

CARDIOVASCULAR

# Influence of the site of measurement on the ability of plethysmographic variability index to predict fluid responsiveness

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## Editor's key points

- Plethysmographic variability index (PVI) can predict i.v. fluid responsiveness in mechanically ventilated patients, but the influence of the monitoring site on sensitivity and specificity is unknown.
- PVI monitored at the forehead, ear, or finger predicted fluid responsiveness in 28 anaesthetized and mechanically ventilated subjects.
- PVI monitored at the forehead or ear provides a useful alternative to the finger in certain situations.

**Background.** Plethysmographic variability index (PVI) is an accurate predictor of fluid responsiveness in mechanically ventilated patients. However, the site of measurement of the plethysmographic waveform impacts its morphology and its respiratory variation. The goal of this study was to investigate the ability of PVI to predict fluid responsiveness at three sites of measurement (the forehead, ear, and finger) in mechanically ventilated patients under general anaesthesia.

**Methods.** We studied 28 subjects after induction of general anaesthesia. Subjects were monitored with a pulmonary artery catheter and three pulse oximeter sensors (the finger, ear, and forehead). Pulse pressure variation, central venous pressure, cardiac index (CI), and PVI measured at the forehead, ear, and finger (PVI<sub>forehead</sub>, PVI<sub>ear</sub>, and PVI<sub>finger</sub>) were recorded before and after fluid loading (FL). Subjects were responders to volume expansion if CI increased >15% after FL.

**Results.** Areas under the receiver-operating curves to predict fluid responsiveness were 0.906, 0.880, and 0.836 for PVI<sub>forehead</sub>, PVI<sub>ear</sub>, and PVI<sub>finger</sub>, respectively ( $P < 0.05$ ). PVI<sub>forehead</sub>, PVI<sub>ear</sub>, and PVI<sub>finger</sub> had a threshold value to predict fluid responsiveness of 15%, 16%, and 12% with sensitivities of 89%, 74%, and 74% and specificities of 78%, 74%, and 67%, respectively.

**Conclusions.** PVI can predict fluid responsiveness in anaesthetized and ventilated subjects at all three sites of measurement. However, the threshold values for predicting fluid responsiveness differ with the site of measurement. These results support the use of this plethysmographic dynamic index in the cephalic region when the finger is inaccessible or during states of low peripheral perfusion.

**Keywords:** cardiac output; fluid responsiveness; monitoring, intraoperative; oximetry; photoplethysmography

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Recent studies have shown that intraoperative optimization of cardiac output (CO) using goal-directed volume expansion has the ability to improve postoperative outcome with a decrease in postoperative morbidity and hospital stay.<sup>1–3</sup> To avoid the potential deleterious effects of volume expansion, preload dependence assessment is crucial to guide fluid therapy to prevent excessive fluid loading (FL), and so robust predictors of fluid responsiveness are needed.<sup>4–5</sup> Dynamic parameters, relying on respiratory variations in stroke volume, have been shown to be better indicators of

fluid responsiveness than static parameters in mechanically ventilated patients under general anaesthesia.<sup>6–7</sup>

Pulse oximetry is a standard intraoperative monitor, is widely available, non-invasive, and mandatory in many countries.<sup>8</sup> Respiratory variations in the plethysmographic waveform amplitude ( $\Delta\text{POP}$ ) can predict fluid responsiveness in mechanically ventilated patients in the operating theatre.<sup>9–11</sup> Plethysmographic variability index (PVI) (Masimo Corp., Irvine, CA, USA) is an algorithm allowing for automated and continuous monitoring of respiratory

variations in the pulse oximetry plethysmographic waveform amplitude, derived from the perfusion index (PI).<sup>12</sup> PVI has the ability to predict fluid responsiveness<sup>13–14</sup> and to improve intraoperative fluid management and postoperative outcome.<sup>15</sup> However, vasomotor tone can impact the plethysmographic waveform and the accuracy of  $\Delta$ POP, PVI, or both to predict fluid responsiveness.<sup>16</sup> Most studies focusing on this topic measured these parameters at the finger.<sup>9–11–14</sup> However, recent studies suggest that other sites of measurement might be more appropriate.<sup>17–20</sup> The choice of an alternative site of measurement with less sensitivity to changes in vasomotor tone, such as the ear or forehead, might then improve the accuracy of PVI.

The goal of this study was to investigate and compare the ability of PVI to predict fluid responsiveness at three different sites of measurement (the finger, ear, and forehead) in mechanically ventilated patients in the operating theatre.

## Methods

The protocol used in the present study was approved by the institutional review board for human subjects of Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale Lyon Sud Est III (Ref: 2010-025 B). After receiving written informed consent, we studied 28 patients referred for cardiac surgery. Patients with cardiac arrhythmias, left ventricular (LV) ejection fraction <40%, or right ventricular (RV) dysfunction were not included.

