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# Abilities of pulse pressure variations and stroke volume variations to predict fluid responsiveness in prone position during scoliosis surgery

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**Background.** Pulse pressure variation (PPV) and stroke volume variation (SVV) are robust indicators of fluid responsiveness in mechanically ventilated supine patients. The aim of the study was to evaluate the ability of PPV and SVV to predict fluid responsiveness in mechanically ventilated patients in the prone position (PP) during scoliosis surgery.

**Methods.** Thirty subjects were studied after the induction of anaesthesia in the supine position [before and after volume expansion (VE) with 500 ml of hetastarch 6%] and in PP (immediately after PP and before and after VE). PPV, SVV, cardiac output (CO), and static compliance of the respiratory system were recorded at each interval. Subjects were defined as responders (Rs) to VE if CO increased $\geq$15%.

**Results.** Three subjects were excluded. In the supine position, 16 subjects were Rs. PPV and SVV before VE were correlated with VE-induced changes in CO ($r^2$=0.64, $P$<0.0001 and $r^2$=0.56, $P$<0.0001, respectively). Fluid responsiveness was predicted by PPV >11% (sensitivity=88%, specificity=82%) and by SVV >9% (sensitivity=88%, specificity=91%). PP induced an increase in PPV and SVV ($P$<0.0001) and a decrease in the static compliance of the respiratory system ($P$<0.0001). In PP, 17 patients were Rs. PPV and SVV before VE were correlated with VE-induced changes in CO ($r^2$=0.59, $P$<0.0001 and $r^2$=0.55, $P$<0.0005, respectively). Fluid responsiveness was predicted in PP by PPV >15% (sensitivity=100%, specificity=80%) and by SVV >14% (sensitivity=94%, specificity=80%).

**Conclusions.** PP induces a significant increase in PPV and SVV but does not alter their abilities to predict fluid responsiveness.

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Intraoperative optimization of cardiac output (CO) using volume expansion (VE) reduces the length of hospital stay, critical care admissions, and mortality after major surgery in various settings.[1–6] In contrast, inappropriate fluid administration can have deleterious effects. Static indicators of fluid responsiveness such as central venous pressure and pulmonary capillary wedge pressure have been shown to be inaccurate in predicting the effect of fluid administration.[7] Several clinical studies demonstrate the usefulness of dynamic indices based on heart–lung interactions for guiding volume resuscitation in patients under mechanical ventilation.[8–12] Mechanical ventilation induces cyclic changes in intrathoracic and transpulmonary pressures that transiently affect left ventricular preload, resulting in cyclic changes in stroke volume (SV) in preload-dependent, but not in preload-independent patients.[13 14] These cyclic changes in SV can be evaluated by the cyclic changes in arterial pulse pressure. Several studies have shown that pulse pressure variation (PPV) and SV variation (SVV) are able to predict fluid

responsiveness in patients in the operating theatre and in intensive care units.[15] However, all these studies were performed in supine patients. Prone position (PP) might impact heart–lung interaction owing to a possible decrease in right ventricular preload and a decrease in compliance of the respiratory system.

Scoliosis surgery is a major orthopaedic operation that can involve substantial blood loss, transfusion, and large fluid shifts. In these patients, an adequate preload is of utmost importance for optimizing cardiac performance and organ perfusion.

We hypothesized that PP induces changes in PPV and SVV but maintains the ability of each variable to predict fluid responsiveness. In order to test this hypothesis, PPV and SVV were measured in individual patients before and after PP along with the relationship between each variable and increases in CO produced by a fluid challenge.

