Prediction of Intradialytic Hypotension using PPG and ECG

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Abstract

Intradialytic hypotension (IDH) is the most common complication during hemodialysis; early prediction and prevention of IDH would dramatically improve the living conditions for patients with end stage renal disease. A recently published study suggests that a decrease in the envelope of the photoplethysmography (PPG) signal can be used for predicting acute symptomatic IDH. In the present study, the PPG based method is extended by introducing a patient dependent detection threshold, which involves information on heart rate variability (HRV) and heart rate turbulence (HRT) from the current dialysis session. This is motivated since several studies have found significant differences in HRV and HRT between hypotension-prone and hypotension-resistant patients. Recordings from 15 patients during 38 hemodialysis sessions were used to evaluate the method. Symptomatic IDH was correctly predicted in 9 out of 14 cases, while 5 out of 24 cases were falsely predicted. The performance was better for acute symptomatic IDH, 5 out of 5 cases were correctly predicted. The present method represents a novel approach to combining information derived from ECG and PPG signals.

1. Introduction

Hemodialysis is since long a well-established treatment of patients with end stage renal decease (ESDR). The treatment improves dramatically the living conditions for this group of patients, but it is also associated with episodes of intradialytic hypotension (IDH) which occur in approximately 25\% of all sessions, thereby making IDH the most common complication during hemodialysis [1].

In many hospitals, the clinical management of IDH remains synonymous to the placement of the patient in Trendelenburg position, i.e., supine body position with the feet held higher than the head [2]. This placement is accompanied with substantial slowing of the ultrafiltration rate so that the reduction in blood volume due to fluid removal is slowed down. These types of actions are invoked when the patient already exhibits symptoms, and it is therefore highly desirable to detect episodes of IDH well in advance so that appropriate measures can be taken.

A recently presented approach to the prediction of acute symptomatic IDH is based on the assumption that capillary vasoconstriction precedes acute symptomatic hypotension [3]. The magnitude of the normalized PPG envelope was used as input data to a test statistic which, when dropping below a fixed threshold, produced a prediction. Heart rate variability (HRV) has been extensively studied for the purpose of discriminating patients prone to hypotension from those who are resistant, but has not been used for real-time prediction [4]. Most studies have concluded that the spectral power can be be used for discrimination, e.g., the ratio between low- and high-frequency power.

The frequent occurrence of ventricular premature beats (VPBs) in dialysis patients renders it possible to study heart rate turbulence (HRT), being a short-term fluctuation in heart rate triggered by a VPB [4]. Blunted or missing HRT reflects autonomic dysfunction, and autonomic neuropathy has been associated with a marked fall in blood pressure during hemodialysis [5]. Consequently, HRT characterization has been suggested as a means to determine a patient’s propensity to IDH [6].

The purpose of the present study is to extend the predictor structure proposed in [3] to include a patient-dependent threshold which involves information on HRV and HRT. In doing so, different thresholds can be applied to patients which are prone and resistant to IDH.

2. Methods

An overview of the predictor is provided by the block diagram in Fig. 1. The upper branch transforms the PPG signal into a test statistic which is performed in a sliding window; the PPG preprocessing is identical to that described...
in [3]. In the lower branch of the block diagram, HRV and HRT are computed from the ECG for use in the patient-dependent threshold. The predictor, also referred to as the detector, is based on the hypothesis that a decrease in the normalized PPG envelope \( x[n] \) reflects capillary vasoconstriction and decreased cardiac output which precede IDH (the normalized envelope is produced by the preprocessor) [3]. This hypothesis is translated to a problem of detecting a change in level of \( x[n] \) in a window that slides in time as new data becomes available. The level detection problem is first treated below for a fixed window, indexed by \( m \), after which it is straightforward to modify the detector for a sliding window.