Anaesthesia was induced with sufentanil (0.5–1.0  $\mu\text{g kg}^{-1}$ ), propofol (1–3  $\text{mg kg}^{-1}$ ), and cisatracurium (0.15  $\text{mg kg}^{-1}$ ). After induction of anaesthesia, an 8 cm, 5 F catheter (Arrow International Inc., Reading, PA, USA) was inserted in the left or right radial artery. A triple-lumen, 16 cm, 8.5 F central venous catheter (Arrow International Inc.) and a 7.5 F pulmonary artery catheter (Swan-Ganz catheter; Baxter Edwards, Lifescience, LLC, Irvine, CA, USA) were inserted via the right internal jugular vein. Pressure transducers (Medex Medical Ltd, Rossendale, Lancashire, UK) were placed at the level of the mid-axillary line and fixed to the operating table at the atrial level throughout the study protocol. All transducers were zeroed to atmospheric pressure. CO was measured by thermodilution using the average of three successive measurements obtained by injection of 10 ml (5%) dextrose at room temperature randomly during the respiratory cycle. Cardiac index (CI) and stroke volume index (SVI) were calculated using standard formulas by dividing CO and stroke volume, respectively, by body surface area. Three pulse oximeter probes were attached to different sites, the first one on the index finger of the right or the left hand via a finger clip (LNOP<sup>®</sup> Adt, Masimo Corp.), one on the left ear via an ear clip (LNOP<sup>®</sup> TC-I, Masimo Corp.), and one on the forehead just above the eyebrow (LNOP<sup>®</sup> TF-I, Masimo Corp.). External pressure was applied to the forehead probe with a headband, as recommended by the manufacturer. The probes were wrapped to prevent outside light from interfering with the signal. These pulse oximeters were connected to a Masimo Radical 7 monitor (Masimo SET, Masimo Corp.) with

PVI software version 7.1.1.5. Pulse oximeter plethysmographic waveforms were recorded from the Radical 7 monitor to a personal computer using PhysioLog software (PhysioLog V1.0.1.1, Protolink Inc., Richardson, TX, USA) for further analysis.

Anaesthesia was maintained with continuous infusion of propofol (5  $\text{mg kg}^{-1} \text{ h}^{-1}$ ) and sufentanil (0.1  $\mu\text{g kg}^{-1} \text{ h}^{-1}$ ) to keep bispectral index (BIS) (Aspect 1000, Aspect Medical Systems Inc., Natick, MA, USA) between 40 and 60. Patients were ventilated in a volume-controlled mode with a tidal volume of 8 ml  $\text{kg}^{-1}$  body weight, a frequency of 10–12  $\text{min}^{-1}$ , an I:E ratio of 1:2, an oxygen inspiratory fraction of 0.5, and a PEEP of 0 cm  $\text{H}_2\text{O}$  (Primus<sup>®</sup>; Dräger, Lübeck, Germany).

## Data recording and analysis

### PVI calculation

PVI is a measure of the dynamic changes in PI during a complete respiratory cycle. For the measurement of oxygen saturation ( $\text{SpO}_2$ ) via pulse oximetry, red and infrared lights are used. A constant amount of light [direct current (DC)] from the pulse oximeter is absorbed by skin, other tissues, and non-pulsatile blood, whereas a variable amount of light [alternating current (AC)] is absorbed by the pulsating arterial inflow. For PI calculation, the infrared pulsatile signal is indexed against the non-pulsatile infrared signal and expressed as a percentage [ $\text{PI} = (\text{AC}/\text{DC}) \times 100$ ], reflecting the amplitude of the pulse oximeter waveform. PVI calculation is then accomplished by measuring changes in PI over a time interval sufficient to include one or more complete respiratory cycles as  $\text{PVI} = [(\text{PI}_{\text{max}} - \text{PI}_{\text{min}})/\text{PI}_{\text{max}}] \times 100$ . PVI is continuously displayed by the Radical 7 monitor and is averaged over 2 min. At each step of the protocol, PVI was recorded for each site of measurement: at the finger ( $\text{PVI}_{\text{finger}}$ ), the ear ( $\text{PVI}_{\text{ear}}$ ), and the forehead ( $\text{PVI}_{\text{forehead}}$ ). PI was also recorded at the finger ( $\text{PI}_{\text{finger}}$ ), the ear ( $\text{PI}_{\text{ear}}$ ), and the forehead ( $\text{PI}_{\text{forehead}}$ ).

