QT dispersion on ECG in acute ischemic stroke and its impact on early prognosis

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ABSTRACT

الأهداف: تقييم آثار تشتيت (QT) المصحح (QTcd) لعلاج المرضى المصابين بمرحلة مبكرة من جلطة نقص التروية غير الفجوية، بغض النظر عن موقع وجود الآفة.

الطريقة: في هذه الدراسة التطلعية العشوائية، تم تقييم المرضى المصابين بالجلطة الدماغية في وحدة العناية المركزة بمستشفى كوكوروفا الجامعي – ادانا – تركيا، خلال الفترة من 2002م وحتى عام 2003م. تم تسجيل الأعراض العصبية لجميع المرضى وفقاً لنقاط غلاسجو للغيبوبة (GCS) وسلم النقاط العصبي الكندي. تم تحديد الأنواع الفرعية للجلطة الدماغية وفقاً لتصنيف مشروع أكسفورد شير لجلطة المجتمع. شملت الدراسة أيضاً المرضى الذين سجلوا مابين 7 إلى 11 نقطة على مقياس غلاسجو للغيبوبة (GSC). تم جمع نتائج تخطيط القلب الكهربائي للمرضى في الساعات الست الأولى، تم حساب (QT) المصحح (QTc) بواسطة صيغة بازيت. تم تحديد تشتيت (QT) المصحح (QTcd) كحد أقصى ناقص – الحد الأدني من فترة (QT).

النتائج: تم تقسيم إجمالي عدد 148 مريضاً (74 ذكراً) مصابا بجلطة دماغية حادة، تراوح العمر بين 36–90 عاماً (متوسط العمر 63.07±12.55) إلى مجموعتين. المجموعة الأولى تكونت من المرضى الناجيين (عدد=109) والمجموعة الثانية تكونت من المرضى المتوفين (عدد=39). لم يكن هنالك فروقات إحصائية ملحوظة في: متوسط العمر، والجنس، وتكرار ارتفاع ضغط الدم، وداء السكر، ومرض الشريان التاجي بين المجموعتين. كان لدى المجموعة الثانية (7.4±3.7) (QTcd) أعلى بشكل ملحوظ مقارنة مع المجموعة الأولى (p=0.002).

خاتمة: أظهرت هذه الدراسة أن قيمة (QTcd) لدى التنبؤ بعلاج المرضى المصابين بمرحلة مبكرة من جلطة نقص التروية غير الفجوية بغض النظر عن موقع وجود الآفة.

Objectives: To evaluate the effects of corrected QT dispersion (QTcd) on patients' prognosis with early stage non-lacunar ischemic stroke, regardless of location of the lesion.

Methods: In this non-randomized prospective study, stroke patients were evaluated in the intensive care unit of Cukurova University Hospital, School of Medicine, Adana, Turkey, from 2002-2003. Neurologic symptoms of all subjects were recorded according to Glasgow Coma Scale (GCS) and Canadian Neurological Scale. Subtypes of stroke were defined according to the Oxfordshire Community Stroke Project classification. Patients with GCS between 7 and 11 were included in the study. Electrocardiograms of the patients were collected in the first 6 hours. Corrected QT (QTc) were calculated by the Bazzett formula. Corrected QT dispersion was defined as maximum minus minimum QT interval.

Results: A total of 148 (74 male) consecutive acute stroke patients, aged between 36-90 years (mean 63.07 ± 12.55), were divided into 2 groups. Group I consisted of surviving patients (n=109) and Group II consisted of expired patients (n=39). There were no statistically significant differences in the mean age, gender distribution, frequency of hypertension, diabetes mellitus, and coronary artery disease between the groups. Group II (7.4 ± 3.7) had significantly higher QTcd (7.4 ± 3.7) compared to Group I (p=0.002).

Conclusion: This study shows the value of QTcd in predicting patients' prognoses with early stage non-lacunar ischemic stroke, regardless of location of the lesion.

