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## Effect of Hemodialysis on the Dispersion of the QTc Interval

### Key Words

QT dispersion  
Hemodialysis

### Abstract

The QTc dispersion reflects the underlying regional heterogeneity of the recovery of the ventricular excitability, thereby it is considered as a novel marker of risk of ventricular arrhythmias. Because a higher incidence of ventricular arrhythmias is described during and after hemodialysis, the aim of this study has been to evaluate the QTc dispersion before and after uncomplicated hemodialysis session. Twenty chronic uremics without heart failure, ischemic heart disease or dialysis hypotension were selected. The QTc dispersion was determined as the difference between the longer and the shorter QTc interval measured on a 12-lead electrocardiogram. Following the hemodialysis session, the QTc dispersion increased from  $30 \pm 9$  to  $54 \pm 17$  ms ( $p < 0.001$ ) associated with the expected reduction of potassium and magnesium and with the increase of extracellular calcium concentration. However, no correlation has been observed between the QTc dispersion increase and the degree of the intradialytic changes of plasma electrolytes, blood pressure or body weight. In summary, the hemodialysis treatment per se does induce an increase of the QTc dispersion, likely due to the rapid changes of electrolyte plasma concentrations. This can potentially contribute to the arrhythmogenic effect of the hemodialysis procedure, reflecting an enhanced regional heterogeneity of ventricular repolarization. The clinical importance of the increase of QTc dispersion as risk factor of ventricular arrhythmias, particularly in hemodialyzed patients suffering from ischemic or hypertrophic heart diseases, should be the matter of further investigations.

### Introduction

Evidence exists that chronic uremics on regular dialysis treatment show a high incidence of ventricular arrhythmias especially during and after the dialysis session [1, 2]. This arrhythmogenic effect of the standard hemodi-

alysis procedure is mainly attributed to the rapid changes of the intra- and extracellular electrolytes [3-5]. It is well known that regional heterogeneity of repolarization times in adjacent areas of the myocardium are associated to higher risk of ventricular tachyarrhythmias [6]. The measurement of the dispersion of the QT interval reflects

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**Table 1.** Changes induced by hemodialysis (HD) session on QTc dispersion, QTc length, heart rate and blood pressure in the studied uremics

	Before HD	After HD	p
QTc dispersion, ms	30 ± 9	54 ± 17	<0.001
QTc, ms	423 ± 45	435 ± 41	<0.05
Heart rate, bpm	71 ± 14	78 ± 21	NS
Systolic BP, mm Hg	152 ± 27	142 ± 18	<0.01
Diastolic BP, mm Hg	93 ± 12	86 ± 10	<0.01

**Table 2.** Changes induced by hemodialysis (HD) on plasma electrolytes, urea and acid-base status

	Before HD	After HD	p
K <sup>+</sup> , mEq/l	5.0 ± 0.9	3.4 ± 0.4	<0.001
Na <sup>+</sup> , mEq/l	138 ± 4	139 ± 2	NS
Magnesium, mEq/l	2.1 ± 0.4	1.5 ± 0.2	<0.01
Total calcium, mg/dl	8.9 ± 0.8	10.8 ± 0.6	<0.001
Phosphorus, mg/dl	4.0 ± 1.0	1.9 ± 0.6	<0.001
Urea, mg/dl	121 ± 41	47 ± 16	<0.001
pH	7.36 ± 0.05	7.47 ± 0.03	<0.01
HCO <sub>3</sub> <sup>-</sup> , mEq/l	20.5 ± 3.1	25.9 ± 3.7	<0.01

regional repolarization differences in the heart [7, 8] which in turn can elicit the onset of arrhythmias by means of re-entry mechanisms. Thereby the inter-lead QT dispersion has been proposed as a novel indicator of arrhythmogenic risk, able to predict severe ventricular arrhythmias or sudden death in patients with hypertrophic cardiomyopathy [9, 10], myocardial infarction [11] or chronic heart failure [12]. It derives that the measurement of QT dispersion in uremics on hemodialysis treatment is an intriguing matter of investigation.

The aim of the present study was to evaluate the effect of uncomplicated hemodialysis session on the QT dispersion in chronic uremic patients without clinically relevant heart diseases.

