

# Arterial and Plethysmographic Waveform Analysis in Anesthetized Patients with Hypovolemia

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## ABSTRACT

**Background:** Respiratory-induced arterial and plethysmographic (pulse oximetry) waveform changes were shown to be good predictors of cardiac output response to increased preload. The aim of this study was to evaluate the reliability of arterial and plethysmographic waveform variables in patients with mild hypovolemia.

**Methods:** Patients undergoing autologous hemodilution were studied. After anesthesia induction, hemodilution was performed by withdrawing blood in steps of 2% of estimated circulating blood volume (ECBV), up to 20%. The patients who did not develop hypotension (systolic blood pressure < 80 mmHg) were studied. Arterial and plethysmographic waveforms were recorded and analyzed off-line at baseline and after each withdrawal of blood. Variations in arterial systolic and pulse pressure were analyzed using standard methods. Plethysmographic waveform variation and delta pulse oximetry plethysmography were determined by using pulse oximetry recordings.

**Results:** There were 33 study participants. Systolic blood pressure decreased by 11%, and heart rate increased from 73 to 76 beats/min after a 20% reduction of ECBV. Systolic pressure and pulse pressure variations increased ( $P < 0.005$ ) after a 4% reduction of ECBV. The values of arterial pressure and pulse oximetry waveform variables al-

most doubled in value after a 20% reduction of ECBV. Systolic pressure variation was the most reliable variable during hypovolemia. Plethysmographic waveform variation increased significantly after a 6% reduction of ECBV and delta pulse oximetry plethysmography after an 8% reduction of ECBV.

**Conclusions:** Arterial and pulse oximetry respiratory-induced changes in waveform variables are reliable indicators of mild hypovolemia in anesthetized patients. The pulse oximetry plethysmographic waveforms accurately reflect arterial waveforms during more progressive hypovolemia.

### What We Already Know about This Topic

- ❖ Respiratory variations in arterial pressure and plethysmographic waveforms correlate with major blood loss, although the effect of mild blood loss is less well known

### What This Article Tells Us That Is New

- ❖ In 33 surgical patients undergoing **controlled blood withdrawal for hemodilution, arterial and pulse oximetry waveform changes with respiration were reliable measures of mild blood loss**

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**E**STIMATION of intravascular volume is one of the basic clinical tasks of the anesthesiologist. Although the limitations of assessing the changes in heart rate (HR) and blood pressure (BP) during blood loss are well known, the clinical diagnosis of hypovolemia is still often based on those two parameters.<sup>1,2</sup> There is a high level of suspicion of hypovolemia in patients with decreased BP and/or tachycardia, but diagnosing hypovolemia when those two signs are within normal limits might be difficult.

Respiratory-induced arterial BP and plethysmographic waveform changes in mechanically ventilated patients have been repeatedly shown to be sensitive indicators of hypovolemia<sup>3-6</sup> as well as sensitive predictors of cardiac output response to fluid infusion<sup>7,8</sup> and other types of preload changes, such as passive leg raising or changing in airway pressure.<sup>9-14</sup> Those dynamic variables have been shown to be better predictors of cardiac output response to fluid loading than the traditional static variables, such as central venous pressure or pulmonary artery occlusion pressure, or even data from transesophageal echocardiography.<sup>15,16</sup> Respiratory-induced varia-

tions in arterial and plethysmographic waveforms and stroke volume have become acceptable physiologic signs of cardiac output responsiveness to fluid loading,<sup>17</sup> and some monitors are already equipped with online automatic measurement of these parameters.

Despite the growing popularity of respiratory-induced arterial and plethysmographic waveform parameters, only few studies have evaluated waveform variations after protocol-driven mild blood volume reduction. These studies evaluated the waveform signal in response to only one step of 10% of the estimated decrease in circulating blood volume (ECBV), and their results have shown significant changes in waveform variables, although the reliability of these changes in estimating less extensive, mild blood loss was not studied.<sup>3,5,6</sup> Waveform changes resulting from smaller amounts of blood loss and the degree of reliability by blood volume changes of less than 10% of the ECBV have never been evaluated. However, during the last 2 decades, some authors have questioned the relevance of those parameters in nonhypotensive patients.<sup>18</sup>

We hypothesized that changes in arterial and plethysmographic respiratory-induced waveform variables reliably reflect the degree of mild blood loss in anesthetized and otherwise hemodynamically stable patients. To test our hypothesis, we evaluated the accuracy of the different respiratory-induced arterial and pulse oximetry plethysmographic waveform variables during mild hypovolemia.

## Materials and Methods

Patients scheduled for elective hip arthroplasty, suprapubic prostatectomy, or nephrectomy and who had a plan for autologous hemodilution were eligible for the study. Exclusion criteria included patients with a hemoglobin concentration less than 13.0 g/dl, a creatinine concentration more than 1.5 mg/dl, with coronary or cerebrovascular event during the past 6 months, or whose cardiac rhythm was other than a normal sinus rhythm. After obtaining institutional review board (Carmel Medical Center, Haifa, Israel) approval for this study and signed written informed consent from the patients, all study participants received standard anesthesia care. Patients treated chronically with  $\beta$ -adrenergic antagonists received regular doses of their medication and 10 mg diazepam orally on the morning of the surgery. Angiotensin-converting enzyme inhibitors were skipped on the day of surgery.

