Assessment of QT Dispersion in Patients with Acute STEMI Receiving Thrombolytic Versus those Performing Primary Percutaneous Coronary Intervention (PCI) Therapy

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Abstract

Background: ECG is a necessary tool for the diagnosis of myocardial infarction and cardiac arrhythmia. The QT interval reflects the duration of ventricular electrical activity, determined by the phases of depolarization and repolarization. QT dispersion (maximum QT interval minus minimum QT interval) was originally proposed as an index of the spatial dispersion of ventricular recovery times.

Aim of the Study: This study was carried out aiming to compare QT dispersion in patients presenting with STEMI and treated with thrombolytic therapy versus those treated with PCI therapies.

Subjects and Methods: The study was carried out at Cardiology Department in Specialized Medical Hospital, Mansoura University from January 2014 to January 2015. Approval to conduct this study was obtained. Also, written consents were obtained from the patients to participate in the study. The study was conducted on 50 patients presented with acute STEMI. Patients were divided into two groups depending on the reperfusion strategy. First group included 25 patients treated with thrombolytic therapy. The second group included another 25 patients treated with PCI therapies. All patients were interviewed using a specially designed questionnaire. Furthermore, anthropometric measurements and laboratory investigations were done. QT intervals of the studied patients were manually calculated at admission (before treatment) and in 24 hours (after treatment). The population enrolled in this study was composed of 35 male patients and 15 female patients with age range between 25 and 75 years. Diabetic patients constituted 56% of the studied sample, whereas patients having hypertension represented 46% of the studied sample. 60% of the studied patients were smokers and dyslipidemia was present in 66% of the studied sample.

Results: Most patients studied were males, diabetic, smoker, and dyslipidemic. Mean age of female patients (54.09±9.35 years) was more than that of male patients (57.47±9.53 years). Patients presented with anterior STEMI were more than those presented with inferior STEMI. There were a significant reduction in QT and QTc dispersions before and after reperfusion regardless of reperfusion strategy (p<0.001 and <0.001 respectively). There were non-significant reduction in QT and QTc dispersions before and after thrombolytic therapy (p=0.147 and p=0.097 respectively), however, there were significant reduction in QT and QTc dispersions after PCI therapies (p<0.001 and p<0.001 respectively). Our study revealed higher significant reduction in QT and QTc dispersions after PCI therapies than after thrombolytic therapy (p=0.005 and p=0.005 respectively). There were non-significant differences in QT and QTc intervals and dispersions before reperfusion according to the site of the infarction (p=0.765 and p=0.0801 respectively). QT maximum and QT minimum were significantly higher in patients with inferior STEMI than those with anterior STEMI after reperfusion (p=0.046 and 0.015 respectively).

Conclusion: Primary PCI is associated with higher significant reduction in QT and QTc dispersion than thrombolytic therapy. So it will be associated with lower incidence of ventricular arrhythmias.

Recommendations: We recommend future larger studies that involve automatic measurements of QT interval which will increase the accuracy of the results to compare different coronary reperfusion strategies.

Key Words: QT dispersion – Thrombolytic therapy – Primary PCI.

Introduction

CAD is a chronic disease with symptoms that require ongoing monitoring and treatment to prevent further complications such as Myocardial Infarction (MI) and chronic heart failure [1].

The Electrocardiogram (ECG) is a necessary tool for the diagnosis of Myocardial Infarction (MI) and cardiac arrhythmia. The QT interval reflects the duration of ventricular electrical activity, determined by phases of depolarization and repolarization, while QT dispersion (QTd), (maximum QT interval minus minimum QT interval) was originally proposed as an index of the spatial dispersion of ventricular recovery times. In reality,
QT dispersion is a crude and approximate measure of a general abnormality of repolarization; it reflects inhomogeneity of ventricular repolarization [2]. This measurement was an attempt to distinguish between myocardium that is homogeneous from myocardium that displays inhomogeneity, which is accompanied by increased dispersion of the ventricular recovery times and prolongation of repolarization [3].