The detection problem is modeled as one of choosing between hypothesis \( H_0 \), in which no change has occurred, i.e., the level is \( A = 1 \), and hypothesis \( H_1 \), when the level reduces to \( A = 1 - \Delta A \) due to an approaching IDH:

\[
H_0 : x[m] = 1 + w[m], \quad m = 0, 1, \ldots, N - 1, \quad (1)
\]

\[
H_1 : x[m] = 1 - \Delta A + w[m], \quad m = 0, 1, \ldots, N - 1, \quad (2)
\]

where \( N \) is the number of samples in the fixed window, and \( \Delta A (0 < \Delta A \leq 1) \) is the unknown reduction in level. The Laplacian model is employed since it better characterizes the noise than the Gaussian model [3]; \( w[m] \) is assumed to be independent and identically distributed, zero-mean with known variance \( \sigma^2 \).

A generalized likelihood ratio test (GLRT) was employed in which \( \Delta A \) is first estimated using maximum likelihood (ML) estimation; thus, the GLRT decides \( H_1 \) if

\[
L_G(x) = \frac{p(x; \hat{A}, H_1)}{p(x; H_0)} > \frac{p(H_0|\theta)}{p(H_1|\theta)} \gamma', \quad (3)
\]

where \( x \) is a vector with the observations \( x[0], x[1], \ldots, x[N-1] \), \( p(x; H_0) \) denotes the probability density function (PDF) of \( x \) under \( H_0 \), \( p(x; \hat{A}, H_1) \) denotes the probability density function (PDF) of \( x \) under \( H_1 \) when the parameter \( A \) is replaced by its maximum likelihood estimate, and \( \gamma' \) is a fixed threshold. The probability \( p(H_1) \) is chosen such that it reflects a patient’s proneness to IDH, e.g., based on the clinical history of the patient or, as done in the present study, based on information conveyed by cardiac activity. The other prior probability is \( p(H_0) = 1 - p(H_1) \).

When \( H_1 \) is true, the ML estimate of \( A \), denoted by \( \hat{A} \), is given by the median of the observations for Laplacian noise. Taking the constraint \( 0 < \Delta A \leq 1 \) into account, the ML estimator is given by

\[
\hat{A} = \min(1, \text{median}\{x[0], x[1], \ldots, x[N-1]\}). \quad (4)
\]

Inserting the Laplacian PDFs in (3) the GLRT gives that \( H_1 \) is decided if

\[
G(x) = 1 + \frac{1}{N} \sum_{m=0}^{N-1} \left( |x[m] - \hat{A}| - |x[m] - 1| \right) > 1 - \frac{1}{N} \sqrt{\frac{\sigma^2}{2}} \ln \left( \frac{p(H_0|\theta)}{p(H_1|\theta)} \gamma' \right). \quad (5)
\]

It is obvious from this equation that the optimal GLRT detector computes the difference between the mean absolute deviation from \( \hat{A} \) and the mean deviation from 1 and compares it to a threshold which depends on \( N, \sigma^2, \gamma' \) as well as on the prior probabilities \( p(H_0|\theta) \) and \( p(H_1|\theta) \). The test statistic is made time-varying, and then denoted \( G(x[n]) \), by simply computing it in a sliding window containing \( x(n), x(n + 1), \ldots, x(n + N - 1) \). The window length is here set to 5 minutes.

Since \( p(H_1|\theta) \) is the probability of IDH, the threshold in (6) can be viewed as being composed of a fixed part \( \gamma_f \) and a patient-dependent part \( \gamma_p \),

\[
\gamma = \gamma_f + \gamma_p, \quad (6)
\]

where

\[
\gamma_f = 1 - \frac{1}{N} \sqrt{\frac{\sigma^2}{2}} \ln \left( \gamma' \right), \quad (7)
\]

\[
\gamma_p = -\frac{1}{N} \sqrt{\frac{\sigma^2}{2}} \ln \left( \frac{1 - p(H_1|\theta)}{p(H_1|\theta)} \right). \quad (8)
\]

