

*Original Article*

## Effects of haemodialysis on maximum P wave duration and P wave dispersion

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**Abstract**

**Background.** Analysing a 12-lead surface electrocardiogram (ECG), the inter-lead variability of the P wave interval, i.e. P wave dispersion, is defined as the difference between the maximum and the minimum P wave duration. Our aim was to assess the effect of haemodialysis on P wave duration and dispersion in non-diabetic patients with end-stage renal failure on chronic haemodialysis.

**Methods.** Twenty-eight patients (14 men and 14 women, mean age  $58 \pm 16$  years, average duration of dialysis  $4.5 \pm 2.8$  years) were examined. Prior to haemodialysis, echocardiography (M-mode and two-dimensional) was performed. Haemodialysis sessions were carried out with polysulfone dialysers and bicarbonate dialysate fluids. Twelve-lead ECGs were recorded at the beginning, 15 and 30 min after starting dialysis, at the end, and 2 h after completion of each session. Ionic parameters were checked during the study. P wave durations were measured with calipers in three consecutive complexes of each lead by one observer.

**Results.** P maximum was  $58 \pm 16$  ms at the beginning, and showed an increase by the end of dialysis to  $98 \pm 8.9$  ms ( $P < 0.0001$ ). Pre-dialysis P dispersion was  $23 \pm 10$  ms and increased to  $41 \pm 16$  ms by the end of the sessions ( $P < 0.0001$ ). In patients with a left atrial diameter larger than 45 mm, P dispersion increased from  $23 \pm 11$  to  $53 \pm 10$  ms ( $P < 0.0003$ ) by the end of the sessions.

**Conclusions.** According to our results, ionic imbalance and dialysis itself may cause changes in P duration and dispersion simultaneously.

**Keywords:** atrial fibrillation; haemodialysis; P wave dispersion; P wave duration

**Introduction**

Atrial fibrillation is one of the most common arrhythmias managed in everyday clinical practice. Its incidence increases with age and the presence of structural heart disease. Although the causes are diverse, hypertensive, ischaemic and valvular heart disease, pericarditis and dilated cardiomyopathy, ionic disturbances, and autonomic dysfunction are common. Most of the patients suffering from kidney disease have these abnormalities. According to recent studies, the estimated prevalence of atrial fibrillation in patients with end-stage renal failure is approximately 13% [1]. Fast ventricular response to atrial tachyarrhythmias may lead to angina pectoris, hypotension, and serious haemodynamic deterioration, also further malignant ventricular arrhythmias may occur [2,3]. Recently, electrophysiological studies have demonstrated that patients suffering from atrial fibrillation have longer intra-atrial and inter-atrial conduction times of sinus impulses [4]. P wave duration lengthening on a 12-lead surface electrocardiogram (ECG) [4,5] and an abnormal signal averaged atrial ECG have also been demonstrated [6]. Inhomogeneous propagation of sinus impulses can be caused by altered micro-architecture and non-uniform anisotropic properties of the atrium, increased heart chamber size, wall thickness [7], and pressure or volume overload conditions [8]. Intracellular or intercellular factors may lead to site-specific conduction differences [9,10]. Arrhythmogeneity depends partly on autonomic tone, mainly on sympathetic overdrive conditions. As a result of atrial structural and electrophysiological heterogeneity, unidirectional blockage may occur, which plays an important role in the genesis of atrial premature complexes and re-entry, which may lead to fibrillation [11].

The purpose of our investigation was to study the possible effects that may result in the change of simple ECG markers: P wave duration (P maximum) and dispersion during haemodialysis. We studied the

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dynamicity of P duration and dispersion changes, so measurements were made at the start of haemodialysis, 15 and 30 min after the start of dialysis, at the end of dialysis, and 2 h after the termination of each session.