### Other haemodynamic measurements

The following variables were also recorded: systolic arterial pressure, mean arterial pressure (MAP), diastolic arterial pressure (DAP), heart rate (HR), end-expiratory central venous pressure (CVP), end-expiratory pulmonary capillary wedge pressure (PCWP), SVI, CI, systemic vascular resistance index (SVRI),  $\text{SpO}_2$ , and the percentage change in arterial pulse pressure [pulse pressure variation (PPV)]. PPV based on Aboy and colleagues<sup>21–22</sup> was automatically and continuously displayed by the Philips<sup>®</sup> monitor (Intellivue MP70, Philips Medical System, Suresnes, France).

### Experimental protocol

For each patient, a complete baseline set of plethysmographic and haemodynamic measurements was performed after induction of general anaesthesia after a 5 min period of haemodynamic stability with no changes in anaesthetic protocol and no volume expansion. Then, an i.v. volume expansion using 500 ml of hetastarch 6% (Volumen<sup>®</sup>; Fresenius Kabi, Bad Homburg, Germany) was infused over

10 min, followed by a new set of haemodynamic measurements 5 min after FL.

### Statistical analysis

All haemodynamic variables are presented as mean (SD) unless otherwise stated. The normality of distribution of data was demonstrated with a Kolmogorov–Smirnov test. Subjects were allocated to two groups according to the percentage change in CI induced by volume expansion. Volume responders were defined by an increase in  $CI \geq 15\%$  and non-responders by an increase in  $CI < 15\%$ .<sup>23</sup> Responders and non-responders group data were compared using unpaired Student's *t*-test. To assess the ability of measured/calculated parameters to identify responders to intravascular fluid administration, receiver-operating characteristic (ROC) curves were generated, varying the discriminating threshold for CI, CVP, PCWP, PI, PVI, and PPV. The optimal threshold value (the value that maximizes the sum of the sensitivity and specificity) was also determined. The areas under the ROC curves were calculated for each variable and compared as described previously.<sup>24</sup>

The variability of PI was evaluated by the coefficient of variation of PI ( $CV_{PI}$ ) for each site of measurement during a 3 min period before and after FL.  $CV_{PI}$  was calculated as the SD divided by the mean of PI, based on a sampling rate of 1 Hz. The mean and SD of the  $CV_{PI}$  for the entire study group were then calculated for each site before and after volume expansion. The  $CV_{PI}$ 's of the cephalic region (the ear and forehead) were compared with the  $CV_{PI}$  of the finger by a one sample *t*-test.

Considering previously published results, power analysis showed that 25 subjects were necessary to detect differences of 0.15 between the PVI and PPV area under the ROC

curve (5% type I error rate, 80% power, two-tailed test).<sup>23</sup> For all comparisons,  $P < 0.05$  was considered significant. Statistical analysis was performed using SPSS software version 13.0 for Windows (SPSS Inc., Chicago, IL, USA).

### Results

Twenty-eight subjects were enrolled in the study. This group consisted of 23 men and five women aged between 38 and 86 yr (mean age, 62 yr). Sixteen subjects received  $\beta$ -blockers before operation; none received vasoactive drugs before surgery.

#### Effects of volume expansion on haemodynamic data

Baseline haemodynamic and plethysmographic data and their changes after intravascular fluid administration are summarized in Table 1. Volume expansion induced significant increases in CI, SVI, CVP, PCWP, and  $PI_{forehead}$  and a significant decrease in  $PVI_{forehead}$ ,  $PVI_{ear}$ ,  $PVI_{finger}$ , PPV, SVRI, and HR. We observed no change in MAP,  $PI_{finger}$ , or  $PI_{ear}$ .

#### Differences in haemodynamic data between responders and non-responders to volume expansion

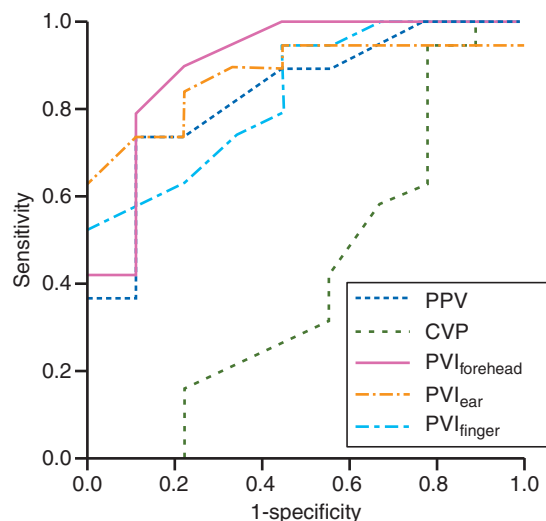
Nineteen subjects were responders and nine were non-responders to volume expansion (Table 1).  $PVI_{forehead}$ ,  $PVI_{ear}$ , and  $PVI_{finger}$  were significantly higher in the responder group than in the non-responder group [20 (4)% vs 13 (5)%,  $P < 0.001$ ; 19 (6)% vs 11 (4)%,  $P = 0.001$ ; and 17 (6)% vs 9 (5)%,  $P = 0.003$ , respectively], as was PPV [16 (6)% vs 9 (4)%,  $P = 0.003$ ]. Interestingly,  $PI_{forehead}$  was significantly lower in responders than in non-responders [0.90 (0.37)% vs 2.06 (1.27)%,  $P = 0.001$ ], as was CI [1.84 (0.51) vs 2.67 (1.56) litre  $min^{-1} m^{-2}$ ,  $P = 0.04$ ]. There was no significant difference in CVP [9 (4) vs 11 (7) mm Hg,  $P = 0.39$ ], PCWP

