Changes in the QT Intervals, QT Dispersion, and Amplitude of T Waves after Hemodialysis

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Background: Increased QT dispersion (QTd) has been associated with an increased risk for ventricular arrhythmias and sudden death in the general population and in various clinical states.

Methods: We investigated the impact of hemodialysis (HD) on QT, QTd, and T-wave amplitude in subjects with end-stage renal failure. Data on 49 patients on chronic HD were studied. The QT, QTd, and the sum of amplitude of T waves (ΣT) in millimetre in the 12 ECG leads, along with a host of other ECG parameters, body weight, blood pressure, heart rate, electrolytes, and hemoglobin/hematocrit were measured before and immediately after HD.

Results: QT decreased (380.9 ± 38.4 – 363.5 ± 36.8 ms, $P = 0.001$), the QTc did not change (406.2 ± 30.8 – 405.4 ± 32.2 ms, $P = 0.8$), the QTd increased (31.3 ± 14.6 – 43.9 ± 18.6 ms, $P = 0.003$), and the ΣT decreased (32.3 ± 15.7 – 25.9 ± 12.6 mm, $P = 0.0001$) after HD. There was no correlation between the change in QTd and the changes in serum cations, heart rate, the subjects' weight, T-wave duration, and ΣT . However, the change in QTc correlated inversely with the change in serum Ca^{++} ($r = -0.339$, $P = 0.021$).

Conclusion: QTd increased, the ΣT decreased, and the QTc and T-wave duration remained stable, after HD. The QTd increase, although may be real, could also reflect measurement errors stemming from the decrease in the amplitude of T waves (as shown recently), imparted by HD; this requires clarification, to use QTd in patient on HD.

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Patients with end-stage renal disease (ESRD) requiring maintenance hemodialysis (HD) have a high mortality rate, which is primarily attributable to cardiovascular disease, including ventricular arrhythmias and sudden death.¹ The incidence of arrhythmias increases during and immediately after HD. These arrhythmias may be caused by the rapid changes in intracellular and extracellular electrolytes during HD in these patients, who also are susceptible to both myocardial ischemia and fibrosis.² Different methods have been employed to predict the occurrence of serious ventricular arrhythmias and detect patients at high risk.

During the last decade, several studies had shown that the dispersion of the QT interval (QTd)

could be used as a predictor of ventricular arrhythmias; in clinical studies, a wide QTd has been shown to be a risk factor for cardiac arrhythmia after myocardial infarction,^{3,4} in congestive cardiac failure,⁵ and with use of certain drugs.⁶ HD has been reported to induce an increase in QTc intervals⁷ and QTd.⁸ In this work, we sought to study the changes in QT interval, QTd, and T-wave amplitude and duration in patients with ESRD before and after HD and the impact of changes in T-wave amplitude on the change of QT interval duration and QTd. Partially this was prompted by our study that documented an increase in QT interval duration in patients with peripheral edema of varying etiologies who subsequently lost weight, and after HD.⁹

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METHODS

Patients

Fifty subjects with ESRD attending a routine mid-week HD session, were recruited in this study; they were receiving biweekly bicarbonate based HD, lasting three to four and a half hours, using polysulfone capillaries and bicarbonate dialysate containing 138 Na⁺, 2.0 K⁺, 1.75 Ca⁺⁺, and 0.5 Mg⁺⁺ mmol/L. Verbal consent was obtained in all cases after an explanation of the study. Before the HD session, the subjects were weighed and a standard 12-lead electrocardiogram (ECG) recorded using an Agilent (HP, currently Philips) M1771A Page writer 200i electrocardiograph at a paper speed of 25 mm/s, and at standardization of 10 mm = 1.0 mV. Filter configurations were: for automatic report filter/base line was 0.15 Hz and noise filter 40 Hz; for manual report, filter/base line was 0.05 Hz, and noise filter 40 Hz. To ensure reproducibility of the ECGs before and after HD, the V1-V6 leads were obtained from fixed chest landmarks made, using a skin marker. A second ECG was immediately recorded after HD, and the subjects were reweighed. Blood was taken before and after HD for measurement of plasma electrolytes, hemoglobin (Hb) and hematocrit (Ht). All HD sessions were uncomplicated.

