Relative Peripheral Blood Volume Changes in Response to Ventricular Premature Beats during Dialysis

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Abstract

The goal of this study is to determine whether peripheral blood volume fluctuations triggered by ventricular premature beats (VPBs) are significantly related to hypotensive symptoms during dialysis treatment. Patients treated with hemodialysis often suffer from cardiovascular disorders and uremic neuropathy, increasing the propensity to homeostatic imbalance that, in turn, may result in intradialytic hypotension, cramps, nausea, dizziness, headache and other complications. VPBs, being abundant in hemodialysis patients, can be viewed as an internal disturbance leading to imbalance through acute blood pressure drop and prolonged tissue deoxygenation.

The present study investigates and quantifies VPB-induced relative peripheral blood volume changes, measured from the fingertip photoplethysmographic (PPG) waveform, and their significance for characterization of physiological recovery of a disturbed circulatory state. The mean decrease in PPG amplitude, corresponding to an initial post-ectopic drop in blood volume delivered to the periphery, was $4 \pm 3\%$ in asymptomatic treatments, whereas $17 \pm 3\%$ in symptomatic dialysis treatments. This result indicates that significant differences exist between the two groups of treatment, providing a potential for development of intradialytic risk predictors.

1. Introduction

The most common treatment option for patients with kidney failure is hemodialysis. Treatment sessions are performed on a regular basis with the use of complex external equipment that partly replaces kidney function by removal of toxic metabolites and excess fluids that accumulate in the patient's blood. Unfortunately, both patient- and dialysis-related factors can lead to adverse intradialytic symptoms. Hypotension is the most common complication, occurring in approximately 25% of all treatments, and is accompanied by cramps, nausea, dizziness, and headache occurring due to impaired cardiovascular compensatory mechanisms [1]. Patients with kidney failure undergoing hemodialysis are also at high risk for ventricular arrhythmia and sudden cardiac death. It has been found that ventricular arrhythmias, accompanied with increased numbers of ventricular premature beats (VPBs), is present in 90% of all dialysis patients [2].

Heart rate turbulence (HRT) analysis utilizes frequent VPBs from ECG, and shows that HRT parameters may help to evaluate the propensity to hypotension during dialysis [3]. Since the ECG is inconvenient to record during treatment, another study reported on the possibility to replace the ECG with the simpler technique of photoplethysmography (PPG) from which HRT parameters can be computed [4]. A promising real-time approach to hypotension prediction based on the analysis of global PPG amplitude demonstrated that relative blood volume changes in the microvascular tissue plays an important role [5].

This study presents a new approach for identifying patients at risk for hypotension, relying on the abundance of VPBs in dialysis patients and averaged normal PPG pulse amplitude values in short intervals surrounding single VPBs. The presence of a VPB-induced fluctuation in blood supply to the periphery, named "pulse amplitude turbulence" (PAT) phenomenon, was identified by tracking of circulatory alterations in post-VPB pulsatile intervals.

2. Materials

2.1. Study population and setup

Eleven patients with end-stage renal disease participated in the clinical study, undergoing regular dialysis treatment thrice a week. The study was approved by the local ethics committee. Data acquisition was performed throughout the entire treatment sessions at Rigshospitalet (Copenhagen, Denmark), lasting from 3 to 5 hours. Patients classified by a nephrologist as hypotension prone were included in the study. The nephrologist's decision

was based on the patient's clinical history one month prior to the study onset, from which the probability of hypotension episodes was determined, resulting in a mean probability of 0.41 for the study population. Treatment was considered symptomatic if one of the adverse events described in Section 1 was encountered and followed by attention of the medical staff. In total, 28 treatments were acquired from 11 patients (7 female and 4 male), age 68 ± 17 (mean±std).

The Gambro AK 200 or AK 200 Systems (Gambro Lundia AB, Sweden) were used for patients who underwent hemodialysis and hemodiafiltration, respectively. Data were acquired using external recording equipment in parallel with the routine hemodialysis equipment. Electrocardiograms were recorded from standard leads V1, V5 and II using the Biopac ECG100C amplifier and sampled at a rate of 1000 Hz with the Biopac MP150 data acquisition system (BIOPAC Systems, Inc., USA). The pulse PPG signals and the oxygen saturation at the fingertip were continuously acquired with the pulse oximeter (LifeSense R, Medair AB, Sweden), and sampled at a rate of 1000 Hz with the Biopac MP150. The recordings from 3 treatments had to be removed from the study due to unstable sensor wearability during the acquisition. The final database consisted of the data from 25 treatments from 10 patients.