## Subjects and methods

Twenty-eight non-diabetic patients (14 males and 14 females, mean age  $58 \pm 16$  years, range 24–85 years) with end-stage renal failure were selected. The studied population had no significant impulse generation or conduction defect, autonomic or metabolic abnormality, or previous episode of atrial fibrillation. Exclusion criteria were: current atrial fibrillation, no P wave on ECG, or no clear point of return to the isoelectric line. The underlying causes of chronic renal failure were chronic glomerulonephritis ( $n = 16$ ), hypertensive and vascular nephropathy ( $n = 5$ ), chronic tubulointerstitial nephropathy ( $n = 5$ ), and polycystic kidney disease ( $n = 2$ ). Prior to haemodialysis, M-mode and two-dimensional images and pulsed and continuous wave Doppler transthoracic echocardiography were performed in all cases with the Acuson Sequoia C 256 Mountain View, CA, USA imaging system using a 3.5-MHz transducer. Left atrial dimension, left ventricular systolic and diastolic function, and left ventricular ejection fraction were determined. Eighty-two per cent of patients had arterial hypertension (arterial blood pressure greater than 140/90 mmHg needing antihypertensive drug therapy), 46% had hypercholesterolaemia (serum cholesterol higher than 5.2 mmol/l). Sixty-four per cent of subjects suffered from ischaemic heart disease proved by stress test, one had a recent myocardial infarction (3.6%), eight patients suffered from mitral valve insufficiency (28.5%), and five subjects had mitral valve stenosis (17.9%). One underwent an operation for an aortic stenosis (Table 1). Two of our patients were administered digitalis (7%), eight subjects took nitrates (28%), three were given a beta blocking agent (39%), 16 took an ACE inhibitor (57%), and calcium antagonists were used in 17 cases (60%). All patients gave informed consent to participate in the study and the Institutional Ethics Committee on Human Research approved the study protocol. Haemodialysis sessions were carried out in standard settings (Fresenius 2008-E devices; Fresenius Medical Care, Bad Homburg, Germany), with F6 and F8 polysulfone dialysers (Fresenius) for 3.5–4.0 h, three times per week. Bicarbonate dialysate fluids contained 140 mmol/l sodium, 2.0 mmol/l potassium, 1.5 mmol/l calcium, and 1.0 mmol/l magnesium. During the sessions no drugs were administered, except isotonic NaCl and sodium heparin. Maintenance therapy consisting of digitalis glucosides, nitrates, beta blocking agents, and antihypertensive agents remained unchanged. Sodium, potassium, calcium, phosphate, and magnesium levels were measured four times during each session, and 2 h after termination of haemodialysis. Serum urea nitrogen, creatinine, cholesterol, triglyceride, and intact parathyroid hormone were also determined. Arterial blood pressure was monitored non-invasively during each session.

All subjects underwent a conventional 12-lead ECG examination five times during the sessions: at the beginning, 15 and 30 min after starting dialysis, at the end, and 2 h after termination of the treatment. Simultaneous 12-lead ECGs were recorded by means of 12-channel ECG equipment (Hewlett Packard Page Writer 200i; M1071A, China), at a paper speed of 25 mm/s. On every occasion, the ECG was obtained in a comfortable supine position. During ECG

**Table 1.** Clinical data of the studied population

Mean age (years)	$58 \pm 16$
Sex (males/females)	14/14
Average time of dialysis (months)	$54 \pm 34$
Ultrafiltration ratio (ml/h)	$1289.6 \pm 413$
Systolic blood pressure (mmHg)	$155.5 \pm 11.2$
Diastolic blood pressure (mmHg)	$89.3 \pm 7.2$
Ischaemic heart disease	18/28 (64%)
Myocardial infarction	1/28 (3.6%)
Hypertension	23/28 (82%)
Intact parathyroid hormone (pmol/l)	$28 \pm 30.1$
Hyperlipidaemia	13/28 (46%)
Aortic stenosis	1/28 (3.6%)
Mitral valve stenosis	5/28 (17.9%)
Mitral valve insufficiency	8/28 (28.5%)
Left ventricular ejection fraction (%)	$52 \pm 11$
Left atrial dimension (mm)	$44.1 \pm 6.9$

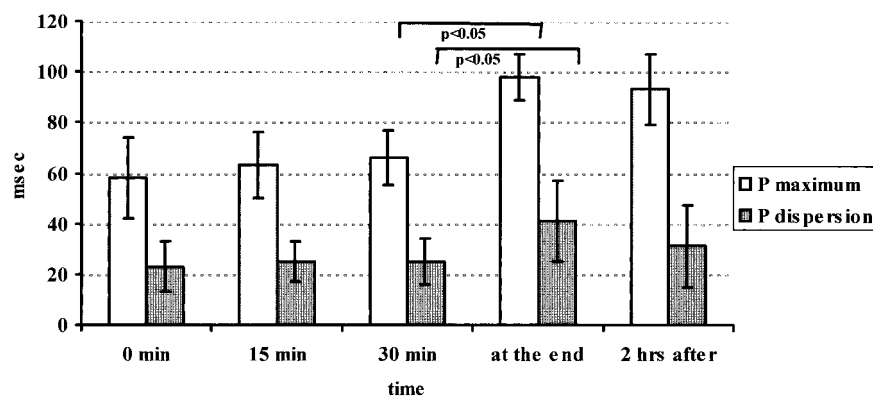
recordings, all patients breathed freely and did not speak. ECG electrodes were not changed or renewed during or after haemodialysis. For measurement of P wave duration, the 12-lead ECG printouts were enlarged on the same photocopier by a factor of three. P wave duration was measured with calipers in all 12 leads by one observer in order to exclude inter-observer variability. P wave duration was measured from the first electrical activity to the offset at the junction between the end of P wave deflection and the isoelectric line. P wave dispersion was defined as the difference between the maximum and minimum value of P wave duration. Three consecutive cardiac cycles were measured and averaged.

