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Tp-e/QT and Tp-e/QTc Ratio in Hemodialysis and Peritoneal Dialysis Patients

Hemodiyaliz ve Periton Diyalizi Hastalarında Tp-e/QT, ve Tp-e/QTc Oranı

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ABSTRACT

OBJECTIVE: Sudden cardiac death and risk of arrhythmia are higher in patients with ESRD. Tp-e/QT, and Tp-e/QTc are novel and more reliable indexes of ventricular arrhythmogenesis and sudden cardiac death than QTc. The aim of this study was to assess ventricular repolarization in patients with hemodialysis and peritoneal dialysis by using the Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio.

MATERIAL and METHODS: A total of 35 healthy controls, 92 hemodialysis patients, and 104 peritoneal dialysis patients were enrolled in the study. The Tp-e interval, Tp-e/QT, and Tp-e/QTc ratio were calculated from the ECGs of the individuals and compared among groups.

RESULTS: QT value was significantly higher in hemodialysis group compared with peritoneal dialysis group ($p<0.001$) and control group ($p<0.001$). However a difference was not found comparing QT values between peritoneal dialysis and control groups. Tp-e, Tp-e/QTc, Tp-e/QT, and QTc values were significantly higher in hemodialysis and peritoneal dialysis group comparing to control group. However a statistically significant difference was not found while comparing QTc values between peritoneal dialysis and control groups (p:0.081). When all patients of ESRD without DM were compared with the control group, Tp-e, Tp-e/QTc, Tp-e/QT, and QTc values were found significantly higher than the healthy control group. The values of Tp-e/QT ($p<0.001$ r:0.314) and Tp-e/QTc (p:0.018 r:0,187) in all patients with kidney disease were found to show positive correlation with duration of dialysis (month).

CONCLUSION: This is the first known study that shows Tp-e/Q, and Tp-e/QTc are higher in hemodialysis and peritoneal dialysis patients.

KEY WORDS: Tp-e/QT, Tp-e/QTc, Tp-e, QTc, Dialysis

ÖZ

AMAÇ: Ani kardiyak ölüm ve aritmi riski son dönem böbrek yetmezliği hastalarında yüksektir. Tp-e/QT, ve Tp-e/QTc' nin ventriküler aritmogenezisi ve ani kardiyak ölümü göstermede QTc' den daha değerli olduğu gösterilmiştir. Çalışmada amacımız hemodiyaliz ve periton diyalizi hastalarında Tp-e intervali, Tp-e/QT ve Tp-e/QTc oranını kullanarak ventriküler repolarizasyonu değerlendirmektir.

GEREÇ ve YÖNTEMLER: 35 sağlıklı kontrol, 92 hemodiyaliz hastası, ve 104 periton diyalizi hastası çalışmaya dahil edildi. Bütün hastaların elektrokardiyografileri çekildi. Tp-e interval, Tp-e/QT ve Tp-e/QTc oranı elektrokardiyografiden elde edilen verilerle hesaplandı ve gruplar arasında karşılaştırıldı.

BULGULAR: QT hemodiyaliz hastalarında periton diyalizi hastalarına ($p<0,001$) ve sağlıklı kontrollere ($p<0,001$) göre yüksek saptandı. Ancak QT periton diyalizi hastalarında sağlıklı kontrollere göre anlamlı fark saptanmadı. QTc, Tp-e, Tp-e/QT, ve Tp-e/QTc hemodiyaliz ve periton diyalizi hastalarında sağlıklı kontrollere göre anlamlı yüksek tespit edildi. Bununla birlikte periton diyalizi ve kontrol grupları arasında QTc değerleri arasında farklılık tespit edilmedi (p:0,081). Diyabetik olmayan bütün son dönem böbrek yetmezliği hastaları sağlıklı kontrollerle karşılaştırıldığında QTc, Tp-e, Tp-e/QT, ve Tp-e/QTc sağlıklı kontrollere göre anlamlı yüksek tespit edildi. Tp-e/QT ($p<0,001$ r:0,314) ve Tp-e/QTc (p:0,018 r:0,187) arasında ortalama diyaliz süresi (ay) ile pozitifkorelasyon saptandı.

SONUÇ: Çalışma Tp-e/QT, ve Tp-e/QTc' nin hemodiyaliz ve periton diyalizi hastalarında sağlıklı kontrollere göre yüksek olduğunu gösteren ilk araştırmadır.