## Methods

### *Patients*

After obtaining approval from the local ethics committee (Comité de Protection des Personnes Sud-Ouest et Outre Mer III, Bordeaux, France) and written informed consent, 30 consecutive patients undergoing scoliosis surgery were enrolled. Exclusion criteria were the following: age $<18$ yr, arrhythmias, BMI $>40$ or $<15$ kg $m^{-2}$, valvular heart disease, left ventricular ejection fraction $<50\%$, or a history of lung disease. Anaesthesia was induced in the supine position with sufentanil and propofol using a target-controlled infusion system.[16 17] Cisatracurium (0.15 mg $kg^{-1}$) was used for muscle relaxation. The trachea was intubated and mechanical ventilation was set up using volume-controlled ventilation. Lungs were ventilated with a tidal volume of 8–10 ml $kg^{-1}$ body weight at a rate of 12–15 $min^{-1}$ (Felix®, Taema, Anthony, France). PEEP was set between 0 and 3 cm $H_2O$ by the attending anaesthetist. Anaesthesia was maintained using a target-controlled infusion of propofol and sufentanil adjusted to maintain the bispectral index between 40 and 50 (BIS-XP™, A2000 monitor; Aspect Medical Systems, Natick, MA, USA).

### *Haemodynamic monitoring*

#### *Cardiac output*

After the induction of anaesthesia, an 8 cm 3 Fr tipped catheter (Vygon, Ecouen, France) was inserted into the right or left radial artery. A dedicated transducer (FloTrac™, Edwards Lifesciences, Irvine, CA, USA) was connected to the radial arterial line on one side and to the Vigileo™ System (Edwards Lifesciences) on the other. The system enables the continuous monitoring of SV and CO by pulse contour analysis without external calibration. The Vigileo™ analyses the pressure waveform 100 times per second over 20 s, capturing 2000 data points for analysis and performing its calculations on the most recent 20 s data. The device calculates SV as $k\times$pulsatility, where pulsatility is the standard deviation of arterial pressure over a 20 s interval and $k$ a factor quantifying arterial compliance and vascular resistance derived from a multivariate regression model including (i) Langewouter's aortic compliance,[18] (ii) mean arterial pressure (MAP), (iii) variance, (iv) skewness, and (v) kurtosis of the pressure curve. The rate of adjustment of $k$ was 1 min (Software 1.14).

#### *Calculation of SVV*

SVV was calculated as the variation of beat-to-beat SV from the mean value during the most recent 20 s data: $SVV=(SV_{max}-SV_{min})/SV_{mean}$. The mean values of the three determinations were used for statistical analysis.

#### *Calculation of PPV*

Pulse pressure was defined as the difference between systolic and diastolic arterial pressure. Maximal ($PP_{max}$) and minimal ($PP_{min}$) pulse pressure values were determined over the same respiratory cycle. PPV was then calculated as: $PPV=(PP_{max}-PP_{min})/[(PP_{max}+PP_{min})/2]$ as previously described.[10] PPV was evaluated in triplicate over each of three consecutive respiratory cycles. The mean values of the three determinations were used for statistical analysis.

### *Prone positioning*

After the induction of anaesthesia, patients were turned to the PP on four pads (two chest and two pelvic supports) to allow the abdomen to hang free.

### *Study protocol*

#### *Measurements*

At each step of the study protocol, the following were recorded: systolic arterial pressure, MAP, diastolic arterial pressure, heart rate (HR), CO, PPV, SVV, and the static compliance of the respiratory system [$C_{st,rs}$=tidal volume/(plateau pressure–PEEP)].

#### *Sets of measurements*

Patients were studied in the supine position and PP. Two sets of measurements were performed in the supine position (T1 and T2) and three in the PP (T3, T4, and T5). After the induction of anaesthesia, patients received 500 ml of hetastarch 6% (Voluven®; Fresenius Kabi, Uppsala, Sweden) given over 10 min. Measurements were performed before (T1) and 3 min after VE (T2). Then, patients were turned to the PP and a third set of measurements was performed 2 min later (T3). Finally, patients received 500 ml of hetastarch 6% given over 10 min during the surgery as decided by the anaesthetist. Measurements were performed before (T4) and after (T5) VE.

During data recording, ventilatory settings were kept constant. Inotropes or vasopressors were not injected and stimulation of the patients was avoided.

