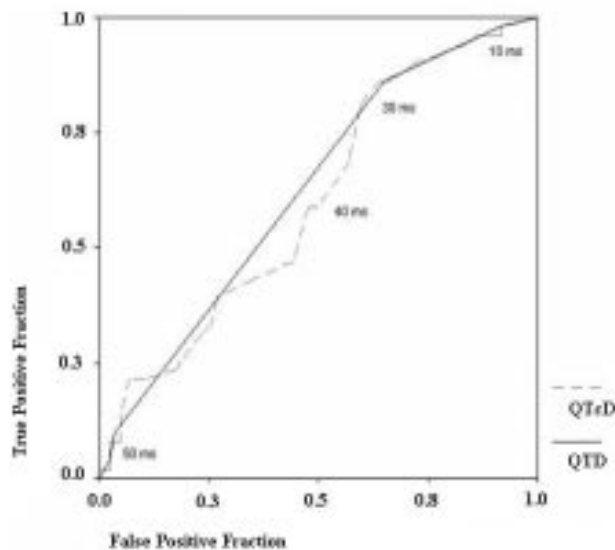


Fig. 2. Receiver operating characteristic curve for QT dispersion and QTc dispersion. QTD = QT dispersion, QTcD = QTc dispersion.

valuable as a diagnostic test in the routine clinical setting.

Conclusion

The present study demonstrated that QTD and QTcD means were markedly greater for patients who had a final diagnosis of ACS. The QTD and QTcD values that were found to be useful in predicting the likelihood of ACS were both 40 ms. However, difficulty with operator measurements of QT dispersion would limit its value as a diagnostic test.

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