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Research

Assessment of Tpe/QT Ratio, Tpe/QTc Ratio, and Tpe Interval in Patients with an Ulcerative Colitis

Ülseratif Kolitli Hastalarda Tpe/QT Oranı, Tpe/QTc Oranı ve Tpe Mesafesinin Değerlendirilmesi

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ABSTRACT

Objective: In this study, our aim was to investigate the change in Tpe/QTc, Tpe/QT ratios, and Tpe interval in patients with ulcerative colitis (UC).

Methods: Our cross-sectional study included 40-patients followed-up with a UC diagnosis and 40 healthy controls. All the patients underwent 12-lead electrocardiography (ECG). In addition to the routine ECG measurements, Tpe/QT and Tpe/QTc ratios and Tpe interval were measured.

Results: Resting heart rate and serum high-sensitive C-reactive protein (hs-CRP) levels were higher with UC patients (p<0.05). Tpe interval and Tpe/QTc ratio values were higher in patients with UC (p<0.05). QT and QTc measurements were similar in the UC patients and healthy controls. Ratio of Tpe to QT and QTc, and Tpe distance measurements positively correlated with the heart rate, UC disease duration, and hs-CRP (p<0.05 for each-one). Tpe/QT, Tpe/QTc ratios, and Tpe interval were found to be independently associated with the heart rate and UC disease duration in a linear regression analyze.

Conclusion: In patients with UC; Tpe/QT, Tpe/QTc ratios, and Tpe interval are increased and are independently associated with a disease duration in these patients. This may be associated with the increased inflammation in the UC patients and its cardiac effects.

Keywords: Ulcerative colitis, Tpe/QT, Tpe/QTc ratios and Tpe interval

ÖZ

Amaç: Bu çalışmada amacımız ülseratif kolitli (ÜK) hastalarda Tpe/QTc, Tpe/QT oranları ve Tpe mesafesindeki değişimi incelemektir.

Gereç ve Yöntem: Kesitsel çalışmamıza ÜK tanısı ile takip edilen 40 hasta ve 40 sağlıklı kontrol dahil edildi. Tüm hastalara on iki derivasyonlu elektrokardiyografi (EKG) çekildi. Rutin EKG ölçümlerine ek olarak Tpe/QT ve Tpe/QTc oranları ve Tpe mesafesi ölçüldü.

Bulgular: ÜK hastalarında istirahat kalp hızı ve serum yüksek duyarlılıklı C-reaktif protein (hs-CRP) düzeyleri daha yüksekti (p<0,05). ÜK'li hastalarda Tpe aralığı ve Tpe/QTc oranı değerleri daha yüksekti (p<0,05). ÜK hastalarında ve sağlıklı kontrollerde QT ve QTc ölçümleri benzerdi. Tpe/QT oranı, Tpe/QTc oranı ve Tpe interval ölçümleri kalp hızı, ÜK hastalık süresi ve hs-CRP ile pozitif korelasyon gösterdi (her biri için p<0,05). Lineer regresyon analizinde Tpe/QT, Tpe/QTc oranları ve Tpe aralığı kalp hızı ve ÜK hastalık süresi ile bağımsız olarak ilişkili bulundu.

Sonuç: ÜK'li hastalarda, Tpe/QT, Tpe/QTc oranları ve Tpe aralığı artar ve bu hastalarda hastalık süresi ile bağımsız olarak ilişkilidir. Bu, ÜK hastalarında artan enflamasyon ve bunun kardiyak etkileri ile ilişkili olabilir.

Anahtar Kelimeler: Ülseratif kolit, Tpe/QT, Tpe/QTc oranları ve Tpe mesafesi

INTRODUCTION

The most common extra-intestinal involvement in the patients with an ulcerative colitis (UC) is the skin, eye, and live. Although the cardiac involvement is much rarer, it is associated with the increased mortality and morbidity of the UC patients (1-3). Cardiac involvement usually occurs as myocarditis, pericarditis, valvular involvement, cardiac arrhythmia, and venous thrombosis (1,2).

