

## Original Article

# Pressure controlled ventilation on stroke volume variation as a predictor of fluid responsiveness in patients

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**Abstract:** Background: Stroke volume variation (SVV), a dynamic index, shows high sensitivity and specificity in predicting the fluid responsiveness of patients undergoing mechanical ventilation. Previous studies have shown that SVV-oriented fluid management performs positive effect in the perioperative maintenance of hemodynamic and better prognosis. It also could be used to predict the fluid responsiveness under one-lung ventilation with constant volume. The present study was aimed to determine the feasibility of stroke volume variation as a predictor for fluid responsiveness under pressure-controlled one-lung ventilation. Methods: Seventy patients were enrolled and divided into two groups with distinct ventilation pressures (20 cmH<sub>2</sub>O and 25 cmH<sub>2</sub>O). ROC curve analysis was performed to evaluate the capacity of SVV for prediction. Results: Sixty-three out of 70 patients completed the study. SVV showed weak correlation with dSVV and dSVI. The optimal threshold value of SVV to discriminate between responders and nonresponders was 9.5% (sensitivity 75.6% and specificity 54.5%). The optimal threshold value of SVV to discriminate between responders and non-responders remains to be 9.5% for both subgroups with 20 cmH<sub>2</sub>O and 25 cmH<sub>2</sub>O. Conclusion: SVV is a poor predictor of fluid responsiveness for patients undergoing pressure-controlled one-lung ventilation.

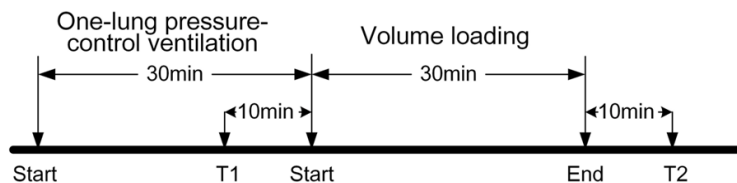
**Keywords:** Goal-oriented fluid management, stroke volume variation, pressure-controlled, one-lung ventilation, fluid responsiveness

## Introduction

The pattern of thoracic surgery has been experiencing a significant change in recent decades. Procedure of pneumonectomy is transforming from open surgery to video assisted thoracoscopic surgery and robot-assisted pneumonectomy. However, the progress on surgical techniques didn't effectively reduce the postoperative mortality, shorten the duration of hospital stays, or decrease the incidence of pulmonary complications [1, 2]. Certain factors have been proved to be associated with the pulmonary complications, among which the perioperative fluid administration is gaining more attentions [3, 4]. The goal-directed therapy is becoming an ideal strategy for fluid administration, due to the complexity of fluid resuscitation in thoracic surgeries.

FloTrac/Vigileo is a real-time, continuous hemodynamic monitoring system that uses arterial-waveform-based analysis. The formation of pulse pressure is proportional to the stroke volume. Combined this law with the analysis of artery waveform, FloTrac/Vigileo system is capable of calculating the stroke volume variation (SVV). SVV is a dynamic index for fluid status determination. Compared with other conventional parameters such as central venous pressure (CVP) and pulmonary arterial wedge pressure (PAWP) [5], SVV shows relatively high sensitivity and specificity, when applied in prediction of body's response to fluid under mechanical ventilation. SVV-guided fluid therapy has been demonstrated as a powerful approach in the perioperative maintaining of hemodynamics stability and improving prognosis in recent years [6]. Multiple studies have

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**Figure 1.** The time course of sample points T1 and T2. All patients were studied at 30 minutes after starting one-lung ventilation.

presented that SVV could be used as a sensitive index for prediction of double-lung infusion response under mechanical ventilation [7-12].

A study conducted by Suehiro and Okutani et al reported that SVV could be used to predict the infusion response with a constant one-lung ventilation volume of 8 mL/kg [13]. However, it is still unknown whether infusion response is predictable by SVV with constant pressure one-lung mechanical ventilation. In this study, we aim to figure out the feasibility of SVV to be used as an index to predict the fluid responsiveness in patients undergoing pressure-controlled one-lung ventilation.

### Methods

This study has been approved by the ethics committee in Xuanwu Hospital Capital Medical University. All the patients involved have signed the informed consents.