### *Statistical analysis*

Results were expressed as median (25–75% inter-quartile range), unless stated otherwise. The effects of VE on haemodynamic parameters were assessed using a non-parametric Wilcoxon rank-sum test. Assuming that a 15% change in CO was required for clinical significance, patients were separated into responders (Rs) and non-responders (NRs) by changes in CO $\geq$15% and $<$15% after the volume challenge, respectively.[10 19] Haemodynamic parameters before VE (T1 and T4) were compared in Rs and NRs with a non-parametric Mann–Whitney test. The relationships between (i) changes in CO and PPV, SVV, HR, and MAP, (ii) SVV and PPV, (iii) changes in PPV or SVV and changes in CO were evaluated using a Spearman rank test.

Receiver operating characteristic (ROC) curves were generated for PPV and SVV varying the discriminating threshold, and areas under the ROC curves [95% confidence interval (CI)] were calculated and compared.[20] Values for each area can be between 0 and 1. A value of 0.5 indicates that the screening measure is no better than chance, whereas a value 1 implies perfect performance. In our study, the area under the ROC curve represented the probability that a random pair of Rs and NRs after VE would be correctly ranked by PPVor SVV.

A *P*-value of 0.05 was considered to be statistically significant. Statistical analysis was performed using Statview for Windows, version 5 (SAS Institute, Cary, NC, USA) and Medcalc (Software 8.1.1.0; Mariakerke, Belgium).

## Results

### *Global analysis*

Three subjects were excluded for arrhythmia during the protocol (ventricular extrasystole, $n$=2; incomplete data, $n$=1). The characteristics of the 27 subjects finally studied are reported in Table 1. Two subjects received β-blockers and three patients received angiotensin-converting enzyme inhibitors. Haemodynamic and respiratory variables at different times are shown in Table 2.

**Table 1** Characteristics of the subjects. Values are mean (range), mean (SD) or number ($n$). LVEF, left ventricular ejection fraction

| **Characteristics** | |
|---|---|
| Age (yr) | 48 (18–74) |
| Sex, F/M ($n$) | 19/8 |
| Height (cm) | 164 (8) |
| Weight (kg) | 60 (11) |
| Body mass index (kg m$^{-2}$) | 22 (4) |
| ASA classification, I/II/III ($n$) | 9/14/4 |
| LVEF (%) | 69 (7) |
| Anaesthesia duration (min) | 243 (37) |
| Levels operated ($n$) | 12 (4) |
| Blood loss (ml) | 1540 (450) |

**Table 2** Haemodynamic and respiratory variables at different times. Values are median (percentile 25th–75th). T1, supine position, before VE; T2, supine position, after VE; T3, immediately after prone positioning; T4, prone position, before VE; T5, prone position, after VE; HR, heart rate; MAP, mean arterial pressure; CO, cardiac output; PPV, pulse pressure variations; SVV, stroke volume variations. P1=T2 *vs* T1; P2=T3 *vs* T2; P3=T5 *vs* T4

| | **T1** | **T2** | **P1** | **T3** | **P2** | **T4** | **T5** | **P3** |
|---|---|---|---|---|---|---|---|---|
| HR (beats min$^{-1}$) | 67 (57–71) | 62 (57–68) | 0.01 | 64 (60–69) | 0.05 | 67 (58–78) | 63 (58–75) | NS |
| MAP (mm Hg) | 64 (56–70) | 74 (59–80) | 0.0001 | 67 (55–77) | 0.05 | 61 (50–68) | 71 (62–84) | 0.0001 |
| CO (litre min$^{-1}$) | 3.7 (3.1–4.5) | 4.4 (3.6–5.2) | 0.0001 | 4.2 (3.6–4.8) | 0.01 | 3.7 (3.2–4.4) | 4.6 (4.0–5.1) | 0.0001 |
| PPV (%) | 12 (9–16) | 5 (3–5) | 0.0001 | 9 (9–12) | 0.0001 | 18 (15–21) | 11 (8–15) | 0.0001 |
| SVV (%) | 11 (8–15) | 5 (3–6) | 0.0001 | 9 (8–10) | 0.0001 | 16 (14–21) | 11 (10–14) | 0.0001 |