**Table 1** Haemodynamic and plethysmographic data in responders and non-responders at baseline and after FL. Data are mean (SD). MAP, mean arterial pressure; HR, heart rate; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; SVI, stroke volume index; CI, cardiac index; SVRI, systemic vascular resistance index; PPV, automated pulse pressure variation; PVI, plethysmographic variability index; PI, perfusion index

	Responders to fluid loading (n=19)	Non-responders to fluid loading (n=9)	P-value	Before fluid loading (n=28)	After fluid loading (n=28)	P-value
MAP (mm Hg)	66 (14)	71 (12)	0.35	67 (13)	71 (14)	0.21
HR (beats $min^{-1}$ )	60 (10)	62 (14)	0.67	61 (11)	58 (10)	0.01
CVP (mm Hg)	9 (4)	11 (7)	0.39	10 (5)	13 (5)	<0.001
PCWP (mm Hg)	12 (5)	16 (12)	0.16	13 (8)	16 (8)	<0.001
SVI (ml $m^{-2}$ )	32 (13)	42 (15)	0.08	35 (14)	44 (18)	<0.001
CI (litre $min^{-1} m^{-2}$ )	1.84 (0.51)	2.67 (1.56)	0.04	2.11 (1.03)	2.50 (0.92)	<0.001
SVRI (dyn $s^{-1} cm^{-5} m^{-2}$ )	2601 (788)	2125 (754)	0.14	2448 (796)	2039 (673)	<0.001
PPV (%)	16 (6)	9 (4)	0.003	14 (6)	7 (3)	<0.001
$PVI_{finger}$ (%)	17 (6)	9 (5)	0.003	15 (7)	11 (6)	0.01
$PVI_{ear}$ (%)	19 (6)	11 (4)	0.001	17 (7)	11 (5)	<0.001
$PVI_{forehead}$ (%)	20 (4)	13 (5)	<0.001	18 (6)	10 (5)	<0.001
$PI_{finger}$ (%)	4.41 (2.56)	4.81 (2.77)	0.71	4.54 (2.59)	4.62 (2.84)	0.81
$PI_{ear}$ (%)	0.63 (0.55)	0.71 (0.59)	0.74	0.65 (0.55)	0.72 (0.65)	0.38
$PI_{forehead}$ (%)	0.90 (0.37)	2.06 (1.27)	0.001	1.27 (0.93)	1.53 (1.08)	0.008

**Table 2** Areas under the ROC curves and cut-off values of haemodynamic and plethysmographic parameters in prediction of fluid responsiveness. AUC, area under the curve; PVI, plethysmographic variability index; PPV, automated pulse pressure variations; PI, perfusion index; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; CI, cardiac index

	AUC	Standard error	Asymptotic 95% confidence interval		P-value	Cut-off	Sensitivity (%)	Specificity (%)
			Lower bound	Upper bound				
PVI <sub>finger</sub>	0.836	0.077	0.685	0.988	0.005	>12%	74	67
PVI <sub>ear</sub>	0.880	0.066	0.751	1.009	0.001	>16%	74	89
PVI <sub>forehead</sub>	0.906	0.066	0.776	1.036	0.001	>15%	89	78
PPV	0.836	0.081	0.678	0.995	0.005	>11%	74	89
PI <sub>finger</sub>	0.538	0.125	0.293	0.783	0.75	<4.20%	58	56
PI <sub>ear</sub>	0.620	0.106	0.412	0.828	0.31	<0.36%	42	89
PI <sub>forehead</sub>	0.854	0.076	0.704	1.003	0.003	<1.37%	95	67
CVP	0.418	0.129	0.165	0.671	0.49	<8 mm Hg	58	33
PCWP	0.386	0.135	0.122	0.650	0.34	<11 mm Hg	56	44
CI	0.760	0.091	0.583	0.938	0.03	<1.64 l min <sup>-1</sup> m <sup>-2</sup>	53	100