Seventy subjects (ASA I-II) scheduled to undergo thoroscopic lobectomy were recruited and randomly assigned to two groups (designated as group A and B, 35 subjects in each group). The ventilation pressures for group A and B are 20 cmH<sub>2</sub>O and 25 cmH<sub>2</sub>O, respectively. Subjects meeting one or more of the following conditions were excluded from the study:

Subjects with insufficiency in cardiac, renal or hepatic function; Obese subjects with body mass index (BMI) over 35; Subjects with valve disease or arrhythmia.

Subjects in two groups fasted routinely before operation. Peripheral venous were open and routine monitoring of HR, ECG, SpO<sub>2</sub> started shortly after patients entering the operation room. Radial artery cannulation (RAC) was performed under local anesthesia. SBP, DBP, MBP, CO, CI, SVI and SVV were measured using FloTrac/Vigileo system. The same model of

FloTrac/Vigileo system was applied throughout the study.

Anesthesia was induced with 0.2 mg/kg etomidate and 0.3 µg/kg sulfentanyl. Cis-atracurium was intravenously infused after the patient's loss of consciousness. Robertshaw double lumen tube (F39 for male, F37

for female) was placed by orotracheal intubation 2 min later and fixed appropriately after the confirmation of correct position by auscultation on both lungs. The pressure-controlled mode was adopted for mechanical ventilation. Pressure was set at 20 cmH<sub>2</sub>O for group A and 25 cmH<sub>2</sub>O for group B. For both groups, the inhaled oxygen concentration was 100% and the end-tidal CO<sub>2</sub> partial pressure was kept between 35 mmHg and 45 mmHg.

Anesthesia was maintained with 4-5 mg/kg/h propofol and 0.2-0.3 µg/kg/min remifentanyl. Depth of anesthesia was maintained at 40-60 using a BIS monitor. All patients were given 3 ml/kg of Ringer's solution intravenously during the induction of anesthesia, and then were maintained with 2 mL/kg/h of Ringer's solution. All the clinical observations were performed 30 min after the one-lung ventilation at lateral decubitus position. Baseline hemodynamics, including HR, MAP, CO, CI, SVI and SVV, were measured simultaneously after induction of anesthesia when CI became stable. After a period of 10 min of stable hemodynamics, volume loading was performed by the administration of 500 ml colloid solution (6% hydroxyethyl starch, MW 70,000) over 30 min. Hemodynamic variables including HR, BP, CO, CI, SVI, and SVV were measured before (T1, 10 minutes) and after (T2, 10 minutes) volume loading (**Figure 1**). No volume loading steps were performed if stable baseline hemodynamic variables were not achieved for 10 minutes. The measurements were obtained during stable periods. Patients were excluded from this study if continuous treatment with vascular active drug was needed. The FloTrac/Vigileo screen was turned away from the attending anesthesiologist; and an independent research staff recorded the FloTrac/Vigileo variables. Patients showing an increase in SVI of 15% or more after VE were defined as responders, whereas patients whose SVI increased by less than 15% were

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**Table 1.** Hemodynamic variables at Sample Points T1 and T2

	T1	T2	P value
HR (beats/min)	63.63±10.34	69.46±10.71	< 0.0001
MAP (mmHg)	83.14±11.90	96.19±13.42	< 0.0001
CI (L/min/m <sup>2</sup> )	2.54±0.62	3.30±0.85	< 0.0001
SVI (mL/m <sup>2</sup> )	40.35±9.56	47.86±10.94	< 0.0001
SVV (%)	8.70±1.96	5.75±1.38	< 0.0001
CO	4.52±1.20	5.90±1.64	< 0.0001
SBP	107.44±32.62	123.52±34.47	< 0.0001
DBP	61.38±18.01	69.33±20.85	< 0.0001

**Table 2.** Hemodynamic data at baseline (T1) in responders and nonresponders to volume expansion

	Responders to Volume Expansion (n = 22)	Nonresponders to Volume Expansion (n = 41)	P value
HR (beats/min)	65.57±10.85	62.55±10.03	0.2257
MAP (mmHg)	82.14±12.94	83.68±11.43	< 0.0001
CI (L/min/m <sup>2</sup> )	2.34±0.48	2.65±0.67	< 0.0001
SVI (mL/m <sup>2</sup> )	36.27±7.10	42.54±10.06	< 0.0001
SVV (%)	9.14±2.36	8.46±1.69	< 0.0001

classified as nonresponders. This cutoff value of 15% was chosen based on the findings from previous studies indicating that this difference is clinically significant for SVI and CO after VE [14, 15]. After all measurements of hemodynamic were done, the surgery was initiated.

