Abstract. Interlead variability of the QT interval in surface electrocardiogram (ECG), i.e., QT dispersion, reflects regional differences in ventricular recovery time, and it has been linked to the occurrence of malignant arrhythmias in different cardiac diseases. The purpose of the study was to assess the effect of hemodialysis on QT and corrected QT (QTc) interval and dispersion in chronic hemodialyzed patients. Data of 34 non-diabetic patients (male/female = 21/13; mean age, 54 ± 15 yr) on chronic hemodialysis were studied. Polysulfone capillaries and bicarbonate dialysate containing (in mEq/L) 135 Na⁺, 2.0 K⁺, 1.5 Ca²⁺, and 1.0 Mg²⁺ were used. Simultaneous 12-lead ECG were recorded before and after hemodialysis in a standard setting. The QT intervals for each lead were measured manually on enlarged (×3) ECG by one observer using calipers. Each QT interval was corrected for patient heart rate: QTc = QT/√RR (in milliseconds [ms]). The average cycle intervals were 853 ± 152 ms predialysis and 830 ± 173 ms postdialysis; the difference was not significant. The maximal QT interval changed significantly from 449 ± 43 to 469 ± 41 ms (P < 0.01). The corrected maximal QT interval increased significantly from 482 ± 42 to 519 ± 33 ms (P < 0.01). The QT dispersion changed from 56 ± 15 to 85 ± 12 ms (P < 0.001) and the corrected QT interval dispersion from 62 ± 18 to 95 ± 17 ms (P < 0.001). During hemodialysis, the serum potassium and phosphate levels decreased from 5.5 ± 0.8 to 3.9 ± 0.5 (mM) and from 2.3 ± 0.5 to 1.6 ± 0.4 (mM), respectively, whereas calcium increased from 2.2 ± 0.23 to 2.5 ± 0.22 (mM). It is concluded that hemodialysis increases the QT and QTc interval and QT and QTc dispersion in patients with end-stage renal failure. Thus, it may be stated that the nonhomogeneity of regional ventricular repolarization increases during hemodialysis. Measurement of QT and QTc dispersion is a simple bedside method that can be used for analyzing ventricular repolarization during hemodialysis.

Patients with end-stage renal failure commonly have different cardiovascular diseases. Although a decline in cardiovascular death has recently been observed in the general population, a similar trend has not been seen in dialysis patients (1,2). According to a number of recent reports, it is known that half of the patients receiving chronic hemodialysis therapy die of cardiovascular disease. The main causes are congestive heart failure, coronary artery disease, and sudden death as a result of hyperkalemia or arrhythmia (3–5). Reported rates of sudden death in these patients range from 1.4 to 25% (3,6).

However, hemodialysis patients have a wide variety of electrocardiographic (ECG) abnormalities and, in certain instances, hemodialysis itself seems to be a cause of ECG changes and different kinds of dysrhythmias. Arrhythmias are often observed after the start of hemodialysis and last at least 5 h after dialysis (5–7).

The arrhythmogeneity depends partly on variable factors such as autonomic tone, and partly on abnormalities in ventricular anatomical structure and metabolism. Nonhomogeneity in conduction velocity and/or repolarization in the different parts of the ventricle could provide a substrate for tachyarrhythmias (8,9). Experimental data have demonstrated a strong link between the vulnerability of the ventricular myocardium and increased temporal dispersion of refractoriness (10). The pathogenic role of increased ventricular repolarization nonhomogeneity was confirmed by clinical and experimental studies (10,11). The exact spatial dispersion of ventricular myocardium can be determined by invasive methods such as the measurement of monophasic action potentials of the left and right ventricle, but it can also be measured by a noninvasive method like surface mapping. Both methods are time consuming and require special technical devices, which limit their use in everyday practice (11).