It is noted that \( \gamma_f \) is identical to the fixed threshold applied in [3], whereas \( \gamma_p \) is novel. In the present study, \( \sigma^2 \) is fixed and set to 0.2 which correspond to a noise level generally found in the normalized PPG envelope, and \( \theta \) consists of two random variables \( \theta_1 \) and \( \theta_2 \), reflecting HRV and HRT.
Spectral analysis of HRV assesses changes in the autonomic nervous system by measuring the power of the low frequency (LF) and the high frequency (HF) bands, defined by 0.04–0.15 Hz and 0.15–0.4 Hz, respectively. The ratio between LF and HF power is considered to be a measure of sympathovagal balance. Since the LF/HF ratio has been related to a patient’s propensity to IDH [4], the LF/HR ratio is taken to define $\theta_1$. Using the method in [7], the ratio is computed during the initial 30 min of the dialysis session when hypotensive events are unlikely to occur.

Heart rate turbulence can be characterized with various parameters of which turbulence onset (TO) and turbulence slope (TS) are the most popular [8]. In the present study, TS is studied since it was significantly different between patients prone and resistant to IDH [6], while this was not the case for TO. Thus, TS defines the random variable $\theta_2$. For both $\theta_1$ and $\theta_2$, smaller values suggest that the patient is more prone to IDH.

Using Bayes’ rule, the conditional probability of IDH can be expressed as

$$p(\mathcal{H}_1|\theta_1, \theta_2) = \frac{p(\theta_1|\mathcal{H}_1)p(\theta_2|\mathcal{H}_1)p(\mathcal{H}_1)}{p(\theta_1|\mathcal{H}_0)p(\theta_2|\mathcal{H}_0)p(\mathcal{H}_0) + p(\theta_2|\mathcal{H}_1)p(\theta_1|\mathcal{H}_1)p(\mathcal{H}_1)}.$$  (9)

For simplicity, all four conditional PDFs that characterize $\theta_1$ and $\theta_2$ in (9) are assumed to be Gaussian, i.e.,

$$p(\theta_j|\mathcal{H}_i) = \mathcal{N}(\bar{\theta}_j|\mathcal{H}_i, \sigma_{j|\mathcal{H}_i}) \quad i = 0, 1, \quad j = 1, 2. \quad (10)$$

A leave-one-out strategy was employed to determine the estimates of the mean $\bar{\theta}_{j|\mathcal{H}_i}$ and the standard deviation $\sigma_{j|\mathcal{H}_i}$: when computing $p(\mathcal{H}_1|\theta_1, \theta_2)$ for one recording, the remaining ones were used for estimation. The prior probabilities in (9) are assumed to be equal, i.e., $p(\mathcal{H}_0) = p(\mathcal{H}_1) = 0.5$ [3].

3. Database

Two datasets are studied for performance evaluation, both recorded at Rigshospitalet in Copenhagen, Denmark. The first dataset (“Db1”) consists of 24 recordings from 11 hypotension-prone patients, and the second dataset (“Db2”) consists of 20 recordings from 7 patients, both hypotension-prone and resistant. Blood pressure, PPG, and the ECG were recorded using the Biopac MP150 data acquisition system (BIOPAC Systems Inc., USA) in parallel with the conventional hemodialysis equipment.

Symptomatic IDH is defined according to the following criteria [4]:

- if pre-dialysis systolic arterial pressure (SAP) was $\geq$ 100 mmHg: any event with SAP $\leq$ 90 mmHg, associated with complaints;
- if SAP was $\leq$ 100 mmHg: any SAP reduction by at least 10% associated with complaints.

Figure 2. The test statistic $G(x[n])$ (blue line), $\gamma_f$ (dotted blue line), and $\gamma$ (dashed green line), using $\gamma_f = 0.6$. Vertical red line indicates time of acute symptomatic IDH. Note that the thresholds coincide for the patient with acute symptomatic IDH.

