

*Original Article***Signal-averaged ECG abnormalities in haemodialysis patients.
Role of dialysis**Maria-Aurora Morales, Celio Gremigni¹, Pietro Dattolo², Marcello Piacenti, Tiziano Cerrai², Antonio Fazi¹, Gualtiero Pelosi, Rossano Vergassola¹ and Quirino Maggiore²CNR Clinical Physiology Institute, Florence and Pisa, ¹Cardiology Department, ²Nephrology and Dialysis Unit, S.M. Annunziata Hospital, Florence, Italy**Abstract**

Background. Late potentials (LP) on the signal-averaged electrocardiogram (SAECG) are predictive of malignant ventricular arrhythmias and sudden cardiac death in patients with ischaemic and non-ischaemic cardiomyopathy. Cardiac dysfunction, both regional and global, as well as supraventricular and ventricular arrhythmias are reported in a high percentage of patients with end-stage renal failure (ESRF). The aim of the study was to assess the prevalence of LP and the effects of haemodialysis on the SAECG of ESRF patients.

Methods. SAECG was recorded immediately before and within 30 min after the end of dialysis in 48 patients in sinus rhythm, free of conduction disturbances on ECG and of signs of congestive heart failure. Serum electrolytes were sampled together with the SAECG recordings. An echo-Doppler exam was performed within 2 weeks of the study. SAECGs were adequate for analysis in 45/48 patients. LP were present when at least two of the following criteria were fulfilled: QRS duration ≤ 115 ms, $LAS_{40} \leq 38$ ms, $RMS_{40} \geq 38$ μ V at 40 Hz high pass bidirectional filter, and noise < 0.7 μ V.

Results. LP were detected in 12/45 patients (25%) on the SAECG before dialysis; of these 12 patients, seven had a history of a previous myocardial infarction and two had documented coronary artery disease (CAD). A significant greater wall motion score index—calculated on a 16 segment model—was reported in patients with LP (1.20 ± 0.20 vs 1.01 ± 0.03 , $P < 0.01$), while left ventricular mass was comparable in the two groups of patients. At the end of dialysis, a significant prolongation of fQRS duration was found both at 25 and 40 Hz filters (from 98 ± 11 to 106 ± 16 ms and from 97 ± 12 s to 102 ± 13 ms, respectively, $P < 0.001$). A significant inverse relationship was seen between the percentage of dialysis-induced serum potassium reduction and fQRS changes at 40 Hz ($r = -0.68$, $P < 0.001$).

Conclusions. LP were detected in a significant proportion of dialysis patients, probably related to underlying CAD with left ventricular dysfunction. Prolongation of fQRS after dialysis could be explained by the acute reduction in serum potassium levels.

Key words: echocardiography; haemodialysis; potassium; signal-averaged ECG; ventricular function

Introduction

Ventricular late potentials are low-amplitude, high-frequency waveforms in the terminal portion of the QRS complex which can be detected by the signal-averaged electrocardiogram (SAECG). They are thought to originate from abnormal areas of ventricular myocardium where activation is delayed by slow conduction, thus predisposing to re-entrant tachycardia [1–5]. A number of reports have demonstrated that the detection of an abnormal signal-averaged ECG can identify a group of patients at risk of serious arrhythmic events and sudden cardiac death [6–11].

Cardiac abnormalities often occur in patients with end-stage renal disease undergoing chronic haemodialysis treatment [12–20]. These abnormalities are left ventricular hypertrophy with increased fibrosis content and deposition of calcium and aluminium salts within the heart tissue [15,21–22]. Such histologic changes could represent a potential substrate for an abnormally delayed and fractionated electrical conduction leading to the appearance of late potentials on the SAECG.

It has been established that haemodialysis treatment can induce supraventricular and ventricular arrhythmias and acute changes on standard ECG waveforms due to the concomitant changes in serum electrolyte levels, acid–base balance and body fluid content [23–28]. Most of the clinical studies performed in dialysis patients have focused on QRS amplitude and T wave changes. So far, systematic studies assessing the role of acute electrolytic and body fluid

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changes induced by haemodialysis on the SAECG parameters are lacking.

