

The effect of hemodialysis adequacy on ventricular repolarization in end-stage kidney disease

Son dönem böbrek hastalarında hemodiyaliz etkinliğinin ventriküler repolarizasyon üzerine etkisi

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ABSTRACT

Objective: Ventricular repolarization (VR) markers may predict ventricular arrhythmias and cardiac arrest. The aim of this study was to investigate the acute effects of a hemodialysis (HD) session and HD adequacy on VR markers in HD patients.

Methods: This cross-sectional study was conducted at 2 university hospitals with 83 patients and VR markers were measured before and after an HD session: QT, QTc, QT minimum, QT maximum, dispersion of QT (QTd), T-peak to T-end (Tp-e) interval, and Tp-e/QT. Kt/V measurements calculated using the second generation Daugirdas formula were used to indicate dialysis adequacy. The patients were divided into 2 groups according to the Kt/V value. Group 1 patients had a Kt/V of ≤ 1.6 with a standard dialysis dose, and Group 2 comprised those with a measurement of >1.6 with a high dialysis dose.

Results: There were 36 patients in Group 1 and 47 patients in Group 2. There were statistically significantly more female patients in Group 2 ($p=0.016$). After an HD session, heart rate increased, blood pressure decreased, and the QT, QTc, QT maximum, QTd, Tp-e interval, and Tp-e/QT were prolonged ($p<0.05$). The VR markers measured were similar in the 2 groups. VR markers were not significantly different in diabetic patients.

Conclusion: HD may be a risk factor for cardiac arrest because of prolonged VR parameters, independent of HD adequacy. A high dialysis dose may not always be best for the heart.

ÖZET

Amaç: Ventriküler repolarizasyon belirteçleri ventriküler aritmileri ve kardiyak arresti öngörebilir. Bu çalışma hemodiyaliz hastalarında hemodiyaliz seansının ve hemodiyaliz etkinliğinin akut etkilerinin ventriküler repolarizasyon üzerine etkisini araştırmayı amaçlamıştır.

Yöntemler: İki üniversite hastanesinde gerçekleştirilen çalışma kesitsel olarak düzenlendi, 83 hemodiyaliz hastasında ventriküler repolarizasyon belirteçleri hemodiyaliz seansının öncesinde ve sonrasında ölçüldü. Bunlar: QT, QTc, QT minimum, QT maksimum, QT dispersiyonu (QTd), Tp-e intervali ve Tp-e/QT. İkinci jenerasyon Daugirdas formülü ile hesaplanan Kt/V diyaliz etkinliğini yansıtır. Hastalar Kt/V değerine göre grup 1 ≤ 1.6 standart diyaliz dozu olarak ve grup 2 >1.6 yüksek diyaliz doz olarak ikiye ayrıldı.

Bulgular: Otuz altı hasta grup 1'de ve 47 hasta grup 2'deydi. Kadın hastalar istatistiksel açıdan anlamlı olarak grup 2'de daha fazlaydı ($p=0.016$). Hemodiyaliz sonrası kalp hızı arttı ve kan basıncı azaldı, QT, QTc, QT maksimum, QTd, Tp-e intervali ve Tpe/QT ise hemodiyaliz seansı sonrasında uzuyordu ($p<0.05$). Ventriküler repolarizasyon belirteçleri iki grup arasında benzer bulundu. Diyabetik hastalarda da ventriküler repolarizasyon belirteçleri Kt/V değerlerinden etkilenmiyordu.

Sonuç: Hemodiyaliz seansı hemodiyaliz etkinliğinden bağımsız olarak ventriküler repolarizasyon parametrelerini uzattığı için hemodiyaliz hastalarında kardiyak arrest için bir risk faktörü olabilir. Yüksek hemodiyaliz dozu kalp için her zaman en iyisi olmayabilir.

