ORIGINAL ARTICLE

Association of Corrected QT and QT Dispersion with Echocardiographic and Laboratory Findings in Uremic Patients under Chronic Hemodialysis

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ABSTRACT

Introduction: Cardiovascular disease is the most common cause of mortality in dialysis patients. Chronic renal failure and hemodialysis (HD) patients may have longer corrected QT (QTc) interval compared with the normal population. Long QTc interval may be a predictor of ventricular arrhythmia and cardiovascular mortality in these patients and hence the aim of this study was the evaluation of the relationship between QTc interval and some echocardiographic findings and laboratory exam results in HD patients. **Materials and Methods:** In a cross-sectional study, 60 HD patients with age >18 years and the dialysis duration >3 months were enrolled. Blood samples were taken, and electrocardiography and echocardiography were done before the dialysis session in the patients. **Results:** Mean age of the patients was 56.15 ± 14.6 years. QTc interval of the patients was 0.441 ± 0.056 s and QT dispersion (QTd) was 64.17 ± 25.93 ms. There was no statistically significant relationship between QTc interval and QTd with duration of dialysis, body mass index, age, and gender ($P > 0.05$). There was also no significant relationship between QTc interval and QTd with mitral regurgitation, tricuspid regurgitation and aortic insufficiency ($P > 0.05$). In addition, QTc interval and QTd of the patients had not any correlation with serum parathormon and serum Ca, K, HCO_3 ($P > 0.05$). **Conclusion:** Based on our results, in HD patients, QTc interval and QTd were not correlated with echocardiographic findings or laboratory exam results. Therefore, it can be concluded that QTc interval prolongation probably has not any correlation with cardiac mortality of the HD patients.

Key Words: Corrected QT interval, echocardiography, hemodialysis, QT dispersion

INTRODUCTION

Cardiovascular disease is the most common cause of mortality in dialysis patients that is responsible for about 60% of their mortality and is also 30 times more common than in general population.[1,2] Different cardiovascular disorders, such as left ventricular hypertrophy (LVH), coronary artery diseases, congestive heart failure (CHF), and arterial hypertension are commonly seen in these patients.[3,4] In addition, calcification of cardiac valves are common and may cause valvular and annular thickening that in turn could lead to valvular stenosis or regurgitation.[5] Some predisposing factors of cardiac disorders in dialysis patients are secondary hyperparathyroidism, long term hypertension, and anemia.[6]

Different electrocardiographic abnormality may be seen in dialysis patients, such as ST, T change, ventricular and supra-ventricular arrhythmia and QT interval prolongation. In the electrocardiogram, QT interval is the time between the start of the Q wave and the end of the T wave. When heart rate increased then QT interval was decreased, so QT interval could be corrected with heart rate. There

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are a number of different correction formulas, but the standard clinical correction is to use Bazett's formula ($QT/\sqrt{R\text{-}R}$, where R-R is the RR interval in seconds). The normal corrected QT (QTc) interval for males and females are ≤430 ms and ≤450 ms, respectively. The borderline QTc for a male is 431-450 and borderline QTc for a female is 451-470 and the abnormal QTc range for a male is >450 and for a female is >470.[7] The QTc interval could be prolonged due to electrolyte abnormalities (hypomagnesaemia and hypokalemia), drug consumption (antihistaminic, antiarrhythmic, and antibiotics), brain trauma and genetic abnormalities (long QT syndrome).[8] Patients with chronic renal failure and dialysis patients had a greater QTc interval and QT dispersion (QTd) (QTd = QTmax — QTmin) compared with the normal population.[9] A single session of HD could be increased QTc in patients undergoing HD.[10] Moreover, QT interval may be a predictor of ventricular arrhythmia and cardiovascular mortality in chronic kidney disease and dialysis patients.[11]

Although there are some studies about QTc and QTc dispersion in hemodialysis (HD) patients with different results; however, there are only a few studies concerning relationship of QTc internal and QTd with echocardiography findings, so the aim of this study was the evaluation of these relationship in dialysis patients.

MATERIALS AND METHODS

In a cross-sectional study, 60 HD patients with age >18 years and the dialysis duration >3 months were enrolled. Exclusion criteria were: Antiarrhythmic drugs consumption, history of cardiac diseases such as arrhythmia, heart block or CHF. Before dialysis session, electrocardiography (ECG) and echocardiography were done for all of the patients. In the 12 leads, ECG QTc were measured based on Bazett's formula. Also, QTd was measured by mentioned formula (QTd = QTmax — QTmin) in 12 leads ECG. The patients were on HD, by Fresenius digital machine (4008B, Germany) and Gambro digital machine (AK95 and AK96, Sweden), 2-3 times/week, as a regular method (4-4.5 h with blood flow of 250-350 mL/min, dialysate flow of 500 ml/min and ultra-filtration based on the patient's condition). The used buffer was bicarbonate powder, and the type of filters were intermediate and high efficient polysulfone membrane (R5, R6) made by SOHA factory under license of Fresenius Company. Serum creatinine, hemoglobin, Ca, parathyroid hormone (PTH), Na, K, HCO_3, and pH were checked by RA1000 machine (made in Italy).