In everyday clinical practice, different methods of surface ECG are being studied for their ability to predict either the occurrence of these ventricular arrhythmias or their clinical relevance (6,11). In the conventional ECG, the prolonged QT interval has been reported to be associated with arrhythmogenesis in a number of cardiac disorders (12). Recent studies have indicated that interlead variability of the QT interval in surface 12-lead ECG (i.e., the QT interval dispersion defined as the difference between maximal and minimal QT interval duration) reflects better the regional differences in ventricular recovery time. This QT dispersion has been linked to the occurrence of arrhythmias in patients with congenital long QT syndromes or with drug-induced tachycardias, and sudden
death in patients with congestive heart failure, hypertrophic cardiomyopathy, hypertensive heart disease, mitral valve prolapse syndrome, etc. (9,11,13–19). Furthermore, there are data about the increased risk of intraoperative death in two patients with renal and liver transplants who had increased QT dispersions (128 ms and 125 ms separately) before surgery (20).

Moreover, in patients awaiting cardiac transplantation and who had QT dispersion longer than 140 ms, there was a fourfold greater risk of death than in patients with QT dispersion shorter than 140 ms. QT dispersion better predicts the risk of sudden death in patients awaiting heart transplantation than the left ventricular ejection fraction (21).

The purpose of our study was to assess the effect of hemodialysis on QT and corrected QT (QTc) interval and QT and QTc interval dispersion in patients with end-stage renal failure 10 min before (pre-HD) and 10 min after each hemodialysis (post-HD).

Materials and Methods

Patients

The data of 34 adult patients, consisting of 21 men and 13 women on chronic hemodialysis with a mean age of 54 ± 15 yr (range, 21 to 78), were studied. The causes of chronic renal failure were as follows: glomerulonephritis (n = 18), tubulointerstitial nephritis (n = 7), nephrosclerosis (n = 5), polycystic kidney disease (n = 2), and other (n = 2) (Table 1). Exclusion criteria were: (1) unmeasurable T waves; (2) atrial fibrillation; (3) bundle branch block; and (4) antihypertensive drugs that lengthen the QT interval. The mean duration of hemodialysis was 22 ± 19 mo (range, 1 to 77). The dialyses were carried out in a standard setting (Fresenius 2008 device; Fresenius Medical Care, Bad Homburg, Germany) with F6 and F8 polysulfone capillaries (Fresenius) for 3.5 to 4 h 2 or 3 times per week. Bicarbonate dialysate containing (in mM) 135 Na+, 2.0 K+, 1.5 Ca2+, and 1.0 Mg2+ was used. During hemodialysis, no drug therapy was applied, except isotonic NaCl or hypertonic (10%) NaCl infusions and sodium heparin. The maintenance drug therapy including digitalis, antihypertensive, antianginal, and beta blocking agents was not changed. The following laboratory tests were performed before hemodialysis and at the end of treatment: serum electrolyte Na+, K+, Mg2+, Ca2+, phosphate, blood urea nitrogen, and creatinine. Arterial BP and heart rate were recorded during the procedure. Intact parathyroid hormone level was determined by RIA (BioRad; normal value 1.2 to 6.8 pmol/L). Different data subgroups were created according to age; gender; the duration of the hemodialysis program; the presence or absence of ischemic heart disease; the presence or absence of hypertension; the use or nonuse of beta blocking agents; and the presence or absence of severe hyperparathyroidism (if the parathyroid hormone [PTH] level was >40 pmol/L).

Methods of Measurement of QT and QTc Interval, and QT and QTc Dispersion

Conventional 12-lead ECG were recorded for assessment of QT dispersion, 10 min before and 10 min after every hemodialysis. Simultaneous 12-lead ECG were recorded by means of a 12-channel ECG recorder (Hewlett Packard Page Writer 200i) at a paper speed of 25 mm/s. On every occasion, the ECG were obtained after a 5-min resting period, with the patients lying comfortably in the supine position. For the analysis of the QT interval, the 12-lead ECG were enlarged on the same photocopier by a factor of three. Three consecutive cardiac cycles were measured and averaged. The QT intervals

