

# Stroke volume variation fail to predict fluid responsiveness in patients undergoing pulmonary lobectomy with one-lung ventilation using thoracotomy

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**Summary** The purpose of this study was to investigate the ability of stroke volume variation (SVV) to predict fluid responsiveness in patients undergoing pulmonary lobectomy with one-lung ventilation (OLV). Thirty patients intubated with double-lumen tube were scheduled for a pulmonary lobectomy requiring OLV for at least 1 hour under general anesthesia. Hemodynamic variables including heart rate, mean arterial pressure, cardiac index (CI), stroke volume index (SVI), central venous pressure (CVP) and SVV were measured before and after volume expansion (VE) (8 mL/kg of 6% hydroxyethyl starch). Fluid responsiveness was defined as an increase in CI  $\geq 10\%$  after VE. Of the 30 patients, 16 (53%) were responders and 14 (47%) were nonresponders to intravascular VE. There were significant increases of CI, SVI in responders after VE ( $p < 0.01$ ), but there were no significant changes in SVV in responders and nonresponders ( $p > 0.05$ ). The baseline value of SVV, CVP, CI and SVI did not correlate significantly with  $\Delta$ CI ( $p > 0.05$ ). The area under the Receiver Operating Characteristic (ROC) curve were 0.507 for SVV (95% confidence interval, 0.294-0.720) and 0.556 for CVP (95% confidence interval, 0.339-0.773), neither was able to predict fluid responsiveness with sufficient statistical power. SVV measured by the Vigileo-FloTrac system was not able to predict fluid responsiveness in patients undergoing pulmonary lobectomy with OLV after thoractomy.

**Keywords:** Stroke volume variation, open-chest condition, fluid responsiveness, thoracotomy

## 1. Introduction

Lung-isolation techniques are primarily designed to facilitate One-Lung Ventilation (OLV) in patients undergoing thoracic, cardiac, mediastinal or esophageal procedures involving the chest cavity. It is essential to maintain optimal organ perfusion by appropriate fluid infusion to achieve the balance between preventing fluid overload and optimizing organ perfusion (1). Preload assessment is crucial to guide fluid therapy during thoracic surgery procedures. However, determining left ventricular preload in the clinical routine is particularly difficult during surgery. Filling pressures like central

venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) are normally used as parameters of right and left heart preload. But these static indicators have been shown to be poor predictors of fluid responsiveness (2).

A recent Vigileo/FloTrac system (Edwards Lifescience, LLC, Irvine, CA, USA) allows for continuous monitoring of the cardiac output (CO) based on pulse contour analysis and of the respiratory variations in stroke volume (SV) based on the analysis of the systemic arterial pressure wave. Stroke volume variation (SVV) is a parameter derived from changes in SV that is dependent on mechanical ventilation and has been found useful for predicting volume response in mechanically ventilated patients during perioperative phase (3,4). Only one study reported that SVV could predict fluid during OLV with PEEP in patients undergoing thoracoscopic lobectomy by using Vigileo system (5). However, all lobectomies in this study were performed under thoracoscopy in the same way. Since SVV during

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OLV could be affected by the surgical procedure, it is still unknown whether SVV could predict fluid responsiveness during OLV with the chest open via a thoracotomy. The aim of this study was to examine the suitability of the established parameter of CVP and especially the new parameter of SVV to predict changes in cardiac index (CI) in patients undergoing pulmonary lobectomy with OLV after thoracotomy.

## 2. Materials and Methods

### 2.1. Patients characteristics

This prospective study was approved by institutional review board of General Hospital of PLA. All patients gave informed consent. From October 2009 to July 2011, a total of 33 patients received a pulmonary lobectomy with OLV and intraoperative infusion with colloids under general anesthesia. All patients were diagnosed with lung cancer preoperatively by computerized tomography (CT) and/or magnetic resonance imaging (MRI). Exclusion criteria applied to patients younger than 18 yr, with fibrillation atrial or intracardiac shunt.