Electrocardiographic Analysis

QT intervals were measured manually with calipers in each ECG lead by one observer (A.D.) who was blinded to the pre- and post-HD status. The start of the QT interval was measured at the beginning of the QRS complex; the end of the QT interval was measured at the return of the T wave to the T-P interval baseline; when a U wave was present, at the offset of the T wave, it was measured at the nadir between the T wave and the U wave. Exclusion criteria were: (1) unmeasurable T waves; (2) atrial fibrillation; (3) bundle branch block and (4) antiarrhythmic drugs that lengthen the QT interval. To allow for changes in heart rate during HD, all QT intervals were corrected for heart rate by dividing their values by the square root of the R-R interval in seconds (Bazett's formula). The mean QTc interval was calculated as the arithmetic mean of QTc intervals measurable in each ECG lead. The QTd was calculated as the maximum QT minus the minimum QT.

To evaluate intraobserver variability in QTc interval and QTd measurements, the ECGs of 15 patients, chosen randomly, were analyzed by a single observer (A.D.) on 2 different occasions. There were no significant differences in QTc interval (407 ± 30 ms vs 407 ± 31 ms) or QTd (31 ± 7 ms vs 32 ± 8 ms) between the two readings; according to the method of Bland and Altman,¹⁰ the mean of the differences was 0.0 ± 5 ms for the QTc interval and -1.0 ± 10 ms for QTd.

Absolute value of the amplitude of T waves in millimetre were measured from peak to nadir, using a magnifying glass; T waves <1.0 mm were set at the fixed levels of 0.25, 0.5, and 0.75 mm. The 0.25 mm amplitude designation was considered when a T wave consisted of a tiny perturbation in the isoelectric line before P waves; the 0.5 mm measurement was considered for the amplitude of T wave estimated as such; the 0.75 mm measurement was considered when the amplitude of T wave was >0.5 mm, but <1.0 mm; the 0 mm was considered when a T wave was strictly isoelectric. The sum of the T waves from all 12 ECG leads (ΣT) was then calculated. The T wave duration was measured in all leads from the first electrical activity to the offset at the junction between the end of T wave deflection and the isoelectric line. The QRS duration was also measured in all leads from the beginning of the QRS complex to the offset at the junction between the end of S wave deflection and the isoelectric line. The amplitude of QRS complexes in all 12 ECG leads were measured from peak to nadir in millimeter to the nearest 0.5 mm employing a magnifying glass and calipers, and the sum (ΣQRS) was calculated. The heart rate was calculated in beats per minute. Also, JT interval was calculated by subtracting QRS duration from QT interval before using the Bazett's formula. The following ECG criteria for left ventricular hypertrophy (LVH) were used: Sokolow-Lyon voltage (sum of the amplitudes of S wave in V1 and R wave in V5 or V6 > 3.5 mV)¹¹ and sex-specific Cornell voltage (sum of the amplitudes of S wave in V3 and R wave in aVL >2.0 mV in women and >2.8 mV in men).¹²

Statistical Analysis

Data are reported as mean $\pm$ SD. Analysis employed the student's *t*-test for paired data to determine the significance of differences. Pearson's correlation coefficient for linear regression analysis of percent change ($\Delta\%$) of the study variables

Table 1. Baseline Characteristics of Subjects

Characteristics	Frequency
Male/female	19/30
Age (yr)	44 ± 14 (21–84)
Coronary heart disease	1 (2%)
Hypertension	21 (42%)
Diabetes	6 (12%)
Dyslipidemia	2 (4%)
Drugs:	
Angiotensin-converting enzyme inhibitors	17 (34%)
Calcium blockers	26 (53%)
Beta-blockers	3 (6%)
Average duration of chronic HD (months)	100 ± 43 (24–216)
Cause of end-stage renal failure	
Glomerulonephritis	7 (14.3%)
Diabetes	6 (12.2%)
Nephrosclerosis	7 (14.3%)
Tubulointerstitial nephritis	4 (8.1%)
Hereditary	1 (2.0%)
Autosomal dominant polycystic	4 (8.1%)
Vascularitis	7 (14.3%)
Unknown	13 (26.5%)

resulting from HD was used. $P < 0.05$ was considered as statistically significant. The SPSS (version 11.5) and Origin statistical packages were used.