All laboratory tests were done before the dialysis session and were checked in a single laboratory. Echocardiography and ECG were done before the dialysis session and by single cardiologist and technician respectively. All data and information were confidential, and for ECG and echocardiography taking an informed consent was taken from each patient.

In echocardiography, left ventricular ejection fraction (LVEF), LVH, pulmonary artery pressure (PAP) and valvular disorders were evaluated. At the end of the study, data were analyzed using SPSS software (version 19, IBM Corporation). $P < 0.05$ was considered as significant level. Pearson correlation coefficient, two-independent samples *t*-test and ANOVA were used for statistical analysis. This study was approved by Ethical Committee of Shahrekord University of Medical Sciences with the Grant Number of 904.

RESULTS

In 60 patients, 37 were males and 23 females. Mean age of the patients were 56.15 ± 14.6 years. Mean body mass indexes (BMIs) (post dialysis) and duration of dialysis were 21.77 ± 3.6 kg/m^2 and 4.25 ± 3.24 years respectively [Table 1]. Mean QTc interval of the patients was 0.441 ± 0.056 s; however, QTc interval in men and women were 0.43 ± 0.04 s and 0.45 ± 0.07 s, respectively ($P > 0.05$). QTd in all of the patients was 64.17 ± 25.93 ms, however in men and women were 62.70 ± 28.05 ms and 66.52 ± 22.48 ms respectively ($P = 0.87$). Mean urea reduction ratio in men and women were 68.14% ± 9.34% and 68.22% ± 3.88%; however, Kt/V was 1.45 ± 0.17 and 1.49 ± 0.16 among men and women, respectively.

Table 1: Characteristics of patients and their association with QTc and QTd

Characteristic	Age (year)	Body weight (kg)	BMI (kg/m^2)	Duration of dialysis (year)	Ca (mg)	PTH (pg/ml)	K (meq/L)	Serum HCO_3 (meq/L)	Serum PH
Value (mean±SD)	56.15±14.6	62.13±14.54	21.77±3.6	4.25±3.24	8.73±0.95	467.85±255.33	5.20±0.71	20.22±3.67	7.32±0.05
QTc: Correlation coefficient+(*P* value)	0.13 (0.29)	0.15 (0.24)	0.04 (0.74)	0.09 (0.94)	0.09 (0.48)	0.07 (0.56)	0.1 (0.43)	0.07 (0.55)	0.07 (0.54)
QTd: Correlation coefficient+(*P* value)	0.069 (0.61)	0.070 (<0.59)	0.001 (0.994)	0.10 (0.40)	0.04 (0.78)	0.16 (0.22)	0.01 (0.94)	0.021 (0.873)	0.07 (0.55)

SD = Standard deviation, BMI = Body mass index, PTH = Parathyroid hormone, QTc = Corrected QT, QTd = QT dispersion

There was no statistically significant relationship between QTc interval or QTd with duration of dialysis, BMI, age, and gender ($P > 0.05$). In ECG, LVH was seen in 23 (38.3%) patients and ST change in 14 patients (23.3%). In echocardiography, mitral regurgitation (MR), tricuspid regurgitation (TR), and aortic insufficiency (AI) were found in 54, 47, and 11 patients respectively [Table 2]. In addition, no significant relation was found between QTc interval and QTd with MR, TR, AI, LVH, septal thickness (ST) and PAP [Table 3]. QTc interval and QTd has also no correlation with serum PTH or Ca, K or HCO_3.

DISCUSSION

Our findings revealed that, in HD patients, QTc interval and QTd had not any correlation with valvular disorders (MR, AI, and TR), LVH or other echocardiographic findings such as PAP and ST. Furthermore, there was no relationship between QTc interval and QTd with serum Ca, K, HCO_3, PTH.

