*Original Article*

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# Pulse pressure variation and stroke volume variation predict fluid responsiveness in mechanically ventilated patients experiencing intra-abdominal hypertension

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**Summary** **The purpose of the present study was to evaluate whether pulse pressure variation (PPV) and stroke volume variation (SVV) can predict fluid responsiveness in patients with intra-abdominal hypertension (IAH) in either a supine or Trendelenburg position. Forty mechanically ventilated patients that exhibited IAH resulting from carbon dioxide insufflation (up to 12 mmHg) underwent fluid therapy in either a supine or Trendelenburg position. Hemodynamic measurements, including PPV and SVV, were obtained before and after fluid therapy. Prediction of fluid responsiveness (> 10% increase in stroke volume) was performed by linear regression analyses. Baseline PPV and SVV values correlated closely with changes in stroke volume induced by fluid therapy, and were significantly higher in patients that subsequently responded to fluid therapy. Fluid responsiveness in patients in a supine position was predicted by a PPV threshold of > 10.5% and an SVV threshold of > 10.5%. Fluid responsiveness in patients in a Trendelenburg position was predicted by a PPV threshold of > 7.5% and an SVV threshold of > 7.0%. PPV and SVV were demonstrated to be sensitive and specific predictors of fluid responsiveness in patients with IAH in both the supine and Trendelenburg positions.**

***Keywords:*** Stroke volume variation, pulse pressure variation, fluid responsiveness, intra-abdominal hypertension, Trendelenburg position

## 1. Introduction

Intraoperative optimization of fluid administration reduces the number of critical care admissions, the length of hospital stays, and incidences of mortality after major surgery in various clinical settings (*1-4*). Frequently used static preload variables such as central venous pressure (CVP) or pulmonary capillary wedge pressure often fail to provide reliable information on cardiac preload and are not capable of predicting a cardiac response to fluid therapy (*5,6*). As an alternative to these static variables, stroke volume variation (SVV) and pulse pressure variation (PPV) have been shown to be sensitive predictors of fluid responsiveness in mechanically ventilated patients undergoing cardiac surgery, neurosurgical procedures, and live transplantation (*7-9*). Left ventricle preload is highly susceptible to changes in the intrathoracic pressure induced by mechanical ventilation. Thus, mechanical ventilation results in cyclic changes of stroke volume (SV) predominantly in preload-dependent patients, but to a lesser degree in preload-independent patients. Alterations of SV can be assessed by the cyclic changes in arterial pulse pressure. Both PPV and SVV are increased with hypovolemia, and variations decrease if intravascular blood volume is restored.

Intra-abdominal pressure (IAP) is frequently increased in critically ill patients. A multiple prospective epidemiological study involving 97 patients revealed that the prevalence of intra-abdominal hypertension (IAH) (defined as a maximal IAP of 12 mmHg or more) was 50.5%, and of abdominal compartment syndrome (defined as a maximal IAP of 20 mmHg or more) was

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8%, in critically ill patients (*10*). However, another prospective cohort study involving 83 patients found that the prevalence of IAH and abdominal compartment syndrome in critically ill patients were 64% and 12%, respectively (*11*). IAH was significantly associated with more severe organ failure, particularly renal and respiratory, and a prolonged intensive care unit stay (*11-13*). IAH was demonstrated to be an independent predictor for in-hospital mortality (*14*).

Appropriate fluid therapy is of the utmost importance for optimizing cardiac performance and organ perfusion during IAH (*15*). It has been shown that cardiac filling pressures, such as CVP and pulmonary artery occlusion pressure, in the presence of elevated IAP may be falsely increased, hence misleading adequate fluid therapy (*16*). Recently, it has been demonstrated that elevated IAP increases the static variables of preload such as PPV and systolic pressure variation (SPV), especially in cases of hypovolemia (*17,18*). However, it is currently unknown whether PPV and SVV can serve as predictors of fluid responsiveness when IAH is present.

The majority of studies have only reported on procedures performed on patients in a supine position. However, a position common in abdominal and gynecological surgeries is the Trendelenburg position. In this position, the patient is laid flat on the back with the feet higher than the head by 15-30 degrees in order to improve surgical exposure of the pelvic organs, as gravity pulls the intestines away from the pelvis. As a result, this position may increase the cardiac preload from the major vessels in the lower extremities, and decrease the compliance of the respiratory system, reducing functional residual capacity as the diaphragm is forced towards the heart, hence affecting heart-lung interactions. Currently, it is unclear whether the Trendelenburg position influences the ability of SVV and PPV to predict fluid responsiveness, especially in patients with IAH.

