

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 markers may predict ventricular arrhythmias and cardiac arrest. This study aimed to investigate the acute effects of a hemodialysis session and hemodialysis adequacy on ventricular repolarization markers in hemodialysis patients.

Methods: The cross-sectional study conducted in two university hospitals and we measured ventricular repolarization markers before and after a hemodialysis session, including QT, QTc, QT minimum, QT maximum, dispersion of QT (QTd), Tp-e interval and Tp-e/QT in 83 hemodialysis patients. Kt/V reflected dialysis adequacy that was calculated using the second generation Daugirdas formula. Patients were divided into two groups according to the Kt/V value, group 1 ≤ 1.6 as standard dialysis dose and group 2 > 1.6 as high dialysis dose.

Results: 36 patients were in group 1 and 47 patients were in group 2. There were statistically significantly more female patients in the group 2 ($p=0.016$). After hemodialysis heart rate increased, blood pressure decreased, QT, QTc, QT maximum, QTd, Tpe interval and Tpe/QT prolonged after hemodialysis session ($p<0.05$). Ventricular repolarization markers were found similar in two groups. In diabetic patients ventricular repolarization markers also did not affected with Kt/V values.

Conclusion: Hemodialysis session may be a risk factor for cardiac arrest in hemodialysis patients because of prolonged ventricular repolarization parameters independently hemodialysis adequacy. High dialysis dose may not always be the 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 ve 83 hemodiyaliz hastasında ventriküler repolarizasyon belirteçleri hemodiyaliz seansının öncesinde ve sonrasında ölçüldü; bunlar QT, QTc, QT minimum, QT maksimum, QT dispersionu (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. Bu çalışmada diyaliz etkinliği ile ventriküler repolarizasyon belirteçleri arasındaki ilişkiyi değerlendirdik.

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, Tpe 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, ischemic heart disease has less mortality than cardiac arrhythmia in hemodialysis patients. Additionally, the dialysis process may induce sudden cardiac death risk due to hemodynamic overload, inflammatory stress, intradialytic myocardial ischemia, and a higher frequency of ventricular repolarization (VR) alteration.^[3]

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

Kt/V is also a formulation and reflects the adequacy of hemodialysis. It is affected by dialysis time, amount of fluid with ultrafiltration, blood urea nitrogen change in HD session. A substantial effect of hemodialysis adequacy on left ventricular remodeling has been reported in previous studies.^[5,6] However, we have not any data about hemodialysis adequacy on VR. This study aimed to investigate the effects of a hemodialysis session and hemodialysis adequacy on VR in hemodialysis patients.

METHODS

Study design and population

In two university hospitals 83 patients were enrolled among 378 chronic hemodialysis patients who met all the criteria. The present study was an observational, cross-sectional study conducted.

The inclusion criteria were as follows: >18 years old, chronic hemodialysis patients, undergoing hemodialysis three times a week for four hours, had normal sinus rhythm and acceptance to participate in the study.

The exclusion criteria were as follows: atrial fibrillation, the presence of left ventricular ejection fraction <40%, stable coronary artery disease and the history of acute coronary syndrome, percutaneous coronary intervention, or cardiac surgery within last six months. We excluded the patients who had Kt/V value <1.2, cause of it reflects ineffective hemodialysis. There were only four patients who had Kt/V value <1.2.

We eliminated ECG related problems like; the presence of bundle branch block, unacceptable ECG records, the presence of second or third-degree atrio-ventricular block. Also, the presence of a U wave on the ECG was a reason for exclusion from the study. We omitted the patients with administration of drugs that prolong the QT interval.

Abbreviations:

| | |
|-----|----------------------------|
| DM | Diabetes mellitus |
| HD | Hemodialysis |
| QTd | QT dispersion |
| VR | Ventricular repolarization |

Hemodialysis schedule and hemodialysis adequacy

The patients were undergoing three times a week. All examination parameters were assessed in second dialysis session of the week. The blood and dialysate flow rates were set at 300 ml/min and 500 ml/min, respectively. Hemodialysis was performed using a low-flux polysulfone dialyzer (Fresenius Fx-10, the surface area of 1.8 m², Fresenius SE & Co. KGaA, Bad Homburg, Germany).

We preferred Kt/V to determine of hemodialysis adequacy because of Kt/V is a useful and reliable indicator.^[7] Kt/V values <1.2 reflect ineffective HD. If Kt/V values are between 1.2 and 1.6, it means standard effective HD session or standard dialysis dose. Kt/V value >1.6 means high effective HD or high dialysis dose. We divided the patients into two groups according to the Kt/V value, ≤1.6 (1.2–1.6) as standard dialysis dose and >1.6 as high dialysis dose.

