

Effect of Valsalva Maneuver on QT Dispersion in Hemodialysis Patients

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Increased QT dispersion seems to be related to an increased risk of arrhythmia and sudden death, a common cause of mortality in hemodialysis (HD) patients. Increase in sympathetic tone has been documented in HD patients. In this study, we aimed to investigate the effect of changes in the autonomic tone on QT dispersion (QTd) in HD patients.

Twenty HD patients (M/F 13/7; age, mean \pm SD, 28 \pm 10 years) and 22 age- and sex-matched healthy controls (M/F 12/10; age, 30 \pm 10 years) were included. The patients were dialyzed three-times weekly; time on dialysis was 17 \pm 8 months. The QT durations were measured from 12 lead surface EKGs and were corrected for RR intervals. Corrected maximum (QT_cmax) and minimum (QT_cmin) QT intervals and their difference (QT_cd) were recorded. The effect of the Valsalva maneuver in the release phase on QT_c intervals and dispersion was assessed.

The HD patients had prolonged values compared to controls: QT_cd, 59 \pm 17 ms versus 35 \pm 7 ms, $p < 0.001$; QT_cmax, 458 \pm 41 ms versus 397 \pm 21 ms, $p < 0.001$; and QT_cmin, 398 \pm 36 ms versus 362 \pm 25 ms, $p < 0.001$. After the Valsalva maneuver no changes were observed in controls: QT_cmax, 397 \pm 21 ms versus 396 \pm 22 ms, $p = 0.9$; QT_cmin, 362 \pm 24 ms versus 358 \pm 19 ms, $p = 0.5$; and QT_cd, 35 \pm 7 ms versus 38 \pm 10 ms, $p = 0.15$. Whereas, in HD patients all values were significantly shortened: QT_cmax, 458 \pm 41 ms versus 427 \pm 35 ms, $p = 0.003$; QT_cmin, 398 \pm 36 ms versus 379 \pm 34 ms, $p = 0.04$; and QT_cd, 59 \pm 17 ms versus 48 \pm 15 ms, $p = 0.01$. The decrease in QTmax was more prominent than the decrease in QTmin, hence QT dispersion was significantly decreased after the Valsalva maneuver, but differences from controls were still significant.

In conclusion, increased sympathetic activity may have a role in the prolonged QT duration and increased QT dispersion in HD patients.

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Key words

Autonomic dysfunction, QT dispersion, Valsalva maneuver

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Introduction

QT dispersion, reflecting inhomogeneity in ventricle repolarization, has been used for predicting patients with risk of malignant arrhythmia and sudden death [1,2]. Recently, increased QT dispersion has also been reported in hemodialysis (HD) patients [3,4]. Increased sympathetic activity in HD patients had been previously reported in studies using microneurographic techniques [5,6]. In the present case-control study, we aimed to investigate the effect of the Valsalva maneuver, which increases parasympathetic tone, on QT dispersion in patients on HD.

Patients and methods

Twenty HD patients (13 male, 7 female; age, mean \pm SD, 28 \pm 10 years) and 22 healthy controls (12 male, 10 female; age 30 \pm 10 years) were included in this study. No difference in age and sex distribution was found between HD patients and controls. The causes of chronic renal failure were primary glomerular diseases (6), chronic pyelonephritis (3), Alport's disease (2), and chronic renal failure of unknown etiology (9). Time on dialysis was 17 \pm 8 months and all patients had been dialyzed for more than 6 months. All HD patients were dialyzed three-times weekly for 3.5 – 4 hours per session, with bicarbonate-containing dialysate bath (Na, 140 mEq/L; K, 1 mEq/L; Cl, 110 mEq/L; HCO₃, 33 mEq/L; Ca, 3 mEq/L; Mg, 1 mEq/L). Demographic features of HD patients and controls are given in Table I.

