Pleth Variability Index Predicts Fluid Responsiveness in Mechanically Ventilated Adults During General Anesthesia for Noncardiac Surgery

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Objective: To investigate whether the pleth variability index (PVI), derived noninvasively from a pulse oximeter probe, would predict fluid responsiveness in patients undergoing noncardiac surgeries.

Design: A clinical, prospective, observational study.

Setting: Operating room of a tertiary care hospital.

Participants: Twenty-nine adult patients undergoing a range of noncardiac surgeries, requiring general anesthesia, tracheal intubation, and mechanical ventilation.

Interventions: Intravenous volume expansion with 500 mL of colloid following induction of general anesthesia and after a period of hemodynamic stability before the start of surgery.

Measurements and Main Results: Baseline values for PVI and stroke volume index, derived from an esophageal Doppler monitor, were compared with final values after the volume expansion. Patients were classified into fluid responders and nonresponders based on a stroke volume index increase of $\geq$10%. The optimal cut-off value for baseline pleth variability index for predicting fluid responsiveness was determined.

There were 17 responders (59%) to the 500-mL volume expansion. Baseline PVI value was significantly different between responders and nonresponders (16.5 $\pm$ 6.4% *v* 10.3 $\pm$ 2.7%; p = 0.004). Receiver operating characteristic analysis demonstrated significant predictive ability of an increase in stroke volume index for PVI with area under the curve of 0.84 (95% confidence interval = 0.69-0.99). The optimal cut-off value for baseline PVI was 10.5%, with a sensitivity of 88% and a specificity of 67%.

Conclusions: Pleth variability index is predictive of fluid responsiveness in adult patients undergoing noncardiac surgery.

KEY WORDS: *Pleth variability index, stroke volume, fluid responsiveness, hemodynamic monitoring, pulse oximeter, esophageal Doppler monitoring*

FLUID ADMINISTRATION commonly is used to improve hemodynamics in the perioperative period. Assessment of fluid responsiveness, described as the ability of the circulation to increase cardiac output in response to volume expansion, is essential to guide fluid therapy and optimize preload.[1] Excessive administration of fluid is associated with adverse outcomes, and a high proportion of hemodynamically unstable patients will not respond to any amount of volume expansion.[2,3]

Dynamic indicators relying on cardiopulmonary interactions in mechanically ventilated patients, such as pulse pressure variation, systolic pressure variation, and stroke volume variation, consistently have been shown to be more accurate than static indicators in predicting fluid or preload responsiveness.[3–8] The pleth variability index (PVI®) is an algorithm that automatically and continuously measures the respiratory variations in the pulse oximeter waveform amplitude.[9] It measures the dynamic changes in perfusion index (PI) over respiratory cycles and is calculated as follows: PVI = $[(PI_{max} - PI_{min})/PI_{max}]$ x 100% (manufacturer technical bulletin, PI = Perfusion index). The main advantages of PVI are that it is totally noninvasive and very easy to use. It only requires a probe to be placed on patients, similar to the ordinary pulse oximeter. Recent studies have shown the ability of PVI to reliably predict fluid responsiveness in patients undergoing cardiac or abdominal surgery as well as in the intensive care unit (ICU) setting.[10–16]

The aim of the current study was to investigate whether PVI could predict fluid responsiveness in mechanically ventilated patients under general anesthesia undergoing a range of noncardiac surgeries. To identify which patients responded to volume expansion, the authors used the esophageal Doppler monitor (EDM), as it offers an alternative measure of cardiac output that is minimally invasive compared to a pulmonary artery catheter, the use of which would be difficult to justify in a general noncardiac surgical patient.[17–19] Furthermore, the use of EDM to guide fluid therapy also has been reported to reduce the incidence of complications and hospital stay after surgery in a number of studies using a goal-directed therapy approach.[20]

METHODS

Following approval of the study by the St. Vincent's Hospital Human Research Ethics Committee-D (Melbourne, Australia) and receipt of written informed consent, 30 adult patients between September 2010 and December 2012 were recruited. Eligible patients included those undergoing noncardiac surgery requiring general anesthesia, tracheal intubation, and mechanical ventilation. Patients with arrhythmias (including atrial fibrillation), ischemic heart disease, cardiac failure, and any contraindications to esophageal probe insertion were excluded.

