Effect of haemodialysis on signal-averaged electrocardiogram P-wave parameters

Andrzej J. Jaroszyński¹, Andrzej G³owniak², Tomasz Sodolski², Wojciech Zaluska¹, Teresa Widomska-Czekajska² and Andrzej Książek¹

¹Clinic of Nephrology and ²Clinic of Cardiology, Medical University of Lublin, Lublin, Poland

Abstract

Background. The P-wave signal-averaged electrocardiogram (SAECG) is a non-invasive technique considered to indicate an increased risk for paroxysmal atrial fibrillation. The study was designed to evaluate the effect of the haemodialysis (HD) process on SAECG parameters in the group of selected HD patients.

Methods. Forty-seven HD patients (without relevant cardiac diseases) were included. SAECGs were performed pre- and post-dialysis together with evaluating extracellular body water by using bioimpedance and biochemical measurements. For each SAECG, filtered P-wave duration (FPD) and root mean square voltage of the final 20 ms of filtered P-wave (RMS20) were established.

Results. The duration of either pre- or post-dialysis FDP was higher in HD patients than in the control group (P < 0.001 and P = 0.005, respectively). The voltage of either pre- or post-dialysis RMS20 was reduced in HD patients compared with controls (P < 0.001 in both cases). HD induced a decrease in the duration of the FDP and a significant increase in the voltage of RMS20 (P < 0.001 in both cases). Stepwise multiple regression identified independent predictors of pre- and post-dialysis FDP as: (1) age; (2) pre- and post-dialysis ECW/kg body weight, respectively and; (3) pre- and post-dialysis haemoglobin levels, respectively. In the case of RMS20, we did not find any independent predictors either pre- or post-dialysis.

Conclusions. Our study revealed that P-wave SAECG parameters are abnormal in a significant portion of HD patients and improved with HD process. We have also demonstrated that patients’ age, volume status as well as the presence of anaemia are important factors influencing P-wave SAECG parameters in HD patients.

Keywords: anaemia; arrhythmias; extracellular body water; haemodialysis; P-wave; signal-averaged electrocardiography

Atrial fibrillation (AF) is one of the most common arrhythmias encountered in clinical practice. Epidemiological surveys have found that independent risk factors for the development of acute AF include age, male gender, ischaemic heart disease, hypertension, heart failure, valvular heart disease, diabetes, alcohol abuse, thyroid disorders, and disorders of the lung and pleura. Onset of AF reduces cardiac output by 10–20% irrespective of the underlying ventricular rate and may lead to serious haemodynamic deterioration (hypotension, angina pectoris with its consequences, malignant ventricular arrhythmias). AF is also associated with a risk of a stroke [1]. AF is a highly prevalent arrhythmia in haemodialysis patients (HD patients). The estimated prevalence of AF in HD patients is approximately 13%. Recent studies have indicated that the presence of AF is associated with a high mortality rate in HD patients [2].

The re-entrant nature of AF requires areas of conduction delay to initiate and sustain arrhythmia. The P-wave signal-averaged electrocardiogram (SAECG) is a non-invasive technique for the detection of microvolt-level cardiac electrical activity in the terminal portion of the P-wave. A high correlation between the P-wave SAECG and direct intra-atrial ECG recording has been demonstrated, validating the use of the P-wave SAECG as a non-invasive surrogate of atrial activation time. Prolongation of the total filtered P-wave duration (FPD) and low root mean square (RMS) voltage for the terminal portion of the filtered P-wave during sinus rhythm are considered to reflect atrial conduction delay and to indicate an
increased risk for paroxysmal AF (including idiopathic), irrespective of the presence of organic heart disease [3–6]. It has been shown that abnormal P-wave SAECG can be used as a predictor of AF development in patients undergoing cardiac surgery and in post-myocardial infarction patients. P-wave SAECG can also be used to detect patients at risk for the transition from paroxysmal to chronic form of AF as well as to predict the relapse after a electrical cardioversion [4,5,7,8]. To the best of our knowledge all previous reports on SAECG parameters in dialysis patients were focused exclusively on ventricular SAECG [9–11] and P-wave SAECG have never been evaluated in HD patients.

The purpose of this study was to estimate the effect of the HD process on parameters of P-wave SAECG in a group of selected HD patients.

Methods

Patients

Forty-seven HD patients (21 F and 26 M), aged 18 to 52 years (mean 37.17 ± 8.51), who remained on HD from 11 to 57 months (mean 32.6 ± 10.8) entered the study. All patients gave written consent, and the studies were approved by members of the local committees of ethics. The causes of ESRD were chronic glomerulonephritis (n = 21), chronic pyelonephritis (n = 8), obstructive nephropathy (n = 6), polycystic kidney disease (n = 3) and unknown (n = 9).