## 2. Materials and Methods

### 2.1. *Patients and anesthesia*

With local ethics committee approval and patient written informed consent, forty mechanically ventilated patients undergoing laparoscopy-assisted gastrointestinal surgery were enrolled in this study. Twenty patients were placed in the supine position and surgical procedures were performed to remove stomach cancer. The remaining twenty patients were placed in the Trendelenburg position for the surgical removal of colon cancer. Patients with preoperative arrhythmias, left ventricle ejection fractions < 50%, valvular heart disease, intracardiac shunts, pulmonary artery hypertension, or severe peripheral vascular obstructive disease were excluded.

The patients were pre-medicated with 0.5 mg atropine (*i.m.*) 30-40 min before their arrival to the operating room. After placement of the routine hemodynamic monitoring equipment and the insertion of arterial and peripheral IV lines, anesthesia was induced with an IV infusion of midazolam (0.05 mg/kg), propofol (1-2 mg/kg), and fentanyl (3 μg/kg), and maintained by using target controlled infusion of propofol (2-4 μg/mL) and a continuous infusion of remifentanil (0.3-0.8 μg/kg/min) to keep the bispectral index between 40 and 50. Neuromuscular blockade was achieved with rocuronium (0.8 mg/kg; IV). Following endotracheal intubation, mechanical ventilation was performed in a volume-controlled mode with an inspired oxygen concentration of 40%, a tidal volume of 8-10 mL/kg, an end-expiratory rate of 0 cm $H_2O$, and an inspiratory/expiratory ratio of 0.5. Respiratory rate was adjusted to maintain an arterial carbon dioxide pressure between 35 and 40 mmHg.

### 2.2. *Hemodynamic monitoring*

After induction of anesthesia, a standard 7 Fr Two-Lumen central venous catheterization set (Arrow International Inc. Salt Lake City, UT, USA) was introduced *via* right internal jugular vein access. CVP was measured using standard transducers and displayed on a monitor. Pressure transducers were zeroed at midaxillary level to ambient pressures. A 3 F tipped arterial catheter (Laboratoires Pharmaceutiques, Vygon, Ecouen, France) was inserted percutaneously into the left radial artery. A transducer (FloTrac, Edwards Life-science, LLC, Irvine, CA, USA) was connected to the radial arterial line on one side and to the Vigileo system (software version 01.01; Edwards Life-science LLC, Irvine, CA, USA). This system enables the continuous monitoring of arterial pressure, cardiac output (CO), SV, and SVV by pulse contour analysis. This system needs no calibration and provides continuous CO measurements from the arterial pressure wave. The Vigileo system analyzes the pressure waveform 100 times/sec over 20 sec, captures 2,000 data points for analysis, and performs its calculations on the most recent 20 sec data. The device calculates SV as $k \times$ pulsatility, where pulsatility is the standard deviation of arterial pressure over a 20 sec interval, and $k$ is a factor quantifying arterial compliance and vascular resistance. The CO was calculated as follows: CO = heart rate (HR) × SV. Except for cardiac pre- and after-load, alteration of HR significantly impacts the measure of CO. However, SV has a close relationship with cardiac pre-load; thus, it was selected as a measure for showing improvement after fluid therapy. SVV, as a percentage change of SV during the ventilatory cycle, was evaluated according to the following equation: SVV (%) = (maximum SV – minimum SV)/mean SV, where maximum and minimum SV are mean values of the four extreme values of SV during a period of

20 sec, and mean SV is the average value for the time period. Additionally, PPV was determined for the same time interval with the following calculation: PPV (%) = (maximum pulse pressure – minimum pulse pressure)/ mean pulse pressure, where maximum and minimum pulse pressures are mean values of the four extreme values of pulse pressure, and mean pulse pressure is the average value for the time period. The CI value was acquired directly from the Vigileo monitoring system.

