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Stroke volume variation for predicting responsiveness to fluid therapy in patients undergoing cardiac and thoracic surgery: A systematic review and meta-analysis

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Abstract

Objectives: To study the utility of stroke volume variation (SVV) in predicting responsiveness to fluid therapy of patients undergoing cardiac and thoracic surgery.

Methods: We searched PubMed, Cochrane Library, EMBASE, and Web of Science database (updated to August 9, 2020) for relevant trials. We used random-effects model to pool value of sensitivity, specificity, and diagnostic odds ratio (DOR) with 95% CI. The area under the curve (AUC) of receiver operating characteristic (ROC) was calculated. Quality of the studies was assessed with the QUADAS-2.

Results: Among the 20 relevant studies, data from 854 patients accepting mechanical ventilation were included in our systematic review. The AUC of ROC was 0.73 (95% CI 0.69–0.77) in the thoracic surgery group, 0.80 (95% CI 0.76–0.83) in the cardiac surgery group and 0.89(95% CI 0.86–0.92) in cardiac intensive care unit (ICU) group. Subgroup analysis showed that in thoracic surgery, high tidal volume (VT) (AUC = 0.81) and non-positive end-expiratory pressure (PEEP) (AUC = 0.74) indicated good responsiveness while in cardiac surgery, non-PEEP (AUC = 0.78) was appropriate. Small volume infusion (AUC = 0.76) was suitable for heart surgery, but large volume infusion (AUC = 0.88) and FloTrac/Vigileo (AUC = 0.80) were suitable for thoracic surgery.

Conclusion: SVV is a reliable measurement parameter for patients undergoing cardiac and thoracic surgery. Nevertheless, technical and clinical variables may affect the predictive value.

Keywords: Stroke volume variation; Fluid responsiveness; Thoracic surgery; Cardiac surgery; Meta-analysis

Strengths and limitations of this study:

- QUADAS-2 scale in Review Manager 5.3 was used to assess the quality of our included studies finding that most of them are of high quality.
- Three different analyzing software were used to compare the predictive value of SVV in different condition and most of their results were consistent, showing high credibility of the conclusion of our meta-analysis.
- Although meta regression analysis, sensitivity analysis and subgroup analysis were conformed, heterogeneity existed in the overall dataset and in most subgroups, which made comparison across trials difficult.
- Most cardiac surgery included in our research were related to coronary artery, which made our conclusions not applicable to all kinds of cardiac surgery.

Background

Fluid therapy is important for maintaining a stable internal environment during thoracic and cardiac surgery 【1】. According to Frank Starling's curve 【2】, the preload of the ventricle is proportional to the cardiac output (CO) in the upcurve. However, if the preload increases in the flat section of the curve, fluid therapy would not yield the desired effect and it could even result in cardiac overload and tissue oedema 【3, 4】. To more accurately predict the blood volume and preload of the ventricle during the perioperative period, goal-directed fluid therapy was suggested.

Anaesthetists previously tended to use some traditional hemodynamic indicators such as central venous pressure (CVP), pulmonary artery diastolic pressure (PADP) and cardiac index (CI) to predict fluid responsiveness 【5】. It could guide the regulation of CO but was of limited utility in reflecting ventricular preload. SVV as a predictive parameter has gained importance since the last decade 【6，7】.

SVV reflects the variation of stroke volume (SV) in 30 seconds and was considered a reliable parameter under the condition of closed chest 【8】. It reflects the effect of respiratory movement on venous return. During inspiration, the increase in intrapulmonary pressure significantly decreases the negative intrapleural pressure, thereby decreasing venous return and CO. During expiration, the opposite changes occur 【9】. Toyoda et al 【6】 reported a curvilinear relationship between the right ventricular end-diastolic volume index (RVEDVI) and SVV. The regression curve accorded better with SVV than with CVP or PADP, showing its reliable prediction performance. In addition, SVV could distinguish several thresholds of RVEDVI more accurately.

Although transoesophageal echocardiography (TEE), serving as a gold standard, had indisputable advantages in diagnosing ventricular preload and guiding fluid therapy, its practicability and availability as a commonly used technique were still limited 【10】. Therefore, SVV offers a good middle ground between conventional indicators and TEE.

Despite many studies conducted to determine whether SVV could be reliably applied to predict fluid responsiveness in cardiac and thoracic surgery patients 【11–30】, there has been no consensus. Several pervious systematic reviews have evaluated the reliability of SVV in predicting the outcome of common surgical operations in children and adults, but no large-sample study has been conducted to evaluate the utility of SVV in cardiac and thoracic surgery. Therefore, this study was conducted to address the issue.

METHODS

The meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement issued in 2009【31】.

Description of investigated indices

SVV is the ratio of the difference between the maximum and the minimum of the SV and the mean of the SV during 30 seconds as follows: $(SV_{max} - SV_{min})/SV_{mean}$.

Search strategy

We searched PubMed, Web of Science, EMBASE, and the Cochrane Library database for relevant literature by using searching terms such as SVV, stroke volume variation, responsiveness, and predict. The initial search was conducted on May 9, 2020 with a language restriction of English.

The search string used was: ((SVV) OR (stroke volume variation)) AND (((((predictor) OR (prediction)) OR (predict)) OR (evolution)) OR (responsiveness)).

Eligibility criterial

We included diagnostic trials evaluating the accuracy and effectiveness of SVV in predicting fluid responsiveness in the operating room (OR) and ICU. We excluded review articles, commentaries, conference reports and research papers on animal or in vitro experimental studies. In addition, we also excluded studies in which the subjects were children or patients with spontaneous breathing, sepsis, shock, or arrhythmia.

Data extraction

The basic characteristics and primary outcomes of each article were independently extracted by two authors (Sheng Huan and Yihao Ji). The characteristics included last name of the first author, publication year, number of patients, position, VT, PEEP, and timing of manoeuvre. The outcomes included TP, FP, TN, FN, sensitivity, specificity, best cut-off (%), AUC, and correlation coefficient. When there were insufficient or missing data, one author (Sheng Huan) contacted the corresponding author to of the included article to obtain the necessary data.

Quality assessment

Two authors (Sheng Huan and Yihao Ji) independently assessed the quality of the included articles using the QUADAS-2 scale in Review Manager 5.3(Cochrane Library, Oxford, UK) 【32】. Disagreements or discrepancies were resolved by discussion with the third author (Guoping Yin). Publication bias was checked using Deeks' Funnel Plot Asymmetry Test 【33】.

Statistical treatment

The Stata software (version 14.0) was used for basic calculations. When the number of included studies within some subgroups was less than four, not meeting the minimum requirements of Stata, we used Review Manager (version 5.3) and R software (version 3.6.3) to analyse data in these subgroups. For comparing the AUC, the Review Manager could only display the summary receiver operating characteristics (SROC).

We used correlation (Mixed Model) of Stata to evaluate whether a threshold effect existed. When the correlation was positive and its P value was >0.05, no threshold effect was considered to exist. We then used a random-effects model to calculate pooled sensitivity, specificity and AUC with 95% CI. Statistical heterogeneity was estimated using the Cochrane Q and I^2 tests 【34】, and it was considered to be present when $I^2 > 50$ % or $P < 0.05$. In such cases, meta-regression analysis, sensitivity analysis, and subgroup analysis were used to determine the sources of heterogeneity.

Patient and public involvement

Patient and public involvement is not applicable for this meta-analysis.

RESULTS

Outcome of literature search and study characteristics

Of the 1371 related articles, 903 articles remained after eliminating duplicates. Then, we excluded 834 articles because they were case reports, review articles, articles related to animal experiments or other irrelevant studies. Among the remaining

69 articles, 14 studies repeated the same content, two studies were not published in English, and data of our interest could not be obtained for 33 articles. Finally, 20 articles were included in our meta-analysis (Fig.1).

The 20 articles included 854 patients. The main kinds of monitoring systems were FloTrac/Vigileo system and PiCCO system. Geerts et al 【28】 used pulmonary artery catheter insertion to measure thermodilution CO and CVP. Kang et al 【29】 used Swan-Ganz and NICOM monitors to detect SV and calculate SVV. We defined VT < 8 ml/kg as "low VT" and VT ⩾ 8 ml/kg as "high VT"; absence of PEEP or PEEP < 5 mmHg was considered non-PEEP. When the infusion volume was set above 5 ml/kg or 250 ml, we considered the study to involve a large bolus group. If not, it was considered a small bolus group. Some patients in the same study accepted fluid challenge with two different systems【27】 or accepted different methods of TV ventilation 【12,17】. We included all such methods and systems in our meta-analysis. The basic characteristics of our included studies are presented in Table 1 and Table 2.

Study	Surgery	Number	Standard	Intervention	Result	Device	PEEP (mmHg)	TV (ml/kg)	Position	Endoscope	Moment of maneuver
Thoracic surgery											
Kang 2016	thoracotomy or VATS with OLV	76	△SVI > 25%	10 mL/kg colloid	Yes	FloTrac-Vigileo system	0	4（OLV）	supine	/	After lung recruitment maneuver and thorax closure, colloid solution at 10 mL/kg of ideal body weight was administered for 30min.
Fu 2015	esophagectomy	24	△CI > 15%	7 mL/kg colloid	Dispute	FloTrac-Vigileo system	5	6（OLV） 8（OLV）	Lateral position	YES	After the procedure of laparoscopic part, the monitoring system was adjusted accordingly.
Fu 2014	pulmonary lobectomy with one-lung ventilation(thoracotomy) (chest opening)	30	△CI > 10%	8 mL/kg colloid	NO	PiCCO	0	8	lateral decubitus position	NA	Hemodynamic measurements were performed before, and within 30s after volume expansion (VE) without stimulation.
Miñana 2020	open lung resection surgery	76	△CI > 10%	250ml crystal-loids or more	NO	PiCCO	5	6(OLV)	lateral position	NA	The study protocol was started once the patient had been placed lateral, with the chest open.
Jeony 2017	Lung cancer surgery	79	△CI > 10%	7 mL/kg colloid	No	FloTrac-Vigileo system	5	6 (OLV)	Lateral position	VATS and open chest	Hemodynamic measurements were conducted 15 minutes after the start of OLV, before fluid loading, and just

										surgery	after finishing fluid loading.
Suehiro 2010	Lobectomy	30	△CI > 25%	500ml colliod	Yes	FloTrac-Vigileo system	5	8	lateral position	thoracoscopy	Hemodynamic variables were measured before and after volume loading.
Suehiro 2011	Lobectomy	37	△CI > 15%	500ml colliod	No(6) Yes(8)	FloTrac-Vigileo system	5	6(OLV) 8(OLV)	lateral position	thoracoscopy	All patients were studied at 30 min after starting OLV. SVV measurements was performed by administration of 500 ml colloid solution for 30 min
Cardiac surgery											
Kim 2013	Coronary surgery (normal pulse pressure)	33	△SVI > 12%	500ml colliod	Yes	FloTrac-Vigileo system	5	10	NA	NA	All hemodynamic data were assessed before sternotomy to maintain consistency of the closed thorax.
Montenij 2016	coronary artery bypass grafting	22	△CO > 15%	7 mL/kg crystalloid	NO	FloTrac-Vigileo system	5-10	8	NA	NA	Between induction of anaesthesia and incision, volume loading was performed in 15 min.
Broch 2011	GABG	81	△SVI > 12%	PLR	Yes	PiCCO	5	8	NA	NA	Measurements were performed after induction of anesthesia before surgery.
Broch 2012	CABG	92	△SVI > 15%	PLR	Yes	PiCCO	5	8	NA	NA	Measurements were performed after induction of anesthesia before surgery.
Hofer 2005	Off-Pump GABG	40	△SVI > 25%	10 mL/kg 6% hydroxyethyl starch solution	Yes	PiCCO	0	10	NA	NA	prior to any surgical intervention, volume replacement was performed
Preisman	CABG	18	SVI > 15%	250ml colliod	NO	TEE,PiCCO	15-20	8-10	NA	NA	After the induction of anaesthesia and after the end of the operation