RESULTS

Forty-nine of 50 pairs of ECGs were judged interpretable. The characteristics of the subjects are shown on Table 1. The results of the changes in measured variables are shown on Table 2. Follow-

ing HD, significant changes in electrolytes, blood pressure, and heart rate were observed in association with a fall of the patients' weight by a mean of 3.36 ± 1.10 kg. Significant ECG changes (Tables 2–7, and Figures 1–3) precipitated by HD included an increase in QRS duration and Σ QRS and a decrease in Σ T and in JT duration (Tables 2–7). However, the changes in T-wave duration and QTc duration were not statistically significant. The QTd showed a statistically significant increase (Tables 2–7). The QTd increases from 31.3 ± 14.6 ms before HD (QTc max = 431.2 ± 53.8 ms, QTc min = 388.2 ± 31.7 ms) to 43.9 ± 18.6 after HD (QTc max = 429.4 ± 33.8 ms, QTc min = 381.9 ± 34.9 ms).

Percentage change in Σ T correlated poorly with $\Delta\%$ in Ca^{++} ($r = 0.173$, $P = 0.246$), K^+ ($r = -0.049$, $P = 0.749$), phosphate ($r = -0.139$, $P = 0.351$), bicarbonate ($r = 0.151$, $P = 0.306$), Hb ($r = -0.001$, $P = 0.993$), Ht ($r = 0.14$, $P = 0.39$), systolic blood pressure ($r = -0.191$, $P = 0.198$), diastolic blood pressure ($r = -0.054$, $P = 0.717$), weight ($r = 0.004$, $P = 0.993$), heart rate ($r = 0.019$, $P = 0.9$), QTc interval ($r = -0.097$, $P = 0.523$), QTd ($r = -0.115$, $P = 0.445$), Σ QRS ($r = 0.198$, $P = 0.182$), QRS duration ($r = 0.148$, $P = 0.35$), and JT duration ($r = -0.21$, $P = 0.25$). Also, there was a poor correlation between $\Delta\%$ in T-wave duration and $\Delta\%$ in QTc interval ($r = 0.139$, $P = 0.358$), QTd ($r = 0.137$, $P = 0.363$), and JT duration ($r = 0.333$, $P = 0.062$).

We further examined the relationship between QTc and QTd with a number of clinical and laboratory variables (Table 6). It was found that the increase in QTd after HD was independent of

Table 2. Study Variables before and after Hemodialysis

Variable	Pre-HD	Post-HD	P
Potassium (mM/L)	5.7 ± 0.8	3.7 ± 0.7	0.0001
Calcium (mg/L)	83.7 ± 8	114 ± 10	0.01
Phosphate (mg/L)	58.3 ± 9.5	54.7 ± 9.4	0.0001
Bicarbonate (mM/L)	16.3 ± 1.8	21.9 ± 1.7	0.0001
Hemoglobin (g/dL)	9.0 ± 1.36	9.8 ± 1.3	0.0001
Hematocrit (%)	30.6 ± 3.4	36.5 ± 4	0.0001
Systolic BP (mm Hg)	136 ± 23.8	124 ± 22.5	0.0001
Diastolic BP (mm Hg)	77 ± 13	71 ± 11	0.0001
Heart rate (beats/min)	74 ± 12	78 ± 12	0.004
Body weight (kg)	56 ± 9	53 ± 9	0.0001
QRS duration (ms)	77.9 ± 11.5	80.5 ± 12.2	0.003
QTc interval (ms)	406.2 ± 30.8	405.4 ± 32.2	0.8
JT duration (ms)	288.5 ± 41.2	273.7 ± 34.4	0.001
QTd (ms)	31.3 ± 14.6	43.9 ± 18.6	0.003
Σ T (mm)	32.3 ± 15.4	25.9 ± 12.6	0.0001
T duration (ms)	116.9 ± 15.7	119.1 ± 20.3	0.389
Σ QRS (mm)	139.1 ± 50.7	177.2 ± 64.8	0.0001