The aim of the present study was to evaluate the prevalence of late potentials in a population of patients undergoing chronic intermittent haemodialysis and the acute effects of dialysis on the SAECG.

Subjects and methods

Patient population

All patients undergoing chronic haemodialytic treatment in our dialysis unit were enrolled in the study with the exception of patients with signs of congestive heart failure, baseline conduction abnormalities and arterial hypotension at the end of the dialytic procedure. Therefore, the final population consisted of 48 consecutive patients, 22 females, with a mean age of 67 ± 13 years on chronic intermittent haemodialysis for 63 ± 55 months (range 1–250 months). Nine patients had a clinical, electrocardiographic and enzymatic diagnosis of a previous myocardial infarction. Twenty eight patients were undergoing cardiovascular therapy: 22 antihypertensive treatment, four digitalis, and four angiotensin-converting enzyme-inhibitors + transdermal nitrates; none of them was using beta-blockers or other antiarrhythmic treatment.

Haemodialysis

All patients underwent maintenance haemodialysis for an average of 4 h three times a week using a Ultramatic Bellico artificial kidney. The blood flow rate (mEq/l) during haemodialysis was 300–350 ml/min. The dialysate contained Na 138 mmol/l, Ca 1.5 mmol/l, K 1.5 mmol/l, Cl 108 mmol/l and acetate 5 mmol/l.

Signal-averaged electrocardiogram

Signal averaging was performed by a commercially available instrument (Del Mar Avionics Mod 65 CEWS, USA). The SAECG was recorded at 30 min intervals immediately before and after the dialysis procedure. For time-domain analysis, signals obtained from three bipolar orthogonal leads were amplified, filtered bidirectionally at frequencies between 25 and 250 Hz and 40 and 250 Hz and combined into a vector magnitude $\sqrt{X^2 + Y^2 + Z^2}$. High frequency QRS duration (fQRS), duration of low amplitude signals $< 40 \mu\text{V}$ (LAS_{40}) and root mean square voltage of signals in the last 40 ms of the high frequency QRS intervals (RMS_{40}) were calculated at both filtering settings. Late potentials were considered present when at least two of the following criteria were fulfilled: $\text{fQRS} \leq 115$ ms, $\text{LAS}_{40} \leq 38$ ms, and $\text{RMS}_{40} \geq 25 \mu\text{V}$ at 40 Hz high pass bidirectional filter [29].

Chemical analysis

Blood samples for electrolyte (potassium, sodium and calcium) and for HCO_3^- serum concentration were taken before and within 30 min after the end of the dialysis procedure from the arterial side of the fistula and determined by standard methods (indirect ISE method for Na^+ , Cl^- and K^+ , colorimetric method for Ca^{2+} and by a Stat 5 Profile Analyser for HCO_3^-).

Cardiac echo-Doppler evaluation

All patients underwent a complete echo-Doppler examination within 2 weeks of the SAECG by means of a commercially available instrument (EsaOte Biomedica SIM 7000 CFM, Italy) and recorded on a video recorder (Panasonic Super VHS, Japan) for subsequent play back and analysis. All exams were performed 24 h after the previous haemodialytic treatment. A complete baseline examination was done, and end-diastolic septal and posterior wall thickness and left ventricular internal dimensions were assessed. The left ventricular mass was calculated according to the Penn-cube formula [30]. The left ventricular wall motion score index was calculated in each patient following the recommendations of the American Society of Echocardiography [31].

Statistical analysis

Data were expressed as mean \pm SD and analysed by Student's *t*-test for both paired and unpaired data. Regression coefficients were calculated between SAECG variables and the laboratory data. A $P < 0.05$ was considered as significant.

Results

Late potentials at baseline

Technically adequate SAECGs with a noise below $0.7 \mu\text{V}$ were obtained before and after haemodialysis in 45/48 patients. Late potentials were recorded in 12/45 (25%) patients before the start of the dialytic procedure. Of these 12 patients, seven had history of a previous myocardial infarction and two had documentation of ischaemic heart disease without signs of myocardial infarction (clinical history for typical anginal pain with positive bicycle exercise ECG in one patient and positive myocardial perfusion scintigraphy during dipyridamole infusion in the other). The prevalence of ischaemic heart disease among patients with a SAECG negative for late potentials was much lower: 2/33 patients only had documentation of a previous myocardial infarction—one transmural with abnormalities in regional left ventricular function and one subendocardial with a normal regional and global left ventricular function—($P < 0.01$ by Fisher exact test). No differences in cardiovascular therapy could be found between patients with and without late potentials on baseline SAECG. Additional patients characteristics are summarized in Table 1.