Statistical analysis was performed using SAS 6.12 for Windows StatSoft, Tulsa, USA. Parameters were characterized with descriptive statistics (case number, mean, standard deviation, median, and quartiles). Temporal change of both ECG markers was determined using Friedman's ANOVA. Relations between variables were assessed using Kruskal–Wallis non-parametric ANOVA. Correlations between ionic parameters and ECG markers were assessed using Spearman rank correlation. Ionic changes in time were established using repeated measures ANOVA. A value of  $P < 0.05$  was considered to be significant.

## Results

P wave duration (P maximum) and dispersion did not show any significant change for the first 30 min of haemodialysis. The average of the P maximum values was  $58 \pm 16$  ms at the beginning, which increased to  $98 \pm 8.9$  ms by the end of dialysis ( $P < 0.0001$ ). P maximum, determined 2 h after completion of sessions, still remained lengthened ( $93 \pm 14$  ms). The average of pre-dialysis P dispersions was found to be  $23 \pm 10$  ms, which increased to  $41 \pm 16$  ms by the end of the sessions ( $P < 0.0001$ ). P dispersion measured 2 h after the end decreased to  $35 \pm 16$  ms, which did not prove to be a significant change compared with its value at termination (Figure 1).

P dispersion showed a significant lengthening ( $P < 0.05$ ) at the end of dialysis in patients with a dilated left atrium, i.e. a diameter greater than 45 mm (Table 2). P maximum did not prove to change significantly in the two subgroups of patients. During



**Fig. 1.** P maximum and dispersion changes during haemodialysis. A significant change occurred regarding both ECG parameters by the end of haemodialysis.

**Table 2.** P maximum and dispersion in the two subgroups of patients

	0 min	15 min	30 min	At the end of haemodialysis	2 h after haemodialysis
Patients with left atrial diameter greater than 45 mm ( <i>n</i> = 14)					
P maximum (ms)	55 ± 17	61 ± 14	65 ± 12	97 ± 11	95 ± 16
P dispersion (ms)	23 ± 11	25 ± 8.5	26 ± 8.4	53 ± 10* ( <i>P</i> < 0.05)	36 ± 18
Patients with left atrial diameter less than 45 mm ( <i>n</i> = 14)					
P maximum (ms)	61 ± 14	65 ± 12	66 ± 12	99 ± 6.1	91 ± 12
P dispersion (ms)	23 ± 10	25 ± 8.5	23 ± 10	28 ± 12	31 ± 22

\**P* < 0.05 was considered to be significant.

the sessions, serum sodium did not show a significant change. Compared with the beginning ( $5.4 \pm 1.02$  mmol/l), serum potassium showed a significant decrease from 30 min ( $4.8 \pm 0.7$  mmol/l) until the end of dialysis ( $3.9 \pm 0.47$  mmol/l; *P* < 0.0001). Two hours after completion of the sessions, blood potassium increased significantly compared with the value at the end of dialysis ( $4.7 \pm 0.6$  mmol/l; *P* < 0.0001). Phosphate levels decreased by the end of dialysis (from  $2.0 \pm 0.5$  to  $1.2 \pm 0.34$  mmol/l; *P* < 0.001), followed by a non-significant increase measured 2 h after completion of the sessions ( $2.6 \pm 0.1$  mmol/l; *P* < 0.0001). Regarding serum magnesium, no significant change occurred (Figure 2).

Using Spearman rank correlation a significant negative relationship was found between P maximum and serum potassium (*P* < 0.0001; *r* = -0.4), also P dispersion and serum potassium proved to correlate significantly negatively (*P* < 0.01; *r* = -0.2). A positive correlation was found between serum calcium and P maximum (*P* < 0.0001; *r* = 0.5), and serum calcium and P dispersion (*P* < 0.009; *r* = 0.21). We did not find a significant relationship between phosphate and the studied ECG markers.

