A STUDY IN THE ELECTROCARDIOGRAPHIC CHANGES IN HAEMODIALYSIS PATIENTS

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ABSTRACT

BACKGROUND

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. In this study, we have compared the electrocardiographic changes in patients with end-stage renal disease before and after haemodialysis. We have assessed the effect of haemodialysis on QT and corrected QT intervals and their dispersions in patients with end-stage renal disease on regular haemodialysis and also the effect of electrolytes- serum potassium, sodium and calcium on QT and corrected QT interval and their dispersions, before and after haemodialysis in patients with end-stage renal disease.

MATERIALS AND METHODS

Hundred patients with end-stage renal disease on twice a week hospital haemodialysis were randomly taken up for this study. The clinical history, examination, ECG (both pre and post HD) and serum electrolytes was done on each patient. ECG was coded and analysed blindly for QT interval, corrected QT and their dispersions by one observer. The obtained data was analysed statistically using the ANOVA test, Student's paired t-test and both simple and multiple linear logistical progression.

RESULTS

This study shows that at the end of HD (post-HD), the data showed significant increases in QT_{max} and QTc_{max} interval prolongation and QT and QTc interval dispersion in patients with end-stage renal failure receiving haemodialysis. 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 ischaemic aetiology, hypertrophic cardiomyopathy as well as the risk of arrhythmia in the long QT syndrome. On analysing the relation between the changes in electrolytes and the increase in the QT and corrected QT dispersions, the study found no correlation between the electrolyte changes and the increase in QT and corrected QT dispersions. The study also points out to the fact that the changes in QT and corrected QT dispersions are independent of gender, presence of hypertension, diabetes mellitus and coronary artery diseases, but is related to the decrease in RR interval following dialysis.

CONCLUSION

It is concluded that the nonhomogeneity of regional ventricular repolarisation in patients with chronic end-stage renal failure receiving haemodialysis maybe suggested by the increase in QT and QTc interval or increase in QT and QTc dispersion. The prolongation of these parameters maybe 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 uraemic patients receiving chronic haemodialysis. Measurement of QT and QTc dispersion is a simple bedside method that can be used for analysing ventricular repolarisation during haemodialysis.

KEYWORDS

ECG, QT Interval, QT Dispersion, Haemodialysis.

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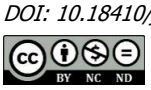

BACKGROUND

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] The main causes are congestive heart failure, coronary artery disease and sudden death as a result of hyperkalaemia or arrhythmia.[3,4,5] Reported rates of sudden death in these patients range from 1.4 to 25%.[3,6]

Arrhythmias are often observed after the start of haemodialysis and last at least 5 hrs. after dialysis.[5,7] Nonhomogeneity in conduction velocity and/or repolarisation 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]

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 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]

AIMS AND OBJECTIVES

Aim of the Study

To study the electrocardiographic changes in patients with end-stage renal disease before and after haemodialysis.

Specific Objectives

1. To assess the effect of haemodialysis on QT and corrected QT intervals and their dispersions in patients with end-stage renal disease on regular haemodialysis.
2. To study the effect of electrolytes like serum potassium, sodium and calcium on QT and corrected QT interval and their dispersions, before and after haemodialysis in patients with end-stage renal disease.

REVIEW OF LITERATURE

Despite improvements in dialysis technology, patients requiring haemodialysis continue to die prematurely. The mechanism responsible for the increased risk of sudden death is not clear, but Holter monitoring in haemodialysis patients has revealed a high incidence of ventricular premature beats and arrhythmias during and immediately after dialysis.[11] The ESRD patients population is characterised as one with the highest mortality rate (even when adjusted for age, race, sex and comorbid conditions)[12] comparable with patients in advanced stages of breast cancer.[13]

The QT Interval

In general, the QT interval represents electrical depolarisation and repolarisation of the left and right ventricles. A lengthened QT interval is a biomarker for ventricular tachyarrhythmias like torsade de pointes and a risk factor for sudden death.

Acquired Long QT Syndrome in Nephrology

In patients with impaired glomerular filtration, QT-liable drugs with renal excretion can produce an unpredictable increase of the plasma concentration leading to a significant prolongation of the QT interval and development of TdP. A well-documented large population-based case-control study of 775 cases of SCD and 6297 matched controls revealed that after adjustment for known confounding factors, current use of noncardiac QTc-prolonging drugs in a general population was associated with almost 3-fold increased risk of SCD (adjusted OR- 2.7; 95% CI- 1.6-4.7).[14,15]

Arrhythmogenic Potentials of Acquired Long QT Syndrome and Haemodialysis

The increase in QTc is not a 'paradoxical' ECG phenomenon and is due to a statistically significant increase in the heart rate (most likely, secondary to the HD-induced reduction of the extracellular fluid), but not due to the changes in the absolute value of the QT interval.[16]

Correction for Heart Rate

The QT interval is dependent on the heart rate. The standard clinical correction is to use Bazett's formula[17] calculating the heart rate-corrected QT interval QT_B. Bazett's formula is as follows-

$$QT_B = \frac{QT}{\sqrt{RR}}$$

Where QT_B is the QT interval corrected for heart rate and RR is the interval from the onset of one QRS complex to the onset of the next QRS complex measured in seconds often derived from the Heart Rate (HR) as 60/HR (here QT is measured in milliseconds).

Upper limit of normal QT interval corrected for heart rate according to Bazett's formula, Fridericia's formula[18] and subtracting 0.02s from QT for every 10 bpm increase in heart rate up to 0.42s (≤420 ms) is chosen as normal QTc of QT_B and QT_F in this diagram.

Definitions of "normal" QTc vary among being equal to or less than 0.40s (≤400 ms),[19] 0.41s (≤410 ms),[20] 0.42s (≤420 ms)[21] or 0.44s (≤440 ms).[22] For risk of sudden cardiac death, "borderline QTc" in males is 431-450 ms and in females 451-470 ms. An "abnormal" QTc in males is a QTc above 450 ms and in females above 470 ms.[23]

QT Dispersion

QT dispersion (maximum QT interval minus minimum QT interval) was originally proposed as an index of the spatial dispersion of ventricular recovery times. In reality, QT dispersion is a crude and approximate measure of a general abnormality of repolarisation.[24]

Attempts to characterise and quantify the inhomogeneity of ventricular repolarisation from the surface electrocardiogram (ECG) using precise mathematical methods such as principal component analysis of the T-wave can be traced back to the 1960s.[25] The QT interval duration varies between leads on the standard ECG, frank orthogonal leads and body surface potential maps.[26-31] These interlead differences called QT interval dispersion or QT range were proposed as an index of the spatial dispersion of the ventricular recovery times.[32] However, there has been much

concern about the validity of the concept and the methodology of the measurement. Despite ongoing controversy, there are a number of reasonable conclusions about the reliability and applicability of the technique.[24,33]

Pathophysiology of QT Dispersion

The initial concept that QT dispersion is an index of inhomogeneity was supported by the link between the dispersion of ventricular recovery times and the genesis of arrhythmias.[34-38] It was generally believed that the standard 12-lead ECG contained information about regional ventricular repolarisation; thus, when increased QT dispersion was seen in cardiac diseases in which ventricular recovery times were known to be heterogeneous. It was assumed that increased QT dispersion was a direct reflection of the disparity of ventricular recovery times.[39]

Data from the United States Renal Data System (USRDS) showed 42% of dialysis patients died of cardiovascular disease with 22.4% of deaths related to cardiac arrest or arrhythmia.[40] Haemodialysis (HD) patients are at an increased risk of sudden death. In addition to the high incidences of coronary artery disease[41] and cardiomyopathy[42] in the patients, disturbances in electrolyte metabolism might contribute to arrhythmia or abnormal conduction. However, serum levels of electrolytes in dialysis patients might have been within normal limits despite the patient having died of sudden death or fatal arrhythmia.[43,44]

QT Dispersion Predicts Ventricular Arrhythmias

QT dispersion, which reflects the differences in heart dipole projections[45] and abnormalities of T-wave loop morphology[46] and has been proposed as a direct measure of the regional heterogeneity of myocardial repolarisation[47] and hence was predisposed to re-entry arrhythmias.[48] Nonhomogeneity in conduction velocity and/or repolarisation in the different areas of the ventricle might provide a substrate for tachyarrhythmias.[49] Patchy myocardial fibrosis resulting from myocardial ischaemia, ventricular dilatation, symptomatic overactivity[50] and neurohormonal activation[18] are all thought to contribute to the risk of increased QT dispersion.