### 2.3. *Study protocol*

After the induction of anesthesia, intraperitoneal insufflation of carbon dioxide was performed to create a pneumoperitoneum to provide surgical visualization of intra-abdominal structures and allow for minimal laparoscopic manipulations. Carbon dioxide was insufflated using an electronic endoflator (26430530, Storz, Tuttlingen, Germany). IAP was increased to 12 mmHg and maintained at this level. When the actual pressure was more than 12 mmHg, an alarm was initiated and the air bleeder was activated to decrease IAP. On establishment of a pneumoperitoneum and prior to any surgical intervention, data of cardiac output index (CI), CO, SV, SVV, and PPV were recorded at this level of IAP. In order to perform fluid therapy, a 6% hydroxyethyl starch solution was infused (mean molecular weight 130,000 Da, molar substitution 0.4) for 15-20 min at a rate of 0.4 mL/kg/min while IAP was maintained at 12 mmHg. The volume of fluid challenge was set at 7 mL/kg. After a 15 min stabilization, the same measurements were recorded at an IAP of 12 mmHg after fluid therapy.

### 2.4. *Statistical analysis*

All hemodynamic variables were analyzed as continuous variables and expressed as the mean ± S.D. Assuming that a 10% change in SV was required for clinical significance, patients were separated into responders (Rs) and non-responders (NRs) by changes in SV ≥ 10% and < 10%, respectively, after fluid therapy. Hemodynamic variables before fluid therapy were compared between Rs and NRs using a two-tailed *t*-test. Hemodynamic variables before and after fluid therapy were compared in Rs or NRs using a non-parametric *Wilcoxon rank sum* test. The correlation between changes in SV and preload variables before fluid therapy was assessed by Pearson's correlation. To assess the ability of different hemodynamic variables to discriminate Rs and NRs after fluid therapy, Receiver Operating Characteristic (ROC) curves were generated for SVV, PPV, CVP, CO, and SV, with evaluation of the discriminating threshold value of each variable. The area under the ROC curve for each variable was calculated and compared by one-way analysis of variance (ANOVA). Values for each area can be between 0 and 1. A value of 0.5 indicates that the screening measures are no better than chance, whereas a value of 1 implies perfect performance. In our study, the area under the ROC curve represented the probability that a random pair of Rs and NRs would be correctly ranked by the hemodynamic variable measurement. For all analyses, $p < 0.05$ was considered to be statistically significant. Statistical analyses were performed using SPSS 15.0 software (SPSS Inc, Chicago, IL, USA).

## 3. Results

### 3.1. *Hemodynamic variables before fluid therapy*

Table 1 summarizes the hemodynamic variables before fluid therapy in patients with IAH in the supine position. Patient data is categorized by whether they were Rs (eleven patients) or NRs (nine patients) to subsequent fluid therapy. A retrospective comparison shows that prior to fluid therapy, there were no significant differences in mean arterial pressure (MAP), heart rate (HR), and CVP, whereas the cardiac output index (CI) and SV were significantly lower in the Rs than in the NRs, and SVV and PPV were significantly higher in the Rs than in the NRs.

Table 2 summarizes the hemodynamic variables before fluid therapy in patients with IAH in the

**Table 1. Hemodynamic variables of responders and non-responders before fluid therapy in patients with IAH in a supine position**

| Items | Responders ($n$ = 11) | Non-responders ($n$ = 9) | $p$ value |
|---|---|---|---|
| MAP (mmHg) | 73.18 ± 11.85 | 74.78 ± 7.73 | NS |
| HR (beat/min) | 69.91 ± 11.44 | 62.89 ± 7.06 | NS |
| CVP (mmHg) | 7.36 ± 2.25 | 7.56 ± 2.65 | NS |
| CI (l/min/m$^2$) | 2.53 ± 0.68 | 3.02 ± 0.74 | $p < 0.05$ |
| SV (mL/beat) | 65.09 ± 15.66 | 81.11 ± 19.12 | $p < 0.05$ |
| SVV (%) | 13.27 ± 1.68 | 8.89 ± 2.26 | $p < 0.05$ |
| PPV (%) | 14.00 ± 2.79 | 8.56 ± 1.81 | $p < 0.05$ |

Values are mean ± S.D., MAP = mean arterial pressure, HR = heart rate, CVP = central venous pressure, CI = cardiac output index, SV = stroke volume, SVV = stroke volume variation, PPV = pulse pressure variation, NS = not significant.

