



## Research article

# Monitoring of plethysmography variability index and total hemoglobin levels during cesarean sections with antepartum hemorrhage for early detection of bleeding



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## ABSTRACT

**Background:** Cesarean sections for parturients with antepartum hemorrhage have the potential risk of massive blood loss. In the current study we investigated the use of Plethysmography variability index (PVI) and non invasive hemoglobin (SPHB) monitoring as well for intraoperative detection of blood loss and intravascular volume status.

**Methods:** One hundred and twenty four full term parturients scheduled for elective CS were included in the study. All patients received general anesthesia after preoxygenation for 5 min, rapid-sequence induction performed with thiopental 3–5 mg/kg and suxamethonium 1.5 mg/kg; Anesthesia was maintained with a 100% of oxygen with 0.5–1 MAC of isoflurane and atracurium 0.5 mg/kg. Standard monitors (pulse oximetry, non-invasive blood pressure, and ECG) were applied. Masimo sensor was applied following best practice guidelines, and automated data collection (ADC) was done. Our primary outcome was to compare PVI values before versus after administration of fluids and blood that was given based on clinical data. Our secondary outcome was to review of SPHB traces plots to determine if and when SPHB may have detected presence of anemic state or critical drop in hemoglobin level when compared to time of clinical awareness of bleeding and confirmation by lab Hb sample measurement.

**Results:** PVI showed a significant negative correlation with CVP ( $p = 0.037$ ) and a significant negative correlation with MAP ( $p = 0.01$ ). Also, it showed significant positive correlation with HR ( $p < 0.001$ ). A highly significant Correlation was found between pre transfusion lab Hb and pre transfusion SpHb ( $p < 0.001$ ). Also post transfusion values showed a highly significant correlation as well ( $p < 0.001$ ). A total of 87 transfusions (91.58%) were found unnecessary when using SpHb as the reference, compared to 58 (61.05%) when using the invasive laboratory measurement.

**Conclusion:** Plethysmography variability index and non invasive hemoglobin monitoring as well can be used for optimization of intravascular volume status during cesarean sections in parturients with antepartum hemorrhage.

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## 1. Introduction

Antepartum hemorrhage is defined as bleeding from the birth canal during the course of pregnancy starting from the 24 weeks of gestation to term [1]. Placenta previa is the main cause of antepartum hemorrhage [2].

The heart's pumping ability results from several factors including the balance between intrathoracic airway pressure and the intravascular fluid volume. Changes in thoracic airway pressure

during normal respiration supplement the normal cardiac pumping ability [3].

Plethysmography variability index (PVI) has the potential to provide useful information concerning changes in the balance between intrathoracic airway pressure and intravascular fluid volume. Trending of PVI may be useful in monitoring surgical patients, both intraoperatively and postoperatively, for appropriate hydration states. For example, a rising PVI may indicate developing hypovolemia [4].

Continuous hemoglobin monitoring can allow a faster detection of significant blood loss, it may enable a rapid assessment of patient's condition as well as a more appropriate blood management and can perhaps reduce needless transfusions [5].

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The Masimo Radical-7 is a non-invasive device recently approved by the Food and Drug Administration that can measure PVI continuously, also Continuous, noninvasive hemoglobin (SpHb<sup>®</sup>) monitoring is possible [6].

The aim of this study is to evaluate the use of continuous non-invasive intraoperative PVI in conjunction with Hb levels monitoring using Masimo Radical-7™ Pulse CO-Oximeter in elective cesarean sections in patients with antepartum hemorrhage to guide for fluid and blood transfusion. Our primary outcome was to Compare PVI values before versus after administration of fluids based on decisions taken on clinical data as estimated blood loss, urinary output, blood pressure, heart rate and central venous pressure. Secondary outcome parameter was to detect whether SPHb detected the presence of anemic state or critical drop in hemoglobin level when compared to time of clinical awareness of bleeding and confirmation by lab Hb sample measurement.

## 2. Methodology

This prospective observational study with retrospective analysis was conducted after the approval of our institutional review board and was registered with clinical trials.gov registry system with trial number NCT02614053. A written informed consent was obtained from 124 participants before inclusion. The study was conducted in the obstetric theatre, Cairo university hospital. American Society of Anesthesiologist (ASA) Physical status I–II. patients aged from 18 to 40 years full-term multigravida parturients with antepartum hemorrhage and a singleton fetus scheduled for elective cesarean section, under general anesthesia were included in the study. Patients with known cardiac problems, significant liver disease, significant renal disease and significant coagulopathy were excluded from the study.

After receiving routine premedications (oral Ranitidine 150 mg and iv ondansetron 4 mg), patients were reassured through description of the whole technique, a peripheral cannula (18 gauge) was inserted under local anesthesia and 15 ml/kg normal saline infused, standard monitors.