ANAHTAR SÖZCÜKLER: Tp-e /QT, Tp-e /QTc, Tp-e, QTc, Diyaliz

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INTRODUCTION

Cardiovascular disease is one of the most important causes of mortality and morbidity in chronic kidney disease (CKD) (1,2). Sudden cardiac death and risk of arrhythmia are higher in patients with end-stage renal disease (ESRD), due to the fact that they have high prevalence of left ventricular hypertrophy, myocardial fibrosis, coronary artery disease and changes in the concentration of electrolytes such as calcium and potassium (3,4). Corrected QT dispersion (QTc) is associated with some life-threatening arrhythmias and cardiac death (5,6). It has been demonstrated that QTc dispersion is higher in hemodialysis and peritoneal dialysis patients (7, 8). The Tp-e interval is measured from the peak of the T wave to the end of the T wave. Tp-e/QT ratio and Tp-e/QTc are calculated with electrocardiography (ECG). Tp-e/QT and Tp-e/QTc are novel indexes of ventricular arrhythmogenesis and are related to a high risk of sudden cardiac death (9-11)**.** The Tp-e/QT ratio has been demonstrated to be a more reliable marker of ventricular arrhythmias compared to the QT interval, QTc, or Tp-e by recent studies. Also, a higher Tp-e/QT ratio has been related with arrhythmic incidents. In the past year, it has been demonstrated that the Tp-e/QT ratio has a considerable relation with malignant ventricular arrhythmia in patients with myocardial infarction (12).

However, Tp-e/QT, and Tp-e/QTc have not been adequately studied in hemodialysis patients and peritoneal dialysis patients. The aim of this study was to assess ventricular re-polarization in patients undergoing hemodialysis and peritoneal dialysis by using the Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio.

METHODS

The study protocol was approved by the Erciyes University Ethical Committee. 35 healthy controls, 92 hemodialysis patients, and 104 peritoneal dialysis patients were enrolled in the study. Hemodialysis and peritoneal dialysis patients had been receiving dialysis for at least 1 year. Patients who had active infections, bundle-branch block (left bundle-branch block, incomplete or complete right bundle-branch block) or intraventricular conduction delay (duration of QRS >120 ms) on ECG, as well as patients with permanent pacemakers; history of percutaneous or surgical revascularization, moderate to severe valve disease, left ventricular dysfunction (ejection fraction <40%), atrial fibrillation, congenital heart disease, systemic conditions (ankylosing spondylitis, rheumatoid arthritis, Marfan's and Ehlers-Danlos disease), and aortic aneurysms were excluded (13,14). All of the hemodialysis patients were receiving hemodialysis 3 times per week with bicarbonate dialysate solution at least for one year. Systolic and diastolic blood pressure was measured in each individual twice, following a 5-minute rest, with an Erka brand sphygmomanometer using an appropriate cuff width. Patients who were on hypertension medication were recorded.

Biochemical Analysis

All samples were obtained in the morning after 12 h of fasting. In hemodialysis patients, blood samples were collected at the start of hemodialysis. Complete blood count measurement was completed with the flow cytometry method; fasting blood glucose, creatinine, albumin, and serum lipids measurements with the enzymatic colorimetric method; ferritin measurements with the immunoturbidimetric method; and sodium, potassium, and chloride measurements with the ion selective electrode method. The Sysmex XT 2000I device was used for complete blood count and the other biochemical parameters were studied using the Modular P, Roche/Hitachi device.

Electrocardiographic Examination

We obtained the 12-lead ECGs of all patients via recorder (Nihon Kohden, cardiofaxs, Tokyo, Japan) with a paper speed of 50 mm/s, while the patient was resting in the supine position on an interdialytic day. All procedures were performed during the same time interval (from 9.00 a.m. to 10.00 a.m.) so as to avoid diurnal variations. ECG measurements were performed manually by two cardiologists, using calipers and a magnifying glass to decrease measurement errors. Subjects who had U waves on their ECGs were not included in the study. The average value of the three examinations was calculated for each lead. The Tp-e interval was measured from the peak of the T wave to the end of the T wave (15,16). We defined the end of the T wave as the intersection of the tangent to the down-slope of the T wave and isoelectric line (17). The QT interval was measured from the beginning of the QRS complex to the end of the T wave and corrected for heart rate (QTc) by using Bazett's formula (QTc=QT/RR-2) (18). The Tp-e interval was measured from the peak of the T wave to the end of the T wave (19). The end of the T wave was defined as the intersection of the tangent to the downslope of the T wave and isoelectric line. Measurements of the Tp-e interval were performed in the precordial leads. The Tp-e/QT ratio and Tp-e/QTc were calculated from these measurements.