2005											and before the transfer to the ICU.
Haas 2012	cardiac surgery with cardiopulmonary bypass	18	△CI ＞10%	4 mL/kg colloid	Yes	PiCCO	5	8	NA	NA	Directly after completion of cardiac surgery and thoracic closure
Canneson 2009	coronary artery bypass grafting	25	△CI ＞15%	500ml colliod	Yes	FloTrac-Vigileo system	0-2	8-10	NA	NA	Baseline hemodynamic measurements were obtained after a 3 min period of hemodynamic stability. and then followed by an IV intravascular volume expansion
ICU after cardiac surgery											
Fischer 2013	ICU C	37	△CI ＞15%	500ml colloid	No	PiCCO Nexfin	NA	NA	NA	NA	Within the first 6 post-operative hours.
Hofer 2008	ICU C	40	25% increase in SV	body position change(from 30° headup position to 30° head-down position)	Yes	PiCCO FloTrac-Vigileo system	5	8-10	NA	NA	Measurements were started during the postoperative period after transfer of patients to the intensive care unit.
Geerts 2011	ICU C	20	△CO ＞7%	passive leg raising (PLR).	Yes	pulmonary artery catheter insertion	5	8-10	NA	NA	NA
Kang 2014	ICU C	54	△CO ＞7%	PLR	Yes	Swan-Ganz NICOM	5	10	NA	NA	NA

De Waal 2009	ICU (Coronary artery bypass grafting)(open chest)	22	△SVI > 12%	7 mL/kg colloid	Yes	PiCCO	5	8/kg	NA	NA	These measurements were performed immediately after stabilization of the patients after arrival in the ICU, i.e. within 1 hour after arrival or within 2 hours after cessation of CPB.

Table.1 The characteristics of the included studies.

Study	TP	FP	TN	FN	Sensitivity	Specificity	Cut-off (%)	AUC	Correlation coefficient
Thoracic surgery									
Kang 2016	33	13	4	25	86.8	65.8	3.5	0.820	NA
Fu 2015	8	6	4	6	66.7	50	8.5	0.767	0.412
Fu 2015	8	3	2	7	80	70	8.5	0.778	0.679
Fu 2014	8	5	8	9	50	64	NA	0.507	-0.171
Miñana 2020	8	3	14	14	36.4	82.4	8	0.47	NA
Jeony 2017	26	39	3	11	0.897	0.22	NA	0.53	NA
Suehiro 2010	14	1	3	13	82.4	92.3	10.5	0.9	0.866
Suehiro 2011	13	9	9	7	58.3	44	10	0.648	NA
Suehiro 2011	18	4	5	8	85.7	66.7	10.5	0.776	NA
Cardiac surgery									
Kim 2013	16	4	5	8	76	67	13	0.808	0.568
Montenij 2016	5	4	4	9	56	69	10	0.7	0.32
Broch 2011	30	9	16	28	65	76	12	0.72	0.57

Broch 2012	35	9	19	31	65	77	11	0.77	0.62
Hofer 2005	17	5	6	12	74	71	12.5	0.823	-0.657
Presiman 2005	26	7	6	32	81	82	NA	0.58	0.58
Haas 2012	4	5	0	13	100	72.2	11	0.87	NA
Cannesson 2009	14	1	3	7	82	88	10	0.871	NA
ICU after cardiac surgery									
Fischer 2013	8	1	19	9	0.3	0.9	NA	0.50	NA
Hofer 2008(PiCCO)	20	4	3	13	87	76	12.1	0.858	0.702
Hofer 2008(Vigileo)	21	3	2	14	91	83	9.6	0.824	0.653
Geerts 2011	7	0	3	10	70	100	7.3	0.90	0.67
Kang 2014	25	4	2	23	92.3	84	13.5	0.942	NA
De Waal 2009	11	3	0	8	100	78	8	0.911	0.745

Table.2 The results of all the included studies.

Assessment of study quality and publication bias

The quality of the 20 included studies was assessed according to the QUADAS-2 (Fig. 2 and Fig. 3).

After using Deeks' Funnel Plot Asymmetry Test to evaluate publication bias, we found the P value of bias to be 0.870, 0.617, and 0.546 for studies mentioning thoracic surgery, cardiac surgery, and cardiac ICU, indicating that no significant publication bias existed in our included studies.

Results of our meta-analysis

Analysis of the data using the Stata/MP 14.0, we found the Spearman correlation coefficient of the thoracic surgery, ICU, and cardiac surgery groups as -0.43 (P = 0.18), -1.0 (P = 1.0), and 1.0 (P = 1.0), respectively, which indicated that there was a significant threshold effect in the thoracic surgery and ICU groups, but there was no significant threshold effect in the cardiac surgery group.

In the thoracic surgery and ICU groups, the AUC of SROC was 0.73 (95% CI 0.69–0.77) and 0.89 (95% CI 0.89–0.92), respectively. The Cochrane-q value of their AUC was 25.829 (P < 0.001, I^2 = 92%) and 15.791 (P < 0.001, I^2 = 87%), indicating significant heterogeneity in both groups.

In the cardiac surgery group, the pooled sensitivity was 0.71 (95% CI 0.65–0.77) and the pooled specificity was 0.76 (95% CI 0.69–0.82). The positive likelihood ratio was 3.0 (95% CI 2.3–3.9), the negative likelihood ratio was 0.38 (95% CI 0.30–0.47), and the diagnostic ratio was 8 (95% CI 5–12). The Cochrane-q value of AUC was > -0.001 (P = 0.5, I^2 = 95%), indicating significant heterogeneity.

Heterogeneity

Meta regression analysis showed that monitoring devices (P < 0.05) in the thoracic surgery group and types (P < 0.01) and volume of fluid infusion (P < 0.01) in the cardiac surgery group were significant reasons for heterogeneity. There was no significant reason to explain the heterogeneity in the ICU group (P < 0. 05).

However, subgroup analysis revealed high heterogeneity (>50%) in all subgroups, which may be attributed to management of surgery and anaesthesia, patient comorbidities, timing of performing fluid challenge, speed of fluid infusion, etc.

Results of sensitivity analysis showed that only in the thoracic surgery group one study 【15】 may contribute to the heterogeneity. Despite excluding this study, the heterogeneity was still significant ($I^2 = 63\%$). Therefore, we concluded that heterogeneity was inevitable and the results were stable.

Comparison between subgroups

The results of our subgroup analysis showed that in both thoracic surgery and cardiac surgery, the colloid type fluid (AUC = 0.76; AUC = 0.85) was superior to the crystalloid type fluid (AUC = 0.47; AUC = 0.70) and non-PEEP ventilation (AUC = 0.740; AUC = 0.778) was better than PEEP ventilation (AUC = 0.736; AUC = 0.689). Postoperative monitoring (AUC = 0.850) was superior to the preoperative monitoring (AUC = 0.691) in cardiac surgery. High VT ventilation (AUC = 0.81) and supine position (AUC = 0.82) may be recommended in thoracic surgery.

In addition, large bolus infusion (AUC = 0.76) was more suitable for thoracic surgery, and small volume infusion (AUC = 0.879) was more suitable for cardiac surgery during fluid therapy. Passive leg raising (PLR) (AUC = 0.886) was a better choice for ICU patients, fluid challenge (AUC = 0.752) was better for thoracic and cardiac surgery. Regrading device, the use of FloTrac/Vigileo (AUC = 0.801) was better for thoracic surgery but there was no particular best choice of system for cardiac surgery. The details are presented in Table 3.

Subgroups	trails number	State					Revman	R	
		AUC	Sensitivity	Specificity	DOR	Youden index	Result	AUC	Youden

									index
Thoracic surgery	**9**	0.73(0.69-0.77)	0.73(0.59-0.83)	0.62(0.46-0.76)	4 (2-10)	0.35			
Lateral position	8	0.71(0.67-0.75)	0.69(0.55-0.81)	0.62(0.43-0.77)	4 (2-8)	0.31			
Supine position	1	0.82(0.73-0.92)	0.87(0.85-0.89)	0.66(0.63-0.69)	-	0.53			
Thoracoscopy	2						High	0.69	0.38
Thoracotomy	7						Low	0.70	0.32
Colloid	8	0.76（0.72-0.79）	0.77(0.66-0.85)	0.59(0.42-0.74)	5 (2-11)	0.36			
Crystalloid	1	0.47（0.30-0.65）	0.36	0.82	-	0.18			
Large bolus	8	0.76（0.72-0.79）	0.77(0.66-0.85)	0.59(0.42-0.74)	5 (2-11)	0.36			
Small bolus	1	0.47（0.30-0.65）	0.36	0.82	-	0.18			
FloTrac/Vigileo	7						High	0.80	
PiCCO	2						Low	0.43	
PEEP	7						Low	0.74	
Non-PEEP	2						High	0.74	
Large VT	4	0.81 [0.77-0.84]	0.73(0.58-0.85)	0.75(0.58-0.86)	8 (3-26)	0.48			
Small VT	5	0.67 [0.63-0.71]	0.73(0.50-0.83)	0.54(0.32-0.74)	3 (1-8)	0.27			
Cardiac surgery	**8**	0.80(0.77-0.83)	0.71(0.65-0.77)	0.76(0.69-0.82)	8 (5-12)	0.47			
FloTrac/Vigileo	3						Low	0.74	0.46
PiCCO	5						High	0.70	0.48
Large bolus	4						Low	0.73	0.46
Small bolus	2						High	0.88	0.62
Crystalloid	1	0.70（0.47-0.92）	0.56	0.69	-	0.25			
Colloid	5	0.85 (0.81-0.88)	0.79(0.70-0.86)	0.76(0.67-0.84)	12 (6-25)	0.55			
Perioperation	6						Low	0.69	0.41
Postoperation	2						High	0.85	0.63
Peep	6						Low	0.69	0.47
Non-Peep	2						High	0.78	0.53
Fluid challenge	6						High	0.75	0.52
PLR	2						Low	0.65	0.41
ICU after cardiac surgery	**6**	0.88(0.86-0.92)	0.85(0.60-0.96)	0.85(0.74-0.92)	32 (9-108)	0.70			
Fluid challenge							Low	0.82	0.41
PLR							High	0.89	0.72

Table.3 The results of subgroup meta-analysis

DISCUSSION

Our study revealed that SVV had excellent predictive performance in monitoring patients accepting cardiac surgery in OR and ICU and had good predictive performance in patients accepting thoracic surgery with one-lung ventilation (OLV). In addition, we found that some operation aspects such as ventilation mode, rehydration mode, timing of intervention, and operation type can significantly affect the performance of SVV, which may also be the reason for the overall heterogeneity in our study.

Ventilation

Protective ventilation, defined as low TV, low inhaled oxygen (FIO2), and PEEP have recently been widely advocated in OLV. However, our meta-analysis found that it may negatively affect SVV monitoring. Ventilation volume rather than airway pressure is the key factor determining pleural pressure and right ventricular afterload 【35】. When TV decreased, the Frank starling curve of the left ventricle markedly moved to the right, making the variation in systolic pressure insignificant. Low TV would not cause any significant variation in SV especially under conditions of low blood volume 【17】.