Echocardiographic data of patients with and without late potentials are summarized in Table 2. It is worth noting that left ventricular mass was comparable in the two groups of patients, while a significantly higher wall motion score index was observed in patients with an abnormal SAECG. Biochemical parameters obtained before haemodialysis were comparable in the two groups of patients, as well as changes in body weight induced by haemodialysis (Table 3).

Effects of dialysis on the signal-averaged ECG

A significant prolongation of QRS duration both at 25–250 and 40–250 high pass filters was observed at

Table 1. Clinical and electrocardiographic characteristics of the patients

	LP positive (n=12)	LP negative (n=33)
Age (years)	68±8	67±14
Dialytic age (months)	69±59	63±55
Previous MI	7	2
ECG		
PAC	1	8
PVC	3	3
First AV block	1	3
LVH	2	9

ECG data obtained from a routine ECG performed before the start of dialysis. MI, myocardial infarction; PAC, premature atrial contractions; PVC, premature ventricular contractions; AV, atrio-ventricular; LVH, left ventricular hypertrophy.

Table 2. 2-D and M-mode echocardiographic parameters in the two groups of patients

	LP positive (n=12)	LP negative (n=33)	P
LV EDD (mm)	54±3	49±6	<0.05
LV EDS (mm)	32±3	30±5	NS
LV EDV	155±26	117±40	<0.05
LV ESV	47±20	39±18	NS
Conc/Ecc Hypert	4/2	13/7	NS
LV mass (g)	158±27	151±52	NS
WMSI	1.2±0.2	1.01±0.08	<0.01

LV, left ventricular; EDD, end-diastolic diameter; EDS, end-systolic diameter; EDV, end-diastolic volume; ESV, end-systolic volume; Conc/Ecc Hypert, concentric/eccentric hypertrophy; WMSI, wall motion score index.

Table 3. Biochemical parameters before hemodialysis and dialysis-induced body weight changes in patients with and without late potentials on SAECG

	LP positive (n=12)	LP negative (n=33)
pH	7.371±0.060	7.373±0.062
HCO ₃ ⁻ (mmol/l)	22.9±2.7	21.8±2.9
K ⁺ (mEq/l)	5.6±0.8	5.6±0.9
Ca ²⁺ (mg/dl)	9.3±0.7	9.2±0.7
Na ⁺ (mEq/l)	140±2	140±3
Δbody weight (kg)	3.9±0.9	4.1±1

the end of the dialysis procedure (98 ± 11 vs 106 ± 16 ms at 25 Hz and 97 ± 11 vs 103 ± 12 ms at 40 Hz, $P < 0.01$). No significant changes in LAS₄₀ and RMS₄₀ were found when SAECGs obtained before and after dialysis were compared both at 25 and 40 Hz. When groups with and without late potentials at baseline were compared, the increase in fQRS duration at the end of the dialytic procedure did not show a significant difference either at 25 or 40 Hz filter (Figure 1).

As a result of dialysis treatment, the following changes in serum electrolytes were recorded: potassium from 5.6 ± 0.9 to 3.4 ± 0.7 mEq/l ($P < 0.001$), calcium

from 9.2 ± 0.5 to 10.1 ± 0.6 mg/dl ($P < 0.05$), bicarbonate from 22 ± 3 to 26 ± 2 ($P < 0.01$) and sodium from 140 ± 3 to 142 ± 4 mEq/l ($P < 0.05$). A significant linear negative relationship between the percentage serum potassium reduction induced by the dialysis procedure and the percentage increase on fQRS duration at 40–250 Hz filter was observed ($r = -0.68$, $P < 0.01$) (Figure 2).

