QT Interval Dispersion

Non-invasive Marker of Ischemic Injury in Patients with Unstable Angina Pectoris?

Oben Döven, MD, Çagdas Özdol, MD, Tamer Sayın, MD, and Dervis Oral, MD

Summary
Prognostic assessment of unstable angina pectoris is a common clinical problem for physicians. Markers of myocardial cell injury, serial electrocardiographic findings and ST segment monitoring are mainly studied for prognosis.

We investigated the relation between myocardial injury and the value of cardiac troponin T and QT interval dispersion in hospitalized unstable angina patients.

This is a prospective study that includes adult patients admitted to an emergency department with Braunwald class IIIB unstable angina pectoris. Eighty-six patients were enrolled in the study (mean age of 57 ± 12 years, 63 males and 23 females). Cardiac troponin T was assayed and QT dispersion calculated from surface ECG. Fifty-eight patients with troponin T < 0.1 ng / ml and 28 patients with troponin T levels ≥ 0.1 formed group 1 and group 2, respectively.

There were no significant differences in sex, age, history of coronary revascularization or ECG findings such as ST depression and T inversions between the two groups. The QT dispersion was significantly greater in patients with elevated cardiac troponin T levels (77 ± 18 msec vs 38 ± 13 msec; p < 0.014).

Because QT interval dispersion exhibited an association with cardiac troponin T levels, it may be used as a non-invasive marker of ischemic injury in patients with unstable angina. (Jpn Heart J 2000; 41: 597-603)

Key words: Unstable angina pectoris, QT dispersion, Troponin T

Identification of patients with acute chest pain at high risk for cardiovascular complications is a common clinical problem for physicians. Surface ECG has been one of the most studied parameters for this purpose.1-4) QT interval on the surface electrocardiogram (ECG) is a measure of total time of ventricular depolarization and repolarization. Regional differences in ventricular repolarization are reflected as differences in QT intervals in leads corresponding to different parts of the myocardium. This heterogeneity is called QT interval dispersion.
Increased QT interval dispersion decreases the threshold for ventricular tachycardia and is associated with a risk of increased mortality. 5-9)

Creatine kinase (CK) and its isoenzyme CK-MB have been used for the diagnosis of myocardial injury for more than a decade. The single values of these tests have limited sensitivity and specificity for the detection of myocardial infarction. Some data suggest that an elevation in cardiac troponin T (cTnT) may be useful for the detection of less severe degrees of myocardial injury that may occur in patients with unstable angina.10,11)

Prior research has demonstrated that troponin T has excellent sensitivity for the diagnosis of acute myocardial infarction and also may be useful for prognostic stratification of patients with unstable angina pectoris.12-15) In this prospective study, we investigated the relation between myocardial injury and the value of troponin T and QT interval dispersion in hospitalized unstable angina patients.

**MATERIALS AND METHODS**

**Patient population:** This is a prospective study consisting of adult patients admitted to an emergency department with Braunwald class IIIB unstable angina pectoris from September 1998 through April 1999, with a chief symptom of anterior or precordial chest pain that could not be explained by any other obvious reason. Acute myocardial infarction patients with ST segment elevation, patients with more than 3 mm horizontal or downsloping ST segment depression accompanied by long lasting (> 30 minutes) severe chest pain, and patients with a diagnostic increase (≥ 2 of normal value) in serum levels of CK-MB in the 24 hours after admission were not included in the study population as diagnosed acute non Q myocardial infarction by a physician. Patients with intraventricular conduction delay (QRS duration ≥ 120 msec), atrial fibrillation and prior myocardial infarction were also excluded from the study. Eighty six patients were included in the final study population with Braunwald class IIIB unstable angina pectoris.

**Data Collection:** Clinical data collected from the emergency department evaluation included the patient’s age, sex, past medical history, physical examination and ECG. Blood was obtained at the time of presentation for cardiac enzyme assay and repeated every 8 hours under the supervision of a physician.

Cardiac troponin T was assayed using excess serum from routine phlebotomy in the emergency department in the first 24 hours. All patients
underwent 1 or more measurement of troponin T after the first 8 hours of their presentation to the emergency department. Troponin T was measured by an immunoassay procedure that uses complementary monoclonal antibodies. Analysis was performed on an ES-300 (Boehringer Mannheim Corporation): the upper limit of the reference interval was 0.1 ng/ml.

**QT analysis:** Standard electrocardiograms with simultaneous 12 lead acquisition were recorded at 50 mm/s. A blinded observer measured the QT intervals manually with calipers from the onset of the QRS to the end of the T wave defined as the return to the TP baseline. When U waves were present, the QT interval was measured to the nadir of the curve between the T and U waves. Three consecutive cycles were measured in each of the standard 12 leads and a mean QT calculated from the three values. When the end of the T wave could not be identified the lead was not included. QT was corrected for heart rate according to Bazett's formula: QTc = QT / RR^1/2. A minimum of six leads was required for QT dispersion to be calculated. The QT dispersion was defined as the difference between the maximum and minimum QT interval occurring in any of the 12 electrocardiographic leads.

**Statistics:** The results were analyzed using a statistical package for social sciences. Continuous variables are presented as the mean ± SD. The significance of the differences was tested by Student's unpaired t test and chi-square test. A value of p < 0.05 was regarded as significant.

