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The Ability of Pleth Variability Index to Predict the Hemodynamic Effects of Positive End-Expiratory Pressure in Mechanically Ventilated Patients Under General Anesthesia

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BACKGROUND: Pleth variability index (PVI) is a new algorithm allowing automated and continuous monitoring of respiratory variations in the pulse oximetry plethysmographic waveform amplitude. PVI can predict fluid responsiveness noninvasively in mechanically ventilated patients during general anesthesia. We hypothesized that PVI could predict the hemodynamic effects of 10 cm H_2O positive end-expiratory pressure (PEEP).

METHODS: We studied 21 mechanically ventilated and sedated patients in the postoperative period after coronary artery bypass grafting. Patients were monitored with a pulmonary artery catheter and a pulse oximeter sensor attached to the index finger. Hemodynamic data (cardiac index [CI], PVI, pulse pressure variation, central venous pressure) were recorded at 3 successive tidal volumes (V_T) (6, 8, and 10 mL/kg body weight) during zero end-expiratory pressure (ZEEP) and then after addition of a 10 cm H_2O PEEP for each V_T. Hemodynamically unstable patients were defined as those with a >15% decrease in CI after the addition of PEEP.

RESULTS: PEEP induced changes in CI and PVI for V_T of 8 and 10 mL/kg. Hemodynamic instability occurred in 5 patients for a V_T of 6 mL/kg, in 6 patients for a V_T of 8 mL/kg, and in 9 patients for a V_T of 10 mL/kg. For V_T of 8 mL/kg, a PVI threshold value of 12% during ZEEP predicted hemodynamic instability with a sensitivity of 83% and a specificity of 80% (area under the receiver operating characteristic curve 0.806; $P = 0.03$). For V_T of 10 mL/kg, a PVI threshold value of 13% during ZEEP predicted hemodynamic instability with a sensitivity of 78% and a specificity of 83% (area under the receiver operating characteristic curve 0.829; $P = 0.01$).

CONCLUSIONS: PVI may be useful in automatically and noninvasively detecting the hemodynamic effects of PEEP when V_T is >8 mL/kg in ventilated and sedated patients with acceptable sensitivity and specificity. (Anesth Analg 2010;110:792–8)

Pulmonary atelectasis can induce gas exchange abnormalities and arterial hypoxemia during anesthesia.[1–3] This phenomenon has been shown to be related to an increase in postoperative morbidity.[4–6] An alveolar recruitment strategy based on the addition of positive end-expiratory pressure (PEEP) in the perioperative period can improve arterial oxygenation and oxygen delivery during anesthesia.[7–10] However, PEEP may also cause a decrease in cardiac output (CO).[11] By increasing intrathoracic pressure, PEEP induces a decrease in right ventricular venous return. This decrease can lead to a significant decrease in CO. In this situation, the addition of PEEP induces a decrease in oxygen delivery related to this decrease in CO and, consequently, may offset the benefits of increasing Pao_2.

Dynamic indicators of fluid responsiveness relying on cardiopulmonary interactions in mechanically ventilated patients, such as ΔPOP[12] (respiratory variations in the pulse oximeter plethysmographic waveform amplitude) or ΔPP (respiratory variations in arterial pulse pressure), have been shown to be superior to static indicators to predict fluid responsiveness.[13] Michard et al.[14] showed that ΔPP can predict the hemodynamic effects of PEEP in mechanically ventilated patients. However, ΔPP monitoring is invasive and not routinely available in daily clinical practice.

The pleth variability index (PVI) is a novel algorithm allowing for automated and continuous calculation of ΔPOP. PVI is related to ΔPOP[15] and can predict fluid responsiveness noninvasively in mechanically ventilated patients under general anesthesia.[16]

The goals of this study were (1) to investigate the ability of PVI to predict the hemodynamic effects of the addition of PEEP, and (2) to assess the influence of tidal volume (V_T) on the predictive value of PVI to discriminate between hemodynamically stable and hemodynamically unstable patients after the addition of PEEP.

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METHODS

The protocol was approved by the IRB for human subjects (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale, Lyon-Sud Est) and written informed patient consent was obtained the day before surgery.

We studied 27 patients in the postoperative period after coronary artery bypass grafting. Patients were excluded if they had cardiac arrhythmias, intracardiac shunt, left ventricular (LV) dysfunction (perioperative LV ejection fraction <50%), right ventricular dysfunction, unstable perfusion index (PI) (defined as a variation in PI >30% over a 1-minute period), vasoactive drugs and/or inotropic support, or any contraindication to the use of PEEP.