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Chronic kidney disease (CKD) is an independent predictor of cardiovascular morbidity and mortality.^[1] Cardiovascular disease, including ventricular arrhythmias and cardiac arrest, is the most frequent cause of death in hemodialysis (HD) patients.^[2] Although coronary atherosclerosis is accelerated, there is less mortality as a result of ischemic heart disease than cardiac arrhythmia among HD patients. The dialysis process may also induce sudden cardiac death due to hemodynamic overload, inflammatory stress, intradialytic myocardial ischemia, and greater ventricular repolarization (VR) alteration.^[3]

Abnormalities in the QT interval, QT dispersion (QTd), and the duration of T-peak to T-end (Tp-e) are accepted as markers of VR. An increase in VR dispersion may predispose the patient to the development of malignant ventricular arrhythmias and cardiovascular mortality.^[4]

Kt/V is a formulation that reflects the adequacy of hemodialysis. It is affected by the length of treatment, the quantity of fluid cleared with ultrafiltration, and the change in the level of blood urea nitrogen that occurs in an HD session. HD adequacy has been reported to have a substantial effect on left ventricular remodeling.^[5,6] However, as yet, to the best of our knowledge, there are no published data about the effect of HD adequacy on VR. The objective of this study was to investigate the effects of an HD session and HD adequacy on VR in HD patients.

METHODS

Study design and population

A total of 83 patients who met all of the criteria were enrolled among 378 chronic HD patients at 2 university hospitals for an observational, cross-sectional study. The inclusion criteria were >18 years of age, chronic HD, HD treatment 3 times a week for 4 hours, normal sinus rhythm, and willingness to participate in the study. The exclusion criteria were atrial fibrillation, the presence of a left ventricular ejection fraction <40%, stable coronary artery disease, cardiac surgery within the previous 6 months, or a history of acute coronary syndrome or percutaneous coronary intervention. Patients with a Kt/V value <1.2 were also excluded, as it indicates ineffective HD. In addition, patients with problems observed on an electrocardiogram (ECG), such as the

presence of bundle branch block or the presence of second or third-degree atrioventricular block, and those with unacceptable ECG records were eliminated. The presence of a U wave on the ECG was also cause for exclusion from the study. Finally, patients who were taking drugs that prolong the QT interval were also omitted.

Abbreviations:

CI	Confidence interval
CKD	Chronic kidney disease
DM	Diabetes mellitus
ECG	Electrocardiogram
HD	Hemodialysis
QTc	Corrected QT
QTd	Dispersion of QT
Tp-e	T-peak to T-end
RRT	Renal replacement therapy
VR	Ventricular repolarization

Hemodialysis schedule and hemodialysis adequacy

The patients were all undergoing HD treatment 3 times a week. The parameters examined were assessed at the second dialysis session of the week. The blood and dialysate flow rates were set at 300 mL/minute and 500 mL/minute, respectively. HD was performed using a low-flux polysulfone dialyzer (Fresenius Fx-10, surface area of 1.8 m²; Fresenius SE & Co. KGaA, Bad Homburg vor der Höhe, Germany).

The practical and reliable Kt/V measure was used to determine HD adequacy.^[7] A Kt/V value <1.2 indicates ineffective HD, while a value between 1.2 and 1.6 is the standard to signify an effective HD session or a standard dialysis dose. A Kt/V value >1.6 signifies highly effective HD or a high dialysis dose. The patients were divided into 2 groups according to a Kt/V value ≤1.6 as a standard dialysis dose and >1.6 as a high dialysis dose (range: 1.2–1.6).

The Kt/v parameter was calculated using the second-generation Daugirdas formula:

$$Kt/V = -\ln(R - 0.008 \times t) + (4 - 3.5R) \times UF/W$$

(R= post-dialysis/pre-dialysis blood urea nitrogen, t= dialysis time (hours), UF=ultrafiltration or pre/post dialysis weight change, and W=post-dialysis weight).^[7]

Clinical, electrocardiographic, and laboratory parameters

Demographic and clinical variables were recorded. The type of vascular access, time in renal replacement therapy (RRT), age when RRT was initiated, and primary kidney disease were recorded. Measurement of arterial blood pressure using a sphygmomanometer and an ECG recording of heart rate were performed at rest for all individuals 10 minutes before the start of HD and 10 minutes after the end of the session.

