Heart Rate Variability during Hemodialysis and Its Relation to Hypotension

D Hernando, R Bailón, P Laguna, L Sörnmo

1Communications Technology Group (GTC), Aragon Institute for Engineering Research (I3A), IIS Aragon, University of Zaragoza, Zaragoza, Spain
2CIBER BBN of Bioengineering, Biomaterials and Nanomedicine, Spain
3Signal Processing Group, Department of Electrical and Information Technology, Lund University, Lund, Sweden

Abstract

Acute hypotensive episodes are common during dialysis sessions, and represent a serious problem. Spectral analysis of heart rate variability (HRV) and baroreflex sensitivity (BRS) is performed to study the behaviour of the autonomic nervous system (ANS) during the hemodialysis. The ratio between the low frequency (LF) and high frequency (HF) power of HRV, as well as BRS in the HF band, are significantly different in patients being prone and resistant to hypotension (p<0.001 and p<0.05, respectively).

Moreover, a very low frequency (VLF) modulation visible in HRV, blood pressure and the series of rotation angles of the heart’s electrical axis have been studied. It turns out that the VLF component is more pronounced and with higher coherence in prone patients (p<0.05), suggesting a possible relation with altered or imbalanced ANS regulation.

1. Introduction

Dialysis-induced hypotension is an important problem in hemodialysis treatment and approximately 30% of all sessions are complicated by cardiocirculatory collapse, leading to premature termination. The origin is still not completely known, but it is clearly multifactorial, and may depend on factors like diabetes and overweight. Hypotension not only causes termination of the session, but may also increase mortality in these patients [1, 2]. This type of event leads to higher costs and an increased need for medical service, extra time and the prolongation of patient rehabilitation. In spite of the improvement of technology and research in this field, hypotension is still one of the most common complication, and it is highly desirable to develop methods to prevent these events.

Spectral analysis of heart rate variability (HRV) is a non-invasive tool which assesses changes of the autonomic nervous system (ANS). Three bands are established in the power spectrum of HRV [3]: very low frequency (VLF: < 0.04 Hz), low frequency (LF: 0.04 to 0.15 Hz) and high frequency (HF: 0.15 to 0.4 Hz). The HF component is considered to be a marker of the parasympathetic activity, being sensitive to the respiratory frequency. The LF component is a marker of the sympathetic modulation, at least when measured in normalized units. Lastly, the VLF component has been linked with humoral and temperature regulation and with slow vasomotor activity. The ratio between the power of LF and HF components is considered to provide an index of sympatho-vagal balance.

Baroreflex sensitivity (BRS) measures reflex changes in interbeat interval induced by changes in arterial pressure, and may reflect impaired ANS regulation [4].

The hypothesis of this study is that hypotension may be related to impairment in autonomic regulation of the cardiovascular system. We studied HRV and BRS in a database of patients undergoing hemodialysis to determine whether hypotensions and/or patients prone to suffer hypotension can be predicted from HRV and BRS measurements. The following parameters have been studied: HRV through the normalized power in the LF and HF bands and the LF/HF ratio, BRS through spectral coherence between HRV and blood pressure variability (BPV) (only computed when a statistically determined threshold is exceeded), and VLF modulation in HRV, BPV and rotation angles of the hearts electrical axis through spectral coherence.

2. Methods and materials

2.1. Study population

The population consists of 16 patients with end-stage renal failure who underwent regular hemodialysis three times a week, and a total of 30 sessions were acquired during the entire clinical treatment at Park Dialyse, Lund,
2.2. Heart rate variability

First, QRS detection marks are obtained from the ECG signal by ARISTOTLE [5], using a rule based on the QRS complex center of gravity. The heart rate (HR) signal is derived from the QRS detection marks, following a method based on the integral pulse frequency modulation (IPFM) model, which also accounts for the presence of ectopic beats [6], and denoted by ARISTOTLE [5], using a rule based on the QRS complex center of gravity. The heart rate (HR) signal is derived from the QRS detection marks, following a method based on the integral pulse frequency modulation (IPFM) model, which also accounts for the presence of ectopic beats [6].

The ECG was recorded using a standard 12-lead configuration, and digitized at a sampling rate of 1000 Hz and amplitude resolution of 0.06 μV (Siemens-Elema AB, Sweden); the blood pressure signal was measured in the finger using a Finapres (Ohmeda, Netherlands) and sampled at a rate of 200 Hz with a MP100 data acquisition system (Biopac, USA).

The subsequent analysis was performed in 5-minute segments where stationarity of the cardiovascular signals was assumed.

During hemodialysis, some patients present a large amount of ectopic beats. Ectopic beats, false detections and misdetections, hereinafter called incidences, were detected and corrected prior to the estimation of \( d_{in}(n) \) based on [6]. The number of incidences, \( I \), in each segment was also computed and analyzed in relation to hypotension and as a measure of the reliability of HRV-derived parameters.

2.3. Baroreflex sensitivity

Systolic blood pressure measures are obtained detecting the maximum value of each pulse wave, using a method based on the derivative of the BP signal and a time-varying threshold. From the value and location of each maximum the systolic blood pressure signal, \( d_{in}(n) \), is computed using spline interpolation at 4 Hz. Using the same procedure as in the previous section, the following signals and parameters are computed: \( d_{in}(n) \), \( d_{in}(n) \), \( P_{LF}^{n} \), \( P_{HF}^{n} \), \( P_{LF}^{n} \) and \( P_{HF}^{n} \).