Ventricular Tachycardia

QT dispersion increased the risk for malignant arrhythmia and sudden death in patients with chronic heart failure,[51] mitral valve prolapse,[52] myocardial infarction,[53] autonomic neuropathy[54] and familial long-QT syndrome.[55] Furthermore, a recent study shows that QTc dispersion is an independent predictor of cardiovascular death and associated with arrhythmia-related death in ESRD patients.[56]

Greater QT Dispersion in Dialysis Patients

Autopsy examinations[57] and quantitative echocardiography have shown interstitial myocardial fibrosis and calcium deposition in uraemic hearts, which increases myocardial nonhomogeneity. Patients with chronic renal failure had a greater QTc interval and QTc dispersion compared with the control subjects.[44,58] It has been reported that a single session of HD might further increase QTc dispersion in both adults and children with chronic HD.[59,60-62]

Dialysis patients with a QTc dispersion longer than 74 ms were shown to be at risk of serious ventricular arrhythmias or sudden death. One study showed that a QT dispersion of 60 ms predicted a 1-year mortality of acute myocardial infarction in uraemic patients.[63]

Transmembrane Electrolyte Shifts during Haemodialysis Aggravate QT Dispersion

Potassium, calcium, magnesium and metabolic acidosis are important factors for the electrical stability of the myocardium.[43,64] In a recent issue of Nephrology, Floccari and his colleagues showed that an increase in QTc dispersion during the first hour of HD when arrhythmias frequently occur was inversely correlated with the rapid removal of serum potassium.[65] The increased QT dispersion during HD might result from low calcium dialysate or influx of magnesium into the cell.[66]

CAPD, continuous ambulatory peritoneal dialysis; HD, haemodialysis
Electrolytes
Large amount of or rapid potassium removal[65]
Low calcium dialysate[44,67]
Intracellular magnesium overload[68,66]
Iron overload in CAPD patients[69]
Rapid bicarbonate gain[43]
Heart disease
Patient with acute myocardial infarct[64]
Left ventricular hypertrophy in HD patients[44]

Table 1. Factors that Increase QTc Dispersion in Dialysis Patients

A strong association of QTc dispersion with transferrin saturation has been observed in PD patients.[69] The linear relationship showed that at 74 ms of QTc dispersion the transferrin saturation was 35.2%.[20] In vitro and in vivo studies have shown that a large iron load might change electrical conduction of the cardiomyocytes and lead to sudden death.[70,71] In the heart, iron deposition is heterogeneous with the greatest amount of iron in the left side of the ventricular septum and free wall (especially in the epicardium) followed by that in the right ventricle and less in the atria. This characteristic pattern of chronic iron deposition within the heart might contribute the arrhythmogenecity of iron when overloaded.[72,73]

Therapeutic Opinions of QTc Dispersion

Prolongation of the QTc dispersion per se has been documented as a risk factor for ventricular arrhythmias in HD patients.[56,65,66] Clinicians should avoid the factors that might increase QTc dispersion, especially when treating patients suffering from ischaemic or hypertrophic heart disease.[60] The dialysate K^+ concentration should be adjusted to avoid rapid potassium removal[65] and the indication for low Ca dialysate should be carefully assessed.[74] Although, the effects of antiarrhythmics or beta agonists have not been

studied in dialysis patients, increased QTc dispersion has been observed in association with these agents in non-uraemic patients.[75,76]

MATERIALS AND METHODS

Study Population and Sample Size

Hundred patients with end-stage renal disease on twice a week hospital haemodialysis were randomly taken up for this study. Each patient was undergoing haemodialysis for three to four hours per session. The dialysis was carried out in a standard setting using polysulfone capillaries and bicarbonate dialysate containing (in mEq/L) 135 Na^1, 2.0 K^1, 1.5 Ca^{21} and 1.0 $Mg.^{21}$

Inclusion Criteria

1. Patients with end-stage renal disease on two times a week hospital haemodialysis for three to four hours.
2. Patients who give consent to enroll in the study.

Exclusion Criteria

1. Patients whose pre-haemodialysis ECG showing atrial fibrillations and frequent extra systole.
2. Patients treated with antiadrenergic drugs or any other drug that may affect QT interval.
3. Patients with permanent pacemaker.
4. Patients with significant valvular heart disease clinically.

Type of Study- Hospital-based observational study.

Methods

Each patient was subjected to the following-

1. History taking as regarding assessment of exclusion criteria, duration of dialysis and causes of renal failure.
2. Examination as regarding detection of exclusion criteria.
3. ECG was done pre and post HD. The twelve-lead ECG was performed at 10 mm/mv and 50 mm/s. ECG was coded and analysed blindly for QT interval, corrected QT and their dispersions by one observer. The QT interval was measured from the onset of the QRS complex to the end of the T wave. When T waves are inverted, the end was taken at the point where the trace returned to the T-P baseline and when U waves are present, the end of the T wave was taken as the nadir between the T and U waves. If the end of the T wave is not clear in a particular lead, then it was excluded from analysis; for any particular ECG, no more than three leads were excluded. Three successive QT interval measurements was performed in each of the 12 leads and the mean value was calculated. The maximum QT interval was corrected for heart rate (QTc max) using Bazett's formula $QTc = QT/\sqrt{(RR)}$.[21]
4. Electrolytes (Na^+, K^+ and Ca^+) was done pre and immediately post HD.

Statistical Analysis

Statistical analysis was done on data entered in the master chart prepared with variables of ECG values of RR intervals, QT intervals of 12 leads, QTc intervals of 12 leads, QT dispersion, QTc dispersion, serum calcium, potassium and sodium before and after dialysis. Other parameters like age, sex, presence of coronary artery disease, hypertension and diabetes mellitus was also considered. The means and Standard Deviations (SD) of all variables was evaluated. ANOVA for analysis of relationship of the means of differences and Student's t-test for paired data will be employed. Linear regression, simple as well as multiple linear regression were also used to assess the relation between serum electrolytes and other parameters to the ECG changes, respectively.

RESULTS

Background Characteristics

This study was conducted on a population of 100 people with end-stage renal disease on twice weekly haemodialysis. Among the 100 patients, 64% were males and 36% were females (Table and Figure 1) of which the mean age group was 51.65 ± 10.45 (Table and Figure 2). Among them, 77% had hypertension (Table and Figure 3), 61% had diabetes mellitus (Table and Figure 4), 33% had coronary artery diseases (Table and Figure 5), 50% of them had both diabetes and hypertension and 25% had all three diseases.