### 2.2. Anesthesia and one-lung ventilation

After the patient arrived in the operating room, routine monitoring including pulse oxymetry, three-lead electrocardiogram and non-invasive arterial pressure was applied. Anesthesia was induced with *i.v.* bolus administration of fentanyl (3-5 µg/kg), and propofol (1.5-2 mg/kg) 2 min later. Following loss of consciousness, orotracheal intubation was facilitated with rocuronium (0.6-0.9 mg/kg). After anesthesia induction, a double-lumen endo-bronchial tube (Tyco Healthcare, Argyle, Mansfield, MA, USA) was inserted and the position was confirmed by fiberoptic bronchoscopy, the airway pressure was kept at 25-35 cm H<sub>2</sub>O. With the proper position of securing the airway, a radial arterial catheter (REFRA-04220, Arrow international Inc., Reading, PA, USA) was inserted and a central venous catheter (ES-04301, Arrow international Inc., Reading, PA, USA) was placed through right internal jugular vein. All pressure transducers were zeroed at midaxillary line to ambient pressure and initial pressures were recorded with the patient in the supine position. After changing the patient's position to lateral decubitus, all pressure transducers were re-positioned at the same value of initially measured pressures in the supine position. Anaesthesia was maintained with target controlled infusion (TCI) of propofol (2-4 µg/mL) and continuous infusion of remifentanyl (0.3-0.8 µg/kg/min) with bispectral index (BIS, Aspect 1000™, Aspect Medical Systems Inc., Natick, MA, USA) kept between 40 and 50. Following the initiation of OLV, patients were ventilated with a tidal volume of 8 mL/kg ideal body weight, a ventilation rate

of 12 cycle/min, inspired oxygen fraction (FIO<sub>2</sub>) was 1.0 and no PEEP was applied.

### 2.3. Hemodynamic monitoring

A dedicated transducer (FloTrac™, Edwards Lifesciences, LLC, Irvine, CA, USA) was connected to the radial arterial line on one side and to the Vigileo System (Vigileo™ Edwards Lifesciences, LLC, Irvine, CA, USA) on the other side. The system enables the continuous monitoring of SV, stroke volume index (SVI), CO, CI and SVV without calibration. The Vigileo (Software version 1.14) analyses the pressure waveform 100 times per second (100 Hz), and performs its calculations on the most recent 20 s data. CI obtained with this device was recorded and used to discriminate responder and non-responder patients after VE. SVV is calculated as the variation of beat-to-beat SV from the mean value during the most recent 20 s data and is displayed continuously. At each step of the study protocol, the following were recorded simultaneously: heart rate (HR), systolic arterial pressure, mean arterial pressure (MAP), diastolic arterial pressure and end-expiratory central venous pressure (CVP).

### 2.4. Study protocol

This study assessed the capability of SVV to predict fluid responsiveness during OLV. The study was started after finishing chest opening (thoracotomy) and collapsing one lung completely. During OLV, values of HR, MAP, CVP, SV/SVI, CO/CI and SVV were measured before (T<sub>0</sub>) and 30 min (T<sub>1</sub>) after fluid loading. Intraoperative infusion with 8 mL/kg of 6% hydroxyethyl starch was started when deemed necessary by the attending anesthesiologists, and completed in 30 min. Hemodynamic measurements were performed before, and within 30s after volume expansion (VE) without stimulation. All patients were studied at 30 min after starting OLV. During the VE, ventilator settings were kept consistent. If obvious hemorrhage (volume > 100 mL) or arrhythmias happened, the infusion protocol would be terminated and patient would be treated accordingly.