Patients with amyloidosis, diabetes mellitus, bundle branch block or atrial fibrillation in electrocardiogram (EKG), or receiving any drug that may lengthen the QT interval were excluded. Patients were evaluated by history, physical examination, EKG, and echocardiography for congestive heart

TABLE I Demographic features of study groups

	Hemodialysis	Controls
Age (years)	28 \pm 10	30 \pm 10
Sex (male/female)	13/7	12/10
Systolic blood pressure (mm Hg)	145 \pm 24	114 \pm 12
Diastolic blood pressure (mm Hg)	84 \pm 14	71 \pm 9
Primary disease		
Primary glomerular diseases	6	
Chronic pyelonephritis	3	
Alport disease	2	
Unknown	9	
Time on dialysis (months)	17 \pm 8	

failure and ischemic heart disease and, if detected, these patients were also excluded. Controls were normotensive, had no cardiac disease, and had normal serum creatinine levels, EKG, and echocardiographic features.

Blood samples were drawn for BUN, serum creatinine, electrolytes (including serum potassium, calcium, and magnesium) on the day of the measurement of QT intervals, the day after HD.

Measurements of QT intervals

QT parameters were measured from a 12-lead EKG recorded the day after HD. Electrocardiograms were recorded by means of a 12-channel EKG recorder (Hewlett-Packard M 1709-A, Corvallis, OR, U.S.A.) at a paper speed of 50 mm/s (gain 10 mm/mV). Before measurement of QT parameters, EKGs were enlarged on the same photocopier by a factor of two. The QT interval was measured from the onset of the QRS complex to the end of T wave. When T waves were inverted, the end was taken at the point where the trace returned to the T-P baseline. In the presence of a U wave, the end of the T wave was taken as the lowest point between the T and U waves. If the end of the T wave was unclear, then it was excluded from analysis. A minimum nine leads were studied in each patient. Minimum (QTmin), maximum (QTmax), duration of QT intervals, and their differences [QT dispersion (QTd)] were measured.

Each QT interval was corrected for patient heart rate according to Bazett's formula [7]:

$$QTc = QT/(RR)^{1/2}.$$

Valsalva maneuver

The Valsalva maneuver with a simultaneous 12-lead EKG recording was carried out by having the patients exhale into a mercury manometer with enough force to reach 35 mm Hg pressure and sustain it for 20 seconds. Analysis of the 20th QT interval after the release of the Valsalva maneuver was used to assess the effect of the Valsalva maneuver on QTd.

Reproducibility

All measures of QT intervals for each lead were performed blindly by one observer. In order to determine intraobserver variability of QT intervals, all EKG strips were measured twice. A Bland-Altman plot for intraobserver variability of QTd is shown in Fig. 1.

Statistics

Statistical analyses were performed with the Statistical Program for Social Sciences (SPSS v8 for Windows, Chicago, IL, U.S.A.). Values are given as mean \pm SD. Comparisons between groups were made by paired and unpaired *t*-test when necessary on log-transformed data. Correlations between parameters were analyzed with the Spearman correlation test. A *p* value of less than 0.05 was accepted as significant.

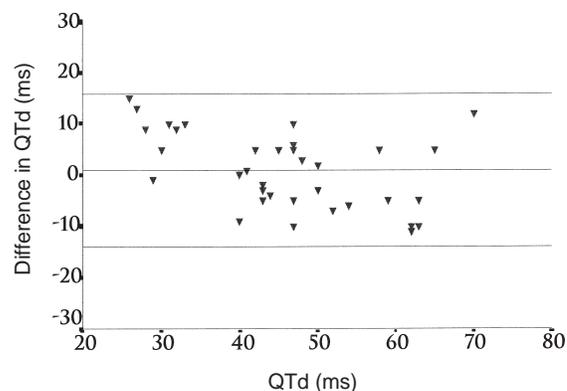


FIGURE 1 Bland-Altman analysis of intraobserver variability of QT dispersion (QTd) in milliseconds (ms).

Results

Biochemical results are given in Table II. There were no severe electrolyte disturbances and the results were unremarkable and consistent with chronic renal failure. On analysis for correlation between electrolyte levels and QTd, no correlation was found between QTd and serum Ca ($r = -0.08$, $p = 0.70$), serum K ($r = 0.16$, $p = 0.49$), serum Mg ($r = -0.07$, $p = 0.81$), or serum intact parathyroid hormone (iPTH) levels ($r = -0.41$, $p = 0.18$) in dialysis patients.