2.2. Annotation and eligibility of VPBs

VPBs were annotated from the ECG by exploring the length of R-R intervals and beat morphology. ECG derived information was used to validate the solely PPG-based VPB detection [4]. VPBs were excluded from further analysis in cases of abrupt ECG or PPG waveform distortion, or when other VPBs surrounded the analyzed one. A minimum number of eight VPBs was used for averaging of the PPG amplitude in pre- and post-VPB intervals, locally characterizing microvascular peripheral blood volume changes, see Section 3.2. The status of meeting the inclusion criteria and presence of hypotension related symptoms in the course of dialysis treatments are summarized in the Table 1.

VPBs were present in 22 treatments from 10 patients, which after application of the inclusion criteria reduced to 14 treatments from 7 patients.

3. Methods

The approach employed in this study focuses on post-VPB intervals of the fingertip PPG recordings in order to capture single VPB-induced local pulse wave amplitude alterations. Normalization with respect to the reference pre-ectopic pulsatile intervals is essential for characterization of instantaneous VPB-induced peripheral blood volume changes using relative measures, whose temporal

Table 1. Number of VPBs satisfying the inclusion criteria and the state of presence or absence of intradialytic symptoms during the analyzed dialysis treatments. See Section 3.1 for distinction between VPB patterns (VPB_{p1} and VPB_{p0}).

Pat:Trt number	Intradialytic symptoms	Amount of VPBs		
		VPB_{p1}	VPB_{p0}	Total
1:1	no	7	16	23
1:2	no	12	1	13
2:1	yes	5	53	58
2:2	yes	2	62	64
2:3	yes	2	22	24
3:1	no	9	0	9
4:1	yes	2	10	12
4:2	yes	1	16	17
4:3	yes	2	10	12
4:4	yes	1	15	16
5:1	yes	18	16	34
5:2	yes	5	13	18
6:1	no	4	4	8
7:1	no	22	15	37

evolution is revealed by tracking the normalized post-VPB amplitude fluctuations present in normal pulses following a VPB. The normalizing factor was determined as an average of a fixed number of regular pulse amplitude values preceding each VPB.

3.1. Pulse detection

PPG recordings were preprocessed in order to reduce the impact of noise using a low-pass FIR filter with a cut-off frequency at 35 Hz. The onset n_o and the peak location n_P of the each pulse in the filtered PPG signals $y(n)$ were determined using a derivative-based detector, by finding zero-crossings of the first derivative followed by the evaluation of local minima and maxima [4].

Different pulse patterns in response to a VPB can occur in the PPG signal [6]. Depending on the degree of cardiac output, VPB may or may not be associated with a PPG pulse, see Fig. 1.

3.2. Pulse amplitude turbulence

Peripheral blood volume changes in response to a VPB result in a compensatory pulse followed by a pulse amplitude turbulence phenomenon of a sudden decrease in a pulsatile PPG component's amplitude followed by its gradual return to the initial level. This phenomenon may be viewed as the amplitude counterpart to the temporal phenomenon called pulse rate turbulence [4]. Pulse rate turbulence is
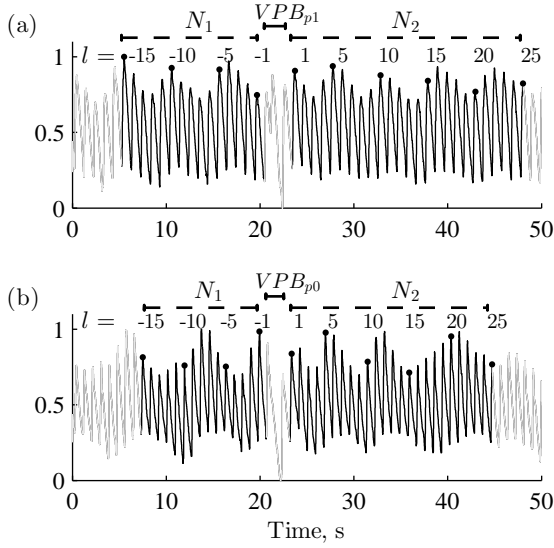
Figure 1. Different pulse responses in PPG signals induced by a single VPB in the same patient at different time instants during the same dialysis treatment. (a) A response expressed as a low amplitude PPG pulse is denoted by VPB_{p1}, and (b) a pulseless PPG response – VPB_{p0}, which is represented by a prolonged compensatory pause. Both VPB_{p1} and VPB_{p0} marked complexes include a compensatory pulse that immediately follows a VPB (last pulse) and one normal pulse that precedes it (first pulse). N_1 and N_2 denote the maximum number of regular PPG pulses l subjected to further analysis in the pre- and post-VPB pulsatile intervals, while VPB_{p1} and VPB_{p0} complexes were not considered further.

