



Accuracy of stroke volume variation and pulse pressure variation in predicting fluid responsiveness undergoing one-lung ventilation during thoracic surgery: a systematic review and meta-analysis

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Background: Stroke volume variation (SVV) and pulse pressure variation (PPV) are based on the interaction between the heart and lungs during mechanical ventilation. However, debate continues as to whether SVV and PPV can accurately predict fluid responsiveness during the one-lung ventilation (OLV). We therefore undertook a systematic review and meta-analysis of clinical trials that investigated the diagnostic value of SVV and PPV in predicting fluid responsiveness undergoing OLV during thoracic surgery.

Methods: The MEDLINE, EMBASE, WANFANG, and CENTRAL databases were systematically searched for studies on the use of SVV and/or PPV in patients undergoing OLV from 2010 to 2021. Heterogeneity was assessed using I^2 statistics. The funnel diagram analysis was used to test publication bias. A fixed-effects model was used to calculate the pooled values of sensitivity, specificity, the diagnostic odds ratio (DOR), and the relevant 95% confidence intervals (95% CIs). The summary receiver operating characteristic (SROC) curves were estimated, and the areas under the SROC curve were calculated.

Results: In total nine studies, comprising 452 patients were ultimately included in this meta-analysis, including 217 (48%) responders and 235 (52%) nonresponders. After combining the correlation coefficients, a slight heterogeneity was found between SVV and PPV in these selected studies ($I^2_{SVV} = 19.7\%$, $I^2_{PPV} = 15.3\%$), and the funnel diagram also showed that the P values of SVV and PPV were 0.33 and 0.26. After the pooled analysis, the respective sensitivity of SVV and PPV in predicting fluid responsiveness was 0.66 and 0.61, the specificity was 0.62 and 0.53, the positive likelihood ratios were 1.7 and 1.3, the negative likelihood ratios were 0.55 and 0.74, and the DORs were 3 and 2. The areas under the SROC curve of SVV and PPV were 0.68 and 0.60, respectively, according to STATA SE16 software, and the combined areas under the receiver operating characteristic (ROC) curve of SVV and PPV were 0.681 and 0.604, respectively, according to MedCalc19.0.4 software.

Conclusions: Current evidence suggests that SVV and PPV are not suitable for guiding intraoperative fluid therapy due to their poor ability to predict fluid responsiveness in patients undergoing OLV, and we need a better indicator instead.

Keywords: Stroke volume variation (SVV); pulse pressure variation (PPV); one-lung ventilation (OLV); fluid therapy; meta-analysis

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Introduction

Goal-directed hemodynamic therapy (GDHT) can affect the prognosis of critical and major surgery patients (1). The real-time and accurate monitoring of stroke volume variation (SVV) and pulse pressure variation (PPV) during anesthesia play an important role in clinical decision making. The FloTrac-Vigileo system is a minimally invasive hemodynamic monitoring method based on arterial pressure waveform analysis, which has many advantages, including that it is sensitive, convenient, and can be applied in real-time (2,3). SVV and PPV are based on the interaction between the heart and lungs under mechanical ventilation, and periodic changes in stroke volume (SV) and pulse pressure (PP) are caused by different changes in lung volume in the inspiratory phase and expiratory phase (4). However, the one-lung ventilation (OLV) condition alters the basic assumption of the SVV and PPV physiological rationale. The receiver operating characteristic (ROC) curve is usually to judge the accuracy, which is considered that the parameter is accurate if the area under the curve (AUC) is greater than 0.7. Fu *et al.* reported that both

SVV had a poor ability (the AUC is 0.57) to predict fluid responsiveness during OLV (5). Conversely, Suehiro *et al.* did not find significant changes of SVV after OLV (the AUC is 0.90) and proved that both SVV and PPV have a good ability to predict fluid responsiveness during OLV (6). The debate continues as to whether SVV and PPV can accurately predict fluid responsiveness in patients during OLV. To our knowledge, one systematic review was carried out 5 years ago that investigated the diagnostic accuracy of SVV and PPV during cardiac and thoracic surgery (3). However, they did not discuss the impact of OLV on SVV and PPV, nor did they use meta-analysis to combine the parameters in the literature. More recently, many additional new studies have been published, and the body of evidence requires updating. Thus, we retrieved the relevant studies on the accuracy of SVV and PPV in OLV and performed a systematic review and meta-analysis in an attempt to reach a conclusion on this issue. We present the following article in accordance with the PRISMA-DTA reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-6030/rc>).

Methods

This study was registered on PROSPERO (registration No. CRD 42022343057).

Data sources and searching strategy

We followed the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) guidelines on conducting meta-analyses of observational cohort studies (7). We retrieved the full texts of the relevant studies, published from 2010 to 2021, from the MEDLINE, EMBASE, WANFANG, and CENTRAL databases, and we conducted our last search on July 4, 2022. The keywords included SVV, PPV, fluid therapy, fluid responsiveness, OLV, and thoracic surgery. There was no language restriction in this search. All the references of the relevant studies were also read and reviewed to identify any additional relevant studies for inclusion in the final analysis.

Highlight box

Key findings

- SVV and PPV are not suitable for guiding intraoperative fluid therapy due to their poor ability to predict fluid responsiveness in patients undergoing OLV.