Blood samples were also taken before and after the HD session to determine the level of blood urea nitrogen, creatinine, sodium, calcium, phosphorus, and potassium. The ECG was performed on all 83 patients at a paper speed and gain of 25 mm/second and 10 mm/mV, respectively. All of the patients had a sinus rhythm. Electrocardiographic intervals were measured by 2 experienced cardiologists blinded to the study. The ECG results were analyzed using a digital caliper with a sensitivity of 1/100 mm and a magnifier. The interobserver agreement rate was 0.952 (95% confidence interval [CI]: 0.940–0.964).

The QT interval on the ECG defines the duration of ventricular depolarization, and was measured from the beginning of the QRS complex to the termination of the T wave. The QT interval recorded by the II or V5 lead has been accepted as the most predictive of ventricular arrhythmia by some authors.^[4] The

heart rate may influence the QT interval. Therefore, a corrected QT (QTc) interval was calculated using Bazett's method [$QTc = QT/(R-R)^{1/2}$]. The QTc was accepted as prolonged when it was higher than 440 ms.^[8] Dispersion of QT (QTd) is another marker of VR. QTd is defined as QT maximum - QT minimum on a surface 12-lead ECG.^[9]

The Tp-e interval was measured as the interval between the peak of the T wave and the end of the T wave on the V6 lead.^[10,11] The Tp-e/QT measured in healthy populations at V6 is in the range of 0.15 to 0.25.^[11]

The local Ethics and Research Committee of the University Hospital approved this study. All of the participating patients provided written, informed consent.

Statistical analysis

Statistical analyses were performed using IBM SPSS

Table 1. Comparison of demographic, clinical, and laboratory characteristics between Kt/V groups

Variables	Kt/V \leq 1.6 (n=36)	Kt/V >1.6 (n=47)	p
Age (years), mean \pm SD	48 \pm 12	50 \pm 16	0.476
Sex (male/female)	25/11	19/28	0.016
Body mass index (kg/m ²), median (min-max)	26 (17–45)	24 (16–36)	0.070
Duration of hemodialysis (years), median (min-max)	2 (1–25)	4 (1–35)	0.298
Age at start of hemodialysis (years), mean \pm SD	44 \pm 15	45 \pm 18	0.689
Smoking, n (%)	12 (33.3)	17 (36.2)	0.971
Alcohol consumption, n (%)	3 (8.3)	1 (2.1)	0.312
Vascular access, n (%)			0.129
Longterm catheter	35 (97.2)	40 (85.1)	
Arteriovenous fistula	1 (2.8)	7 (14.9)	
Underlying kidney disease, n (%)			0.630
Arterial hypertension	9 (25)	16 (34)	
Diabetes mellitus	13 (36)	11 (23.4)	
Glomerulonephritis	5 (13.9)	3 (6.4)	
Polycystic kidney disease	1 (2.8)	1 (2.1)	
Urological disorders	3 (8.3)	5 (10.6)	
Other	5 (13.9)	11 (23.3)	
Hypertension, n (%)	23 (63.9)	33 (70.2)	0.709
Diabetes mellitus, n (%)	14 (38.9)	15 (31.9)	0.669
Serum sodium (mEq/L), mean \pm SD	134 \pm 3	136 \pm 3	0.137
Serum calcium (mg/dL), mean \pm SD	8.6 \pm 0.9	8.7 \pm 0.9	0.723
Serum phosphorus (mg/dL), mean \pm SD	5.1 \pm 1.1	5.0 \pm 1.6	0.866
Hemoglobin (gr/dL), median (min-max)	11.4 (8–16.3)	11.1 (6.6–17.6)	0.646
Ultrafiltration (mL) mean \pm SD	3008 \pm 954	2918 \pm 898	0.660

SD: Standard deviation; Min: Minimum; Max: Maximum.

