MEDICO RESEARCH CHRONICLES
ISSN NO. 2394-3971
DOI No. 10.26838/MEDRECH.2019.6.2.495
OPEN ACCESS
Contents available at: www.medrech.com

COMPARISON OF QTc AND QT DISPRESION IN PREDICTION OF CARDIO-VASCULAR MORTALITY AND MORBIDITY AMONG THE PATIENTS WITH CHRONIC RENAL FAILURE

Dr. Nikhil Pursnani[1], Dr. Mohan Lal Pursnani[2], Dr. Satyanand Sathi[3]*, Dr. Prabhat Kumar Agrawal[4], Dr. Ashish Gautam[4], Dr. Apoorva Jain[1], Dr. Ravindra Singh Chahar[5]

1. Assistant Professor, Dept. of Medicine, S.N. Medical college & hospital, Agra
2. Professor, Dept. of Medicine, F. H. Medical college, Tundla
3. Assistant Professor, Department of Medicine, SMMH Medical College, Saharanpur
4. Associate professor, Dept. of Medicine, S.N. Medical college & hospital, Agra
5. Senior consultant physician, Dept. of Cardiology, SNMC and hospital, Agra

ARTICLE INFO

Article History
Received: March' 2019
Accepted: April' 2019
Keywords: Dialysis, Qt interval, CRF, Sodium, Potassium, Cardiac arrythmia.

Corresponding author*
Dr. Satyanand Sathi

ABSTRACT

Introduction: QT interval dispersion (QT-d), measured as the difference between the maximum and minimum QT interval on a standard 12 lead electrocardiograph (ECG), is a normal phenomenon. Corrected QT interval (a rate related QT interval), QTc can be calculated on QT/√R-R and normally is ≤0.44 second. Corrected QT interval dispersion can predict adverse cardiovascular outcome however QTd is a measure of regional heterogeneity in myocardial repolarization. **Aim:** The objective of the present study is to assess the effects of cardiovascular morbidity and mortality by comparing the predictive values of QTc and QTd in the patients with chronic renal failure. Along with this the study also evaluates the relationship of QTc and QTd with serum sodium and potassium. **Materials and methods**: Patients of chronic renal failure were included in the study. Patients of both gender and age of above 15 years with CRF on hemodialysis were selected for the study. Routine biochemistry levels, including sodium, potassium, and ionized calcium was measured pre and post hemodialysis at the time of ECG. Patients over 15 years of age with serum creatinine level >1.5 mg/dl and blood urea >40 mg/dl were included in the study. **Results:** A total of 40 patients from both genders (24 males and 16 Females) were studied. 7 patients (20.5%) of CRF died of various causes in the 1-year follow-up period. 6 (15%) patients died due to cardiovascular causes whereas 1 (2.5%), the patient died due to blood transfusion reaction. There is a statistically significant difference found between the mean values of QTd and QTc between predialysis and post dialysis measurement. The t value shows the QTd value is more significant in case of prediction of Hypertension, CHF, IHD and Arrhythmias in CRF patients on haemodialysis. The QTc interval calculation may represent a simple method of monitoring patients with high risk of sudden death.

INTRODUCTION:

QT interval dispersion (QT-d), measured as the difference between the maximum and minimum QT interval on a standard 12 lead electrocardiograph (ECG), is a normal phenomenon. It was initially proposed as an index of spatial dispersion of ventricular recovery time.[1] Recent investigation suggests a difference in heart dipole projection and abnormalities of T-wave loop morphology as the main cause. It reflects repolarization abnormality.[2,3]

QT interval includes both ventricular depolarization and repolarization and varies with heart rate.

Corrected QT interval (a rate related QT interval), QTc can be calculated on QT/√R-R and normally is ≤0.44 second.[4]

Chronic renal failure is a pathophysiological process with multiple aetiologies resulting in attrition of nephron numbers and function, ESRD represents a clinical state or condition in which there has been an irreversible loss of endogenous renal function of a degree sufficient to render the patient permanently dependent upon renal replacement therapy in order to avoid life-threatening uraemia.[5]

The pathophysiology of CRF involves initiating mechanism specific to the underlying etiology as well as a set of progressive mechanism that is a common consequence following long term reduction of renal mass irrespective of etiology. Such reduction of renal mass causes structural and functional hypertrophy of surviving nephrons.[6]

Corrected QT interval dispersion can predict adverse cardiovascular outcome however QTd is a measure of regional heterogeneity in myocardial repolarization.[7]

Haemodialysis relies on the principle of solute diffusion across a semipermeable membrane. Movement of metabolic waste products takes place down a concentration gradient from the circulation into the dialysate.