The RR interval at the beginning was found to be  $863 \pm 203$  ms, which had decreased to  $783 \pm 94$  ms by

the end of dialysis and it remained shortened at the value of  $784 \pm 95$  ms measured 2 h after finishing the treatment. No atrial fibrillation occurred during the sessions.

## Discussion

There are few data about the importance of atrial arrhythmias and atrial fibrillation in patients with end-stage renal failure during haemodialysis. After a publication survey on this topic, a report was found on P wave duration changes during haemodialysis. Among the 21 patients studied by Shapira *et al.* [12] 18 showed an increase from  $75 \pm 3.1$  to  $92.9 \pm 3.4$  ms, whereas three showed a decrease from  $90.1 \pm 4.7$  to  $71.1 \pm 4.5$  ms during haemodialysis. Eighty per cent of patients with atrial fibrillation are associated with organic heart disease including valvular, ischaemic, hypertensive (particularly if left ventricular hypertrophy is also present) heart disease, hypertrophic, or dilated cardiomyopathy [13]. Atrial fibrillation is characterized by multiple circulating re-entrant wavelets due to disorganized atrial depolarization [14]. Increased atrial dimension, decreased conduction velocity, and shortened atrial refractory time, are considered to be important reasons for this mechanism. Recently, non-invasive ECG methods have been introduced to assess the atrial arrhythmia risk of

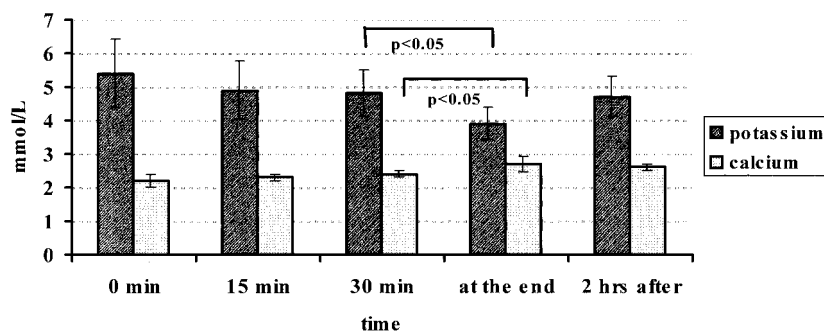


Fig. 2. Serum potassium and calcium changed significantly by the end of haemodialysis.

patients. P wave duration and dispersion are considered to be one of the most important non-invasive ECG markers in this field [15,16]. Individuals with a history of paroxysmal atrial fibrillation have significantly longer intra-, and inter-atrial conduction time of sinus impulses. The increase of P wave duration is thought to be an accepted indicator of atrial conduction prolongation and, thus, might be useful in atrial arrhythmia risk stratification. The heterogeneity of electrophysiological and structural properties of the atrium may play a role in the genesis of unidirectional block of premature impulses. Also, intracellular and intercellular factors (regulatory proteins, ionic channels, etc.), and metabolic imbalance may lead to non-uniform anisotropic conduction of the atrial myocardium. The site-dependent inhomogeneous atrial conduction may result in increased variability of the P wave duration, and thus increase P wave dispersion.

In this report, 28 patients with end-stage renal failure (with no history of atrial fibrillation) were studied during haemodialysis sessions. P wave duration and dispersion were calculated from a 12-lead surface ECG. At the end of the sessions the examined ECG parameters were found to be significantly increased compared with those at the beginning, and they still remained lengthened 2 h after the termination of the treatment. None of our patients showed a decrease in the studied ECG parameters. Regarding left atrial dimension measured by echocardiography, an increased P dispersion occurred at the end of dialysis in patients with an atrial diameter larger than 45 mm. The data suggest that an enlarged left atrium may result in increased atrial arrhythmogeneity. On the basis of our data obtained from Spearman rank correlation, we conclude that changes in calcium and potassium levels may have an unfavourable effect on atrial arrhythmogeneity.

## Conclusion

Changes in P wave duration and dispersion might be the result of ionic imbalance and haemodialysis itself. Renal replacement therapy may lengthen P wave dispersion in patients with enlarged left atrium. The

role of these ECG markers for the prediction of atrial arrhythmias in end-stage renal failure patients should be evaluated in prospective studies.

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