What is known and what is new?

- Dynamic preload variables, such as SVV and PPV, are based on heart-lung interactions for guiding volume administration in mechanically ventilated patients. However, the debate continues as to whether SVV and PPV can accurately predict fluid responsiveness in patients undergoing OLV during thoracic surgery;
- This study retrieved the relevant studies on the accuracy of SVV and PPV in OLV and performed a systematic review and meta-analysis in an attempt to reach a conclusion on this issue.

What is the implication, and what should change now?

- In the future, a multicenter and large sample research needs to be conducted and analyzed.

Study selection and inclusion criteria

The study selection process was independently performed by 2 reviewers. The selection of studies was conducted systematically based on the prespecified PICOS (participants, interventions, comparisons, outcome, and study design) eligibility criteria: (I) participants: mechanically ventilated adult patients (≥ 18 years) with OLV during thoracic surgery; (II) interventions: fluid responsiveness test after OLV; (III) comparisons: parameters of patients who were responsive and non-responsive to fluid challenge; (IV) outcomes: AUCs and the threshold values of SVV and PPV; (V) study design: randomized clinical trials. Quality assessment was performed for each included study according to the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) document.

Studies conducted with patients with arrhythmia or spontaneous breathing were excluded, as were studies with patients who did not undergo OLV, animal experiment articles, reviews, and editorials.

Statistical analysis

The qualities of the selected studies on SVV and PPV were evaluated based on the QUADAS-2 tool before the analysis, which consists of 4 key domains (i.e., patient selection, the index test, the reference standard, and the flow of patients through the study), and the timing of the index test(s) and reference standard (8). We used Stata SE16 and MedCalc 19.0.4 for the meta-analysis. Heterogeneity was assessed using I^2 statistics. The I^2 results were divided using the boundary values of 25%, 50% and 75%, which represented low, medium and high heterogeneity, respectively (9). The criteria for determining heterogeneity in the tunnel diagram analysis were symmetry and a P value < 0.05 . Next, the pooled sensitivity, specificity, positive likelihood ratios, negative likelihood ratios, diagnostic odds ratios (DORs), and relevant 95% confidence intervals (95% CIs) were obtained. The effect sizes were converted into standard normal metrics, and a weighted average of these transformed scores was then calculated. The AUC greater than 0.7 was considered to have high accuracy. The AUC was pooled by a weighted average of areas from individual studies, and they were combined using MedCalc 19.0.4 based on the weighted average of each study (10). The combined sensitivity, specificity and the summary ROC (SROC) curve were calculated by StataSE16, and the accuracy of the SVV and PPV was comprehensively determined by the area under the

combined SROC curves (11,12).

Results

Search results and study characteristics

A total of 47 studies were identified after an initial search. After repeated screening, and the exclusion of articles that related to animal experiments, did not use OLV during the operation, did not have the full text available, did not use the fluid infusion test, or did not include a ROC curve analysis of the OLV, 9 eligible articles were ultimately included in the meta-analysis (5,6,13-19) (*Figure 1*).

The nine studies included a total of 452 patients, including 217 (48%) responders and 235 (52%) nonresponders to intravascular volume expansion. The operations included the radical resection of esophageal cancer and lobectomy/the segmental resection of the lung, and the methods of lung surgery included thoracotomy and thoracoscopy. The methods of OLV included double-lumen endotracheal intubation and single-lumen endotracheal intubation combined with a bronchial occlude. The tidal volume of the patients during OLV was 6–8 mL/kg, and the positive end expiratory pressure (PEEP) was 0–5 cmH_2O , except for one study, in which the tidal volume was 10 mL/kg (15). SV, cardiac output (CO), cardiac index (CI) and SVV were monitored by the FloTrac-Vigileo system monitor (Edwards Lifesciences, Irvine, CA, USA). PPV was monitored by the Philips IntelliVue MP70 or MP50 system (Phillips, Suresnes, France). However, in one study, a hemodynamic esophageal Doppler probe (Arrow International, Everett, Washington, USA) was used to monitor SV, CO, CI, and Adobe Photoshop CS2 (Adobe Systems Inc., San Jose, CA, USA) Software was used to calculate PPV (16). Among the nine selected studies, the accuracy of SVV was counted in eight studies (5-6,13,15-19), and the accuracy of PPV was counted in five studies (13,14,16-18). Hydroxyethyl starch (HES) was adopted for the fluid responsiveness test in each study, at a dose of 7–10 mL/kg in six studies (5,13-17), a dose of 500 mL in two studies (6,19), and a dose of 250 mL in one study (16). The standards of fluid responsiveness were as follows: Δ [stroke volume index (SVI)] was used in five studies ($\geq 10\%$ in one study (18), $\geq 15\%$ in two studies (13,17), $> 25\%$ in two studies (6,15)], Δ CI was used in three studies ($\geq 10\%$ in one study (11), $> 15\%$ in two studies (14,19)], and Δ SV $\geq 10\%$ was used in one study (16). The characteristics of the individual studies are presented in *Table 1*.