Each patient received 7 ml/kg lactated Ringer's solution during the induction of general anesthesia by 1.5  $\mu$ g/kg fentanyl and 2.0–2.5 mg/kg propofol. Tracheal intubation was facilitated with 0.6 mg/kg rocuronium, positive pressure ventilation was applied (tidal volume 8 ml/kg of ideal body weight), and anesthesia was maintained with nitrous oxide/oxygen (1:1) + isoflurane (end-expiratory concentration 0.4%) throughout the period of blood autodonation. The frequency of mechanical ventilation was adjusted to remain between 8 and 12 to keep end-tidal carbon dioxide at 33–37 mmHg.

Blood was withdrawn by steps of 2% of ECBV up to 20% of ECBV (10 steps), which was calculated by the

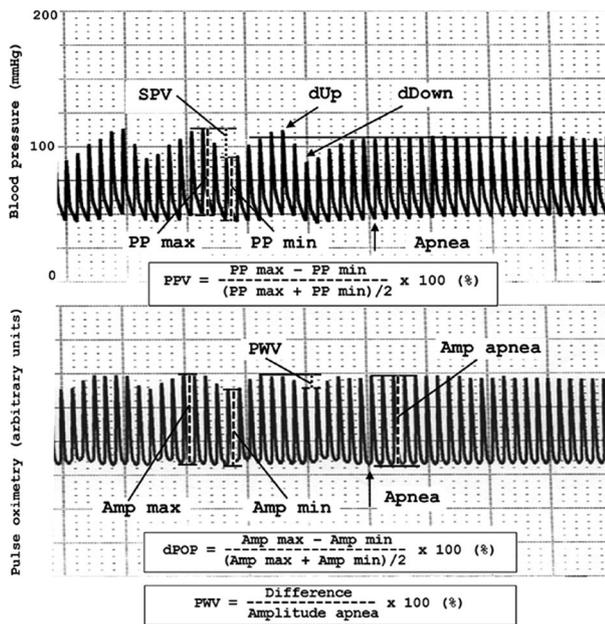
following formula:  $([1486 \times \text{body surface area}] - 825) + (1578 \times \text{body surface area})$  for men and  $([1.06 \times \text{age}] + [822 \times \text{body surface area}] + (1395 \times \text{body surface area}))$  for women.<sup>19</sup> Blood was collected in a citrate phosphate dextrose adenine bag. The criteria for blood withdrawal discontinuation were as follows: a decrease in systolic BP by more than 20% from the values observed immediately before start of blood withdrawal, a systolic BP less than 80 mmHg, or the occurrence of dysrhythmia. Each step of blood withdrawal with concomitant recording of waveforms took about 3 min, with no pauses between steps. Blood volume was replaced with an equal volume of colloid solution after the completion of blood withdrawal (6% hydroxyethyl starch 200/0.5; Fresenius Kabi, Deutschland GmbH, Germany). Autologous blood was retransfused to the patient at the end of the surgical procedure.

Arterial and plethysmographic (pulse oximetry) waveforms were recorded with a Datex-Ohmeda AS-3 (Datex, Helsinki, Finland) recorder and analyzed off-line at baseline and after each step of blood withdrawal. A pulse oximeter probe was placed on the patient's index finger and wrapped with a towel to prevent interference from outside light. The pulse oximeter of the monitor was set for the manual size mode and the signal was kept at the same scale throughout the study period. Arterial and plethysmographic waveforms were recorded using the printer module of the monitor. Paper recordings were scanned at a resolution of 300 dpi. The computer images were measured using the format shape function of Word (Office 2003; Microsoft Co., Redmond, WA) with the lock-to-grid function disabled. All the measured points were verified by two independent researchers.

The systolic pressure variations (SPV), dUp, dDown, and pulse pressure variations (PPV) were analyzed using standard methods (fig. 1).<sup>4,9</sup> The plethysmographic waveform variations (PWV) of the pulse oximetry signal were calculated as follows: the difference between the maximal and minimal plethysmographic signals divided by the amplitude of the plethysmographic signal during apnea (fig. 1).<sup>6</sup> The delta pulse oximetry plethysmographic (dPOP) waveform amplitude was calculated as follows:  $(\text{POP}_{\text{max}} - \text{POP}_{\text{min}})/([\text{POP}_{\text{max}} + \text{POP}_{\text{min}}]/2)$  (fig. 1).<sup>20</sup> Only patients who tolerated all 10 steps (*i.e.*, 20% of circulating blood volume) of the blood withdrawal protocol were included in this analysis.

