# Short Term Variability of Oxygen Saturation during Hemodialysis Is a Warning Parameter for Hypotension Appearance

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### Abstract

Acute hypotension is a frequent complication of hemodialysis. Blood oxygenation may play a role in hypotension and hypoxemia may be considered as a marker of hemodynamic surrogate instability. Continuous, non-invasive monitoring of oxygen saturation  $(SO_2)$  during hemodialysis is now possible, by means of sensors measuring  $SO_2$  in blood entering the dialyzer. The aim of the present work was to analyze the short-term variability of SO<sub>2</sub> during hemodialysis in sessions with and without hypotension to correlate the SO<sub>2</sub> variability to hemodynamic instability. Our preliminary results showed an interesting, yet to be fully understood, role of  $SO_2$  in anticipating hypotension onset.

### 1. Introduction

During the last 40 years a lot has been achieved in dialysis regarding both monitors safety and membranes overall performances Anyway, intradialytic symptoms still remain a major concern for nephrologists: in particular, hypotension is the most frequent.

Intradialytic hemodynamic monitoring systems have been developed to have continuous surveillance of the main hemodynamic variables (heart rate, body temperature, blood pressure itself, cardiac output, ecc...).

In a second moment, the further evolution was towards the retroactive control systems, to force some of the variables involved in the genesis of the hemodynamic stability, along a pre-determined, ideal, trend. In this view, various bio-feedback mechanisms have been proposes along the years, for example, to tackle hypovolemia-related hypotension. Their scientific rationale is the control of either blood volume or directly natremia, in order to pilot plasma refilling towards the vascular compartment [1].

Despite the great achievements obtained, the forecasting of acute hypotension during hemodialysis still remains a complex problem, likely involving more than one variable.

 $SO_2$  can be considered an indirect expression of the hemodynamic stability. Moreover, in dialysis, it has always been regarded as a bio-compatibility marker for membranes [2]. Nowadays,  $SO_2$  changes during dialysis are easy to measure with a fully, non-invasive sensor assembled on the arterial line.

We planned this study to analyze the short-term variability of  $SO_2$  during hemodialysis in relationship with hemodynamic tolerance.

# 2. Methods

## 2.1. Patients

Twenty hypotension-prone patients with ESRD in renal replacement therapy with three times a week 4-hour maintenance double-needle haemodialysis at the dialysis division of Malpighi Hospital (Bologna, Italy) were enrolled (N=20, 6 males and 14 females; age  $70\pm12$  years old range 45 to 96; and dry weight  $65\pm16$  Kg, range 40 to 106; weight loss  $2,9\pm0,9$  Kg range 0,6 to 4,5). All the participants provided informed consent for participation in this study. All the patients were classified as hypotension-prone based on recent incidence of hemodialysis-induced hypotension (at least two of their most recent 12 treatments complicated by acute hypotension).

Intradialytic hypotension was defined on the basis of systolic pressure (SP) values: (1) SP  $\leq$  90 mmHg, accompanied by symptoms and therapeutic maneuvers (saline or hypernatric infusions, plasma expander, Trendelenburg or other maneuvers, reduction in blood

flow, stop of ultrafiltration); (2) SP reduction  $\ge 25 \text{ mmHg}$ compared to the pre-dialysis value, in the presence of symptoms and therapeutic maneuvers: (3) SP  $\leq$  90 mmHg, accompanied by a reduction of at least 20 mmHg from the pre-dialysis value.

#### 2.2. **Hemodialysis treatments**

Bicarbonate hemodialysis (BD) were adminstrated. The monitor used to deliver the treatments was the Bellco Formula 2000, equipped with the Hemox sensor on the arterial blood line. Dialyzer, heparin dose, blood flow (Q<sub>B</sub>) were set as usual for every patient: blood flow was 299±11 ml/min, QD was set to 500 ml/min and dialysis length was 232±13 min. Patients were studied two times during their mid-week BD session for two consecutive weeks.

#### 2.3. Measurements and data collection

Systolic and diastolic arterial blood pressures were measured in pre-dialysis phase and every 15 minutes during the treatment by an automatic oscillometric sphygmomanometer (SPHYGMO, Bellco, Italy). The occurrence of typical low blood pressure symptoms (muscular cramps, headache, dizziness, vomiting, nausea, sweating) and time of appearance were also recorded. At the end of each study session, acute hypotension episodes and the time of hypotension onset were assessed by reviewing pressure data and symptoms off-line. Sessions with hypotension were classified as positive and sessions without hypotension were classified as negative.

SO<sub>2</sub> signal was acquired with a frequency of 1 sample per 5 seconds (fc = 0.2 Hz) by means of the Hemox sensor (BellCo, Italy) and stored in a personal computer (DELL Latitude D520).

#### 2.4. Data analysis

SO<sub>2</sub> digital signal was filtered with a numerical lowpass filter (ft = 0,1 Hz) to remove high frequency components. To calculate SO<sub>2</sub> short-term variability, data were extracted from filtered SO<sub>2</sub> time series by shifting a 4-min long window (48 points, 1 point each 5 second) producing epochs overlapping by 75% (1 min time-shift). For each epoch, long term fluctuations having a period greater than the window-length were removed by linear regression, and standard deviation (SD) was then computed to characterize SO<sub>2</sub> short-term variability (1 point per minute). In the positive sessions, the SO2 analysis was ended 15 minutes before the first hypotension episode.

A critical threshold of 0.85 was fixed and a hypotension was predicted when the SD exceeded this threshold. Overshoot time (OT) was calculated as the last SD value above 0.85 in the 30 minutes that preceded

hypotension occurrence.

Likelihood ratios were calculated as well. The positive Sensitivity

1 – Specificity likelihood ratio (LR+) defined as indicated the increase of hypotension risk when SD exceeds 0,85; the negative likelihood ratio (LR-) defined

1 – Sensitivity

*Specificity* the indicated decrease of as hypotension risk when SD < 0.85.

#### 3. **Results**

A total of 40 sessions were analyzed. On the basis of hypotension presence, 20 were classified as positive and 20 as negative. The incidence of positive sessions was: 2/2 in 7 patients, 1/2 in 6, and 0/2 in the remaining 7. Pressure, SO<sub>2</sub> and SO<sub>2</sub> short term variability (SD) data, in an esemplificative case of a session with hypotension, are shown in Figures 1-2.



Figure 1. Example of positive session Panel A: Blood pressure Panel B: S0<sub>2</sub> filtered signal Panel C: Standard deviation



Figure 2. Example of negative session Panel A: Blood pressure Panel B: S0<sub>2</sub> filtered signal Panel C: Standard deviation

The off-line overall prediction, based on the  $SO_2$  variability, was 88% (17/20 positive and 18/20 negative sessions).

The positive likelihood ratio (LR+), was 8,5, indicating that the SO<sub>2</sub> variability index increases significantly the likelihood of positive prediction when greater than 0,85.

Notably, OT anticipated hypotension of 14 ±9 min.

The negative likelihood ratio (LR-) was 0,17, indicating that the SO<sub>2</sub> variability index decreases significantly the likelihood of positive prediction when lower than 0,85.

### 4. Discussion and conclusions

Changes of intradialytic  $SO_2$  variability anticipate hypotension, likely as a result of the ups and downs of cardiac output and tissue perfusion. Continuous monitoring of  $SO_2$  variability may provide useful information to forecast the onset of hypotension. In this view, the study may pave the way to an automatic alarm system including  $SO_2$  changes as a warning variable, offering the opportunity of preventive manoeuvres to avoid hypotension. Further analysis on a larger group, yet in progress, are needed to confirm our results.

### References

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