Sex	Count	Percent
Male	64	64.0
Female	36	36.0

Table 1. Distribution According to Sex

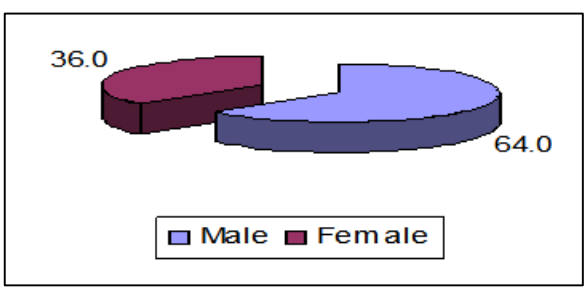

Figure 1. Distribution According to Sex

HTN	Count	Percent
No	23	23.0
Yes	77	77.0

Table 2. Distribution According to HTN

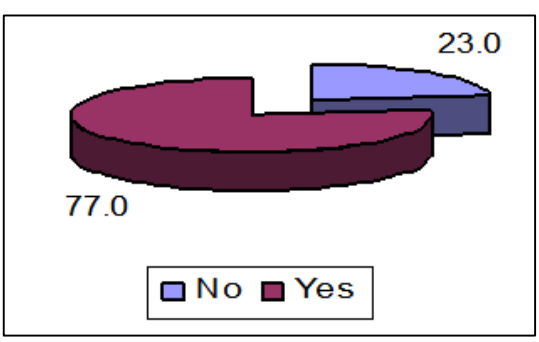

Figure 2. Distribution According to Hypertension

DM	Count	Percent
No	39	39.0
Yes	61	61.0

Table 3. Distribution According to Diabetes Mellitus

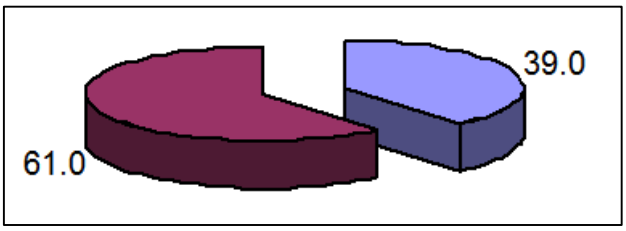

Figure 3. Distribution According to Diabetes Mellitus

CAD	Count	Percent
No	67	67.0
Yes	33	33.0

Table 4. Distribution According to Coronary Artery Disease

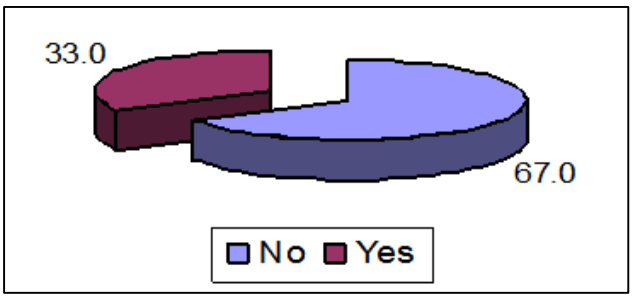

Figure 4. Distribution According to Coronary Artery Disease

Comparison of QT Before and After Dialyses

	Stage	Mean	SD	N	Mean Difference	Paired t	P
QT1	Before	403.1	20.5	100	1.980	1.02	0.311
	After	405.1	20.4	100			
QT2	Before	400.4	18.6	100	5.340	2.52*	0.013
	After	405.7	23.5	100			
QT3	Before	398.9	18.6	100	1.920	0.90	0.368
	After	397.0	24.8	100			
QTR	Before	418.0	23.0	100	6.180	2.31*	0.023
	After	424.2	20.0	100			
QTL	Before	417.4	18.2	100	10.620	5.52**	0.000
	After	428.0	18.2	100			
QTF	Before	418.4	18.3	100	10.160	4.91**	0.000
	After	428.6	19.8	100			
QTV1	Before	438.8	14.6	100	13.440	10.09**	0.000
	After	452.2	17.2	100			
QTV2	Before	440.0	13.0	100	9.960	8.35**	0.000
	After	450.0	15.6	100			
QTV3	Before	440.2	13.7	100	7.140	4.87**	0.000
	After	447.4	20.5	100			
QTV4	Before	434.7	13.8	100	5.740	3.48**	0.001
	After	440.4	18.9	100			
QTV5	Before	432.2	15.0	100	6.240	3.72**	0.000
	After	438.5	17.8	100			
QTV6	Before	432.3	15.2	100	3.040	1.80	0.075
	After	435.3	18.6	100			
QT Max.	Before	445.5	12.6	100	11.980	11.05**	0.000
	After	457.5	18.4	100			
QT Min.	Before	385.9	13.2	100	2.460	2.12*	0.037
	After	388.4	17.1	100			

Table 5. Comparison of QT Interval Before and After Dialysis

**- Significant at p value <0.001.
*- Significant at p value <0.05.

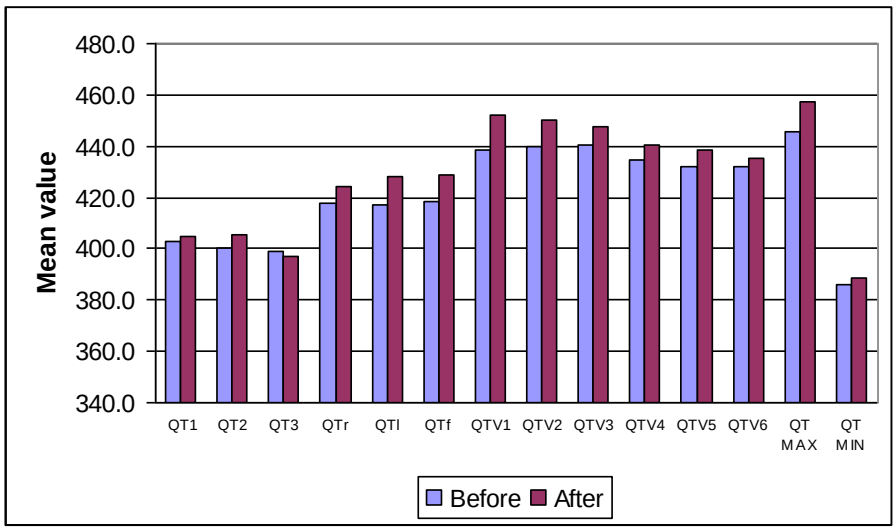

Figure 5. Comparison of QT Interval Before and After Dialysis

On comparing the QT intervals of all the patients before and after haemodialysis, this study shows that there has been a significant increase in the QT interval in ECG taken after dialysis in all leads except lead 1 and V6 as compared to that taken before dialysis.

The QT max increased significantly from 445.5 ± 12.6 to 457.5 ± 18.4 with a p value of <0.001 (Table and Figure 6).

This observation goes in hand with that of the study conducted by Mahmud Malhis and et al[77] wherein QT max increased from 446 ± 47 to 465 ± 52 ms (p value <0.05). This is also similar to the study conducted by Istvan Lorincz et al[78] and Nauman Tarif et al.[79]

Comparison of QTd Before and After Dialysis

QTd	Mean	SD	N	Mean Difference	Paired t	P
Before	59.6	9.1	100	9.520	8.74**	0.000
After	69.1	12.4	100			

Table 6. Comparison of QTd Before and After Dialyses

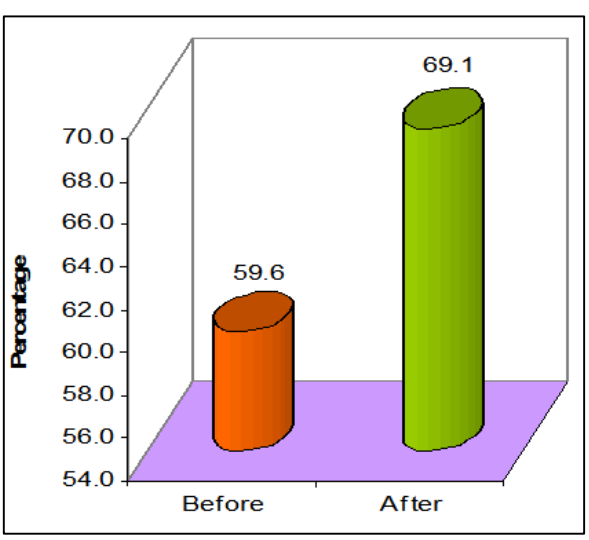

Figure 6. Comparison of QTd Before and After Dialyses

This shows that there is a significant increase in the value of QT dispersion from 59.6 ± 9.1 to 69.1 ± 12.4 with a p value <0.001 (Table and Figure 7). Similar results were noted in studies of Istvan Lorincz et al[78] also in those of Mahmud Mahlis[77] et al and Nauman Tarif et al.[79]

