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Technical note

# Relative peripheral blood volume changes induced by premature ectopic beats and their role in hemodialysis

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ABSTRACT

Hemodialysis patients often suffer from cardiovascular disorders and uremic neuropathy, increasing the propensity to homeostatic imbalance that, in turn, may result in intradialytic complications like cramp, nausea, and, worse, hypotension. Ectopic beats, being abundant in such patients, may lead to imbalance through repeated, sudden drops in blood pressure. By exploring the properties of postectopic peripheral circulation recovery, treatment sessions prone to intradialytic complications may be better identified. This paper introduces a novel method for quantifying changes in peripheral blood volume due to ventricular or supraventricular premature beats (VPBs or SVPBs). Using the fingertip photoplethysmographic pulse waveform, VPB and SVPB-induced changes in relative peripheral blood volume are quantified by the postectopic pulse amplitude. Two parameters are proposed for characterizing (i) the initial drop in peripheral blood volume following an ectopic beat, and (ii) the degree of postectopic peripheral circulation recovery. A small set of data from 16 hemodialysis sessions in 9 hypotension-prone patients are used to illustrate the method. In asymptomatic sessions, the first parameter was found to be $8 \pm 13\%$ (mean $\pm$ std), whereas, in symptomatic sessions, it increased to $32 \pm 13\%$, suggesting that postectopic pulse amplitude recovery is related to intradialytic complications; similar results were obtained for the second parameter. Postectopic pulse amplitude recovery may also be of interest in other applications where relative changes in peripheral blood volume play a role.



## 1. Introduction

Patients with chronic kidney disease undergoing dialysis are at high risk for cardiovascular disorders, since kidney failure affects cardiac structure and function through hemodynamic and metabolic changes [1,2]. Resulting adverse cardiomyopathic and vasculopathic conditions are associated with sudden cardiac death, conduction abnormalities, and certain types of arrhythmias. In a recent study, ventricular arrhythmia was found to be present in 90% and supraventricular arrhythmia in 80% of patients with chronic kidney disease; both types of arrhythmia were exacerbated by dialysis [3]. Dialysis-related factors such as decreased circulating blood volume, sympathetic overactivity, and variation in metabolite concentrations were pointed out as causes to electrical instability of the heart.

Ventricular premature beats (VPBs) are frequent in hemodialysis patients [4,5], and increase in number as the treatment session progresses and excess potassium is removed [6]. Furthermore, patients with regional wall motion abnormalities, ischemic heart disease, and left ventricular hypertrophy have more frequent VPBs during hemodialysis than patients without these conditions. Since VPBs are abundant in hemodialysis patients, interest has recently been directed to methods for exploring different aspects related to the occurrence of VPBs. For example, ECG-based analysis of heart rate turbulence (HRT) [7], has not only been established as a powerful predictor of mortality after myocardial infarction, but HRT analysis has been considered for intradialytic risk stratification. Using the standard HRT parameter “turbulence slope”, propensity to acute intradialytic hypotension may be assessed [8,9], see also [10].

Since it is inconvenient to wear ECG electrodes throughout a hemodialysis session, and calls for clinical staff who need to spend time on attaching electrodes, the much simpler photoplethysmographic (PPG) technique can be used since the accuracy of HRT parameters is not compromised when using the PPG [11]. The PPG

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is a noninvasive, optical technique suitable for tracking changes in microvascular blood volume; the sensor is usually attached to the fingertip [12]. In hemodialysis, the benefits of the PPG have been demonstrated for continuous intradialytic assessment of blood pressure [13], peripheral vascular regulatory function [14], hemodynamic stability [15], respiratory function [16], and fluid removal [17]. The prediction of acute intradialytic hypotension represents yet another problem addressed by using the PPG [18]: the method is based on the assumption that the global PPG amplitude, determined in a sliding minute-long window, provides a measure of change in relative blood volume in the microvascular tissue.

This technical note introduces a novel method for quantifying changes in peripheral blood volume due to VPBs or supraventricular premature beats (SVPBs), information which may be used to identify patients at risk for intradialytic complications. The proposed method requires the availability of several ectopic beats, of ventricular and/or supraventricular origin, so that the PPG pulse amplitude can be computed in a short interval centered around the premature ectopic beats. It is hypothesized that changes in blood supply to the periphery due to the premature ectopic beats are reflected by changes in the pulse amplitude during the postectopic pulse interval. Here, such amplitude changes are referred to as *pulse amplitude recovery* (PAR). Two simple PAR parameters are proposed in Section 3, reflecting the initial circulatory disturbance and the degree of postectopic recovery of reduced peripheral microvascular circulation; both parameters are expressed as percentages. Using data acquired from hemodialysis patients (Section 2), the parameters are studied in Section 4 with respect to differences between sessions with and without complications.