Alvarado et al 【36】 found that low PEEP (0–10 mmHg) had no significant effect on cardiac preload because most of the pressure generated by the ventilator would be released to the atmosphere 【16】, whereas high PEEP (10–15 mmHg) would mistakenly indicate blood volume 【37】. This phenomenon would become more evident in OLV, in agreement with our result. However, another meta-analysis reported an opposite conclusion that the AUC of SVV is not affected by PEEP levels or driving pressures 【36】, which may be explained by the difference between OLV and normal ventilation. It suggests that the effect of respiratory pressure and VT on

SVV depends primarily on the degree to which these variables transmitted to the pulmonary circulation, rather than absolute value.

Intervention

Fluid therapy with large bolus showed better reliability in thoracic surgery, whereas small bolus fluid therapy was more used useful in cardiac surgery, and this could be because patients undergoing cardiac surgery usually have cardiac dysfunction and cannot tolerate a large bolus during in a short period, whereas thoracic surgery patients often exhibit heavy bleeding. Regarding the type of fluid, the colloid rather than crystalloid type can quickly compensate for fluid loss to achieve satisfactory CO 【8】 and significantly increase RVEDVI 【38】. By transfer of approximately 300 ml of venous blood from the lower body toward the right heart, PLR was often used in the ICU to mimic a fluid challenge, which agreed with our result that PLR suited ICU patients and fluid therapy suited OR patients 【29】. Interestingly, Ma found that PLR may replace fluid challenge as a more reliable intervention in protection ventilation patients during cardiac surgery 【39】.

Monitoring device

The FloTrac/Vigileo system was better in thoracic surgery but was contradictory in cardiac surgery. It has lower thresholds than the PiCCO system and could predict the insufficiency of blood volume earlier and with greater sensitivity even if the wave of hemodynamic status remained weak or unchanged in OLV 【27】. In addition, it requires no calibration and is considered to be less affected by arterial compliance and elasticity 【40】. However, misestimation of blood volume is possible when a rapid wave of CO occurs 【41】.

The PiCCO system can be used only after correction for low-temperature saline, and it is difficult to continuously calibrate the system during surgery in cases of heavy bleeding 【42】. Its latest version incorporates adapted vascular compliance measurement from every 10 minutes to every minute based on a modification algorithm 【43】. Wiesenack et al 【44】 reported a significant correlation between baseline SVV and changes of SVI after updating the algorithm of PiCCO system, which was opposite to their previous negative result that linear regression analysis between SVV and changes of SVI did not reveal a significant relationship.

Cardiac insufficiency and arrhythmia

Although our analysis did not include studies with arrhythmia patients, wide pulse pressure has been considered to seriously affect SVV prediction 【18】. Similarly, in shock patients with circulatory failure, the diagnostic value of SVV was greatly limited 【45】. However, Cannesson et al 【46】reported that a new SVV algorithm using multi-parameter signal recognition to reject ectopic beats could work well even in patients with arrhythmia.

Heart failure could decrease the ventricular output due to the increasing afterload during inspiration 【47】. Right ventricular dysfunction would also lead to false positive functional parameters of preload 【48】. However, some studies found that patients with slightly impaired LV function (50%≥EF≥30%) still had values on the steep upcurve of the Frank-Starling curve and were equally responsive to fluid therapy as healthy patients according to SVV 【10,23】.

Others

Previous studies have shown that SVV is suitable for laparoscopic surgery in different positions such as supine, lateral decubitus, or prone positions. However, thoracoscopy creates a continuous intrathoracic pressure, which compresses the mediastinum and contralateral lung, further reducing lung compliance 【49,35】. Due to the small sample size, our results have limited power in judging preference between thoracoscopy and thoracotomy. Moreover, we found that the supine position is more suitable than the lateral position to monitor SVV.

Opening the chest cavity would increase the aortic impedance and decrease venous return, strongly affecting the correlation between SV and pulse pressure 【23】. SVV correlated with the ventricular preload when the pericardium is closed 【30,50】. Our results showed that SVV monitoring after cardiac surgery had a better predictive value than that before cardiac surgery, which may result from cure of cardiac dysfunction. Interestingly, Kang et al 【11】 found that SVV also has good diagnostic value during lung recruitment manoeuvre.

More than vasoactive drugs affecting CO calculation, the classification criteria between responders and non-responders, system error, and thresholds were apparently potential factors influencing the predictive value of SVV.

Limitations and strengths

Our meta-analysis has some limitations. First, heterogeneity existed in the overall dataset and in most subgroups, so our conclusion should be interpreted with caution. Second, the best cut-off value of our included articles was too wide, ranging from 3.5 to 13.5. Physicians should refer to the related articles when choosing the appropriate cut-off value. Third, we did not discuss the effect of vasoactive drugs on SVV because of lack of relevant data. Fourth, most studies on cardiac surgery patients involved coronary artery surgery, which prevents us from applying our conclusions to all cardiac surgery types. Therefore, multicentre and large-sample studies should be performed.

There are also several strengths in our research. First, this is the first diagnostic meta-analysis studying the utility of SVV in predicting responsiveness to fluid therapy of patients undergoing cardiac and thoracic surgery. Second, most of our included studies are of high quality. Third, we used three different software to compare the predictive value of SVV between subgroups, so our results have high credibility.

CONCLUSION

SVV had excellent predictive performance in patients accepting cardiac surgery in OR and ICU and had good predictive performance in patients accepting thoracic surgery with OLV. Colloid infusion, high VT (≥8), and non-PEEP ventilation can effectively improve the accuracy of SVV in both thoracic and cardiac surgery. PLR was more suitable for ICU, whereas fluid challenge is more appropriate for OR. When performing fluid challenge, a large bolus in thoracic surgery and a small bolus in cardiac surgery were the preferred options. To monitor SVV, the FloTrac/Vigileo system was better than the PiCCO system in thoracic surgery.

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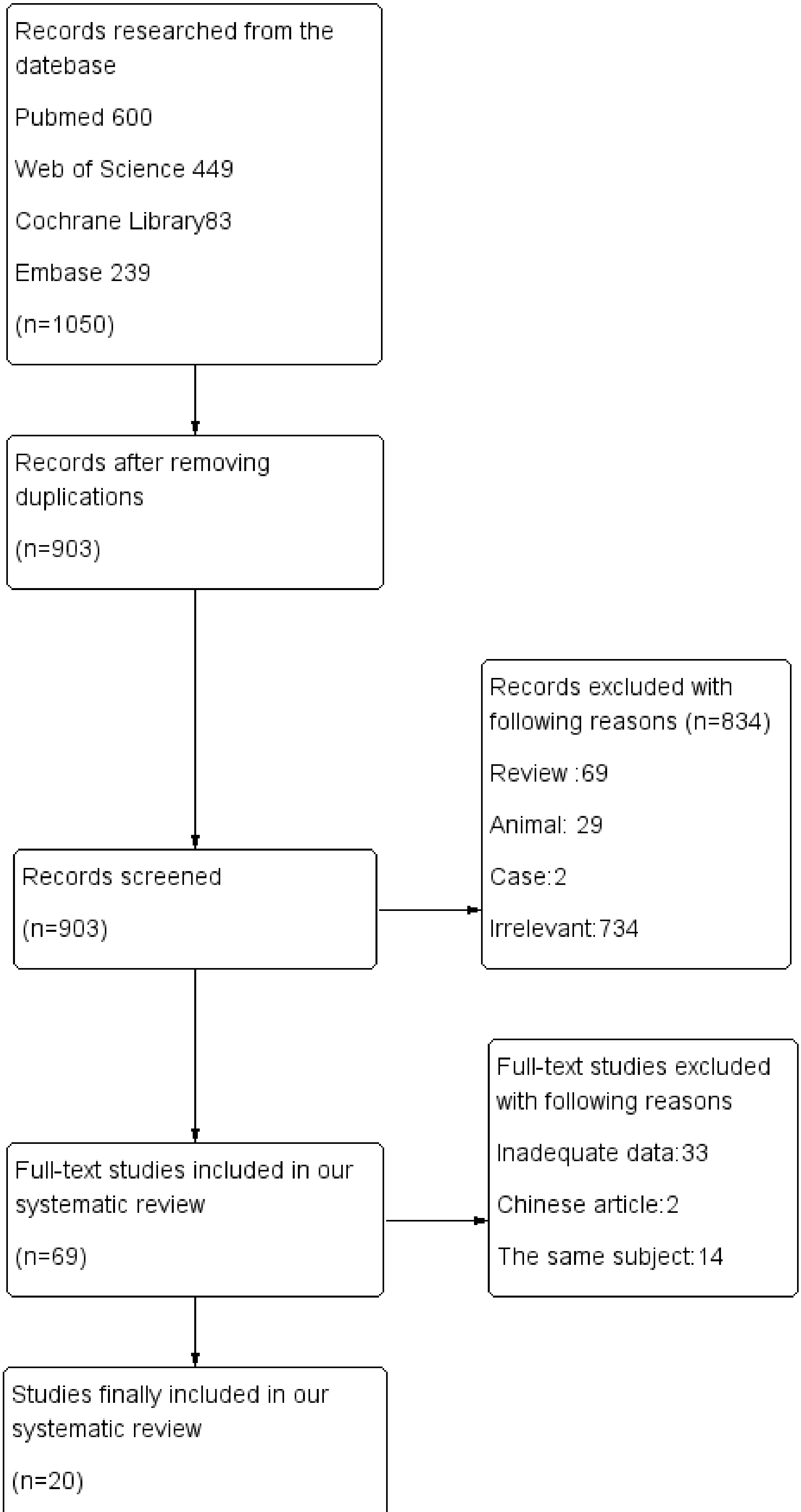
Competing interests: None declared.

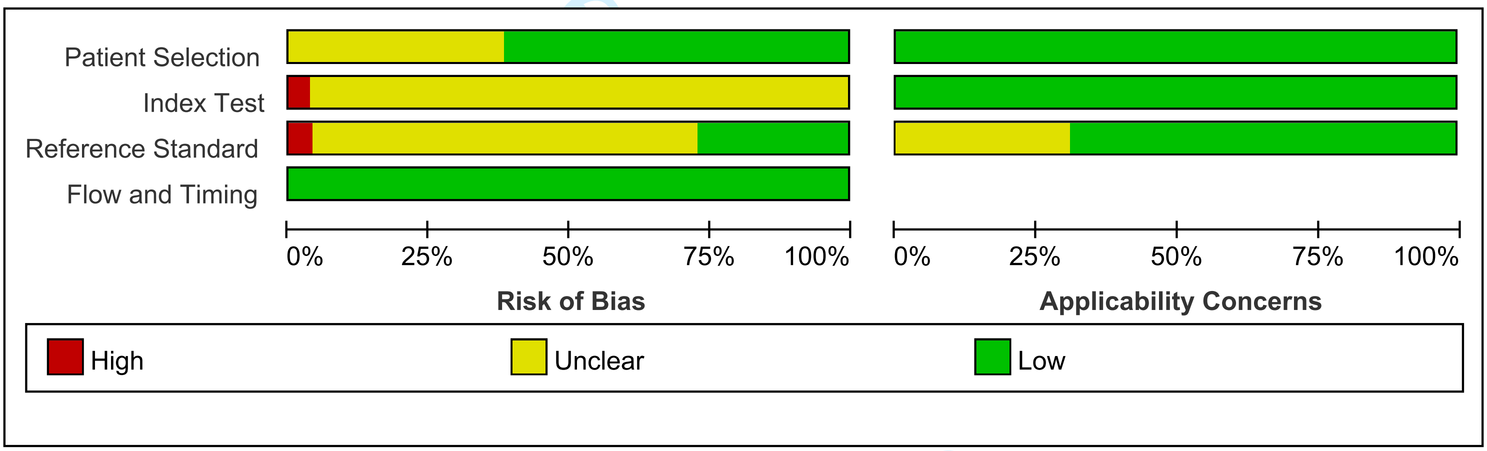
Data availability statement: All data relevant to the study are included in the article or uploaded as online supplemental information. No additional data available.