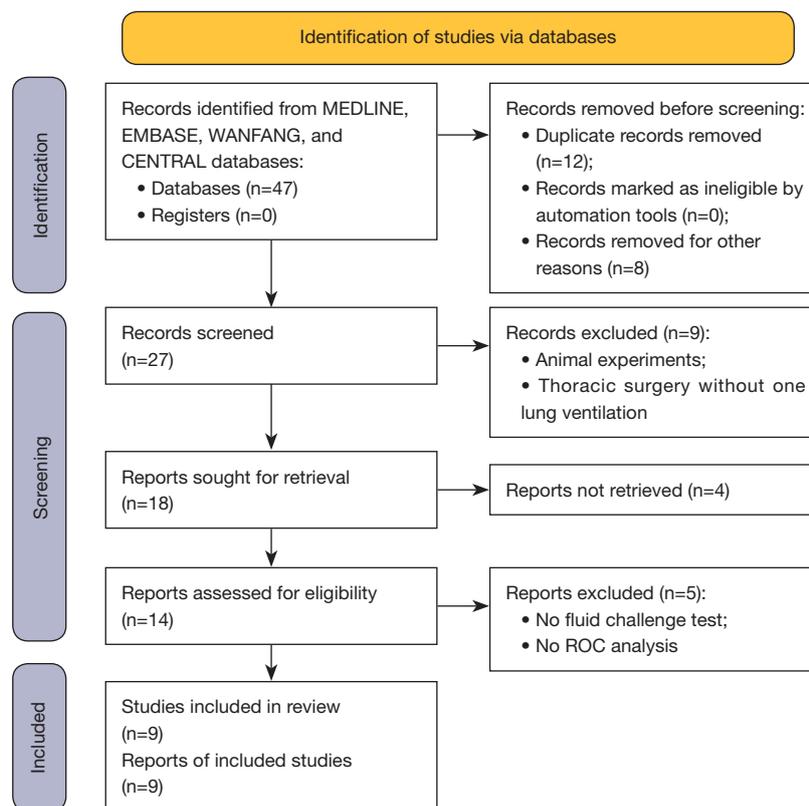


Figure 1 Flow chart showing article identification and selection during the review process. ROC, receiver operating characteristic.

Quality assessment

The quality of the included studies was assessed using the QUADAS-2 tool, and the results are set out in *Table 2*. Two studies included patients undergoing esophageal surgery (13,16), while patients in the other studies underwent lung surgery. Eligibility criteria were sufficiently described in all selected studies. One out of 9 (11%) papers were scored as unclear risk of bias on reference standard (16), and another 1 out of 9 (11%) papers were scored as unclear risk of bias on flow and timing (15). The reference standard employed in the recognized standard in distinguishing between responders and non-responders is the increase in CI or SVI, whose variation shall be at least 10%. However, it was unclear whether the standard for fluid responsiveness used in one study was sufficiently accurate, which selected the increase in SV as the reference standard (16). The researchers reported there were an appropriate time interval between the fluid challenge test and reference standard, except for the study by Kang *et al.* (15). Because the measurement of cardiac performance was taken immediately after fluid challenge, there was no disease progression

bias for all studies. There was no partial or differential verification bias in all studies. No studies reported uninterpretable test results and missing or incomplete data. All other papers were scored as low risk of bias.

Synthesis

After strict screening applying the inclusion and exclusion criteria, a total of nine studies were included in the final analysis. After combining the correlation coefficients, we found that there was a slight heterogeneity between the SVV and PPV in the selected studies, and the I^2 values of SVV and PPV were 19.7% (16.2–21.5%) and 15.3% (14.7–18.1%). The funnel diagram analysis also showed that the P values of SVV and PPV were 0.33 and 0.26 (*Figures 2,3*), and $P < 0.05$ represented statistically significant difference. Heterogeneity and the funnel diagram analysis showed that heterogeneity, publication bias had little influence on the pooled results. Thus, the fixed-effects model was selected to combine and comprehensively analyze the effect size of each study.

Table 1 Characteristics of the included studies

Study	Year	Sample size (lung/esophagus)	Type of operation (thoracotomy/thoracoscopy)	Tidal volume (mL/kg)	PEEP (cmH ₂ O)	SVV	PPV	Infusion volume	Distinguish between responders and non-responders
Fu <i>et al.</i> (5)	2014	30 (30/0)	30/0	8	0	Yes	No	8 mL/kg HES	Δ CI >10%
Suehiro <i>et al.</i> (6)	2010	30 (30/0)	0/30	8	5	Yes	No	500 mL HES	Δ SVI >25%
Fu <i>et al.</i> (13)	2015	45 (0/45)	0/45	6/8	5/0	Yes	Yes	7 mL/kg HES	Δ SVI >15%
Lee <i>et al.</i> (14)	2011	49 (49/0)	8/41	6/10	5/0	Yes	Yes	7 mL/kg HES	Δ CI \geq 15%
Kang <i>et al.</i> (15)	2016	76 (76/0)	17/59	7	0	Yes	No	10 mL/kg HES	Δ SVI >25%
Kimura <i>et al.</i> (16)	2021	30 (19/11)	0/30	6	5	Yes	Yes	250 mL, HES	Δ SV >10%
Choi <i>et al.</i> (17)	2021	40 (40/0)	0/40	6	5	Yes	Yes	7 mL/kg HES	Δ SVI \geq 15%
Jeong <i>et al.</i> (18)	2017	79 (79/0)	39/40	6	5	Yes	Yes	7 mL/kg HES	Δ SVI \geq 10%
Suehiro <i>et al.</i> (19)	2011	73 (73/0)	0/73	6/8	5	Yes	No	500 mL HES	Δ CI \geq 15%

PEEP, positive end expiratory pressure; SVV, stroke volume variation; PPV, pulse pressure variation; HES, hydroxyethyl starch; CI, cardiac index; SV, stroke volume; SVI, stroke volume index.

