

## QT interval changes and reversibility of QT dispersion in patients with acute pancreatitis

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### ABSTRACT

**Background/Aims:** QT dispersion is a sign of heterogeneity of ventricular myocardial wall and is associated with cardiac mortality and morbidity. Data regarding with the persistence of QT interval changes in cases with acute pancreatitis (AP) that required clinical follow-up, are insufficient. Therefore, in this study, we aimed to evaluate the QT interval changes during attack and after remission of the disease, in cases with AP.

**Materials and Methods:** The cases admitted to the Gastroenterohepatology Clinic with the diagnosis of AP were included into the study. Ranson's score parameters, electrocardiography and echocardiography of all patients included into the study were evaluated. Electrocardiographic changes were evaluated two times, during attack and after remission of the disease.

**Results:** A total of 134 subjects (F/M:54/80, 41/59%) diagnosed as AP were included into the study. Seventy two (54%) of the AP cases included into the study were biliary, 32 (24%) were alcohol dependant, 19 (14%) were idiopathic, 9 (7%) were hyperlipidemic and 2 (1%) were ERCP related cases. Mean age of the patents was 57.7±15 years old (range: 19-82 years old) and mean Ranson's score was 3.8±1.9 (range: 1-7), according to the numerical scoring system. We compared QT interval changes during the attack and after the remission of AP and found significant increase in QT dispersion levels during acute attack of AP (p<0,001).

**Conclusion:** The most common electrocardiographic changes in AP patients are QT interval changes including QT dispersion. QT dispersion which was emerged during the attack recovered after the remission of the disease.

**Keywords:** Acute pancreatitis, ECG, QT dispersion

### INTRODUCTION

Acute pancreatitis (AP) is a systemic inflammatory disorder of the pancreas with a rising incidence around the globe (1). Significant morbidity and mortality can be seen in AP patients due to the systemic complications and multi-organ failure. Cardiac involvement has an important place during systemic involvement and cardiac dysfunction in AP patients was confirmed by many studies (2-4). AP has frequently been reported to be associated with transient electrocardiographic (ECG) changes such as ST-T changes mimicking myocardial infarction, sinus bradycardia (5), repolarization changes (6), nonspecific T wave changes and accelerated atrial or nodal rhythms (7) have also been reported in early phase of acute pancreatitis. In addition, QT interval changes, particularly early repolarization

was described to be the most common ECG finding of AP patients (8,9). QT dispersion was defined as an index of the spatial dispersion and attributed to difference of ventricular recovery times (10). It has also been reported that QT dispersion has a high sensitivity rate for prediction of severe tachyarrhythmias such as sustained ventricular tachycardia (11). Increased QT dispersion was reported in two studies with limited AP patients (12,13). In addition, the data regarding with the persistence of QT dispersion were also insufficient. As mentioned, the persistence of QT dispersion in patients with AP requires long-term follow-up due to the increasing frequency of tachyarrhythmias such as sustained ventricular tachycardia. In this study, we aimed to investigate QT changes during the attack and after the remission of AP.

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## MATERIALS AND METHODS

The patients admitted to our Gastroenterohepatology department and diagnosed as AP were included into the study. AP diagnosis was made by characteristic findings and symptoms, (upper abdominal pain and/or guarding and/or rebound tenderness), elevated serum enzymes ( $\geq 3$ -fold amylase and/or lipase) and abdominal ultrasonography (performed two times before and after 24 hours) and/or contrast enhanced computerized tomography (CT) performed after 48-72 hours. Acute pancreatitis was considered to be biliary in origin if stones or sludge were detected in the gallbladder and/or common bile duct and alcoholic in origin if the patient or his/her relatives reported consumption of  $>60$  g of pure alcohol per day. Serum triglyceride level more than 750 mg/dL and exclusion of other etiologies were accepted as hyperlipidemic etiology. Patients were classified as having an idiopathic etiology if the history and laboratory findings ruled out known etiologic factors and ultrasonography and/or contrast enhanced CT revealed a normal biliary tract.