In HD patients, cardiac abnormalities such as vascular calcification are common and are associated with the development of LVH, that may cause increased cardiac arrhythmias and mortality.[12,13] Elevation of calcium-phosphorus product can also cause valvular calcification and stenosis in these patients. Mitral and aortic calcification and stenosis are common in these patients; however, tricuspid and pulmonic valve calcification is rare. Valvular abnormality could increase the patients' morbidity and mortality.[14,15] QTc interval prolongation in chronic kidney disease and HD patients was shown in some studies such as Covic *et al*. and Ljutic *et al*. studies which postdialysis QTc interval was 434 ± 29 ms and 445.7 ± 36.9 ms respectively,[16,17] while in our patients QTc interval was 444.6 ± 54.5 ms. Selby and McIntyre in a review article reported that HD can increase QTc interval and QTd and is also capable of inducing arrhythmias and increasing mortality especially in patients with ischemic heart disease.[18] In Nakamura *et al*. study on 48 dialysis patients, throughout the follow-up period, there was a higher incidence of cardiovascular death in patients with prolongation of QTc dispersion after HD.[19] Kantarci *et al*. showed that the serum potassium was significantly higher in HD patients when compared to continuous ambulatory peritoneal dialysis (CAPD) patients and rate of QT interval dispersions was significantly higher in HD and CAPD patients when compared with healthy controls. They concluded that there is a tendency to cardiac arrhythmias in HD patients during the postdialysis period.[9] Maule *et al*. showed that after the HD session, QTc increased in 56% and decreased in 43% of the patients but it was not related to the presence of autonomic neuropathy.[20] After dialysis session, cell-associated Mg levels and QTd increased significantly in Averbukh *et al*. study, so he concluded that excess daily Mg intake and increased concentrations of cell-associated Mg could be responsible for QTc prolongation in these patients.[21] Change in serum electrolytes during HD may also be responsible at least partially, to increase QTc or QTd. For example, increase of QTc interval after a dialysis session, and its correlation with plasma calcium level, postdialysis blood pressure, LVEF and ST was shown in Covic *et al*. study.[16] Cupisti *et al*. showed that QTd increased during HD due to serum K^+ depletion and then return to baseline 2 h after the end of dialysis. QT prolongation during dialysis may also predispose to arrhythmia especially in the cardiac disease patients,[22] Näppi *et al*. demonstrated that HD increases QTd if a low-calcium dialysate is used. Therefore, use of a low-calcium dialysate may predispose HD patients to ventricular arrhythmias.[23] Genovesi *et al*. in his study on 16 HD patients showed that QTc interval has a reverse correlation with K^+ and Ca^{2+} concentrations of dialysate.[24] However, in HD children, Ozdemir *et al*. found that QTc interval has no correlation with the patients' sex, age and presence of hypertension or LVH but patients with left ventricular systolic dysfunction had significantly greater QTc dispersion. Similar to our study, the changes in serum Ca or K of the patients during

Table 2: Severity of valvular disorders in the patients

Valvular abnormality	Normal	Mild	Moderate	Severe
MR	6	46	8	0
TR	13	35	11	1
AI	49	10	1	0

MR = Mitral regurgitation, TR = Tricuspid regurgitation, AI = Aortic insufficiency

Table 3: Echocardiographic findings and their association with QTc and QTd

Variables	Septal thickness	PAP	LVEF	LVH	MR	TR	AI	PE
Value or number	13.23±1.67 (mm)	33.83±13.25 (mm Hg)	51.92±4.61 (%)	23 (38%)	No=6 Yes=54	No=13 Yes=47	No=49 Yes=11	No=51 Yes=9
P (QTc)	0.182	0.008	0.75	0.59	0.39	0.11	0.27	0.39
P (QTd)	0.07	0.85	0.73	0.2	0.6	0.38	0.82	0.75

QTc = Corrected QT, QTd = QT dispersion, PAP = Pulmonary artery pressure, LVEF = Left ventricular ejection fraction, LVH = Left ventricular hypertrophy, MR = Mitral regurgitation, TR = Tricuspid regurgitation, AI = Aortic insufficiency, PE = Pericardial effusion

dialysis were not associated with the QTc interval in this study.[25] Moreover, in Hekmat *et al*.'s study on 49 HD patients, QTc interval had not correlation with serum electrolytes and blood gas findings.[26] In Voiculescu *et al*. study, there was no statistically significant correlation between QT interval and serum concentrations of Mg, PO_4 in HD patients too. In addition, QTc interval was not dependent from LVEF, arrhythmias or sudden death.[27] Our results had some similarities with some of above-mentioned studies as well as some differences with the others. The observed controversy between our study and some of these studies might be due to the discrepancy in the number of cases or racial differences of the patients, and more importantly, the fact that we did not compare predialysis and postdialysis QTc interval.

We could not find any study on the correlation of QTc interval with LVH or valvular heart disease in HD patients; however, there are some studies related to the correlation of QTc and LVH with other diseases or conditions. For example, Mayet *et al*. reported that QTd has correlated with left ventricular mass index in hypertensive individuals.[28] Lonati *et al*. found that in athletes, LVH induced by physical training activity is not associated with an increase in QTd, whereas pathological increase in LVH secondary to hypertension could increase QTd.[29] The study of Dimopoulos *et al*. on the evaluation of QTd and left ventricular mass index in elderly hypertensive and normotensive patients reported that hypertensive patients had greater left ventricular mass index and higher QTd. QTd were also found to be independent predictors of left ventricular mass index.[30] The study had some limitations such as small sample size and lack of QTc measurement after HD session and comparison of it before and after procedure.

CONCLUSION

By our knowledge, this is one of the first studies on the correlation of QTc or QTd with valvular abnormality and LVH in HD patients. There were a few studies about the relationship of QTc and LVH in nonrenal patients, so we could not compare our results with other studies. Based on our results, in HD patients, QTc interval or QTd was not correlated with echocardiographic findings or laboratory exam results. Therefore, it can be concluded that QTc interval prolongation probably has not any correlation with cardiac mortality of the HD patients.

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