## Statistical Analysis

Values are presented as mean  $\pm$  SD unless otherwise stated. Comparisons of variables before and after blood withdrawal were performed with the paired *t* test. The relationship between hemodynamic variables and the steps of blood withdrawal was analyzed by a linear mixed model.<sup>21</sup> A mixed model takes into account the within-patient correlation and includes all available data for each patient. Each step of ECBV reduction was taken as a fixed categorical variable (with 11 levels) to estimate differences from baseline. Compound symmetry structure was assumed for the covariance matrix of the repeated measures. Applying the Bonferroni



**Fig. 1.** Arterial and pulse oximeter plethysmographic waveform analysis. Systolic pressure variation (SPV) is the difference between maximal and minimal systolic blood pressure; delta Up (dUp) is a maximal inspiratory minus apneic systolic blood pressure; delta Down (dDown) is an apneic minus minimal systolic blood pressure during expiration; pulse pressure (PP) is a difference between systolic and diastolic blood pressure,  $PP_{max}$  = maximal PP during inspiration;  $PP_{min}$  = minimal PP during expiration; PPV = pulse pressure variation. Plethysmographic waveform variation (PWV) was measured as a difference between maximal and minimal pulse oximeter signals divided by the pulse oximeter signal amplitude during apnea. Pulse oximetry plethysmographic (POP) max and min are defined as maximal and minimal waveform amplitudes over one respiratory cycle.

correction, a *P* value less than 0.005 was considered significant for comparisons with the baseline value, as 10 differences were tested.<sup>22</sup> The *F* value of the mixed model test was used to compare the magnitude of the relationship between hemodynamic variables during all stages of blood withdrawal.

The mean coefficient of variation (SD/mean) was used to compare the variability of the parameters. Correlations between SPV and PPV, PWV, and dPOP for each step of blood withdrawal were calculated using the Pearson correlation coefficient.

To test the slope difference of two periods of ECBV reduction, that is, steps 0–5 and steps 6–10, a second mixed model<sup>21</sup> was performed. The model includes time as a fixed continuous variable and as an indicator variable for period (first five steps = 0 and the last five steps = 1), and interaction (that estimates the difference in slopes of the two periods).

The Pearson correlation coefficient of each waveform variable to the stages of blood withdrawal in every patient was calculated to estimate the supplemental value of each variable. Statistical calculations were performed with the SPSS 15.0 (SPSS Inc., Chicago, IL).

**Table 1.** Demographic Data and Medical History

Parameters	Concomitant Diseases and Chronic Medications	Values
Age (yr)		54.1 ± 11.1
Male/female (n)		21/12
BMI (kg/m <sup>2</sup> )		27.4 ± 6.1
ECBV (ml)		4711 ± 872
Hb (g%)		13.7 ± 1.2
Medical history (n)	IHD	2
	HTN	8
	DM	5
	PVD	1
	COPD	8
Current medications (n)	β-adrenergic antagonists	4
	ACE inhibitors	5

Data are mean ± SD.

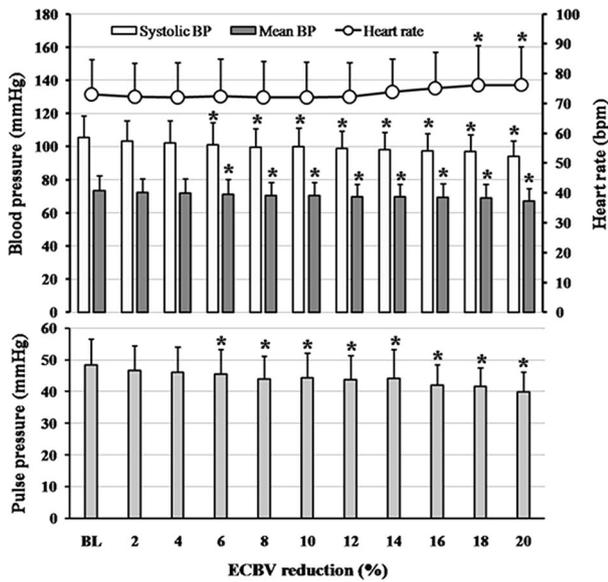
ACE = angiotensin-converting enzyme; BMI = body mass index; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; ECBV = estimated circulating blood volume; Hb = hemoglobin; HTN = hypertension; IHD = ischemic heart disease; PVD = peripheral vascular disease.

## Results

Total 109 patients were recruited in the study, and 33 of them tolerated withdrawal of 20% of estimated blood volume without decrease in systolic BP below 80 mmHg and or by more than 20% of baseline value. The demographic data of the 33 study participants who tolerated gradual 20% blood withdrawal without significant hypotension are presented in table 1. Because of the small number of patients with concomitant diseases and receiving medications chronically, we did not perform quantitative analysis. The entire procedure, from the initiation of recording at baseline until the recording after 20% of ECBV withdrawal, took 25–30 min. As a result of blood withdrawal, the hemoglobin concentration decreased from 13.7 ± 1.2 g/dl to 13.0 ± 1.3 g/dl (*P* < 0.0001) before replacement with colloid. Peak airway pressure did not change during the study period; it was 20.7 ± 4.6 cm H<sub>2</sub>O at the beginning and 20.6 ± 4.6 cm H<sub>2</sub>O at the end of blood withdrawal.