No linear or non-linear relationship was found between QRS duration changes at 25 and 40 Hz filter and calcium, sodium, bicarbonate and body weight. Likewise, the changes in LAS₄₀ and RMS₄₀ bore no relationship to the changes in the biochemical parameters.

Discussion

In this study, we recorded ventricular late potentials in 25% of patients under maintenance haemodialysis treatment, which is well above the prevalence reported in normal subjects (0–7%) [4]. Our data suggest that such a high prevalence was due mainly to the presence of previous myocardial infarction. Thus, underlying coronary artery disease may be considered as the probable substrate for detection of late potentials in patients undergoing chronic haemodialytic treatment. Actually, the presence of necrotic areas intermingled with areas of both viable and normal myocardium have been documented to be a favourable substrate for the appearance of late potentials on SAECGs in patients with a previous myocardial infarction [2,3]. In this study, a significantly higher wall motion score index was recorded in patients with late potentials on SAECG. It is noteworthy that ventricular arrhythmias have been reported in a sizeable proportion of patients on chronic haemodialysis; in such patients, Lown's classes 4A and 4B arrhythmias were significantly associated with the presence of left ventricular dysfunction [32]. Of the 32 patients with normal SAECG, only two patients had a previous myocardial infarction and one of them had a normal global and regional left ventricular function after a small non-Q infarction. We cannot completely rule out the presence of silent myocardial ischaemia in at least some of the patients with negative late potentials; a stress test for coronary artery disease in these patients would probably have defined the study population more accurately. However, these tests are not free of side effects and bear a potential hazard, so they cannot be safely proposed for every patient, especially when the pre-test probability of coronary artery disease is low.

A previous study recorded late potentials in only 14% of 33 haemodialysed patients [33] which is well below the 25% observed in our study. This discrepancy can be explained partly by the younger age and the much lower prevalence of myocardial infarction in that population as compared with ours. Moreover, in that study, the criteria used for defining late potentials did not conform, as ours did, to the recommendations of the Committee of the European Society of Cardiology,