**Table 2. Hemodynamic variables of responders and non-responders before fluid therapy in patients with IAH in the Trendelenburg position**

| Items | Responders ($n$ = 9) | Non-responders ($n$ = 11) | $p$ value |
|---|---|---|---|
| MAP (mmHg) | 76.10 ± 10.77 | 87.00 ± 4.99 | NS |
| HR (beat/min) | 74.50 ± 13.40 | 66.00 ± 12.11 | NS |
| CVP (mmHg) | 7.33 ± 3.61 | 8.64 ± 2.20 | $p < 0.05$ |
| CI (l/min/m$^2$) | 2.71 ± 0.48 | 3.09 ± 0.67 | $p < 0.05$ |
| SV (mL/beat) | 64.10 ± 11.03 | 83.80 ± 25.21 | $p < 0.05$ |
| SVV (%) | 12.70 ± 2.95 | 7.73 ± 3.32 | $p < 0.05$ |
| PPV (%) | 13.10 ± 3.14 | 8.81 ± 3.37 | $p < 0.05$ |

Values are mean ± S.D., MAP = mean arterial pressure, HR = heart rate, CVP = central venous pressure, CI = cardiac output index, SV = stroke volume, SVV = stroke volume variation, PPV = pulse pressure variation, NS = not significant.

Trendelenburg position. Patient data is similarly categorized by response to subsequent fluid therapy, with nine patients categorized as Rs, and eleven as NRs. Prior to fluid therapy, there were no significant differences in MAP and HR, whereas CI, SV and CVP were significantly lower in the Rs than in the NRs, and SVV and PPV were significantly higher in the Rs than in the NRs.

### 3.2. *The effect of fluid therapy on hemodynamic variables*

Table 3 summarizes the hemodynamic variables before and after fluid therapy in patients with IAH in the supine position. Fluid therapy did not significantly change MAP, HR, or CI in Rs and NRs. However, fluid therapy was associated with an increase in SV and CVP in the Rs, whereas these measures did not differ before and after fluid therapy in the NRs. More importantly, fluid therapy induced significant decreases in PPV and SVV in both Rs and NRs.

Table 4 summarizes the hemodynamic variables before and after fluid therapy in patients with IAH in the Trendelenburg position. After fluid therapy, MAP, HR and CVP were not significantly changed in Rs and NRs. Fluid therapy was associated with an increase in SV and CI in the Rs, but did not differ before and after fluid therapy in the NRs. As occurred in patients in the supine position, fluid therapy induced significant decreases in PPV and SVV in both Rs and NRs in the Trendelenburg position.

### 3.3. *Fluid responsiveness to fluid therapy*

Figure 1 illustrates the correlations between the change in SV and hemodynamic variables before fluid therapy in patients with IAH in the supine position. There was no significant correlation between the change in SV

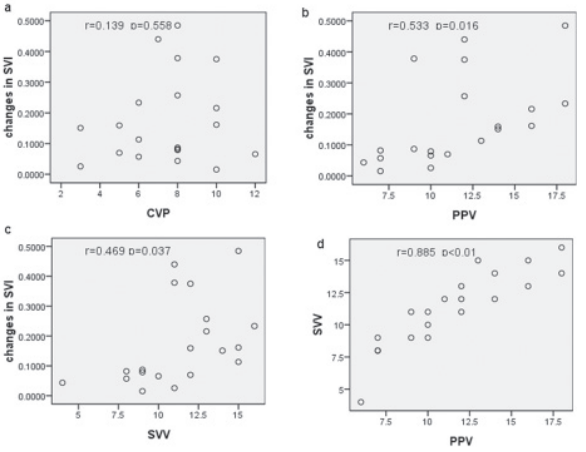


**Figure 1. Prediction of fluid responsiveness in patients with IAH in the supine position.** No correlation was observed between baseline CVP and the change in SV after fluid therapy **(a)**; Conversely, baseline PPV and SVV correlated closely with the change in SV induced by fluid therapy **(b** and **c)**; Moreover, baseline PPV correlated significantly with baseline SVV **(d)**.

**Table 3. Hemodynamic variables of responders and non-responders before and after fluid therapy in patients with IAH in a supine position**