Then, BRS parameters are computed in the LF and HF bands as [7]: \( \alpha_{LF} = \frac{P_{LF}^{n}}{P_{HF}^{n}} \) and \( \alpha_{HF} = \frac{P_{HF}^{n}}{P_{LF}^{n}} \), respectively.

BRS parameters are considered only if the spectral coherence between \( d_{in}(n) \) and \( d_{in}(n) \) is above a statistically determined threshold of 0.7. The threshold is determined as the 97th percentile of the statistical distribution of the maximum value of the spectral coherence between two white noises. Spectral coherence is estimated using the minimum variance distortionless response (MVDR) method [8], which presents higher spectral resolution than Welch periodogram, which is needed especially in the study of VLF modulation (see Section 2.5).

2.4. Series of rotation angles

The series of rotation angles of the heart’s electrical axis are estimated from the ECG using a least squares minimization of the normalized distance between a reference QRS-vectorcardiographic loop and each observed loop subjected to rotation, amplitude scaling and time synchronization [9]. The envelope of each of the three rotation angles is low-pass filtered using a cut-off frequency of 0.03 Hz, and denoted \( \varphi_{x,y}(n) \), \( \varphi_{x,y}(n) \) and \( \varphi_{z,y}(n) \).

2.5. VLF modulation

The MVDR method is used to estimate the spectral coherence between \( d_{x,y}(n) \), \( d_{x,y}(n) \) and the envelopes of the rotation angle series for each 5-min segment. For segments with a maximum coherence value exceeding the threshold (0.7), the value and the location of the maximum are calculated and denoted \( \Gamma_{x,y} \) and \( \Gamma_{x,y} \), respectively, where \( X_{1} \) and \( X_{2} \) represent \( d_{x,y}(n) \), \( d_{x,y}(n) \), or \( \varphi_{x,y}(n) \), \( \varphi_{x,y}(n) \) being the envelope showing the highest coherence among \( \varphi_{x,y}(n) \), \( \varphi_{x,y}(n) \) and \( \varphi_{z,y}(n) \).

### Table 1. Study population characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>R</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td># Patients</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td># Measurements</td>
<td>11</td>
<td>19</td>
</tr>
<tr>
<td>Male/Female</td>
<td>6/1</td>
<td>6/3</td>
</tr>
<tr>
<td>D / ND</td>
<td>3/4</td>
<td>5/4</td>
</tr>
<tr>
<td>Age (year)</td>
<td>58.6 ± 13.5</td>
<td>65.6 ± 10.6</td>
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<tr>
<td>Weight (kg)</td>
<td>86.9 ± 19.5</td>
<td>83.1 ± 19.9</td>
</tr>
</tbody>
</table>
Table 2. Median±MAD of HRV and BRS parameters in prone (P) and resistant (R) groups. NS: non-significant, p > 0.05.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P</th>
<th>R</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$I_{LF}$</td>
<td>0.43 ± 0.03</td>
<td>0.79 ± 0.01</td>
<td>&lt;0.0005</td>
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<tr>
<td>$I_{LF}$</td>
<td>0.77 ± 0.05</td>
<td>3.99 ± 0.71</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>$I$</td>
<td>2 ± 1</td>
<td>5.5 ± 3</td>
<td>NS</td>
</tr>
<tr>
<td>$\alpha_{LF}^{2}$</td>
<td>0.26 ± 1.0e-04</td>
<td>1.83 ± 1.8e-04</td>
<td>NS</td>
</tr>
<tr>
<td>$\alpha_{HF}^{2}$</td>
<td>0.24 ± 1.2e-05</td>
<td>4.64 ± 9.2e-05</td>
<td>&lt;0.05</td>
</tr>
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Table 3. Median±MAD of HRV and BRS parameters PD and RD groups. NS: non-significant, p > 0.05.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PD</th>
<th>RD</th>
<th>p-value</th>
</tr>
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<tr>
<td>$I_{LF}$</td>
<td>0.28 ± 0.02</td>
<td>0.60 ± 0.01</td>
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<tr>
<td>$I_{LF}$</td>
<td>0.38 ± 0.06</td>
<td>1.53 ± 0.12</td>
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<tr>
<td>$\alpha_{LF}^{2}$</td>
<td>0.23 ± 1.2e-05</td>
<td>3.69 ± 9.2e-05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 4. Median±MAD of HRV and BRS parameters PND and RND groups. NS: non-significant, p > 0.05.

\[ \varphi_{\Delta X}(n), \] where the VLF modulation is visible. Table 5 shows the p-value corresponding to the parameters which characterize VLF modulation in P and R groups, as well as in D and ND groups. While there are not significant differences in VLF parameters in D and ND groups, P and R groups show significantly different maximum coherence values and different periods of time where the coherence is above the threshold.

### 4. Discussion and conclusion

Despite the fact that different approaches to reducing the incidence of intradialytic hypotension have been proposed and extensively evaluated in recent years, the problem has not yet found a satisfactory solution. Many patients suffer from a large number of ectopic beats, sometimes implying...
that the HRV analysis may not be reliable, so that alternate measurements of ANS activity can be helpful [10]. Still, knowledge on ANS by HRV analysis is desirable, and it has been shown that such analysis can be used to classify a patient into prone or resistant. The origin of this VLF modulation is still uncertain and it may be related to other fields, where it has also been observed [13, 14].

### References