Fig. 1 The search, included and exclusion of the literature

Fig. 2 The result of quality assessment of the included articles (overview)

Fig. 3 The result of quality assessment of each articles


Records researched from the datebase
Pubmed 600
Web of Science 449
Cochrane Library83
Embase 239
(n=1050)
Records after removing duplications
(n=903)
Records excluded with following reasons (n=834)
Review :69
Animal: 29
Case:2
Irrelevant:734
Records screened
(n=903)
Full-text studies excluded with following reasons
Inadequate data:33
Chinese article:2
The same subject:14
Full-text studies included in our systematic review
(n=69)
Studies finally included in our systematic review
(n=20)


Patient Selection
Index Test
Reference Standard
Flow and Timing
0%
25%
50%
75%
100%
Risk of Bias
Applicability Concerns
High
Unclear
Low

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Belloni 2008	+	−	−	+	+	+	+
Broch 2011	?	?	?	+	+	+	+
Broch 2012	?	?	?	+	+	+	+
Cannesson 2009	+	?	?	+	+	+	+
De Waal 2009	+	?	?	+	+	+	+
Fischer 2013	+	?	?	+	+	+	+
Fu 2014	+	?	?	+	+	+	+
Fu 2015	+	?	?	+	+	+	+
Geerts 2011	+	?	?	+	+	+	+
Haas 2012	+	?	?	+	+	+	+
Hofer 2005	+	?	+	+	+	+	?
Hofer 2008	+	?	+	+	+	+	?
Jeony 2017	+	?	?	+	+	+	+
Kang 2014	+	?	?	+	+	+	+
Kang 2016	+	?	?	+	+	+	?
Kim 2013	+	?	+	+	+	+	+
Kobayashi 2009	+	?	?	+	+	+	?
Miñana 2020	+	?	?	+	+	+	+
Montenij 2016	?	?	?	+	+	+	+
Presiman 2005	?	?	+	+	+	+	+
Reuter 2002	?	?	+	+	+	+	+
Reuter 2003	?	?	+	+	+	+	+
Rex 2007	?	?	+	+	+	+	?
Suehiro 2010	?	?	?	+	+	+	?
Suehiro 2011	?	?	?	+	+	+	?
Wyffels 2010	?	?	?	+	+	+	?

− **High** ? **Unclear** + **Low**

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Page 1 (**Title**)
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Page 1 , 2 (**Abstract**)
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 1 , 2 (**Background**)
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page1 , 2 (**Background**)
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Page 3 (**Methods**)
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Page 4 (**Eligibility criterial**)
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 4 (**Search strategy**)
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Page 4 (**Search strategy**)
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 4 (**Data Extraction**)
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 4 (**Data Extraction**)
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Page 4 (**Data**

PRISMA 2009 Checklist

			Extraction)
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Page 4，5 (**Quality assessment**)
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Page 5 (**Statistical treatment)**
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Page 5 (**Statistical treatment)**

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Page 5 (**Statistical treatment)**
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Page 6 (**Identification of eligible studies characteristics of the studies** , Fig. 1**)**
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Page 6 (**Characteristics of the studies,** Table 1, 2)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Page 6 (**Assessment of study quality and publication**

PRISMA 2009 Checklist

			bias)
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Page 5, 6 (**Outcome of literature search and study characteristics**)
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Page 14 (**Results of our meta-analysis, Comparison between subgroups**)
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Page 6 (**Assessment of study quality and publication bias,** Table 4**)**
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Page 13, 14 (**Heterogeneity**)
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Page 16, 17, 18, 19 (**Discussion**)
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Page 19 **(Limitations)**
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page20 (**Conclusions)**
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	**N/A**

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

Stroke volume variation for predicting responsiveness to fluid therapy in patients undergoing cardiac and thoracic surgery: A systematic review and meta-analysis

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Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Anaesthesia, Cardiovascular medicine, Surgery
Keywords:	Thoracic surgery < SURGERY, Cardiac surgery < SURGERY, Anaesthesia in cardiology < ANAESTHETICS, ANAESTHETICS

Stroke volume variation for predicting responsiveness to fluid therapy in patients undergoing cardiac and thoracic surgery: A systematic review and meta-analysis

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Word count: 4971

Keywords: Stroke volume variation; Fluid responsiveness; Thoracic surgery; Cardiac surgery; Meta-analysis

Abstract

Objective: To evaluate the reliability of stroke volume variation (SVV) for predicting responsiveness to fluid therapy in patients undergoing cardiac and thoracic surgery.

Design: Systematic review and meta-analysis.

Data sources: PubMed, EMBASE, Cochrane Library, Web of Science up to August 9, 2020.

Methods: Quality of included studies were assessed with the QUADAS-2 tool. We conducted subgroup analysis according to different anesthesia and surgical method with Stata V.14.0, Review Manager V.5.3 and R V.3.6.3. We used random-effects model to pool sensitivity, specificity, and diagnostic odds ratio (DOR) with 95% CI. The area under the curve (AUC) of receiver operating characteristic (ROC) was calculated.

Results: Among the 20 relevant studies, 7 were conducted during thoracic surgery, 8 were conducted during cardiac surgery and the remained 5 were conducted in intensive critical unit (ICU) after cardiac surgery. Data from 854 patients accepting mechanical ventilation were included in our systematic review. The pooled sensitivity and specificity were 0.73 (95％CI 0.59-0.83) and 0.62 (95％CI 0.46-0.76) in the thoracic surgery group, 0.71 (95％CI 0.65-0.97) and 0.76 (95％CI 0.69-0.82) in the cardiac surgery group, 0.85 (95％CI 0.60-0.96) and 0.85 (95％CI 0.74-0.92) in cardiac ICU group. The AUC was 0.73 (95% CI 0.69-0.77), 0.80 (95% CI 0.76-0.83), and 0.89(95% CI 0.86-0.92), respectively. Results of subgroup of FloTrac/Vigileo system (AUC =0.80, Youden index =0.38) and large tidal volume (TV) (AUC =0.81, Youden index =0.48) in thoracic surgery, colloid (AUC =0.85, Youden index =0.55) and postoperation (AUC =0.85, Youden index =0.63) in cardiac surgery, passive leg raising (PLR) (AUC =0.90, Youden index =0.72) in cardiac ICU were reliable.

Conclusion: SVV had good predictive performance in cardiac surgery or ICU after cardiac surgery and had fair predictive performance in thoracic surgery. Nevertheless, technical and clinical variables may affect the predictive value potentially.

Strengths and limitations of this study:

- As far as we know, this is the first systematic review and meta-analysis discussing the predicative value of fluid responsiveness of SVV during thoracic and cardiac perioperation.
- We assessed the included studies with QUADAS-2 tool in Review Manager V.5.3 to ensure their quality.
- Three different software (Stata V.14.0, Review Manager V.5.3, and R V.3.6.3) were used to compare the predictive value of SVV between different subgroups.
- A limitation was the existence of overall heterogeneity among our included studies.
- We did not discuss whether the SVV is suitable for children in thoracic and cardiac surgery due to a lack of relevant studies.

Introduction

Fluid therapy is the most important factor for maintaining a stable internal environment during perioperative period, especially in thoracic and cardiac surgery.[1] In recent years, more and more studies have showed that goal directed fluid therapy (GDFT) can provide individual treatment for patients, preventing perioperative patients from potentially hypervolemia or hypervolemia and reducing complications or mortality. According to Frank Starling's curve,[2] the preload of the ventricle is proportional to the cardiac output (CO) in the raising stage. However, if the preload reaches the platform stage, fluid therapy would not yield the desired effect but result in cardiac overload and tissue edema.[3 4] Therefore, it is urgent to find an effective method of hemodynamics monitoring sensitive to fluid responsiveness.

Anaesthetists previously tended to use traditional hemodynamic indicators to monitor hemodynamics and predict fluid responsiveness, such as central venous pressure (CVP), pulmonary artery diastolic pressure (PADP), and cardiac index (CI). [5] However, it was of limited utility in reflecting actual ventricular preload, which may be affected by many non-cardiovascular factors. On the other hand, although transoesophageal echocardiography (TEE), serving as a gold standard of evaluating cardiac function, has indisputable advantages in monitoring ventricular preload and guiding fluid therapy, its complex manipulations and potential complications prevent it from being widely used in thoracic and cardiac surgery.[6] Stroke volume variation (SVV) offers a good middle ground between them, and combine their superiority and security during perioperative peroid.[7]

SVV means the variation of stroke volume (SV) in 30 seconds and was considered a reliable parameter under the condition of closed chest.[8] It reflects the effect of respiratory movement on venous return. During inspiration of mechanical ventilation, the increase of intrapulmonary pressure significantly decreases the negative intrapleural pressure, thereby decreasing venous return and CO. During expiration, the opposite changes occur.[9] When the body has insufficient circulating blood volume, the variation of SV fluctuates obviously with the switching between inspiratory and expiration. Thus, the fluid responsiveness can be predicted according to SVV, so as to judge the condition of blood volume. Toyoda et al[10] reported a curvilinear relationship between the right ventricular end-diastolic volume index (RVEDVI) and SVV. They found the regression curve accorded better with SVV than with CVP or PADP, showing its reliable predictive value of RVEDI.

Several meta-analysis have synthesised present evidence and evaluated the reliability of SVV in common surgery of children and adults, but there was still no a systematic review discussing whether SVV could be applied for thoracic and cardiac surgery. Lots of trials have been conducted to investigate this issue.[11-30] Unfortunately, they haven't been able to reach a consensus so far. A series of studies proved good reliability of SVV in predicting fluid responsiveness during such surgery.[11 16 18 20-22 24-25 27-30] However, some other studies are not convincing due to different anesthesia and surgical strategy, such as model of mechanical ventilation, position, method of fluid therapy, moment of maneuvers, etc.[12-15 17 19 23 26] Fu et al[12]and Suehiro et al[17]reported that SVV was not suitable for thoracic surgery when a protection ventilation was conducted. Miñana et al[15] found that SVV successfully predicted fluid responsiveness only in thoracoscopy but not thoracotomy. Moreover, Fishcher et al[26] reported that SVV also could not give a good performance within the first 6 post-operative hours in cardiac ICU. There seems to be a great deal of debate about which anesthesia or surgical strategy SVV is more appropriate for in thoracic and cardiac surgery. However, no large-sample study has been conducted to evaluate the utility of SVV in such conditions and surgery. The purpose of this meta-analysis was to review relevant literatures and systematically evaluate the predictive value of SVV in such surgery, and provide evidence and guidance for the clinical application of SVV.

METHODS

The meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement issued in 2009.[31]

Description of investigated indices

SVV is the ratio of the difference between the maximum and the minimum of the SV and the mean of the SV during 30 seconds as follows: $(SV_{max} - SV_{min})/SV_{mean}$.

Eligibility criterial

We included diagnostic trials evaluating the accuracy and effectiveness of SVV in predicting fluid responsiveness in the operating room (OR) and ICU. We excluded review articles, commentaries, case reports and research papers on animal or in vitro experimental studies. In addition, we also excluded studies of which the subjects were pregnant women or patients with spontaneous breathing, sepsis, shock, and arrhythmia.

Search strategy

We searched PubMed, Web of Science, EMBASE, and the Cochrane Library database for relevant literature by using searching terms such as SVV, stroke volume variation, responsiveness, and predict. The full search strategy was described in the online supplemental file. The initial search was conducted on August 9, 2020 with a language restriction of English.