Kt/v is calculated using the second generation Daugirdas formula.^[7]

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

(R=post-dialysis/pre-dialysis blood urea nitrogen, t=dialysis time (hour), UF=ultrafiltration or pre/post dialysis weight change and W=post-dialysis weight).

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 in the clinical history and archives. Measurement of arterial blood pressure and ECG recording were performed at rest in all individuals 10 minutes before the start of HD and 10 minutes after the end of the HD session.

Arterial blood pressure was measured by a sphygmomanometer and heart rate was measured by electrocardiography before and after each HD session.

Blood samples were taken before and after HD session to determine blood urea nitrogen, creatinine, sodium, calcium, phosphorus, and potassium levels in a local laboratory.

All 83 patients underwent a 12-lead electrocardiogram; the 12-lead ECG was performed conventionally at a paper speed and gain of 25 mm/s and 10 mm/mV, respectively. The ECG was performed at rest in all individuals 10 minutes before the start of HD and 10 minutes after the end of the HD session. All of the patients had a sinus rhythm. Electrocardiographic intervals were measured by two experienced cardiologists blinded to the study. ECGs were analyzed with the help of a digital caliper with a sensitivity of 1/100

mm and a magnifier. Inter-observer agreement rates were 0.952 (95% CI: 0.940, 0.964).

The QT interval on the ECG defines the duration of ventricular depolarization. The QT interval 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 leads is accepted as most predictive capacity ventricular arrhythmia by some authors.^[4] The heart rate may influence the QT interval. Therefore, the corrected QT (QTc) interval calculated using Bazett's method [$QTc = QT/(R-R)^{1/2}$]. The QTc was accepted prolonged when it was higher than 440 ms.^[8] Dispersion of QT (QTd) is another marker of VR. QTd is defined as QT maximum minus QT minimum on the surface 12-lead ECG.^[9]

Tp-e interval was measured as the interval between the peak of the T wave and the end of the T wave on

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

| Variables | Kt/V ≤1.6 (n=36) | Kt/V >1.6 (n=47) | p |
|--|------------------|------------------|-------|
| Age (years), mean±SD | 48±12 | 50±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 hemodialysis (years), median (min-max) | 2 (1–25) | 4 (1–35) | 0.298 |
| Age of onset of hemodialysis (years), mean±SD | 44±15 | 45±18 | 0.689 |
| Smoking consumption, 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) | |
| Base 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) | |
| Others | 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±SD | 134±3 | 136±3 | 0.137 |
| Serum calcium (mg/dL), mean±SD | 8.6±0.9 | 8.7±0.9 | 0.723 |
| Serum phosphorus (mg/dL), mean±SD | 5.1±1.1 | 5.0±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±SD | 3008±954 | 2918±898 | 0.660 |

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

the V6 lead.^[10,11] Tp-e/QT measured in healthy populations at V6 is in the range of 0.15 to 0.25.^[11] We calculated the Tp-e/QT at the V6 lead.

The local Ethics and Research Committee of the University Hospital approved this study. All patients were informed with written consent.

Statistical Analysis

Statistical analyses were performed using SPSS 19.0 software (SPSS Inc., Chicago, IL, USA). The distribution of the data was assessed by the Shapiro-Wilk test. Continuous variables were expressed as mean \pm standard deviation or median (min-max), and categorical variables as frequency and percent. The Fisher Exact Chi-square test or The Chi-Square test with Yates Correction was used to determine for difference between groups for categorical variables. Continuous variables were compared with the independent sample t-test or the Mann-Whitney U test for two groups. Comparison of repeated measures was performed using the paired t-test or Wilcoxon signed ranks test. Sex, diabetes mellitus, ultrafiltration, QT, QTc, QTd and Tp-e interval were taken into multivariable logistic regression analysis was performed to determine the risk of dialysis dose by Backward LR method. A post-hoc power analysis was performed using GPower 3.0.10. We found the power as 99% in post-hoc power

analysis. A p-value of less than 0.05 was considered statistically significant for all tests.

RESULTS

36 patients were in the Kt/V \leq 1.6 group and 47 patients were in the Kt/V $>$ 1.6 group. Comparison of demographic, laboratory and clinical data between Kt/V groups are presented in Table 1. We didn't find any difference between Kt/V groups except sex. There were more female patients in high dialysis dose group (p=0.016).