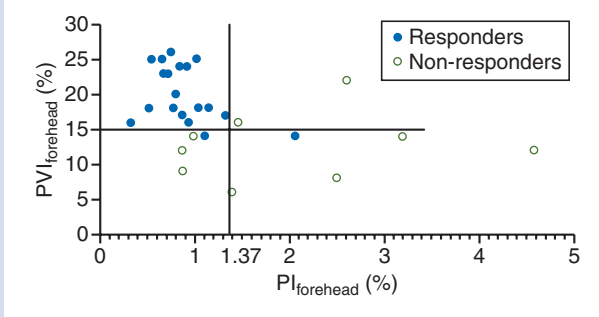


**Fig 1** ROC curves comparing the ability of PVI recorded at the forehead, ear, and finger (PVI<sub>forehead</sub>, PVI<sub>ear</sub>, and PVI<sub>finger</sub>), automated PPV and CVP at baseline to discriminate between responders and non-responders to intravascular volume expansion.

[12 (5) vs 16 (12) mm Hg,  $P=0.16$ ], PI<sub>ear</sub> [0.63 (0.55)% vs 0.71 (0.59)%,  $P=0.74$ ], or PI<sub>finger</sub> [4.41 (2.56)% vs 4.81 (2.77)%,  $P=0.71$ ] between the two groups.

### Prediction of fluid responsiveness

Areas under ROC curves (se) and the optimal threshold value for each parameter are presented in Table 2. The greater areas were obtained with PVI<sub>ear</sub> and PVI<sub>forehead</sub> ( $P=0.001$  for both) (Fig. 1). Optimal threshold values of PVI were higher at the forehead and ear (15% and 16%, respectively) than at the finger (12%). Areas under ROC curves obtained with PI<sub>ear</sub>, PI<sub>finger</sub>, CVP, and PCWP showed no significant difference from 0.5 (Fig. 1). The three sites of measurement



**Fig 2** Individual data for PVI and PI recorded at the forehead (PVI<sub>forehead</sub> and PI<sub>forehead</sub>) according to responders and non-responders.

of PVI were able to predict fluid responsiveness with the best site being the forehead, then the ear and finger; however, there was no statistical difference between these three areas.

Individual data of PVI<sub>forehead</sub> and PI<sub>forehead</sub> according to responders and non-responders to FL are shown in Figure 2. A PI<sub>forehead</sub> below 1.37% predicted fluid responsiveness with a sensitivity of 67% and a specificity of 95% ( $P<0.005$ ). Interestingly, looking at the threshold values of PI<sub>forehead</sub> and PVI<sub>forehead</sub> together increased the specificity from 78% to 100%, and the positive and negative predictive values to predict fluid responsiveness (Table 3).

### Signal stability analysis

Four subjects were excluded from CV<sub>PI</sub> calculation because of discontinuous collection of the plethysmographic signal during the PI recording. The CV<sub>PI</sub> calculated for each site at baseline and after volume expansion are presented in Table 4. There was no significant difference in CV<sub>PI</sub> between each site before and after volume expansion. However, CV<sub>PI</sub>



**Table 3** Prediction of fluid responsiveness by PVI and the association of PVI and PI recorded at the forehead. PVI, plethysmographic variability index; PI, perfusion index

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
$PVI_{\text{forehead}} > 15\%$	89	78	89	78
$PVI_{\text{forehead}} > 15\%$ and $PI_{\text{forehead}} < 1.37$	89	100	100	82

**Table 4** Coefficients of variation of perfusion index at the forehead, ear, and finger at baseline and after FL. Data are mean (SD).  $CV_{PI_{\text{forehead}}}$ , coefficient of variation of perfusion index at the forehead;  $CV_{PI_{\text{ear}}}$ , coefficient of variation of perfusion index at the ear;  $CV_{PI_{\text{finger}}}$ , coefficient of variation of perfusion index at the finger. \*Significantly different from  $CV_{PI_{\text{forehead}}}$  before FL ( $P < 0.05$ ). <sup>§</sup>Significantly different from  $CV_{PI_{\text{forehead}}}$  after FL ( $P < 0.05$ )

	Before fluid loading	After fluid loading
$CV_{PI_{\text{finger}}}$	0.130 (0.090)*	0.117 (0.085) <sup>§</sup>
$CV_{PI_{\text{ear}}}$	0.088 (0.079)	0.066 (0.072)
$CV_{PI_{\text{forehead}}}$	0.095 (0.078)	0.075 (0.097)

were nevertheless significantly lower for the ear and forehead than for the finger whatever the period of recording.