Statistics for Windows, Version 19.0 (IBM Corp., Armonk, NY, USA). The distribution of the data was assessed with the Shapiro-Wilk test. Continuous variables were expressed as mean \pm SD or median (min-max), and categorical variables as frequency and percentage. The Fisher's exact test or a chi-square test with Yates Correction was used to determine differences between groups of categorical variables. Continuous variables were compared with an independent sample t-test or the Mann-Whitney U test for 2 groups. Comparison of repeated measures was performed using a paired t-test or the Wilcoxon signed rank test. The variables of sex, diabetes mellitus (DM), ultrafiltration, QT, QTc, QTd, and Tp-e interval were used in multivariate logistic regression analysis with the backward elimination method to determine risk according to the dialysis dose. A post-hoc power analysis was performed using multivariate logistic regression and G*Power version 3.0.10 software (Erdfelder, E., Faul, F., & Buchner, A., 1996). A power of 99% was observed in post-hoc analysis. A p value of <0.05 was considered statistically significant for all tests.

RESULTS

In all, there were 36 patients in the Kt/V \leq 1.6 group and 47 patients in the Kt/V >1.6 group. A comparison of demographic, laboratory, and clinical data between the 2

groups is presented in Table 1. No significant difference in these characteristics was seen, with the exception of a female prevalence in the high dialysis dose group (p=0.016). A comparative analysis of laboratory, hemodynamic, and electrocardiographic variables recorded before and after HD is shown in Table 2. Body weight; levels of serum creatinine, blood urea nitrogen, and potassium; and the systolic, diastolic, and mean blood pressure decreased after HD. Heart rate increased after HD (78 \pm 11 bpm vs 82 \pm 14 bpm; p<0.001). All of the VR parameters were prolonged after HD, other than the QT minimum. There was no statistically significant difference in the QT minimum after HD (p=0.838). The QTd was 38 \pm 19 ms before HD and 49 \pm 36 ms after HD (p=0.037). The Tp-e interval was 101 \pm 16 before HD and 113 \pm 43 ms after HD (p=0.002).

The comparative analysis of VR markers before and after HD according to Kt/V group is provided in Table 3. The VR markers of QT, QTc, QT minimum, QT maximum, QTd, Tp-e, and Tp-e/QT were similar before and after HD. The magnitude of change in VR markers before and after HD was calculated as a percentage and was found to be similar in the 2 Kt/V groups.

A comparative analysis of the Kt/V value and VR markers in diabetic and non-diabetic HD patients can

Table 2. Laboratory, hemodynamic, and electrocardiographic variables before and after hemodialysis session

Variables (n=83)	Before hemodialysis	After hemodialysis	p
Weight (kg)	72 \pm 14	69 \pm 14	<0.001
Urea (mg/dL)	61 \pm 15	16 \pm 7	<0.001
Creatinine (mg/dL)	8.5 (4.5–14.7)	2.7 (1.0–5.9)	<0.001
Serum potassium (mEq/L)	5.1 (3.7–7.5)	3.4 (2.0–5.0)	<0.001
Heart rate (bpm)	78 \pm 11	82 \pm 14	<0.001
Systolic blood pressure (mmHg)	132 \pm 21	112 \pm 22	<0.001
Diastolic blood pressure (mmHg)	76 \pm 10	67 \pm 11	<0.001
Mean blood pressure (mmHg)	94 \pm 12	82 \pm 13	<0.001
QT (ms)	407 \pm 35	418 \pm 55	0.025
QTc (ms)	464 (391–552)	480 (399–592)	<0.001
QT minimum (ms)	368 (281–451)	368 (271–466)	0.838
QT maximum (ms)	407 \pm 35	418 \pm 55	0.018
QTd (ms)	38 \pm 19	49 \pm 46	0.037
Tp-e (ms)	101 \pm 16	113 \pm 43	0.002
Tp-e/QT	0.245 (0.183–0.310)	0.252 (0.175–0.395)	0.004

QTc: Corrected QT; QTd: Dispersion of QT; Tp-e: T-peak to T-end; SD: Standard deviation; Min: Minimum; Max: Maximum.