All patients were fasted for more than 6 hours and did not receive any intravenous (IV) fluids prior to admission to the operating room. Standard anesthetic monitoring equipment was applied before the induction of general anesthesia, and the blood pressure (BP), heart rate (HR), and oxygen saturation were recorded continually. A Masimo Rainbow® SET Pulse CO-Oximetry (Masimo Corporation, Irvine, CA) probe was attached to the index finger of either the right or left hand, contralateral to the side of the BP cuff. IV fluid administration during induction was limited to that required to flush the line with drug delivery. Induction of anesthesia was based on IV midazolam (1-3 mg), fentanyl (1-2 μg/kg) or alfentanil (10-20 μg/kg), and propofol (1-3 mg/kg). The choice of muscle relaxant was left to the anesthesiologists. The patients were intubated with a cuffed

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endotracheal tube. Maintenance was with sevoflurane to achieve a BIS™ under 60. All patients' lungs were ventilated in a volume-controlled mode with a tidal volume of 8mL/kg of their ideal body weight, at a frequency of 10 to 14 breaths/min, and positive end-expiratory pressure set at 0 cm H_2O to achieve an end-tidal carbon dioxide of 30 to 34 mmHg. A CardioQ-ODM™ (Deltex Medical, Chicester, West Sussex, UK) probe was inserted via the mouth or nose and gently manipulated until an appropriate audible and spectral Doppler signal was obtained and displayed on the monitor.

The clocks in the Masimo Rainbow® SET Pulse CO-Oximetry, the CardioQ-ODM™, and the anesthetic machine were all synchronized. A 10-minute period was allowed to elapse after anesthesia induction and prior to surgery to allow for hemodynamic stability. The following baseline hemodynamic measurements were recorded after a period of stability was demonstrated (ie, <5% difference in 2 consecutive baseline readings obtained 1 minute apart): PVI and PI derived from the Masimo Rainbow® SET Pulse CO-Oximetry, stroke volume index (SVI), cardiac index (CI), and corrected flow time (FTc) derived from the CardioQ-ODM™. Other standard parameters, which were automatically and periodically recorded by the anesthetic machine (systolic BP, diastolic BP, mean arterial pressure, and HR), also were noted.

Volume expansion consisting of 500 mL of Voluven™ (6% hydroxyethyl starch 130/0.4 in 0.9% sodium chloride; Fresenius Kabi, Pymble, NSW, Australia) was given over 5 minutes. Three minutes following the end of volume expansion, a set of 3 measurements were taken at 1-minute intervals. The 3 readings were then averaged and accepted as the final post-bolus values. During the study period, no additional fluids or vasoactive drugs were administered by the anesthesiologist unless there was an episode of systolic BP drop of more than 30% from baseline or below 80 mmHg. Patients receiving vasoactive drugs were excluded from the study due to the effects of these drugs on PVI measurement. Any stimulation of the patients before data recording also was avoided. The attending anesthesiologists were blinded to the information on the study devices.

Data are expressed as mean ± SD. Hemodynamic variables before and after volume expansion were compared using a paired t-test. Patients were allocated to 2 groups according to the percentage ΔSVI after volume expansion: Responders were defined as ΔSVI ≥10% and nonresponders as ΔSVI <10%. The differences between responders and nonresponders were evaluated using the Student's t-test or the Mann-Whitney U-test as appropriate. A receiver operating characteristic (ROC) curve for PVI was generated, and the optimal cut-off value was determined by the highest Youden index (calculated as: sensitivity + specificity − 1). The Spearman rank method was used to test correlation. P values of <0.05 were considered significant. Considering previously published results, power analysis showed that at least 25 patients were necessary to achieve a power of 80% to detect differences in ROC curve areas of 0.15 with a 5% type-I error rate.[12]