| Items | Responders ($n$ = 11) | | | Non-responders ($n$ = 9) | | |
|---|---|---|---|---|---|---|
| | Before | After | $p$ value | Before | After | $p$ value |
| MAP (mmHg) | 73.18 ± 11.85 | 79.00 ± 11.87 | NS | 74.78 ± 7.73 | 80.11 ± 8.96 | NS |
| HR (beat/min) | 69.91 ± 11.44 | 67.64 ± 9.36 | NS | 62.89 ± 7.06 | 64.33 ± 7.68 | NS |
| CVP (mmHg) | 7.36 ± 2.25 | 10.09 ± 2.81 | $p < 0.05$ | 7.56 ± 2.65 | 9.33 ± 3.04 | NS |
| CI (l/min/m$^2$) | 2.53 ± 0.68 | 3.15 ± 0.79 | NS | 3.02 ± 0.74 | 3.32 ± 0.82 | NS |
| SV (mL/beat) | 65.09 ± 15.66 | 82.00 ± 16.85 | $p < 0.05$ | 81.11 ± 19.12 | 85.56 ± 20.10 | NS |
| SVV (%) | 13.27 ± 1.68 | 7.27 ± 2.19 | $p < 0.05$ | 8.89 ± 2.26 | 6.11 ± 1.83 | $p < 0.05$ |
| PPV (%) | 14.00 ± 2.79 | 7.09 ± 2.39 | $p < 0.05$ | 8.56 ± 1.81 | 5.89 ± 1.27 | $p < 0.05$ |

Values are mean ± S.D., MAP = mean arterial pressure, HR = heart rate, CVP = central venous pressure, CI = cardiac output index, SV = stroke volume, SVV = stroke volume variation, PPV = pulse pressure variation, NS = not significant.

**Table 4. Hemodynamic variables of responders and non-responders before and after fluid therapy in patients with IAH in the Trendelenburg position**

| Items | Responders ($n$ = 9) | | | Non-responders ($n$ = 11) | | |
|---|---|---|---|---|---|---|
| | Before | After | $p$ value | Before | After | $p$ value |
| MAP (mmHg) | 76.10 ± 10.77 | 84.20 ± 10.09 | NS | 87.00 ± 4.99 | 88.20 ± 7.57 | NS |
| HR (beat/min) | 74.50 ± 13.40 | 71.40 ± 14.24 | NS | 66.00 ± 12.11 | 67.80 ± 14.20 | NS |
| CVP (mmHg) | 7.33 ± 3.61 | 10.33 ± 4.77 | NS | 8.64 ± 2.20 | 10.91 ± 2.74 | NS |
| CI (l/min/m$^2$) | 2.71 ± 0.48 | 3.31 ± 0.61 | $p < 0.05$ | 3.09 ± 0.67 | 3.44 ± 0.66 | NS |
| SV (mL/beat) | 64.10 ± 11.03 | 79.10 ± 13.11 | $p < 0.05$ | 83.80 ± 25.21 | 88.90 ± 24.88 | NS |
| SVV (%) | 12.70 ± 2.95 | 7.10 ± 1.59 | $p < 0.05$ | 7.73 ± 3.32 | 5.36 ± 1.36 | $p < 0.05$ |
| PPV (%) | 13.10 ± 3.14 | 6.50 ± 1.78 | $p < 0.05$ | 8.81 ± 3.37 | 5.27 ± 1.49 | $p < 0.05$ |

Values are mean ± S.D., MAP = mean arterial pressure, HR = heart rate, CVP = central venous pressure, CI = cardiac output index, SV = stroke volume, SVV = stroke volume variation, PPV = pulse pressure variation, NS = not significant.

and CVP before fluid therapy ($r = 0.139$, $p = 0.558$). In contrast, both the SVV and PPV before fluid therapy correlated significantly and closely with the change in SV induced by fluid expansion ($r = 0.469$, $p = 0.037$; $r = 0.533$, $p = 0.015$, respectively). Moreover, the baseline PPV correlated with the baseline SVV prior to fluid therapy ($r = 0.885$, $p < 0.01$).

Figure 2 illustrates the correlations between the change in SV and hemodynamic variables before fluid therapy in patients with IAH in the Trendelenburg position. There was no significant correlation between the change in SV and CVP before fluid therapy ($r = 0.109$, $p = 0.647$). Conversely, both the SVV and PPV before fluid therapy correlated significantly and closely with the change in SV induced by fluid expansion as was observed in patients in the supine position ($r = 0.884$, $p < 0.001$; $r = 0.831$, $p < 0.001$, respectively). Additionally, the baseline PPV was significantly correlated with the baseline SVV prior to fluid therapy ($r = 0.940$, $p < 0.01$).