An accurate assessment of QT dispersion requires all 12 leads of the ECG to be recorded simultaneously in order to avoid the effect of heart rate changes on QT dynamics. As a result, simultaneous 12-lead recordings have been proposed as the gold standard for the measurement of QT dispersion. Since rate-related changes in the QT interval develop slowly, QT dispersion measurements based upon simultaneous recording of six or even only three QRS complexes during ectopic-free sinus rhythm is acceptable for practical purposes [4].

Ischemia can increase QT dispersion. Percutaneous Coronary Intervention (PCI) is widely used to manage ischemia in patients with coronary artery disease. However, there is lack of information on the influence of elective PCI on ECG parameters, especially QT parameters [5].

Thrombolytic therapy has been a major advance in the management of acute myocardial infarction. Thrombolytic therapy works by lysing infarct artery thrombi and achieving reperfusion, thereby reducing infarct size, preserving left ventricular function, and improving survival. The most effective thrombolytic regimens achieve angiographic epicardial infarct-artery patency in only 50% of patients within 90 minutes [6].

Aim of the work:

The aim of this study is to compare QT dispersion in thrombolytic versus percutaneous coronary intervention therapies in patients with CAD and to evaluate the effect of thrombolytic therapy and PCI on electrocardiographic QT interval, corrected QT interval, QT dispersion, and the implications of such assessment for prediction of ventricular arrhythmias.

Subjects and Methods

The study population included 50 patients admitted to Cardiology Department at Specialized Medical Hospital in Mansoura University during the period January 2014 to January 2015 with acute STEMI. Acute STEMI was defined using the third universal definition of MI which signifies detection of rise and/or fall of cardiac biomarker values (preferably Troponin) with at least one value above the 99th percentile of the upper reference limit and with at least one of the following: Symptoms of ischemia, new or presumably new significant ST-T changes (0.1mV in at least two contiguous leads) or new LBBB, development of pathological Q waves in the ECG, imaging evidence of new loss of viable myocardium, or new regional wall motion abnormality and identification of an intracoronary thrombus by angiography or autopsy. ECG localization of MI was assessed: Anterior MI (include anterior, anteroseptal, anterolateral and extensive anterior) and inferior MI (include inferior, inferoposterior, and inferolateral) [7].

Exclusion criteria:

Patients were excluded from the study for any of the following reasons: NSTEMI, prior history of MI or surgical revascularization, atrial fibrillation or flutter, bundle branch block or any other intraventricular conduction abnormalities, pre-excitation on ECG, ventricular pacing rhythm, cardiogenic shock, need for urgent CABG or repeat PCI during a 24-hour period after the procedure, electrolyte disturbance, history of medications that may affect QT (anti-arrhythmic, anti-psychotic, and anti-depressant drugs) and if QT interval could not be reliably measured in at least nine leads.

Patients included in the study were divided into two groups depending on the reperfusion strategy. First group consists of 25 patients reperfused by fibrinolytic therapy. Thrombolytic agent used was Streptokinase in a dose 1.5 million units intravenous given over 30-60min [8]. Coronary angiography was not done in patients who received thrombolytic therapy in the acute phase of MI. Second group consists of another 25 patients reperfused by primary PCI (aspiration device, PTCA, and/or combined with stenting). Aspirin, clopidogrel, and intravenous heparin were routinely given to study patients.

Measurements of QT intervals were calculated at admission (before treatment) and in 24 hours ECGs (after treatment). At the time of both these ECGs, patients were not taking antiarrhythmic drugs and their electrolyte status was normal.

All standard 12-lead ECGs were recorded at a paper speed of 25mm/sec and 10mm/mV gain [9]. ECGs were recorded using ECG Cardimax electrocardiogram device, Fukuda Denshi FX-2111 model 93908-02, Tokyo, Japan.