<table>
<thead>
<tr>
<th>Table 1. Clinical data of patientsa</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Average age (yr)</td>
</tr>
<tr>
<td>Average duration of chronic HD (±SD, months)</td>
</tr>
<tr>
<td>Weight loss during dialysis (L)</td>
</tr>
<tr>
<td>Systolic BP at the beginning of HD (±SD, mmHg)</td>
</tr>
<tr>
<td>Systolic BP at the end of HD (±SD, mmHg)</td>
</tr>
<tr>
<td>Diastolic BP at the beginning of HD (±SD, mmHg)</td>
</tr>
<tr>
<td>Diastolic BP at the end of HD (±SD, mmHg)</td>
</tr>
<tr>
<td>Cause of end-stage renal failure</td>
</tr>
<tr>
<td>glomerulonephritis</td>
</tr>
<tr>
<td>tubulointerstitial nephritis</td>
</tr>
<tr>
<td>nephrosclerosis</td>
</tr>
<tr>
<td>autosomal dominant polycystic kidney disease</td>
</tr>
<tr>
<td>renal tubular acidosis</td>
</tr>
<tr>
<td>unknown origin</td>
</tr>
<tr>
<td>Cardiac complications</td>
</tr>
<tr>
<td>angina pectoris</td>
</tr>
<tr>
<td>old myocardial infarction</td>
</tr>
<tr>
<td>valvular heart disease</td>
</tr>
<tr>
<td>cardiomyopathy</td>
</tr>
<tr>
<td>sick sinus syndrome</td>
</tr>
<tr>
<td>supraventricular tachycardia</td>
</tr>
<tr>
<td>Medication</td>
</tr>
<tr>
<td>digoxin</td>
</tr>
<tr>
<td>antiarrhythmic medication (beta blockers)</td>
</tr>
<tr>
<td>other (antihypertensive drugs)</td>
</tr>
</tbody>
</table>

a HD, hemodialysis.

for each lead were measured manually with calipers by one observer. The QT interval was measured from the first deflection of the QRS complex to the point of T wave offset, defined by the return of the terminal T wave to the isoelectric TP baseline. In the presence of U wave interrupting the T wave, the terminal portion of the visible T wave was extrapolated to the TP baseline to define the point of T wave offset. If the end of T wave could not be reliably determined, the lead was not included in the analysis. Each QT interval was corrected for patient heart rate using Bazett’s formula: QTc = QT/√RR (ms), where QTc is the corrected QT interval. QT, QTc dispersions were defined as differences between the minimal and maximal QT and QTc values in each of the 12 leads studied (22).

Reproducibility

To determine the intraobserver variability of QT interval and QT interval dispersion measurement, all ECG strips were evaluated by one investigator on two different occasions. The intraobserver variability was demonstrated by Bland and Altman plot methods (Figures 1 and 2). The mean difference in QT interval between the two
measurements, the relative error, was 4.5% and in the QT dispersion it was 11%.

Statistical Analyses

Data were expressed as mean ± SD. The relationship of mean differences between intervals and dispersions in groups (pre-HD and post-HD) and differences among subgroups (ischemic heart disease, hypertension, gender, parathyroid hormone level) were analyzed using ANOVA. A linear regression was used for evaluation of correlation between intervals and dispersions, and to compare ages and duration of HD program. *P* < 0.05 was considered significant. The intraobserver variabilities of ECG measurements were calculated as relative errors according to the formula \( \frac{A - B}{A + B}/2 \), where A represents the first and B the second measurement (23). Statistical package SAS for Windows 6.12 version was used for the analysis.

Results

The data of patients were classified into two groups: Data at the beginning of hemodialysis were grouped under pre-HD, and the data at the end of hemodialysis under post-HD. Our results are summarized in Figures 3 and 4. They show the mean values with SD of measured relative risk (RR) intervals, the maximal QT interval and QT dispersion, and the maximal QTc interval and QTc dispersion of groups pre-HD and post-HD. There were no significant differences between the RR intervals. The average cycle intervals were 853 ± 152 ms before hemodialysis and 830 ± 175 ms after hemodialysis (*P* = 0.52).