Data extraction and quality assessment

Backgrounds and conclusions of the included literatures were screened independently by two authors, following the inclusion and exclusion criteria. Then, the full content was read in detail. Disagreements or discrepancies were resolved by discussion with the third author. The information was extracted from the included studies as follows: study characteristics (last name of the first author, publication year, sample number, operations, fluid therapy, reference standard, position, TV, positive end-expiratory pressure, endoscopy, and moments of manoeuvers) and outcome indicators (TP, FP, TN, FN, sensitivity, specificity, best cut-off, AUC, and correlation coefficient). When there were insufficient or missing data, one author contacted the corresponding author of the included article to obtain the necessary data.

The quality of our included studies was assessed by two authors independently using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) in Review Manager 5.3(Cochrane Library, Oxford, UK).[32] QUADAS-2 mainly consists of four parts (case selection, trials to be evaluated, gold standard, case process and progress). All components would be assessed in terms of bias risk, and the first three components would also be assessed in terms of clinical. In addition, publication bias was also checked using Deeks' Funnel Plot Asymmetry Test in Stata V.14.0.[33] quality assessment was performed independently by two authors. Disagreements were reconciled through discussion until a consensus was reached.

Statistical treatment and Quality assessment

The Stata software V.14.0 was used for basic calculations. Subgroup analysis on primary outcomes stratified by intervention, TV, positive end-expiratory pressure (PEEP), position, endoscopy and moments of maneuvers was conducted. When the number of included studies within some subgroups was less than four, not meeting the minimum requirements of Stata V.14.0, we used Review Manager V.5.3 and R V.3.6.3 to process data in these subgroups. For comparing the AUC, the Review Manager V.5.3 could only display the summary receiver operating characteristics (SROC) and the R V.3.6.3 could only give the result of mean AUC. The operative performance is graduated as follows:

o AUC 0.9-1 excellent operative performance

o AUC 0.8-0.9 good operative performance.

o AUC 0.7-0.8 fair operative performance.

We used correlation (Mixed Model) of Stata to evaluate whether a threshold effect existed. When the correlation was positive and its P value was >0.05, no threshold effect was considered to exist. We then used a random-effects model to calculate pooled sensitivity, specificity and AUC with 95% CI. Statistical heterogeneity was estimated using the Cochrane Q and I^2 tests,[34] and it was considered to be present when $I^2 > 50$ % or $P < 0.05$. In such cases, meta-regression analysis and sensitivity analysis were used to determine the sources of heterogeneity.

Patient and public involvement

Patient and public involvement is not applicable for this meta-analysis.

RESULTS

Outcome of literature search and study characteristics

Of the 795 related articles, 645 articles remained after eliminating duplicates. Then, we excluded 576 articles because they were case reports, review articles, articles related to animal experiments or other irrelevant studies. Among the remaining 69 articles, 14 studies repeated the same content, two studies were not published in English, and data of our interest could not be obtained for 33 articles. Finally, 20 articles were included in our meta-analysis (figure 1).

The 20 articles included 854 patients. The main kinds of monitoring systems were FloTrac/Vigileo system and PiCCO system. Geerts et al[28] used pulmonary artery catheter insertion to measure thermodilution CO and CVP. Kang et al[29] used Swan-Ganz and NICOM monitors to detect SV and calculate SVV. We defined TV < 8 ml/kg as 'low TV' and TV ⩾ 8 ml/kg as 'high TV'; absence of PEEP or PEEP < 5 mmHg was considered non-PEEP. When the infusion volume was set above 5 ml/kg or 250 ml, we considered the study to involve a large bolus group. If not, it was considered a small bolus group. Some patients in the same study accepted fluid challenge with two different systems[27] or accepted different methods of TV ventilation.[12 17] We included both conditions of these studies in our meta-analysis. The basic characteristics of our included studies are presented in Table 1 and Supplementary Table1.

Table 1: The characteristics of the included studies

Study	Year	Surgery	Number	Standard	Intervention	Result	Device	PEEP (mmHg)	TV (ml/kg)	Position	Endoscope	Moment of maneuver
Thoracic surgery												
Kang et al[11]	2016	Pulmonary lobectomy	76	△SVI＞25%	10 ml/kg colloid	Yes	FloTrac-Vigileo system	0	4	Supine	NO	After lung recruitment maneuver and thorax closure.
Fu et al[12]	2015	Esophagectomy	24	△CI＞15%	7 mL/kg colloid	No Yes	FloTrac-Vigileo system	5	6 8	Lateral	YES	After the procedure of laparoscopic part.
Fu et al[13]	2014	Pulmonary lobectomy	30	△CI＞10%	8 mL/kg colloid	NO	PiCCO system	0	8	Lateral decubitus	NO	Before, and within 30s after volume expansion （VE）without stimulation.
Miñana et al[14]	2020	open lung resection	76	△CI＞10%	250ml crystalloids	NO	PiCCO system	5	6	lateral	NO	Once the patient had been placed lateral, with the chest open.
Jeong et al[15]	2017	Lung cancer surgery	79	△CI＞10%	7 ml/kg colloid	No	FloTrac-Vigileo system	5	6	Lateral	Dispute	15 minutes after the start of OLV, before and after finishing fluid loading.
Suehiro et al[16]	2010	Lobectomy	30	△CI＞25%	500ml colloid	Yes	FloTrac-Vigileo system	5	8	Lateral	YES	Before and after volume loading.
Suehiro et al17	2011	Lobectomy	37	△CI＞15%	500ml colloid	No Yes	FloTrac-Vigileo system	5	6 8	Lateral	YES	30 min after starting OLV.
Cardiac surgery												
Kim et al[18]	2013	Coronary surgery	33	△SVI＞12%	500ml colloid	Yes	FloTrac-Vigileo system	5	10	NA	NA	Before sternotomy to maintain consistency of the closed thorax.
Montenij et al[19]	2016	CABG	22	△CO＞15%	7ml/kg crystalloid	NO	FloTrac-Vigileo system	5-10	8	NA	NA	Between induction of anaesthesia and incision.
Broch et al[20]	2011 2011	CABG	81	△SVI＞12%	PLR	Yes	PiCCO system	5	8	NA	NA	After induction of anesthesia before surgery.
Broch et al[21]	2012	CABG	92	△SVI＞15%	PLR	Yes	PiCCO system	5	8	NA	NA	After induction of anesthesia before surgery.
Hofer et al[22]	2005	Off-Pump CABG	40	△SVI＞25%	10mL/kg colloid	Yes	PiCCO system	0	10	NA	NA	Prior to any surgical intervention or volume replacement.
Preisman et al[23]	2005	CABG	18	△SVI＞15%	250ml colloid	NO	TEE,PiCCO	15-20	8-10	NA	NA	After the induction of anaesthesia, after the end of the operation, and before transfer to the ICU.
Haas et al[24]	2012	Cardiac Surge	18	△CI＞10%	4 mL/kg colloid	Yes	PiCCO system	5	8	NA	NA	After completion of cardiac surgery and thoracic closure.
Cannesson et al[25]	2009 2009	CABG	25	△CI＞15%	500ml colloid	Yes	FloTrac-Vigileo system	0-2	8-10	NA	NA	After a 3 min period of hemodynamic stability.
ICU after cardiac surgery												
Fischer et al[26]	2013	ICU	37	△CI＞15%	500ml colloid	No	PiCCO s	NA	NA	NA	NA	within the first 6 post-operative hours
Hofer et al[27]	2008	ICU	40	△SV＞25%	PLR	Yes	PiCCO system FloTrac-Vigileo system	5	8-10	NA	NA	After transfer of patients to the intensive care unit.

Geerts et al[28]	2011	ICU	20	△CO>7%	PLR	Yes	Pulmonary artery catheter	5	8-10	NA	NA	NA
Kang et al[29]	2014	ICU	54	△CO>7%	PLR	Yes	Swan-Ganz NICOM	5	10	NA	NA	NA
De Waal et al[30]	2009	ICU	22	△SVI>12%	7ml/kg colloid	Yes	PiCCO system	5	8	NA	NA	After stabilization of the patients arrivingl in the ICU.

PEEP, positive end-expiratory pressure; SV, stroke volume; TV, tidal volume; PLR, passive leg raising; VATS, video-assisted thoracic surgery; CPB, cardiopulmonary bypass; VE, volume expansion; ICU, intensive critical unit; CABG, coronary artery bypass grafting.

Assessment of study quality and publication bias

The quality of the 20 included studies was assessed with the QUADAS-2 tool. The result showed most of our included studies were of good quality (Fig. 2 and Fig. 3).

After using Deeks' Funnel Plot Asymmetry Test to evaluate publication bias, we found the P value of bias to be 0.870, 0.617, and 0.546 for studies mentioning thoracic surgery, cardiac surgery, and cardiac ICU, indicating that no significant publication bias existed in our included studies.

Results of our meta-analysis

Analysis of the data using the Stata/MP 14.0, we found the Spearman correlation coefficient of the thoracic surgery, ICU, and cardiac surgery groups was -0.43 (P = 0.18), -1.0 (P = 1.0), and 1.0 (P = 1.0), respectively, which indicated that there was a significant threshold effect in the thoracic surgery and ICU groups, but there was no significant threshold effect in the cardiac surgery group.

In the thoracic surgery and ICU groups, the AUC of SROC was 0.73 (95% CI 0.69–0.77) and 0.89 (95% CI 0.89–0.92), respectively. The Cochrane-q value of their AUC was 25.829 (P < 0.001, I^2 = 92%) and 15.791 (P < 0.001, I^2 = 87%), indicating significant heterogeneity in both groups.

In the cardiac surgery group, the pooled sensitivity was 0.71 (95% CI 0.65–0.77) and the pooled specificity was 0.76 (95% CI 0.69–0.82). The positive likelihood ratio was 3.0 (95% CI 2.3–3.9), the negative likelihood ratio was 0.38 (95% CI 0.30–0.47), and the diagnostic ratio was 8 (95% CI 5–12). The Cochrane-q value of AUC was > -0.001 (P = 0.5, I^2 = 95%), indicating significant heterogeneity.

Heterogeneity

Meta regression analysis showed that monitoring devices (P < 0.05) in the thoracic surgery group and types (P < 0.01) and volume of fluid infusion (P < 0.01) in the cardiac surgery group were significant reasons for heterogeneity. There was no significant reason to explain the heterogeneity in the ICU group ($P < 0.05$).

However, subgroup analysis revealed high heterogeneity (>50%) in all subgroups, which may be attributed to management of surgery and anaesthesia, patient comorbidities, timing of performing fluid challenge, speed of fluid infusion, etc.

Results of sensitivity analysis showed that only in the thoracic surgery group one study[15] may contribute to the heterogeneity. Despite excluding this study, the heterogeneity was still significant ($I^2 = 63\%$). Therefore, we concluded that heterogeneity was inevitable and the results were stable.

Comparison between subgroups

The results of our subgroup analysis were showed as follows. When the sample number of subgroups sample was larger than 4, Stata V.14.0 was used to compare the difference between subgroups. In thoracic surgery, the AUC and Youden index of subgroup of lateral position were 0.71(95% CI 0.67–0.75) and 0.31. The AUC and Youden index of subgroup of supine position were 0.82(95% CI 0.73–0.92) and 0.53. The AUC and Youden index of subgroup of colloid were 0.76(95% CI 0.72–0.79) and 0.36. The AUC and Youden index of subgroup of crystalloid were 0.47(95% CI 0.30–0.65) and 0.18. The AUC and Youden index of subgroup of large bolus infusion were 0.76(95% CI 0.72–0.79) and 0.36. The AUC and Youden index of subgroup of small bolus infusion were 0.47(95% CI 0.30–0.65) and 0.18. The AUC and Youden index of subgroup of large TV were 0.71(95% CI 0.67–0.75) and 0.31. The AUC and Youden index of subgroup of small TV were 0.67(95% CI 0.63–0.71) and 0.27. In cardiac surgery, the AUC and Youden index of subgroup of crystalloid were 0.70(95% CI 0.47–0.92) and 0.25. The AUC and Youden index of subgroup of colloid were 0.85(95% CI 0.81–0.88) and 0.55.