Statistical Analysis

Statistical analyses were carried out using the Statistical package for Social Sciences for Windows version 15.0 (SPSS, Chicago, IL, USA). Results for continuous variables were demonstrated as mean±standard deviation. By using chi-square test to find categorical variables, we determined statistical significant differences between the groups. To compare continuous variables, the Student t test or Mann-Whitney U test were used where appropriate. The values were statistically analyzed using one-way ANOVA and post hoc Tukey multiple comparison tests. Associations between the variables were explored using the Pearson correlation and Spearman's rho (for data that were not normally distributed). Statistical significance was defined as $P< 0.05$

RESULTS

The laboratory parameters of all groups are shown in Table I. Baseline characteristics of patients with CKD are demonstrated in Table II.

QT values were prominently higher in the hemodialysis group compared with the peritoneal dialysis groups and control group. Tp-e, Tp-e/QTc, Tp-e/QT, and QTc values were significantly higher in the hemodialysis and peritoneal dialysis groups compared with the control group, yet a statistical difference was not detected for these parameters between the hemodialysis and peritoneal dialysis groups (Table III). When all ESRD patients without DM were compared with the control group, the value of Tp-e, Tp-e/QTc, Tp-e/QT, and QTc were detected to be significantly higher than in the healthy control group (Table IV). The values of Tp-e/QTc (p:0.018 r:0,187) (Figure 1) and Tp-e/QT (p<0.001 r:0.314) (Figure 2) in all patients with kidney disease were detected to show a positive correlation with the duration of dialysis.

DISCUSSION

The main findings of our study are that Tp-e, Tp-e/QTc, Tp-e/QT, and QTc were significantly higher in the hemodialysis and peritoneal dialysis groups compared with the control group. When all ESRD patients were compared with the control group, Tp-e, Tp-e/QTc, Tp-e/QT, and QTc were detected to be significantly higher in the ESRD without DM group than in the healthy control group. The values of Tp-e/QT and Tp-e/QTc in all patients with kidney disease were detected to show a positive correlation with the duration of dialysis

The mechanism of ventricular repolarization prolongation in patients with end-stage renal failure was associated with traditional and CKD-related risk factors. Several CKD-related risk factors such as inflammation (20), hyperferritinemia, hyperparathyroidism, hyperphosphatemia (21), and structural changes in uremic myocardium (22-24) are frequently present in patients with CKD. An increased prevalence of left ventricular dysfunction, autonomic dysfunction, myocyte dysfunction, altered electrolyte metabolism, and cardiac fibrosis may also contribute to arrhythmic risk in patients with kidney disease.

It has been shown that QT dispersion was higher in hemodialysis patients than healthy control in previous studies. Hashemi et al. showed that QT dispersion was higher in hemodialysis and peritoneal dialysis patients than in the healthy control group (25). Maule et al. reported that patients with ESRD have higher QTc (26). QTc was reported to be significantly higher in PD patients by Wu et al. (27). These results are in accordance with our findings.

Table I: Laboratory parameters of the study group patients.