Measurements of QT and RR intervals were manually performed. QT interval was measured
from the beginning of the Q wave to the end of the T wave. The end of the T wave was defined as a return to the isoelectric baseline. U wave when present, the QT was measured to the nadir of the curve between the T and U waves. If the end of the T wave could not be determined reliably or if the T waves were isoelectric or of very low amplitude, measurements were not done and these leads were excluded from the study [2].

All patients had a minimum of eight ECG leads that were measurable, at least four precordial leads required for inclusion of the patient. All of the ECGs were in sinus rhythm.

In order to exclude the effect of heart rates on QT intervals, QT intervals were corrected (QTc) according to Bazett’s formula (QTc = QT/square root of the RR interval in seconds) [10] if the heart rate between 60-110b/min and according to Hodgess’s formula QTc = QT + 1.75 (HR-60) [10] if the heart rate is less than 50b/min or more than 110 b/min to avoid under correction and over correction, respectively.

QT and QTc dispersions were defined as the difference between the maximum and minimum QT, and the maximum and minimum QTc interval measurements, respectively [2].

Data collection:
A pre-designed interview questionnaire was used to collect personal data, smoking habit, history of hypertension, diabetes mellitus, chronic kidney disease or medications for them and positive family history of premature CAD that is defined as the presence of documented CAD in a first-degree relative male less than 55 years or female less than or equal to 65 years [11].

The following investigations were performed for every patient: Plasma glucose concentration, plasma lipoprotein profile, electrolyte profile, complete blood count, serum creatinine and blood urea.

Statistical analysis:
The collected data were revised, organized, tabulated and statistically analyzed using Statistical Package for Social Sciences (SPSS) version 22 for windows. Data are presented as the Mean ± Standard Deviation (SD), frequency, and percentage. Categorical variables were compared using the chi-square (Χ²) and Fisher’s exact tests. Continuous variables were compared by the Student t-test (two-tailed). Comparison of ECG data before and after treatment by the paired t-test for normally distributed data. Mann-Whitney U test was used to compare nonparametric data. Pearson and spearman correlation coefficients were used to evaluate the relationship between continuous variables. The level of significance was accepted if the p-value <0.05 [12].

Results
The population enrolled in this study composed of 50 CAD patients, 35 were males and 15 were females with age range between 25 and 75 years (mean age was 55.10±9.44 years, mean age of male patients was 54.09±9.35 years, and mean age of female patients was 57.47±9.53 years).

Table (1): Demographic and clinical characteristics of the studied patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (N=50)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (M ± SD)</td>
<td>55.10±9.44</td>
<td>–</td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>35</td>
<td>70.0</td>
</tr>
<tr>
<td>Female</td>
<td>15</td>
<td>30.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>28</td>
<td>56.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23</td>
<td>46.0</td>
</tr>
<tr>
<td>Smoking</td>
<td>30</td>
<td>60.0</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>33</td>
<td>66.0</td>
</tr>
<tr>
<td>Site of infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>29</td>
<td>58.0</td>
</tr>
<tr>
<td>Inferior</td>
<td>21</td>
<td>42.0</td>
</tr>
</tbody>
</table>