When the sample number of subgroups was smaller than 4, R V.3.6.3 was used to calculated the pool sensitivity, pool specificity, and mean AUC, and Review manager V.5.3 was used to compare the difference between AUC of SROC of subgroups. In thoracic surgery, the mean AUC and Youden index of subgroup of thoracoscopy were 0.73 and 0.38. The mean AUC and Youden index of subgroup of thoracotomy were 0.67 and 0.32. The result of Review Manager V.5.3 showed that AUC of thoracoscopy was larger than that of thoracotomy. The mean AUC and Youden index of subgroup of FloTrac/Vigileo system were 0.80 and 0.38. The mean AUC and Youden index of subgroup of PiCCO system were 0.42 and 0.19. The result of Review Manager V.5.3 showed that AUC of FloTrac/Vigileo system was larger than that of PiCCO system. The mean AUC and Youden index of subgroup of non-PEEP were 0.74 and 0.39. The mean AUC and Youden index of subgroup of PEEP system were 0.67 and 0.33. The result of Review Manager V.5.3 showed that AUC of non-PEEP system was larger than that of PEEP.

In cardiac surgery, the mean AUC and Youden index of subgroup of FloTrac/Vigileo system were 0.73 and 0.46. The mean AUC and Youden index of subgroup of PiCCO syetem were 0.66 and 0.48. The result of Review Manager V.5.3 showed that AUC of FloTrac/Vigileo system was smaller than that of PiCCO system. The mean AUC and Youden index of subgroup of small bolus infusion were 0.86 and 0.62. The mean AUC and Youden index of subgroup of large bolus infusion were 0.73 and 0.46. The result of Review Manager V.5.3 showed that AUC of small bolus infusion was larger than that of large bolus infusion. The mean AUC and Youden index of subgroup of postoperation were 0.85 and 0.63. The mean AUC and Youden index of subgroup of preoperation were 0.70 and 0.41. The result of Review Manager V.5.3 showed that AUC of postoperation was larger than that of preoperation. The mean AUC and Youden index of subgroup of non-PEEP were 0.77 and 0.53. The mean AUC and Youden index of subgroup of PEEP were 0.67 and 0.47. The result of Review Manager V.5.3 showed that AUC of non-PEEP was larger than that of PEEP. The mean AUC and Youden index of subgroup of fluid challenge were 0.73 and 0.52. The mean AUC and Youden index of subgroup of PLR were 0.65 and 0.47. The result of Review Manager V.5.3 showed that AUC of fluid challenge was larger than that of PLR.

In cardiac ICU, the mean AUC and Youden index of subgroup of PLR were 0.90 and 0.72. The mean AUC and Youden index of subgroup of fluid challenge were 0.73 and 0.41. The result of Review Manager V.5.3 showed that AUC of PLR was larger than that of fluid challenge. The details are presented in Table 2.

Table.2 The results of subgroup meta-analysis

Subgroups	Number	State V.14.0				Revman V.5.3	R V.3.6.3	
		AUC(95% CI)-ROC	Sensitivity(95% CI)	Specificity(95% CI)	DOR(95% CI)	Result of AUC comparison	AUC	Youden index
Thoracic surgery	**9**	0.73(0.69-0.77)* △	0.73(0.59-0.83)	0.62(0.46-0.76)	4 (2-10)			0.35
Lateral position	8	0.71(0.67-0.75) ◇	0.69(0.55-0.81)	0.62(0.43-0.77)	4 (2-8)			0.31
Supine position	1	0.82(0.73-0.92)	0.87(0.85-0.89)	0.66(0.63-0.69)	-			0.53
Thoracoscopy	3					High	0.73	0.38
Thoracotomy	5					Low	0.67	0.32
Colloid	8	0.76（0.72-0.79）	0.77(0.66-0.85)	0.59(0.42-0.74)	5 (2-11)			0.36
Crystalloid	1	0.47（0.30-0.65）	0.36	0.82	-			0.18
Large bolus	8	0.76（0.72-0.79）	0.77(0.66-0.85)	0.59(0.42-0.74)	5 (2-11)			0.36
Small bolus	1	0.47（0.30-0.65）	0.36	0.82	-			0.18
FloTrac/Vigileo	6					High	0.80*	0.38
PiCCO	2					Low	0.42	0.19
PEEP	6					Low	0.67	0.33
Non-PEEP	2					High	0.74	0.39
Large TV	4	0.81 [0.77-0.84] ◇	0.73(0.58-0.85)	0.75(0.58-0.86)	8 (3-26)			0.48
Small TV	5	0.67 [0.63-0.71]	0.73(0.50-0.83)	0.54(0.32-0.74)	3 (1-8)			0.27
Cardiac surgery	**8**	0.80(0.77-0.83)△	0.71(0.65-0.77)	0.76(0.69-0.82)	8 (5-12)			0.47
FloTrac/Vigileo	3					Low	0.73	0.46
PiCCO	5					High	0.66	0.48
Large bolus	4					Low	0.73	0.46
Small bolus	2					High	0.86	0.62
Crystalloid	1	0.70（0.47-0.92）	0.56	0.69	-			0.25
Colloid	5	0.85 (0.81-0.88)	0.79(0.70-0.86)	0.76(0.67-0.84)	12 (6-25)			0.55
Preoperation	6					Low	0.70	0.41
Postoperation	2					High	0.85	0.63
Peep	6					Low	0.67	0.47
Non-Peep	2					High	0.77	0.53
Fluid challenge	6					High	0.73	0.52
PLR	2					Low	0.65	0.41

ICU after cardiac surgery	**6**	0.88(0.86-0.92)*	0.85(0.60-0.96)	0.85(0.74-0.92)	32 (9-108)			0.70
Fluid challenge	2					Low	0.73	0.41
PLR	4					High	0.90	0.72

PEEP, positive end-expiratory pressure; TV, tidal volume; PLR, passive leg raising; ICU, intensive critical unit; AUC, area under curve; DOR, diagnostic Odds Ratio.

* P <0.05 compared to cardiac surgery group

△ P<0.05 compared to ICU group

◇ P<0.05 compared within subgroup

DISCUSSION

Fluid therapy is essential during perioperative period. Unfortunately, it is often ignored and anesthesiologists just simply estimated infusion volume based on their experience or conventional indicators. Precise prediction of responsiveness to fluid therapy could greatly reduce the risk of heart failure or tissue edema. SVV has been proved to have a good performance in various kinds of surgery. However, there was still much contradiction in whether SVV could be applied in thoracic or cardiac surgery.

In this study, we systematically reviewed the relevant literatures about reliable and effectiveness of SVV in above-mentioned surgery. A total of 20 studies were included, involving 854 participants accepting thoracic and cardiac surgery to assess predictive value of SVV. Regarding the quality of included studies, most studies had good description of design and protocol so that the overall quality was rated as medium to high quality.

Previous studies have disputed the diagnostic value of SVV during thoracic and cardiac surgery, mainly due to different anesthesia or surgical factors, such as ventilation mode, rehydration method, intervention moments, operative position, etc. Our study found that SVV had good predictive performance in monitoring patients accepting cardiac surgery in OR (AUC=0.80) and ICU (AUC=0.89) and fair predictive performance in patients accepting thoracic surgery (AUC=0.73). In addition, SVV was recommended in the condition of low TV, FloTrac/Vigileo system, non-PEEP, thoaracoscopy, supine, colloid infusion of large bolus during thoracic surgery, condition of FloTrac/Vigileo system, postoperation, non-PEEP, fluid challenge, and colloid infusion of small bolus during cardiac surgery, and condition of PLR in cardiac ICU. Next, we would discuss the potential impact of different anesthesia management or surgical manipulation on the reliability of SVV.

Protective ventilation, defined as low TV, low inhaled oxygen (FIO2), and PEEP, has recently been widely advocated in thoracic surgery with one-lung ventilation (OLV). However, our meta-analysis found that it may negatively affect accuracy of SVV. Ventilation volume rather than airway pressure is the key factor determining pleural pressure and right ventricular preload.[35] When TV decreased, the Frank starling curve of the left ventricle markedly moved to the right, making the variation in systolic pressure insignificant. Low TV would not cause significant variation in SV especially in the condition of hypovolemia.[17] Alvarado et al[36] found that low PEEP (0–10 mmHg) had no significant effect on cardiac preload due to release of most pressure generated from the ventilator to the atmosphere[16], whereas high PEEP (10–15 mmHg) would mistakenly make SVV predict actual blood volume[37]. This phenomenon would become more evident in OLV, in agreement with our result. However, another study reported an opposite conclusion that SVV is not affected by PEEP or driving pressures[36], which may be explained by the difference between OLV and normal ventilation. This suggests that the effect of respiratory pressure and TV on SVV depends primarily on the degree to which these variables transmitted to the pulmonary circulation, rather than absolute value. As far as our result were concerned, high TV without PEEP may be better recommended in thoracic surgery when SVV monitoring. This may also be the reason for the high accuracy of SVV in perioperative patients with cardiac surgery, because all patients received normal mechanical ventilation with 8 ml/kg TV and non-PEEP. However, it cannot be ignored that the use of non-protective ventilation during period of OLV may cause damage to the healthy lung. In total, the applicability of SVV in thoracic surgery is fair and limited.

We found that fluid therapy with large bolus had better reliability of SVV in thoracic surgery, whereas small bolus fluid therapy was more recommended in cardiac surgery. Patients undergoing cardiac surgery usually have cardiac dysfunction, not tolerating a large bolus during in a short period, whereas in thoracic surgery patients often experience heavy bleeding and need large bolus of colloid to maintain body blood volume. Regarding the type of fluid, the colloid rather than crystalloid could quickly compensate for fluid loss to achieve satisfactory CO[8] and significantly increase RVEDVI.[38] Ma et al[39] found that PLR could replace fluid challenge as a more effective intervention in protection ventilation patients during cardiac surgery. By transfer of approximately 300 ml of venous blood from the lower body toward the right heart, PLR can mimic a fluid challenge and increase systemic filling pressure without influencing vascular resistance. However, our result showed that fluid challenge has larger AUC than PLR in cardiac surgery, and PLR was more suitable for ICU patients, especially those with cardiovascular dysfunction.[29] Precious systematic review has showed that the change of CO and pulse press induced by PLR can reliably predict the response of CO to volume expansion in adult patients with acute circulatory failure. The preload of right and left ventricles was increased to a sufficient extent to induce fluid responsiveness, having the same effect as the liquid challenge. PLR has been proposed by consensus conference of the European Society of Intensive Care Medicine for a long time and became a useful maneuver of predict fluid responsiveness in the high-risk patients.[40 41]

As to monitoring device, FloTrac/Vigileo system was better recommended in thoracic surgery. It has lower thresholds than the PiCCO system and predicts the insufficiency of blood volume earlier with good sensitivity even if the wave of hemodynamic status remained weak in OLV.[27] In addition, it need no calibration and was less affected by arterial compliance and elasticity.[42] However, misestimation of blood volume may happen when a rapid wave of CO occurs.[43] The PiCCO system can be used only after correction for low-temperature saline, and it is difficult to continuously calibrate the system during surgery in cases of heavy bleeding.[44] It was reported that latest version of PiCCO system incorporates adapted vascular compliance measurement from every 10 minutes to every one minute based on a modification algorithm[45], giving a more accurate result of SVV. Wiesenack et al[46] reported a significant correlation between baseline SVV and changes of SVI after updating the algorithm of PiCCO system, which was opposite to their previous negative result. Therefore, the version update of monitoring device may make SVV more and more suitable for difficulty conditions.