Table 3. Comparison of ventricular repolarization predictors according to Kt/V group

Variables	Kt/V ≤1.6 (n=36)	Kt/V >1.6 (n=47)	p
QT interval, before hemodialysis (ms)	402±35	410±35	0.306
QT interval, after hemodialysis (ms)	398 (295–560)	424 (324–630)	0.156
QT interval, change (%)	1.3 (-16.3–19.8)	1.2 (-15.1–47.5)	0.636
QTc, before hemodialysis (ms)	461±30	463±34	0.847
QTc, after hemodialysis (ms)	481±42	489±38	0.376
QTc, change (%)	5.2 (-8.4–17.6)	4.3 (-9.3–30.8)	0.594
QT minimum, before hemodialysis (ms)	364±31	372±32	0.251
QT minimum, after hemodialysis (ms)	361±32	375±40	0.096
QT minimum, change (%)	-0.2 (-16–29.8)	0 (-17.7–13.8)	0.411
QT maximum, before hemodialysis (ms)	403±35	410±35	0.331
QT maximum, after hemodialysis (ms)	398 (295–560)	424 (324–630)	0.180
QT maximum, change (%)	1.5 (-16.3–19.8)	1.2 (-15.1–47.5)	0.776
QTd, before hemodialysis (ms)	36 (4–119)	38 (10–104)	0.672
QTd, after hemodialysis (ms)	33 (10–166)	39 (6–221)	0.575
QTd, change (%)	5.3 (-78–1700)	14.7 (-86–807)	0.927
Tpe, before hemodialysis (ms)	103±18	100±14	0.515
Tpe, after hemodialysis (ms)	105 (64–414)	106 (73–186)	0.723
Tpe, change (%)	6.7 (-27.1–218.4)	7.1 (-16.6–72.2)	0.312
Tpe/ QT, before hemodialysis (ms)	0.260 (0.189–0.310)	0.240 (0.183–0.310)	0.122
Tpe/ QT, after hemodialysis (ms)	0.267 (0.175–0.395)	0.250 (0.180–0.355)	0.730
Tpe/ QT, change (%)	3 (-25.8–36.3)	1.5 (-11.7–47.7)	0.471

QTc: Corrected QT; QTd: Dispersion of QT; Tp-e: T-peak to T-end.

be seen in Table 4. There were 22 non-diabetic patients in Group 1 and 32 in Group 2. Of the diabetic patients, 14 were in Group 1 and 15 were in Group 2. No significant difference was observed in VR parameters in diabetic and non-diabetic patients between Kt/V groups.

Multivariate logistic regression analysis was performed to determine the risk factors associated with dialysis dose. The VR variables of sex, the presence of DM, ultrafiltration, and the QT, QTc, QTd and Tp-e interval values were analyzed, but an association was only seen between HD dose and sex (odds ratio: 3.349, 95% CI: 1.34–8.38; p=0.010) (Table 5).

DISCUSSION

The risk of ventricular arrhythmia and sudden cardiac death caused by arrhythmia is elevated in HD patients.^[2] Cardiovascular mortality is greater in patients with CKD than in the general population.^[12] Prolonged

time on HD, a drop of 30 mmHg in systolic blood pressure during HD, concomitant diseases, increased sympathetic activity, and electrolyte imbalance may also contribute to the risk of sudden death in HD patients. The dialysis process and existing disorders result in a higher frequency of pathological VR. In CKD, the QTc interval is greater compared with the healthy population.^[13,14] Furthermore, QTd has been found to be significantly higher in HD patients in comparison with control subjects.^[15]