### *Fluid responsiveness in the supine position (T1 vs T2)*

Sixteen subjects were Rs and 11 were NRs. Before VE, PPV and SVV were correlated ($r^2$=0.71; $P$<0.0001) and were significantly higher in Rs than in NRs ($P$<0.0001 and <0.0005, respectively) (Fig. 1). After VE, HR, MAP, PPV, SVV, and CO showed significant changes (Table 3). There was no correlation between baseline values of HR or MAP and the VE-induced changes in CO ($P$>0.05). In contrast, the baseline PPV and SVV correlated significantly with VE-induced changes in CO ($r^2$=0.64; $P$<0.0001 and $r^2$=0.56; $P$<0.0001, respectively). VE induced a significant decrease in PPV ($P$<0.0001) and in SVV ($P$<0.0001), which were significantly correlated with the VE-induced increase in CO ($r^2$=0.62; $P$<0.0001 and $r^2$=0.66; $P$<0.0001, respectively). An 11% PPV threshold discriminated between Rs and NRs with a sensitivity of 88% (95% CI: 62–98) and a specificity of 82% (95% CI: 48–97), AUC=0.949 (95% CI: 0.789–0.993). A 9% SVV threshold discriminated between Rs and NRs with a sensitivity of 88% (95% CI: 62–98) and a specificity of 91% (95% CI: 59–99), AUC=0.932 (95% CI: 0.765–0.990) (Fig. 2). There was no difference between the area under the ROC curves for PPV and SVV.

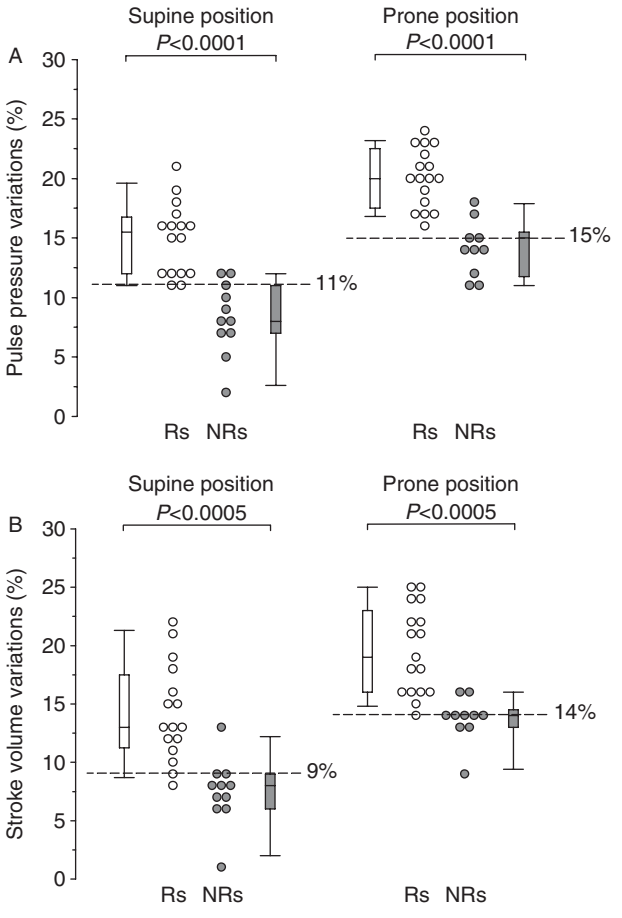


**Fig 1** Median values, inter-quartile range, and individual values of PPVs (A) and SVVs (B) before VE in Rs and in NRs, in the supine position and prone position.