Our analysis did not include studies with arrhythmia patients because it is reported that wide pulse pressure could seriously affect accuracy of SVV[18]. Similarly, in shock patients or patients with heart failure, the diagnostic value of SVV was greatly limited[47]. However, Cannesson et al[48]reported that a new SVV algorithm using multi-parameter signal recognition to reject ectopic beats could work well even in patients with arrhythmia. Heart failure could seriously decrease the ventricular output due to the increasing afterload during inspiration[49]. Right ventricular dysfunction would also lead to false positive prediction of preload[50]. Interestingly, some studies found that SVV applied in patients with slightly impaired LV function ($50\% \geq EF \geq 30\%$) still had good values .[10 23] This showed that SVV may have a potential value in predicting fluid responsiveness of patients with mild cardiac dysfunction. Moreover, we found monitoring after main operative manipulation had a better predictive value than that monitoring before that, which may result from partial cure of cardiac dysfunction.

Previous studies have shown that SVV is suitable for laparoscopic surgery in different positions such as supine, lateral decubitus, or prone positions. However, thoracoscopy, different from other endoscopy, creates a continuous intrathoracic pressure, which compresses the mediastinum and contralateral lung and further reducing lung compliance.[35 51] Oppositely, opening the chest cavity would increase the aortic impedance and decrease venous return, strongly affecting the correlation between SV and pulse pressure.[23] Therefore, SVV correlated closely with the ventricular preload when the pericardium is closed.[30 52] Our result also showed supine position is better in thoracic surgery when monitoring with SVV. However, the applicability of SVV may be further limited because the lateral position is mostly used when thoracic surgery is in progress. Interestingly, Kang et al[11] found that SVV also has good diagnostic value during lung recruitment manoeuver. This may prove that SVV was suitable for different time periods in surgery, not just during operative manipulation.

Systolic pressure variation (SPV) and pulse pressure variation (PPV) are also widely used in guiding intraoperative fluid therapy. However, present studies suggested that SVV may be more applicable in patients with high-risk non cardiac surgery.[53] Some studies found correlation coefficients between baseline SVV with ΔSVI were higher than PPV, and SPV with ΔSVI. SV is derived from the arterial pressure waveform, and relies on the PulseCO algorithm. SPV and PPV, on the other hand, is based on absolute measures of arterial waveform analysis， which may not reflect true CO as accurately as former. [54]

As development of anesthesiology and surgery, number of patients accepting thoracic and cardiac surgical operations increased rapidly. Perioperative haemodynamic monitoring combined with GDFT has been demonstrated to usefully reduce mortality and cardiac dysfunction. More and more anaesthetists and surgeons are now aware of the importance of body fluid balance and cardiac perfusion during perioperative period. Despite this, the reliability of minimally invasive cardiac output monitoring indicator is not widely accepted, and a lack of consensus on monitoring method and device has done little to promote the popularization of GDFT, especially in undeveloped areas and grass-rooted hospital. There is increasing evidence that fluid therapy should be defined as 'the right amount of the right type at the right time', but this is hard to be perfectly performed. When a patient showed hypotension or pallor, it does not imply that this patient blindly needs large bolus of crystalloid or colloid infusion. The specific liquid therapy needs to be reasonably and individually analysed and chosen according to anesthetic management and surgical manipulation.

The use of SVV monitoring for high-risk surgery was firstly put forward by the National Institute for Clinical Excellence (NICE) in the UK in 2012. During recent years, it is obvious that the popularization of SVV monitoring has been more prompted. However, whether these monitoring device and indicators accurately predict responsiveness of fluid therapy in high-risk patients and when the necessary fluid therapy is required are still not clear. More studies related with SVV in thoracic and cardiac surgical should be conducted.

In view of authors, our study assisted rational decisionmaking and provide clinical consistency for the high-risk thoracic and cardiac patients in guiding fluid therapy and for this cohort the potential complication and complexity of minimally. SVV in perioperative period of thoracic and cardiac surgery may be justified.

Limitations and strengths

Our meta-analysis has some limitations. First, heterogeneity existed in the overall dataset and in most subgroups, so our conclusion should be interpreted with caution. Second, the best cut-off value of our included articles was too wide, ranging from 3.5 to 13.5. Physicians and anesthesists should refer to the related articles when choosing the appropriate cut-off value. Third, we did not discuss the effect of vasoactive drugs on SVV because of lack of relevant data. Fourth, most studies on cardiac surgery patients involved coronary artery surgery, which prevents us from applying our conclusions to all cardiac surgery types. Therefore, multicentre and large-sample studies should be performed.

There are also several strengths in our research. First, this is the first diagnostic meta-analysis studying the reliability of SVV in predicting responsiveness to fluid therapy of patients undergoing cardiac and thoracic surgery. Second, most of our included studies are of high quality. Third, we used three different software to compare the predictive value of SVV between subgroups, so our results have a high credibility.

CONCLUSION

SVV has good predictive performance in patients accepting cardiac surgery in OR and ICU, and has fair predictive performance in patients accepting thoracic surgery with OLV. Colloid infusion, high TV, and non-PEEP ventilation can effectively improve the accuracy of SVV in both thoracic and cardiac surgery. PLR was more suitable in ICU, whereas fluid challenge is more appropriate in OR. When performing fluid challenge, a large bolus in thoracic surgery and a small bolus in cardiac surgery were the preferred options. Regarding the monitoring device, the FloTrac/Vigileo system was better recommended than the PiCCO system during surgery.

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Contributors SH and GY conceived and designed the meta-analysis; SH and YJ conducted the database search, screened and extracted data for the meta-analysis, prepared extracted data for the procedures. SH and JD had primary responsibility in writing this article. SH and YJ performed statistical analysis and contributed to article screening, data collection and extraction. SH, YJ, JD, SS and GZ contributed to the data analysis. SS and GZ critically revised the manuscript. All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

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Patient consent for publication Not applicable.

Data availability statement All data relevant to the study are included in the article or uploaded as online supplemental information. No additional data available.

Data sharing statement Data are available in a public, open access repository.

Ethical Approval Statement This study does not involve animal subjects.

Supplementary Table 1 The results of all the included studies

Fig. 1 The search, included and exclusion of the literature

Fig. 2 The result of quality assessment of the included articles (overview)

Fig. 3 The result of quality assessment of each articles

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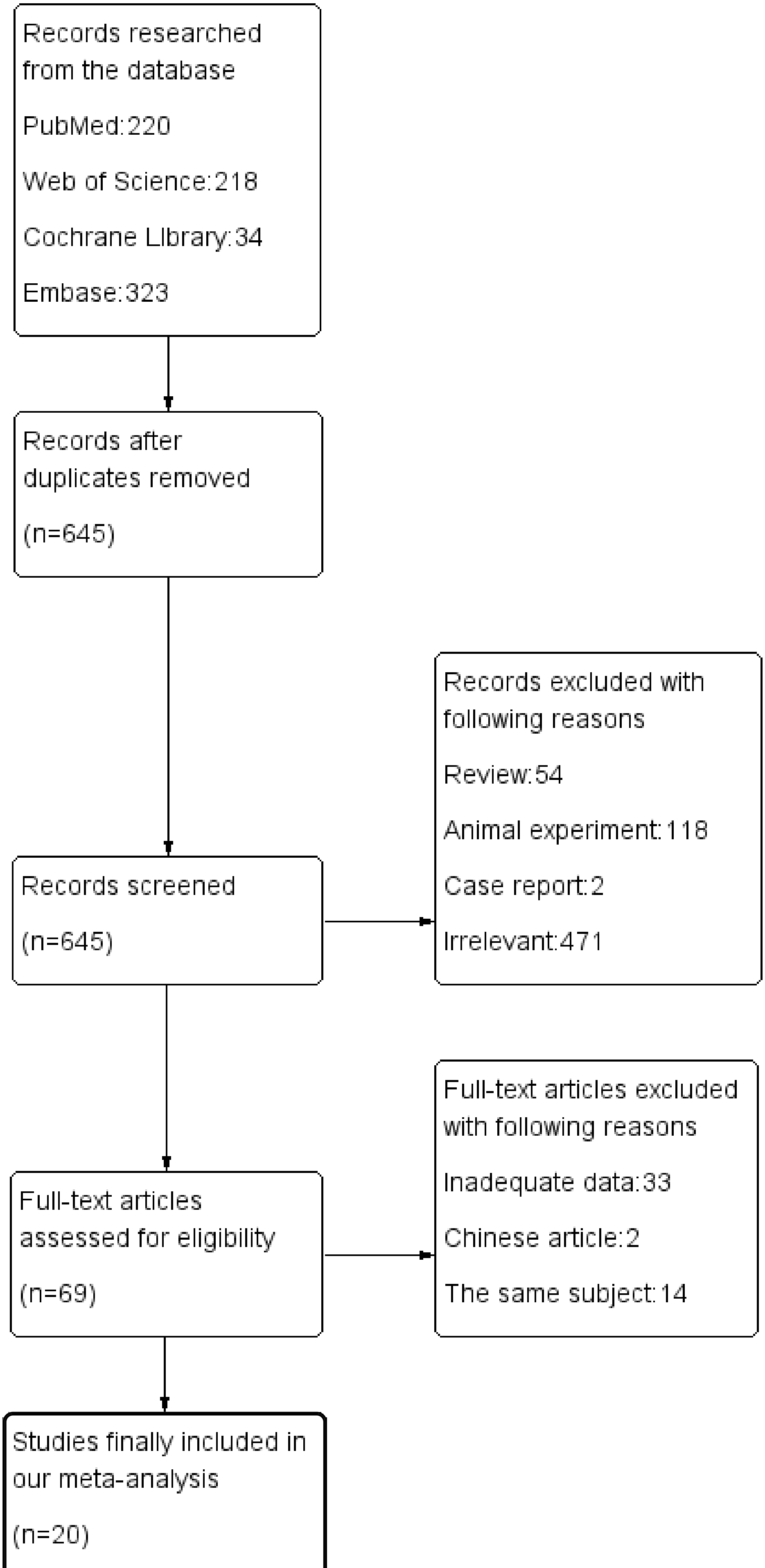
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Records screened
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Chinese article:2
The same subject:14
Full-text articles assessed for eligibility
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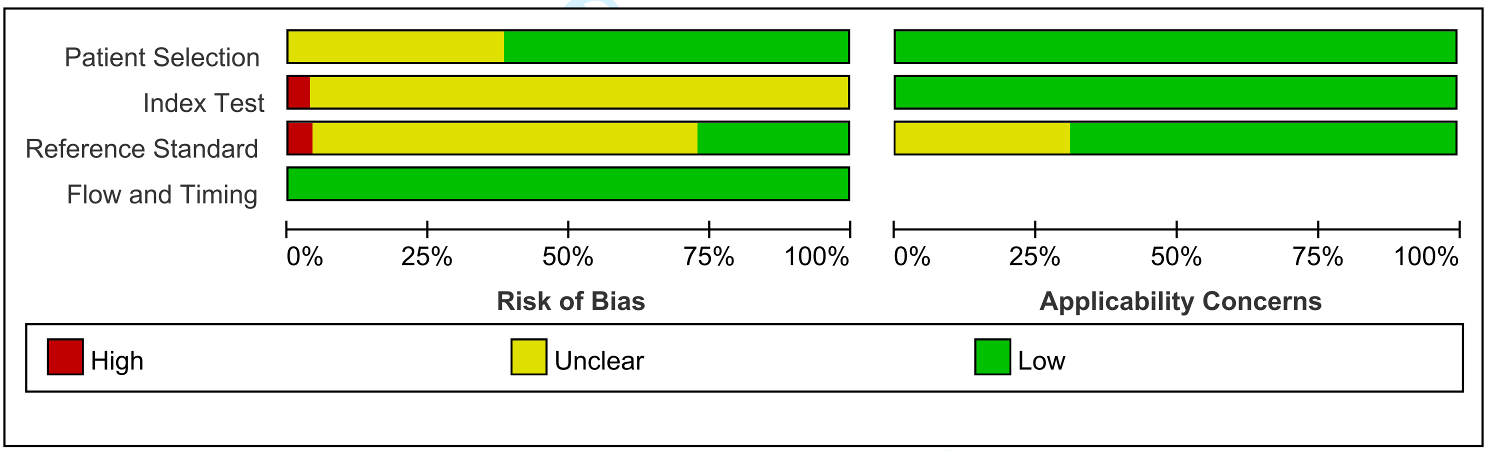
Studies finally included in our meta-analysis
(n=20)