The objective of the present study is to assess the effects of cardiovascular morbidity and mortality by comparing the predictive values of QTc and QTd in patients with chronic renal failure. Along with this the study also evaluated the relationship of QTc and QTd with serum sodium and potassium.[8]

MATERIALS AND METHOD:

Subject Population:

The study was conducted and approved by the ethical committee of the postgraduate department of medicine, S. N. Medical College, Agra and FH Medical College, Tundla. Patients admitted in the Department of S.N. Medical College Agra and F.H. Medical College, Tundla for the period from December 2017 to June 2018 were taken for study. Patients of chronic renal failure were included in the study, written informed consent was taken from all the patients included for the study and they are informed about the procedure of the study. The inclusion and exclusion criteria were laid down.

Inclusion Criteria

Patients of both gender and age of above 15 years with CRF on hemodialysis were selected for the study. Cases were kept under follow up for cardiovascular morbidity and mortality for a period of 1 year.

Exclusion Criteria

Patients having a history of ischemic heart disease, myocardial infarction or congestive heart failure or on drugs that cause a change in QT interval. Patients from the population who didn't give consent for the study were not included.

Routine biochemistry levels, including sodium, potassium, ionized calcium was measured pre and post hemodialysis at the time of ECG.

Diagnostic Criteria for CRF.

Clinical criteria of Chronic Renal Failure were kept as more than 6 months of ill health. Diagnostic of CRF was established by detailed clinical history and thorough clinical examination and investigations. Patients over 15 years of age with serum creatinine level >1.5 mg/dl and blood urea >40 mg/dl were included in the study.[9]

Kidney Morphology evaluation

On ultrasonography normal kidney was considered with 9 to 12 cm in length and with intact corticomedullary differentiation.[10]

Methodology:

Each selected patient was subjected to:

1. Clinical history evaluation
2. Physical Examination
3. 12 leads standard electrocardiography
4. Routine investigation
5. Other investigations
    a. Hemogram with GBP
    b. Blood Urea
    c. Serum Creatinine
    d. Serum Na^+, K^+
    e. Serum Ionized Calcium
    f. Urine
        i. Routine
        ii. Microscopy
    g. X-Ray Chest Postero-anterior view
    h. USG Abdomen

Electrocardiograph

ECG with bundle branch blocks atrial fibrillation and those with T wave measurement errors in three or more leads were excluded.

Among ECG that was included for each lead, three consecutive cardiac cycles were measured and averaged. The lead with maximal and minimal QT and QTc interval were determined. QTd for an ECG was defined as the difference between the maximal and minimal QT within the 12 leads.

The QTd value was determined by finding out arithmetic means of all QTd values obtained from electrocardiogram taken before and after hemodialysis as each patient included in the study was subjected to hemodialysis for a period of at least one month.[11]

Similarly, the arithmetic mean of the QTc from the 12 leads of each ECG recording was assumed as the QTc interval length. Sokolow-Lyon Voltage (SV_1 plus RV_5 or V_6) as an index for LVH was measured

Norma Value of QTc was considered <440 milliseconds.

Normal Value of QTd was considered 30- 60 millisecond.

RESULTS:

A total of 40 patients from both genders (24 males and 16 Females) were studied. All the patients were divided in different age brackets and maximum no. of patients were found to be in age groups 36-45 and 46-55 which contains 12 patients in each group. Whereas minimum no. of patients was found in age groups of 66-75 and 76-85 years which accounts for 2 patients in each group. The demographic distribution selected subjects are given in Table 1.

Table 1: Demographic distribution of patients with CRF

Age Groups (Years)	No. of patients n (%)	Male	Female
25-35	7 (17.50)	4	3
36-45	12 (30)	6	6
46-55	12 (30)	9	3
56-65	5 (12.50)	4	1
66-75	2 (5)	1	1
76-85	2 (5)	0	2
Total	**40 (100)**	**24**	**16**

Etiology of CRF

All the patients were observed for the etiology of CRF and found that maximum no. of patients was reported with chronic glomerulonephritis and diabetic nephropathy together and accounts for 60% patients whereas Polycystic kidney disease and Hypertension were accounts for 10% patients.