### Standard Hemodynamics

Although the increase in HR became significant after 18% of ECBV withdrawal, the changes were small and clinically insignificant (fig. 2). The HR increased only by 4% after a 20% reduction of ECBV. Similarly, the changes in systolic and mean arterial BPs were mild, although the decrease was already significant after a 6% withdrawal of ECBV (fig. 2). The maximal reduction of 11% in systolic BP was observed after withdrawal of 20% of ECBV. The decrease in arterial pulse pressure was also gradual and reached statistical significance after 6% ECBV withdrawal (fig. 2). However, the magnitude of reduction was only 16% after a 20% withdrawal of ECBV (table 2). As mea-



**Fig. 2.** Heart rate, systolic blood pressure, mean blood pressure, and pulse pressures during all stages of blood withdrawal. The data are presented as mean ± SD. *P* values are significant (\*) at <0.005 compared with baseline (BL). ECBV = estimated circulating blood volume.

sured by the coefficient of variation, the changes of HR and arterial pressures were consistent during all stages of the study (table 2).

**Pulse Oximeter Plethysmography Waveform Variables**

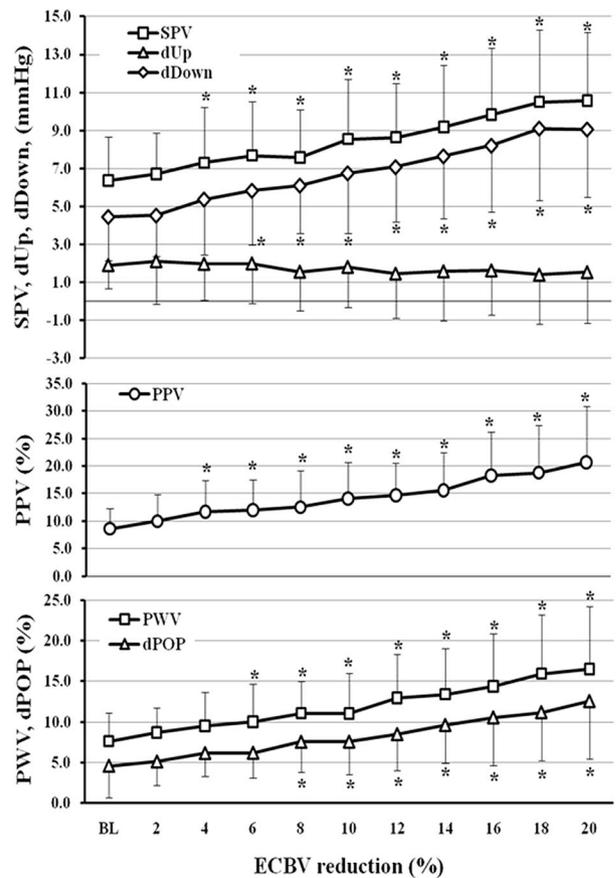
The values of plethysmographic waveform variables, PWV and dPOP, increased gradually during the steps of blood withdrawal. The PWV value became significantly different

**Table 2.** Relationships of Hemodynamic Variables to the Steps of Hypovolemia, Coefficient of Variation, and Percent of Change during Blood Volume Reduction

Variables	<i>F</i> <sub>(10, 320)</sub>	Coefficient of Variation (%)	% Change after 20% ECBV Withdrawal
HR	8.2	16.4	4
SBP	14.3	11.4	11
MBP	8.6	11.6	8.5
PP	10.9	17.6	16
SPV	54.8	33.7	87
dDown	28.6	59.8	103
PPV	34.9	46.4	148
PWV	31.6	43.2	117
dPOP	15.6	54.9	174

*F* = value of the mixed model test, *P* < 0.00001. Coefficient of variation = mean value of coefficient of variations of all steps of blood withdrawal including baseline. Percent of change is calculated as percent of change after 20% estimated circulating blood volume (ECBV) withdrawal compared with baseline.

dDown = delta down; dPOP = delta pulse oximetry plethysmographic waveform amplitude; HR = heart rate; MBP = mean blood pressure; PP = pulse pressure; PPV = pulse pressure variation; PWV = plethysmographic waveform variation; SBP = systolic blood pressure; SPV = systolic pressure variation.

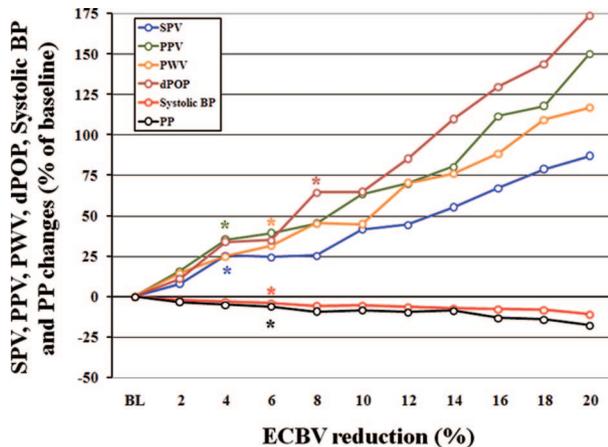


**Fig. 3.** Systolic blood pressure variations (SPV) and their components, dUp and dDown, pulse pressure variation (PPV) of arterial blood pressure, plethysmographic waveform variation (PWV), and pulse oximetry plethysmographic waveform variation (dPOP) during all stages of blood withdrawal. The data are presented as mean ± SD. \* Significant compared with baseline (BL) (*P* < 0.005). ECBV = estimated circulating blood volume.