Comparison of RR Interval Before and After Dialysis

RR Interval	Mean	SD	N	Mean Difference	Paired t	P
Before	823.9	44.6	100	22.670	17.25**	0.000
After	801.2	43.8	100			

Table 7. Comparison of RR Interval Before and After Dialyses

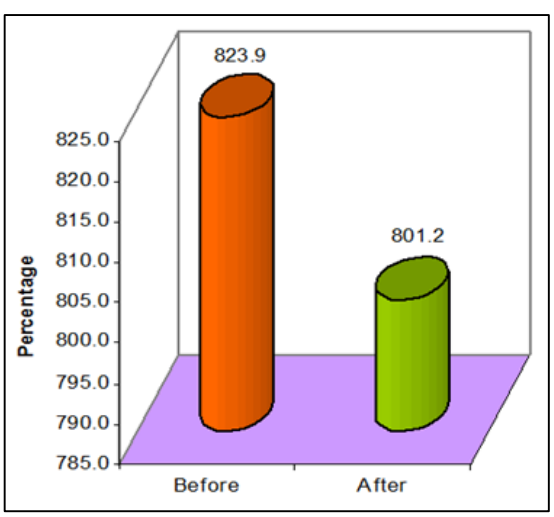

Figure 7. Comparison of RR Interval Before and After Dialyses

There has been a significant decrease in the RR interval in patients after dialysis as compared to before dialysis from 823.9 ± 44.6 to 801.2 ± 43.8 with a p value <0.05 (Table and Figure 8). This is in par with the studies of Lorincz Istvan et al.[78] This study result does not go in hand with that of Mahmud Mahlis[77] et al and Nauman Tarif et al,[79] wherein there was no significant decrease in the RR interval as that observed in this study.

Comparison of QTc Intervals and Their Dispersions Before and After Dialysis

	Stage	Mean	SD	N	Mean Difference	Paired t	P
QTC1	Before	444.6	25.7	100	8.420	3.70*	0.311
	After	453.0	25.0	100			
QTC2	Before	441.6	23.8	100	12.081	5.09**	0.013
	After	453.6	27.3	100			
QTC3	Before	440.0	25.8	100	3.935	1.59	0.368
	After	444.0	30.1	100			
QTCR	Before	461.2	32.8	100	13.195	4.16**	0.023
	After	474.4	25.9	100			
QTCL	Before	460.3	22.7	100	18.403	8.09**	0.000
	After	478.7	24.0	100			
QTCF	Before	461.4	22.4	100	17.950	7.31**	0.000
	After	479.3	26.1	100			
QTCV1	Before	483.9	19.4	100	21.858	13.03**	0.000
	After	505.7	22.7	100			
QTCV2	Before	485.3	19.2	100	17.935	12.11**	0.000
	After	503.2	21.2	100			
QTCV3	Before	485.5	20.2	100	14.798	8.38**	0.000
	After	500.3	26.4	100			
QTCV4	Before	479.4	19.5	100	13.138	6.59**	0.001
	After	492.6	23.9	100			
QTCV5	Before	476.7	20.5	100	13.688	6.77**	0.000
	After	490.4	23.5	100			
QTCV6	Before	476.8	21.7	100	10.086	5.02**	0.075
	After	486.9	24.7	100			
QTC Max.	Before	491.4	19.0	100	20.300	14.35**	0.000
	After	511.7	24.2	100			
QTC Min.	Before	425.6	18.2	100	8.748	6.35**	0.037
	After	434.4	22.3	100			

Table 8. Comparison of QTc Intervals Before and After Dialyses

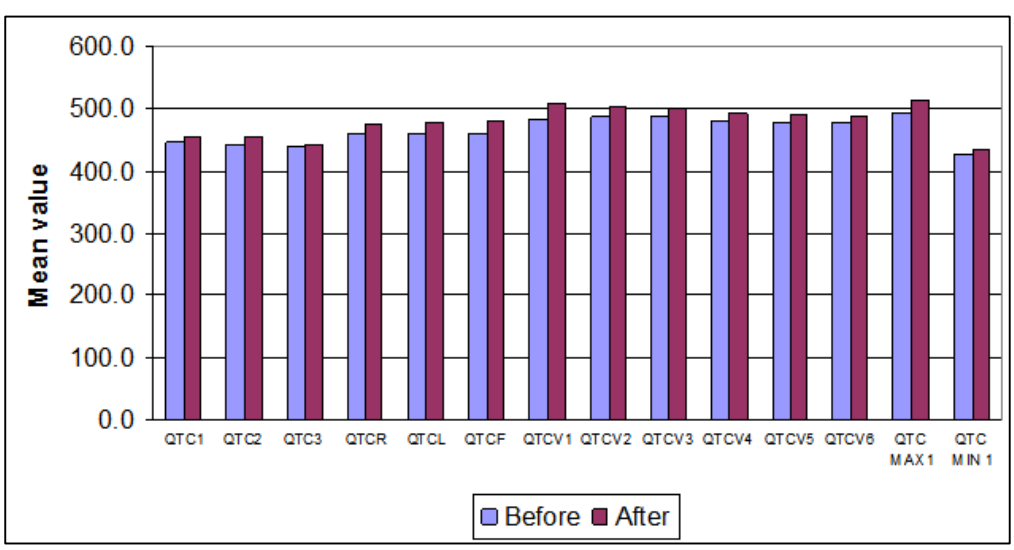

Figure 8. Comparison of QTc Intervals Before and After Dialyses

It has been found that there has been a significant increase in the QTc interval after dialysis as compared to before dialysis with an increase of QTc max. from 491.4 ± 19.0 to 511.7 ± 24.2 and QTc min. from 425.6 ± 18.2 to 434.4 ± 22.3 with a p value 0.000 and 0.037, respectively (Table and Figure 9). On measuring the dispersion, the QTc dispersion also showed a significant increase from 65.7 ± 10.2 to 77.3 ± 13.9 with a p value <0.001 (Table and Figure 10). This is in agreement with the study conducted by Mahmud Malhis et al[77] in which the QTc max. increased from 472 ± 38 to 492 ± 58 with a p value <0.01 and QTc dispersion from 72 ± 46 to 98 ± 56 with a p value <0.001 and that of Lorincz Istvan et al.[78] QTc max. from 449 ± 43 to 469 ± 41 and QTc dispersion from 62 ± 18 to 95 ± 17 p value <0.001. This study goes in hand with other researchers like Nauman Tarif et al.[79]

Comparison of QTc Dispersions Before and After Dialyses

QTcd	Mean	SD	N	Mean Difference	Paired t	P
Before	65.7	10.2	100	11.552	9.38**	0.000
After	77.3	13.9	100			