On analysis of QT parameters, both QTmax and QTmin were significantly prolonged in HD patients compared to controls (Table III). Heart rates were similar in the two groups. In HD patients, QTmax was prolonged to a greater extent than QTmin; therefore, QTd was also significantly increased. QT dispersion was 59 ms for HD patients and 35 ms for controls.

On analyzing the effect of the Valsalva maneuver on QT parameters in HD patients, both QTmax and QTmin were significantly decreased after the Valsalva maneuver (Table IV). The decrease in QTmax was more prominent than the decrease in QTmin; hence QTd was significantly decreased after the Valsalva maneuver. However, no change in QT parameters was observed after the Valsalva maneuver in controls, indicating that the Valsalva maneuver has no effect

TABLE II Biochemical results of hemodialysis patients

	Hemodialysis
BUN (mg/dL)	70 \pm 14
Creatinine (mg/dL)	9.8 \pm 2.52
Na (mmol/L)	138 \pm 4
K (mmol/L)	5.2 \pm 0.7
Mg (mmol/L)	1.50 \pm 0.65
Ca (mg/dL)	8.98 \pm 1.19
HCO ₃ (mEq/L)	21.4 \pm 3.6
iPTH (ng/dL)	327 \pm 308

on QT intervals in controls (Table V). Figure 2 shows the changes in QTd after the Valsalva maneuver in HD patients and controls. QT dispersion decreased to 48 ms after the Valsalva maneuver in HD patients but did not reach the level seen in controls (35 ms).

Discussion

Cardiovascular diseases are responsible for 50% of deaths in HD patients. The main causes of cardiovascular mortality are congestive heart failure, ischemic heart disease, and sudden death [8,9]. The results of these EKG monitoring studies indicated that ventricular premature beats and arrhythmias increase during and after HD [10]. Recent studies reported increased QTd in HD patients compared to controls [3,4]. Increased QTd predicts increased cardiovascular deaths in

TABLE III Results of QT parameters in hemodialysis patients and controls

	Hemodialysis	Controls	p Value
QT _c min (ms)	398±36	362±25	< 0.001
QT _c max (ms)	458±41	397±21	< 0.001
QT _c d (ms)	59±17	35±7	< 0.001

c = corrected; d = dispersion.

TABLE IV Results of Valsalva maneuver on QT parameters in hemodialysis patients

	Before Valsalva	After Valsalva	p Value
QT _c min (ms)	398±36	379±34	0.04
QT _c max (ms)	458±41	427±35	0.003
QT _c d (ms)	59±17	48±15	0.01

c = corrected; d = dispersion.

TABLE V Results of Valsalva maneuver on QT parameters in controls

	Before Valsalva	After Valsalva	p Value
QT _c min (ms)	362±24	358±19	NS
QT _c max (ms)	397±21	396±22	NS
QT _c d (ms)	35±7	38±10	NS

c = corrected; NS = non significant; d = dispersion.

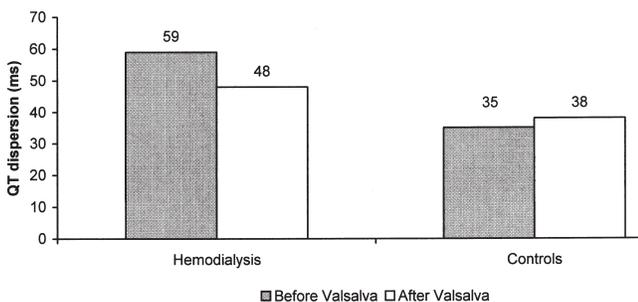


FIGURE 2 Effects of Valsalva maneuver on QT dispersion in study groups.

hypertrophic cardiomyopathy and myocardial infarction, and may be the predictor of the same in HD patients. It has also been reported that QTd increased after HD [3,4,11]. Rapid changes in serum electrolyte levels and acid-base status have been implicated in the changes observed in QTd; however, no correlation was found between QTd and serum electrolyte and iPTH levels [3,11]. We also did not find any correlation between QTd and serum electrolytes and iPTH in the present cross-sectional study.