The study group consisted of 19 men and 8 women, aged between 38 and 84 years (mean age, 65 ± 13 years). Fifteen patients received β-blockers preoperatively.

An 8-cm 5F-tipped catheter (Arrow International, Reading, PA) was inserted in the left or right radial artery, and a triple-lumen 16-cm 8.5F central venous catheter (Arrow International) and a pulmonary artery catheter (PAC) (7.5F Swan-Ganz catheter; Baxter Edwards, Lifescience, LLC, Irvine, CA) were inserted in the right internal jugular vein. Pressure transducers (Medex Medical, Rossendale, Lancashire, UK) were placed on the midaxillary line and fixed to the bed to keep the transducer at the atrial level during the study protocol. All transducers were zeroed to atmospheric pressure. Correct position of the pulmonary artery catheter in West zone 3 was verified using the method of Teboul et al.[17] CO was measured by thermodilution using the average of 5 successive measurements obtained by randomly injecting 10 mL dextrose at room temperature during the respiratory cycle. Cardiac index (CI) and stroke volume index were calculated by dividing CO and stroke volume by body surface area, respectively. A pulse oximeter probe (LNOP® Adt, Masimo Corp., Irvine, CA) was attached to the index finger of either the right or left hand and was wrapped in a dark blanket to prevent outside light from interfering with the signal. This pulse oximeter was connected to a Masimo Radical 7 monitor (Masimo SET, Masimo Corp.) with PVI software (version 7.0.3.3).

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 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 nonpulsatile blood, whereas a variable amount of blood (alternating current [AC]) is absorbed by the pulsating arterial inflow. For PI calculation, the infrared pulsatile signal is indexed against the nonpulsatile infrared signal and expressed as a percentage (PI = [AC/DC] × 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 PVI = ([PImax − PImin]/PImax) × 100. PVI is continuously displayed by the Radical 7 monitor.

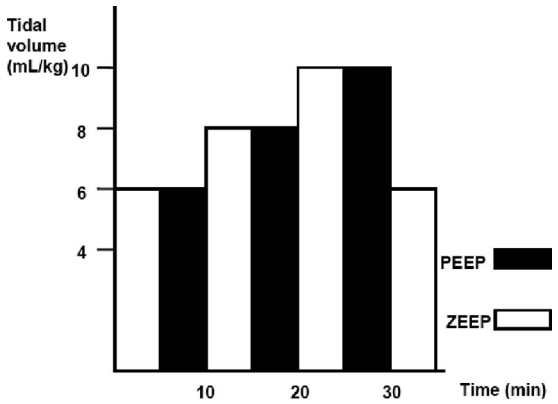

Figure 1. Tidal volume and end-expiratory pressure used in the experimental protocol. ZEEP = zero end-expiratory pressure; PEEP = positive end-expiratory pressure of 10 cm H_2O.

Respiratory Variations in Pulse Pressure Analysis

Pulse pressure (PP) was defined as the difference between systolic and diastolic pressure. Maximal (PPmax) and minimal (PPmin) values were determined over the same respiratory cycle. ΔPP was then calculated as described by Michard et al.[18]: ΔPP = (PPmax − PPmin)/ ([PPmax + PPmin]/2). The measurements were repeated on 3 consecutive respiratory cycles and averaged for statistical analysis.

Other Hemodynamic and Respiratory Measurements

At each step of the protocol, the following variables were recorded by an observer blinded to the other data: systolic arterial blood pressure, mean arterial blood pressure, diastolic arterial blood pressure, heart rate, end-expiratory central venous pressure (CVP), end-expiratory pulmonary capillary wedge pressure (PCWP), Spo_2, stroke volume index, CI, systemic vascular resistance index, peak airway pressure, and plateau airway pressure.