Ranson's score parameters obtained by using findings within the first 48 hours were used for prognostic evaluation. All computerized tomography (CT) scans were reviewed by radiologists dedicated to abdominal imaging, who were blinded to the laboratory data and clinical course. Serum calcium concentration (mg/dL) was calculated by correcting with  $0.8 \times [4 - \text{albumin (g/dL)}]$ .

In this study, patients with known congestive heart failure, pulmonary embolism, systemic and pulmonary hypertension, atrial fibrillation, paroxysmal supraventricular arrhythmia, chronic renal failure, cirrhosis, chronic obstructive pulmonary disease, valvular heart diseases and congenital heart diseases and those with a history of consumption of antiarrhythmic drugs were not included.

### Electrocardiography (ECG) and echocardiography

Standard 12-lead ECG were performed with the subject in supine position during quiet respiration and recorded at 25 mm/sec. ECG patterns was evaluated according to the commonly adopted clinical criteria. Early repolarization was defined as an elevation of the QRS-ST junction (j point) in at least two leads at the time of admission of the patients. QT interval was assessed as an interval beginning from depolarization of QRS complex to the end of the T wave in each lead -defined as a return to the T-P baseline-. QT interval was measured until nadir of the notch between T and U waves in the presence of the U wave. QT interval dispersion was defined as difference between maximum and minimum QT intervals in milliseconds (ms) measured in ECG leads. Corrected QT (QTc) was evaluated according to the Bazett formula. QTc was defined to be prolonged QT when it was  $> 440$  ms in males and  $>460$  ms in females. Echocardiography was applied by the same cardiologist within the first day of acute presentation. Transthoracic echocardiography images were obtained from parasternal long-axis window and

four apical windows with 2,5-3,5 MHz transducer by using GE Vivid 3 ultrasound machine. Echocardiographic measurements were performed according to the recommendations for quantitation of the left ventricle (LV) by two dimensional echocardiography of the American Society of Echocardiography. Left ventricular volumes and ejection fraction were obtained by the modified biplane Simpson's method. Left atrial, LV end-diastolic and end-systolic dimensions, interventricular septal thickness, and LV end-diastolic posterior wall thickness were measured from the parasternal long-axis view. From the apical 4-chamber view, mitral inflow early (E) and late diastolic (A) velocities were measured and then the tissue doppler imaging (TDI) cursor was placed on the lateral wall of the LV, 1 cm apical to the mitral annulus. From TDI of the LV lateral annulus, systolic velocity (Sa), E and A were recorded.

### Ethics

The study protocol was approved by the local ethics Committee and Research Hospital and informed consent was obtained from all patients before inclusion into the study.

### Statistical analysis

Scale variables were presented as mean $\pm$ standard deviation (mean $\pm$ SD). Student's t test was used for comparison of parametric quantitative data. Categorical data was evaluated using Chi-square analysis or with Pearson's correlation as appropriate. Nonparametric data were evaluated by spearman's correlation. Paired t test was used to determine the difference between acute attack and after remissions of QT changes. A p value  $<0.05$  was considered to be statistically significant. SPSS (statistical package for social sciences, for Windows, release 12.0.0 standard version) software was used for statistical evaluations.

### RESULTS

A total of 134 subjects (F/M:54/80, 41/59%) diagnosed as AP were included into the study. Seventy two (54%) of the AP cases included into the study were biliary, 32 (24%) were alcohol dependant, 19 (14%) were idiopathic, 9 (7%) were hyperlipidemic and 2 (1%) were ERCP related cases. Mean age of the patients was  $57.7 \pm 15$  years old (range: 19-82 years old) and mean Ranson's score was  $3.8 \pm 1.9$  (range: 1-7) according to the numerical scoring system. Seven of the patients were necrotizing and the others were edematous AP patients. Follow-up period was ranged from 6 to 12 months. In this study, two of the patients with edematous AP were died during the follow-up period.

Eighty-eight of AP cases (66%) had ECG changes. ECG changes were seen most frequently in patients with biliary (73%) and alcohol dependant (21%) AP. The most frequently seen electrocardiographic findings were repolarization changes on lateral chest derivations (57%), left anterior hemi-block (44%) and sinus tachycardia (20%), respectively.