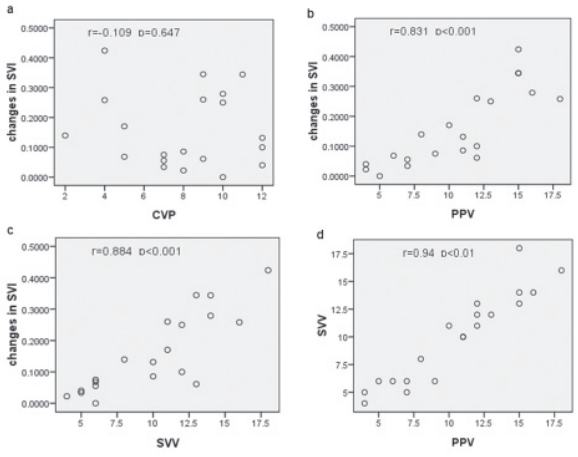


**Figure 2. Prediction of fluid responsiveness in patients with IAH in the Trendelenburg position.** No correlation was observed between baseline CVP and the change in SV after fluid therapy **(a)**. Conversely, baseline PPV and SVV correlated closely with the change in SV induced by fluid therapy **(b** and **c)**. Moreover, baseline PPV correlated significantly with baseline SVV **(d)**.

### 3.4. *Discriminating thresholds between Rs and NRs*

The discriminating thresholds of hemodynamic variables between Rs and NRs in the supine position were evaluated by constructing ROC curves (Figure 3). The areas under the ROC curves were: 0.955 for PPV, 0.960 for SVV, 0.399 for CO, 0.480 for CVP, and 0.197 for SV. The areas for PPV and SVV were statistically greater than those for SV, CVP and CO ($p < 0.01$). A PPV threshold of 10.5% allows for discrimination between Rs and NRs with a sensitivity of 90.9% and a specificity of 88.9%. An SVV threshold of 10.5% allows for discrimination between Rs and NRs with a sensitivity of 100% and a specificity of 77.8%.

The discriminating thresholds of hemodynamic variables between Rs and NRs in the Trendelenburg position were also evaluated by constructing ROC curves (Figure 4). The areas under the ROC curves were: 0.859 for PPV, 0.854 for SVV, 0.493 for CO, 0.372 for CVP, and 0.327 for SV. The areas for PPV and SVV were statistically greater than those for SV, CVP and CO ($p < 0.01$). A PPV threshold of 7.5% allows for discrimination between Rs and NRs with a sensitivity of 100% and a specificity of 54.5%, and an SVV threshold of 7% allows for discrimination between Rs and NRs with a sensitivity of 100% and a specificity of 63.6%.

## 4. Discussion

To optimize cardiac performance and organ perfusion, it is imperative that optimal preload conditions are

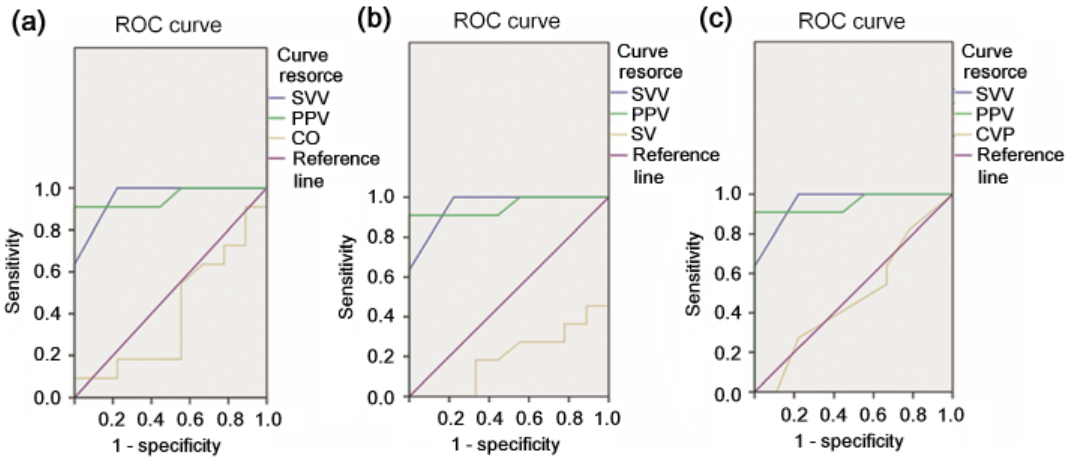


**Figure 3. ROC analyses for PPV, SVV, CO, SV and CVP as predictors of increases in SV of more than 10% after fluid therapy in patients with IAH in the supine position.** Areas under the ROC curves for PPV and SVV were significantly greater than those for CO **(a)**, SV **(b)**, and CVP **(c)**. A PPV threshold of > 10.5% allows for discrimination between Rs and NRs with a sensitivity of 90.9% and a specificity of 88.9%. Overall sensitivity and specificity between Rs and NRs were 100% and 77.8% with a SVV threshold of > 10.5%.