Another factor that may be implicated in prolonged QTd is autonomic dysfunction. It has been proposed that the increase in arrhythmias and QTd was due to changes in autonomic tone during HD [11,12], but this proposition has not been extensively investigated. Kirvela *et al.* [12] observed significantly increased QTd in diabetics with autonomic dysfunction compared to diabetics without this disorder.

In our study, corrected QTmax and QTmin were significantly shortened after the Valsalva maneuver. The decrease in corrected QTmax (QT_cmax) was more prominent, which caused a decrease in QTd. However, the decrease of QT_cd from 59 ms to 48 ms after the Valsalva maneuver was not enough to bring QT_cd to levels seen in controls (35 ms, $p = 0.001$). According to our data, the Valsalva maneuver had no observable effect on QTd in normal controls. However, the ameliorating effect of the Valsalva maneuver (increase in parasympathetic tone) on QTd seems to indicate that autonomic dysfunction may be a factor in the increased QTd seen in HD patients. The decrease in QTd after the Valsalva maneuver indicates that increased parasympathetic tone might have balanced the increased sympathetic tone in HD patients.

In conclusion, HD patients had significantly increased QTd compared to controls. After the Valsalva maneuver, increased QTd regresses in HD patients, but does not return to normal. However, no significant change in QTd after the Valsalva maneuver was observed in controls. This finding suggests increased sympathetic activity may be involved in increased QTd in HD patients.

References

- 1 Buja G, Miorelli M, Turrini P, Melacini P, Nava A. Comparison of QT dispersion in hypertrophic cardiomyopathy between patients with and without ventricular arrhythmias and sudden death. *Am J Cardiol.* 72:973-6, 1993.
- 2 Barr CS, Naas A, Freeman M, Lang CC, Struthers AD. QT dispersion and sudden unexpected death in chronic heart failure. *Lancet.* 343:327-9, 1994.
- 3 Morris STW, Galiatsou E, Stewart GA, Roger RSC, Jardine AG. QT dispersion before and after hemodialysis. *J Am Soc Nephrol.* 1081:160-3, 1999.
- 4 Lorincz I, Matyus J, Zilahi Z, Kun C, Karanyi Z, Kakuk G. QT dispersion in patients with end-stage renal failure and during hemodialysis. *J Am Soc Nephrol.* 10:1297-302, 1999.
- 5 Converse RL, Jacobsen TN, Toto RD, Jost CMT, Cosentino F, Fouad-Tarazi F, Victor RG. Sympathetic overactivity in

- patients with chronic renal failure. *N Engl J Med.* 327: 1912–18, 1992.
- 6 Hansen J, Victor RG. Direct measurement of sympathetic activity: New insights into disordered blood pressure regulation in chronic renal failure. *Curr Opin Nephrol Hypertens.* 3:636–43, 1994.
 - 7 Bazett HC. An analysis of time-relations of electrocardiograms. *Heart.* 7:353–70, 1918.
 - 8 Sarnak MJ, Levey AS. Epidemiology of cardiac disease in dialysis patients. *Semin Dial.* 12:69–76, 1999.
 - 9 United States Renal Data System. *USRDS Annual Data Report.* Baltimore, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Division of Kidney, Urologic and Hematologic Diseases, 1997.
 - 10 Gruppo Emodialisi e Patologie Cardiovascolari. Multicentre, cross-sectional study of ventricular arrhythmias in chronically haemodialysed patients. *Lancet.* 2:305–9, 1988.
 - 11 Cupisti A, Galetta F, Morelli E, Tintori G, Sabilia G, Meola M, Barsotti G. Effect of hemodialysis on the dispersion of the QTc interval. *Nephron.* 78:429–32, 1998.
 - 12 Kirvela M, Yli-Hankala A, Lindgren L. QT dispersion and autonomic function in diabetic and nondiabetic patients with renal failure. *Br J Anaesth.* 73:801–4, 1994.