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Identification of patients prone to hypotension during hemodialysis based on the analysis of cardiovascular signals

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ABSTRACT

Intradialytic hypotension (IDH) is a major complication during hemodialysis treatment, and therefore it is highly desirable to identify, at an early stage during treatment, whether the patient is prone to IDH. Heart rate variability (HRV), blood pressure variability (BPV) and baroreflex sensitivity (BRS) were analyzed during the first 30 min of treatment to assess information on the autonomic nervous system. Using the sequential floating forward selection method and linear classification, the set of features with the best discriminative power was selected, resulting in an accuracy of 92.1%. Using a classifier based on the HRV features only, thereby avoiding that continuous blood pressure has to be recorded, accuracy decreased to 90.2%. The results suggest that an HRV-based classifier is useful for determining whether a patient is prone to IDH at the beginning of the treatment.

1. Introduction

Hemodialysis is a well-established treatment for patients with severe kidney problems. A serious problem during treatment is intradialytic hypotension (IDH), which occur in about 20% of all sessions [1], causing symptoms such as dizziness and vertigo, and possibly also premature termination of the session [1,2]. The causes of hypotension are multifactorial, of which the primary factor is the decrease in blood volume that occurs during hemodialysis. This decrease results from fluid withdrawal of the vascular compartment during ultrafiltration and insufficient refilling of fluid from the interstitial compartment to the vascular compartment. Other factors include impaired peripheral vasoconstriction, autonomic dysfunction, arteriosclerosis, cardiovascular pathologies, hydration, and medication [3]. The occurrence of IDH not only leads to higher costs and increased need for medical service, but, more seriously, to increased mortality [4,5]. Therefore, it is desirable to determine, at an early stage of each treatment, whether a patient is prone or resistant to IDH.

Spectral analysis of heart rate variability (HRV) is a well-known technique for assessing information on the autonomic nervous system (ANS). The following two frequency bands are commonly studied [6]: high frequency (HF: 0.15 to 0.4 Hz) and low frequency (LF: 0.04 to 0.15 Hz). The HF power component mostly reflects parasympathetic activity, being influenced by respiration. The LF power component largely reflects sympathetic modulation when normalized with respect to LF and HF bands [6]. The ratio between the power of the LF and HF components is considered to be an index of sympathovagal balance [6]. Several studies have already investigated HRV information in hemodialysis patients, mainly the LF/HF ratio [4,7,8]. For example, it has been observed that the LF component tends to dominate during sessions without IDH in the sympathovagal balance when measuring the LF/HF ratio [9], and the power of this ratio drops markedly at the time of crisis in sessions with hypotension [10].

In terms of normal cardiovascular control, changes in the regulation of the heart rate produced by the ANS can be expected to affect blood pressure regulation as assessed by blood pressure variability (BPV). With respiration, arterial blood pressure typically falls on inspiration and rises on expiration, thus affecting the HF component of BPV. The LF component is related to variations in the sympathetic nervous system mediated through vasoconstriction, as well as to the interaction between vasoactive agents and hormones and the autoregulatory processes [11]. Usually, HRV and BPV exhibit high coherence so that baroreflex sensitivity (BRS) can be computed.

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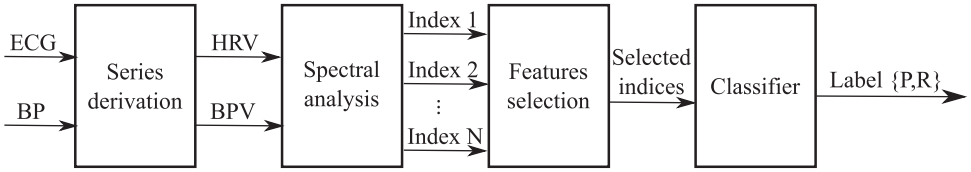

Fig. 1. Framework.

BRS indices characterize RR interval changes induced by changes in arterial pressure, and reflect impaired autonomic regulation [12]. BRS indices have been studied before in hemodialysis patients, the results suggesting that such indices cannot discriminate between IDH prone and resistant patients [13].

The hypothesis of this study is that IDH is related to impaired autonomic regulation of the cardiovascular system. A novelty is that information from both the electrocardiogram (ECG) and the blood pressure (BP) signal is combined to assess ANS activity. As another novelty, only the first 30 min of the treatment are analyzed, when hypotensive events are unlikely to occur [14], for characterizing the ANS status in prone and resistant patients.

From the ECG and BP signals, HRV, BPV and BRS related indices are extracted and studied in terms of their power to discriminate between IDH prone and resistant patients, see Fig. 1. A multivariate classifier is designed which analyzes the signals at the beginning of the treatment, and which makes use of information on diabetes since ANS is usually impaired in diabetic patients. A simplified classifier is also studied which does not require information on blood pressure, as it is costly and cumbersome to record continuously.