Table 9. Comparison of QTc Dispersions Before and After Dialyses

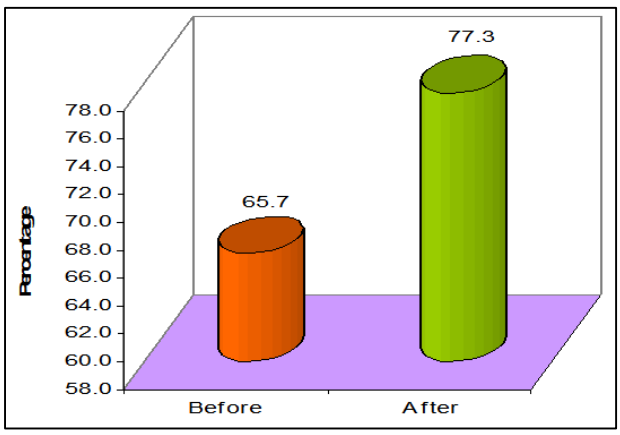

Figure 9. Comparison of QTc Dispersions Before and After Dialyses

Comparison of Electrolytes Before and After Dialyses

S. Potassium	Mean	SD	N	Mean Difference	Paired t	P
Before	5.2	0.5	100	9.520	8.74**	0.000
After	3.7	0.6	100			

Table 10. Comparison of S. Potassium Before and After Dialyses

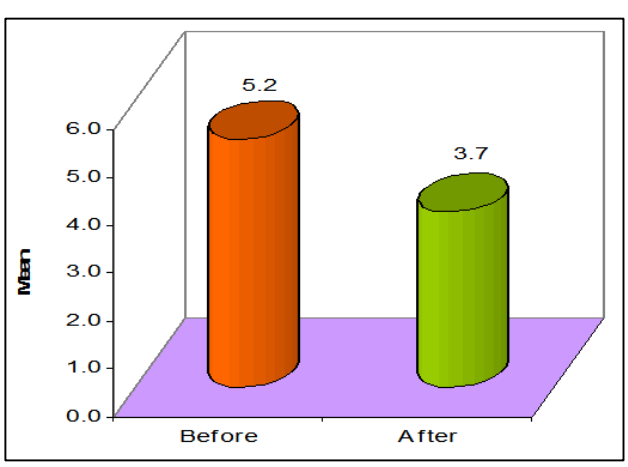

Figure 10. Comparison of S. Potassium Before and After Dialyses

On comparing the serum electrolytes, potassium decreased significantly from 5.2 ± 0.5 to 3.7 ± 0.6 with p value <0.001. There was significant increase in serum calcium from 7.4 ± 0.4 to 8.1 ± 0.6 with p value <0.001 and serum sodium from 131.5 to 132.3 (Table and Figure 11, 12, 13). This was in accordance with the studies of other similar researchers like Istvan Lorincz et al,[78] Mahmud Mahlis[77] et al and Nauman Tarif et al.[79]

Comparison of S. Calcium Before and After Dialyses

S. Calcium	Mean	SD	N	Mean Difference	Paired t	P
Before	7.4	0.4	100	0.6	12.41**	0.000
After	8.1	0.6	100			

Table 11. Comparison of S. Calcium Before and After Dialyses

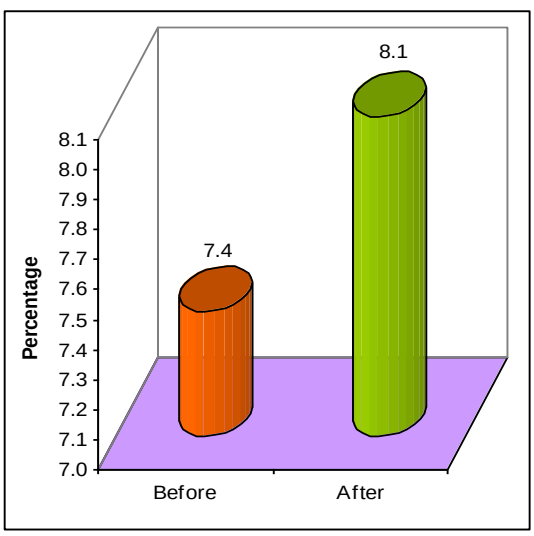

Figure 11. Comparison of S. Calcium Before and After Dialyses

Comparison of S. Sodium Before and After Dialyses

S. Sodium	Mean	SD	N	Mean Difference	Paired t	P
Before	131.5	4.4	100	0.8	4.6**	0.000
After	132.3	4.1	100			

Table 12. Comparison of S. Sodium Before and After Dialyses

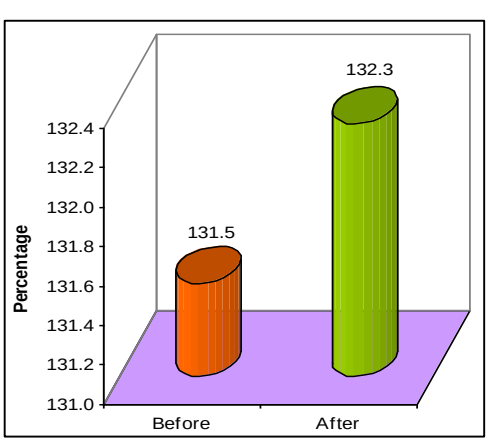

Figure 12. Comparison of S. Sodium Before and After Dialyses

Parameters	M. Malhis et al		N. Tarif et al		I. Lorincz et al		Current Study	
	Pre HD	Post HD	Pre HD	Post HD	Pre HD	Post HD	Pre HD	Post HD
QT Max.	446 ± 47	465 ± 72	-	-	449 ± 43	469 ± 41	445.5 ± 12.6	457.5 ± 18.4
QTC Max.	472 ± 38	492 ± 58	429.1 ± 19.9	440.3 ± 24.8	485 ± 42	519 ± 34	491.4 ± 19	511.7 ± 24.2
QTd	60 ± 29	76 ± 32	-	-	57 ± 15	85 ± 13	59.6 ± 9.1	69.1 ± 12.4
QTcd	72 ± 46	98 ± 56	-	-	62 ± 18	95 ± 17	65.7 ± 10.2	77.3 ± 13.9
RR	828 ± 132	798 ± 122	-	-	853 ± 15.2	830 ± 17.5	823.9 ± 44.6	801.2 ± 43.8
Sodium	136 ± 3.4	138 ± 5.2	132.67 ± 2.3	134.24 ± 2.5	139 ± 3.9	128 ± 2.09	131.5 ± 4.4	132.3 ± 4.1
Potassium	5.7 ± 0.9	3.9 ± 0.8	5.2 ± 0.88	3.3 ± 0.77	5.53 ± 0.83	3.97 ± 0.5	5.2 ± 0.5	3.7 ± 0.6
Calcium	7.9 ± 0.8	8.4 ± 0.9	2.24 ± 0.25	-	2.2 ± 0.23	2.54 ± 0.23	7.4 ± 0.4	8.1 ± 0.6

Table 13. Comparison of Current Study with Other Reference Studies

Prediction of change in QTd and QTcd with change in S. potassium, S. calcium and S. sodium as a result of dialyses.

	B	Std. Error	p
(Constant)	12.69	2.73	0.000
S. potassium change	-2.10	1.66	0.208

Table 14. Prediction of Change in QTd with Change in Potassium as a Result of Dialyses

$R = 0.1269$; $R^2 = 0.0161$.

The regression coefficient of change in QTd is 12.69 from the result. It can be inferred that as the change in QTd increases with the decrease in potassium as a result of dialysis conducting. For every unit, decrease in potassium between the dialysis, increase of 12.69 unit in QTd between the dialysis can be observed. The R value, correlation between decrease in potassium and increase in QTd as a result of dialysis is 0.1269. It means that there is not much relation between decrease in potassium and increase in QTd as a result of dialysis. R^2 of the regression analysis is 0.016, which indicates that decrease in potassium determine only 1.6 percent of variation in the increase in QTd as a result of dialysis. It was similar to that for QTc dispersion as well.

The R value for the changes in other electrolytes like calcium and sodium were also not significant enough to produce a correlation to the increase in the QT and QTc dispersions.

	B	Std. Error	p
(Constant)	15.57	3.08	0.000
S. potassium change	-2.65	1.87	0.159

Table 15. Prediction of Change in QTcd with Change in Potassium as a Result of Dialyses

$R = 0.1420$; $R^2 = 0.0202$.

	B	Std. Error	p
(Constant)	11.52	1.73	0.000
S. calcium change	-3.08	2.08	0.142

Table 16. Prediction of Change in QTd with Change in S. Calcium as a Result of Dialyses

$R = 0.1480$; $R^2 = 0.0219$.