(pulse oximetry, non-invasive blood pressure, and ECG) were applied. Masimo sensor was applied following best practice guidelines, and automated data collection (ADC) started using PC and Pulse Ox Software for ADC.

All patients received general anesthesia after preoxygenation for 3 min, rapid-sequence induction was done with thiopental in a dose of 3–5 mg/kg and suxamethonium 1.5 mg/kg. After induction and endotracheal intubation a large bore venous access, a central venous line, an arterial line and an indwelling urinary catheter were inserted.

Anesthesia was maintained with a 100% of oxygen with 0.5–1 MAC of isoflurane. Atracurium 0.5 mg/kg was given for muscle relaxation after suxamethonium action fades. Patients were ventilated to maintain an EtCO<sub>2</sub> of 4–4.6 kPa. After umbilical cord clamping, an infusion of 10 U oxytocin and fentanyl 2 µg/kg were given. At the end of surgery, inhalational anesthetic was discontinued, neuromuscular block was antagonized with neostigmine 50 µg/kg and atropine 20 µg/kg and the patient was extubated upon responding to commands, all patients were then transferred to PACU for postoperative monitoring.

Baseline PVI as well as Hb were recorded and then patients received continuous intraoperative PVI & Hb monitoring using Radical-7 Pulse cooximeter, v7748, connected to a R2-25 adult disposable sensor (Revision E, Masimo, Irvine, CA) After induction of anesthesia, the sensor was placed on the ring finger of the hand contralateral to the arterial line. Intermittent blood sampling was done for serum Hb analysis by the central laboratory. Blood

samples were taken when estimated blood loss (EBL) was 20% of total blood volume. Crystalloids (Ringer acetate) were used to replace blood loss (3 ml crystalloid for every 1 ml blood loss) as long as patient is hemodynamically stable and estimated blood loss (EBL) was <20% of total blood volume as detected from the suction apparatus, surgical field and surgical gauzes Blood transfusion was started when (EBL) was >20% of total blood volume and/or lab. Hb dropped to less than 8 gm/dl. The PVI, lab Hb and SpHb values were recorded at baseline as well as before and after any transfusion.

## 3. Statistical analysis and sample size calculation

Our primary outcome was to Compare PVI values before versus after administration of fluids. A minimum of 100 patients will be needed for a study power of 80% and an alpha error of 0.05. The number will be increased to 120 patients to compensate for possible dropouts. Data were collected and tabulated. Statistical analysis was done using SPSS (Statistical Package for Social Sciences) program V15 (IBM corp. U.S.A.) Frequency and percentage were used for non-numerical variables, while mean and standard deviation were used for numerical variables. Calculation of Bias and its SD between SpHb and lab Hb was done. Pearson correlation coefficient (*r*) was calculated to test linear relationship between two numerical variables. Results were considered statistically significant if *P* value was less than 0.05.

## 4. Results

Our study included 124 female patients. The demographic data included age, weight, height, and gestational age (Table 1).

Patients hemodynamic data (PVI, CVP, MAP and HR, were recorded throughout the operation as shown in the table below (Table 2).

From the start of the operation till the delivery of the baby PVI showed significant negative correlation with CVP ( $r = -0.238$ ,  $p = 0.022$ ) (Fig. 1) and a significant negative correlation with MAP ( $r = -0.280$ ,  $p = 0.032$ ). Also, it showed a significant positive correlation with HR ( $r = 0.294$ ,  $p < 0.001$ ). In patients where hysterectomy decision was taken (25 patients) PVI following hysterectomy showed significant negative correlation with CVP ( $r = -0.316$ ,  $p = 0.022$ ) and a significant negative correlation with MAP ( $r = -0.303$ ,  $p = 0.023$ ) (Fig. 2). Also, it showed significant positive correlation with HR ( $r = 0.289$ ,  $p = 0.031$ ). At the end of the operation in both situations whether hysterectomy was done or not PVI showed significant negative correlation with CVP ( $r = -0.224$ ,  $p = 0.037$ ) and a significant negative correlation with MAP ( $r = -0.211$ ,  $p = 0.01$ ). Also, it showed a significant positive correlation with HR ( $r = 0.342$ ,  $p < 0.001$ ). (Fig. 3).

Regarding hemoglobin levels, our results showed that Pre-transfusion lab Hb and SpHb showed significant correlation ( $r = 0.444$ ,  $p < 0.001$ ) (Fig. 4), also Post-transfusion lab Hb and SpHb showed significant positive correlation ( $r = 0.643$ ,  $p < 0.001$ ) as well (Fig. 5).

A total of 95 transfusions were performed in this study with a mean number of blood units  $2.76 \pm 1.42$  units. A transfusion was determined as necessary when there was either an observed change in hemoglobin by 2 g/dl, or when there was an observed total hemoglobin value below 8 g/dl A total of 87 transfusions (91.58%) may have been determined as unnecessary when using SpHb as the reference. Using the invasive laboratory measurement, 58 of the transfusions (61.05%) may have been considered as unnecessary (Table 3)

**Table 1**

Demographic data. Data are presented as mean ± SD.