2. Database

Two databases have been analyzed from patients with endstage renal failure on hemodialysis treatment thrice a week, each session lasting between 2 and 5 h. Both databases contain ECG and BP signals. The continuous arterial blood pressure signal was acquired with a Finapres (Finapres Medical Systems BV, Holland) and sampled at 200 Hz with a Biopac (BIOPAC Systems Inc., USA) data acquisition system. The ECG was recorded during dialysis using the standard 12-lead configuration, and sampled at a rate of 1000 Hz. Synchronization between the ECG and BP signals was performed manually, leading to a misalignment on the order of magnitude of a few ms, which has negligible significance in the present application.

The first database consists of 28 sessions from 15 patients (the number of sessions for each patient varies from 1 to 4, see Table 1) treated at Park Dialys, Lund, Sweden, and Helsingborg Hospital, Helsingborg, Sweden [7]. Each patient was classified by a nephrologist as either resistant (R) or prone (P) to IDH based on the clinical history, e.g., the number of hypotensive events per month. The second database consists of 29 sessions from 11 patients. These patients underwent hemodialysis treatment in Copenhagen, Denmark. Due to poor quality of the BP signal, 5 sessions had to be excluded so that only 24 sessions from 9 patients were used for BPV and BRS analysis. Based on clinical history, all patients in the second database were classified as prone to IDH. The databases were merged and a total of 52 sessions from 24 patients were analyzed of which 21 sessions belonged to 10 patients with diabetes, see Table 1.

Table 1
Study population characteristics.

Characteristic	Resistant	Prone
# Patients/# Sessions	7/11	17/41
# Ses. each patient	2,1,1,2,1,2,2	2,1,2,1,4,4,3,2,2,3,4,2,2,1,2,3,3
# Diabetic patients/# Ses.	3/4	7/17
Male/Female	6/1	9/8
Age (years)	59 ± 14	65 ± 11
Weight (kg)	87 ± 20	77 ± 20

3. Methods

3.1. Heart rate variability

The beat occurrence times t_k are obtained from the ECG using a multi-lead wavelet-based detector [15]. The heart rate signal is derived from t_k using a method based on the integral pulse frequency modulation model. This method assumes that ANS activity can be modeled as a modulating signal $m(t)$ which, together with a DC level, is integrated until it reaches a threshold T, when a beat occurs and the process is reset [16]. The threshold T represents the mean interval length between successive beats in the analyzed interval. From t_k, the instantaneous heart rate is obtained as [17]:

$$d_{\mathrm{HR}}(t) = \frac{1 + m(t)}{T} \tag{1}$$

where $1/T$ represents the mean heart rate and $m(t)/T$ represents the heart rate variability. The signal $d_{\mathrm{HR}}(t)$ is sampled with a rate of $F_s = 4$ Hz to produce the discrete signal $d_{\mathrm{HR}}(n) = d_{\mathrm{HR}}(t)|_{t=n\frac{1}{F_s}}$.

3.2. Blood pressure variability

The blood pressure signal is low-pass filtered with a cut-off frequency of 40 Hz (forward/backward filtering) to remove noise. The peaks of the low-pass filtered signal, $s(n_k)$ (discrete-time), are found by locating the zero crossings of the differentiated signal, implemented by the first order difference: $s'(n) = s(n) - s(n-1)$, where $s(n)$ is the low-pass filtered blood pressure signal. A protective rule is applied to the detected peaks, imposing a refractory period to make sure that a certain distance elapses between successive beat detections. The distance is set to 0.5 s.

Signal segments lost due to calibration of the blood pressure device need to be detected and removed from further analysis. An amplitude threshold is used in successive 5-min segments, where a "gap" is found if there is more than 5 s without any valid peak above the threshold. The pairs $(n_k, s(n_k))$ are interpolated using cubic splines to generate the systolic blood pressure signal $d_{\mathrm{BP}}(n)$ sampled at a rate of 4 Hz. If the segment contains a gap, $d_{\mathrm{BP}}(n)$ is obtained using a shorter segment which does not contain that gap, as long as it exceeds 3 and a half minute. If shorter, the segment is removed for further analysis.

3.3. Spectral indices

Classification of resistant and prone patients is based on a set of spectral parameters determined during the first 30 min of the treatment session. The minimum variance distortionless response (MVDR) method [18,19] is applied for estimation of power spectral densities since, in general, it offers higher spectral resolution than does the classical periodogram. The respective spectra of $d_{\mathrm{HR}}(n)$ and $d_{\mathrm{BP}}(n)$ are computed in successive 5-min segments, using a resolution