Comparative analysis of laboratory, hemodynamic and electrocardiographic variables are shown in Table 2 before and after HD. Body weight, serum creatinine, BUN, potassium, systolic, diastolic and mean blood pressure decreased after HD. Heart rate increased after HD (78 \pm 11 bpm, 82 \pm 14 bpm, p<0.001). All of the VR parameters prolonged after HD except QT minimum. There was no statistically significant difference after HD QT minimum (p=0.838). QTd was 38 \pm 19 ms before HD and 49 \pm 36 ms after HD (p=0.037). Tp-e interval was 101 \pm 16 before HD, 113 \pm 43 ms after HD (p=0.002).

The comparative analysis of VR markers before and after HD according to the Kt/V groups was shown in Table 3. The VR markers including QT, QTc, QT minimum, QT maximum, QTd, Tp-e and Tp-e/QT

Table 2. Laboratory, hemodynamic and electrocardiographic variables in the 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 (mm Hg) | 132 \pm 21 | 112 \pm 22 | <0.001 |
| Diastolic blood pressure (mm Hg) | 76 \pm 10 | 67 \pm 11 | <0.001 |
| Mean blood pressure (mm Hg) | 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 |
| Tpe (ms) | 101 \pm 16 | 113 \pm 43 | 0.002 |
| Tpe/QT | 0.245 (0.183–0.310) | 0.252 (0.175–0.395) | 0.004 |

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

Table 3. Comparison of ventricular repolarizations predictors according to Kt/V groups

| 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 |

were similar before and after HD indifferent Kt/V groups. Further, we calculated and analyzed the magnitude of change in VR markers before and after HD

as a percentage. The values of change in VR markers before and after HD were also found similar indifferent Kt/V groups.

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

| | Kt/V ≤1.6 | Kt/V >1.6 | p |
|--------------------------------|---------------------|---------------------|-------|
| QT interval, non-diabetic (ms) | 398 (295–560) | 415 (324–630) | 0.245 |
| QT interval, diabetic (ms) | 420±48 | 445±54 | 0.197 |
| QTc, non-diabetic (ms) | 474±45 | 483±37 | 0.434 |
| QTc, diabetic (ms) | 492±36 | 502±37 | 0.483 |
| QT minimum, non-diabetic (ms) | 350±29 | 369±39 | 0.065 |
| QT minimum, diabetic (ms) | 377±32 | 387±41 | 0.492 |
| QT maximum, non-diabetic (ms) | 398 (295–560) | 415 (324–630) | 0.252 |
| QT maximum, diabetic (ms) | 422±46 | 445±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±24 | 116±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±0.044 | 0.260±0.049 | 0.733 |

Table 5. Multivariable logistic regression analysis

| Indicators | Rank | OR | 95% CI | p |
|-------------------|------|-------|-----------|-------|
| 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 |

Comparative analysis of the Kt/V value and VR markers in diabetic and non-diabetic HD patients was shown in Table 4. Among the non-diabetic patients, 22 were in group 1 and 32 were in the group 2. Among the diabetic patients, 14 were in group 1 and 15 were in group 2. We didn't find any significant difference between VR parameters and the Kt/V groups in diabetic and non-diabetic patients.

Multivariable logistic regression analysis was performed to determine the risk factors of dialysis dose. Indicators were selected among the significantly different parameters in the study groups and VR predictors that were sex, diabetes mellitus, ultrafiltration, QT, QTc, QTd and Tp-e interval. As a result, we only found an association between HD dose and sex (OR: 3.349, 95% CI: 1.34–8.38, p=0.010) in Table 5.

DISCUSSION

The risk of ventricular arrhythmia and sudden cardiac death caused by arrhythmia is increased in HD patients.^[2] Also, cardiovascular mortality is higher in patients with CKD rather than in the general population.^[12] Prolonged time on hemodialysis, a drop of 30 mmHg in systolic blood pressure during hemodialysis, concomitant diseases, increased sympathetic activity, and electrolyte imbalance might 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 increased compared to the healthy population.^[13,14] QTd has been found to be significantly higher compared to control subjects in HD patients.^[15]

Analysis of the VR surface ECG is essential for the prediction of ventricular arrhythmia in HD patients. The effect of HD on VR is still controversial.

The change of the predictors of VR in HD session have been found different findings in various studies. Kalanzti et al. found that QT, the QTc interval, and QTd were not changed after HD.^[16] In another study, QTc was not changed but QTd was significantly increased after HD.^[17] Astan et al. and Lorincz et al. found that QT, the QTc interval, and QTd increased after HD.^[18,19] Valentim et al. found that an increased QTc interval and QTc dispersion were associated with dialysis.^[20] Based on these studies, the relevance of VR markers is unclear and controversial and needs further investigation in patients with the end-stage renal disease.