A paired t-test was used to compare the hemodynamic variables in **Table 1** before and after volume loading. An un-paired t-test was used to compare the changes of hemodynamic variables for the responders in **Table 2**. The association between SVV and each of dSVV and dSVI is assessed using Pearson correlation and regression.

The descriptive statistics for the hemodynamic variables were shown as Mean ± SD. Receiver operating characteristic (ROC) curves were generated for SVV by varying the discriminating the threshold of the variable. A significance level of 0.05 was used. CRAN R software was used for statistical analysis.

### Results

Among all 70 recruited subjects, 63 of them completed this study (43 males and 20 fe-

males, 34 in group A and 29 in group B). Lobectomies were performed under thoracoscopy in the same way for all patients. Twenty-nine patients had left-sided operations and 34 had right-sided operations. BMI has a mean of 24.67 and SD of 3.23, with a maximum of 31.62.

All hemodynamic variables changed significantly after volume loading. Systolic and diastolic blood pressures were computed based on variable ABP in the raw data (see **Table 1**).

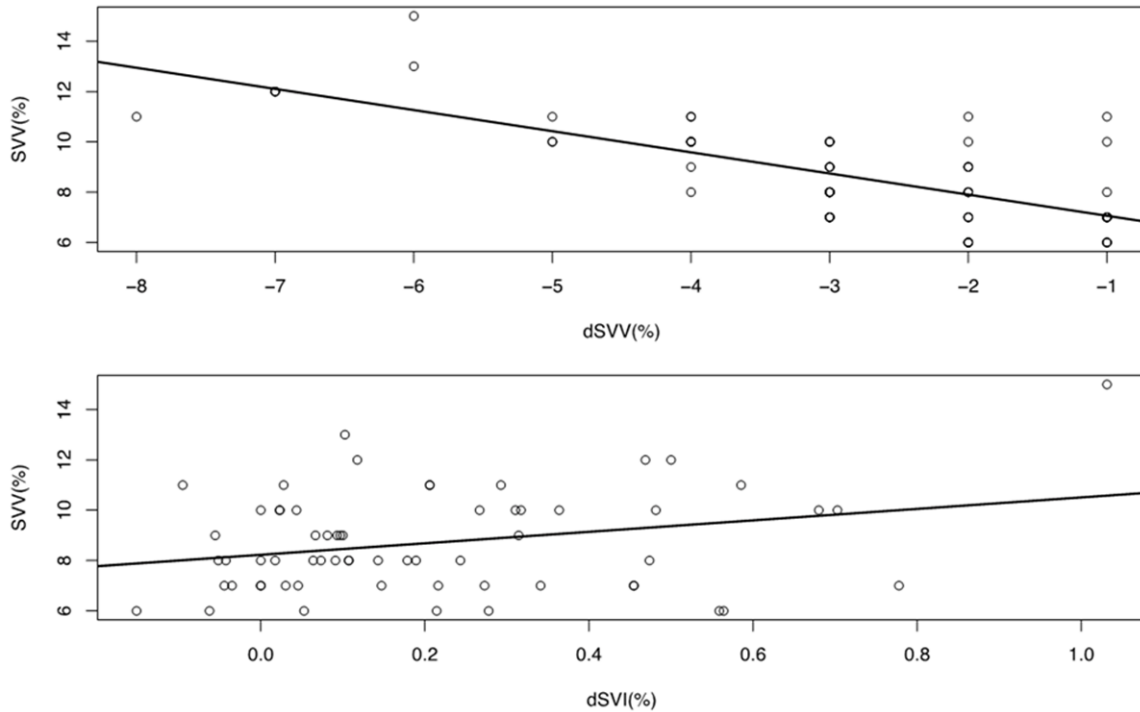
Among the 63 patients, 22 (35%) were responders to intravascular volume expansion and 41 (65%) were nonresponders. Their hemodynamic data at baseline (T1) are shown in **Table 2** (Column 2 and 3). We found that all hemodynamic variables except HR changed significantly for responders after volume loading (last column of **Table 1**).

SVV before volume loading was significantly correlated with dSVV and dSVI. The linear relation was moderate strong between SVV and dSVV, but not very strong between SVV and dSVI (**Figure 2**).