Twelve lead electrocardiographic (ECG) changes are associated with a serious ventricular arrhythmia. These ECG parameters are interval of QT-QTc, dispersion of QT-QTc, and T wave-peak and end-distance (Tpe interval). QT-QTc are related to a ventricular repolarization and depolarization. Tpe is mostly a sign of a ventricular repolarization and could be more meaningful in evaluating especially the repolarization. During the repolarization ventricular transmural dispersion is associated with the ratio of Tpe to QT and QTc (4). Increased Tpe interval is associated with an increased risk of a ventricular arrhythmia and shows abnormality in a ventricular repolarization (5). As far as we have investigated, although it has been shown that the QTc and QTc dispersion has increased in the patients with UC (6-9), there is no study about the ratio of Tpe to QT and QTc and distance of Tpe used in a ventricular repolarization assessment in the recent years.

In this study, our aim was to investigate the change in the Tpe/QT ratio, Tpe/QTc ratio, and Tpe interval in patients with the UC.

METHODS

Between January 2019 and January 2020, a total of 59 UK patients who were followed-up in the Gastroenterology Clinic in University of Health Sciences, Adana City Research and Training Hospital were scanned. Written informed consent was not necessary for those who did not include any patients' data in the study. After the exclusion criteria, a total of 40 patients diagnosed with the UC and 40 healthy controls that were similar in the age and gender were included. Taking a medical treatment known to affect the QT-QTc interval, history of sudden cardiac arrest or syncope, persons with under 18 years-old, failure to obtain the QTc and Tpe measurements, mild-advanced valvular disease, known ischemic heart disease (IHD), or major risk factors for IHD such as: hypertension, diabetes mellitus, and systolic and diastolic heart failure were the exclusion criterion.

Local Ethics Committee approved our study (Cukurova University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee, decision number: 72, date: 14.02.2020). The demographic data were recorded from the UC patients and healthy controls. Active disease duration of the patients with the UC was noted. Glucose, creatinine, sodium, aspartate aminotransferase, blood urea nitrogen, alanine aminotransferase, potassium, calcium, triglyceride, high-sensitive C-reactive protein (hs-CRP), and low-density lipoprotein cholesterol levels were measured (Abbott Aeroset, MN, USA).

Twelve-lead Electrocardiographic Evaluation

Twelve-lead ECGs carried out by an ECG Device of MAC 2000 (GE-medical, Inc, WI-USA) in a sinus rhythm, 1 mv/10 mm and 25 mm/sec speed, and standard calibration was obtained from all the individuals. QT-interval was measured (the time from where QRS started to the point where the T wave merges with the isoelectric line was calculated). Bazett Formula was used for QTc measurement ($QTc=QT/\sqrt{R\text{-}R}$). It was evaluated whether there was a supraventricular extrasystole and ventricular extrasystole along with the cardiac axis. Tpe is defined as the distance from the peak of the T wave to the end of the T wave. V_5 was used for measurements (10). The ratio of the Tpe to QT-QTc were calculated.

Statistical Analysis

All the analyses were conducted using SPSS-24.0 (Chicago, IL, USA). The Kolmogorov-Smirnov test was used. The data are expressed as the means ± the standard deviations and as percentages and numbers for the categorical variables. Student-t test and Mann-Whitney U test was used. The categorical variables were compared by the chi-square (χ^2) test. We use kappa coefficient to examine the inter-intra observer variability of the ECG parameters. Parameters associated with a Tpe distance, Tpe/QTc, and Tpe/QTc were determined with an univariate Spearman's or Pearson's correlation analyses.

RESULTS

ECG measurement was successfully obtained. Cohen kappa values were >90% that evaluate the interobserver variability for all the ECG evaluation (p<0.001 for all the comparisons). The study population was divided into two groups (UC patients and healthy controls).

Gender and age were similar between both the groups. The resting heart rate, one of the clinical parameters, was higher in the UC patients. Among the laboratory parameters, hs-CRP level was significantly higher in the UC patients. Other ECG and laboratory measurements were same for each group (Table 1).