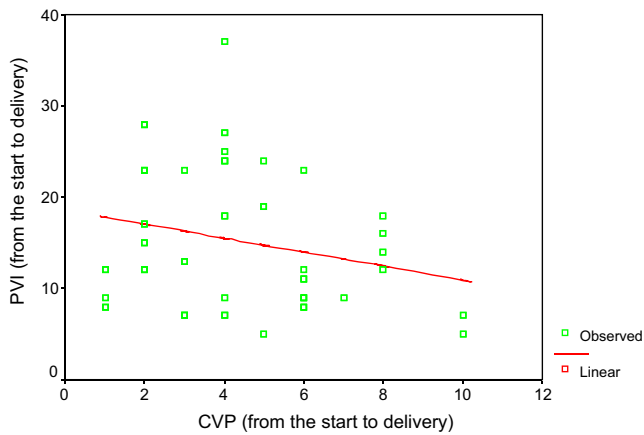
	Minimum	Maximum	Mean	SD
Age (years)	18	40	29.63	6.72
Gestational age (weeks)	34	38	36.36	1.81
Weight (kilogram)	55	120	73.71	21.21
Height (centimeter)	150	171	158.32	7.64

**Table 2**

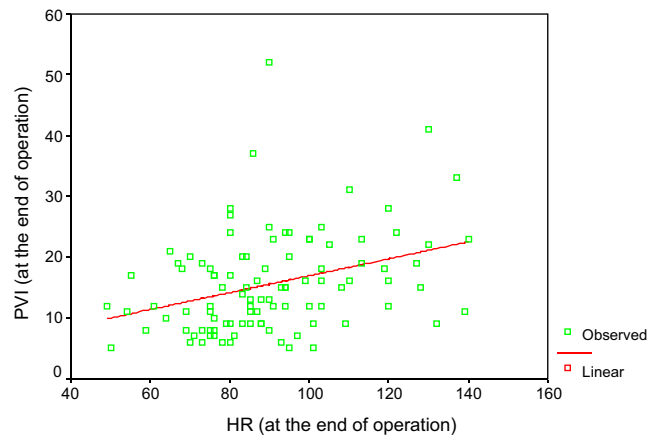
Hemodynamic data. Data are presented as mean ± SD.

Hemodynamic data		Minimum	Maximum	Mean	SD
From the start till baby delivery	PVI	5	37	15.76	7.77
	CVP	1	10	4.43	2.36
	HR	59	140	96.1	18.84
	MAP	68	124	86.58	10.99
Post hysterectomy	PVI	5	52	14.53	7.99
	CVP	1	6	3.38	1.15
	HR	49	137	84.86	18.87
	MAP	62	110	84.95	8.84
End of operation	PVI	5	52	15.7	8.25
	CVP	1	10	3.94	1.88
	HR	49	140	90.29	20.06
	MAP	62	124	86.03	10.53

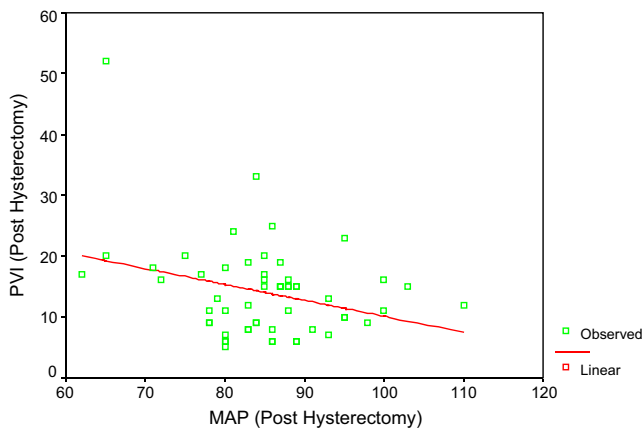
PVI: plethysmography variability index, CVP: central venous pressure (cm H2o), HR: heart rate (BPM), MAP: mean arterial pressure (mm Hg).



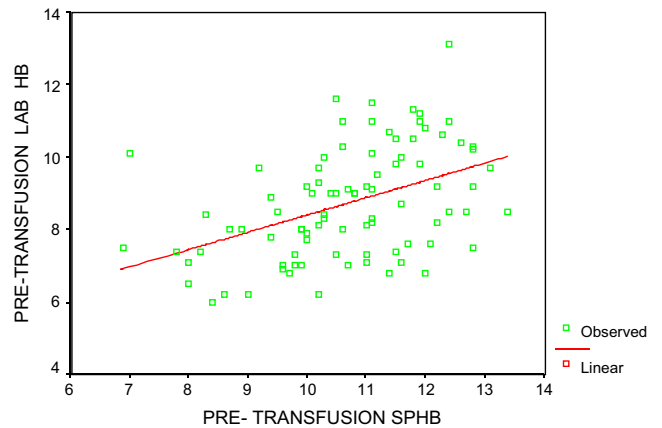
**Figure 1.** Linear regression curve showing negative correlation between PVI (pleth. Variability index) and CVP (central venous pressure).