Table 3. QRS Duration (in ms) before and after Hemodialysis

	QRS Duration before HD	QRS Duration after HD	P
V ₁	83.55 ± 18.72	86.22 ± 16.96	0.278
V ₂	90.00 ± 19.77	93.33 ± 14.77	0.190
V ₃	94.22 ± 17.89	93.33 ± 15.95	0.660
V ₄	88.00 ± 17.78	87.82 ± 21.25	0.955
V ₅	84.00 ± 16.29	85.77 ± 17.89	0.456
V ₆	76.00 ± 16.29	78.22 ± 16.41	0.342
I	68.44 ± 15.66	67.11 ± 17.13	0.473
II	69.33 ± 15.72	74.66 ± 18.29	0.017
III	74.22 ± 18.40	75.11 ± 18.66	0.57
AVR	64.54 ± 13.46	68.18 ± 12.44	0.044
AVL	69.54 ± 17.51	70.90 ± 19.97	0.262
AVF	74.54 ± 16.90	81.13 ± 21.30	0.003

Table 5. T Amplitude (in mm) before and after Hemodialysis

	T Amplitude before HD	T Amplitude after HD	P
V ₁	2.09 ± 1.72	2.37 ± 2.39	0.198
V ₂	4.87 ± 3.62	3.74 ± 2.70	0.013
V ₃	6.48 ± 3.83	4.79 ± 3.45	0.0001
V ₄	4.90 ± 4.48	3.38 ± 3.15	0.001
V ₅	3.74 ± 3.30	2.25 ± 2.12	0.0001
V ₆	2.92 ± 2.10	2.00 ± 1.34	0.0001
I	1.53 ± 1.08	1.27 ± 0.90	0.047
II	2.43 ± 1.61	1.95 ± 1.09	0.022
III	1.51 ± 0.98	1.25 ± 0.88	0.063
AVR	1.80 ± 1.04	1.63 ± 0.77	0.250
AVL	0.73 ± 0.85	0.71 ± 0.83	0.827
AVF	1.92 ± 1.22	1.65 ± 1.23	0.180

gender, hypertension, LVH, diabetes, and the presence of hypokalemia after HD. Furthermore, $\Delta\%$ in QTd correlated poorly with $\Delta\%$ in Ca^{++} ($r = -0.028$, $P = 0.85$), K^+ ($r = 0.271$, $P = 0.071$), phosphate ($r = -0.121$, $P = 0.423$), bicarbonate ($r = -0.04$, $P = 0.79$), Hb ($r = 0.182$, $P = 0.227$), Ht ($r = 0.186$, $P = 0.215$) subjects' weight ($r = 0.031$, $P = 0.84$), diastolic blood pressure ($r = 0.004$, $P = 0.977$), systolic blood pressure ($r = 0.081$, $P = 0.594$), heart rate ($r = -0.23$, $P = 0.124$), and QRS duration ($r = 0.275$, $P = 0.081$). However, QTc interval was significantly greater after HD in women than in men, in diabetic patients, and in patients with LVH. In patients with hypertension, QTc interval was prolonged at baseline and after HD in comparison with patients without hypertension. However $\Delta\%$ in QTc correlated

inversely with $\Delta\%$ in serum Ca^{++} ($r = -0.339$, $P = 0.021$) and directly with $\Delta\%$ in heart rate ($r = 0.413$, $p = 0.004$), QRS duration ($r = 0.376$, $P = 0.015$), and Hb ($r = 0.413$, $P = 0.004$). There was no correlation between $\Delta\%$ in QTc and $\Delta\%$ in JT intervals ($r = 0.115$, $P = 0.53$), K^+ ($r = 0.097$, $P = 0.527$), phosphate ($r = -0.075$, $P = 0.621$), bicarbonate ($r = 0.75$, $P = 0.621$), Ht ($r = 0.174$, $P = 0.248$) subjects' weight ($r = 0.02$, $P = 0.89$), diastolic blood pressure ($r = 0.093$, $P = 0.541$), and systolic blood pressure ($r = 0.0001$, $P = 0.999$).