We compared QT changes during the attack and after the remission of AP and found significant increase in QT maximum,

minimum and dispersion levels during the acute attack of AP (Figure 1) (Table 1).

We did not find QT prolongation in our study patients. In addition, we did also not find neuromuscular hyperactivity and tetany in AP patients who exhibited hypocalcemia. There was a significant positive correlation between serum calcium and albumin ( $r=0,314$ ,  $p=0,043$ ).

Echocardiography was performed in all cases with AP. Echocardiography data were within the normal ranges in all participants.

## DISCUSSION

In the current study, the most common electrocardiographic changes in patients with AP were QT interval changes. The most common ECG finding observed in this study is consistent with report of QT interval changes as an early repolarization in a study performed by Rubio-Tapia et al (14). However, Rubio-Tapia et al. (14) stated it as an unimportant finding with the term of "nonspecific repolarization". While early repolarization was described as a benign situation in the beginning, it was shown to be a prognostic parameter of ventricular tachyarrhythmias in the studies performed in recent years (15-18). It is not exactly known why the lateral early repolarization occurs. The increase in ventricular myocyte sensitivity due to cardiac depressant factors (such as kinin and myocardial depressant factor) in AP cases may have a role. Also, the QT dispersion like early repolarization is another change at this interval. In the current study, we found that QT dispersion was significantly increased in patients with acute pancreatitis. Currently, the data regarding with the etio-pathogenesis of QT dispersion were insufficient. The increase in QT dispersion was considered as a sign of inhomogeneity of ventricular repolarization and it was also considered to be a marker of cardiac electrical instability (19-21). Sakagami et al, and Ates et

al. showed increased QT dispersion in alcohol-dependant and biliary AP cases (12-13). However, these two studies have been performed with a limited number patients. Our study confirmed the QT changes in early phase of AP. In addition, we demonstrated for the first time the recovery of QT changes after the remission of the disease.

Although the exact mechanism of cardiovascular changes remain topics of continued research, various hypotheses have been speculated for the underlying mechanism of electrocardiographic changes during the course of AP, including toxic effects of the pancreatic proteolytic enzymes such as myocardial depressant factor and kinins on the myocardium, autonomic imbalance with vagal predominance, coronary artery spasm, metabolic and electrolyte abnormalities, prothrombotic derangements, hemodynamic instability, and systemic inflammatory response-induced cardiac damage (22-25).

In conclusion, the most common electrocardiographic changes in AP patients is QT interval changes including QT dispersion. We do not advise long-term follow-up of patients with AP for increased risk of tachyarrhythmias such as ventricular tachycardia because of the reversibility of QT dispersion.

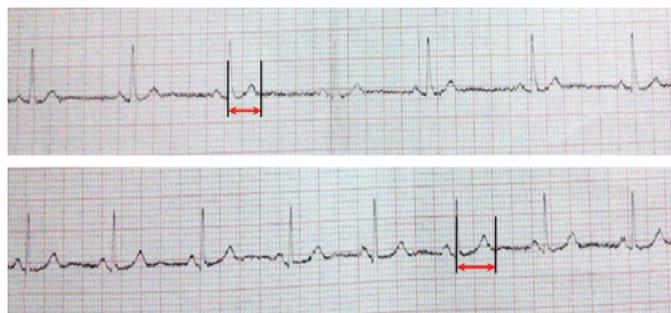
**Conflict of Interest:** No conflict of interest was declared by the authors.

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**Table 1.** QT changes of acute pancreatitis subjects during attack and after remission of the disease

	During attack	After remission	p
QT max (ms)	430.7±23.9	388.8±21.45	<0.001
QT min (ms)	381.2±23.38	361.2±16.45	<0.001
QT dispersion (ms)	48.7±21	24.85±16.13	<0.001



**Figure 1. a, b** QT maximum value of a patient was 360 msn after the resolution (a) and, was 420 msn during attack (b) of acute pancreatitis.

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