Table 2 Quality assessment of the included diagnostic accuracy studies using the QUADAS-2 tool

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Fu <i>et al.</i> (5)	⊙	⊙	⊙	⊙	⊙	⊙	⊙
Suehiro <i>et al.</i> (6)	⊙	⊙	⊙	⊙	⊙	⊙	⊙
Fu <i>et al.</i> (13)	⊙	⊙	⊙	⊙	⊙	⊙	⊙
Lee <i>et al.</i> (14)	⊙	⊙	⊙	⊙	⊙	⊙	⊙
Kang <i>et al.</i> (15)	⊙	⊙	⊙	?	⊙	⊙	⊙
Kimura <i>et al.</i> (16)	⊙	⊙	?	⊙	⊙	⊙	⊙
Choi <i>et al.</i> (17)	⊙	⊙	⊙	⊙	⊙	⊙	⊙
Jeong <i>et al.</i> (18)	⊙	⊙	⊙	⊙	⊙	⊙	⊙
Suehiro <i>et al.</i> (19)	⊙	⊙	⊙	⊙	⊙	⊙	⊙

⊙, low risk; ?, unclear risk. QUADAS-2, Quality Assessment of Diagnostic Accuracy Studies-2.

The data obtained directly from the original literature or indirectly through our calculations are set out in the table, including the number of true positive results, false positive results, false negative results, true negative results, and AUCs for SVV and PPV in each study (Tables 3,4). The results of the comprehensive analysis showed that the sensitivity of SVV and PPV in predicting fluid responsiveness was 0.66 (SVV, 95% CI: 0.56–0.74) and 0.61 (PPV, 95% CI: 0.52–0.69), respectively, the specificity was 0.62 (SVV, 95% CI: 0.52–0.71) and 0.53 (PPV, 95% CI: 0.42–0.63), the positive likelihood ratios were 1.7

(SVV, 95% CI: 1.3–2.4) and 1.3 (PPV, 95% CI: 1.0–1.7), respectively, the negative likelihood ratios were 0.55 (SVV, 95% CI: 0.39–0.78) and 0.74 (PPV, 95% CI: 0.55–1.00), respectively, and the DORs were 3 (SVV, 95% CI: 2–6) and 2 (PPV, 95% CI: 1–3), respectively (Table 5, and Figures 4,5). The areas under the SROC curve of SVV and PPV were 0.68 (SVV, 95% CI: 0.64–0.72) and 0.60 (PPV, 95% CI: 0.56–0.64), respectively, according to STATA SE16 software (Figures 6,7), and the combined AUCs of SVV and PPV were 0.681 (SVV, 95% CI: 0.665–0.698) and 0.604 (PPV, 95% CI: 0.578–0.640), respectively, according to

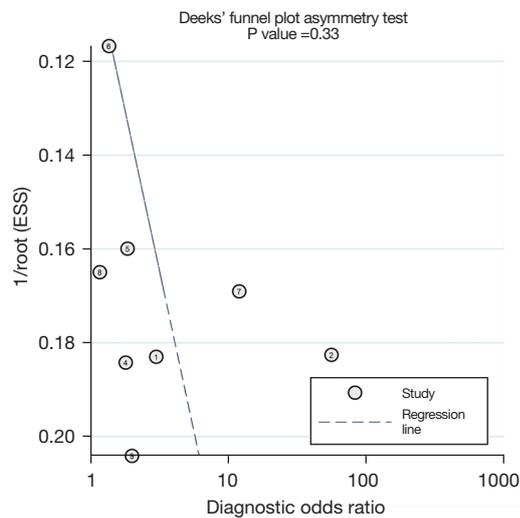


Figure 2 Funnel chart of SVV. ESS, explained sum of squares; SVV, stroke volume variation.

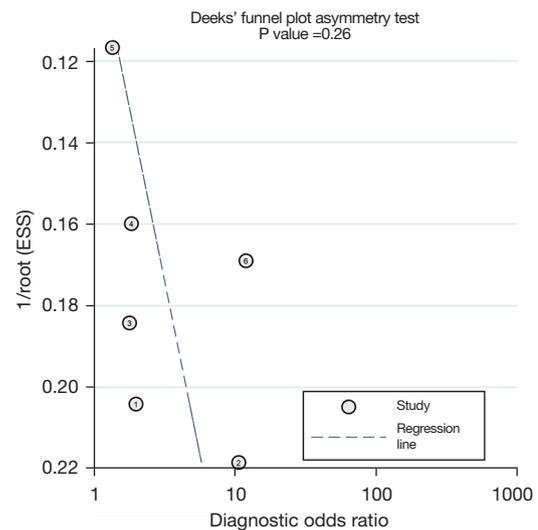


Figure 3 Funnel chart of PPV. ESS, explained sum of squares; PPV, pulse pressure variation.