Analysis of VR on a surface ECG is essential for the prediction of ventricular arrhythmia in HD patients. The effect of HD on VR is still debatable. Various studies have reported different findings in terms of predictors of VR in HD. Kalantzi et al.^[16] found that QT, the QTc interval, and QTd were not changed after HD. In another study, QTc was not changed but QTd was significantly increased after HD.^[17] Astan et al.^[18] and Lorincz et al.^[19] found that QT, the QTc interval, and QTd increased after HD. Valentim et al.^[20]

Table 4. Ventricular repolarization predictors in Kt/V groups according to the presence of diabetes

	Kt/V ≤ 1.6	Kt/V > 1.6	<i>p</i>
QT interval, non-diabetic (ms)	398 (295–560)	415 (324–630)	0.245
QT interval, diabetic (ms)	420 \pm 48	445 \pm 54	0.197
QTc, non-diabetic (ms)	474 \pm 45	483 \pm 37	0.434
QTc, diabetic (ms)	492 \pm 36	502 \pm 37	0.483
QT minimum, non-diabetic (ms)	350 \pm 29	369 \pm 39	0.065
QT minimum, diabetic (ms)	377 \pm 32	387 \pm 41	0.492
QT maximum, non-diabetic (ms)	398 (295–560)	415 (324–630)	0.252
QT maximum, diabetic (ms)	422 \pm 46	445 \pm 54	0.224
QTd, non-diabetic (ms)	38 (12–166)	35 (6–221)	0.591
QTd, diabetic (ms)	26 (10–133)	56 (14–118)	0.158
Tpe, non-diabetic (ms)	98 (64–414)	104 (73–174)	0.666
Tpe, diabetic (ms)	113 \pm 24	116 \pm 29	0.703
Tpe/QT ratio, non-diabetic	0.255 (0.181–0.395)	0.244 (0.197–0.355)	0.930
Tpe/QT ratio, diabetic	0.266 \pm 0.044	0.260 \pm 0.049	0.733

QTc: Corrected QT; QTd: Dispersion of QT; Tpe: T-peak to T-end.

Table 5. Multivariate logistic regression analysis

Indicators	Rank	OR	95% CI	<i>p</i>
Ultrafiltration	1	1.000	0.99–1.00	0.887
QTd	2	1.004	0.97–1.00	0.791
QTc	3	1.023	0.98–1.02	0.425
Diabetes mellitus	4	1.845	0.66–5.12	0.240
Tpe	5	1.020	0.98–1.05	0.246
QT	6	0.996	0.98–1.00	0.523
Sex	–	3.349	1.34–8.38	0.010

QTc: Corrected QT; QTd: Dispersion of QT; Tpe: T-peak to T-end.

found that an increased QTc interval and QTc dispersion were associated with dialysis. Based on these studies, the relevance of VR markers is unclear and needs further investigation in patients with end-stage renal disease.

In our study, the QT, QTc, QT maximum, QTd, Tpe intervals, and Tpe/QT were statistically significantly prolonged after HD.

QTd indicates the heterogeneity of VR. Okin et al.^[21] found that in healthy individuals, a QTd > 58 ms increased the risk of cardiovascular mortality 3.2-fold. QTd was increased after HD in our study (38 \pm 19 ms vs 49 \pm 36 ms; $p=0.037$). The Tpe interval is an index of the transmural dispersion of VR on ECG. The Tpe interval has been proposed as a means to indi-

cate patients at increased risk of ventricular arrhythmia.^[22] In the healthy population, the Tpe interval at the V5 point was reported to be 94 \pm 10 ms in men and 92 \pm 11 ms in women.^[23] However, there is no consensus regarding the cut-off value of the Tpe interval, and further research is needed to provide a definition. In our study, the Tpe interval was longer both pre and post HD compared with healthy subjects.

The Tpe/QT is an indicator of cardiac arrhythmia and is significantly higher in patients at risk of an arrhythmic event.^[11] It has an advantage over other markers of VR because it does not need to be corrected according to the heart rate. The Tpe/QT was increased post HD in comparison with pre HD results in the present study. According to our findings, HD appeared to have an adverse effect on VR and could be associated with arrhythmic events due to the increase in QT, QTc, QT maximum, QTd, Tpe interval, and Tpe/QT after HD.