from baseline after a 6% withdrawal of ECBV, and the dPOP value became significantly different after an 8% withdrawal of ECBV, with the changes of both variables reaching more than 100% from baseline values after a 20% withdrawal of ECBV (table 2, fig. 3). The relationship (measured by the *F* value of a mixed model) between these two variables and the steps of blood withdrawal was stronger, and the coefficient of variation (variability of variable) was lower in PWV compared with that of dPOP (table 2).

**Arterial BP Waveform Variables**

The SPV and PPV became significantly different from baseline values after a 4% reduction of the ECBV during gradual blood withdrawal, and the dDown became significantly different from baseline values after a 6% reduction of the ECBV during gradual blood withdrawal (figs. 3, 4). The changes were more than 80% for each of those variables after a 20% withdrawal of the ECBV. The dUp component of the SPV did not change significantly, although the absolute value became negative in five pa-



**Fig. 4.** Changes in systolic blood pressure (SBP; red line), pulse pressure (PP; black line), systolic pressure variations (SPV; blue line), pulse pressure variation (PPV; green line), plethysmographic waveform variation (PWV; orange line), and pulse oximetry waveform amplitude (dPOP; brown line) plotted against all stages of blood withdrawal. Asterisk signifies the first step of blood withdrawal when there was a significant difference from baseline (BL). The values during all the following stages were also significantly different from BL. Values of SD are not shown for the sake of simplicity (shown in figs. 2 and 3). SPV and PPV are seen as being the first two variables that became significantly different from BL. Among the examined four waveform variables, the SPV has the lowest variability (table 2) and highest consistency (table 3), making it the most reliable of the tested variables even though the degree of change from BL was larger in the dPOP and PPV. ECBV = estimated circulating blood volume.

tients, indicating considerable hypovolemia. The degree of changes in the SPV and PPV during the first five steps of blood withdrawal was less prominent compared with the ensuing steps of blood volume reduction ( $P = 0.006$  for the SPV and  $P = 0.002$  for the PPV). The dDown did not show any difference in the pattern of changes between the early and later stages of blood withdrawal.

The strength of the relationship ( $F$  value) between the SPV and the step of blood withdrawal was stronger and the coefficient of variation was lower compared with those of the PPV, signifying that changes in the SPV were more closely dependent on the step of blood withdrawal and that there was less variability between individual subjects (table 2).

### Interactions among Waveform Variables

The Pearson coefficient of correlation between waveform variables and stages of blood withdrawal in each patient was used to estimate the supplemental value of the parameters. The correlations with the steps of blood withdrawal were not significant in two patients for SPV, in four patients for PPV, in five for PWV, and in 11 for dPOP (fig. 5 and table 3). Three of the four patients with nonsignificant correlations of their PPV with steps of blood withdrawal had a significant correlation between their SPV and steps of blood withdrawal, although only one patient

had no correlation of all waveform variables with steps of blood withdrawal.

Correlations between the SPV and PPV, PWV, and dPOP increased with deeper hypovolemia. Both plethysmographic variables correlated well with the corresponding arterial waveform variables (*i.e.*, PWV with SPV and dPOP with PPV), and those correlations were greater at deeper stages of blood withdrawal (fig. 6 and table 4).