	B	Std. Error	p
(Constant)	13.91	1.95	0.000
S. calcium change	-3.64	2.35	0.125

Table 17. Prediction of Change in QTcd with Change in S. Calcium as a Result of Dialyses

$R = 0.1545$; $R^2 = 0.0239$.

	B	Std. Error	p
(Constant)	10.34	1.19	0.000
S. sodium change	-1.01	0.62	0.103

Table 18. Prediction of Change in QTd with Change in S. Sodium as a Result of Dialyses

$R = 0.1638$; $R^2 = 0.0268$.

	B	Std. Error	p
(Constant)	12.44	1.35	0.000
S. sodium change	-1.10	0.70	0.118

Table 19. Prediction of Change in QTcd with Change in S. Sodium as a Result of Dialyses

$R = 0.1575$; $R^2 = 0.0248$.

This study shows that there is no relation between the changes in serum electrolytes to the changes in the QT and QTc dispersions (Tables 14-19). This is also at par with the results of other researchers. None of the studies could show any association between the electrolyte changes to the changes in the dispersions though there were significant individual changes in electrolytes.

Independent Predictors of Change in QTd and QTcd as a Result of Dialyses

	B	Std. Error	p
Constant	8.80	5.23	0.096
Sex (dummy female)	0.75	2.57	0.771
HTN (dummy presence)	-2.75	2.65	0.303
DM (dummy presence)	0.53	2.73	0.845
CAD (dummy presence)	0.97	2.43	0.691
Change in S. potassium	-0.80	2.02	0.692
Change in S. calcium	-1.40	2.23	0.532
Change in S. sodium	-1.14	0.65	0.082
Change in RR interval	0.22	0.09	0.017

Table 20. Independent Predictors of Change in QTd as a Result of Dialyses (Multiple Regression Analysis)

$R = 0.376$; $R^2 = 0.141$.

	B	Std. Error	p
Constant	9.14	5.81	0.119
Sex (dummy female)	1.24	2.86	0.665
HTN (dummy presence)	-2.86	2.95	0.336
DM (dummy presence)	0.44	3.03	0.885
CAD (dummy presence)	1.24	2.71	0.649
Change in S. potassium	-0.82	2.25	0.716
Change in S. calcium	-1.45	2.48	0.560
Change in S. sodium	-1.29	0.72	0.078
Change in RR interval	0.30	0.10	0.004

Table 21. Independent Predictors of Change in QTcd as a Result of Dialyses (Multiple Regression Analysis)

$R = 0.412$; $R^2 = 0.169$.

As a result of the comparison of different subgroups like gender, presence of hypertension, diabetes and coronary artery disease in multiple regression analysis to the changes in QT and QTc dispersions, these variables were found to be independent and no correlation could be framed (Tables 20, 21). This is in par with the study conducted by Istvan Lorincz et al[78] where they found all these subgroups to be independent to the changes in the QT and QTc dispersions. But, studies of Mahmud Mahlis et al and Nauman Tarif et al though did not show any correlation between hypertension and gender to the changes in the QT and QTc dispersions, there was significant increase in QT and QTc dispersions in patients with diabetes and coronary artery diseases. The only subgroup in this study that showed a relation to the increase in QT and QTc dispersion was the decrease in RR interval with a p value <0.05. Though this finding is not in accordance with the other similar studies, a study by Gussak HM et al[16] came forward with the finding that QTc interval changes are due to a satisfactorily significant decrease in RR interval and not a paradoxical phenomenon.

DISCUSSION

This study shows that at the end of HD (post HD), the data showed significant increases in QTmax and QTcmax interval prolongation and QT and QTc interval dispersion in patients with end-stage renal failure receiving haemodialysis.

According to several publications, the normal range for QT dispersion is 40 to 50 ms with a maximum of 65 ms and if the QT dispersion values are greater than 65 ms, the patients are at risk for serious ventricular arrhythmias or sudden death. In this study, the average value QT dispersion was 69.1 ms and QTc dispersion was 77.3 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, diabetes and concomitant ischaemic heart disease. This study also analysed the relation between the changes in serum electrolytes to the increase in the QT and QTc dispersions. Though, there was significant decrease in potassium and increase in calcium values, the study showed no correlation between the electrolyte changes and the increase in the QT and QTc dispersions, but showed significant relation to the decrease in RR interval. As stated by Gussak HM et al,[16] these decrease in RR interval leading an increase in QTc intervals could be attributed secondary to the HD-induced reduction of the extracellular fluid.

The results of this current study indicate that the nonhomogeneity of regional ventricular repolarisation increases during haemodialysis, 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 ischaemic aetiology, hypertrophic cardiomyopathy, as well as the risk of arrhythmia in the long QT syndrome.

SUMMARY

- 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 haemodialysis on QT and corrected QT (QTc) interval and dispersions in chronic haemodialysed patients.
- Data of 100 end-stage renal disease patients (male/female 64/36; mean age, 51.65 ± 10.45 yrs.) on twice a week haemodialysis were studied. Polysulfone capillaries and bicarbonate dialysate containing (in mEq/L) 135 Na^1, 2.0 K^1, 1.5 Ca^{21} and 1.0 Mg^{21} were used. Simultaneous 12-lead ECG were recorded before and after haemodialysis in a standard setting. The QT intervals for each lead were measured manually on enlarged ECG by one observer using calipers. Each QT interval was corrected for patient's heart rate-QTc=QT/√(RR) (in milliseconds (ms)).
- Statistical analysis was done on data entered in the master chart prepared with variables of ECG values of RR intervals, QT intervals of 12 leads, QTc intervals of 12 leads, QT dispersion, QTc dispersion, serum calcium, potassium and sodium before and after dialysis. Other parameters like age, sex, presence of coronary artery disease, hypertension and diabetes mellitus was also considered. The means and Standard Deviations (SD) of all variables will be evaluated. ANOVA for analysis of relationship of the means of differences and Student's t-test for paired data will be employed. Linear regression- simple as well as multiple linear regression was also used to assess the relation between serum electrolytes and other parameters to the ECG changes, respectively.
- The maximal QT interval changed significantly from 445.5 ± 12.6 to 457.5 ± 18.4 with a p value of <0.001.
- The RR interval decreased significantly from 823.9 ± 44.6 to 801.2 ± 43.8 (mM) with p value <0.001.
- The corrected maximal QT interval increased significantly from 491.4 ± 19.0 to 511.7 ± 24.2 ms with a P value <0.001).

- The QT dispersion changed from 59.6 ± 9.1 to 69.1 ± 12.4 with a p value <0.001.
- The corrected QT interval dispersion from 65.7 ± 10.2 to 77.3 ± 13.9 with a p value <0.001.
- During haemodialysis, the serum potassium levels decreased from 5.2 ± 0.5 to 3.7 ± 0.6 (mM), whereas calcium increased from 7.4 ± 0.4 to 8.1 ± 0.6 (mM) and serum sodium from 131.5 ± 4.4 to 132.3 ± 4.1 (mM), respectively.
- It is concluded that haemodialysis increases the QT and QTc interval and QT and QTc dispersion in patients with end-stage renal failure.
- On analysing the relation between the changes in electrolytes and the increase in the QT and corrected QT dispersions, the study found no correlation between the electrolyte changes and the increase in QT and corrected QT dispersions.
- The study also points out to the fact that the changes in QT and corrected QT dispersions are independent of gender, presence of hypertension, diabetes mellitus and coronary artery diseases, but is related to the decrease in RR interval following dialysis.
- Thus, it maybe stated that the nonhomogeneity of regional ventricular repolarisation increases during haemodialysis.
- Measurement of QT and QTc dispersion is a simple bedside method that can be used for analysing ventricular repolarisation during haemodialysis.

CONCLUSION

It is concluded that the nonhomogeneity of regional ventricular repolarisation in patients with chronic end-stage renal failure receiving haemodialysis maybe suggested by the increase in QT and QTc interval or increase in QT and QTc dispersion. The prolongation of these parameters maybe 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 uraemic patients receiving chronic haemodialysis.