Table (2): Comparison of some demographic and clinical characteristics of the studied patients according to reperfusion strategy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Thrombolytic therapy (N=25)</th>
<th>PCI therapies (N=25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (M ± SD)</td>
<td>57.80±8.94</td>
<td>52.40±9.32</td>
<td>0.042</td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16</td>
<td>19</td>
<td>64.0</td>
</tr>
<tr>
<td>Female</td>
<td>9</td>
<td>6</td>
<td>36.0</td>
</tr>
<tr>
<td>DM:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14</td>
<td>14</td>
<td>56.0</td>
</tr>
<tr>
<td>No</td>
<td>11</td>
<td>11</td>
<td>44.0</td>
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<tr>
<td>HTN:</td>
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<td></td>
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</tr>
<tr>
<td>Yes</td>
<td>14</td>
<td>9</td>
<td>56.0</td>
</tr>
<tr>
<td>No</td>
<td>11</td>
<td>16</td>
<td>44.0</td>
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<tr>
<td>Smoking:</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Yes</td>
<td>16</td>
<td>14</td>
<td>56.0</td>
</tr>
<tr>
<td>No</td>
<td>9</td>
<td>11</td>
<td>44.0</td>
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<tr>
<td>Dyslipidemia:</td>
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<tr>
<td>Yes</td>
<td>21</td>
<td>12</td>
<td>84.0</td>
</tr>
<tr>
<td>No</td>
<td>4</td>
<td>13</td>
<td>16.0</td>
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<tr>
<td>Site of infarction</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>14</td>
<td>15</td>
<td>56.0</td>
</tr>
<tr>
<td>Inferior</td>
<td>11</td>
<td>10</td>
<td>44.0</td>
</tr>
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</table>
Table (2) showed significant difference regarding age between patients treated with thrombolytic therapy and those with PCI based treatment strategy (57.80±8.94 and 52.40±9.32, respectively). Also, dyslipidemia was more among patients treated with thrombolytic therapy based strategy than those treated with primary PCI based strategy (84.0% and 48.0%, respectively). On the other hand, there were no significant differences between the two groups regarding other demographic and clinical characteristics.

Fig. (1) showed comparison of the HR and QT intervals of the studied patients before and after thrombolytic therapy regardless of reperfusion strategy. This figure demonstrates that there were no statistically significant differences noticed regarding HR, QT maximum, and QT minimum before and after reperfusion therapy (p=0.352, 0.187 and 0.081, respectively). Whereas there were a significant reduction from admission to 24 hour ECGs in all studied patients treated with thrombolytic agent or primary PCI regarding QT dispersion, QTc maximum, and QTc dispersion. On the other hand, QTc minimum was significantly increased after 24 hours of thrombolytic therapy.

Table (3): Comparison of the HR and QT intervals of the studied patients before and after thrombolytic therapy.

Table (4) showed significant changes in all QT and QTc measurements before and after PCI therapies, except HR and QT maximum.

Table (5) showed significant reduction in QT dispersion and QTc dispersion in patients treated with primary PCI therapies when compared with those treated with thrombolytic therapy (p=0.005 and 0.005, respectively). However, other QT interval measurements did not significantly vary between both groups.

Fig. (2) showed that there were no significant differences between anterior and inferior MI regarding QT and QTc measurements. Fig. (3) showed that there was significant reduction in HR after reperfusion in patients presented with inferior MI when compared with those presented with anterior MI (p=0.030). Also, there were significant reduction in the QT maximum and QT minimum after reperfusion in those presented with anterior MI when compared with those presented with inferior MI (p=0.046 and 0.015, respectively).
Increased QT dispersion reflects inhomogeneous ventricular repolarization, which may provide a background for significant ventricular arrhythmias [13]. Prolonged QT dispersion is associated with a higher risk of malignant ventricular arrhythmias in patients with the long QT syndrome, hypertrophic cardiomyopathy, and myocardial infarction [14]. Kosar et al., [13] showed that effective management of acute MI or ventricular arrhythmias may reduce QT dispersion.

During acute MI increased QT dispersion is a well-known finding. Also it was found that QT dispersion is significantly greater in patients with MI who had malignant ventricular arrhythmias than in those without arrhythmias [15]. Van de Loo et al., [16] reported that; patients with acute MI who developed ventricular fibrillation within the first 24 hours after admission, QT dispersion was significantly longer (88±30msec) than in those without ventricular fibrillation (56±24msec).

On the other hand, other researchers noticed that in patients with reperfusion, QT interval was prolonged transiently within 12 hours and shortened later, whereas in patients without reperfusion QT interval became prolonged progressively on serial ECGs recorded within 72 hours after the onset of symptoms [19].

As regarding site of infarction; patients in our study presented with anterior MI were more than those presented with inferior MI (58.0% and 42.0%, respectively). These findings coincide with those reported by Cavusoglu et al., [20]; in which anterior and inferior MI were 57.14% and 42.86%, respectively.