DISCUSSION

The incidence of ventricular arrhythmias among HD patients has been shown to be high.¹³ Arrhythmias may be life threatening, although their predictive power for mortality in the HD population has

Table 4. T Duration (in ms) before and after Hemodialysis

	T Duration before HD	T Duration after HD	P
V ₁	103.1 ± 33.8	114.9 ± 27.0	0.027
V ₂	136.8 ± 30.6	146.3 ± 36.0	0.183
V ₃	152.2 ± 30.8	152.6 ± 40.0	0.942
V ₄	144.4 ± 28.1	141.0 ± 45.6	0.631
V ₅	126.7 ± 26.1	124.4 ± 42.5	0.780
V ₆	111.9 ± 32.7	120.0 ± 40.7	0.307
I	111.1 ± 25.0	108.3 ± 28.8	0.586
II	117.6 ± 24.6	112.4 ± 27.2	0.269
III	104.9 ± 27.2	100.5 ± 28.8	0.366
AVR	99.1 ± 20.2	102.7 ± 23.4	0.4
AVL	90.0 ± 30.0	107.3 ± 28.6	0.5
AVF	108.8 ± 21.9	110.7 ± 34.0	0.73

Table 6. QTc (in ms) before and after Hemodialysis

	QTc before HD	QTc after HD	P
V ₁	387.54 ± 23.9	380.58 ± 26.66	0.28
V ₂	401.20 ± 18.83	385.82 ± 23.92	0.024
V ₃	401.20 ± 18.83	389.82 ± 22.42	0.077
V ₄	401.20 ± 18.83	389.82 ± 22.42	0.077
V ₅	401.20 ± 18.83	389.82 ± 22.42	0.077
V ₆	401.20 ± 18.83	394.41 ± 21.93	0.305
I	403.27 ± 25.42	389.00 ± 33.71	0.229
II	403.27 ± 25.42	386.45 ± 32.52	0.204
III	406.76 ± 24.75	387.85 ± 34.47	0.207
AVR	403.27 ± 25.42	386.45 ± 32.52	0.204
AVL	399.77 ± 15.03	371.57 ± 30.39	0.06
AVF	403.27 ± 25.42	386.45 ± 32.52	0.204

Table 7. JT Duration (in ms) before and after Hemodialysis

	JT Duration before HD	JT Duration after HD	P
V ₁	283.0 ± 46.0	269.5 ± 38.9	0.014
V ₂	282.8 ± 48.7	262.0 ± 37.2	0.001
V ₃	278.5 ± 46.8	267.2 ± 39.3	0.018
V ₄	284.9 ± 44.6	272.9 ± 39.0	0.04
V ₅	291.4 ± 43.5	278.6 ± 43.8	0.014
V ₆	297.0 ± 45.8	286.0 ± 40.8	0.034
I	305.9 ± 46.1	292.2 ± 39.4	0.007
II	310.0 ± 43.7	289.5 ± 43.5	0.0001
III	301.0 ± 43.7	288.6 ± 36.4	0.006
AVR	306.0 ± 44.4	288.0 ± 35.8	0.002
AVL	295.1 ± 41.2	269.7 ± 89.0	0.095
AVF	296.6 ± 44.0	280.5 ± 42.3	0.002

not yet been shown.¹⁴ Nowadays, one of the noninvasive ways of assessing ventricular repolarization is based on the measurement of the QT interval and QTd. The QTd has been suggested to reflect regional variation in action potential duration.^{15,16} However, several recent articles^{17–19} pointed out that the true pathophysiological meaning of QTd is still not known. Also Kors et al.¹⁹ have shown that a measuring error of QT duration is dependent on T amplitude, i.e., the lower the T amplitude in a lead, the greater presumably the measurement error of QT duration. They have suggested that QTd is related to T wave morphology and shown that ECGs with narrow, tall T loops have small QTd values, whereas wide, small T loops have the largest QTd.

Figure 1. Changes in QTc interval before and after an uncomplicated hemodialysis session; P = NS by Student's *t*-test. **Figure 2.** Changes in QT dispersion before and after an uncomplicated hemodialysis session; P = 0.003 by Student's *t*-test.

The significant increase in QTd in our patients was attributed only to a significant reduction in the minimum QTc, and not to an increase in the maximum QTc duration, possibly due to an error in measuring the minimum QTc (vide supra), or due to other factors perhaps electrolyte changes imparting an effect on the T-wave amplitudes.