In our study, QT, QTc, QT maximum, QTd, Tp-e intervals and Tp-e/QT statistically significantly prolonged after hemodialysis.

QTd indicates the heterogeneity of VR. Okin et al. showed that, in healthy individuals, a QTd>58 ms increases the risk of cardiovascular mortality by 3.2-fold.^[21] QTd was increased after HD in our study (38±19 ms vs 49±36 ms, p=0.037). The Tp-e interval is an index of the transmural dispersion of VR on ECG. The Tp-e interval has been also proposed to indicate patients at an increased risk of ventricular arrhythmia.^[22] In healthy population, the Tp-e interval was found at the V5 point of 94±10 ms; 92±11 ms in men and women respectively.^[23] However, there is no consensus regarding the cut-off value of the Tp-e interval, and further investigations are needed to define this. In our study the Tp-e interval was found longer both pre and post HD from healthy subjects.

The Tp-e/QT is also 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 Tp-e/QT increased post HD comparing pre HD in the present study. According to our findings we can say HD had an adverse effect on VR and arrhythmic events because of the increase in QT, QTc, QT maximum, QTd, Tp-e interval and Tp-e/QT after HD.

To the best of our knowledge, there are no previously published papers about the efficacy 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 defined as ≥ 1.2 .^[25-27] Several studies have shown that the effect of dialysis dose was associated with gender. Men have been to need more HD session time to obtain the same Kt/V than women.^[28] This result may be related the larger body mass index and body surface area. Besides high dialysis dose or high effective HD session was found to reduced mortality in women.^[28,29] Based on these studies, Spanish guidelines recommend that women should aim for a Kt/V value of >1.6 .^[27] In our study women was also found higher in the Kt/V > 1.6 group. Likewise we only found a significant relationship between sex and dialysis dose in multivariable regression analysis.

We did not find any study about the relationship between hemodialysis adequacy and VR. In our study, VR markers were not significantly different in patients with standard dialysis dose and high dialysis dose. According to this finding, we can say VR parameters were not related to hemodialysis adequacy. Moreover, we can state that high hemodialysis dose cannot provide the desired effect on VR.

Diabetes mellitus (DM) is a chronic disease that affects cardiovascular system by endothelial dysfunction, oxidative stress, atherosclerosis and autonomic neuropathy.^[30] Cardiac autonomic neuropathy is a serious complication of DM and affects 30% of the patients with DM.^[31] As a result of the cardiac autonomic dysfunction, sympathetic autonomic nervous system activity increases in DM patients that is associated with malignant ventricular arrhythmias and sudden cardiac death.^[32] In a recent study, Tokatli et al. were found that Tp-e interval, Tp-e/QT and Tp-e/QTc were prolonged in patients with type 2 DM without CKD.^[33] Besides they found a positive correlation between HbA1c level and glucose level with Tp-e interval, Tp-e/QT, and Tp-e/QTc. In the present study, when we compared the clinical and electrocardiographic variables regarding QTc intervals with a cut-off value of 440 ms, ninety percent of diabetic HD patients had a higher QTc interval ($p=0.025$). There is no consensus on the target Kt/V in the diabetic population in previous studies. Also, we investigated the relationship between HD adequacy and VR parameters in DM subgroups. However we didn't find a significant difference between VR parameters and HD dose in diabetic patients. According to this finding, we can say that the HD adequacy in diabetic patients has no effect on VR parameters.

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 adverse cardiovascular outcome in patients on renal replacement therapy, increase hemoglobin levels have failed to show benefits in mortality in patient with administering erythropoietin stimulating agent.^[35] In another study, ventricular arrhythmia was found in 35% of CKD patients and was associated with increased hemoglobin level.^[36] Besides the high body iron stores was found related to increase the risk of increased QTc in patients with chronic ambulatory peritoneal dialysis.^[37] In our study hemoglobin level was similar in Kt/V groups.

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

Conclusion

In summary, during a 4-hour HD session, in addition to changes in biochemical parameters, systolic and diastolic blood pressure, and heart rate, electrocardiographic VR markers were significantly different. Thus, we can say that HD session may be a risk factor for cardiac arrest in hemodialysis patients, especially for diabetic patients. However, we didn't find any relation between VR parameters and HD adequacy. These findings were not changed in the diabetic subgroup. As a result, high dialysis dose may not always be the best for the heart.

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Anahtar sözcükler: Diyaliz dozu; hemodiyaliz; hemodiyaliz etkinliği; Kt/V; QT interval; ventriküler repolarizasyon.