Static compliance of the respiratory system was calculated by dividing the expiratory V_T by the pressure difference between end-inspiratory plateau pressure and total end-expiratory pressure.[19]

Study Protocol

Patients were studied in the intensive care unit within the first postoperative hour. Anesthesia was maintained with propofol 2 mg/kg/h and sufentanil 0.2 μg/kg/h. A heat blanket was set to maintain a core temperature >36°C. All patients were sedated and their lungs mechanically ventilated in a volume-controlled mode with an I:E ratio of 1:2, a respiratory frequency of 12 to 15/min, an active inspiration with a constant flow of 60 L/min, an inspiratory pause of 60%, and an oxygen inspiratory fraction of 0.5 (Evita XL, Dräger Medical, Telford, PA). We used these respiratory settings to obtain a peak airway pressure and a plateau airway pressure. Measurements were performed in duplicate, first during 0 cm H_2O PEEP (zero end-expiratory pressure [ZEEP]), and then 3 minutes after the addition of 10 cm H_2O PEEP under successive V_T values of 6, 8, and 10 mL/kg ideal body weight (Fig. 1). Attention was given to maintain PVI and PI stable before data recording.

Statistical Analysis

All data are presented as mean ± SD. Normality of the distributions was tested using a Kolmogorov-Smirnov test.

The number of patients was derived from previously published results,[14] and it was calculated that 20 patients were necessary to achieve a power of 80% with a 5% type I error rate. Changes in hemodynamic variables induced by successive V_T and the addition of PEEP were assessed using a 1-way repeated-measures analysis of variance. Patients were divided into 2 groups (hemodynamically unstable group versus hemodynamically stable group) according to the hemodynamic effect induced by the addition of PEEP. Hemodynamically unstable was defined as >15% decrease in CI after the addition of PEEP.[14] Hemodynamic instability (HI) and non-HI group data were compared using an unpaired Student *t* test. Receiver operating characteristic (ROC) curves were generated for CVP, ΔPP, and PVI varying the discriminating threshold of each parameter, and area under the ROC curves were calculated and compared.[20] Briefly, the value corresponding to the highest sum of sensitivity and specificity was defined as the optimal cutoff value. A P value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS 13.0 for Windows (SPSS, Chicago, IL).

RESULTS

Twenty-seven patients were enrolled. Among them, 6 patients were excluded (2 for unstable PI, 2 awoke during the study protocol, and 2 for arrhythmias). The mean Pao_2 was 19.86 ± 5.27 kPa at baseline.

Hemodynamic and respiratory data at each step of the protocol for the 21 patients studied are shown in Tables 1 and 2.

Changes in Plethysmographic and Hemodynamic Data Induced by Changes in V_T

Sequential increase in V_T from 6 to 10 mL/kg induced significant changes in PVI (from 9% ± 3% to 12% ± 6%; $P <$ 0.001) (Table 1).

Changes in Plethysmographic and Hemodynamic Data Induced by Changes in PEEP

For each V_T level, the addition of PEEP induced significant changes in PVI (from 9% ± 3% to 12% ± 6%; $P = 0.001$ for V_T 6 mL/kg; from 10% ± 4% to 15% ± 7%; $P < 0.001$ for V_T 8 mL/kg; and from 12% ± 6% to 18% ± 8%; $P < 0.001$ for V_T 10 mL/kg) (Table 1). At the same time, we observed a significant decrease in CI induced by the addition of PEEP for V_T 8 and 10 mL/kg (from 2.88% ± 1.09% to 2.61% ± 1.10%; $P = 0.01$ for V_T 8 mL/kg; from 2.96% ± 1.12% to 2.55% ± 1.08%; $P < 0.001$ for V_T 10 mL/kg).

PVI to Predict HI Induced by the Addition of PEEP

At V_T 6 mL/kg, 5 patients were hemodynamically unstable, which was induced by the addition of PEEP. We observed no significant difference between PVI at ZEEP in the HI group and in the non-HI group (9% ± 2% vs 8% ± 3%, $P = 0.55$). Similarly, ΔPP was not significantly different at ZEEP between the HI group and the non-HI group (6% ± 4% vs 5% ± 4%, $P = 0.35$). CI, CVP, and PCWP were not different (Tables 3–5, Fig. 3).

At V_T 8 mL/kg, 6 patients were hemodynamically unstable, which was induced by the addition of PEEP. PVI was significantly higher in the HI group than in the non-HI group