QT dispersion reflects the nonhomogeneous recovery of ventricular excitability and predicts ventricular arrhythmias. The causes of the prolongation of QT dispersion in dialysis patients are multifactorial including fibrosis and hypertrophy of the heart, changes of cellular or interstitial fluid composition during dialysis and iron overload. There are higher percentages of ESRD patients with dialysis therapy that have prolonged QT dispersion and hence are susceptible to ventricular arrhythmias. Due to its high reproducibility and noninvasive methodology, QT dispersion should be a routine test in the care of dialysis patients. The factors contributing to greater QTc dispersion should be avoided in patients with end-stage renal disease undergoing haemodialysis.

RECOMMENDATIONS

1. Regular monitoring of heart rate and ECG should be made mandatory in patients with end-stage renal disease undergoing haemodialysis.
2. Due to its high reproducibility and noninvasive methodology, QT and QTc dispersion should be a routine test in the care of dialysis patients.
3. The factors contributing to greater QTc dispersion, specifically drugs prolonging QT interval should be avoided in patients with end-stage renal disease undergoing haemodialysis.
4. Regular monitoring of serum electrolytes should be made compulsory in all dialysis patients.
5. All patients undergoing haemodialysis must be cautiously observed for arrhythmias.
6. Additional studies are needed to clarify whether increased postdialysis QT dispersion results in an increased occurrence of arrhythmias.

REFERENCES

[1] Lorincz I, Zilahi ZS, Kun CS, et al. ECG abnormalities in haemodialysis [Letter]. Am Heart J 1997;134:1138-1140.

[2] US Renal Data System. In: USRDS 1990 annual data report, US Department of Health and Human Services, National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, August 1990.

[3] Leier CV, Boudolulas H. Renal disorders and heart disease. In: Braunwald E, ed. Heart disease: a textbook of cardiovascular medicine. 5th edn. Philadelphia: Saunders 1997:1914-1938.

[4] Chazan JA, Pono LM. Sudden death in patients with chronic renal failure on haemodialysis. Dial Transplant 1987;16:447-448.

[5] Morrison G, Michelson EL, Brown S, et al. Mechanism and prevention of cardiac arrhythmias in chronic haemodialysis patients. Kidney Int 1980;17(6):811-819.

[6] Abe S, Yoshizawa M, Nakanishi N, et al. Electrocardiographic abnormalities in patients receiving haemodialysis. Am Heart J 1996;131(6):1137-1144.

[7] Redaelli B, Cavalli A, Latini R, et al. Multicentre cross-sectional study of ventricular arrhythmias in chronically haemodialysed patients. Lancet 1988;2(8606):305-309.

[8] Tomaselli GF, Beuckelmann DJ, Calkins HG, et al. Sudden cardiac death in heart failure: the role of abnormal repolarization. Circulation 1994;90:2534-2539.

[9] Pye MP, Cobbe SM. Mechanism of ventricular arrhythmias in cardiac failure and hypertrophy. Cardiovasc Res 1992;26(8):740-750.

[10] Zabel M, Portnoy S, Franz MR. Electrocardiographic indexes of dispersion of ventricular repolarization: an isolated heart validation study. J Am Coll Cardiol 1995;25(3):746-752.

[11] Gruppo Hemodialisi e Patologie Cardiovascolari. Multicentre, cross-sectional study of ventricular arrhythmias in chronically haemodialysed patients. Lancet 1988;332:305-339.
[12] National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002;39(2 Suppl 1):S1-S266.
[13] Styblo TM, Wood. Traditional prognostic factors for breast cancer. In: Bland KI, Copeland EM, eds. The breast: comprehensive management of benign and malignant diseases. 2nd edn. Philadelphia: Saunders 1998.
[14] Straus SM, Sturkenboom MC, Bleumink GS, et al. Non-cardiac QTc-prolonging drugs and the risk of sudden cardiac death. Eur Heart J 2005;26(19):2007-2012.
[15] Salvi V, Karnad DR, Panicker GK, et al. Update on the evaluation of a new drug for effects on cardiac repolarization in humans: issues in early drug development. Br J Pharmacol 2010;159(1):34-48.
[16] Gussak HM, Gellens ME, Gussak I, et al. Q-T interval dispersion and its arrhythmogenic potential in hemodialyzed patients: methodological aspects. Nephron 1999;82(3):278.
[17] Bazett HC. An analysis of the time-relations of electrocardiograms. Heart 1920;7:353-370.
[18] Fridericia LS. The duration of systole in the electrocardiogram in normal subjects and of patients with heart disease. Acta Medica Scandinavica 1920;53:469-486.
[19] Yanowitz FG. Lesson III. Characteristics of the Normal ECG. University of Utah School of Medicine 2010.
[20] Matthew Fitz, Loyola University Chicago Stritch School of Medicine > Medicine I; March 23, 2010.
[21] ecglibrary.com >A normal adult 12-lead ECG. 2010.
[22] Richard E Klabunde Image for Cardiovascular Physiology Concepts > Electrocardiogram (EKG, ECG)
[23] medscape.com > QTc Prolongation and Risk of Sudden Cardiac Death: Is the Debate Over? 2006.
[24] Malik M, Batchvarov VN. Measurement, interpretation and clinical potential of QT dispersion. J Am Coll Cardiol 2000;36(6):1749-1766.
[25] Horan LG, Flowers NC, Brody DA. Principal factor waveforms of the thoracic QRS complex. Circ Res 1964;15:131-145.
[26] Wilson FN, Macleod AG, Barker PS, et al. Determination of the significance of the areas of the ventricular deflections of the electrocardiogram. Am Heart J 1934;10(1):46-61.
[27] Rudehill A, Sundqvist K, Sylvén C. QT and QT-peak interval measurements. A methodological study in patients with subarachnoid haemorrhage compared to a reference group. Clin Physiol 1986;6(1):23-37.
[28] Campbell RW, Gardiner P, Amos PA, et al. Measurement of the QT interval. Eur Heart J 1985;6(Suppl D):81.
[29] Cowan JC, Yusoff K, Moore M, et al. Importance of lead selection in QT interval measurement. Am J Cardiol 1988;61(1):83-87.
[30] Butrous GS, Dabbas N, Patel PR, et al. Measurement of the QT interval. In: Butrous GS, Schwartz PJ, eds. Clinical aspects of ventricular repolarization. London: Farrand Press 1989:p.41.
[31] Mirvis DM. Spatial variation of QT intervals in normal persons and patients with acute myocardial infarction. J Am Coll Cardiol 1985;5(3):625.
[32] Day CP, McComb JM, Campbell RW. QT dispersion: an indication of arrhythmia risk in patients with long QT intervals. Br Heart J 1990;63(6):342-344.
[33] Rautaharju PM. QT and dispersion of ventricular repolarization: the greatest fallacy in electrocardiography in the 1990s. Circulation 1999;99(18):2477-2478.
[34] Han J, Moe GK. Nonuniform recovery of excitability in ventricular muscle. Circ Res 1964;14:44.
[35] Allessie MA, Bonke FI, Schopman FJ. Circus movement in rabbit atrial muscle as a mechanism of tachycardia. II. The role of nonuniform recovery of excitability in the occurrence of unidirectional block, as studied with multiple microelectrodes. Circ Res 1976;39(2):168-177.
[36] Kuo CS, Munakata K, Reddy CP, et al. Characteristics and possible mechanism of ventricular arrhythmia dependent on the dispersion of action potential durations. Circulation 1983;67(6):1356-1367.
[37] Kuo CS, Amlie JP, Munakata K, et al. Dispersion of monophasic action potential durations and activation times during atrial pacing, ventricular pacing, and ventricular premature stimulation in canine ventricles. Cardiovasc Res 1983;17(3):152.
[38] Kuo CS, Atarashi H, Reddy CP, et al. Dispersion of ventricular repolarization and arrhythmia: study of two consecutive ventricular premature complexes. Circulation 1985;72(2):370-376.
[39] Gavrilescu S, Luca C. Right ventricular monophasic action potentials in patients with long QT syndrome. Br Heart J 1978;40(9):1014-1018.
[40] www.usrds.org/download/1996/ch04.pdf.
[41] Parfrey PS, Foley RN, Harnett JD, et al. Outcome and risk factors of ischemic heart disease in chronic uremia. Kidney Int 1996;49(5):1428-1434.
[42] Bleyer AJ, Tell GS, Evans GW, et al. Survival of patients undergoing renal replacement therapy in one center with special emphasis on racial differences. Am J Kidney Dis 1996;28(1):72-81.
[43] Yetkin E, Ileri M, Tandogan I, et al. Increased QT interval dispersion after hemodialysis: role of peridialytic electrolyte gradients. Angiology 2000;51(6):499-504.
[44] Yildiz A, Akkaya V, Sahin S, et al. QT dispersion and signal-averaged electrocardiogram in haemodialysis and CAPD patients. Perit Dial Int 2001;21(2):186-192.
[45] Lee TM, Su SF, Wang TD, et al. Increased ventricular repolarization inhomogeneity during postural changes

