Prediction of Dialysis-induced Hypotension

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Abstract— **Intradialytic hypotension is the most common acute complication during conventional hemodialysis treatment. Clinical methods for prediction of acute hypotension during treatment is of great importance in the daily routine as it may prevent such events. This paper presents a method for predicting acute intradialytic hypotension using information from a pulse oximeter which reflects vasoconstriction and cardiac output. The method is based on monitoring changes in the DC level of a measure denoted relative magnitude of the capillary pulse (RMCP), here modeled as a DC level in Laplacian noise. Hypothesis testing is performed in order to obtain an optimal detector for monitoring these changes. The prediction performance was evaluated on 28 treatments from 11 hypotension prone patients who underwent hemodialysis treatment. Continuous blood pressure, photoplethysmography (PPG) signal, and oxygen saturation were acquired during the 28 treatments. A total of 7 acute symptomatic hypotension occurred during the treatments. The proposed method was able to predict all cases with acute intradialytic hypotension without producing any false alarms; hypotension was predicted with an average of 38 min in advance.**

Keywords— **Hemodialysis, Intradialytic Hypotension, Prediction Model, Surveillance, Pulse Oximeter.**

I. INTRODUCTION

Dialysis-induced hypotension continues to be a major complication in end-stage renal disease patients undergoing hemodialysis, despite considerable effort to shed light on its underlying cause. Such hypotension not only causes discomfort to the patient, but may also increase mortality [1]. Since dialysis-induced hypotension leads to increased need for medical service and higher costs, it is very desirable to develop clinical methods for prediction of intradialytic hypotension which may lead to the prevention of such events.

The etiology of dialysis-induced hypotension is often considered to be volume depletion, originating from an ultrafiltration rate which exceeds the reabsorption rate. Volume depletion causes a reduction in the blood volume returning to the heart, resulting in decreased cardiac filling and thus decreased cardiac output; which may lead to hypotension.

Besides hypovolemia, other factors contribute to intradialytic hypotension as well, of which failing compensatory mechanisms are often considered (e.g., reflected by the autonomic nervous system, cardiac output, and capillary vasoconstriction). Decreased cardiac output will reduce the amount of blood which reaches the capillaries, and thus causes the magnitude of the capillary pulse to decrease. Capillary vasoconstriction is an important autonomic counterregulation which prevents hypotension, by increasing blood pressure. The blood volume in the capillaries will decrease during capillary vasoconstriction, causing the magnitude of the capillary pulse to decrease. Thus, both cardiac output and capillary vasoconstriction will contribute to a decrease in the magnitude of the capillary pulse prior to a hypotension.

II. EQUIPMENT AND DATA SETS

A. Equipment

Data were acquired with a blood pressure monitor and a pulse oximeter instrument, operating in parallel with the conventional hemodialysis equipment. Two types of dialysis machines were used in this study. The Gambro AK 200 and the Gambro AK 200 Systems (Gambro Lundia AB, Sweden) were used for patients who underwent hemodialysis and hemodialysis filtration, respectively. The dialyzer filters were selected according to each patient's individual requirements.

A continuous arterial blood pressure signal was acquired with a Portapres (Finapres Medical Systems BV, Holland) and sampled at a rate of 1000 Hz with a Biopac MP150 data acquisition system (BIOPAC Systems, Inc., USA). The blood pressure was measured with two finger-cuffs wrapped around the mid-phalanx of two different fingers on the hand of the access-free arm. The blood pressure was measured with one finger-cuff at a time, where measurements were performed during 15 minutes on one cuff before the measurements were changed to the other cuff for 15 minutes, and so forth. The blood pressure was not measured during eating, since the finger-cuff was removed due to patient comfort. If blood pressure measurements failed completely, they were measured manually. Blood pressure was also measured manually at the start and end of treatment as a reference. The measurement hand was held close to the heart

O. Dössel and W.C. Schlegel (Eds.): WC 2009, IFMBE Proceedings 25/VII, pp. 173–176, 2009.
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level during treatment. Different cuff sizes and adjacent fingers were used when inaccurate blood pressure measurements were obtained.

The PPG signal and the oxygen saturation were continuously acquired with a pulse oximeter (LifeSense®, Medair AB, Sweden) and also sampled at a rate of 1000 Hz with the Biopac MP150 data acquisition system (BIOPAC Systems, Inc., USA). The pulse oximeter used a finger sensor which was attached to the same hand as where blood pressure was measured, on one of the fingers free from a blood pressure finger-cuff. The sensor was attached to the finger during the entire treatment.