Table 1. Hemodynamic Data by Tidal Volume and PEEP Status

	V_T 6 mL/kg ZEEP (1)	V_T 6 mL/kg PEEP	V_T 8 mL/kg ZEEP	V_T 8 mL/kg PEEP	V_T 10 mL/kg ZEEP	V_T 10 mL/kg PEEP	V_T 6 mL/kg ZEEP (2)
HR (bpm)	72 ± 13	71 ± 13	72 ± 13	72 ± 13	73 ± 13	73 ± 13	72 ± 12
MAP (mm Hg)	76 ± 13	72 ± 12	76 ± 12	73 ± 14	78 ± 13	75 ± 14	80 ± 14[a]
CVP (mm Hg)	11 ± 4	12 ± 4[b]	11 ± 4	12 ± 4[b]	10 ± 4	12 ± 4[b]	11 ± 4
PCWP (mm Hg)	15 ± 6	17 ± 5[b]	15 ± 5	17 ± 5[b]	14 ± 5	16 ± 5[b]	14 ± 5
CI (L/min/m^2)	2.88 ± 1.18	2.71 ± 1.17	2.88 ± 1.09	2.61 ± 1.10[b]	2.96 ± 1.12	2.55 ± 1.08[b]	2.80 ± 1.07
SVI (mL/m^2)	40 ± 13	38 ± 13	40 ± 12	36 ± 13[b]	40 ± 12	35 ± 12[b]	39 ± 12
SVRI (dyn/s/cm^5/m^2)	2017 ± 769	2008 ± 802	1960 ± 553	2064 ± 700	2005 ± 621	2177 ± 737	2196 ± 717
ΔPP (%)	5 ± 4	7 ± 6	6 ± 4	9 ± 6[b]	6 ± 4	10 ± 6[b]	4 ± 3
PVI (%)	9 ± 3	12 ± 6[b]	10 ± 4	15 ± 7[b]	12 ± 6[a]	18 ± 8[b]	8 ± 4
PI (%)	1.60 ± 1.25	1.52 ± 1.22	1.51 ± 1.10	1.26 ± 1.09[b]	1.30 ± 1.01[a]	0.99 ± 0.89[b]	1.20 ± 0.99[a]

Data are mean ± SD.

HR = heart rate; MAP = mean arterial blood pressure; CVP = central venous pressure; PCWP = pulmonary capillary wedge pressure; CI = cardiac index; SVI = stroke volume index; SVRI = systemic vascular resistance index; ΔPP = respiratory variations in arterial pulse pressure; PVI = pleth variability index; PI = perfusion index; ZEEP = zero end expiratory pressure; PEEP = positive end-expiratory pressure; V_T = tidal volume.

[a] Significantly different from V_T 6 mL/kg at ZEEP (1) ($P < 0.05$).

[b] Significantly different from ZEEP for the same V_T ($P < 0.05$).

Table 2. Respiratory Data Produced by Tidal Volume and Positive End-Expiratory Pressure (PEEP) Status

	V_T 6 mL/kg ZEEP (1)	V_T 6 mL/kg PEEP	V_T 8 mL/kg ZEEP	V_T 8 mL/kg PEEP	V_T 10 mL/kg ZEEP	V_T 10 mL/kg PEEP	V_T 6 mL/kg ZEEP (2)
Peak pressure (cm H_2O)	30.1 ± 4.5	35.6 ± 4.3[a]	31.0 ± 5.7	37.4 ± 4.6[a]	32.1 ± 5.7[b]	39.1 ± 4.1[a]	28.0 ± 5.5[b]
Plateau pressure (cm H_2O)	11.3 ± 2.6	19.4 ± 1.8[a]	13.5 ± 3.3[b]	22.0 ± 2.8[a]	15.7 ± 4.3[b]	25.0 ± 3.2[a]	10.2 ± 2.7[b]
Static compliance (mL/cm H_2O)	34.8 ± 9.7	41.2 ± 9.9[a]	39.3 ± 12.7[b]	44.2 ± 13.9	42.7 ± 13.7[b]	43.4 ± 11.3	39.4 ± 11.5[b]

Data are mean ± SD.

[a] Significantly different from zero end-expiratory pressure (ZEEP) for the same V_T ($P < 0.05$).

[b] Significantly different from tidal volume (V_T) 6 mL/kg at ZEEP (1) ($P < 0.05$).

Table 3. Plethysmographic and Hemodynamic Data at Zero End-Expiratory Pressure (ZEEP) and for Successive Tidal Volumes of 6, 8, and 10 mL/kg in Hemodynamically Stable (HS) and Hemodynamically Unstable (HU) Patients Induced by the Addition of PEEP