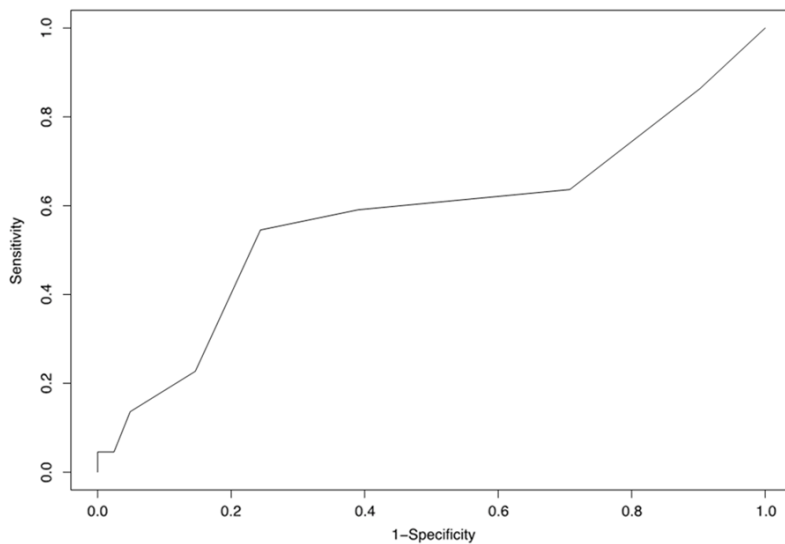
The overall performance for SVV in predicting the responsiveness of the stroke volume to intravascular volume expansion was evaluated by constructing ROC curves. The area under the ROC curve was 0.574 for SVV (95% confidence interval 0.41-0.737). The optimal threshold value of SVV to discriminate between responders and nonresponders was 9.5% (sensitivity 75.6% and specificity 54.5%, **Figure 3**).

Comparative analysis was conducted between the results of the two subgroups with airway pressure 20 cmH<sub>2</sub>O and 25 cmH<sub>2</sub>O. **Table 3** shows the mean and standard deviation of each of the hemodynamic variable for the two subgroups at T1 and T2, respectively. The differences between the two subgroups were compared using a t-test. Results showed that the mean values were not significantly different for all hemodynamic variables between the two groups at T1 and T2. In addition, we compared the differences between the two subgroups among the responders and the results showed that none of the differences was significant at level 0.05. In summary, no significant differ-

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**Figure 2.** Top panel: regression line  $SVV = 6.21 - 0.84 \text{ dSVV}$  with  $R\text{-squared} = 0.52$ , Pearson correlation coefficient =  $-0.722$  ( $p\text{-value} < 0.0001$ ). Bottom panel: regression line  $SVV = 8.23 + 2.28 \text{ dSVI}$  with  $R\text{-squared} = 0.078$ . Pearson correlation coefficient =  $0.28$  ( $p\text{-value} = 0.026$ ).



**Figure 3.** ROC curve for SVV in predicting the responsiveness of the stroke volume to intravascular volume expansion.

ence was found among all hemodynamic variables between the two groups with pressure 20 and 25, respectively.

The overall performance for SVV in predicting the responsiveness of the stroke volume to

intravascular volume expansion was evaluated by constructing ROC curves for the two subgroups, respectively (see **Figure 4**). The area under the ROC curve for the group with pressure 25 was 0.637, while the area for the other group was 0.507. The optimal threshold value of SVV to discriminate between responders and non-responders remained to be 9.5% for both subgroups.

### Discussion

The assessment of fluid responsiveness and volume status during perioperative period has been one of the major goals of invasive hemodynamic monitoring. Previous studies have shown the limitations of traditional fluid therapy monitoring method in hemodynamics [16, 17]. SVV is a sensitive index in fluid infusion response prediction and a dynamic

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**Table 3.** Hemodynamic variables at Sample Points T1 and T2 between the two subgroups (20 versus 25)