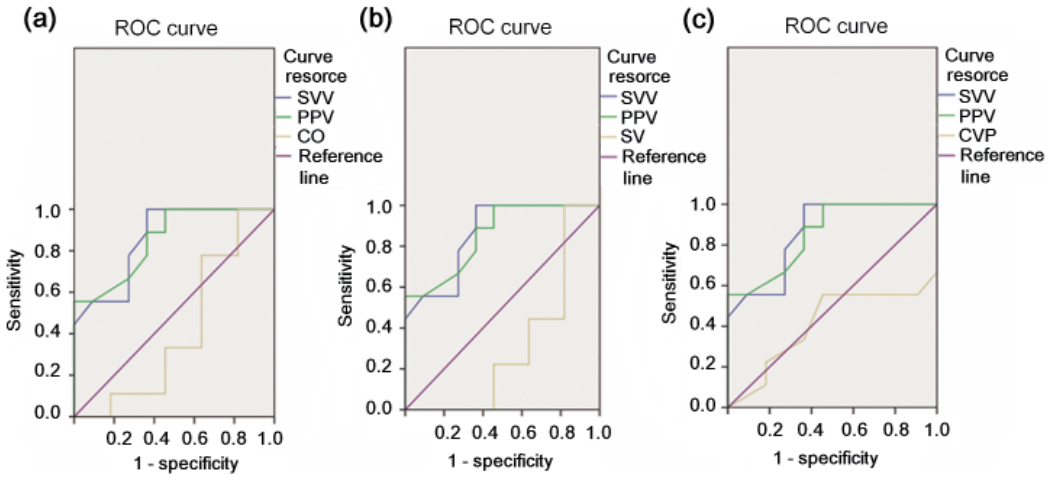


**Figure 4. ROC analyses for PPV, SVV, CO, SV and CVP as predictors of increases in SV of more than 10% after fluid therapy in patients with IAH in the Trendelenburg position.** Areas under the ROC curves for PPV and SVV were significantly greater than those for CO **(a)**, SV **(b)** and CVP **(c)**. A PPV threshold of > 7.5% allows for discrimination between Rs and NRs with a sensitivity of 100% and a specificity of 54.5%. Overall sensitivity between Rs and NRs was 100% with a SVV threshold of > 7.0%.

achieved in patients undergoing surgical procedures. Measurements of cardiac filling pressures, namely CVP and pulmonary artery occlusion pressure, are insensitive and sometimes misleading in the assessment of circulating blood volume (*5,6*). A more accurate method for preload assessment is based on the heart-lung interactions and the measurement of PPV and SVV by arterial waveform analysis in mechanically ventilated patients. Many studies have demonstrated that PPV and SVV are highly sensitive in predicting fluid responsiveness in mechanically ventilated patients undergoing cardiac surgery, neurosurgical procedures, and live transplantation (*7-9*). However, some procedures utilize the insufflation of carbon dioxide, such as for minimal laparoscopic manipulations, which induce IAH. The induction of IAH, as well as the adoption of the Trendelenburg position, has potential hemodynamic and respiratory consequences. The influence of IAH on the predictive ability of PPV and SVV is currently under debate. To our knowledge, no patient-based clinical investigations have been performed to clarify whether PPV and SVV can reliably predict fluid responsiveness in patients with IAH in supine or Trendelenburg positions.