### *Fluid responsiveness in PP*

Seventeen subjects were Rs and 10 were NRs. Before VE, PPV and SVV were correlated ($r^2$=0.77; $P$<0.0001) and were significantly higher in Rs than in NRs ($P$<0.0001 and <0.0005, respectively) (Fig. 1). After VE, MAP, PPV, SVV, and CO showed significant changes (Table 4). There was no correlation between baseline values of HR or MAP and the VE-induced changes in CO ($P$>0.05). In contrast, baseline PPV and SVV correlated significantly with VE-induced changes in CO ($r^2$=0.59; $P$<0.0001 and $r^2$=0.55; $P$<0.0005, respectively). VE induced a significant decrease in PPV ($P$<0.0001) and SVV ($P$<0.0001), which correlated significantly with the VE-induced increase in CO ($r^2$=0.57; $P$<0.0001 and $r^2$=0.57; $P$<0.0001, respectively). A 15% PPV threshold discriminated between Rs and NRs with a sensitivity of 100% (95% CI: 80–100) and a specificity of 80% (95% CI: 44–97), AUC=0.959 (95% CI: 0.803–0.994). A 14% SVV threshold discriminated between Rs and NRs with a sensitivity of 94% (95% CI: 71–99) and a specificity of 80% (95% CI: 44–97), AUC=0.938 (95% CI: 0.774–0.992) (Fig. 2). There was no difference between the area under the ROC curves for PPV and SVV.

### *Effects of PP on haemodynamic and respiratory variables*

PP induced a significant decrease in CO ($P$<0.01) and MAP ($P$<0.05), and a significant increase in PPV ($P$<0.0001), SVV ($P$<0.0001), and HR ($P$<0.05). PPV and SVV values before PP were not correlated with the PP-induced changes in CO ($P$>0.05). PP induced a significant decrease in $C_{st,rs}$ [31 (27–40) *vs* 25 (22–33) ml (cm $H_2O$)$^{-1}$; $P$<0.0001].

## Discussion

Our data suggest that PPV and SVV are able to predict fluid responsiveness in prone patients during spine surgery. Recently, Marks and colleagues[21] studied the changes in systolic pressure variations induced by the PP in 25 subjects undergoing spine surgery. They showed that systolic pressure variations were not different in the PP compared with the supine position. However, changes in the compliance of the respiratory system were not shown and fluid challenge was not done in the PP.

In the present study, we demonstrate a significant increase in PPV and SVV induced by PP. Several mechanisms could explain this phenomenon. Although there are no data directly supporting that right ventricular preload is reduced by prone positioning, we can suggest that the position of the heart at a hydrostatic level above the head and limbs causes a reduction in venous return.[22–24] The cyclic

**Table 3** Haemodynamic variables before and after VE in fluid Rs and NRs in the supine position. Values are median (percentile 25th–75th). T1, supine position, before VE; T2, supine position, after VE; HR, heart rate; MAP, mean arterial pressure; CO, cardiac output; PPV, pulse pressure variations; SVV, stroke volume variations. P1, T2 *vs* T1 in fluid Rs; P2, T1 in fluid NRs *vs* T1 in fluid Rs; P3, T2 *vs* T1 in fluid NRs

| | **Responders ($n$=16)** | | | **Non-responders ($n$=11)** | | | |
|---|---|---|---|---|---|---|---|
| | **T1** | **T2** | **P1** | **T1** | **T2** | **P2** | **P3** |
| HR (beats min$^{-1}$) | 68 (62–72) | 63 (62–66) | 0.01 | 57 (56–70) | 57 (52–69) | NS | NS |
| MAP (mm Hg) | 64 (54–77) | 74 (63–88) | 0.001 | 58 (57–70) | 64 (56–77) | NS | NS |
| CO (litre min$^{-1}$) | 3.3 (2.9–3.9) | 4.2 (3.7–4.8) | 0.001 | 4.8 (3.6–5.1) | 5.3 (3.8–5.5) | 0.005 | 0.01 |
| PPV (%) | 16 (12–17) | 5 (4–6) | 0.001 | 8 (7–11) | 5 (3–5) | 0.0001 | 0.01 |
| SVV (%) | 13 (12–17) | 5 (3–8) | 0.005 | 8 (6–9) | 5 (3–6) | 0.0005 | 0.001 |