	V_T 6 mL/kg			V_T 8 mL/kg			V_T 10 mL/kg		
	HU (n = 5)	HS (n = 16)	P	HU (n = 6)	HS (n = 15)	P	HU (n = 9)	HS (n = 12)	P
HR (bpm)	72 ± 10	72 ± 14	0.98	74 ± 12	71 ± 14	0.71	78 ± 11	70 ± 13	0.16
MAP (mm Hg)	81 ± 11	74 ± 13	0.28	76 ± 14	75 ± 11	0.87	78 ± 17	78 ± 11	0.96
CVP (mm Hg)	10 ± 3	11 ± 4	0.44	9 ± 4	12 ± 3	0.08	9 ± 4	12 ± 4	0.08
PCWP (mm Hg)	14 ± 6	15 ± 6	0.60	14 ± 3	15 ± 6	0.55	14 ± 5	15 ± 5	0.51
CI (L/min/m^2)	2.36 ± 0.54	3.04 ± 1.28	0.27	2.46 ± 0.50	3.04 ± 1.22	0.28	2.94 ± 0.99	2.94 ± 1.27	0.99
SVI (mL/m^2)	33 ± 6	42 ± 14	0.15	33 ± 4	43 ± 13	0.10	38 ± 11	42 ± 13	0.50
SVRI (dyn/s/cm^5/m^2)	2551 ± 935	1851 ± 653	0.07	2217 ± 315	1857 ± 601	0.18	2036 ± 616	2015 ± 680	0.94
ΔPP (%)	6 ± 4	5 ± 4	0.35	9 ± 5	4 ± 3*	0.01	9 ± 3	4 ± 3*	0.001
PVI (%)	9 ± 2	8 ± 3	0.55	13 ± 5	9 ± 4*	0.03	16 ± 7	10 ± 4*	0.01
PI (%)	1.44 ± 1.13	1.65 ± 1.32	0.75	0.96 ± 0.47	1.74 ± 1.21	0.15	1.07 ± 0.8	1.47 ± 1.15	0.38

Data are mean ± SD.

V_T = tidal volume; HR = heart rate; MAP = mean arterial blood pressure; CVP = central venous pressure; PCWP = pulmonary capillary wedge pressure; CI = cardiac index; SVI = stroke volume index; SVRI = systemic vascular resistance index; ΔPP = respiratory variations in arterial pulse pressure; PVI = pleth variability index; PI = perfusion index; PEEP = positive end-expiratory pressure.

Table 4. Plethysmographic and Hemodynamic Data at Positive End-Expiratory Pressure (PEEP) and for Successive Tidal Volumes of 6, 8, and 10 mL/kg in Hemodynamically Stable (HS) and Hemodynamically Unstable (HU) Patients Induced by the Addition of PEEP

	V_T 6 mL/kg			V_T 8 mL/kg			V_T 10 mL/kg		
	HU (n = 5)	HS (n = 16)	P	HU (n = 6)	HS (n = 15)	P	HU (n = 9)	HS (n = 12)	P
HR (bpm)	70 ± 13	72 ± 13	0.75	74 ± 11	71 ± 14	0.68	77 ± 11	70 ± 13	0.21
MAP (mm Hg)	73 ± 12	72 ± 13	0.83	72 ± 20	74 ± 12	0.8	75 ± 20	74 ± 10	0.82
CVP (mm Hg)	11 ± 2	13 ± 4	0.46	11 ± 4	13 ± 3	0.22	11 ± 4	13 ± 4	0.27
PCWP (mm Hg)	17 ± 6	17 ± 5	0.92	16 ± 4	18 ± 6	0.40	16 ± 5	17 ± 5	0.61
CI (L/min/m^2)	1.90 ± 0.48	2.96 ± 1.21	0.08	1.94 ± 0.49	2.88 ± 1.17	0.08	2.32 ± 0.78	2.73 ± 1.27	0.4
SVI (mL/m^2)	28 ± 7	41 ± 13*	0.04	26 ± 4	40 ± 13*	0.02	30 ± 9	39 ± 14	0.1
SVRI (dyn/s/cm^5/m^2)	2735 ± 941	1781 ± 625*	0.02	2515 ± 606	1883 ± 668	0.06	2386 ± 769	2020 ± 703	0.27
ΔPP (%)	10 ± 9	7 ± 5	0.37	14 ± 6	7 ± 4*	0.01	13 ± 6	8 ± 5*	0.04
PVI (%)	19 ± 5	10 ± 5*	0.003	23 ± 8	13 ± 5*	0.002	24 ± 8	13 ± 5*	0.002
PI (%)	1.13 ± 0.86	1.62 ± 1.30	0.49	0.80 ± 0.55	1.45 ± 1.2	0.22	0.72 ± 0.52	1.20 ± 1.06	0.23

Data are mean ± SD.