Table 1. Patient Demographics

Age, median (years)	55 (range, 20–83)
Sex (male/female)	18/11
ASA score (I/II/III)	6/17/6
Type of surgery (*N*)	
Colorectal	6
General	2
Hepatobiliary	7
Maxillofacial	2
Orthopedic	5
Spinal	1
Thoracic	2
Urologic	4

Abbreviation: ASA, American Society of Anesthesiologists.

Table 2. Hemodynamic Variables Before and After Volume Expansion

	Baseline value	Final value	p value
Heart rate (bpm)	80 ± 20	73 ± 17	<0.001
Systolic blood pressure (mmHg)	106 ± 23	103 ± 16	0.413
Diastolic blood pressure (mmHg)	62 ± 14	60 ± 10	0.340
Mean arterial pressure (mm Hg)	76 ± 16	74 ± 11	0.356
Stroke volume index (mL/m^2)	35.6 ± 9.1	42.3 ± 11.9	<0.001
Cardiac index (L/min/m^2)	2.7 ± 0.8	3.1 ± 1.0	0.001
Flow time corrected (msec)	365 ± 42	388 ± 36	0.011
Pleth variability index (%)	13.9 ± 6.0	8.7 ± 4.9	<0.001
Perfusion index (%)	8.3 ± 4.0	8.7 ± 4.0	0.548

NOTE: Data are presented as mean ± SD.

All statistical analysis was performed using Stata 12.1 (StataCorp LP, College Station, TX).

RESULTS

One patient was excluded from the study due to use of a vasopressor after the induction of anesthesia. The remaining 29 patients were investigated, and their demographics are summarized in Table 1. The 500-mL fluid bolus was associated with a significant decrease in HR, an increase in CI, an increase in SVI, an increase in FTc, and a decrease in PVI (Table 2). Using ΔSVI ≥10% to define fluid responsiveness, there were 17 responders (59%) to the 500-mL fluid bolus and 12 nonresponders (Table 3). At baseline, the hemodynamic parameters that were significantly different between responders compared with nonresponders were PVI (16.5 ± 6.4% *v* 10.3 ± 2.7%; p = 0.004) and FTc (351 ± 34 msec *v* 385 ± 46 msec; p = 0.028). ROC analysis demonstrated significant predictive ability of an increase in SVI for PVI (Fig 1). Area under the curve was 0.84 (95% confidence interval = 0.69-0.99). A baseline PVI value of >10.5% had 88% sensitivity and 67% specificity for predicting a 10% SVI increase. There was a statistically significant negative linear correlation between percentage changes in PVI and SVI (r = −0.44, p = 0.004; Fig 2).

DISCUSSION

This study showed that baseline PVI was predictive of fluid responsiveness to a 500-mL infusion of colloid in noncardiac patients. A baseline PVI value of 10.5% allowed discrimination between responders and nonresponders with good sensitivity (88%) and specificity (67%). The data support previous studies that demonstrated the ability of PVI to accurately predict fluid responsiveness in cardiac, general surgical, colorectal, and ICU patients.[10–16] In this study, patients presented for a wider range of low-risk noncardiac surgeries for which invasive monitoring would not be indicated. The advantage of the non-invasive nature of PVI in this setting is, therefore, very appealing.

Fluid therapy optimization in the perioperative period has been considered as a major contributor to improve oxygen delivery.[2] Static indicators of cardiac preload, such as central venous pressure and pulmonary artery occlusion pressure, repeatedly have been shown to be inaccurate measures of volume status and fluid responsiveness.[21,22] Instead, the use of dynamic preload variables such as PVI, pulse-pressure variation, systolic pressure variation, and stroke volume variation for prediction of fluid responsiveness has been shown to be