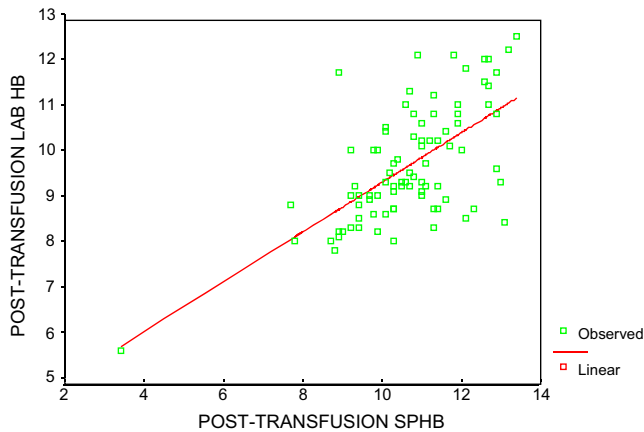
**Figure 3.** Linear regression curve showing significant positive correlation between PVI & HR (heart rate) .



**Figure 2.** Linear regression curve showing negative correlation between PVI and MAP (mean arterial pressure).



**Figure 4.** Linear regression curve showing significant positive correlation between pre transfusion lab HB and pre transfusion SpHB.



**Figure 5.** Linear regression curve showing significant positive correlation between post transfusion lab HB and post transfusion SpHB.

**Table 3**  
Frequency and percentage of necessary and possibly unnecessary transfusions.

Reference	Total number of necessary transfusions	Total number of possibly unnecessary transfusions
SpHb (gm/dl)	8 (8.42%)	87 (91.58%)
Lab HB (gm/dl)	37 (38.95%)	58 (61.05%)

## 5. Discussion

We reported that Plethysmography variability index (PVI) has the ability to provide useful information regarding the changes in the balance between the intravascular fluid volume status and the intrathoracic airway pressure. Also the results of the current study showed that continuous non invasive monitoring of hemoglobin (SpHb) may be a useful tool to decrease unnecessary blood transfusion.

Pleth variability index (PVI), showed to be useful for the management of patients on mechanical ventilation under general anesthesia with goal directed fluid therapy in the study by Cannesson et al. [4] Fu et al., found that PVI has significantly changed following volume expansion during complex surgical procedures [7]. Feissel et al., concluded that PVI is an interesting method for prediction of fluid responsiveness during early phase of septic shock patients [8]. A meta analysis done by Yin and Ho included 10 studies involving 328 patients, they came out with a result that PVI can predict fluid and preload responsiveness in the peri-operative as well as critically ill patients [9]. On the contrary, although Haas et al. [10] found a significant correlation between Stroke Volume Variations (SVV) and PVI after cardiopulmonary bypass in patients undergoing cardiac surgery, they found that PVI, MAP and CVP has no significant correlation which is against the results of the current study. Basal Lab Hb and SpHb showed significant correlation ( $p < 0.001$ ), these results go in line with Vos in the study done on patients undergoing hepatic resection [11]. On the contrary Marques et al. found that a bias of  $1.08 \pm 0.82$  g/dl was detected

between SpHb and lab.Hb [12]. Also in the study done by Miller et al. the accuracy of SpHb in 20 patients doing spine surgery was investigated, they concluded that a difference of  $-1.5$  g/dL was found between SpHb and lab.Hb in 39% of their findings [13].

Pre-transfusion and Post-transfusion lab Hb and SpHb showed significant correlation ( $p < 0.001$ ). However, the percentage of unnecessary blood transfusions, using either SpHb or labHb was 91.58%, 61.05% respectively may be attributed to being a blind study with retrospective analysis. The decision of blood transfusion was taken depending on lab. Hb, the estimated blood loss & finally on the clinical data rather than real time hemoglobin readings.

Limitations to our study are that PVI readings can be affected in states of low perfusion, with vasopressors use and in cases of severe hypothermia, so technical improvements of both sensor and the software as well are necessary to improve its accuracy. Also, the number of unnecessary blood transfusions might be reduced if the SpHb readings were taken into consideration.

In conclusion Plethysmography variability index (PVI) as well as non invasive spHb can be used as a useful monitor of intravascular volume status. Trending of PVI and spHb may be useful in surgical patients monitoring, both intraoperatively and postoperatively, for optimization of fluid and blood transfusion decisions.

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