also induced by a single VPB and normally responds to it by a transient fluctuation in rhythm.

The characterization of PAT is based on the peak-to-peak upslope amplitude of the PPG waveforms which surround a VPB. This amplitude is denoted by

$$a_+(k_i + l), \quad i = 1, \ldots; \ l = \ldots, -1, 1, \ldots \quad (1)$$

where k_i is the index of the i-th VPB, and l is the index of the surrounding waveforms. To reduce the influence of respiration as well as of other types of noise, $a_+(k_i + l)$ is aligned with respect to k_i and then ensemble averaged over all VPBs, resulting in the amplitude series $\bar{a}_+(l)$, where $l = 0$ defines the occurrence time of the VPB. Ensemble averaging of VPBs is illustrated by the example in Fig. 2 for the two patient groups (asymptomatic/symptomatic); thus, each curve is the result of ensemble averaging as well as the mean over all treatments in each of the groups.

The PAT parameter proposed in this study reflects how the normalized peak-to-peak upslope amplitude recovers
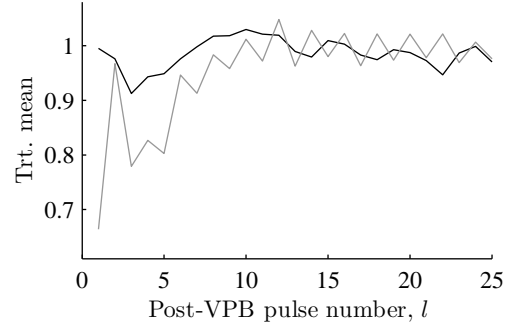

Figure 2. Dynamics of the ensemble averaged PPG signal upslope in short post-ectopic intervals during the asymptomatic (black line) and symptomatic (grey line) dialysis treatments.

after the VPB. Its definition is given by

$$r(l) = \frac{\dfrac{1}{L} \displaystyle\sum_{m=1}^{L} \bar{a}_+(l+m)}{\dfrac{1}{N_1} \displaystyle\sum_{m=-N_1}^{-1} \bar{a}_+(m)}, \quad l = 0, 1, \ldots \quad (2)$$

where a sliding window of length L has been introduced to improve the amplitude estimate of the post-ectopic segment. The normalization factor results from averaging the N_1 amplitudes before the VPB. It is noted that complete recovery is reflected by $r(l)$ approaching one as l increases.

In the present study, a window length of $L = 6$ was used, and the normalization factor was based on $N_1 = 15$ amplitudes in the pre-ectopic segment.

4. Results

Out of the 14 studied treatments, 5 were successful or asymptomatic (4 patients) and 9 contained dialysis-related complications (3 patients). PPG amplitude dynamics in post-VPB intervals were evaluated by determining the mean of $\bar{r}(l)$ for all treatments in each of the two groups.

Peripheral blood volume drop. The evaluation of initial peripheral blood volume drop following a VPB in the normalized post-ectopic PPG intervals were significantly different (Student's t-test, $p < 0,05$) in the asymptomatic and symptomatic groups. For dialysis treatment without intradialytic symptoms, the initial drop in peripheral blood volume after a VPB was found to be $4 \pm 3\%$ (mean±std). On the contrary, a much larger initial drop in peripheral blood volume, $17 \pm 3\%$, was observed in treatments with adverse symptoms, see Fig. 3.