Table 3 Paired sensitivity and specificity of the studies examining whether SVV can be used to predict fluid responsiveness

Reference	No. of fluid challenges				Sensitivity (%)	Specificity (%)	AUC-ROC (95% CI)
	TP	FP	FN	TN			
Fu <i>et al.</i> (5)	10	5	6	9	62.5	64.2	0.507 (0.294–0.720)
Suehiro <i>et al.</i> (6)	12	1	3	14	82.4	92.3	0.900 (0.809–0.991)
Fu <i>et al.</i> (tidal volume 6 mL/kg) (13)	8	6	4	6	66.7	50.0	0.767
Fu <i>et al.</i> (tidal volume 8 mL/kg) (13)	8	3	2	8	80	70.0	0.885
Kang <i>et al.</i> (15)	33	13	5	25	86.8	65.8	0.820 (0.724–0.915)
Kimura <i>et al.</i> (16)	9	5	8	8	52.9	61.5	0.65 (0.45–0.81)
Choi <i>et al.</i> (17)	10	10	7	13	58.8	56.5	0.64 (0.45–0.82)
Jeong <i>et al.</i> (18)	15	22	14	28	51.7	56.0	0.53 (0.42–0.65)
Suehiro <i>et al.</i> (tidal volume 8 mL/kg) (19)	18	5	3	10	85.7	66.7	0.776 (0.630–0.922)
Suehiro <i>et al.</i> (tidal volume 6 mL/kg) (19)	10	11	7	9	69.5	64.3	0.648 (0.495–0.802)

SVV, stroke volume variation; TP, true positive; FP, false positive; TN, true negative; FN, false negative; AUC-ROC, area under the receiver operating characteristic curve; 95% CI, 95% confidence interval.

MedCalc19.0.4 software (Tables 6,7).

Discussion

SVV and PPV are common, dynamic hemodynamic monitoring indicators used to predict fluid responsiveness in patients undergoing mechanical ventilation during general anesthesia and usually have good sensitivity and specificity (20). However, in some special cases, such as

OLV in thoracic surgery, the accuracy of SVV and PPV is still controversial. Some studies have reported that the destruction of the integrity of the pleural cavity on the side of thoracotomy or video-assisted thoracoscopic surgery was not enough to affect the periodic changes in the venous return, which leads to the reduction and false negative results of SVV (5,16-18) and PPV (14,16-18).

This is the first meta-analysis in which researchers tested the predictive response of SVV in patients undergoing

Table 4 Paired sensitivity and specificity of the studies examining whether PPV can be used to predict fluid responsiveness

Reference	No. of fluid challenges				Sensitivity (%)	Specificity (%)	AUC-ROC (95% CI)
	TP	FP	FN	TN			
Fu <i>et al.</i> (tidal volume 6 mL/kg) (13)	13	1	5	5	72.2	83.3	0.778
Fu <i>et al.</i> (tidal volume 8 mL/kg) (13)	9	2	1	9	90.0	81.8	0.890
Lee <i>et al.</i> (tidal volume 6 mL/kg) (14)	11	2	2	10	84.6	83.3	0.857 (0.712–1.003)
Lee <i>et al.</i> (tidal volume 10 mL/kg) (14)	7	6	5	6	58.3	50.0	0.524 (0.283–0.766)
Kimura <i>et al.</i> (16)	12	2	12	4	50.0	66.7	0.608 (0.37–0.74)
Choi <i>et al.</i> (17)	10	10	7	13	58.8	56.5	0.630 (0.47–0.83)
Jeong <i>et al.</i> (18)	18	20	11	30	62.1	60.0	0.550 (0.52–0.74)

PPV, pulse pressure variation; TP, true positive; FP, false positive; TN, true negative; FN, false negative; AUC-ROC, area under the receiver operating characteristic curve; 95% CI, 95% confidence interval.

Table 5 Summary performance estimates

Parameter	SVV estimate (95% CI)	PPV estimate (95% CI)
Sensitivity	0.66 (0.56 to 0.74)	0.61 (0.52 to 0.69)
Specificity	0.62 (0.52 to 0.71)	0.53 (0.42 to 0.63)
Positive likelihood ratio	1.7 (1.3 to 2.4)	1.3 (1.0 to 1.7)
Negative likelihood ratio	0.55 (0.39 to 0.78)	0.74 (0.55 to 1.00)
Diagnostic odds ratio	3 (2 to 6)	2 (1 to 3)

SVV, stroke volume variation; PPV, pulse pressure variation; 95% CI, 95% confidence interval.

OLV during thoracic surgery. We examined nine studies comprising a total of 452 patients. Our meta-analysis results showed that the combined sensitivity, combined specificity, and area under the SROC curve of SVV were 0.66, 0.62, and 0.68, respectively, and the combined sensitivity, combined specificity, and area under the SROC curve of PPV were 0.61, 0.53, and 0.60, respectively. Additionally, neither SVV nor PPV had good diagnostic accuracy and neither were suitable for guiding intraoperative fluid therapy due to their poor prediction of fluid responsiveness in patients undergoing OLV.