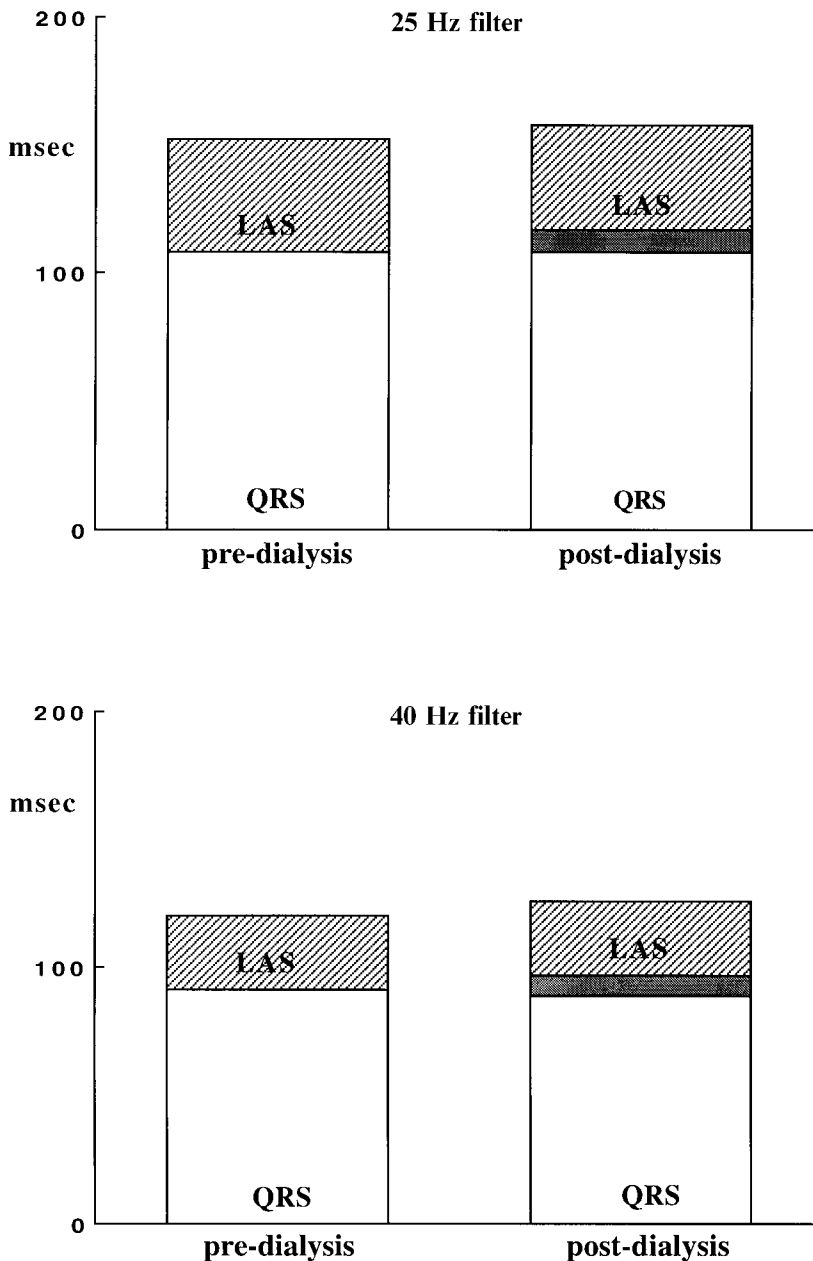


Fig. 1. Duration of fQRS and LAS₄₀ before and after dialysis. The black area represents the prolongation of fQRS in ms.

the American Heart Association and the American College of Cardiology [29].

Some authors have reported that left ventricular hypertrophy can induce a prolongation of QRS duration on the SAECG due to a longer depolarization time [34]. Patients under maintenance haemodialysis show a very high prevalence of left ventricular hypertrophy [35,36] which might be responsible for the prolongation of QRS duration. This explanation appears unlikely, since we did not detect a significant difference in left ventricular mass between the groups with and without late potentials on pre-dialysis SAECG.

We also found that the dialysis session induced a prolongation of the total filtered QRS duration at 25

and 40 Hz bidirectional filters. This prolongation was due to the widening of the initial portion of the QRS rather than to the prolongation of the late portion of the fQRS. In fact the terminal part of the fQRS signal (LAS₄₀ amplitude signals duration) was practically unchanged before and after haemodialysis (Figure 1).

The prolongation of fQRS duration after dialysis is not surprising. Studies on QRS duration in experimental settings have demonstrated that a reduction in serum potassium levels can induce an increase in QRS duration on conventional surface electrocardiograms due to a generalized slowing of conduction in the myocardial fibres rather than to a focal block within the bundle branches [37–39]. Indeed, we found a significant relationship between the serum potassium

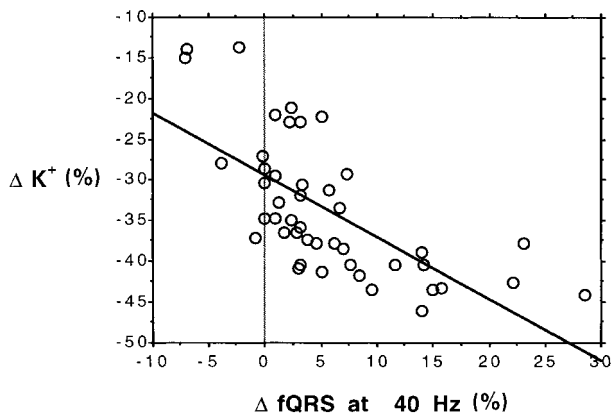


Fig. 2. Relationship between fQRS changes and K^+ changes after haemodialysis. $r = -0.68$.

reduction and the prolongation of fQRS duration recorded after dialysis, supporting the role of serum potassium changes in the genesis of these abnormalities. Conversely, there was no relationship between fQRS prolongation and dialysis-induced changes in serum sodium and calcium or body weight changes.

In conclusion, an abnormal SAECG can be recorded in a high proportion of patients undergoing chronic haemodialysis; moreover, acute changes in serum potassium levels can determine a significant prolongation of fQRS duration at the end of dialysis. As we did not perform a Holter monitoring in our patients, we cannot conclude whether the electrophysiological abnormalities detected in this study predispose to the development of severe ventricular arrhythmias.

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