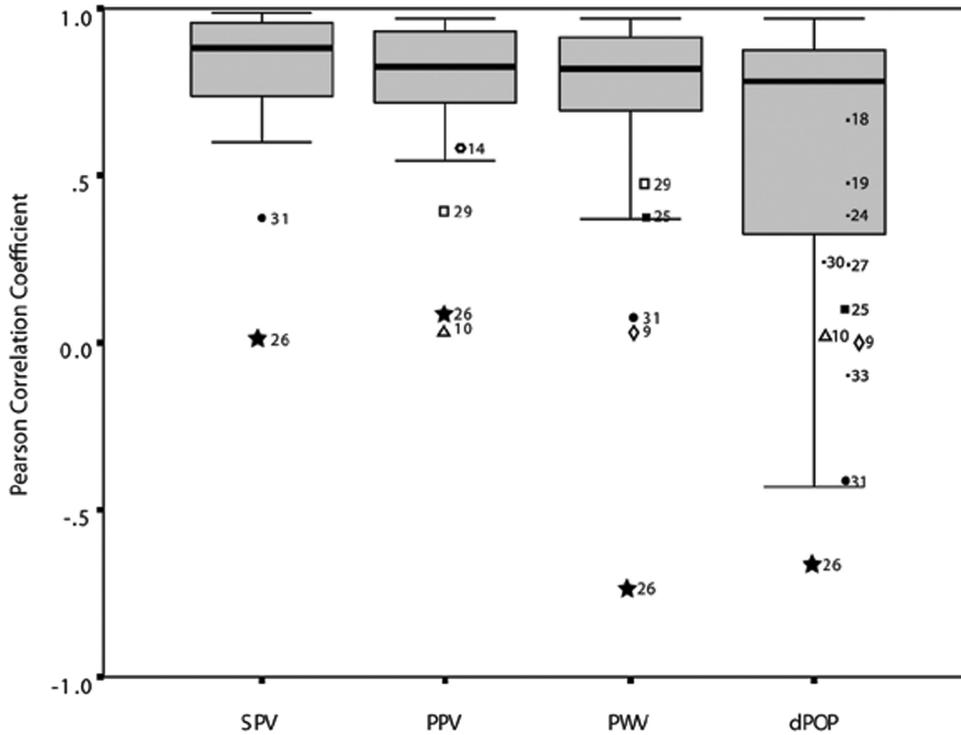
### Discussion

Our hypothesis was that arterial and pulse oximeter plethysmographic waveforms are reliable indicators of hypovolemia in otherwise hemodynamically stable patients. The findings of the study that supported this hypothesis are follows: (1) reduction of even 4% of ECBV causes significant changes in respiratory-induced arterial waveform variables in otherwise hemodynamically stable patients; (2) respiratory-induced plethysmographic waveform signals follow arterial waveform changes with some delay and correlate accurately with the arterial BP waveforms at more advanced stages of blood loss; (3) respiratory-induced arterial waveform changes are more prominent during more extensive stages of hypovolemia than during early stages; and (4) SPV is the most reliable hemodynamic variable during graded hypovolemia.

The respiratory-induced arterial waveform variables, such as SPV, dDown, and PPV, have repeatedly been shown to be sensitive predictors of cardiac output response to volume loading and other factors that affect venous return.<sup>7,8,10,12,23</sup> Arterial waveform variables have been used by several authors as guides for intraoperative fluid management.<sup>24,25</sup> However, those data are difficult to extrapolate for the purpose of diagnosing mild hypovolemia. This is the first study to evaluate the clinically relevant reliability of both respiratory-induced arterial and plethysmographic waveform variations during gradually developing hypovolemia without arterial hypotension.

Our study simulates a clinically important situation in which substantial blood loss occurs without considerable changes in BP and HR (an only 11% change of systolic BP and a  $< 10\%$  change in HR and mean BP). The early and consistent increase in values of waveform variables during blood withdrawal strongly supports the idea that these parameters are reliable indicators of mild hypovolemia in otherwise hemodynamically stable patients.

In our study group, SPV correlated better with blood volume reduction than PPV and had a smaller variability between patients throughout the study compared with other variables. These results are different from the previous studies by Michard *et al.*,<sup>26</sup> who found PPV to be a more sensitive and specific predictor of cardiac output changes after an increase in preload. There are several explanations for this discrepancy. We used a gradual multistep approach to reduce blood volume in contrast to the one-step increase in the preload that had been used in that and most of the previous



**Fig. 5.** Box plots of Pearson correlation coefficients between waveform variables and the steps of blood withdrawal. The *line* across the *box* indicates the median. The *box* represents the interquartile range (the difference between the 75th and 25th percentiles), which contains 50% of the values. The *whiskers* are lines that extend from the *box* to the highest and lowest values, excluding outliers (cases with values > 1.5 box lengths from the upper or lower edge of the *box*). The marked ID of patients indicate those with nonsignificant correlation. dPOP = pulse oximetry waveform amplitude; PPV = pulse pressure variation; PWV = plethysmographic waveform variation; SPV = systolic pressure variations.

studies.<sup>7,8,14,16,23,27</sup> In addition, they estimated cardiac response to volume expansion by an arbitrary threshold of cardiac output response, usually 10–15%, which probably affected the results.<sup>7,8,14,23,26,27</sup> Our data support the notion that SPV is at least reliable and even more consistent than PPV in reflecting hypovolemia and lend credence to the contention that it is easier to observe until automatic determination will become widely available.<sup>28</sup>

The supplemental effect of different waveform variables is clearly evident in our data. By analyzing only their PPV, the diagnosis of hypovolemia could have been missed in four of the 33 patients in our group, whereas the additional measurement of SPV would have decreased the number of missed diagnoses to one. Although some waveform variables had more prominent changes than the SPV

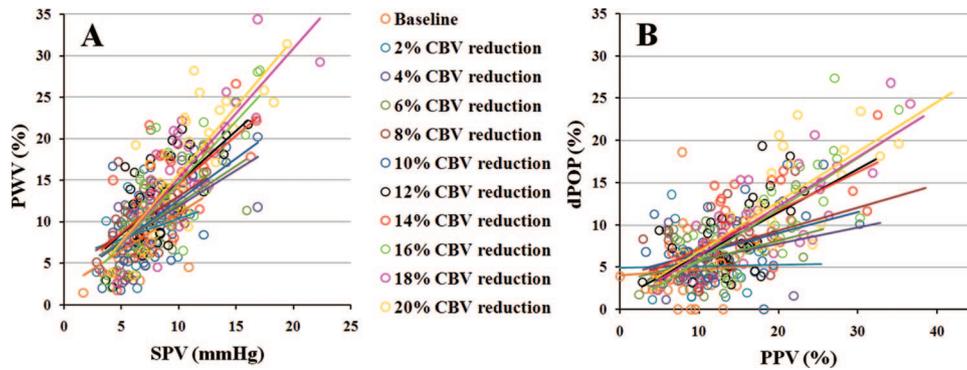
(fig. 4), SPV is more reliable by being more consistent during all stages of blood withdrawal.