The exclusion criteria were: organic heart disease (evaluated by history, clinical examination and ECG) such as old infarction, ischaemic heart disease (Canadian Cardiovascular Society class > I), heart failure (New York Heart Association class > I), valvular and pericardial heart disease; diabetes; abnormal thyroid function tests; clinically significant episodes of hypotension during HD; pulmonary hypertension; sinus sick syndrome; ejection fraction (EF) < 50%; left atrial dimension (LAD) > 45 mm; current AF or flutter. None of HD patients received anti-arrhythmics (class I or III) or digitalis. HD patients with pre-dialysis serum calcium below 2.15 mmol/l, and potassium over 4.12±0.22 h. Bicarbonate dialysate containing (in mmol/l) 32 bicarbonate, 138 sodium, 2.0–2.5 potassium, 1.0 magnesium, 1.5 calcium was used in all HD patients. During HD, no medication was applied except heparin.

Haemodialysis

HD patients were dialysed thrice weekly with polysulphone dialysers (Fresenius). The mean time of HD session was 4.12±0.22 h. Bicarbonate dialysate containing (in mmol/l) 32 bicarbonate, 138 sodium, 2.0–2.5 potassium, 1.0 magnesium, 1.5 calcium was used in all HD patients. During HD, no medication was applied except heparin.

SAECG recording and processing

SAECGs were recorded in an electrically shielded and noise-proof room 1 h before and after (not exceeding 1 h) a single HD session. The technique used has been described previously [12]. Equipment constructed in the National Institute of Cardiology (Warsaw, Poland) was applied for signal recording and processing. The P-wave was derived from three bipolar orthogonal (Frank) leads. The signals from each lead were amplified (×1000) and passed through a band pass filter (cut-off frequency 25–250 Hz), and subsequently converted from analog to digital mode with 12-bit accuracy. The signal-averaging process was synchronized by the R-wave trigger. Ectopic beats, if present, were identified and rejected. The P-wave signal averaging was performed until residual noise < 1.0 μV was achieved. Approximately 150–200 beats were averaged and stored. The filtered (Butterworth bidirectional filter) and averaged signals for the X, Y and Z leads were combined into a spatial magnitude calculated as follows: \( (X^2 + Y^2 + Z^2)^{1/2} \). The onset and offset of P-wave was defined as a point at which the atrial signal exceeded and returned to the 1.0 μV level, respectively. The following parameters were measured and calculated automatically: filtered P-wave duration (FPD); root mean square voltage of the final 20 ms of filtered P-wave (RMS20).

Biochemical measurement

The following biochemical and haematological parameters were measured pre- and post-dialysis by using automated analyser: serum sodium, potassium, magnesium, calcium, phosphate, creatinine, urea, pH, bicarbonate, haematocrit, and haemoglobin (Hb). Serum albumin was determined by using standard patient check-up methods before the HD. Serum intact PTH (i-PTH) was measured by using ELISA before HD. The dialysis adequacy was evaluated by the estimation of equilibrated Kt/V [13]. Blood samples were taken immediately after the end of HD session (after 10–15 s of 50–100 ml/min blood flow).

Fluid balance assessment

Body weight loss induced by the HD process was calculated for each patient. A whole body bioimpedance technique was used for a spectrum of frequencies ranging from 5 to 500 kHz (Hydra 4008 Analyser, supplied by Xitron Technologies Inc.) to obtain the values of extracellular water (ECW), intracellular water (ICW) and total body water (TBW). Electrodes were placed on the wrist and on the ankle on the contralateral access side of the patient, as described elsewhere [14]. Throughout the dialysis, patients were in the supine position to eliminate the effect of position changes on bioimpedance volume estimation. Data was collected

Mean blood pressure

Mean blood pressure (MBP) was calculated from the following standard equation: \( \text{MBP} = \frac{1}{3} \text{of the systolic blood pressure} + \frac{2}{3} \text{of the diastolic blood pressure} \).
3 times at 15 s intervals before dialysis, and at the end of each HD [14].

Statistical analysis

Statistical analysis was carried out on an IBM PC using Statistica Version 5. Results were tested for normality. Data are expressed as mean ± SD, except data relating to i-PTH that is presented as median and range. The statistical significance of the differences between pre- and post-dialysis groups’ means were compared by Student’s t-test for paired data. Linear regression analysis was performed by using Pearson test. Multiple stepwise regression analysis was performed to estimate the potential influence of various factors on SAECG parameters. In the case of FDP and RMS20, the following independent parameters were entered into the model: age, duration of dialysis, PTH, albumin, pre-dialysis or post-dialysis values of sodium, potassium, calcium, phosphorus, magnesium, bicarbonate, Hb, urea, MBP and ECW/kg body weight. Probability values of less than 0.05 were accepted as significant.