The maximal QT interval changed significantly from 449 ± 43 to 469 ± 41 ms (*P* < 0.01). The corrected maximal QT interval (QTc) increased significantly from 485 ± 42 to 519 ± 34 ms (*P* < 0.03). The QT interval dispersion changed from 57 ± 13 ms (*P* < 0.001), and the corrected QT interval dispersion from 62 ± 18 to 95 ± 17 ms (*P* < 0.001). Both QT and QTc intervals and QT and QTc dispersions increased significantly at the end of hemodialysis (*P* < 0.001). There were no differences between the average values of the QT and QTc intervals and between the QT and QTc dispersions.

During hemodialysis, the serum potassium level decreased from 5.5 ± 0.8 to 3.97 ± 0.55 mM and phosphate level from 2.37 ± 0.51 to 1.58 ± 0.38 mM, whereas calcium increased from 2.2 ± 0.23 to 2.5 ± 0.23 mM. Both potassium and phosphate level changes were significant (*P* < 0.001), as was the change in calcium level, which increased significantly (*P* < 0.001). There were no changes in the levels of sodium and magnesium (Table 2).
As a result of the comparison of different subgroups, the basal (pre-HD) maximal QT and QTc interval prolongation and QT and QTc interval dispersion were independent of gender, age of patients, hypertension, and duration of chronic hemodialysis program and hyperparathyroidism, but not of concomitant cardiac disease (Tables 3 and 4). There was no correlation between the increase of QT$_{\text{max}}$ and QTc$_{\text{max}}$ prolongation and QT and QTc interval dispersion at the end of HD (post-HD) and the patients’ age, gender, hypertension, duration of chronic dialysis treatment, and concomitant cardiac abnormalities, namely, ischemic heart disease (Tables 3 and 4).

**Table 3.** The results of QT$_{\text{max}}$ interval and QT interval dispersion in subgroups of hemodialyzed patients

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of Patients</th>
<th>QT$_{\text{max}}$ Interval (ms)</th>
<th>QT Dispersion (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pre-HD</td>
<td>Post-HD</td>
</tr>
<tr>
<td>IHD</td>
<td>9</td>
<td>451.4 ± 26.5</td>
<td>468.1 ± 34.0</td>
</tr>
<tr>
<td>No IHD</td>
<td>25</td>
<td>449.5 ± 45.7</td>
<td>466.1 ± 46.0</td>
</tr>
<tr>
<td>BB</td>
<td>8</td>
<td>444.6 ± 41.8</td>
<td>469.1 ± 32.0</td>
</tr>
<tr>
<td>No BB</td>
<td>26</td>
<td>451.7 ± 41.6</td>
<td>465.9 ± 45.9</td>
</tr>
<tr>
<td>HYP</td>
<td>29</td>
<td>447.8 ± 38.1</td>
<td>462.4 ± 40.2</td>
</tr>
<tr>
<td>No HYP</td>
<td>5</td>
<td>461.2 ± 57.1</td>
<td>488.0 ± 52.2</td>
</tr>
<tr>
<td>PTH &lt;40 pmol/L</td>
<td>25</td>
<td>447.4 ± 39.0</td>
<td>458.9 ± 43.1</td>
</tr>
<tr>
<td>PTH &gt;40 pmol/L</td>
<td>9</td>
<td>456.1 ± 47.1</td>
<td>484.8 ± 37.2</td>
</tr>
<tr>
<td>Male</td>
<td>21</td>
<td>456.0 ± 36.9</td>
<td>468.3 ± 46.7</td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>439.7 ± 47.3</td>
<td>463.8 ± 36.1</td>
</tr>
</tbody>
</table>

$^a$ HD, hemodialysis; IHD, ischemic heart disease; BB, beta blocker therapy; HYP, hypertension; PTH, parathyroid hormone level.