VPB isolation criteria. For artifact-free PPG signals, it was shown that VPB isolation criteria can be reduced to 15
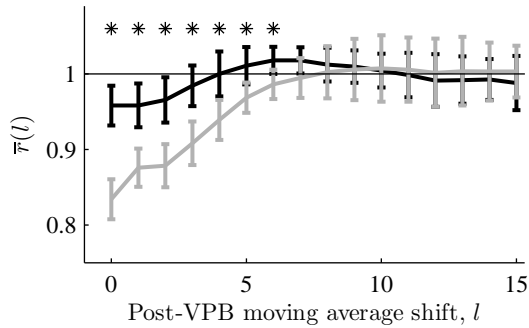
Figure 3.   Mean±std post-VPB moving average values normalized with the treatment-specific pre-VPB references for the two groups of dialysis treatments: asymptomatic (black line) and symptomatic (grey line). Significantly different (p-value$< 0,05$) respective pairs of the two groups are marked by asterisks.
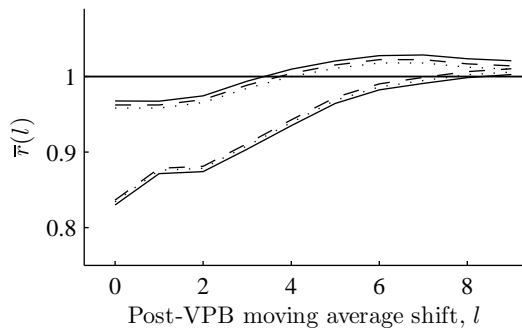

Figure 4.   Pre-ectopic PPG interval length influence on the results of the two dialysis treatment groups (upper – asymptomatic, lower – symptomatic) when N_1 of the normalizing factor is equal to 5 (dotted line), 10 (dashed line), and 15 (solid line) amplitudes.

post-ectopic and 5 pre-ectopic normal pulses surrounding a single VPB, with no qualitative alterations to the results obtained so far, see Fig. 4.

5.   Discussion

Analysis of relative peripheral blood volume changes from the PPG waveform demonstrated the possibility to distinguish between the two hemodialysis treatment groups according to the presence/absence of hypotension-related symptoms in patients with VPBs. An indicator signifying the initial post-VPB peripheral blood volume drop demonstrated good distinctive capacity. Larger drop in pe-

ripheral blood volume in symptomatic treatments can be explained by higher degree hemodynamic instability that VPBs trigger. The reasons for that are not clear, but they are likely to be related to dialysis settings, patient's physical properties, cardiac condition, and other diagnoses.

The study was based on a small dataset, particularly due to the length of isolation intervals around a VPB. The obtained result on the possibility to reduce the length by 30% in pre-ectopic and by 40–50% in post-ectopic pulsatile interval, combined with the reasonable guarantee of PPG signal quality, gives a good perspective to reduce the necessity of further data exclusion.

The main limitation of the study is that only hypotension-prone patients were available, and therefore another study should be pursued which investigate a larger number of hypotension-resistant and -prone patients.

Acknowledgements

References

[1] Daugirdas JT, Blake PG, Ing TS, editors. Handbook of dialysis, 4th ed. Wolters Kluwer/Lippincott Williams & Wilkins, 2006.

[2] Shamseddin MK, Parfrey PS. Sudden cardiac death in chronic kidney disease: epidemiology and prevention. Nat Rev Nephrol, 2011;7(3):145-154.

[3] Solem K, Laguna P, Martínez JP, Sörnmo L. Model-based detection of heart rate turbulence. IEEE Trans Biomed Eng, 2008;55(12):2712-22.

[4] Gil E, Laguna P, Martínez Cortes J, Barquero-Perez O, Garcia-Alberola A, Sörnmo L. Heart Rate Turbulence Analysis Based on Photoplethysmography. IEEE Trans Biomed Eng, 2013;PP(99).

[5] Solem K, Olde B, Sörnmo L. Prediction of intradialytic hypotension using photoplethysmography. IEEE Trans Biomed Eng, 2010;57:1611-19.

[6] Zheng D, Allen J, Murray A. Determination of aortic valve opening time and left ventricular peak filling rate from the peripheral pulse amplitude in patients with ectopic beats. Physiol Meas, 2008;29:1411-19.

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