Results

Baseline characteristics of the studied patients are shown in Table 1. Mean pre-dialysis Hb level was 10.91 ± 1.43, ranging from 8.60 to 14.02 g/dl. Twenty-three HD patients who (48.9%) qualified for the study had pre-dialysis Hb levels below 11 g/dl. Mean post-dialysis Hb level was 12.36 ± 1.58, ranging from 9.11 to 15.301 g/dl. Ten (21.3%) HD patients had post-dialysis Hb level below 11 g/dl.

As expected, serum levels of potassium and phosphorus decreased, while the serum level of calcium significantly increased during the HD process. No significant changes between pre-dialysis and post-dialysis measurements were found in sodium and magnesium serum levels. The values of pH and serum bicarbonate levels significantly increased post-dialysis. Changes in electrolytes and acid base parameters are presented in Table 2.

The TBW, ECW and ECW/TBW ratio significantly decreased post-dialysis. No statistically significant changes between pre-dialysis and post-dialysis measurements were found in ICW, whereas the ICW/TBW ratio increased significantly after the dialysis. Changes of whole body bioimpedance parameters associated with HD are shown in Table 3. Mean pre-dialysis vs post-dialysis body weight loss was 2370 ± 940, ranging from 600 to 4700 g. The results of the analysis performed by using the Pearson test showed significant correlations between pre- vs post-dialysis body weights loss and ΔTBW (r = 0.366, P = 0.011), as well as ΔECW (r = 0.648, P < 0.001). The relation between pre- and post-dialysis body weight loss and ΔICW was NS.
The durations of both pre- and post-dialysis FDP were significantly higher in patients than in the control group ($P < 0.001$ and $P = 0.005$, respectively). FDP values were higher than 140 ms in 38.3% of HD patients pre-dialysis and in 19.1% post-dialysis. RMS values were lower than 3.0 $\mu$V in 55% of HD patients pre-dialysis and in 29.8% post-dialysis. The voltage of both pre- and post-dialysis RMS20 were significantly reduced in HD patients compared with the control group ($P < 0.001$ in both cases). Haemodialysis process induced a significant decrease in the duration of the FDP and a significant increase in the voltage of RMS20 ($P < 0.001$ in both cases). Table 4 illustrates the P-wave SAECG parameters in HD patients (pre- and post-dialysis) and in the control group. No significant changes in any of the estimated parameters were found between men and women.

The results of the analysis performed by using the Pearson test showed significant correlations between (1) pre- and post-dialysis FDP and HD patients’ age ($r = 0.404$, $P = 0.005$ and $r = 0.496$, $P < 0.001$, respectively); (2) pre- and post-dialysis FDP and pre- and post-dialysis ECW/kg body weight ($r = 0.432$, $P = 0.002$ and $r = 0.452$, $P = 0.001$, respectively); (3) pre- and post-dialysis FDP and pre- and post-dialysis Hb levels ($r = -0.376$, $P = 0.009$ and $r = -0.401$, $P = 0.005$, respectively); (4) pre- and post-dialysis RMS20 and HD patients’ age ($r = -0.367$, $P = 0.011$ and $r = -0.398$, $P = 0.006$); (5) post-dialysis RMS20 and post-dialysis ECW/kg body weight ($r = -0.301$, $P = 0.040$).

Despite the significant changes in electrolyte concentrations (sodium, potassium, calcium, phosphorus and bicarbonate), there were no significant correlations between these changes and changes in FDP or RMS20 values. No significant correlations were also noted between changes in electrolyte concentrations and post-dialysis SAECG parameters.

Likewise, pre- and post-dialysis SAECG data as well as changes in SAECG parameters following HD showed no relationship to the estimated echocardiographic parameters.

The results of multiple regression analysis showing independent variables influencing the estimated P-wave SAECG parameters are presented in Table 5. The independent predictors of pre-dialysis FDP were: (1) age, (2) pre-dialysis ECW/kg body weight and (3) pre-dialysis Hb level. In the case of post-dialysis FDP, the independent predictors were: (1) age, (2) post-dialysis ECW/kg body weight and (3) post-dialysis Hb level. In the case of RMS20 we did not find any independent predictors of either pre- or post-dialysis.