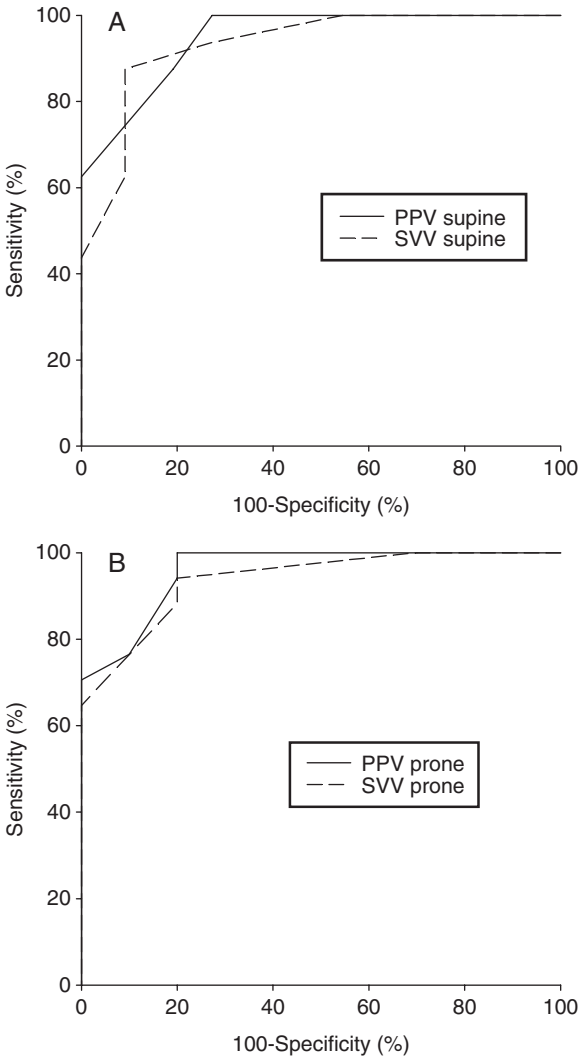


**Fig 2** ROC curves showing the ability of PPVs and SVVs to predict fluid responsiveness in the supine position (A) and prone position (B).

effects of mechanical ventilation on the heart would be more pronounced because of a decrease in right ventricular preload. Secondly, we observed a significant increase in plateau pressure during PP as a result of a decrease in the compliance of the respiratory system. It has been shown that reducing chest compliance induces an increase in SVV.[25 26] An increase in inspiratory pressure should impede venous return, and hence induce a leftward shift on the Frank–Starling curve.[15] Conversely, it has been shown that an increase in chest wall compliance induced by opening the chest (sternotomy) decreases SVVs.[27] In the PP, abdominal compression may induce inferior vena cava compression and a decrease in right ventricular preload. However, the position used in the study (four pads) is not known to induce an increase in intra-abdominal pressure and we made sure that the abdomen hung free because of the risk of bleeding intraoperatively.[23] Unfortunately, we did not measure intra-abdominal pressure and cannot exclude that the increase in PPV and SVV was not due to an increase in intra-abdominal pressure.

Our study suggests that PPV is able to predict fluid responsiveness in the PP, but with a threshold higher than in the supine position (15% *vs* 11%). This finding is in accordance with a previous experimental study evaluating the ability of PPV to predict fluid responsiveness in the event of a decrease in the compliance of the respiratory system secondary to increased intra-abdominal pressure.[28] The authors showed an increase in the absolute value of PPV, although its ability to predict fluid responsiveness in this specific setting remained unchanged. The optimal threshold of PVV for predicting fluid responsiveness increased dramatically (20.5% *vs* 11.5%).

Our results confirm that SVV obtained with the Vigileo™ device is able to predict fluid responsiveness in the supine position.[8 29–31] However, this was the first time that SVV was tested in PP and we found an increase in SVV values in PP probably for the same reasons as for PPV. We did not find any difference between PPV and SVV for predicting fluid responsiveness in PP, so calculation of the SVV algorithm is not or only slightly impacted by body position.