### 2.5. Statistical analysis

All data are presented as mean ± S.D. Distribution normality was assessed using Kolmogorov-Smirnov test. Changes in haemodynamic measures induced by VE were assessed using one-way analysis of variance (ANOVA). Patients were divided into two groups according to the percent increase in CI after intravascular VE. Responders were defined as patients demonstrating an increase in CI ≥ 10% after intravascular VE and non-responders as patients whose CI changed < 10%. Receiver operating characteristic

**Table 2. Anti-HBV response of TCM and related active compounds in clinical trials**

Items	Baseline	Volume expansion	<i>p1</i>	Baseline	<i>p2</i>	Volume expansion	<i>p3</i>
HR (beat/min)	71.2 ± 10.3	68.4 ± 11.9	0.760	71.9 ± 10.9	0.620	69.7 ± 9.5	0.120
MAP (mmHg)	72.8 ± 10.6	78.6 ± 8.2	0.661	77.7 ± 12.1	0.073	84.8 ± 11.9	0.514
CI (l/min/m <sup>2</sup> )	2.9 ± 1.0	3.1 ± 1.1	0.649	2.7 ± 0.6	0.063	3.5 ± 0.7	0.001
CVP (mmHg)	6.89 ± 2.23	8.26 ± 3.02	0.065	6.95 ± 2.45	0.124	8.34 ± 3.14	0.087
SVI (mL/m <sup>2</sup> )	41.3 ± 13.6	44.7 ± 16.7	0.705	39.9 ± 15.2	0.291	51.6 ± 15.8	0.003
SVV(%)	8.6 ± 2.8	7.1 ± 2.1	0.260	8.4 ± 3.1	0.095	6.9 ± 2.4	0.083

Values are mean ± S.D. HR, heart rate; MAP, mean arterial pressure; CI, cardiac output index; CVP, central venous pressure; SVI, stroke volume index; SVV, stroke volume variation. *p1*, volume expansion value vs. baseline value in non-responders; *p2*, baseline value in responders vs. baseline value in non-responders; *p3*, volume expansion value vs. baseline value in responders.

(ROC) curves were generated for SVV, SVI, CI, CVP and MAP. The areas under the ROC curves by varying the discriminating threshold for each parameter were calculated and compared according to the method described by Hanley and McNeil (6). Threshold value for each parameter was determined by considering values that yielded the greatest sensitivity and specificity. Pearson's test was used to test correlation. A *p*-value less than 0.05 was considered as statistically significant. All statistic analysis was performed using SPSS 15.0 software (SPSS Inc, Chicago, IL, USA).

### 3. Results

#### 3.1. Patients selection

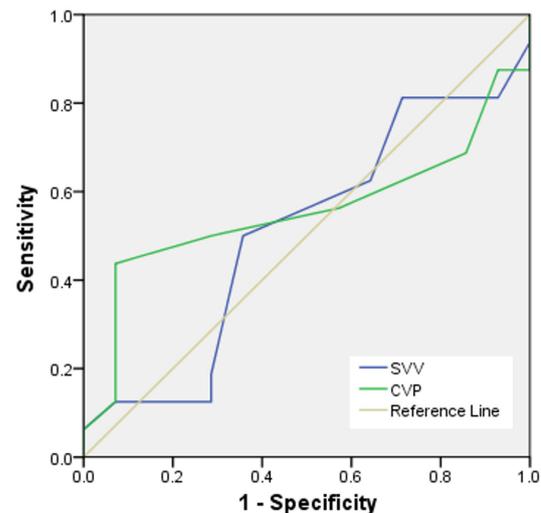
Thirty-three patients were initially included. Among them, three patients were excluded from analysis because of arrhythmia (two patients; one had ventricular premature contraction, one had atrial fibrillation) or obvious hemorrhage (one patient; bleeding > 100 mL during volume loads) during the protocol. Thirty patients in this study consisted of 21 males and 9 females from 47 to 58-year-old (mean age, 52.4 ± 4.7 year). There was no case requiring the administration of vasoactive agents during volume loading, BP and HR were kept in normal range.