Table 1. Comparison of demographic and laboratory findings patients with ulcerative colitis and control group

	Ulcerative colitis (+) n=40	Control group n=40	p
Age (year)	38.5±4.8	37.8±5.9	0.536
Male % (n)	50 (15)	50 (15)	1.000
Smoking % (n)	50 (15)	50 (15)	1.000
Disease duration (years)	4.15±2.19	-	-
Blood pressure for systolic (mmHg)	120±17	124±13	0.271
Blood pressure diastolic (mmHg)	70±9.6	72±8.3	0.327
Heart rate (pulse/minute)	71±14	62±4.4	<0.001
Body mass index (kg/m²)	27.5±1.7	27.9±1.5	0.365
Glucose (mg/dL)	93±8.2	90±12	0.153
Urea (mg/dL)	25.5±7.6	27.1±8.2	0.350
Creatinine (mg/dL)	0.65±0.19	0.60±0.08	0.871
Sodium (mEq/L)	139±6.5	140±3.7	0.457
Potassium (mEq/L)	4.36±0.60	4.34±0.32	0.871
Aspartate aminotransferase (u/L)	20.1±5.9	18.2±2.8	0.063
Alanine aminotransferase (u/L)	17.4±5.1	17.5±2.4	0.877
Calcium (mg/dL)	9.74±0.66	9.45±0.52	0.869
Low-density lipoprotein cholesterol (mg/dL)	92±24	101±24	0.091
Triglycerides (mg/dL)	115±34	118±39	0.745
hs-CRP (mg/dL)	2.74±1.12	1.15±0.20	<0.001

hs-CRP: High-sensitive C-reactive protein

QTc and QT measurements were similar between both the groups. Ratio of Tpe to QT and QTc, and Tpe distance were significantly higher in the patients with UC (Table 2). Tpe distance, the ratio of Tpe to QT, and QTc positively related with the hs-CRP and UC disease duration (Table 3). Tpe/QT, Tpe/QTc ratios, and Tpe interval were found to be independently associated with the hs-CRP and UC disease duration in a linear regression analysis (Table 4). Most significant relation was found hs-CRP-UC disease duration and Tpe-interval.

DISCUSSION

Most important evidence of this investigation was that without the QT and QTc prolongation, Tpe distance, Tpe/QTc ratio, and Tpe/QT ratio were higher in the patients with UC in contrast to healthy controls. As we observed, this is the first study to show the increase of the ventricular repolarization parameters such as: Tpe distance, ratio of Tpe to QTc, and QT in patients with UC. We also found that the hs-CRP and UC disease duration have a close and positive relationship with a Tpe distance, ratio of Tpe to QTc, and QT.

Ventricular depolarization starts from the endocardium to the epicardium. During the ventricular repolarization, dispersion between the endocardial and the epicardial region occurs. Tpe distance, which is associated with a transmural ventricular repolarization, is between the T wave peak and the end distance and this interval (4,11). In the literature, there are studies about the Tpe distance and the ratios of the Tpe to QT are associated with the arrhythmic situations and sudden cardiac death (5,12-14). Increased Tpe distance, ratio of Tpe to QT are associated with a normal arrhythmia and a sudden cardiac death. The dispersion in the repolarization between the endocardial and the epicardial region in the ventricular myocardium causes slow conduction in the endocardium and epicardium. It may especially be increasing the re-entry-related arrhythmias.

Although there are studies evaluating the QT and QTc distance and QT dispersion, which are among the ventricular repolarization parameters, there is no study investigating the Tpe distance, ratio of Tpe to QTc, and QT in patients with UC (6-9). In most of the studies, the findings indicate that the QTc and QTc dispersion are markedly elongated in the

Table 2. Comparison of ventricular repolarization parameters patients with ulcerative colitis and control group

	Ulcerative colitis (+) n=40	Control group n=40	p
QT distance (msn)	403±38	401±23	0.889
QTc distance (msn)	431±35	427±27	0.372
Tpe distance (msn)	87.8±9.1	72.7±7.4	0.002
The ratio of Tpe to QT	0.227±0.048	0.191±0.025	0.010
The ratio of Tpe to QTc	0.203±0.028	0.185±0.023	0.002

Table 3. Correlation of Tpe distance, the ratio of Tpe to QT, and QTc with the clinical and laboratory parameters

	Tpe distance		The ratio of Tpe to QT		The ratio of Tpe to QTc	
	r	p	r	p	r	p
Pulse (per min)	0.380	<0.001	0.068	0.463	0.100	0.278
Disease duration (years)	0.560	<0.001	0.190	0.021	0.290	0.009
hs-CRP	0.474	<0.001	0.217	0.017	0.310	0.001

hs-CRP: High-sensitive C-reactive protein

Table 4. A linear regression analysis for parameters significantly correlated with Tpe distance, the ratio of Tpe to QT and QTc