Arterial waveforms changed more dramatically during ECBV withdrawal of 12–20% compared with 2–10%. There are at least two possible explanations for such a difference. Stroke volume is more sensitive to changes in preload when operating on the steep portion of the Frank–Starling curve; a similar decrease in preload results in a larger decrease in stroke volume that is reflected in higher variability in arterial systolic and pulse pressure, as well as in the plethysmographic waveform signal. An additional explanation for nonlinear changes in stroke volume could be a more effective recruitment of blood volume during the early stages of hypovolemia by mobilization of blood from an “unstressed” volume within the

**Table 3.** Summary of Intercept and Slope of Pearson Coefficient of Correlations between Waveform Variables and the Steps of Blood Volume Reduction

	SPV		PPV		PWV		dPOP	
	b <sub>0</sub>	b <sub>1</sub>						
Mean	6.298	0.433	8.563	1.157	7.426	0.882	4.185	0.783
SD	2.284	0.272	4.121	0.769	3.042	0.607	3.223	0.812
Median	6.050	0.419	8.175	1.023	7.011	0.940	3.975	0.762

b<sub>0</sub> = intercept; b<sub>1</sub> = slope; dPOP = delta pulse oximetry plethysmographic waveform amplitude; PPV = pulse pressure variation; PWV = plethysmographic waveform variation; SPV = systolic pressure variation.



**Fig. 6.** (A) Respiratory variations of the plethysmographic waveform variation (PWV) plotted against arterial systolic pressure variations (SPV). (B) Respiratory variations in the pulse oximetry photoplethysmographic waveform amplitude (dPOP) plotted against the arterial pulse pressure variation (PPV) in a scatterplot. The circles represent the values of the two variables in all patients at the same step of blood volume reduction and are presented with the same color. Each color of the regression lines represents the same step of blood withdrawal. Two values from the PPV and dPOP plot were removed for lack of space. Correlations within both comparisons improved with increased stages of blood withdrawal. CBV = circulating blood volume.

venous system that exists in normovolemic subjects, mostly in the splanchnic venous system.<sup>29</sup> It is reasonable to speculate that compensation from the venous system occurs to a greater extent at early stages of hypovolemia than at later ones when unstressed volume is already decreased.

Unlike the arterial signal that can be accurately measured, the plethysmographic pulse oximetry signal is not standardized, and, in addition, it is processed and filtered in different ways by different manufacturers.<sup>30,31</sup> The use of PWV to assess changes in blood volume, similar to arterial waveform variations, was first mentioned more than 2 decades ago.<sup>32</sup> Since then several studies have described different methods of analyzing the pulse oximetry plethysmographic signal.<sup>6,20,33–38</sup> In our current as well as previous studies, we used normalized plethysmographic AS signals (pulsatile) during apnea as reference points to calculate respiratory-induced PWV. We also measured respiratory dPOP that has also been used in several recent studies.<sup>20,36–38</sup> Contrary to previous studies that found the plethysmographic signal to be similar to the arterial waveform signal, we found some discrepancy between them. We observed low correlations of both the PWV and the dPOP with the arterial waveform

variables at baseline and during early stages of blood withdrawal; these correlations significantly improved at more advanced stages of hypovolemia. This is in agreement with recent data that demonstrated a discrepancy between arterial and plethysmographic signals observed in an intensive care unit.<sup>39</sup> In this study, the plethysmographic variables showed a similar relationship with arterial waveforms, and significant improvement was seen in the correlation between them at more extensive stages of blood withdrawal (fig. 6). The difference between the PWV and the dPOP at early stages of hypovolemia and the significantly greater inconsistency between the dPOP and the PWV compared with the arterial waveform signals supports the need for an accurate evaluation of each new variable generated from pulse oximetry plethysmographic signals before introduction of the technique into wide clinical use.<sup>28</sup>

There are several limitations to this study. The selection of patients with mild hypovolemia was based on an arbitrary threshold of systolic BP = 80 mmHg or within 20% of baseline. These two threshold limits were not prospectively evaluated, although they are frequently used in clinical practice as safety limits.<sup>40</sup> The volume of withdrawn blood could not be precisely