### Discussion

Our study generated three major findings: (1) FPD was prolonged and RMS20 was reduced in the HD patients compared with the control group; (2) HD process improved the P-wave SAECG parameters; (3) HD patients’ age, low Hb level, and increased ECV volume were found to be independent predictors of the FDP.

Several studies have validated the role of P-wave SAECG as a non-invasive method for detecting patients at risk for paroxysmal AF in various clinical settings [3–8]. It is important to note, however, that there is a relatively large diversity of the results coming from various studies and no consensus about the cutoff values of P-wave SAECG parameters have ever been achieved. This is largely due to different methodological standards of filtering techniques, especially different noise end points and different definitions of onset and

### Table 3. Whole body bioimpedance parameters measured before (pre-dialysis) and after dialysis treatment (post-dialysis)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-dialysis</th>
<th>Post-dialysis</th>
<th>$P$ (pre- vs post-dialysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBW (l)</td>
<td>34.21 ± 7.95</td>
<td>32.07 ± 7.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TBW/kg b.w. (l/kg)</td>
<td>0.501 ± 0.07</td>
<td>0.488 ± 0.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ECW (l)</td>
<td>16.74 ± 3.10</td>
<td>14.26 ± 2.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ECW/kg b.w. (l/kg)</td>
<td>0.247 ± 0.028</td>
<td>0.219 ± 0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICW (l)</td>
<td>17.55 ± 5.24</td>
<td>17.89 ± 5.49</td>
<td>0.073</td>
</tr>
<tr>
<td>ICW/TBW (n)</td>
<td>0.498 ± 0.062</td>
<td>0.454 ± 0.069</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ECW/kg b.w. (l/kg)</td>
<td>0.247 ± 0.028</td>
<td>0.219 ± 0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Δ body weight</td>
<td>2.483 ± 0.85</td>
<td>2.483 ± 0.85</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Δ body weight, mean pre- vs post-dialysis body weight loss; TBW/kg b.w., TBW divided by body weight; ECW/kg b.w., ECW divided by body weight.

### Table 4. Comparison of the parameters measured before (pre-dialysis) and after dialysis treatment (post-dialysis) in patients and in the control group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-dialysis</th>
<th>Post-dialysis</th>
<th>Controls</th>
<th>$P$ (pre- vs post-dialysis)</th>
<th>$P$ (controls vs pre-dialysis)</th>
<th>$P$ (controls vs post-dialysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDP (ms)</td>
<td>137.5 ± 14.36</td>
<td>128.4 ± 15.56</td>
<td>116.6 ± 14.1</td>
<td>&lt;0.001</td>
<td>0.005</td>
<td>0.005</td>
</tr>
<tr>
<td>RMS20 (μV)</td>
<td>1.81 ± 0.44</td>
<td>2.62 ± 0.85</td>
<td>3.32 ± 0.77</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ΔFDP (ms)</td>
<td>9.18 ± 7.86</td>
<td>13.51 ± 10.28</td>
<td>20.89 ± 12.34</td>
<td>&lt;0.001</td>
<td>0.005</td>
<td>0.005</td>
</tr>
<tr>
<td>ΔRMS (μV)</td>
<td>−0.82 ± 0.80</td>
<td>−0.24 ± 0.38</td>
<td>−0.56 ± 0.48</td>
<td>&lt;0.001</td>
<td>0.401</td>
<td>0.102</td>
</tr>
</tbody>
</table>
offset of the filtered P-wave. Therefore it is difficult to compare our results directly to the available data from other studies.

We have demonstrated that both pre- and post-dialysis FPD were prolonged and RMS20 were reduced in the HD patients compared with the controls. In our study, the mean pre-dialysis FDP was 137.5 ± 14.36 ms and was comparable to that observed in patients with organic heart disease and paroxysmal AF [6], as well as patients after coronary artery bypass surgery developing paroxysmal AF [15]. In most studies, FDP values of >140 ms were considered abnormal [3–4]; however, other cutoff values were also proposed, ranging from 120 to 155 ms [8,16]. In the case of RMS20, the cutoff value ranges between 1.9 and 3.5 μV [6,7]. In our study, we found the that mean pre-dialysis RMS20 was 1.81 ± 0.44 and was comparable to that observed in patients at risk for recurrence of atrial fibrillation after successful electrical cardioversion [7], and was even lower than in patients with organic heart disease and paroxysmal AF [6,16]. Further research is needed to find out whether the P-wave SAECGs have the predictive value for AF risk estimation in HD patients.