Table 2: Aetiology of the patients with CRF

Disease	No. of patients n (%)	Male	Female
Chronic Glomerulonephritis	12 (30)	8	4
Diabetic Nephropathy	12 (30)	7	5
Obstructive Nephropathy	6 (15)	6	0
Chronic Pyelonephritis	6 (15)	2	4
Polycystic Kidney Disease	2 (5)	1	1
Hypertension	2 (5)	1	1
Total	40 (100)	25	15

Mortality of the patients with CRF:

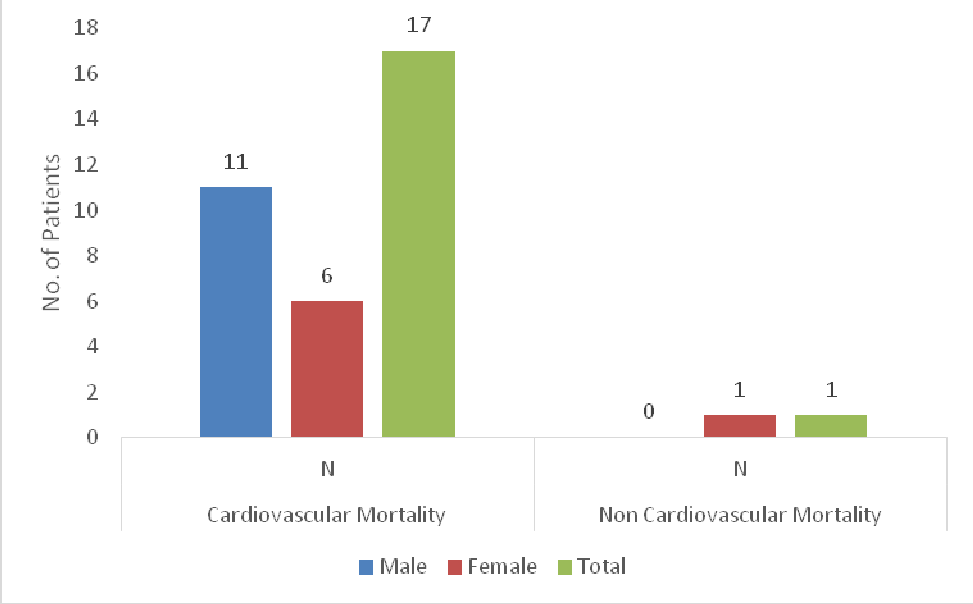

Fig 1: Reported Mortality of the patients with CRF

Table 3: Mortality reported in the population of patients with CRF

Gender	Cardiovascular Mortality		Non-Cardiovascular Mortality	
	N	%	N	%
Male	4	10	0	0
Female	2	8	1	2.5
Total	6	18	1	2.5

7 patients (20.5%) of CRF died of various causes in the 1-year follow-up period. 6 (15%) patients died due to cardiovascular causes whereas 1 (2.5%), the patient died due to blood transfusion reaction. However, no death observed during a dialysis procedure.

Duration of survival from the date of dialysis till the time of death was variable.

Hypotensive Episodes:

10 patients of CRF were having hypotensive episodes at the start of dialysis within 2 hours. These episodes were corrected later in dialysis. 5 of these patients were

having evidence of autonomic neuropathy and 5 patients were having evidence of pericarditis.

Hypertensive Episodes.

13 Patients of CRF developed hypertensive episode during dialysis frequently. These episodes of hypertension were controlled by ultrafiltration and/ or sublingual nifedipine.

Incidences of Cardiac Arrhythmias

Table 4: Incidences of cardiac arrhythmias in dialysis patients

Event Occurred	Incidences of Arrhythmias		Patients expired due to sudden cardiac death		Patients Survived	
	N	%	N	%	N	%
Before Dialysis	0	0	0	0	0	0
After Dialysis	14	35	8	20	28	70

No patients were reported with an episode of cardiac arrhythmia before dialysis but after dialysis 14 (35%) patients were developed with cardiac arrhythmia out of which 8 (20%) died due to sudden cardiac death, 28 (70%) patients were survived.

Laboratory Data before and after Haemodialysis

All the patients were screened and the data is presented in Table 5.