#### 3.2. Changes in hemodynamic variables after volume expansion

Hemodynamic measurements in the responders and nonresponders at baseline and after VE are given in Table 1. After VE, no significant changes were found in the nonresponders, while in the responders, there were significant changes of CI (from 2.7 ± 0.6 to 3.5 ± 0.7 l/min/m<sup>2</sup>; *p* = 0.001), SVI (39.9 ± 15.2 to 51.6 ± 15.8 mL/m<sup>2</sup>; *p* = 0.008). At the same time we observed no significant changes in both SVV and CVP in responders. Before VE, there was no difference in CI, SVI, CVP, MAP and SVV at baseline (Table 1).

#### 3.3. Fluid responsiveness to fluid therapy

There were no significant correlations between baseline



**Figure 1. ROC curve compared the SVV and CVP in the abilities to discriminate the responders and the non-responders.** Patients were classified as the responders to fluid loading, when increases in cardiac index (CI) were at least 10%. ROC analysis showed that both SVV and CVP failed to predict fluid responsiveness in patients undergoing pulmonary lobectomy with OLV. Diagonal segments are produced by ties.

values of CVP, MAP, SVI, CI and the percent change in CI after fluid expansion ( $r = -0.213$ ,  $p = 0.114$ ;  $r = 0.011$ ,  $p = 0.954$ ;  $r = -0.202$ ,  $p = 0.294$ ;  $r = -0.123$ ,  $p = 0.517$ , respectively). And the baseline value of SVV also did not correlate significantly with the change in CI induced by fluid expansion ( $r = -0.171$ ,  $p = 0.367$ ).

#### 3.4. Dynamic indices and static indices to predict fluid responsiveness

The overall performance for SVV and CVP in predicting the responsiveness of the stroke volume to intravascular VE was evaluated by constructing ROC curves (Figure 1). The area under the ROC curve was 0.507 for SVV (95% confidence interval, 0.294-0.720), the area under the ROC curve was 0.556 for CVP (95% confidence interval, 0.339-0.773). The ROC analysis showed that both SVV and CVP failed to predict fluid responsiveness with sufficient statistical power in patients undergoing pulmonary lobectomy with OLV. There was no significant difference in the area under ROC curves between SVV and CVP.

#### 4. Discussion

OLV is necessary in a variety of thoracic surgery to collapse one lung for surgical procedure. Several studies have demonstrated that SVV could predict fluid responsiveness in two-lung mechanically ventilated patients, and more efficiently than CI, CVP, MAP, which is in accordance with increasing evidence that static preload indicators are not suited for functional hemodynamic monitoring (3,4,7). Only one study evaluated the ability of SVV to predict fluid responsiveness in patients undergoing OLV, and they found that SVV measured by the Vigileo-FloTrac system was able to predict fluid responsiveness in patients undergoing surgery with OLV with acceptable levels of sensitivity and specificity. Of note, all surgeries were performed under thoracoscopy in the same way (5). With the chest opening via thoracotomy, whether SVV derived from Vigileo-FloTrac system could predict fluid responsiveness in patients with OLV is still unknown. In the present study, we found that SVV measured by the Vigileo-FloTrac system was not able to predict fluid responsiveness in patients undergoing pulmonary lobectomy with OLV after thoracotomy.

Several studies have found that the dynamic volume responsive measurements like SVV and pulse pressure variation (PPV) obtained with PiCCO system may be more suitable for monitoring the volume status of patients particularly under open-heart conditions during cardiac surgery and especially after sternotomy (8,9). Conversely, the others found that SVV and PPV were unable to predict fluid responsiveness in open chest condition (10,11). It has been shown that opening the chest via a sternotomy may result in an increase in CI and a decrease in SVV (9,10). The ventilated lung is actually not open to the atmosphere because its pleura are still intact and the mediastinum separates lungs from the atmosphere after sternotomy. But with the chest opening by thoracotomy, much of the pressure generated by the ventilator would not be transmitted to the pulmonary vessels but rather to the atmosphere (5). So SVV could not be predictive of fluid responsiveness in open-chest condition after thoracotomy.