## Discussion

This present study shows that  $PVI_{\text{forehead}}$  and  $PVI_{\text{ear}}$  provide a prediction of fluid responsiveness in mechanically ventilated and anaesthetized patients in the operating theatre as accurately as PPV and  $PVI_{\text{finger}}$ . Contrary to the usual practice, using  $PVI_{\text{forehead}}$  combined with  $PI_{\text{forehead}}$  (available on the same device) seems to be the most appropriate measurement method.

PVI is an algorithm allowing automated and continuous monitoring of respiratory variation of photoplethysmographic waveform amplitude. Despite limits of application of dynamic parameters such as arrhythmias, LV dysfunction, or small tidal volumes,<sup>25 26</sup> ~40% of the patients undergoing an anaesthetic procedure met the criteria for the use of PVI.<sup>27</sup> All studies concerning PVI have involved the finger plethysmograph. However, it has been suggested that the choice of an alternative site of measurement, such as the ear lobe or forehead, might affect the ability of PVI to accurately predict fluid responsiveness, mainly for two reasons. First, the effect of ventilation on the plethysmographic signal is expressed more strongly if probes are placed on the head (probably because of a shorter distance between the heart and the cephalic region than between the heart and fingers).<sup>19</sup> The higher values of  $PVI_{\text{forehead}}$  and  $PVI_{\text{ear}}$  compared with  $PVI_{\text{finger}}$  observed in responder patients highlight this fact. Secondly, PI depends on the distensibility of the vascular wall and the intravascular pulse pressure.<sup>16 20</sup> So any change in local conditions (such as acute changes in vasomotor tone) could alter PI, and consequently, PVI, since this index reflects variations in PI over a given period.

It should be noted that the vasculature of the head is relatively more resistant to sympathetically mediated vasomotor tone changes than that of the finger.<sup>17 18</sup>

$CV_{PI}$  was higher at the finger than in the cephalic region, although values of PVI were highest at the ear and forehead. Since the  $CV_{PI}$  is not linked just to respiratory variations of PI, we hypothesize that these variations of PI at the finger are predominantly dependent on variations in vasomotor tone, independently of the volume status. Of note, we have not evaluated the coefficient of variation of PVI before and after FL because the value of PVI displayed by the monitor is already averaged over a period of 2–3 min. Vasomotor tone can be explored by analysing low frequencies of the PI using spectral analysis.<sup>28</sup> Unfortunately, we were unable to perform spectral analysis on low PI frequencies because of filters placed on the monitors provided by the manufacturer. Consequently, we cannot draw definitive conclusions regarding the cause of these smaller PI variations or regarding a potential better PVI measurement site. As with a number of devices, PVI is a 'black box' with a protected algorithm. Because of this, there could be a loss of important information, specifically venous modulation during the respiratory cycle, that could give us supplementary information about fluid responsiveness.

We suppressed the venous component using an external headband so as not to alter the PI. It could be interesting to study the PVI and PI of the forehead and ear sensor without compression. This could confirm previous studies<sup>19</sup> by exploring both arterial and venous components of the photoplethysmographic signal in further studies should the manufacturer be more forthcoming with details of the algorithm used to calculate PVI.<sup>29</sup>

Many factors can decrease the alternating current of the PI (such as vasoconstriction, cold, surgical stress, or use of vasoactive drugs).<sup>16 19</sup> Nevertheless, general anaesthesia reduces the oscillatory components of the perfusion signal related to sympathetic, myogenic activity and the component modulated by the endothelium.<sup>30</sup> This is why our subjects were studied during steady-state conditions, under deep general anaesthesia, with a BIS between 30 and 60, and none of the subjects received vasoconstrictors.

Despite the fact that  $CV_{PI}$  was lower in the cephalic region, the ROC curve observed for  $PVI_{\text{forehead}}$  and  $PVI_{\text{ear}}$  was not statistically better compared with the  $PVI_{\text{finger}}$ . These devices need to be tested during surgical procedures, where vasomotor tone can be exerted. Forget and colleagues have previously demonstrated the feasibility of PVI during

major abdominal surgery with a probe on the finger. In that study, PVI-based goal-directed fluid management resulted in less crystalloid administration perioperatively and lower lactic acid levels after operation.<sup>15</sup>

Interestingly, using a  $PI_{\text{forehead}}$  cut-off value of  $<1.37\%$  in the face of a  $PVI_{\text{forehead}} >15\%$  increased the specificity of PVI. This agrees with a recent article<sup>31</sup> that showed that the area under the curve for the forehead plethysmographic amplitude (which is related to the PI), as opposed to the finger site, was strongly correlated ( $r^2 > 0.59$ ) with stroke volume changes during low body negative pressure in healthy volunteers. Therefore, PI could be used as an additional tool for haemodynamic monitoring. Moreover, PI has already been linked to systemic and tissue perfusion, particularly in neonates.<sup>32</sup> Of note, forehead plethysmography is based on transreflectance contrary to ear and finger plethysmography which are based on transmittance. Nevertheless, the haemodynamic state seems to influence these two different measurement techniques in the same manner.<sup>28</sup> The reason why, in our study, the ratio AC/DC (i.e. the PI) is more sensitive to preload dependence when measured on the forehead as opposed to the other sites is not yet understood.