Our findings indicate that baseline PPV and SVV correlate significantly and closely with the change in SV induced by fluid therapy, and baseline PPV are strongly correlated with baseline SVV in mechanically ventilated patients with IAH. These results indicate that PPV and SVV are still accurate indices of fluid responsiveness during IAH even when the patients are placed in the Trendelenburg position. Our findings are in accordance with a previously published article by Jacques *et al*. who reported in an animal experimental study that PPV and SVV remained the reliable indices of fluid responsiveness in the presence of 30 mmHg of IAP, and threshold values discriminating Rs and NRs were higher than during normal IAP (*18*). Although, another experimental animal study by Renner *et al*. indicated that only PPV, and not SVV, was a sensitive and specific predictor of fluid responsiveness during increased IAP (*19*). These inconsistencies are likely due to the differences in the measurement methods used to calculate SVV. Renner *et al*. acquired SVV with a PiCCO system (Pulsion Medical Systems, Munich, Germany). This device needs a femoral artery and derives SV from pulse contour analysis of arterial femoral pressure. The measurement of SVV may be biased due to vascular constraint in the presence of IAH. Gruenewald *et al*. report that IAH affects the continuous CO and SV measurement base on pulse contour analysis with a PiCCO system, which is likely due to the elevated femoral arterial impedance (*20*). In the present study, SVV was measured using the Vigileo system by means of a radial artery catheter. SVV from pulse contour analysis of radial pressure may be more reliable than pulse contour analysis of femoral pressure, as arterial radial impedance should be not affected by IAH. Jacques *et al*. measured the SVV using an ultrasound transit-time flow probe around the aortic root (*18*). This measurement is less likely to be influenced by IAH. The strong correlations we found between PPV and SVV further reinforce the reliability of this SV measurement. Likewise, Jacques *et al*. also demonstrated that there was a significant correlation between PPV and SVV. In contrast to SVV and PPV, the preload variable of CVP failed to predict fluid responsiveness in the presence of IAH, as there was no correlation between baseline CVP and change in SV induced by fluid therapy. Our findings are consistent with most studies in which static preload variables do not predict fluid responsiveness (*5,6*).

The areas under the ROC curves show the ability of the hemodynamic parameters to discriminate

between Rs and NRs after fluid therapy. Our study shows that areas under the curves for PPV and SVV are statistically greater than for CVP, demonstrating the superiority of PPV and SVV over CVP as predictors of fluid responsiveness in the presence of IAH. In the supine position, we found a threshold value of 10.5% for PPV and of 10.5% for SVV to induce an SV increase of 10% or more. In the Trendelenburg position, we found a threshold value of 7.5% for PPV and of 7.0% for SVV to induce an SV increase of 10% or more. These threshold values in the Trendelenburg position were lower than those in the supine position, which may result from the effect of head-down tilting on cardiac preload. Russo *et al*. demonstrated that head-down positioning was capable of increasing the venous return, enlarging left ventricular end-diastolic volume, and elevating the SV in normal and elevated IAP (*21*). Hirvonen *et al*. demonstrated that the Trendelenburg position in awake and anesthetized patients increased pulmonary arterial pressures, CVP and pulmonary capillary wedge pressures, and these pressures further increased at the beginning of IAH (*22*). The elevated IAP influences the intrathoracic pressure by pushing the diaphragm upward, thus decreasing respiratory system compliance (*23*). Moreover, IAH during carbon dioxide-induced pneumoperitoneum decreases the venous return from the lower extremities, thus reducing the left ventricular end-diastolic volume and shortening cardiac preload (*24,25*). An experimental animal study indicated the threshold value for PPV dramatically increased from 11.5% to 20.5% after elevating IAP up to 25 mmHg (*19*). Thus, we postulate that threshold values may be gradually increased with the elevation of IAP. To our knowledge, the present study is the first patient-based clinical investigation devoted to clarifying the discriminating thresholds for PPV and SVV in the presence of IAH. Therefore, we did not compare the threshold values with the previously published investigations, nor did we measure the discriminating threshold values between Rs and NRs in the absence of IAH.

Some limitations of our study should be noted. Firstly, fluid therapy was performed at a moderate IAP of 12 mmHg, and therefore it remains unclear whether the higher grade of IAP influences the feasibility of PPV and SVV in predicting fluid responsiveness. Secondly, we did not perform hemodynamic measurement and fluid expansion before the IAP was applied. Consequently, the effect of IAP on the discriminating threshold values could not be clarified. Thirdly, the IAH was pre-operatively induced by increasing abdominal volume with carbon dioxide insufflation, which may be different from conditions that occur secondarily to abdominal compression in critically ill patients. Fourthly, the hemodynamic measurement was performed only with the FloTrac system. Future studies may include the use of thermodilution and echo techniques to further demonstrate the efficacy of hemodynamic indices. Thus, our results cannot be directly extrapolated to critically ill patients.

In conclusion, we demonstrate that PPV and SVV are sensitive and specific predictors of fluid responsiveness in patients with IAH. The Trendelenburg position does not alter their abilities to predict fluid responsiveness, although it reduces the discriminating threshold values for PPV and SVV between Rs and NRs of fluid therapy.

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