B. Patient group

Eleven patients with end-stage renal failure participated in the study who underwent regular hemodialysis treatment three times a week. The study was voluntary and approved by the local ethics committee. The data were acquired during the entire clinical treatment at Rigshospitalet (Copenhagen, Denmark), lasting from 3 to 5 hours. A physician classified the patients as either hypotension resistant or hypotension prone, and only hypotension prone patients were included in the study. The physician's decision was based on each patient's clinical history, such as the number of hypotension episodes per month. The average probability of hypotension during a treatment in the last month for the 11 patients were 41.4%. There were a total of 4 male and 7 female patients, with an average age of 64.0 years and a standard deviation (std) of 12.3 years, and an average weight of 70.3 kg and a std of 20.0 kg.

A total of 28 treatments were acquired from the 11 patients, however, 25 treatments were evaluated since the pulse oximeter could not be used in 3 treatments due to cold hands or sensor problems. There were 17 treatments without blood pressure drops, classified as treatments with stable blood pressure. A total of 7 symptomatic acute hypotensive episodes, defined by a sudden unexpected blood pressure drop, occurred in 5 treatments (2 treatments with double blood pressure drops). In 2 treatments there were a hypotensive episode, caused by a slow blood pressure drop (gradual decrease) over the entire treatment, and in 1 treatment the patient had consistently low blood pressure. The clinical staff made notes during the dialysis treatment, e.g., the time of hypotension.

III. METHODS

A. Method overview

This study presents a new method for prediction of intradialytic hypotension using the photoplethysmography (PPG) signal and oxygen saturation delivered by a pulse oximeter. The method is based on a measure denoted relative magnitude of capillary pulse (RMCP) which estimates the PPG pulse amplitude, thus reflecting both cardiac output and capillary vasoconstriction [2]. The different processing blocks of the method are presented in Figure 1.

B. Method description

In the first processing block, the DC level and the baseline wander are removed from the PPG signal. Then, in the second block, the RMCP signal *x[n]* is obtained as the running sum of the absolute values during one minute of the baseline filtered PPG signal, *p[k]* (down-sampled to 200 Hz). The RMCP signal was sampled every T_s = 5 s due to the slow varying nature of the signal. Thus, the RMCP signal, *x[n]*, may be obtained according to,

$$x[n] = \sum_{k=nK-L+1}^{nK} \left| p[k] \right| \tag{1}$$

where K = 1000 (i.e., corresponding to 5 s) and L = 12000 (i.e., corresponding to 1 min). All values in *x[n]* are normalized with respect to its initial values (an estimate of the DC level during the first 5 min of the recording), since

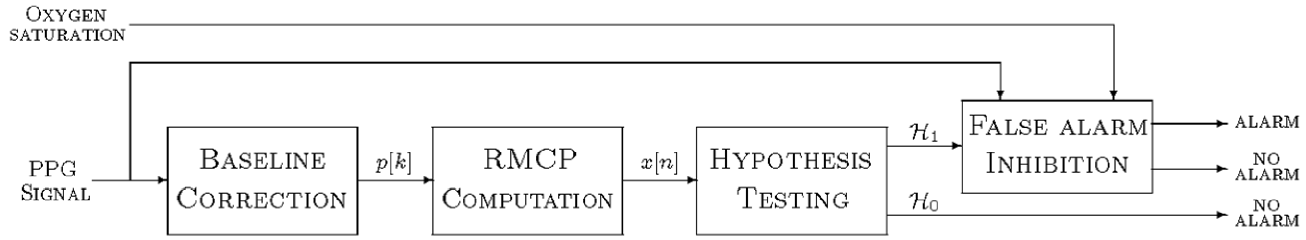

Fig. 1 Block diagram of the RMCP-based method used for prediction of hypotension. The two input signals, the PPG signal and oxygen saturation, may be obtained with a pulse oximeter.

only relative values are of interest.