V_T = tidal volume; HR = heart rate; MAP = mean arterial blood pressure; CVP = central venous pressure; PCWP = pulmonary capillary wedge pressure; CI = cardiac index; SVI = stroke volume index; SVRI = systemic vascular resistance index; ΔPP = respiratory variations in arterial pulse pressure; PVI = pleth variability index; PI = perfusion index.

* $P < 0.05$.

Table 5. Areas Under the Receiver Operating Characteristic Curves and Cutoff Values of Various Parameters at Successive Tidal Volumes for the Prediction of Hemodynamic Instability Induced by PEEP

			Asymptomatic 95% confidence interval					
	Area under the curve	Standard error	Lower bound	Upper bound	P	Cutoff	Sensitivity (%)	Specificity (%)
Tidal volume 6 mL/kg								
ΔPP	0.631	0.152	0.334	0.929	0.39	8	60	82
PVI	0.656	0.119	0.422	0.890	0.30	9	60	69
CVP	0.363	0.128	0.112	0.613	0.36	7	80	13
Tidal volume 8 mL/kg								
ΔPP	0.833	0.097	0.643	1.023	0.02	7	83	87
PVI	0.806	0.113	0.583	1.028	0.03	12	83	80
CVP	0.239	0.117	0.010	0.468	0.07	9	67	13
Tidal volume 10 mL/kg								
ΔPP	0.907	0.064	0.643	1.015	0.01	7	89	83
PVI	0.829	0.095	0.643	1.015	0.01	13	78	83
CVP	0.259	0.111	0.043	0.476	0.07	8	78	17

Data are mean ± SD.

PEEP = positive end-expiratory pressure; ΔPP = respiratory variations in arterial pulse pressure; PVI = pleth variability index; CVP = central venous pressure.

(13% ± 5% vs 9% ± 4%, P = 0.03). Similarly, ΔPP was significantly higher in the HI group than in the non-HI group (9% ± 5% vs 4% ± 3%, P = 0.01). CI, CVP, and PCWP were not different. A PVI >12% at ZEEP predicted a significant decrease in CI after the addition of PEEP with a sensitivity of 83% and a specificity of 80% (Tables 3–5, Fig. 3).

At V_T 10 mL/kg, 9 patients were hemodynamically unstable, which was induced by the addition of PEEP. PVI was significantly higher in the HI group than in the non-HI group (16% ± 7% vs 10% ± 4%, $P = 0.01$). ΔPP was also significantly higher in the HI group than in the non-HI group (9% ± 3% vs 4% ± 3%, $P = 0.001$). CI, CVP, and PCWP were not different. A PVI >13% at ZEEP predicted a significant decrease in CI after the addition of PEEP with a sensitivity of 78% and a specificity of 83% (Tables 3–5, Fig. 3).

DISCUSSION

This study shows that PVI is affected by V_T and by PEEP. Moreover, for a V_T ≥8 mL/kg, PVI is able to predict the hemodynamic effects of PEEP.

Dynamic indicators have consistently been shown to be superior to static indicators for prediction of fluid responsiveness in the intensive care unit and in the operating room. The dynamic indicators rely on the cardiopulmonary interactions in patients under general anesthesia and mechanical ventilation. Positive pressure insufflation increases pleural pressure (leading to a decrease in right ventricular filling) and transpulmonary pressure (increasing right ventricular afterload and, consequently, decreasing right ventricular stroke volume). Moreover, positive pressure ventilation (PPV) also induces changes in LV loading conditions. These phenomena are responsible for the respiratory variations observed in LV stroke volume.[13] With greater V_T, there are corresponding increases in cyclic perturbations in cardiac filling, and hence, increased PPV.

In this study, we approached the relationship between PVI and fluid responsiveness in the opposite manner from which it is usually studied. Rather than study the predictive effects of PPV on fluid responsiveness by giving fluids, we studied the relationship by decreasing preload. By increasing PEEP from 0 to 10 cm H_2O, our aim was to decrease systemic venous return and, consequently, to decrease CO. Because factors leading to a decrease in CO induced by PEEP are similar to factors inducing respiratory variations of LV stroke volume or on its surrogates (systemic arterial pulse pressure or pulse oximeter plethysmographic waveform amplitude), we postulated that both PPV and PVI would be able to predict the effects of the addition of PEEP on CI. Few studies have reported the hemodynamic effects of PEEP with dynamic indicators.[14] Michard et al.[14] showed that changes in CI induced by adding PEEP were correlated with ΔPP ($r = -0.91$, $P < 0.001$) in ventilated patients with acute lung injury. This study included 14 patients ventilated with V_T between 7 and 12 mL/kg body weight.