	Group-20 T1	Group-25 T1	Group-20 T2	Group-25 T2
HR (beats/min)	62.59±10.57	64.85±10.12	69.91±11.69	68.93±9.61
MAP (mmHg)	83.69±10.11	82.48±13.90	95.88±11.25	96.56±15.82
CI (L/min/m <sup>2</sup> )	2.61±0.68	2.45±0.54	3.34±0.82	3.26±0.89
SVI (mL/m <sup>2</sup> )	41.91±10.54	38.52±8.07	48.50±10.78	47.10±11.26
SVV (%)	8.68±2.10	8.72±1.81	5.76±1.42	5.72±1.36

index in patient's volume determination. It is a hotspot for clinical practice that whether SVV measurement would be influenced by the change of venous return, pre load and pot load of heart, in the condition of thoracic operation. FloTrac/Vigileo system is one of the minimally invasive methods of monitoring for clinical application. The Vigileo/FloTrac system allows for automatic and continuous monitoring of SVV, which is easy to evaluate and may indicate fluid responsiveness during mechanical ventilation. Positive-pressure ventilation induces cyclic changes in left ventricular stroke volume that are related mainly to the expiratory decrease in left ventricular preload because of the inspiratory decrease in right ventricular filling and ejection. SVV obtained with the Vigileo/FloTrac system has shown good correlation for predicting fluid responsiveness in patients under VCV during major surgery [5, 14, 15].

One-lung ventilation is required in thoracic surgery, due to the demand of surgical vision field and operation. Routine ventilation could be divided into volume-controlled and pressure-controlled. Volume-controlled ventilation ensures the delivery of a defined tidal volume and uses a square waveform flow delivery method that produces high peak airway pressures in low-compliance states. On the other hand, pressure-controlled ventilation (PCV) uses a decelerating inspiratory flow delivery method, which has been known to reduce the peak airway pressure and allows a more homogeneous gas distribution [18].

The capability of SVV to predict fluid responsiveness in patients undergoing OLV has been evaluated [15]. The ventilation in these studies was volume controlled, with tidal volume over 8 ml/kg. This setting may cause excessive peak pressure in one-lung ventilation. Previous studies showed that ventilation with airway pres-

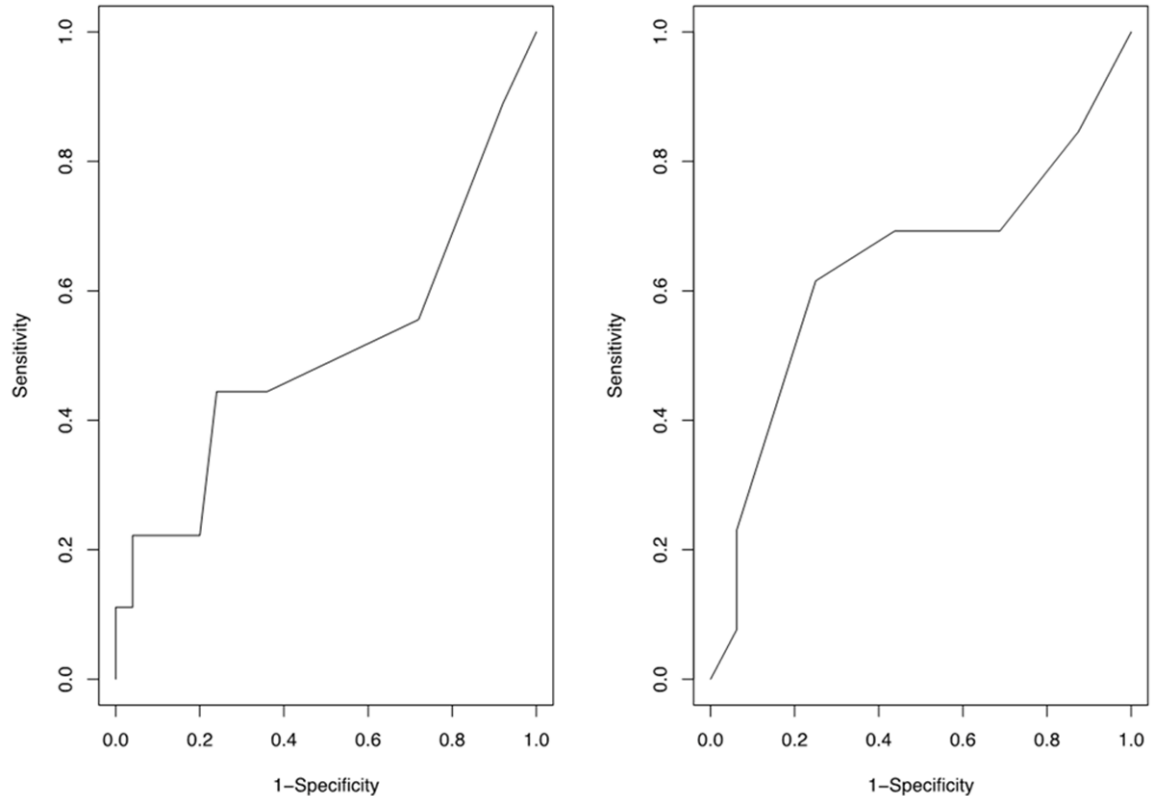
sure higher than 30 cmH<sub>2</sub>O could increase the risk of pulmonary barotrauma, stimulate the release of inflammatory factors, aggravated lung injury and result in the postoperative lung complications [18, 19]. The application of pressure-controlled ventilation can help to lower peak airway