To the best of our knowledge, there are no previously published papers about the effect of HD on VR markers. Kt/V is a parameter that measures the efficacy of HD. Kt/V reflects dialysis adequacy and is associated with quality of life and adherence.^[24] The minimum target of Kt/V calculated according to the Daugirdas formula is ≥ 1.2 .^[25–27] Several studies have demonstrated that dialysis dose is associated with

gender. Men need more HD session time than women to obtain the same Kt/V.^[28] This may be related to a greater body mass index and larger body surface area. A high dialysis dose or highly effective HD has been found to reduce mortality in women.^[28,29] Spanish guidelines recommend that women should aim for a Kt/V value of >1.6.^[27] In our study, there were more women in the Kt/V >1.6 group, and the only significant relationship seen in multivariate regression analysis was that between sex and dialysis dose.

A review of the literature did not reveal any previous research of a relationship between hemodialysis adequacy and VR. In our study, the VR markers were not significantly different between patients with a standard dialysis dose and a high dialysis dose. According to this finding, VR parameters would not appear to be related to hemodialysis adequacy. Moreover, we can state that a high hemodialysis dose will not provide the desired effect on VR.

DM is a chronic disease that affects the cardiovascular system through endothelial dysfunction, oxidative stress, atherosclerosis, and autonomic neuropathy.^[30] Cardiac autonomic neuropathy is a serious complication of DM and affects 30% of DM patients.^[31] As a result of cardiac autonomic dysfunction, sympathetic autonomic nervous system activity increases in DM patients, which is associated with malign ventricular arrhythmias and sudden cardiac death.^[32] In a recent study, Tokatli et al.^[33] found that Tp-e interval, Tp-e/QT, and Tp-e/QTc were prolonged in patients with type 2 DM without CKD. In addition, they found a positive correlation between the glycosylated hemoglobin level and glucose level and the Tp-e interval, Tp-e/QT, and Tp-e/QTc. In the present study, when we compared clinical and ECG variables regarding QTc intervals with a cut-off value of 440 ms, 90% of the diabetic HD patients had a higher QTc interval ($p=0.025$). Previous studies have yielded no consensus on a target Kt/V in the diabetic population. We investigated the relationship between HD adequacy and VR parameters in DM subgroups; however, we didn't find a significant difference in VR parameters in diabetic patients according to HD dose. HD adequacy had no effect on VR parameters in diabetic patients.

Anemia is a common complication of end-stage kidney disease due to erythropoietin deficiency and is one of the potential factors promoting the risk of

arrhythmia and sudden cardiac death in CKD.^[34] Although anemia is an independent risk factor for an adverse cardiovascular outcome in patients on RRT, increased hemoglobin levels have failed to show benefits in terms of mortality in patient taking an erythropoietin-stimulating agent.^[35] In another study, ventricular arrhythmia was found in 35% of CKD patients and was associated with an increased hemoglobin level.^[36] High body iron stores were found to be related to an increased risk of elevated QTd in patients with chronic ambulatory peritoneal dialysis.^[37] In our study, the hemoglobin level was similar in the 2 Kt/V groups.

Some limitations of this study should be noted. Although we found that hemoglobin level was similar in the different Kt/V groups, body iron stores and the use of erythropoietin-stimulating agent were not considered. We excluded patients taking drugs that prolong the QT interval; however, we didn't examine angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker use. Angiotensin II directly induces cardiomyocyte hypertrophy, independent of afterload. The blockade of angiotensin II may influence VR. The use of these medications may have affected the findings.

Conclusion

During a 4-hour HD session, besides to changes in biochemical parameters, systolic and diastolic blood pressure, and heart rate, there were significant differences in electrocardiographic VR markers. We could not find any relationship between VR parameters and HD adequacy. Furthermore, the VR findings were not significantly different in the diabetic subgroup. As a result, a high dialysis dose may not always be best for the heart.

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