In our study, we found that both ΔPP and PVI were able to predict the effects of PEEP on CO but only when V_T was ≥8 mL/kg. Our findings are consistent with the results from De Backer et al.,[21] showing that ΔPP was not an accurate predictor of fluid responsiveness in septic patients ventilated with V_T of 6 mL/kg in the intensive care unit.[22] This corresponds to the finding in patients receiving norepinephrine in the intensive care unit where Charron et al.[23] showed that ΔPP was affected by V_T. The higher the V_T, the higher the ΔPP. However, because cardiopulmonary interactions depend on respiratory compliance, some authors found that dynamic indicators of fluid responsiveness are still valuable in septic or acute respiratory distress syndrome conditions even when V_T is low (6.4 ± 0.7 mL/kg) and when PEEP is high.[24,25]

We believe that in the perioperative setting, high respiratory compliances explain the inability of such small V_T values to predict fluid responsiveness with dynamic indices. V_T tends to influence the optimal threshold value of PVI (ranging from 12% to 13% according to V_T), and PVI at ZEEP was different according to V_T. These results emphasize the importance of the respiratory settings when using PVI or any other dynamic indicators. Several studies used different V_T and/or PEEP values,[26–28] thus making it more difficult to obtain a valuable threshold value. A recent experimental study confirms the importance of V_T for the assessment of fluid responsiveness using dynamic indicators.[29]

In this study, we found differences in PVI and ΔPP threshold values for the prediction of fluid responsiveness. PVI values were significantly higher than ΔPP values. This is in contrast to published studies in which we found that PVI and ΔPP threshold values were similar in the evaluation of fluid responsiveness assessment.[16] Because these studies were conducted in the operating room and in very standardized conditions, the difference in these findings is likely attributable to the difference in study protocols. In our study, it is likely that changes in venous pool at the site of measurement had an effect on PVI, because the plethysmographic waveform relies in part on light absorption by venous blood.[30] By increasing PEEP, we can postulate that we increased the venous congestion in extrathoracic compartments. This hypothesis is supported by the fact that PI decreased after the addition of PEEP, whatever the V_T. The decrease in stroke volume and the venous congestion induced by PEEP would then increase the constant absorption (DC) and decrease the PI. This may explain the differences in PVI and ΔPP values. However, further studies are required to explore this phenomenon.

Study Limitations

Our study has some limits. First, results should be interpreted with caution because of the small sample size. These results cannot be extrapolated to the general population (patients were free of pulmonary disease, cardiac dysfunction, and rhythm disorder). We studied only 1 level of PEEP. Nevertheless, this level seems to be the most appropriate to avoid alveolar derecruitment after a recruitment maneuver.[10]

Because PVI reflects variations in PI over a given period of time, any change in local conditions such as a variation in vasomotor tone may alter PI and, consequently, PVI. Recently, Landsverk et al.[31] found a poor agreement between ΔPOP and ΔPP in patients receiving vasoactive drugs in the intensive care unit. These results were in contradiction with results from previously published studies from our team and from others conducted in this setting.[27,28,32–34] The authors explained their results by the effect of vasomotor tone on the constant absorption portion of the photoplethysmographic waveform. However, our group of patients was more homogeneous and was studied in a steady-state condition (Figs. 2 and 3), the patients were under deep anesthesia (inducing a decrease in cyclic changes observed in microcirculation[35]), and were not given any vasoactive drugs. These conditions may strengthen the PVI