The effect of HD was estimated exclusively with reference to ventricular SAECG. Some authors [9] reported the beneficial effect of HD process on ventricular SAECG, while others [10,11] observed that SAECG indices worsened during HD. The influence of fluid removal as well as changes in electrolyte concentration due to HD process on ventricular SAECG is not clear. Some authors [9,17] found the relation between volume overload and some SAECG parameters; others [10] contest this view. The relation between serum potassium reduction induced by HD and the increase of filtered QRS duration was also observed only by Morales et al. [10].

In our study, pre-dialysis P-wave SAECG parameters tended to improve after HD. Interestingly, significant changes in electrolyte levels could not be correlated with SAECG changes. The mechanism by which HD changed P-wave SAECG parameters could not be determined with certainty on the basis of our study. The association of FPD with increased ECW volume (ECW/kg body weight) is of considerable importance, because ECW volume can be modified by the HD process. The association of fluid overload and P-wave SAECG abnormalities can be explained on the basis of both experimental and clinical studies. Myocardial stretch due to excessive volume overload results in electrophysiological changes in refractoriness and conduction, essential components of re-entry and proarrhythmia, and can induce arrhythmias [17,18]. In HD patients, excess fluid accumulates within the ECV and fluid overload is a well-known factor leading to myocardial dysfunction, hypertension, cardiac arrhythmias, increasing inhomogeneities of myocardium repolarization phase and elevating cardiovascular mortality [17–19]. Further studies are required to determine the possible clinical importance of the relation between FPD and HD patients’ volume status. If more detailed studies of volume status estimation using complementary techniques (i.e. inferior vena cava diameter, vasoactive hormones) confirm our results, FPD may become useful haemodynamic parameter, helpful in patients’ dry weight estimation.

The incidence of AF is known to increase as patients get older either in general population [1] or in HD patients [2]. Taking into consideration that the population on dialysis is getting older, the relation between age and P-wave SAECG is of significance. In our study, HD patients’ age was the independent predictor of FPD. The association of FPD and age may give the evidence that age-related atrial conduction delay observed by some authors in healthy subjects [3] or patients with lone paroxysmal AF [5] is also present in HD patients and is detectable by the results of the P-wave SAECG.

In our study, Hb level was the independent factor that inversely affected the FPD. According to our knowledge, the association of Hb levels and FPD has not been previously reported in the literature. Widespread consensus exists that anaemia is an independent risk factor of cardiac diseases and poor outcome either in the general population or in HD patients correlating with the incidence of ischaemic heart disease, heart failure, cardiac arrhythmias and increased mortality [17]. In the studied population, only 51% HD patients matched the pre-dialysis target Hb level of 11 g/dl recommended in the National Kidney

### Table 5. Factors influencing signal-averaged P-wave duration estimated by multivariate stepwise regression analysis

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variables</th>
<th>B</th>
<th>St. error</th>
<th>Beta</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-dialysis</td>
<td>Model (R = 0.578, R² = 0.334)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0.407</td>
<td>0.143</td>
<td>0.356</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>ECW1/kg b.w.</td>
<td>1.435</td>
<td>0.578</td>
<td>0.310</td>
<td>0.017</td>
</tr>
<tr>
<td></td>
<td>Haemoglobin</td>
<td>−2.474</td>
<td>1.174</td>
<td>−0.264</td>
<td>0.041</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>118.8</td>
<td>17.81</td>
<td>&lt;0.000</td>
<td></td>
</tr>
<tr>
<td>Post-dialysis</td>
<td>Model (R = 0.660, R² = 0.436)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0.506</td>
<td>0.145</td>
<td>0.409</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>ECW2/kg b.w.</td>
<td>1.980</td>
<td>0.643</td>
<td>0.357</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>Haemoglobin</td>
<td>−1.995</td>
<td>0.983</td>
<td>−0.237</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>98.56</td>
<td>17.41</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

ECW1/kg b.w., pre-dialysis ECW value divided by pre-dialysis body weight; ECW2/kg b.w., post-dialysis ECW value divided by post-dialysis body weight.
Foundation’s Kidney Disease Outcomes Quality Initiative guidelines [20]. Further studies are required to determine the possible clinical importance of the relation between Hb level and P-wave SAECG parameters.

The limitations of our study include the relatively small patient numbers and the impossibility of controlling all possible factors that might influence P-wave SAECG parameters. Further studies are required to confirm our results as well as determine possible clinical importance of P-wave SAECG parameter estimation in HD patients.

Our study indicated that P-wave SAECG parameters are abnormal in a significant proportion of HD patients and improve with HD process. We have also demonstrated that patients’ age, volume status as well as the presence of anaemia are important factors influencing P-wave SAECG parameters in HD patients.

Conflict of interest statement. None declared.

References


Received for publication: 5.2.05
Accepted in revised form: 2.9.05