	Control Group (n:35)	Hemodialysis Group (n: 92)	Peritoneal Dialysis Group (n: 104)	p
Gender (m/f)	20/15	51/41	63/41	0.435
Age (years)	52.06±12.73	53.83±13.34	54.53±13.95	0.431
SBP(mmHg)	124.57±18.56	132.23±20.59	128.55±18.42	0.115
DBP (mmHg)	79.28±11.32	80.86±9.57	79.91±11.88	0.719
Creatinine (mg/dl)	0.88±0.16	7.68±2.22*	8.04±3.38*	<0.001
Sodium (mmol/L)	139.77±1.55	134.71±17.12	136.46±4.38	0.187
Potassium (mmol/L)	4.45±0.14	4.72±0.68	4.52±0.57	0.135
Triglyceride (mg/dl)	92.29±44.50	180.79±81.36*	207.32±118.7*	<0.001
LDL (mg/dl)	112.47±18.90	98.94±26.60α	121.42±52.55	0,006
HDL(mg/dl)	54.76±11.54	34.36±9.23*α	42.70±23.01*	<0.001
Albumin (mg/dl)	4.47±0.176	3.56±0.321*	3.77±0.703*	<0.001
Calcium (mg/dl)	9.51±0.338	8.90±0.73*	8.88±0.76*	0,001
phosphorus (mg/dl)	3.41±0.45	4.67±1.27*	4.35±1.35*	0,001
Hemoglobin (g/dl)	14.13±1.66	10.99±1.45	11. 80±1.6	<0.001
Platelet counts (10^3/ul)	278.74±82.61	233.70±105.96	259.33±87.71	0.066

***:** P<0.05: versus control group, **α:** P<0.05 versus peritoneal dialysis group. **SBP:** Systolic blood pressure, **DBP:** Diastolic blood pressure, **LDL:** Low density lipoprotein, **HDL:** High density lipoprotein.

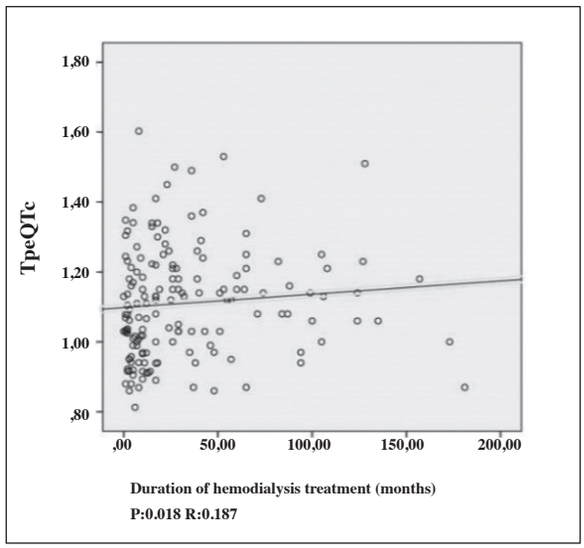

Figure 1: *The relation between of Tp-e/QTc and, duration of dialysis.*

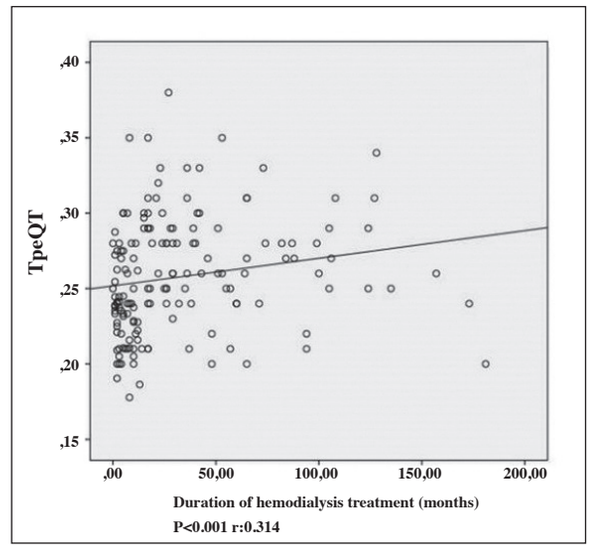

Figure 2: *The relation between of Tp-e/QT and, duration of dialysis.*

Table II: Baseline characteristics of patients with chronic kidney disease.

	Hemodialysis Group (n:92)	Peritoneal Dialysis Group (n:104)	p
Etiology			
Diabetes Mellitus	27(29.4)	36(34.6)	0.720
Hypertension	21(22.8)	29(27.9)	0.680
Glomerulonephritis	6(6.6)	5(4.8)	0.906
Nephrolithiasis	9/-(9.7)	5(4.8)	0.183
Unknown	25(27.2)	22(21.2)	0.433
Polycystic kidney disease	4(4.3)	6(5.8)	0.402
Amyloidosis	0	1(0.9)	0.490
Medications			
Erythropoietin	75 (81.5)	45(43.2)	<0.001
Beta-blockers	20(21.7)	25 (24.2)	0.751
Angiotensin Converting Enzyme Inhibitors	24 (26.1)	40(38.4)	0.735
Statin	6 (6.5)	15(14.4)	0.690
Vitamin D	36 (39.1)	48(46.1)	0.438
Ca canal blocker	16 (17.3)	28(26.9)	0.163

Values are expressed as n (%) for $\chi 2$ analysis.