The central hypothesis in this study is the problem of detecting a change in the DC level of the RMCP signal, here believed to precede hypotension. The detection procedure is solved using hypothesis testing (third block) and is based on a linear model in which the DC level is either unchanged (hypothesis H_0) or changed (hypothesis H_1) [3],

$$\begin{aligned} H_0 &: x[n] = A_0 + w[n] && n = 0,1,\ldots,N-1 \\ H_1 &: x[n] = A_0 - \Delta A + w[n] && n = 0,1,\ldots,N-1 \end{aligned} \tag{2}$$

where $x[n]$ is the observed RMCP signal, A_0 is the initial DC level of the RMCP (here equal to one since only relative changes are measured), ΔA is the unknown change in DC level (with $0 < \Delta A \leq 1$), N is the number of samples in the time window (here set to 60, i.e., corresponding to 5 min), and $w[n]$ is assumed to be independent and identically distributed (IID) zero mean Laplacian noise with known variance, σ^2. The Laplacian distribution is assumed since outliers are common in the RMCP signal.

Two different DC level change detectors are used, where the first is based on the maximum likelihood estimation (MLE) of the DC level in (2), which is easily shown to be the median of the observations $x[n]$ [4], denoted x_{med}, i.e.,

$$x_{med} = median\{x[0], x[1], \ldots, x[N-1]\}. \tag{3}$$

The second DC level change detector is obtained from the Neyman-Pearson theorem [3] in which the probability of detection P_D is maximized for a given probability of false alarm $P_{FA} = \alpha$ by deciding H_1 if

$$L(\bar{x}) = \frac{p(\bar{x}; H_1)}{p(\bar{x}; H_0)} > \gamma, \tag{4}$$

where $p(\bar{x}; H_i)$ denotes the probability density function (PDF) of $\bar{x}$ under H_i, where $\bar{x}$ is an N×1 vector with the observed data $x[0], x[1], \ldots, x[N-1]$. The threshold γ is found from

$$P_{FA} = \int_{\{\bar{x}: L(\bar{x}) > \gamma\}} p(\bar{x}; H_0)\, d\bar{x} = \alpha. \tag{5}$$

Since, the PDF under H_1 in (2) contains the unknown parameter ΔA, the generalized likelihood ratio test (GLRT) is employed in which the MLE of ΔA is inserted into the likelihood ratio test in (4) [3]. The test statistic from the GLRT decides H_1 if

$$G(\bar{x}) = 1 + \frac{1}{N} \sum_{n=0}^{N-1} \left(\left| x[n] - x_{med} \right| - \left| x[n] - 1 \right| \right) < \gamma', \tag{6}$$

where γ' is a threshold determined by a given P_{FA}. This detector evaluates the difference between the mean deviation from the median and the mean deviation from one (which is the initial DC level). In order to monitor the DC level continuously, a sliding window is applied to the RMCP signal such that x_{med} in (3) and $G(\bar{x})$ in (6) are evaluated in each window.

The hypothesis H_1 is decided the first time the DC level change detector drops below the threshold γ', and thus determines the time instant of alarm which predicts that hypotension will occur. The time of alarm is an important parameter in order to evaluate performance of the method in terms of P_D and P_{FA}. However, an equally important performance parameter is the time of prediction, which is defined as the time difference between the true time of hypotension and the time of alarm.

Before an alarm is triggered by the detector, its validity is tested with the help of the PPG signal and/or the oxygen saturation (false alarm inhibition, last block). The pulse oximeter requires a restarting period after saturation in the PPG signal, during which the capillary pulse information is lost. As a consequence, the RMCP signal will be zero during the restarting period, which may trigger a false alarm. Thus, an alarm is disregarded when the saturation in the PPG signal is longer than one second (a very short saturation will not cause a restarting period).

The capillary pulse information may be distorted or lost even if the PPG signal is not saturated. If the pulse oximeter sensor is moved or touched, both the RMCP signal and the oxygen saturation may decrease, without the PPG signal being saturated. Thus, when the oxygen saturation is zero or in case of a sudden large drop (abnormal oxygen saturation), an alarm is disregarded irrespective of the value in the PPG signal. A false alarm would be triggered if the pulse oximeter sensor is removed from the finger, but the alarm is disregarded since both the PPG signal and the oxygen saturation will be zero.