### Patients and Methods

Twenty chronic uremics (11 m, 9 f, aged 49 ± 17 years) on hemodialysis treatment entered the study. Ten patients were on a 3-times-weekly dialysis schedule and 10 patients were on a once-weekly dialysis combined with dietary treatment [13, 14]. All the patients were treated with acetate-free biofiltration lasting 3.5–4 h. The dialysate composition was: potassium 2 mmol/l, calcium 2 mmol/l, magne-

sium 0.37 mmol/l, sodium 139 mmol/l. Patients affected by diabetes, heart failure, ischemic heart disease, atrial fibrillation or conduction disturbances were excluded. Two-dimensional echocardiographic examination was performed in all the studied patients: the detection of a global or regional deficit of contractility, or an ejection fraction lower than 60% were regarded as exclusion criteria. Antihypertensive treatment was clonidine in 7 cases, nifedipine in 3 cases, ACE inhibitor in 3 cases and atenolol in 1 case. No patient was on pharmacological treatment known to affect the QT interval.

Before and 15 min after the end of the hemodialysis session, 12-lead electrocardiogram recordings were performed by Cardiovit CS-100 ECG Recorder (Schiller AG, Baar, Switzerland), at 50 mm/s paper speed (gain 10 mm/mV). The measurements of QT interval in all possible leads were blindly performed by a single observer. The QT interval was taken from the onset of the QRS complex to the end of the T wave. In the presence of a U wave the nadir between T and U was taken as the final point.

For each electrocardiogram recording we took measurements of three consecutive QT intervals from each lead and calculated the arithmetic means; these QT values were then corrected (QTc) by the heart rate according to Bazett's formula. The QTc dispersion was determined as the difference between the maximum and the minimum value of the QTc interval in different leads (ten at least) of the same recording. The arithmetic mean of the QTc from the 12 leads of each electrocardiogram recording was assumed as the QTc interval length.

Blood pressure and heart rate were taken at the same time of the electrocardiogram recordings. Plasma levels of electrolytes, urea, hematocrit, blood pH and bicarbonate were determined at the start and at the end of the hemodialysis session. No clinically significant hypotensive episodes were observed during the hemodialysis treatments.

All the results are expressed as mean ± standard deviation. Statistical evaluation has been performed using Student's t test for paired data and Pearson's correlation test. Differences were considered as statistically significant when  $p < 0.05$ .

### Results

The results are shown in tables 1 and 2. After the hemodialysis session, the QTc dispersion increased (Table 1) and this phenomenon was invariably observed in all the 20 studied patients, as it appears in figure 1. Also the QTc interval length increased after dialysis (table 1), but this change did not occur in all the studied patients.

As expected by dialysis treatment, plasma concentrations of K<sup>+</sup> and Mg<sup>2+</sup> decreased whereas calcium plasma levels increased (table 2). However, no correlation has been found between the degree of the electrolytes' intradialytic changes and the amount of the QTc dispersion increase. No significant relations were also observed between the increase of QTc dispersion and blood pressure, acid-base status or hematocrit at the beginning of the hemodialysis session, or ultrafiltration (2.2 ± 1.0 kg), age, sex or duration of dialysis.

The increase of QTc dispersion occurred both in the patients on 3-times-weekly hemodialysis ( $30 \pm 11$  vs.  $57 \pm 19$  ms,  $p < 0.001$ ) and in those on once-weekly hemodialysis ( $30 \pm 7$  vs.  $51 \pm 15$  ms,  $p < 0.01$ ) schedule. At the start of dialysis, plasma levels of urea were higher in the former than in the latter ( $143 \pm 42$  vs.  $98 \pm 26$  mg/dl,  $p < 0.05$ ) group, whereas no significant differences were detected as far as the electrolytes, hematocrit, blood pressure or body weight gain were concerned. This can be achieved, despite the lower dialytic dose in the once-weekly dialysis patients, thanks to their higher residual renal function (creatinine clearance ranging from 2 to 6 ml/min/1.73 m<sup>2</sup>) and to the conservative dietary treatment.