Table III: Electrocardiographic parameters of study group patients.

	Control Group (n:35)	Hemodialysis Group (n:92)	Peritoneal Dialysis Group (n:104)	P
Tp-e	81.48±5.54	95.11±16.87*	97.35±12.10*	<0.001
QT	356.51±21.79	378.58±37.46*α	360.86±27.98	<0.001
Tp-e/QT	0.22±0.02	0.25±0.04*	0.26±0.033*	<0.001
Tp-e/QTc	0.99±0.11	1.12±0.22*	1.15±0.14*	<0.001
QTc	82.03±5.48	85.76±7.65*	84.73±5.42*	0.015

***:** P<0.05 versus control group, **α:** P<0.05 versus peritoneal dialysis group.

Table IV: Electrocardiographic parameters of the control group and the ESRD group without Diabetes Mellitus.

	Control Group (n:35)	ESRD without Diabetes Mellitus (n:120)	P
Tp-e	81.48±5.54	93.67±12.08	<0.001
QT	356.51±21.79	366.05±30.35	0.093
Tp-e/QT	0.22±0.02	0.25±0.03	<0.001
Tp-e/QTc	0.99±0.11	1.11±0.15	<0.001
QTc	82.03±5.48	84.30±6.06	0.048

ESRD: End stage renal disease.

Recently, a novel index of arrhythmogenesis, the Tp-e/QT, and the Tp-e/QTc ratio have been suggested to be more accurate measures for the dispersion of ventricular repolarization compared to QTc and Tp-e intervals (19). It was demonstrated that Tp-e/QT ratio was a strong predictor of sudden cardiac death (28) and was significantly elevated in those who suffered malignant ventricular arrhythmias (29). In accordance with our study, Tun et al. demonstrated that Tp-e was significantly higher in the end-stage renal disease group than in the control group (30). To the best our knowledge, there is no study comparing the relation of Tp-e/QT, Tp-e/QTc in patients with hemodialysis and peritoneal dialysis. However, there is a study showing alteration of Tp-e/QT between predialysis and postdialysis in patients with ESRD. Kalantzi et al. demonstrated that hemodialysis induced ventricular arrhythmia (31). In contrast to this study, we investigated the value of Tp-e/QT and Tp-e/QTc in peritoneal dialysis and hemodialysis patients compared to the healthy control group. Oour study group (n: 231) was also larger than theirs (n: 65).

Recent studies have shown that ventricular repolarization is related with age, blood pressure values , and diabetes mellitus (32,17). In our study, the mean age of the blood pressure values were not different among peritoneal dialysis, hemodialysis, and healthy control groups.

It was shown that Tp-e/QT was higher in patients with diabetes mellitus compared to the healthy control group (17). In our study group, there were 27 hemodialysis patients with diabetes mellitus and 36 peritoneal dialysis patients with diabetes mellitus. When all patients of ESRD without DM were compared with control group, the values of Tp-e, Tp-e/QTc, Tp-e/QT, and QTc were identified to be significantly higher than in the healthy control group.

We also demonstrated that the values of Tp-e/QT, and Tp-e/QTc in all patients with kidney disease show positive correlation with the duration of dialysis treatment. In accordance with our study, Bozbas et al. have shown that duration of dialysis therapy is an independent factor affecting ventricular arrhythmia development in these patients (33).

CONCLUSION

We identified that the values of Tp-e/QT, and Tp-e/QTc which are higher in hemodialysis and peritoneal dialysis patients than in the healthy control group, and the values of Tp-e/QT, and Tp-e/QTc in all patients with kidney disease show a positive correlation with the duration of dialysis.

Conflict of Interest Disclosures (none)

None of the authors has a personal or financial relationship that has any potential to inappropriately influence (bias) his or her actions or manuscript, and no financial or other potential conflicts of interest exist (includes involvement with any organization with a direct financial, intellectual, or other interest in the subject of the manuscript) regarding the manuscript. In addition, there are no grants and sources of financial support related to the topic or topics of the manuscript.

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