We found a poor relationship between PPV before prone positioning and the change in CO induced by PP. In other words, the PP-induced changes in CO were not only preload-dependent. All subjects received VE before prone positioning and their volume status was optimized, as attested by their low PPV [5% (3–5)]. Despite that, CO decreased significantly in PP. Even if the right ventricular preload is decreased by blood sequestration and by an increase in inspiratory pressure, other mechanisms are involved in the PP-induced changes in CO. However, because our study was not designed to elucidate why CO

**Table 4** Haemodynamic variables before and after VE in fluid Rs and NRs in prone position. Values are median (percentile 25th–75th). T4, prone position, before VE; T5, prone position, after VE; HR, heart rate; MAP, mean arterial pressure; CO, cardiac output; PPV, pulse pressure variations; SVV, stroke volume variations. P1, T5 *vs* T4 in fluid Rs; P2, T4 in fluid NRs *vs* T4 in fluid Rs; P3, T5 *vs* T4 in fluid NRs

| | **Responders ($n=17$)** | | | **Non-responders ($n=10$)** | | | |
|---|---|---|---|---|---|---|---|
| | **T4** | **T5** | **P1** | **T4** | **T5** | **P2** | **P3** |
| HR (beats $min^{-1}$) | 68 (58–80) | 63 (58–75) | NS | 65 (58–76) | 63 (58–73) | NS | NS |
| MAP (mm Hg) | 61 (52–68) | 77 (67–84) | 0.001 | 62 (48–66) | 64 (56–68) | NS | 0.05 |
| CO (litre $min^{-1}$) | 3.4 (3.2–4.0) | 4.6 (4.1–5.1) | 0.001 | 4.3 (3.4–4.8) | 4.6 (3.4–5.3) | NS | 0.05 |
| PPV (%) | 20 (18–22) | 10 (7–12) | 0.001 | 14 (12–15) | 11 (10–14) | 0.0001 | 0.05 |
| SVV (%) | 19 (16–23) | 12 (10–14) | 0.0005 | 14 (13–14) | 11 (11–13) | 0.0005 | NS |

decreases during PP, we cannot determine which mechanisms are involved. Furthermore, if a VE had not been given before turning the subjects to the PP, changes in PPV and CO would likely have been greater.

Optimizing SV or CO during major surgery can reduce length of hospital stay, critical care admissions, and mortality.[1–6] However, all these studies were performed in patients in the supine position. As we demonstrated that PPV is useful in predicting fluid responsiveness in the PP, it would be interesting to perform a study evaluating the impact of CO optimization using PPV or SVV on outcome.

Our study has some limitations. First, Rs and NRs to VE were defined by CO obtained by the Vigileo™/FloTrac™ system. The accuracy of the Vigileo™ device to assess CO has been tested in numerous settings with various results.[32–35] However, it has been shown that the device is able to track changes in SV and CO induced by VE, PEEP, and mechanical ventilation.[8 36 37] Recent studies evaluating fluid responsiveness used the Vigileo™/FloTrac™ system as the reference to define response to VE.[38 39] However, there are no data about the ability of the device to track changes in CO induced by PP, which could induce significant changes in systemic vascular resistance. This could have impacted our results. Secondly, the PP used in the study involves the heart being positioned at a hydrostatic level above the head and limbs, and a four-pad support to allow the abdomen to hang free. Our results might not be extrapolated to other PP with abdominal compression. Thirdly, we excluded subjects with spontaneous breathing activity or cardiac arrhythmias because respiratory variations in haemodynamic signals are ineffective.[15] Fourthly, the study was performed in subjects sedated and mechanically ventilated with a tidal volume of $\geq$8 ml $kg^{-1}$, and PPV is affected by tidal volume under mechanical ventilation.[40] Fifthly, Rs were defined by an increase in CO $\geq$15% after VE. A cut-off of 15% is usually used to cope with the intrinsic variability of CO measurements and to define a clinically relevant change.[10 41] However, defining this threshold determines the results obtained by the ROC analysis, and different thresholds would provide different results. Finally, our low sample size might limit the interpretation of the results.

In conclusion, our results suggest that PP induces a significant increase in the absolute value of PPV and SVV but does not affect their ability to predict fluid responsiveness.

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