Acute symptomatic IDH is defined by a sudden drop in systolic blood pressure (30 mmHg per 10 min before hypotension).

Two different issues were investigated with respect to IDH prediction. Firstly, prediction of acute symptomatic IDH was evaluated on Db1, since Db2 did not contain any such event. The dataset Db1 was divided into two groups: patients with acute symptomatic IDH and patients without symptomatic IDH, containing 5 and 14 recordings, respectively. Secondly, prediction of symptomatic IDH (both acute or non-acute) was evaluated by combining Db1 and Db2 and then dividing the resulting dataset into two groups: patients with and patients without symptomatic IDH. After exclusion of PPG recordings with poor signal quality (at least 20% of the 5-min segments did not reflect hear rate), the two groups contained 14 and 24 recordings.

4. Results

The prediction of IDH is illustrated for one patient with chronic symptomatic IDH and another patient without symptomatic IDH, see Fig. 2. The thresholds $\gamma$ and $\gamma_f$ are practically identical in the recording with acute symptomatic IDH, see Fig. 2(a), whereas $\gamma$ is lower than $\gamma_f$ for the patient without symptomatic IDH, see Fig. 2(b). The reason for a lower $\gamma$ in the latter case is that the HRV/HRT values indicates that this patient is less prone to IDH. In the former case the HRV/HRT values did not add any information about the patient’s propensity to IDH.
Table 1. Sensitivity and specificity in predicting acute symptomatic IDH and symptomatic IDH, respectively.

<table>
<thead>
<tr>
<th>γ_f</th>
<th>Acute Symptomatic IDH</th>
<th>Symptomatic IDH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>0.4</td>
<td>40%</td>
<td>100%</td>
</tr>
<tr>
<td>0.6</td>
<td>100%</td>
<td>93%</td>
</tr>
<tr>
<td>0.8</td>
<td>100%</td>
<td>64%</td>
</tr>
</tbody>
</table>

Table 2. HRV and HRT results from recordings with acute symptomatic IDH and no symptomatic IDH in Db1.

<table>
<thead>
<tr>
<th></th>
<th>Acute Symptomatic IDH</th>
<th>No Symptomatic IDH</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$x_{HRT}$</td>
<td>1.11 ± 1.00</td>
<td>2.87 ± 3.67</td>
<td>N.S.</td>
</tr>
<tr>
<td>$x_{HRV}$</td>
<td>1.48 ± 1.42</td>
<td>2.06 ± 1.89</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

The sensitivity and specificity in predicting acute symptomatic IDH and symptomatic IDH, respectively, is displayed in Table 1 for different values of $\gamma_f$. Setting the fixed threshold $\gamma_f$ to 0.6, acute symptomatic IDH was correctly predicted in 5 out of 5 recordings and falsely in 1 out of 14 recordings, whereas symptomatic IDH was correctly predicted in 9 out of 14 recordings and falsely in 5 out of 24 recordings. In all cases, the prediction results obtained with $\gamma_f$ were virtually identical to those obtained for $\gamma_f$.

To shed light on the above results, the parameters $\theta_1$ and $\theta_2$ were compared for the sessions in Db1 with acute symptomatic IDH without symptomatic IDH, respectively, see Table 2. Both $\theta_1$ and $\theta_2$ were lower in the recordings with acute symptomatic IDH, although the differences were not significant. HRT computation was feasible in 5 out of 5 recordings with acute symptomatic IDH, and 9 out of 14 recordings without symptomatic IDH. For the present datasets, the results suggest that information on HRV and HRT does not improve prediction performance significantly.

5. Conclusions

An extension to the PPG based method for predicting IDH [3] is presented. The method takes into account the magnitude of the PPG signal as well as the a priori probability of a patient developing IDH during each specific dialysis session; HRV and HRT estimated from the ECG in each dialysis session is used to determine these a priori probabilities. The prediction performance is promising, as 5 out of 5 episodes of acute symptomatic IDH could be accurately predicted.

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References


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