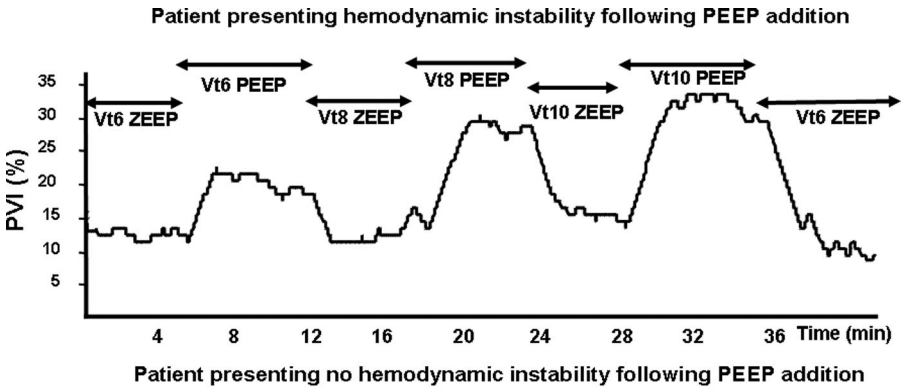

Figure 2. Pleth variability index (PVI) evolution during tidal volumes (V_T) and positive end-expiratory pressure (PEEP) variations in a hemodynamically unstable patient (top) and in a hemodynamically stable patient (bottom). The top of the figure shows a typical patient whose hemodynamic profile was unstable after the addition of PEEP. Note the high PVI (14%) under zero end-expiratory pressure (ZEEP) at the start of the experiment. The higher the V_T, the higher the PVI at ZEEP. The PVI increased significantly after the addition of PEEP (from 14% to 22% under 6 mL/kg V_T, from 16% to 35% under 10 mL/kg V_T). The bottom of the figure shows a typical patient whose hemodynamic profile was stable. Note the low PVI (9%) under ZEEP at the start of the experiment. The PVI remains low during the increase of V_T (10% under a V_T of 10 mL/kg). The PVI increases slightly after the addition of PEEP (from 10% to 15% under a V_T of 10 mL/kg).

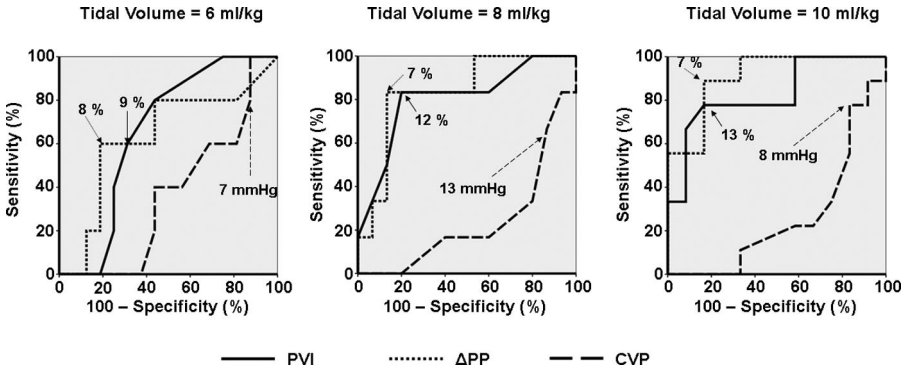

Figure 3. Receiver operating characteristic curves for pleth variability index (PVI), respiratory variations in the arterial pulse pressure (ΔPP), and central venous pressure (CVP) describing their ability to predict hemodynamic instability induced by the addition of positive end-expiratory pressure (PEEP) for 3 different levels of tidal volume (V_T).

value. However, because the ΔPP is less affected by vasomotor tone and venous congestion, the area under the ROC curve of ΔPP is better than the area under the curve for PVI. Moreover, this new index will have to be validated in daily clinical practice and may still be improved.[36]

The compliance at V_T 10 mL/kg was higher than the compliance at V_T 6 mL/kg (Table 2). This fact can be explained by an alveolar recruitment caused by the progressive increase in the V_T and the application of a 10 cm H_2O PEEP for each V_T. Because dynamic indicators of fluid responsiveness depend on pulmonary compliance, we may have decreased the sensitivity of PVI and ΔPP at V_T 10 mL/kg. Interestingly, the increase in compliance was sustained at the end of the experiment (when applying the V_T at 6 mL/kg), explaining the trend toward lower values of PVI and ΔPP compared with the beginning of the experiment.

In this study, we used the 7.0.3.3 version of the PVI software. The new available software (version 7.1.1.5) uses a longer period of smoothing for PVI. Its aim is to decrease the variability of PVI value over time. However, with this newer version, acute changes in loading conditions may have a later effect on PVI value. Future versions of the software should allow users to adjust this parameter.

Finally, these threshold values have been derived retrospectively and will have to be confirmed in prospective studies.

In conclusion, in patients with normal lung function and receiving no inotropes or vasoactive drugs, PVI is able to predict the hemodynamic effects of 10 cm H_2O of PEEP in mechanically ventilated patients after cardiac surgery when V_T is ≥8 mL/kg. Therefore, PVI may help the physician to optimize the respiratory uptake in oxygen and its delivery to the tissues.

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