Table 5: Laboratory database of patients with CRF before and after dialysis

Parameters	Before dialysis (Mean ± SD)	After Dialysis (Mean ± SD)	t Value	p-Value
QTc (m. Second)	420 ± 35	470 ± 44	4.9	<0.01
QTd (m. Second)	52.08 ± 4.3	64.10 ± 3.2	13.9	<0.01
Sodium (meq/L)	134.33 ± 11.40	127.58 ± 12.12	2.6	<0.05
Potassium (meq/L)	4.38 ± 0.72	3.52 ± 0.56	5.9	<0.01
Blood Urea (mg%)	214.55 ± 94.07	110.40 ± 79.77	5.3	<0.01
Serum Creatinine (mg%)	10.83 ± 3.9	6.37 ± 2.8	5.8	<0.01
Ionized Calcium (meq/L)	1.02 ± 0.16	1.25 ± 0.28	2.5	<0.05

All the patients were having anemia before dialysis out of which 30 (75 %) patients showed improvement in hemoglobin level. Predialysis mean hemoglobin was 5.3 gm% which and the mean post dialysis hemoglobin became 6.1 gm%.

The reduction in the predialysis and post dialysis, blood urea concentration and serum creatinine concentration were statistically significant. The changes in the other parameters like serum sodium, potassium, and ionized calcium concentration were also statistically significant.

The changes in QTc and QTd was highly significant. The t value QTc and QTd were 4.9 and 13.9 respectively indicating that QTd was more significant in the prediction of cardiovascular mortality.

Relationship between QTc and QTd before and after dialysis in developing cardiovascular morbidity:

QTc and QTd values were assessed before and after dialysis associated with different cardiovascular morbidity.

Table 6: Relationship between QTc and QTd in the patients with CRF, before and after dialysis

Type of Cardiovascular Morbidity	No. of Cases	QTc		t Value	p-Value	QTd		t Value	p-Value
		Before	After			Before	After		
Hypertension	2	430 ± 36	470 ± 44	4.7	<0.01	52.10 ± 4.3	64.12 ± 3.1	12	<0.01
CHF	4	430 ± 19	470 ± 15	3.1	<0.01	52.04 ± 3.9	63.06 ± 4.2	3.8	<0.01
IHD	13	420 ± 37	470 ± 54	2.6	<0.01	53.02 ± 4.0	63.04 ± 2.8	6.4	<0.01
Pericarditis	7	450 ± 7	490 ± 7	5.6	<0.01	54.04 ± 0.7	65.12 ± 5.7	2.8	<0.01
Arrythmia	14	430 ± 40	490 ± 48	3.6	<0.01	55.08 ± 3.5	65.10 ± 2.4	7.5	<0.01

There is a statistically significant difference found between the mean values of QTd and QTc between predialysis and post dialysis measurement. The t value shows the QTd value is more significant in case of prediction of Hypertension, CHF, IHD and Arrhythmias in CRF patients on hemodialysis.

DISCUSSION

The study was designed to measure the changes in QTc and QTd with plasma concentration of dialyzable electrolyte before and after hemodialysis. It was confirmed that Serum Na^+, $K^{+,}$ and ionized calcium levels are the main determinants of QTc and QTd in hemodialysis. The result of this study may add a new dimension of recent reports indicating the usefulness of QTc and QTd as a predictor of sudden death after myocardial ischemia, in heart failure of ischemic etiology, hypertrophic cardiomyopathy as well as the risk of arrhythmias in long QT syndrome. Supported by the summary of findings done by Puddu E. Paolo M. D. et al., 1986, where it was noted the in patients with ischemic heart disease; the QTc interval calculation may represent a simple method of monitoring patients with a high risk of sudden death.

Through the study, it was evident that 30% of patients were developed with cardiac arrhythmia after dialysis. These findings of the present study are supported by the findings of Carytan D. M. *et al.*, 2016, where the cardiac arrhythmia remain the main reason after hemodialysis and cardiac morbidity[12].

The changes in the plasma electrolyte concentration and their association with QTc and QTd in the patients with CRF is found to be significant in the findings of the present study which is similar to the results of the study done by Adamasco Cupisiti[13] et al. (1999) and Yan Quing Tong[14] et al. (2007). Adrian Covic[15] et al (2002), also concluded that hemodialysis increases QTc interval in ESRD patients mainly related to rapid changes in plasma electrolytes concentration.

The present study also indicating that QTd was more significant in the prediction of cardiovascular mortality. And there is a significant difference found between QTd and QTc. These findings are in line with the findings of Neki N. S. et al., 2016, which concluded that QTc prolongation has a positive linear correlation with Cardiac Autonomic Neuropathy and can be used as the prognostic tool for the diagnosis of the same.[16]

There is a significant difference found between the predialysis and postdialysis measurement of Qtd and QTc. The findings are in accordance with the study done by Niaki M. R. K. et al., 2013, where researchers reported that the prolongation of QT intervals has a relation with the presence of potassium ion.[17]

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