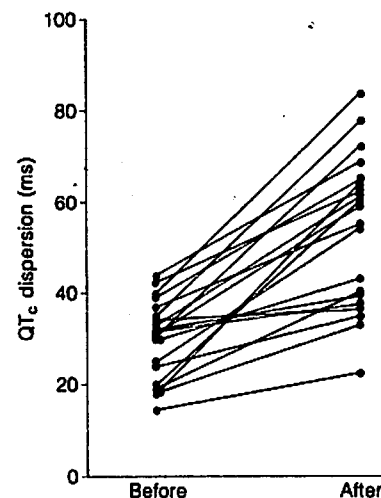
## Discussion

Ventricular arrhythmias are one of the most severe complications in hemodialysis patients, occurring especially during and after the hemodialysis session [1, 2]. They can represent a serious life-threatening condition although do not seem to predict the overall mortality in the hemodialyzed population [15].

The changes of cellular or interstitial fluid composition can account for increased susceptibility to ventricular arrhythmias. Namely, the rapid reduction of plasma potassium concentration as well as the elevation of ionized calcium plasma levels [3] can elicit cardiac arrhythmias. Actually, Redaelli et al. [5] demonstrated that the arrhythmogenic effect of hemodialysis was reduced when a constant plasma-dialysate K<sup>+</sup> gradient was used instead of the constant low K<sup>+</sup> dialysate concentration. Also low intracellular K<sup>+</sup> concentration was found to be associated with an increased risk of ventricular arrhythmias [4].

A link between regional heterogeneity of duration of ventricular recovery and severe ventricular arrhythmias is reported [6]. Since increased values of QTc dispersion reflect regional differences of the myocardial repolarization [7], they are considered as a predictor of arrhythmogenic risk [6, 10–12]. However, a relation between increased QT dispersion and incidence of arrhythmias was not observed in a group of patients with left ventricular hypertrophy [16].

In the present study we clearly demonstrate that the hemodialysis treatment induces a significant increase of the QTc dispersion. This confirms our preliminary data [17] that are in keeping with those of Locati et al. [18] although others have not observed similar results [19]. This finding has been detected in chronic uremics on



**Fig. 1.** Changes of the dispersion of QTc interval in the 20 chronic uremics before and after the hemodialysis session.

maintenance or infrequent hemodialysis schedule, with no clinically relevant cardiopathies and during uncomplicated hemodialysis sessions, just in order to evaluate the influence of the hemodialysis treatment itself on the QTc dispersion.

The present study has been performed using one hemodialysis technique with the aim to reduce variabilities potentially due to different dialysis procedures, and a soft hemodiafiltration, that is acetate-free biofiltration, has been chosen because it is generally well tolerated. Hence our results reflect the effect of this dialysis procedure but similar data were obtained also using unspecified standard hemodialysis techniques [18]. Potassium and magnesium are two of the most important factors for the electrical stability of the myocardium, involved in creating normal cellular excitability, impulse propagation and regular ventricular recovery. Of consequence, it is likely that the dialysis-induced electrolytic disequilibrium, namely the rapid reduction of extracellular concentration of K<sup>+</sup> and Mg<sup>2+</sup>, can be the main cause of the increased QTc dispersion. However, no correlation has been observed between the degree of QTc dispersion increase and the degree of the electrolyte changes following hemodialysis treatment. This absence of relation could have been determined by the relatively small number of patients. Moreover, other factors may affect the QTc dispersion, as the

anatomic-functional heterogeneity among different areas of the ventricular myocardium that hence may variably respond to the rapid electrolytic changes or to the autonomic nervous modifications occurring during hemodialysis.

To define the pathogenesis of the increase of QTc dispersion following hemodialysis, well-designed study protocols and more patients are needed because of the high number of dialytic or individual factors potentially affecting this parameter. Finally, the question arises as to whether the increasing of QTc dispersion is really associated to severe ventricular arrhythmias in uremics, particularly when the hemodialysis treatment is performed in

patients suffering from severe left ventricular hypertrophy, heart failure, ischemic heart disease, arrhythmic or conduction disturbances. Further studies enrolling a larger number of patients should be planned to investigate this aspect.

In summary, the dispersion of QTc interval does increase after the hemodialysis treatment. Theoretically this phenomenon may be regarded as one of the factors contributing to the well-known arrhythmogenic effect of hemodialysis. The role of the dialysis-induced increase of the QTc dispersion as predictor of severe arrhythmias or sudden death remains to be assessed.

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