pressure, thus to decrease the risk of following ventilator-associated lung injuries [20, 21]. Pressure controlled mechanical ventilation was adopted in the present study to explore whether SVV could be used to predict the fluid responsiveness. Considering the difference in patients' lung compliances, two airway pressures, 20 cmH<sub>2</sub>O and 25 cmH<sub>2</sub>O, were applied in this study. The results of the present study suggest that SVV before volume loading was significantly correlated with dSVV and dSVI. The linear relation was moderately strong between SVV and dSVV, but not very strong between SVV and dSVI.

The authors evaluated the overall performance of SVV in predicting the responsiveness of the stroke volume to intravascular volume expansion. Results showed that the area under the ROC curve was 0.574 for SVV (95% CI 0.41-0.737), the optimal threshold value of SVV to discriminate between responders and non-responders was 9.5% (sensitivity 75.6% and specificity 54.5%). SVV is not very good in predicting the fluid infusion response under one-lung ventilation with constant pressure. We also performed the ROC curve analysis with varied ventilation pressure. Results showed that SVV is better in predicting the responsiveness of the stroke volume to intravascular volume expansion in the group with airway pressure 25 cmH<sub>2</sub>O than that in the other group (with airway pressure 20 cmH<sub>2</sub>O). The area under the ROC curve for the group with pressure 25 is 0.637, while the area for the other group is 0.507. Overall speaking, SVV is poor in predicting the responsiveness of the stroke volume to intravascular volume expansion among the patients with airway pressure 20 and 25, respectively, and altogether.

One limitation of the study was that SVI obtained by the Vigileo/FloTrac system was used to determine the responders and the non-

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**Figure 4.** The overall performance for SVV in predicting the responsiveness of the stroke volume to intravascular volume expansion. Left panel: pressure = 20; Right panel: pressure = 25.

responders to volume expansion. The earlier validation studies of the FloTrac/Vigileo system have demonstrated conflicting results [22, 23]. However, with the updated software, the recent clinical studies have demonstrated promising results [24]. Jo et al demonstrated that the CO measured by the FloTrac/Vigileo system was reliable even in patients with a decreased ejection fraction of LV and in a low cardiac output status during off-pump coronary bypass surgery [25].

Another limitation of this study was that other variables of fluid responsiveness, such as CVP, PCWP, and transthoracic echocardiography-derived assessment, were not measured simultaneously with SVV. The SVV value has to be considered after a period of hemodynamic stability in order to avoid misleading values that may have been induced by any acute change in HR or MAP. It is important to observe a steady hemodynamic state before accepting the SVV value [5].

The thresholds of SVV to predict fluid responsiveness under two pressures are both 9.5%,

but with poor sensitivity. This is likely due to the diversity in the patients' thorax size. The fixed airway pressure may have different impacts on the filling of thoracic great vessels and left ventricle, lead to the poor correlation between dSVI and SVV, before and after the infusion. Thus SVV is not an effective predictor for fluid responsiveness, in the condition of constant ventilation pressure. Pressure Control Ventilation-Volume Guarantee (PCV-VG), another approach for mechanical ventilation, is more intelligent and accord with human physiology. Under the precondition of ensuring appropriate tidal volume, ventilator feeds back the PIP for the following ventilation to decrease the ventilation pressure as much as possible, by automatic and continuous evaluation of association between lung compliance, ventilation volume and pressure. The further trial could be conducted with PCV-VG, to test whether SVV is a good predictor for fluid responsiveness.

SVV is a poor predictor of fluid responsiveness for patients undergoing pressure-controlled one-lung ventilation.

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### Disclosure of conflict of interest

None.

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