Recent studies have shown that the method of attachment of a pulse oximeter can affect the ability of the device to accurately determine the optimal waveform.<sup>28</sup> Moreover, Shelley and colleagues<sup>33</sup> have found that forehead plethysmography can be affected by the presence of a strong venous signal, which can contribute to misinterpretation of the plethysmographic waveform in patients with a pulse oximeter probe attached to their forehead. The ear and finger plethysmographic probes are outfitted with a clip, which prevents venous stasis and therefore reflects a more reliable arterial waveform. In our study, we applied external pressure on the forehead probe with a dedicated headband in order to obtain an optimal plethysmographic waveform<sup>28</sup> and to suppress the impact of venous pulsation.<sup>33</sup>

Several factors can affect vasomotor tone during the perioperative period such as surgical stress, regional sympathetic blocks, sedation depth, cold, and vasoconstrictors and these can consequently affect PI. Further studies are necessary to confirm the ability of PVI to assess fluid responsiveness during surgical procedures.

Threshold values of dynamic indicators of fluid responsiveness such as  $PVI^{13\ 14\ 34}$  vary among studies and settings, and the existence of an inconclusive 'grey zone' has been evoked.<sup>9</sup> We believe that values in this grey zone should be interpreted warily, and additional indices should be used (such as the  $PI_{\text{forehead}}$  in our study) to make decisions.

In conclusion, PVI can predict fluid responsiveness whatever the site of measurement in the operating theatre during general anaesthesia may be. Despite a lower variability of forehead and ear PI, the cephalic region is not better than the finger site at monitoring the PVI in this setting. However, it is a viable alternative when the finger site cannot be monitored. Further studies should be performed during surgical procedures to examine the potential

increased accuracy of predicting fluid responsiveness by using the  $PVI_{\text{forehead}}$  and  $PVI_{\text{ear}}$ .

## Conflict of interest

M.C. is a paid consultant for Masimo Corp., Edwards Lifesciences, Conmed, and Covidien.

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## References

- Gan TJ, Soppitt A, Maroof M, et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. *Anesthesiology* 2002; **97**: 820–6
- Venn R, Steele A, Richardson P, Poloniecki J, Grounds M, Newman P. Randomized controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures. *Br J Anaesth* 2002; **88**: 65–71
- Hamilton MA, Cecconi M, Rhodes A. A systematic review and meta-analysis on the use of preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. *Anesth Analg* 2010, 21 Oct [Epub ahead of print]
- Solus-Biguenet H, Fleyfel M, Tavernier B, et al. Non-invasive prediction of fluid responsiveness during major hepatic surgery. *Br J Anaesth* 2006; **97**: 808–16
- Cannesson M. Arterial pressure variation and goal-directed fluid therapy. *J Cardiothorac Vasc Anesth* 2010; **24**: 487–97
- Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med* 2009; **37**: 2642–7
- Michard F. Changes in arterial pressure during mechanical ventilation. *Anesthesiology* 2005; **103**: 419–28
- Haynes AB, Weiser TG, Berry WR, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med* 2009; **360**: 491–9
- Cannesson M, Attouf Y, Rosamel P, et al. Respiratory variations in pulse oximetry plethysmographic waveform amplitude to predict fluid responsiveness in the operating room. *Anesthesiology* 2007; **106**: 1105–11
- Natalini G, Rosano A, Taranto M, Faggian B, Vittorielli E, Bernardini A. Arterial versus plethysmographic dynamic indices to test responsiveness for testing fluid administration in hypotensive patients: a clinical trial. *Anesth Analg* 2006; **103**: 1478–84
- Pizov R, Eden A, Bystriski D, Kalina E, Tamir A, Gelman S. Arterial and plethysmographic waveform analysis in anesthetized patients with hypovolemia. *Anesthesiology* 2010; **113**: 83–91
- Cannesson M, Delannoy B, Morand A, et al. Does the pleth variability index indicate the respiratory induces variation in the plethysmogram and arterial pressure waveforms? *Anesth Analg* 2008; **106**: 1189–94
- Cannesson M, Desebbe O, Rosamel P, et al. Pleth variability index to monitor the respiratory variations in the pulse oximeter plethysmographic waveform amplitude and predict fluid responsiveness in the operating theatre. *Br J Anaesth* 2008; **101**: 200–6