It should be emphasized that HRT analysis resembles PAR analysis since both characterize the aftermath of ectopic beats. However, completely different physiological phenomena are characterized: while HRT relates to a short-term change in heart rate, PAR relates to a short-term change in peripheral blood perfusion.

## 2. Materials

The dataset consists of 11 hypotension-prone patients (7 females, age 64 ± 12 years (mean ± std)) with end-stage renal disease who underwent regular hemodialysis treatment thrice a week at Rigshospitalet, Copenhagen, Denmark. The patients were classified by a nephrologist as hypotension-prone from clinical history, such as the number of hypotensive events per month. Data acquisition was performed throughout the entire treatment session, lasting from 3 to 5 h; a total of 28 sessions were acquired. A session was labeled symptomatic when an intradialytic complication occurred, i.e., hypotension, cramp, nausea or dizziness, and was accompanied by attention from the staff. The study was approved by the local ethics committee. The dataset has previously been studied in [18].

The machines Gambro AK 200 or AK 200 S (Gambro Lundia AB, Sweden) were used for patients who underwent hemodialysis and hemodiafiltration, respectively. The dialyzer filter was selected according to each patient's individual requirements. Data were acquired using external sensors operating in parallel with the hemodialysis equipment. The electrocardiogram (ECG) was recorded with the Biopac ECG100C amplifier, and sampled at a rate of 1000 Hz with the Biopac MP150 data acquisition system (BIOPAC Systems, Inc., USA). The PPG signal was continuously acquired at the fingertip with a pulse oximeter (LifeSense©, Medair AB, Sweden), also sampled at 1000 Hz using the Biopac MP150. The acquisition of ECG and PPG signals was time-synchronized since the same acquisition board was used. Thanks to this, matching of QRS complexes with the corresponding PPG waves is straightforward.

Based on the ECG, premature ectopic beats were manually annotated by two independent experts and grouped into VPBs and SVPBs. A premature ectopic beat was excluded from further analysis whenever another ectopic beat occurred within an "isolation interval" defined by $D_1$ beats before and $D_2$ beats after the premature ectopic beat. Moreover, if less than $K$ premature ectopic beats remained after application of the isolation criterion, the entire session was excluded from further analysis. In the PPG signal, segments for which the heart rate could not be reliably determined were excluded from further analysis [9]. The following parameter values were used in the present study: $D_1 = 6$, $D_2 = 16$, and $K = 8$.

Applying these exclusion criteria, the original 28 sessions from 11 patients reduced to 16 sessions from 9 patients. For these 9 patients, VPBs were more frequent than SVPBs in symptomatic sessions (96% vs. 53%), whereas the reverse observation applied to asymptomatic sessions, i.e., SVPBs were more frequent than VPBs (47% vs. 4%), see Table 1.

In the PPG signal, different types of pulse pattern occur in response to a premature ectopic beat. Depending on the degree of blood pumping efficiency, an ectopic beat may or may not be associated with a distinguishable pulse [19]. Three types of PPG responses may be defined, namely, a pulseless response (denoted $P_0$), a pulse-related response (denoted $P_1$), and an indeterminate type of pulse response defined by an amplitude less than 10% of a normal PPG

**Table 1**
Patient information, presence of intradialytic complications during hemodialysis treatment, and the number of premature ectopic beats after application of exclusion criteria.

| Patient: Session# | Age/Gender | Complications | Premature ectopic beats | | |
|---|---|---|---|---|---|
| | | | Quantity | VPBs, % | SVPBs, % |
| 1:1 | 61/F | No | 41 | 46 | 54 |
| 1:2 | | No | 51 | 2 | 98 |
| 1:3 | | No | 9 | 11 | 89 |
| 2:1 | 76/M | No | 44 | 82 | 18 |
| 3:1 | 66/M | No | 494 | 88 | 12 |
| 3:2 | | Yes | 448 | 100 | 0 |
| 4:1 | 63/F | No | 15 | 7 | 93 |
| 5:1 | 58/F | Yes | 573 | 98 | 2 |
| 5:2 | | Yes | 469 | 98 | 2 |
| 5:3 | | Yes | 594 | 99 | 1 |
| 5:4 | | Yes | 652 | 91 | 9 |
| 6:1 | 56/M | No | 39 | 100 | 0 |
| 7:1 | 59/M | No | 169 | 99 | 1 |
| 7:2 | | Yes | 80 | 93 | 7 |
| 8:1 | 75/F | Yes | 35 | 91 | 9 |
| 9:1 | 84/F | No | 41 | 43 | 57 |
| Average | – | – | 100[a]/420[s] | 53[a]/96[s] | 47[a]/4[s] |

[a] Asymptomatic sessions.
[s] Symptomatic sessions.