IV. RESULTS

Detection probability P_D (sensitivity) was evaluated on the 7 acute hypotensive episodes using both x_{med} and $G(\bar{x})$. The same methods were used in order to estimate probability of false alarm P_{FA} (1-specificity), which was evaluated on the 17 treatments with stable blood pressure. The $G(\bar{x})$ method achieves a performance of P_D=100% and P_{FA}=6%, while the x_{med} method offers a performance of P_D=100% and P_{FA}=0%. Thus, x_{med} was able to predict all cases with acute intradialytic hypotension without producing any false alarms.

The method based on x_{med} has an average prediction time of 38 min with the performance of P_D=100% and P_{FA}=0%, which is well in time to allow clinical staff to take actions to prevent the onset of hypotension or to alleviate symptoms.

Examples of x_{med} obtained from the RMCP signal during two hemodialysis treatments are displayed in Figure 2 and Figure 3. In Figure 2, data from a patient with stable blood pressure is shown, where x_{med} is almost constant during the entire treatment for this patient. Data from a patient with acute symptomatic hypotension is presented in Figure 3. An evident DC level change occurs in the RMCP signal prior to the actual hypotension. The patient is eating in the period from 120 to 140 minutes, and the hypotension occurs slightly after the eating is finished, at 144 minutes.

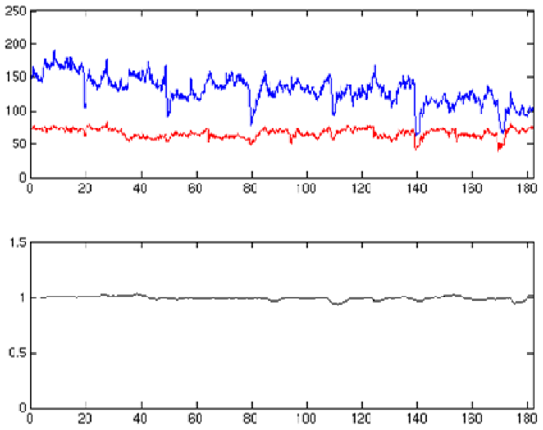

Fig. 2 A patient with stable blood pressure during treatment, horizontal axis in minutes. *Top figure:* Blood pressure in *mmHg*, BP (diastole, systole). *Bottom figure:* x_{med} from the RMCP.

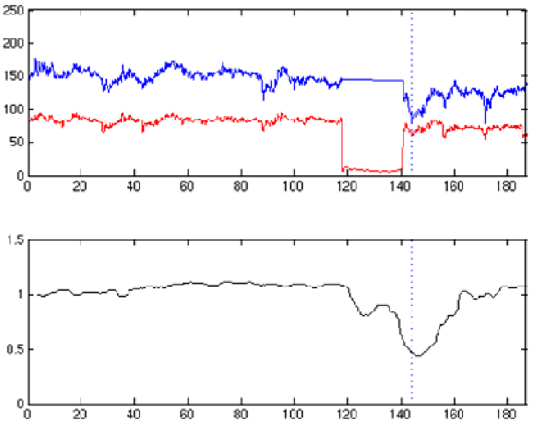

Fig. 3 A patient with an acute symptomatic hypotension occurring at the dotted line (144 min), horizontal axis in minutes. *Top figure:* Blood pressure in *mmHg*, BP (diastole, systole). *Bottom figure:* x_{med} from the RMCP.

V. CONCLUSIONS

A multi-signal approach method based on the information from a pulse oximeter is developed for prediction of hypotension during hemodialysis. Three different signals are used in the method: the RMCP signal, the PPG signal, and oxygen saturation. The RMCP signal, estimated from the PPG pulse amplitude, reflects both capillary vasoconstriction and cardiac output. The PPG signal from a pulse oximeter has, to our knowledge, never been used in order to predict dialysis-induced hypotension.

The prediction performance of the method was evaluated on 28 treatments from 11 hypotension prone patients. There were a total of 7 acute symptomatic hypotension during the treatments. The proposed method was able to predict all the cases with acute intradialytic hypotension (sensitivity = 100%) without producing any false alarms (specificity = 100%). The hypotension was predicted with an average of 38 min in advance, which is well in time to allow clinical staff to take actions to prevent the onset of hypotension or to alleviate symptoms.

ACKNOWLEDGMENT

This study was supported by grants from Gambro AB, Lund, Sweden and The Swedish Research Council. The authors thank Sören Ladefoged and Joakim Cordtz at the Department of Nephrology, Rigshospitalet, Copenhagen, Denmark, for being supportive during the data acquisition.

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