Pan et al., [21] clarified that QTc dispersion change after primary PCI considered as independent predictor for the development of major cardiovascular events (which was defined as life threatening arrhythmias, nonfatal MI, heart failure hospitalization, and death) at one year follow-up. As they found that every 10msec reduction in QTc dispersion associated with a 49.8% decrease in the risk for the development of major cardiovascular events.

In our patients, there was no significant change in QT maximum and minimum before and after reperfusion, which coincides with Cavusoglu et al., [20], Nikiforos et al., [22], and Alasti et al., [23]. Whereas, a significant change was noticed among the studied sample as regarding; QT dispersion, QTc maximum, QTc minimum, and QTc dispersion. These findings are consistent with data reported by Cavusoglu et al., [20], Nikiforos et al., [22], Aydinlar et al., [5], and Alasti et al., [23].
De Boer et al., [24] had documented that treatment of acute MI with thrombolytic agents or primary PTCA leads to reestablishment and maintenance of coronary patency, preserves myocardial function, and improves survival. Also, it’s known that establishing sustained patency of the artery leading to reduction of the electrophysiological instability so reducing the QT dispersion [25].

In acute MI, early thrombolytic therapy is known to reduce mortality. Improvement in the left ventricular functions and reduction of late arrhythmias by enhancing electrical stability of the heart may decrease the rate of sudden deaths. Thus, thrombolytic therapy is expected to have a positive effect on late arrhythmic events after infarction [26].

We did not found a significant reduction in QT dispersion in our patients before and after thrombolytic therapy. Our findings are in agreement with other reports [13,27-30]. On the other hand, Cavusoglu et al., [20] and Nikiforos et al., [22] had concluded that patients treated with thrombolytic therapy were associated with a significant reduction in QT and QTc dispersions.

Choi et al., [31] demonstrated that QT dispersion decreased in coronary artery disease patients with no history of myocardial infarction at one month following a successful PCI. Another study performed by Aydinlar et al., [5] revealed a reduction in QT dispersion immediately after percutaneous transluminal coronary angioplasty. According to our data, a successful full revascularization of patients with acute STEMI is associated with a significant reduction in QT dispersion.

Furthermore, there were significant reduction in the QT and QTc measurements before and 24 hours after PCI but not in the QT maximum and minimum interval measurements. These findings are in agreement with Cavusoglu et al., [20]; Alasti et al., [23] and Alici et al., [32]. They found that these two measurements did not vary significantly between admission and 24 hours after PCI treatment.

Although there was a significant reduction in QT and QTc dispersions in both groups (those treated with thrombolytic therapy and those treated with primary PCI), we noticed that QT and QTc dispersions were shorter in the primary PCI group than in the thrombolytic group. These findings can be related to the higher TIMI 3 flow patency rate obtained by primary PCI. This is important in the context of the fact that PCI is generally associated with better clinical outcomes when compared with thrombolytic therapy. Also, Cavusoglu et al., [20] showed that PTCA is associated with a more significant decrease in QT and QTc dispersions compared to thrombolysis.

Our study revealed that QT and QTc dispersions are greater in anterior MI than inferior MI [33]. Furthermore, it has been reported that QT and QTc dispersions are dependent on the infarct size, and the greater values of QT and QTc dispersions associated with anterior MI can be explained by larger infarction [34].

On the other hand, it has been found that no significant differences in QT measurements between patients presented with anterior MI and those presented with inferior MI before and after reperfusion regardless to reperfusion strategy.

Our findings are incompatible with a study conducted by Cavusoglu et al., [20] who observed a significant reduction of QT and QTc dispersions with reperfusion therapy in both sites of MI.

The major limitation of the present study may be represented by the small number of the patients. So, designing a larger study with more cases could be more informative.

A limitation of QT interval assessment is that it is not always measurable in every lead or may be difficult to measure with precision in certain leads.

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