The new information in our study is that HD leads to a decrease in T-wave amplitude; this may explain the prolongation of QTd after HD according to the hypothesis of Kors et al. In this case, we can hypothesize that the prolongation of QTd after HD reported in our study and in some other studies is mainly related to difficulties of measuring the end

Figure 3. Changes in ΣT before and after an uncomplicated hemodialysis session; P = 0.0001 by Student's *t*-test.

Table 8. The Results of QTc Interval and QT Dispersion in Subgroups of Hemodialysed Patients

Subgroup	No of Patients	QT c Interval (ms)		QT Dispersion (ms)	
		Pre-HD	Post-HD	Pre-HD	Post-HD
Female	30	406 ± 30	409 ± 33 ^a	31 ± 17 ^a	49 ± 24
Male	19	408 ± 31	402 ± 26	38 ± 16	47 ± 17
Hypertension	20	422 ± 33 ^a	419 ± 35 ^a	33 ± 15	54 ± 20 ^a
Nonhypertension	29	396 ± 23	398 ± 26	34 ± 19	44 ± 21
LVH	10	409 ± 32	418 ± 37 ^a	37 ± 9 ^b	47 ± 20
No LVH	39	406 ± 30	404 ± 30	33 ± 18	49 ± 22
Diabetes	6	407 ± 32	412 ± 24 ^c	36 ± 15	48 ± 17
No diabetes	43	407 ± 30	406 ± 33	33 ± 17	48 ± 22
K+Post-HD < 3.5 mM/L	17	413 ± 34 ^a	405 ± 28	35 ± 18	47 ± 2
K+Post-HD ≥ 3.5 mM/L	32	404 ± 28	408 ± 34	33 ± 17	49 ± 20

^aP < 0.0000; ^bP = 0.007; ^cP = 0.01.

HD = Hemodialysis; LVH = left ventricular hypertrophy.

of T wave when it is too small. However, despite the probable lack of association of QTd with true heterogeneity of repolarization, or possible systematic error in measurements of QT duration, depending on the T-wave amplitude and morphology¹⁹ increased QTd has been demonstrated to predict risk in a variety of clinical populations.³⁻⁴ The prognostic value of increased QTd may reflect an ability to quantify abnormalities of repolarization as distinct from true heterogeneity of repolarization.¹⁸ Also, the mechanism of decrease in T amplitude after HD is not clear and it may reflect some alteration of repolarization after HD. So until a good noninvasive marker to assess heterogeneity of ventricular repolarization is found, some authors suggest that QTd can still be useful to reflect global repolarization abnormalities in 12-lead ECG.²⁰

In patients with ESRD, the cardiac structural and functional changes can alter the repolarization and are at least partly responsible for the high overall incidence of cardiac arrhythmias.^{21,22} However, although the arrhythmogenic effect of HD is well known, the exact cause of HD-induced arrhythmias has remained elusive. There are some contributing factors according to publications in this field: (1) the differences between the serum and intracellular K⁺, or rapid decrease of serum K⁺;²³ (2) serum Ca⁺⁺ and Mg⁺⁺ level changes;²⁴ (3) decrease of the circulatory volume;²⁵ (4) fast correction of metabolic acidosis;²⁶ and (5) increased parathyroid hormone level.²⁷ The result of our study showed that QTc interval has remained stable after HD, whereas QTd increased significantly post-HD.

Although there was no correlation of the changes in the QTc, QTd, and K⁺, patients with hypokalemia after HD showed statistically significant shortening of QTc; the QTc increased post-HD in both the patients who were normokalemic, and hypokalemic after the procedure (Table 8). The lengthening of QTd was larger for patients with post-HD normokalemia, although for both subgroups the change was not statistically significant. These counterintuitive changes may represent a type 2 statistical error, because of the small number of patients evaluated in each subgroup (Table 8). Also there is no doubt that more work is needed, focusing on the effects of HD on repolarization indices in the context of changing electrolyte milieu.