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Acute ischemic stroke has 12.2% and 19% mortality rates for the following 7 and 28 days.[1] The majority of the deaths occur due to direct effects of brain damage on the early days of the stroke. Cardiac complications are less frequent but may be responsible for the mortality. One percent of the deaths is related to myocardial infarction during the first 28 days.[2] Cardiac arrest due to sudden fatal ventricular arrhythmias, chronic congestive heart failure, and dilated cardiomyopathy are some other cardiac causes of approximately 6% of mortality during the acute stroke phase.[3,4] In addition, the QT dispersion (QTd) is considered to be a marker of electrical instability of the ventricular myocardium, and it may be associated with an increased incidence of ventricular arrhythmias and sudden death.[5,6] The QT dispersion can also be seen with ischemic heart disease, hypertension, diabetes mellitus, and left ventricular hypertrophy. Recent studies show that the QT variability might influence mortality in stroke patients.[7] In the first study on this subject, it was found that QTd was significantly longer in patients with involvement of the insular cortex compared to the patients without this involvement.[8] In another study, early mortality rate was found to be higher in patients with acute ischemic stroke and QTc prolongation.[9] The aim of the present study was to investigate the relation between QTd and prognoses of patients with acute ischemic stroke.

Methods. This was a prospective, non-randomized comparative, and controlled study, from June 2002 to May 2003, all patients (n=148) diagnosed with non-lacunar acute ischemic stroke in the Neurology Intensive Care Unit, Cukurova University Hospital, Adana, Turkey, were included consecutively in the present study. This study was approved by the local ethical committee and written consent was received either from the patients or their first-degree relatives (in case of unconsciousness).

Inclusion criteria. The diagnosis of stroke was made by history, neurological examination, and CT. Acute ischemic stroke was diagnosed according to general and neurological examination. Inclusions were made as soon as a diagnosis of acute ischemic stroke was confirmed by a consultant neurologist. Neurologic and mental states were evaluated according to the Canadian Neurological Scale (CNS) and Glasgow Coma Scale (GCS).[10,11] Patients with GCS between 7 and 11 were included in the study.

Exclusion criteria. Patients with non-lacunar ischemic stroke who had a history or clinical or laboratory evidence of coronary artery disease (CAD), valvular heart disease, heart failure, cardiac arrhythmia, any whose ECG showed bundle branch block, and a kind of cardiomyopathy were excluded. Besides, patients taking any medication (antiarrhythmic drug, digoxine, lithium carbonate, tricyclic antidepressant drugs, phenothiazines, erythromycin stearate, levodopa and theophylline) known to affect repolarization parameters on the ECG were not involved in this study. Patients with a correctable cause of an electrolyte imbalance (serum potassium and/or calcium and magnesium levels) were excluded from study.

Neurologic assessment. Subtypes of stroke were defined as lacunar infarct (LACI), total anterior circulation infarct (TACI), partial anterior circulation infarct (PACI), and posterior circulation infarct (POCI) according to the classification made by the Oxfordshire Community Stroke Project (OCSP).[12] Cerebral CT was carried out in the Emergency Department. The CT examinations were repeated in the 72nd hour in patients who had a normal CT in the beginning.

General assessment. Data from the patients' records regarding blood pressure, hyperlipidemia, diabetes mellitus, cigarette smoking, previous stroke, and coronary heart disease were recorded. Patients with a sustained blood pressure ≥140 mm Hg systolic and 90 mm Hg diastolic or using an antihypertensive medication were defined as hypertensive.[13] Coronary artery disease was diagnosed if the patients had a history of myocardial infarction, coronary artery bypass grafting or percutaneous transluminal coronary angioplasty, angina, abnormal stress test, or positive coronary angiograms. Diabetes mellitus was defined as hyperglycemia, requiring antidiabetic drugs, or fasting blood sugar over 126 g/dl.[14] Serum potassium and/or calcium and magnesium levels were between normal ranges in the first 24 hours.