Some of the included studies reached contradictory conclusions. However, the following reasons may account for this: (I) insufficient sample sizes (the sample size of some studies was only 30, which may have affected the judgment of results); (II) different methods and judgment standards of liquid reaction tests may have led to conclusion errors; and (III) differences in surgical types and procedures. For example, esophageal surgery requires more enhancement in the field of visual surgery than pulmonary surgery. Different

degrees of lung traction by different operators during surgery may lead to variations in the detected parameter values, which may have affected the accuracy of the results.

SVV and PPV are dependent on cardiopulmonary interactions, which are periodic changes in venous return and trans pulmonary pressure caused by mechanical ventilation (21). They are important volume indexes in the GDHT and are also important components of enhanced recovery after surgery. However, the accuracy of SVV and PPV in predicting fluid responsiveness is affected by many factors, such as tidal volume, respiratory rate, arrhythmia, pleural integrity, and cardiac function during mechanical ventilation (22).

During OLV, the patients are usually placed in the lateral position, and changes in body position have been shown to have no statistically significant effect on the monitoring results of SVV (23). Additionally, research has found no statistically significant difference in the effects of left and right lateral positions on circulatory function and blood volume status (24). Low PEEP is often used in lung

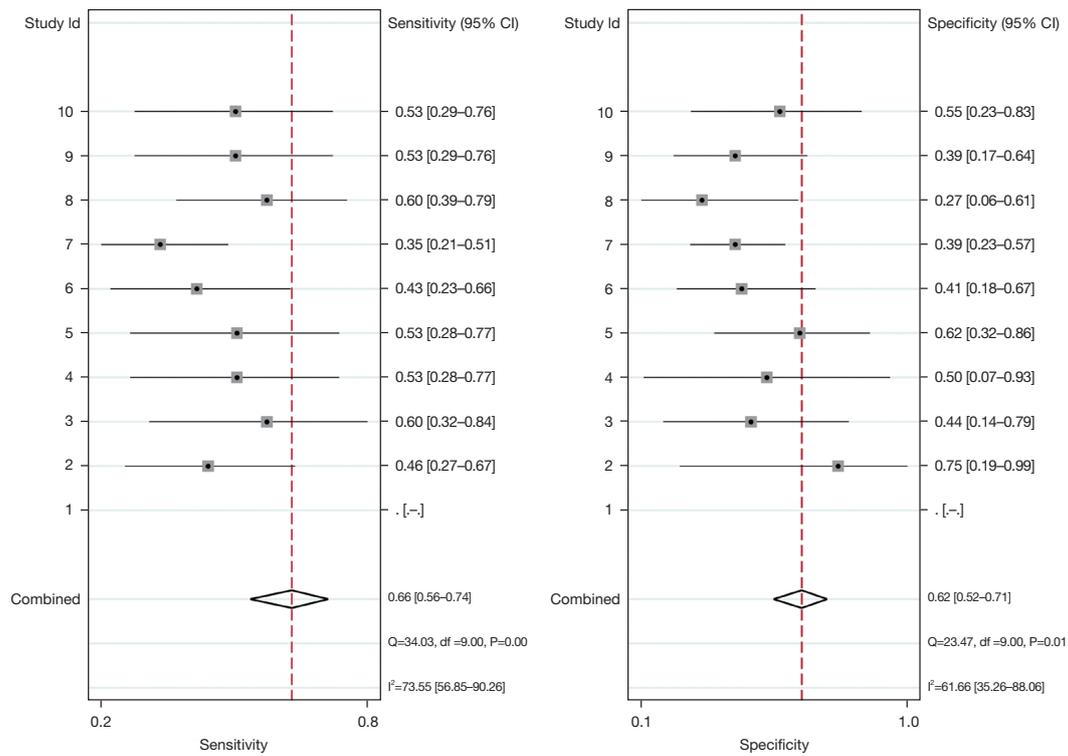


Figure 4 Forest plot for combined sensitivity and specificity of SVV. 95% CI, 95% confidence interval; SVV, stroke volume variation.