in patients with syndrome X. Am J Cardiol 1998;82(5):615-620.
[46] Kors JA, van Herpen G, van Bemmel JH. QT dispersion as an attribute of T-loop morphology. Circulation 1999;99:1458-1463.
[47] Schouten EG, Dekker JM, Meppelink P, et al. QT interval prolongation predicts cardiovascular mortality in an apparently healthy population. Circulation 1991;84(4):1516-1523.
[48] Ostovan M, Khosropanah S, Hooshmand S. Adjacent QT dispersion: a good predictor of ventricular arrhythmias after myocardial infarction. Cent Eur J Med 2008;3(2):179-182.
[49] Aronson RS. Mechanisms of arrhythmias in ventricular hypertrophy. Journal of Cardiovascular Electrophysiology 1991;2(3):249-261.
[50] Zipes DP. The long QT interval syndrome. A Rosetta stone for sympathetic related ventricular tachyarrhythmias. Circulation 1991;84(3):1414-1419.
[51] Barr CS, Naas A, Freeman M, et al. QT dispersion and sudden unexpected death in chronic heart failure. Lancet 1994;343(8893):327-329.
[52] Tieleman RG, Crijns HJ, Wiesfeld AC, et al. Increased dispersion of refractoriness in the absence of QT prolongation in patients with mitral valve prolapse and ventricular arrhythmias. Br Heart J 1995;73(1):37-40.
[53] Higham PD, Furniss SS, Campbell RW. QT dispersion and components of the QT interval in ischaemia and infarction. Br Heart J 1995;73(1):32-36.
[54] Maule S, Veglio M, Mecca F, et al. Autonomic neuropathy and QT interval in hemodialysed patients. Clin Auton Res 2004;14(4):233-239.
[55] Linker NJ, Colonna P, Kekwick CA, et al. Assessment of QT dispersion in symptomatic patients with congenital long QT syndromes. American Journal of Cardiology 1992;69(6):634-638.
[56] Beaubien ER, Pylypchuk GB, Akhtar J, et al. Value of corrected QT interval dispersion in identifying patients initiating dialysis at increased risk of total and cardiovascular mortality. Am J Kidney Dis 2002;39(4):834-842.
[57] Ansari A, Kaupke CJ, Vaziri ND, et al. Cardiac pathology in patients with end-stage renal disease maintained on haemodialysis. Int J Artif Organs 1993;16(1):31-36.
[58] Kantarci G, Ozener C, Tokay S, et al. QT dispersion in hemodialysis and CAPD patients. Nephron 2002;91(4):739-741.
[59] Morris ST, Galiatsou E, Stewart GA, et al. QT dispersion before and after haemodialysis. J Am Soc Nephrol 1999;10(1):160-163.
[60] Cupisti A, Galetta F, Morelli E, et al. Effect of hemodialysis on the dispersion of the QTc interval. Nephron 1998;78(4):429-432.
[61] Lorincz I, Matyus J, Zilahi Z, et al. QT dispersion in patients with end-stage renal failure and during haemodialysis. J Am Soc Nephrol 1999;10(6):1297-1302.
[62] Ozdemir D, Mese T, Agin H, et al. Impact of haemodialysis on QTc dispersion in children. Nephrology 2005;10(2):119-123.
[63] Wang CL, Lee WL, Wu MJ, et al. Increased QTc dispersion and mortality in uremic patients with acute myocardial infarction. Am J Kidney Dis 2002;39(3):539-548.
[64] Antzelevitch C, Shimizu W, Yan GX, et al. Cellular basis for QT dispersion. J Electrocardiol 1998;30(Suppl):168-175.
[65] Floccari F, Aloisi E, Nostro L, et al. QTc interval and QTc dispersion during haemodiafiltration. Nephrology 2004;9(6):335-340.
[66] Suzuki R, Tsumura K, Inoue T, et al. QT interval prolongation in the patients receiving maintenance haemodialysis. Clin Nephrol 1998;49(4):240-244.
[67] Nappi SE, Virtanen VK, Saha HH, et al. QTc dispersion increases during haemodialysis with low-calcium dialysate. Kidney Int 2000;57(5):2117-2122.
[68] Averbukh Z, Rosenberg R, Galperin E, et al. Cell-associated magnesium and QT dispersion in haemodialysis patients. Am J Kidney Dis 2003;41(1):196-202.
[69] Wu VC, Huang JW, Wu MS, et al. The effect of iron stores on corrected QT dispersion in patients undergoing peritoneal dialysis. Am J Kidney Dis 2004;44(4):720-728.
[70] Kuryshev YA, Brittenham GM, Fujioka H, et al. Decreased sodium and increased transient outward potassium currents in iron-loaded cardiac myocytes. Implications for the arrhythmogenesis of human siderotic heart disease. Circulation 1999;100:675-683.
[71] Schwartz KA, Li Z, Schwartz DE, et al. Earliest cardiac toxicity induced by iron overload selectively inhibits electrical conduction. J Appl Physiol 2002;93(2):746-751.
[72] Buja LM, Roberts WC. Iron in the heart. Etiology and clinical significance. Am J Med 1971;51(2):209-221.
[73] Fitchett DH, Coltart DJ, Littler WA, et al. Cardiac involvement in secondary haemochromatosis: a catheter biopsy study and analysis of myocardium. Cardiovasc Res 1980;14(12):719-724.
[74] Nigro G, Politano L, Santangelo L, et al. Is the value of QT dispersion a valid method to foresee the risk of sudden death? A study in becker patients. Heart 2002;87(2):156–157.
[75] Faber TS, Zehender M, Krahnefeld O, et al. Propafenone during acute myocardial ischemia in patients: a double-blind, randomized, placebo-controlled study. J Am Coll Cardiol 1997;29(3):561-567.
[76] Insulander P, Juhlin-Dannfelt A, Freyschuss U, et al. Electrophysiologic effects of salbutamol, a beta2-selective agonist. J Cardiovasc Electrophysiol 2004;15(3):316-322.

[77] Malhis M, Al Bitar S, Farhood S. Changes in QT interval in patients with end-stage renal disease before and after haemodialysis. Saudi Journal of Kidney Diseases Transplantation 2010;21(3):460-465.
[78] Covic A, Diaconita M, Gusbeth-Tatomir P, et al. Haemodialysis increases QTc interval but not QTc dispersion in ESRD patients without manifest cardiac disease. Nephrol Dial Transplant 2002;17:2170-2177.
[79] Tarif N, Yamani H, Bakhsh AJ, et al. Electrocardiography and serum potassium before and after haemodialysis. Saudi Journal Of Kidney Diseases Transplantation 2008;19(1):47-53.