Electrocardiography. Twelve-lead ECGs with a speed of 25 mm/s were recorded in the first 6 hours of hospitalization. All ECG recordings were analyzed by 2 blinded cardiologists. The QT intervals were manually measured and defined as the distance between the start point of the QRS complex to the end point of the T wave and T wave's end point at the isoelectric line. If the U wave was present, then the lowest point of T and U wave junction was accepted as the end of QT interval. Corrected QT (QTc) was calculated by the Bazzett formula (QTc = QT/(RR)1/2). Corrected QT dispersion (QTcd) was defined as maximum minus minimum QTc interval. ST segment changes, T wave abnormalities, bundle branch blocks, atrial and ventricular arrhythmias were also inspected. All neurologic and cardiologic events during hospitalization were recorded. The relation between QTcd and in-hospital mortality was evaluated.

Statistical analysis. Statistical Package for Social Sciences (SPSS) version 9.0 (SPSS Inc., Chicago, Illinois, USA) was used for the statistical analysis. Continuous and categorical data were presented as mean ± standard deviation and percentages respectively. Student's t test (for normally distributed data) and the Mann-Whitney (for non-normally distributed data) were used to analyze

the continuous data. The Chi-Square test was used to analyze the categorical data. *P* value less than 0.05 was accepted as statistically significant.

Results. The patients of this study totalled 148 (male 74, female 74), with a mean age of 63.07 ± 12.55 (range 36-90) years. Mean duration of the patients' stay in hospital was 13.8 days (2-45 SD 5.9). The subjects were divided into 2 groups (Group I and Group II) according to in-hospital mortality. Group I consisted of surviving patients (n=109), and Group II of expired patients (n=39). Demographic characteristics of the patients are shown in **Table 1**. **Table 2** shows the clinical subtypes in both groups. As can be observed from the table, no statistically significant differences were found between the 2 groups. Risk factors such as hypertension, DM and previous stroke history are summarized in **Table 1**. There were no statistically significant differences between the groups. Echocardiographic pathologies were seen in 68 patients of a total of 88 patients with echocardiography in Group I (77.3%), and 19 of the 23 (82.6%) in Group II (p=0.777) had echocardiographic diastolic dysfunction. Corrected QT and QTcd were prolonged in both groups; but particularly Group II had relatively higher QTcd (**Table 3**) compared to Group I (**Figures 1 & 2**).

Discussion. In this study, it is obviously demonstrated that QTcd has negative prognostic effects on the early stage of acute stroke in the university clinic. Increased QTcd is an independent predictor for in-hospital

Table 1 - Clinical characteristics of the patients.

Clinical characteristics	Group I (n=109)	Group II (n=39)	*P*-value
Age	63.85±12.42	60.90±12.80	0.209
Gender			0.135
Male	50	24	
Female	59	15	
Hypertension (%)	87 (79.8)	28 (71.8)	0.419
Diabetes mellitus (%)	38 (34.9)	19 (48.7)	0.182
Previous stroke history (%)	28 (25.7)	11 (28.2)	0.925
Smoking: no. (%)			0.634
(previous + current)			0.999
Female	20 (40)	11 (45.8)	
Male	7 (11.8)	2 (13.3)	
Lipid profiles			
HDL cholesterol (mg/dL)	42±13	44±17	0.151
LDL cholesterol (mg/dL)	115±32	116±41	0.121
Triglycerides (mg/dL)	154±131	151±155	0.980
Hospitalization (day)	15.22±6.78	10.18±6.89	0.0001

HDL - high-density lipoprotein
LDL - low-density lipoprotein

Table 2 - Distribution of the cases according to Oxfordshire Community Stroke Project classification.

Stroke Classification	Group I n (%)	Group II n (%)
TACI	83 (56.1)	21 (53.8)
PACI	40 (27.0)	10 (25.6)
POCI	25 (16.9)	8 (20.5)
Total	**148 (100)**	**39 (100)**

TACI - total anterior circulation infarct, PACI - partial anterior circulation infarct, POCI - posterior circulation infarct

Table 3 - Corrected QT interval and QTcd values in both groups Qtc.