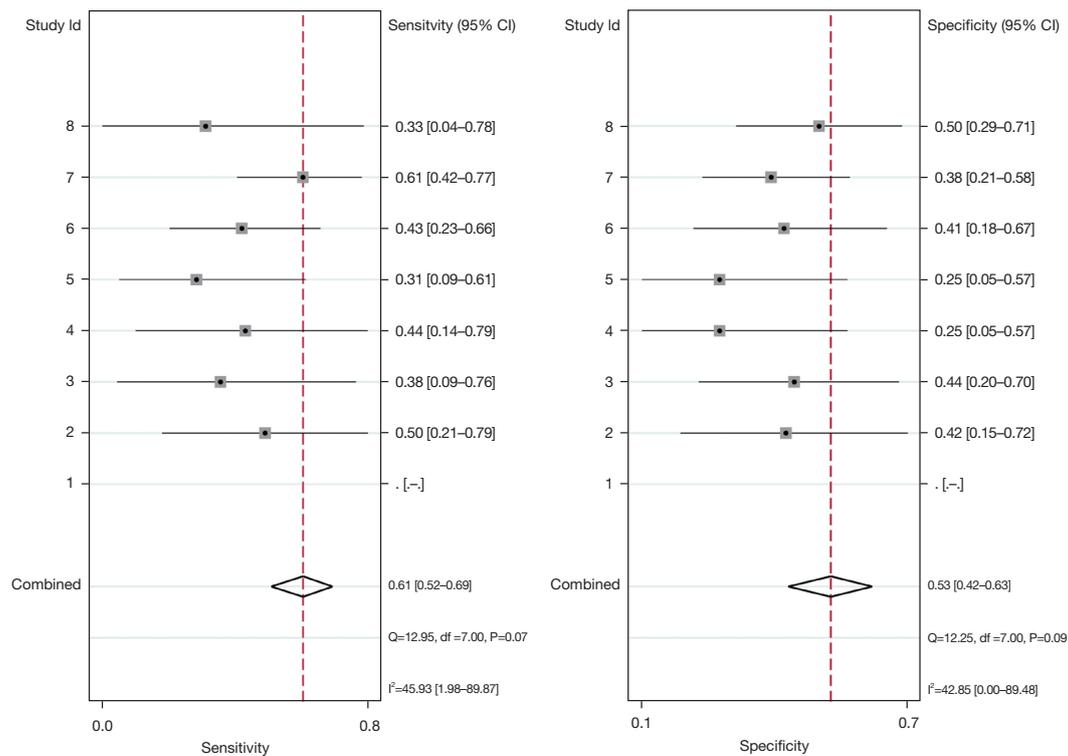


Figure 5 Forest plot for combined sensitivity and specificity of PPV. PPV, pulse pressure variation; 95% CI, 95% confidence interval.

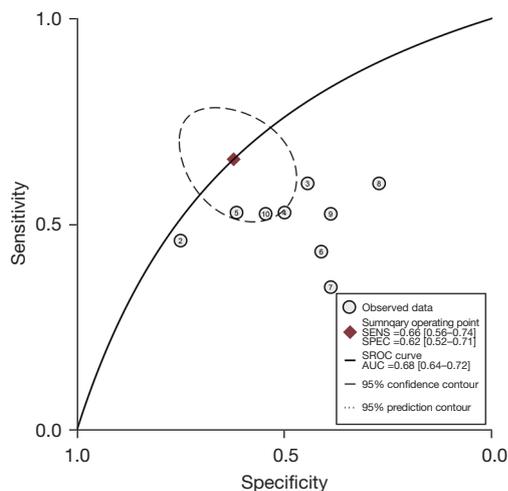


Figure 6 Combined SROC curve of SVV. SENS, sensitivity; SPEC, specificity; SROC, summary receiver operating characteristic; AUC, area under the curve; SVV, stroke volume variation.

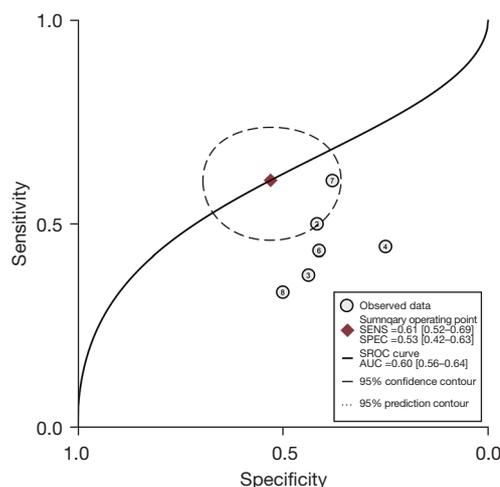


Figure 7 Combined SROC curve of PPV. SENS, sensitivity; SPEC, specificity; SROC, summary receiver operating characteristic; AUC, area under the curve; PPV, pulse pressure variation.

Table 6 The combined AUCs of SVV

Study	ROC area	95% CI	Weight (%)
Fu <i>et al.</i> (5)	0.507	0.448 to 0.566	7.62
Suehiro <i>et al.</i> (6)	0.900	0.841 to 0.959	7.62
Fu <i>et al.</i> (tidal volume of 6 mL/kg) (13)	0.767	0.694 to 0.840	5.01
Fu <i>et al.</i> (tidal volume of 8 mL/kg) (13)	0.885	0.816 to 0.954	5.59
Kang <i>et al.</i> (15)	0.820	0.781 to 0.859	17.13
Kimura <i>et al.</i> (16)	0.650	0.591 to 0.709	7.62
Choi <i>et al.</i> (17)	0.640	0.601 to 0.679	17.13
Jeong <i>et al.</i> (18)	0.530	0.497 to 0.563	23.72
Suehiro <i>et al.</i> (tidal volume 8 mL/kg) (19)	0.776	0.698 to 0.854	4.28
Suehiro <i>et al.</i> (tidal volume 6 mL/kg) (19)	0.648	0.570 to 0.726	4.28
Total (fixed-effects)	0.681	0.665 to 0.698	100.00

AUC, area under the curve; ROC, receiver operating characteristic; 95% CI, 95% confidence interval; SVV, stroke volume variation.

protection ventilation strategies, and relevant studies have also shown that low PEEP will not affect the accuracy of SVV (25).