**Table 4.** Pearson Correlation Coefficients between SPV–PWV and PPV–dPOP during Blood Volume Reduction

Steps of Blood Volume Reduction	SPV–PWV				PPV–dPOP			
	<i>r</i>	<i>P</i> Value	<i>b</i> <sub>0</sub>	<i>b</i> <sub>1</sub>	<i>r</i>	<i>P</i> Value	<i>b</i> <sub>0</sub>	<i>b</i> <sub>1</sub>
0 (BL)	0.553	0.001	2.073	0.893	0.058	0.756	4.021	0.068
1 (2%)	0.314	0.097	5.479	0.489	0.026	0.894	4.913	0.019
2 (4%)	0.562	0.001	3.291	0.862	0.280	0.127	3.994	0.190
3 (6%)	0.529	0.002	3.055	0.909	0.385	0.033	3.303	0.242
4 (8%)	0.547	0.002	4.050	0.907	0.356	0.058	3.963	0.271
5 (10%)	0.632	0.000	2.468	1.013	0.395	0.025	4.138	0.247
6 (12%)	0.658	0.000	2.371	1.273	0.568	0.001	1.253	0.513
7 (14%)	0.667	0.000	2.772	1.174	0.664	0.000	2.646	0.455
8 (16%)	0.802	0.000	−0.074	1.480	0.777	0.000	−0.232	0.605
9 (18%)	0.821	0.000	−0.286	1.561	0.792	0.000	0.553	0.584
10 (20%)	0.787	0.000	−0.583	1.630	0.752	0.000	2.124	0.505

*b*<sub>0</sub> = intercept; *b*<sub>1</sub> = slope; BL = baseline; dPOP = delta pulse oximetry plethysmographic waveform amplitude; PPV = pulse pressure variation; PWV = plethysmographic waveform variation; *r* = Pearson correlation coefficient; SPV = systolic pressure variation.

equal to the 20% of real blood volume because the actual blood volume was not measured but rather calculated by a formula.<sup>19</sup> Despite these limitations, we believe that we have described a reasonable approximation of a human model of mild gradual hypovolemia that lasts for less than 30 min.

In conclusion, respiratory-induced arterial waveform changes are reliable indicators of small degrees of blood loss in otherwise hemodynamically stable anesthetized and mechanically ventilated patients. The SPV was the most reliable variable for estimating blood loss. The respiratory-induced plethysmographic waveforms accurately follow changes in arterial waveforms at more advanced stages of blood withdrawal.

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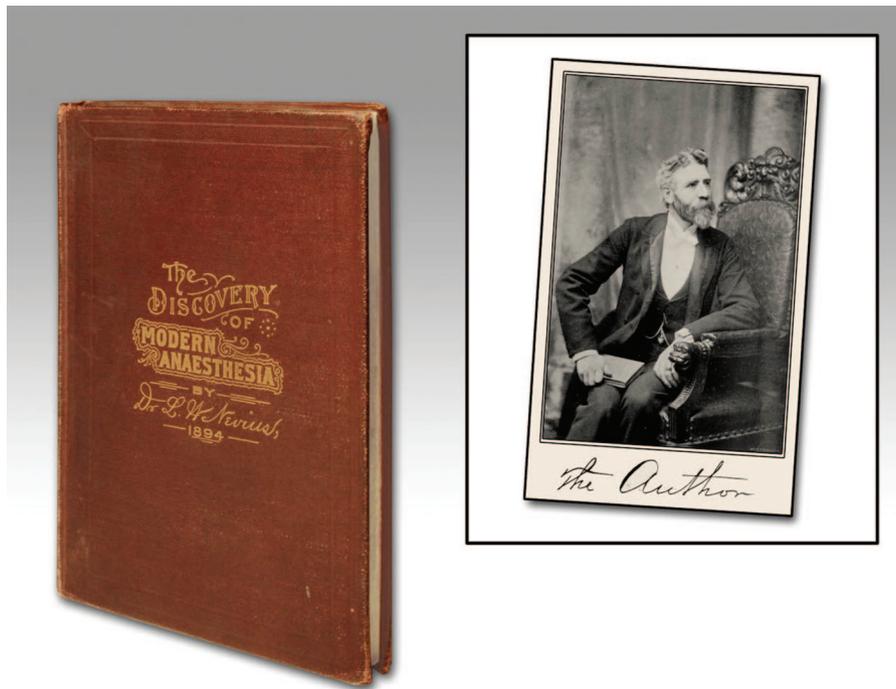
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## ANESTHESIOLOGY REFLECTIONS

### Nevius' 1894 *Discovery of Modern Anesthesia*



From the stacks of the Wood Library-Museum, this elegant volume is awkwardly titled *The Discovery of Modern Anesthesia. By Whom It Was Made. A Brief Statement of Facts*. Authored by dentist Laird W. Nevius (1845–1915), this book attempted to fairly portray the leading figures behind dental and surgical anesthesia. This was a remarkable effort, particularly since Nevius was a disciple of G. Q. Colton, who clearly backed Horace Wells as the “Discoverer of Anesthesia.” Upon reviewing Nevius’ book in 1894, the journal *Dental Cosmos* observed that the “whole controversy, from 1847 to the present time, has been no more marked by acrimony than it has been by a disposition to laud those who applied the scientific discoveries more than the original suggestors [sic] of the agents to be employed.” (Copyright © the American Society of Anesthesiologists, Inc. This image appears in color in the *Anesthesiology Reflections* online collection available at [www.anesthesiology.org](http://www.anesthesiology.org).)

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