QTc interval and QTcd value	Group I	Group II	*P*-value
Minimum QTc interval (ms)	429.4±41.6	430.1±28.4	0.901
Maximum QTc interval (ms)	434.4±29.3	440.9±70.5	0.579
QTcd (ms)	7.4±3.7	10.1±4.6	0.002

QTc - Corrected QT, QTcd - corrected QT dispersion

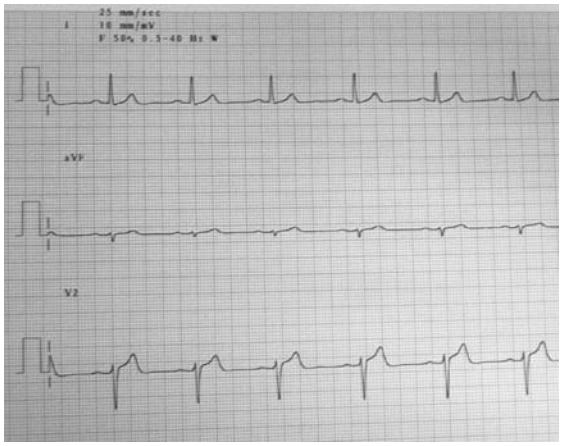

Figure 1 - QTc interval (<360 msn) of a patient.

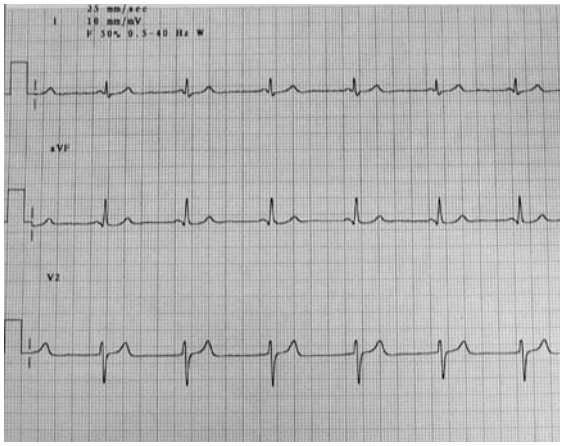

Figure 2 - QTc interval (>360 msn) of a patient.

mortality of ischemic stroke patients. However, no such relation was observed between clinical stroke subtypes and QTcd. Current evidence suggests that a close relation between the CNS and cardiovascular system exists in the early stage of cerebrovascular incidents. The QT dispersion, ST changes T spikes or inversion or abnormal U waves can emerge in the acute stage of stroke due to repolarization disturbance. Long QT dispersion or a long QTc interval is associated with acquired coronary artery disease, carotid intima-media thickness, left ventricular systolic dysfunction, left ventricular hypertrophy, and arrhythmias.[15] Besides, it is also well known that a new arrhythmia and cardiac autonomic changes may occur less frequently.[15] All these effects are related to involvement of the autonomic cardiac control center.[16-18] Based on experimental and clinical studies, it was identified that some cerebral regions (such as insula, amygdala, and lateral hypothalamus) affect the cardiac autonomic control.[1,8] The QT dispersion is a deterministic factor of electrical instability of myocardium and it reflects repolarization differences of the ventricular surface. These differences are important in determining patients who have the propensity towards arrhythmia and QTd, which in turn may lead to ventricular arrhythmia. Patients with QTd have higher risks for sudden cardiac death.[15] In addition, prolonged QTd and its relation to general population mortality was approached from a different perspective. It was reported that QTd was the most important indicator of stroke mortality.[9,18,22] Prognostic effect of QTd on the acute stage of cerebrovascular diseases was investigated in several studies.[9,18,19,20-25] It was indicated that QTd had a negative prognostic effect on all ischemic stroke,[9,20] intracerebral hemorrhage[19,21-23] and subarachnoid hemorrhage.[24,25]

One limitation in our study is that autonomic dysfunction was not investigated with other methods such as blood pressure changes and heart rate variability. However, QTc interval may be an easy and contributing method in predicting prognosis in daily clinical practice for neurologist in acute ischemic stroke. Further studies are necessary before any definite conclusion can be drawn.

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