	Tpe distance		The ratio of Tpe to QT		The ratio of Tpe to QTc	
	β	p	β	p	β	p
Heart rate	0.187	0.054	-	-	-	-
Disease duration (years)	0.487	<0.001	0.264	0.023	0.290	0.009
hs-CRP	0.240	0.014	0.123	0.045	0.334	<0.001

R square for Tpe-interval, Tpe/QT and Tpe/QTc as 401-290-361, respectively, hs-CRP: High-sensitive C-reactive protein

patients with UC (6-8). However, in the study conducted by Dogan et al. (9), there was no significant difference in the QTc and QT dispersion (the longest and shortest QTc difference) in the UC patients compared to the healthy controls. In the same study, these parameters were also not associated with a disease duration and the activity (9). Yorulmaz et al. (8) reported that the QT dispersion was higher in the UC patients than the healthy controls. While QTc dispersion was associated with a systolic blood pressure and patient's age, no relationship was found between a disease duration and the QTc dispersion (8). In our study, the QT and QTc intervals obtained supported the study where the QT and QTc prolongation were not detected from the previous articles. However, the increase in the Tpe distance, ratio of Tpe to QTc, and QT, in patients with UC was markedly more important than the QTc distances. Increased QT and QTc dispersion, QTc duration, Tpe/QTc, Tpe distance have been shown to be risk factors for the ventricular arrhythmia and sudden death (4,5). In our study, Tpe interval, Tpe/QT, and Tpe/QTc were shown to be increased for the first time in patients with UC. So, it is important.

In our study and in the previous studies, it has been shown that there may be prolonged ventricular repolarization parameters without the cardiac involvement and cardiovascular disease (6-8). In these studies, and in our study, serum electrolytes were normal, and there are no drugs that prolongs the ventricular repolarization. It was thought that the prolongation in the repolarization among UC patients from our previous study, and previous studies resulted from a myocardial repolarization of an electrical remodeling caused by the increased intra-cardiac inflammation, because of the increased systemic inflammatory process. The increased inflammatory process also does endothelial damage and dysfunction in the intra-cardiac vascular system, as in the entire vascular endothelium. This leads to depolarization/repolarization abnormality in the cardiac myocytes (15,16). Although this physiopathology is not clearly shown in our study, indirectly supporting findings were obtained. The

most important parameter was increased serum hs-CRP, which is an important indicator of the systemic inflammation in the UC patients, and the duration of the disease was related to the Tpe interval, Tpe/QT, and Tpe/QTc.

In our study there are some important limitations. The most important limitation is the cross-sectional design of the study, and another limitation is the number of the patients enrolled in the study. In our study, the number of patients were limited to 40. Therefore, in the regression analysis, ventricular repolarization parameters were found to be associated only with the hs-CRP and UC disease duration. In addition, arrhythmic event and clinical follow-up parameters could not be evaluated due to the low number of the patients and no clinical follow-up.

In our study, taking medication and medical treatment that may cause QT prolongation was accepted as an exclusion criterion. In the patients with UC, the risk of atrial and ventricular arrhythmia increases (2,17,18), but in our study, although no arrhythmia symptoms were observed, more significant results could be obtained, if 48 hours Holter examination was performed.

CONCLUSION

Tpe distance and the ratio of Tpe to QTc are increased in the UC patients. This may be due to a neuroendocrine system activity and serum electrolytes in the UC patients. Also, QTc evaluation, which was routine in patients diagnosed with UC, it was thought that the Tpe-interval and Tpe/QT ratios should be measured and monitored more closely in terms of a hypopotassemia and hypomagnesemia.

ETHICS

Ethics Committee Approval: This study approved by Cukurova University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (decision no: 72, date: 14.02.2020).

Informed Consent: Written informed consent was not necessary for those who did not include any patients' data in the study.

Authorship Contributions

Surgical and Medical Practices: E.G., H.E.S., M.K., Concept: E.G., H.E.S., M.K., Design: E.G., H.E.S., B.Ş.A., A.A., M.K., Data Collection or Processing: B.Ş.A., M.Z.A., Y.K.İ., Analysis or Interpretation: B.Ş.A., M.Z.A., Y.K.İ., A.A., Literature Search: H.E.S., B.Ş.A., M.Z.A., Y.K.İ., M.K., Writing: E.G., H.E.S., A.A., M.K.

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