$^b$ $P = 0.011$, IHD versus no IHD (pre-HD).
The patients are at risk for serious ventricular arrhythmias or sudden death (18,34). In our patients, the average value QT dispersion was 85 ms and QTc was 95 ms at the end of HD. The post-HD QT and QTc interval prolongation and QT and QTc interval dispersion lengthening were independent of gender, patient age, hypertension, duration of chronic hemodialysis program and hyperparathyroidism, and concomitant cardiac disease (Tables 3 and 4). According to continuous ECG and BP monitoring, there were no major arrhythmias including non-sustained and sustained ventricular tachycardias, or ventricular fibrillations, and serious hypotensive episodes (<90 mmHg for systolic BP or decrease in systolic BP >30 mmHg) during HD. Our results indicate that the nonhomogeneity of regional ventricular repolarization increases during hemodialysis, which is suggested by increased QTmax and QTcmax interval and QT and QTc interval dispersion. The results of this study may add a new dimension to recent reports indicating the usefulness of QT dispersion as a predictor of sudden death after myocardial infarction, in heart failure of ischemic etiology, hypertrophic cardiomyopathy, as well as the risk of arrhythmia in the long QT syndrome (8,9,13,14–16).

It is concluded that the nonhomogeneity of regional ventricular repolarization in patients with chronic end-stage renal failure receiving hemodialysis may be suggested by the increase in QT and QTc interval or increase in QT and QTc dispersion. The prolongation of these parameters may be a further noninvasive marker of susceptibility to ventricular arrhythmias. Additional studies are needed to clarify whether increased postdialysis QT dispersion results in an increased occurrence of arrhythmias. QT and QTc dispersion is an easily obtainable, noninvasive, simple, inexpensive, and widely available method of risk stratification in uremic patients receiving chronic hemodialysis.

**Table 4. The results of rate corrected QT, QTcmax interval, and QTc interval dispersion in subgroups of hemodialyzed patients**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of Patients</th>
<th>QTcmax Interval (ms) Pre-HD</th>
<th>QTcmax Interval (ms) Post-HD</th>
<th>QTc Dispersion (ms) Pre-HD</th>
<th>QTc Dispersion (ms) Post-HD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHD</td>
<td>9</td>
<td>488.1 ± 43.3</td>
<td>522.0 ± 35.1</td>
<td>66.4 ± 19.7b</td>
<td>100.6 ± 16.4</td>
</tr>
<tr>
<td>No IHD</td>
<td>25</td>
<td>476.6 ± 43.6</td>
<td>510.8 ± 31.2</td>
<td>51.5 ± 10.4</td>
<td>81.1 ± 9.0</td>
</tr>
<tr>
<td>BB</td>
<td>8</td>
<td>487.1 ± 46.0</td>
<td>517.4 ± 35.6</td>
<td>62.4 ± 17.6</td>
<td>94.4 ± 17.9</td>
</tr>
<tr>
<td>No BB</td>
<td>26</td>
<td>478.3 ± 33.6</td>
<td>523.7 ± 29.9</td>
<td>62.0 ± 23.4</td>
<td>98.0 ± 15.2</td>
</tr>
<tr>
<td>HYP</td>
<td>29</td>
<td>484.3 ± 76.2</td>
<td>531.3 ± 28.3</td>
<td>66.5 ± 10.8</td>
<td>90.3 ± 18.1</td>
</tr>
<tr>
<td>No HYP</td>
<td>5</td>
<td>485.1 ± 43.3</td>
<td>517.0 ± 34.8</td>
<td>61.6 ± 19.8</td>
<td>96.0 ± 17.1</td>
</tr>
<tr>
<td>PTH &lt;40 pmol/L</td>
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<td>484.3 ± 42.9</td>
<td>513.1 ± 37.8</td>
<td>61.8 ± 19.0</td>
<td>93.3 ± 16.0</td>
</tr>
<tr>
<td>PTH &gt;40 pmol/L</td>
<td>9</td>
<td>484.8 ± 45.5</td>
<td>532.0 ± 18.9</td>
<td>63.3 ± 19.1</td>
<td>99.6 ± 19.4</td>
</tr>
<tr>
<td>Male</td>
<td>21</td>
<td>484.8 ± 43.9</td>
<td>518.7 ± 33.2</td>
<td>63.0 ± 19.6</td>
<td>92.4 ± 14.8</td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>485.2 ± 43.3</td>
<td>519.4 ± 37.0</td>
<td>60.9 ± 17.8</td>
<td>100.7 ± 20.4</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 3.

Acknowledgment

We thank Dr. Ben Thomas for helpful assistance in preparing the manuscript.

**References**