**RESULTS**

Eighty-six patients were enrolled in the study [mean age of 57 ± 12 years, 63 (73%) males and 23 (27%) females]. Six (7%) patients had undergone a previous CABG operation and 9 (11%) patients had undergone percutaneous transluminal coronary angioplasty (Table I). We divided the patients into two groups according to their troponin T levels. Fifty-eight patients with troponin T < 0.1 ng/ml formed group 1 and 28 patients with troponin T levels ≥ 0.1 formed group 2. There were no differences in clinical presentation or ECG findings between the two groups. All patients received aspirin (300 mg/day). Patients were also treated with nitrates (n = 80), calcium antagonists (n = 34), beta blockers (n = 62) and heparin (n = 78).

Table II shows the results of the QT analysis at 24 hours. Even though the calculated QTc intervals were similar between the two groups, QT dispersion was significantly greater in patients with elevated troponin T levels (p = 0.014).
Table I. Characteristics of Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 ± 12 (35-82)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>63 (73%)</td>
</tr>
<tr>
<td>Mean heart rate (beat / min)</td>
<td>73 ± 10 (55-105)</td>
</tr>
<tr>
<td>Previous CABG (n)</td>
<td>6 (7%)</td>
</tr>
<tr>
<td>Previous PTCA (n)</td>
<td>9 (11%)</td>
</tr>
<tr>
<td>ECG at presentation (n)</td>
<td></td>
</tr>
<tr>
<td>ST depression</td>
<td>49 (57%)</td>
</tr>
<tr>
<td>T inversion</td>
<td>37 (43%)</td>
</tr>
<tr>
<td>cTn T (n)</td>
<td></td>
</tr>
<tr>
<td>&lt; 0.1 ng / ml</td>
<td>58 (67.4%)</td>
</tr>
<tr>
<td>≥ 0.1 ng / ml</td>
<td>28 (32.6%)</td>
</tr>
</tbody>
</table>

Table II. Clinical and QT Analysis of Patient Groups

<table>
<thead>
<tr>
<th></th>
<th>cTn T (-)</th>
<th>cTn T (+)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 58</td>
<td>n = 28</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>55 ± 11</td>
<td>61 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>42 (67%)</td>
<td>21 (75%)</td>
<td>NS</td>
</tr>
<tr>
<td>ST depression (n)</td>
<td>32 (57%)</td>
<td>17 (61%)</td>
<td>NS</td>
</tr>
<tr>
<td>T inversion (n)</td>
<td>26 (43%)</td>
<td>11 (39%)</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate (beat / min)</td>
<td>71 ± 9</td>
<td>74 ± 12</td>
<td>NS</td>
</tr>
<tr>
<td>QTc (msec)</td>
<td>424 ± 34</td>
<td>436 ± 21</td>
<td>NS</td>
</tr>
<tr>
<td>QT dispersion (msec)</td>
<td>38 ± 13</td>
<td>77 ± 18</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Interactive Graph

Figure. QT dispersions in the cardiac troponin T negative and positive patients with Braunwald class IIIB unstable angina pectoris.
DISCUSSION

Prognostic assessment of unstable angina pectoris resulting from sub-total thrombotic occlusion of the coronary arteries is a common clinical problem for physicians. In clinical practice, prognosis is based on clinical history, objective findings and laboratory data. Early identification of patients with high risk angina, however, has largely focused on the markers of myocardial cell injury, serial electrocardiographic findings and ST segment monitoring.13-18)

Troponin T in one of the most studied laboratory parameters, and among the data potentially available, serum levels of cardiac troponin T have significantly greater prognostic value than other laboratory parameters in patients with unstable angina pectoris.13,14,19) Multivariate analysis showed that serum levels of troponin T is an independent factor with high sensitivity and specificity for poor prognosis.14)

QT interval dispersion reflects regional variations in ventricular repolarization and cardiac electrical instability, which is a substrate for ventricular arrhythmia. Previous studies showed that QT interval dispersion increases during episodes of myocardial ischemia in patients with coronary artery disease, however, only a limited number of studies have thus far examined the relation between the extent of myocardial ischemia and degree of QT interval dispersion.20-24)

Our study is, to the best of our knowledge, the first to examine the degree of QT dispersion with troponin T levels in high risk patients with Braunwald class IIIB unstable angina. Elevations of cardiac troponin T were detected in the first 24 hours among 28 (32.6%) of the 86 patients with unstable angina. We found a significant association between dispersion of ventricular repolarization (the difference between maximum and minimum QT interval measurements in any of the 12 leads on a standard electrocardiogram) and cellular injury in patients with class IIIB unstable angina who had elevated troponin T. This association was independent of age, sex, and drug assignment.

This study also shows that microscopic levels of injury detected by elevated troponin T may result in modification of ventricular repolarization in a large area of the myocardium to be detected by surface ECG. This level of injury may change extracellular potassium and / or intracellular hydrogen which modify ventricular repolarization hours after the ischemic episodes, and also explains the considerable change in QT behavior between the leads.

In conclusion, increased QT interval dispersion is a non invasive
marker of ischemic cellular injury in patients with Braunwald class IIIB unstable angina, and since it is closely correlated with elevated cardiac troponin T levels, it may be used to identify high risk patients.

REFERENCES