Positive intrathoracic pressure following mechanical ventilation induces a reduction in left ventricular preload. This is reflected by variations in the SV. These variations during a defined interval have proven to be useful parameters of cardiac preload (12). But the ventilatory issues, such as tidal volume (13), positive end-expiratory pressure (14), and chest and lung compliance (15) may also have effects on SVV. SVV could predict fluid responsiveness in patients undergoing thoracoscopic lobectomy during OLV only when tidal volume is at least 8 mL/kg (13) and with PEEP (14). Another study showed that PPV could predict fluid responsiveness in patients who received

protective OLV with tidal volume of 6 mL/kg,  $\text{FIO}_2$  of 0.5 and positive end-expiratory pressure (PEEP) of 5 cm  $\text{H}_2\text{O}$  for lung surgery using thoracotomy, but not in patients who received conventional OLV with tidal volume of 10 mL/kg,  $\text{FIO}_2$  of 1.0 and no PEEP (16). In this study, OLV was started with a tidal volume of 8 mL/kg,  $\text{FIO}_2$  of 1.0 and no PEEP was applied. But during OLV, if the same tidal volume is applied, the ventilated lung is exposed to double the tidal volume of two-lung ventilation. This could increase right ventricular afterload and exaggerate the cyclic variation in stroke volume (17). In addition, the venous return could be influenced by the mechanical ventilation under chest opening due to the decrease in chest compliance and airway pressure. Previous studies have showed that SVV could predict fluid responsiveness in patients undergoing OLV only when tidal volume is at least 8 mL/kg (13), so in this study tidal volume was set as 8 mL/kg, which had been used previously in two-lung ventilation (3,4) or one-lung ventilation (13).

Mechanical ventilation method, hypoxic pulmonary vasoconstriction in the non-ventilated lung and significant pulmonary arteriovenous shunt amount through the non-ventilated lung can influence the predictive value of SVV for fluid responsiveness, regardless of the patient's preload state. Due to pulmonary vascular resistance increase induced by hypoxic pulmonary vasoconstriction in non-ventilated lung, the blood flowed to the ventilated-side lung (18). During OLV, there is a 20-30% shunt through the non-ventilated lung even with optimal management. This shunt amount does not contribute to the generation of SVV because there is no cyclic change of intra-thoracic pressure in the non-ventilated lung (19). The results showed that SVV before the fluid challenge in both responders and nonresponders was fairly normal, we speculated that SVV was mainly associated with pulmonary flow distribution, did not correlate positively with tidal volume. The results of our study indicate that SVV failed to predict fluid responsiveness in patients undergoing pulmonary lobectomy with OLV after thoracotomy.

Some limitations of our study should be noted. Firstly, we measured CO with Vigileo-FloTrac system, but not a calibrated thermodilution CO monitor. Although thermodilution is considered as the clinical standard method to measure CO, but CO measured by Vigileo-FloTrac system correlated well with that measured by thermodilution. And due to the cost-effect, we did not prefer a calibrated thermodilution CO monitor or transesophagus echocardiograph. Secondly, we did not estimate shunt fraction, so could not draw a conclusion whether the less shunt fraction contributes to the bigger SVV that can predict fluid responsiveness. Thirdly, we could have compared two different ventilation strategies (*i.e.* lung-protective and conventional) to investigate SVV as a predictor of fluid

responsiveness during one-lung ventilation for lung surgery using thoracotomy, whether a clinically more relevant lung protective ventilation strategy would have yielded different results.

In conclusion, we evaluated the capability of SVV in predicting fluid responsiveness in patients receiving OLV. It was found that SVV measured by the Vigileo-FloTrac system was not able to predict fluid responsiveness in patients undergoing pulmonary lobectomy with OLV after thoracotomy.

### Acknowledgements

Dr. Qiang Fu was supported by a Japan-China Sasagawa medical research fellowship. Thanks to Dr. Junko Kouhei and Prof. Makoto Ozaki (Tokyo Women's Medical University) for their kind guidance and help.

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(Received November 5, 2013; Revised January 19, 2014; Accepted February 6, 2014)