During OLV, the integrity of the pleural cavity and the periodicity of pulmonary respiration on the operative side are destroyed, regardless of whether a thoracotomy or thoracoscopic surgery were performed (26). The following questions arise: (I) does the periodicity of intrapleural pressure caused by mechanical ventilation that relies only

on the positive pressure of the other side change the venous return blood volume and lead to a change in SV? (II) Does the accuracy of SVV and PPV be affected during OLV? According to our meta-analysis results, the accuracy of SVV and PPV were greatly affected by OLV.

First, low tidal volume (6–8 mL/kg) is widely known to be a major factor that may lead to prediction failure. Many studies have shown that the sensitivity and specificity of SVV and PPV in predicting fluid responsiveness are related

Table 7 The combined AUCs of PPV

Study	ROC area	95% CI	Weight (%)
Fu <i>et al.</i> (tidal volume of 6 mL/kg) (13)	0.778	0.705 to 0.851	4.59
Fu <i>et al.</i> (tidal volume of 8 mL/kg) (13)	0.890	0.821 to 0.959	5.12
Lee <i>et al.</i> (tidal volume 6 mL/kg) (14)	0.857	0.753 to 0.961	2.23
Lee <i>et al.</i> (tidal volume 10 mL/kg) (14)	0.524	0.428 to 0.620	2.61
Kimura <i>et al.</i> (16)	0.608	0.549 to 0.667	6.97
Choi <i>et al.</i> (17)	0.650	0.611 to 0.689	15.69
Jeong <i>et al.</i> (18)	0.630	0.610 to 0.650	62.77
Total (fixed-effects)	0.604	0.578 to 0.640	100.00

AUC, area under the curve; ROC, receiver operating characteristic; 95% CI, 95% confidence interval; PPV, pulse pressure variation.

to tidal volume, and their accuracy is greatly reduced when tidal volume is <8 mL/kg (27). However, during OLV, the tidal volume is usually 6–8 mL/kg. Excessive tidal volume will increase airway pressure and cause lung injury, and also limit surgical vision (28). If the tidal volume is too small, the trans-pulmonary pressure will also decrease, and its periodic changes will not be enough to cause changes in the blood flow of the vena cava, pulmonary artery, and aorta. The Frank-Starling curve moves to the left. Thus, patients occupying the flat part of the Frank-Starling curve may theoretically occupy the steep part of the curve during low tidal volume ventilation, which will result in decreased accuracy (29).

Second, the increase in the intrapulmonary shunt rate (Q_s/Q_t) during OLV leads to an increase in intrapulmonary shunts due to the doping of intrapulmonary vein blood on the non-ventilated side. At this time, the airway pressure increases significantly, which increases the vascular resistance. Part of the blood flow will transfer to the collapsed opposite lung, which easily results in hypoxia. Hypoxic pulmonary vasoconstriction (HPV) during OLV is considered an important mechanism for preventing hypoxemia, but HPV and autonomic regulation are weakened due to the influence of anesthesia methods, drugs and other factors during surgery. Studies have shown that the intrapulmonary shunt rate and hypoxic vasoconstriction may be important factors affecting the accuracy of CI, which suggests that they may affect the accuracy of dynamic hemodynamic indicators, such as SVV and PPV, but the specific mechanism remains unclear (30,31).

Third, dynamic indicators distinguish the steep part of the Frank-Starling curve according to the periodic change in cardiopulmonary interaction, which not only depends

on the change in venous return but also on the change in right ventricular afterload and left ventricular transmural pressure. OLV will cause an increase in intrapulmonary shunt and dead space ventilation due to the collapse of the affected side and atelectasis of the healthy side, resulting in hypercapnia. Hypercapnia defined as the arterial carbon dioxide pressure (P_aCO_2) >48 mmHg is an independent predictor of right ventricular dysfunction in patients with chronic obstructive pulmonary disease receiving low tidal volume mechanical ventilation, which can cause pulmonary vasoconstriction, increase the afterload of the right heart, decrease the function of the right heart, and affect the accuracy of SVV and PPV (31,32).

Limitations and strengths

Our meta-analysis had some limitations. First, as heterogeneity was found in the whole data set, the conclusions should be interpreted carefully. Second, the effects of vasoactive drugs on SVV and PPV could not be discussed due to a lack of relevant data. Third, as the types of surgery included mainly involved the lung and esophagus, our conclusions are not applicable to all patients undergoing OLV surgery. In the future, multicenter and large sample research needs to be conducted.

Our meta-analysis also had several strengths. First, this is the first diagnostic meta-analysis in which the reliability of SVV and PPV was studied in terms of predicting fluid responsiveness in patients under OLV. Second, the quality of the included articles was good. Third, we used two different software programs to compare the combined ROC curves of SVV and PPV, and the results of the two software analyses were consistent, which increases the reliability of

our results.

Conclusions

This was the first meta-analysis to examine the accuracy of SVV and PPV in terms of predicting fluid responsiveness in patients undergoing OLV. Our results indicate that SVV and PPV are not suitable for guiding intraoperative fluid therapy due to their poor prediction of fluid responsiveness in patients undergoing OLV, and we need a better indicator instead.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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