In the study by Nappi et al,⁷ QTc and QTd increased with the dialysate Ca⁺⁺ concentration of 1.25 mmol/L, whereas in patients who underwent HD with the dialysate Ca⁺⁺ concentration of 1.75 mmol, QTc interval was decreased and QTd tended to increase. Cupusti et al.⁸ found that QTd increased significantly during HD with high-calcium (2.0 mmol/L) dialysate. Furthermore, Vichnu et al.²⁸ have studied the influence of electrolyte abnormalities on QTd; they showed that hyperkalemia, hypocalcemia, and hypercalcemia are not associated with increased dispersion of ventricular repolarization. In our study, we have used the same dialysate Ca⁺⁺ concentration at 1.75 mM/L in all patients. This high Ca⁺⁺ dialysate leads to an increase in serum Ca⁺⁺ after HD which itself lead to a shortening of the QTc interval.^{28,29} We have confirmed this result by demonstrating that the QTc

interval changes are inversely related to the changes in serum Ca^{++} . However, no correlation was found between the HD-induced changes in QTd and T-wave amplitude and changes in serum calcium, or other electrolytes, or the heart rate. There was a statistically significant increase in heart rate in our patients, although by a mean of only 4 beats (Table 2); this could have been a response to the significant drop of systolic and diastolic blood pressure which was also noted, and/or the sympathetic arousal (independent to the blood pressure reduction, or due to it) known to be present in patients with ESRD, with further accentuation after HD.³⁰ Such sympathetic surge post-dialysis may have a proarrhythmic effect, and this particular matter needs to be evaluated because there is a potential for therapeutic intervention employing β -blockers. Of interest also was the correlation of the increase in heart rate and QTc, which could predispose to enhanced arrhythmogenicity.

In the present study, the difference in QTc duration between men and women in baseline condition was not significant, but we observed a greater prolongation of the QTc interval after HD in women than in men; this was also found by Genovesi et al.³¹ There is no clear explanation for these sex differences. We didn't find any difference in Ca^{++} concentration before and after HD between men and women. The possibility that sex differences in Ca^{++} handling or Ca^{++} receptor density that have been described in vitro³² might have contributed to a greater effect of HD on ventricular repolarization in women. This may explain the data reported by Leggat et al.³³ who found that death was preceded by withdrawal from dialysis significantly more frequently in women than in men.

A comment is in order about the difference noted in this and our previous work.⁹ In that study HD led to increase in QTc, although we found in the present study a stable QTc. In both studies an increase in ΣQRS ⁹ and QRSd ³⁴ with HD was noted. However the previous study was based on observations of a single patient during 26 HD sessions, whereas the present study examined 49 patients undergoing HD. In some other previous work with patients developing peripheral edema with subsequent alleviation in some patients, reduction of the fluid overload (which can be viewed as a parallel of HD) resulted in increase in ΣQRS , amplitude of P waves, QRSd , and QTc.^{9, 35, 36} The stability of the QRS duration and ΣT in the present study is counterintuitive. Perhaps alleviation of peripheral

edema of patients with varying etiologies, should not be equated with HD. Also perhaps the increase in serum Ca^{++} and decrease in serum K^{+} values after HD produce the variation noted in our previous work (where K^{+} and Ca^{++} were stable) and the present study. Indeed the T-wave amplitude decreased after HD in a previous study,³⁷ in agreement with the present investigation.

QTc did not change in the present study, probably due to an increase in the QRS duration and a decrease in the JT interval (Table 2), the former due to an increase in the amplitude of the QRS complexes, and the latter due to a decrease in the amplitude of the T waves with HD. JT has been suggested to be a better marker of repolarization duration in patients with wider QRS complexes, but this does not apply to our patients who before and after HD had normal QRS duration values.

CONCLUSIONS

It is concluded that HD induced increase of QTd, stable QTc duration, and decrease ΣT ; the increased QTd may have clinical implications, in reference to an imparted increased risk for arrhythmias or sudden death. These changes need first to be corroborated by other investigators, particularly in reference to (a) a possible underlying influence of a measurement error of QTc and QTd, as the amplitude of the T wave decreases with HD,^{18, 19, 37} (b) the possible effect of the varying compositions of used dialysates, and (c) the different post-HD resulting levels of serum K^{+} and Ca^{++} , or the changes in these two cations during HD.

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