- 14 Zimmermann M, Feibicke T, Keyl C, et al. Accuracy of stroke volume variation compared with pleth variability index to predict fluid responsiveness in mechanically ventilated patients undergoing major surgery. *Eur J Anaesthesiol* 2010; **27**: 555–61
- 15 Forget P, Lois F, de Kock M. Goal-directed fluid management based on the pulse oximeter-derived pleth variability index reduces lactate levels and improves fluid management. *Anesth Analg* 2010; **111**: 910–4
- 16 Landsverk SA, Hoiseith LO, Kvandal P, Hisdal J, Skare O, Kirkeboen KA. Poor agreement between respiratory variations in pulse oximetry photoplethysmographic waveform amplitude and pulse pressure in intensive care unit patients. *Anesthesiology* 2008; **109**: 849–55
- 17 Awad AA, Ghobashy MAM, Ouda W, Stout RG, Silverman DG, Shelley KH. Different responses of ear and finger pulse oximeter waveform to cold pressor test. *Anesth Analg* 2001; **92**: 1483–6
- 18 Awad AA, Stout RG, Ghobashy MAM, Rezkanna HA, Silverman DG, Shelley KH. Analysis of the ear pulse oximeter waveform. *J Clin Monit Comput* 2006; **20**: 175–184
- 19 Shelley KH, Jablonka DH, Awad AA, Stout RG, Rezkanna H, Silverman DG. What is the best site for measuring the effect of ventilation on the pulse oximeter waveform? *Anesth Analg* 2006; **103**: 372–7
- 20 Shelley KH. Photoplethysmography: beyond the calculation of arterial oxygen saturation and heart rate. *Anesth Analg* 2007; **105**: S31–6
- 21 Aboy M, McNames J, Thong T, Phillips CR, Ellenby MS, Goldstein B. A novel algorithm to estimate the pulse pressure variation index deltaPP. *IEEE Trans Biomed Eng* 2004; **51**: 2198–203
- 22 Cannesson M, Sliker J, Desebbe O, et al. The ability of a novel algorithm for automatic estimation of the respiratory variations in arterial pulse pressure to monitor fluid responsiveness in the operating room. *Anesth Analg* 2008; **106**: 1195–200
- 23 Michard F, Boussat S, Chemla D, et al. Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. *Am J Respir Crit Care Med* 2000; **162**: 134–8
- 24 Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology* 1983; **148**: 839–43.
- 25 De Backer D, Heenen S, Piagnerelli M, et al. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. *Intensive Care Med* 2005; **31**: 517–23
- 26 Desebbe O, Boucau C, Farhat F, Bastien O, Lehot JJ, Cannesson M. The ability of pleth variability index to predict the hemodynamic effects of positive end-expiratory pressure in mechanically ventilated patients under general anesthesia. *Anesth Analg* 2010; **110**: 792–8
- 27 Maguire S, Rinehart J, Vakharia SMD, Cannesson M. Respiratory variation in pulse pressure and plethysmographic waveforms: intraoperative applicability in a North American academic center. *Anesth Analg* 2011; **112**: 94–6
- 28 Reisner A, Shaltis PA, McCombie D, Asada HH. Utility of the photoplethysmogram in circulatory monitoring. *Anesthesiology* 2008; **108**: 950–8
- 29 Feldman JM. Can clinical monitors be used as scientific instruments? *Anesth Analg* 2006; **103**: 1071–2
- 30 Landsverk SA, Kvandal P, Bernjak A, Stefanovska A, Kirkeboen KA. The effects of general anesthesia on human skin microcirculation evaluated by wavelet transform. *Anesth Analg* 2007; **105**: 1012–9
- 31 McGrath SP, Ryan KL, Wendelken SM, Rickards CA, Convertino VA. Pulse oximeter plethysmographic waveform changes in awake, spontaneously breathing, hypovolemic volunteers. *Anesth Analg* 2011; **112**: 368–74
- 32 Sahni R, Schulze KF, Ohira-Kist K, Kashyap S, Myers MM, Fifer WP. Interactions among peripheral perfusion, cardiac activity, oxygen saturation, thermal profile and body position in growing low birth weight infants. *Acta Paediatr* 2010; **99**: 135–9
- 33 Shelley KH, Tamai D, Jablonka D, Gesquiere M, Stout RG, Silverman DG. The effect of venous pulsation on the forehead pulse oximeter wave form as a possible source of error in SpO<sub>2</sub> calculation. *Anesth Analg* 2005; **100**: 743–7
- 34 Loupec T, Nanadoumgar H, Frasca D, et al. Pleth variability index predicts fluid responsiveness in critically ill patients. *Crit Care Med* 2011; **39**: 294–9