Patient Selection
Index Test
Reference Standard
Flow and Timing
0%
25%
50%
75%
100%
Risk of Bias
0%
25%
50%
75%
100%
Applicability Concerns
High
Unclear
Low

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Belloni 2008	+	−	−	+	+	+	+
Broch 2011	?	?	?	+	+	+	+
Broch 2012	?	?	?	+	+	+	+
Cannesson 2009	+	?	?	+	+	+	+
De Waal 2009	+	?	?	+	+	+	+
Fischer 2013	+	?	?	+	+	+	+
Fu 2014	+	?	?	+	+	+	+
Fu 2015	+	?	?	+	+	+	+
Geerts 2011	+	?	?	+	+	+	+
Haas 2012	+	?	?	+	+	+	+
Hofer 2005	+	?	+	+	+	+	?
Hofer 2008	+	?	+	+	+	+	?
Jeony 2017	+	?	?	+	+	+	+
Kang 2014	+	?	?	+	+	+	+
Kang 2016	+	?	?	+	+	+	?
Kim 2013	+	?	+	+	+	+	+
Kobayashi 2009	+	?	?	+	+	+	?
Miñana 2020	+	?	?	+	+	+	+
Montenij 2016	?	?	?	+	+	+	+
Presiman 2005	?	?	+	+	+	+	+
Reuter 2002	?	?	+	+	+	+	+
Reuter 2003	?	?	+	+	+	+	+
Rex 2007	?	?	+	+	+	+	?
Suehiro 2010	?	?	?	+	+	+	?
Suehiro 2011	?	?	?	+	+	+	?
Wyffels 2010	?	?	?	+	+	+	?

− **High** ? **Unclear** + **Low**

Pubmed:

("thoracic procedures*"[tw] OR "thoracic operation*"[tw] OR "chest surgery*"[tw] OR "thoracic surgical procedures*"[tw] OR "operation on chest*"[tw] OR "major thoracic surgery*"[tw] OR "Thoracic Surgery"[Mesh] OR "heart operation*"[tw] OR "cardiac operations*"[tw] OR "open heart surgery*"[tw] OR "cardiac surgical procedures*"[tw] OR "cardiac operation*"[tw] OR "heart surgical*"[tw] OR "Cardiac Surgical Procedures"[Mesh] OR "critical care unit*"[tw] OR "intensive care*"[tw] OR "intensive care unite*"[tw] OR "intensive care unit*"[tw] OR "Recovery Room*"[tw] OR "Respiratory Care Units*"[tw] OR "Intensive Care Units"[Mesh]) AND ("evaluation*"[tw] OR "predication*"[tw] OR "predictor*"[tw] OR "Physiological Monitoring*"[tw] OR "Monitoring, Physiologic"[Mesh]) AND ("fluid infusion*"[tw] OR "fluid challenge*"[tw] OR "fluid therapy*"[tw] OR "passive leg raising*"[tw] OR "reaction*"[tw] OR "response*"[tw] OR "responsiveness*"[tw]) AND ("SVV*"[tw] OR "stroke volume variation*"[tw] OR "volume variation*"[tw] OR "cardiac output variation*"[tw] OR "stroke volume"[Mesh])

220

Web of Science:

TS=(("thoracic procedures*" OR "thoracic operation*" OR "chest surgery*" OR "thoracic surgical procedures*" OR "operation on chest*" OR "major thoracic surgery*" OR "Thoracic Surgery*" OR "heart operation*" OR "cardiac operations*" OR "open heart surgery*" OR "cardiac surgical procedures*" OR "cardiac operation*" OR "heart surgical*" OR "Cardiac Surgical Procedures*" OR "critical care unit*" OR "intensive care*" OR "intensive care unite*" OR "intensive care unit*" OR "Recovery Room*" OR "Respiratory Care Units*" OR "Intensive Care Units") AND ("evaluation*" OR "predication*" OR "predictor*" OR "Physiological Monitoring*" OR "Monitoring, Physiologic*") AND ("fluid infusion*" OR "fluid challenge*" OR "fluid therapy*" OR "passive leg raising*" OR "reaction*" OR "response*" OR "responsiveness*") AND ("SVV*" OR "stroke volume variation*" OR "volume variation*" OR "cardiac output variation*" OR "stroke volume*"))

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(thoracic NEXT procedures* OR thoracic NEXT operation* OR chest NEXT surgery* OR thoracic NEXT surgical NEXT procedures* OR operation NEXT on NEXT chest* OR major NEXT thoracic NEXT surgery* OR Thoracic NEXT Surgery* OR heart NEXT operation* OR cardiac NEXT operations* OR open NEXT heart NEXT surgery* OR cardiac NEXT surgical NEXT procedures* OR cardiac NEXT operation* OR heart NEXT surgical* OR Cardiac NEXT Surgical NEXT Procedures* OR critical NEXT care NEXT unit* OR intensive NEXT care* OR intensive NEXT care NEXT unite* OR intensive NEXT care NEXT unit* OR Recovery NEXT Room* OR Respiratory NEXT Care NEXT Units* OR Intensive NEXT Care NEXT Units) AND (evaluation* OR predication* OR predictor* OR Physiological NEXT Monitoring* OR Monitoring, Physiologic*) AND (fluid NEXT infusion* OR fluid NEXT challenge* OR fluid NEXT therapy* OR passive NEXT leg NEXT raising* OR reaction* OR response* OR responsiveness*) AND (SVV* OR stroke NEXT volume NEXT variation* OR volume NEXT variation* OR cardiac NEXT output NEXT variation* OR stroke NEXT volume*)

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Embase:

("thoracic procedures*" OR "thoracic operation*" OR "chest surgery*" OR "thoracic surgical procedures*" OR "operation on chest*" OR "major thoracic surgery*" OR "Thoracic Surgery*" OR "heart operation*" OR "cardiac operations*" OR "open heart surgery*" OR "cardiac surgical procedures*" OR "cardiac operation*" OR "heart surgical*" OR "Cardiac Surgical Procedures*" OR "critical care unit*" OR "intensive care*" OR "intensive care unite*" OR "intensive care unit*" OR "Recovery Room*" OR "Respiratory Care Units*" OR "Intensive Care Units") AND ("evaluation*" OR "predication*" OR "predictor*" OR "Physiological Monitoring*" OR "Monitoring, Physiologic*") AND ("fluid infusion*" OR "fluid challenge*" OR "fluid therapy*" OR "passive leg raising*" OR "reaction*" OR "response*" OR "responsiveness*") AND ("SVV*" OR "stroke volume variation*" OR "volume variation*" OR "cardiac output variation*" OR "stroke volume*")

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Supplementary Table1 The results of all the included studies.										
Study	Year	TP	FP	TN	FN	Sensitivity(%)	Specificity(%)	Cut-off	AUC	Correlation coefficient
Thoracic surgery										
Kang er al[11]	2016	33	13	4	25	86.8	65.8	3.5	0.82	NA
Fu et al[12]	2015	8	6	4	6	66.7	50.0	8.5	0.77	0.41
Fu et al[12]	2015	8	3	2	7	80.0	70.0	8.5	0.78	0.68
Fu et al[13]	2014	8	5	8	9	50.0	64.0	NA	0.51	-0.17
Miñana et al[14]	2020	8	3	14	14	36.4	82.4	8.0	0.47	NA
Jeony et al[15]	2017	26	39	3	11	89.7	22.0	NA	0.53	NA
Suehiro et al[16]	2010	14	1	3	13	82.4	92.3	10.5	0.90	0.87
Suehiro et al[16]	2011	13	9	9	7	58.3	44.0.	10.0	0.65	NA
Suehiro et al17	2011	18	4	5	8	85.7	66.7	10.5	0.78	NA
Cardiac surgery										
Kim et al[18]	2013	16	4	5	8	76.0	67.0	13.0	0.81	0.57

Montenij et al[19]	2016	5	4	4	9	56.0	69.0	10.0	0.70	0.32
Broch et al[20]	2011	30	9	16	28	65.0	76.0	12.0	0.72	0.57
Broch et al[21]	2012	35	9	19	31	65.0	77.0	11.0	0.77	0.62
Hofer et al[22]	2005	17	5	6	12	74.0	71.0	12.5	0.82	-0.66
Presiman et al[23]	2005	26	7	6	32	81.0.	82.0	NA	0.58	0.58
Haas et al[24]	2012	4	5	0	13	100.0	72.2	11.0	0.87	NA
Cannesson et al[25]	2009	14	1	3	7	82.0	88.0	10.0	0.87	NA
ICU after cardiac surgery										
Fischer et al[26]	2013	8	1	19	9	30.0.	90.0	NA	0.50	NA
Hofer et al[27] (PiCCO)	2008	20	4	3	13	87.0	76.0	12.1	0.86	0.70
Hofer et al[27] (Vigileo)	2008	21	3	2	14	91.0	83.0	9.6	0.82	0.65
Geerts et al[28]	2011	7	0	3	10	70.0	100.0	7.3	0.90	0.67
Kang	2014	25	4	2	23	92.3	84.0	13.5	0.94	NA

et al[29]										
De Waale t al[30]	2009	11	3	0	8	100.0	78.0	8.0	0.91	0.75

TP, true positive; FP, false positive; TN, true negative; FN, false negative; AUC, area under the curve

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	Page 1 (**Title**)
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	Page 1 , 2 (**Abstract**)
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 2, 3 (**Background**)
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	Page 2, 3 (**Background**)
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	Page 2, 3 (**Background**)
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Page 3 (**Eligibility criterial**)
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 3, 4 (**Search strategy**)
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	Page 3, 4 (**Search strategy**)
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 4 (**Data Extraction**)
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 4 (**Data Extraction**)
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	Page 4 (**Data Extraction**)

PRISMA-DTA Checklist

Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	Page 4 (**Quality assessment**)
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	Page 4 (**Statistical treatment)**
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	Page 4 (**Statistical treatment)**

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	Page 4 (**Statistical treatment)**
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Page 4 (**Statistical treatment)**
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	Page 5 (**Identification of eligible studies characteristics of the studies** , Fig. 1**)**
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	Page 5, 6, 7 (**Characteristics of the studies,** Table 1)
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	Page 7 (**Assessment of study quality and publication bias)**

PRISMA-DTA Checklist

Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	Page 5, 6, 7 (**Characteristics of the studies,** Table 1)
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	Page 8, 9,10 (**Comparison between subgroups,** Table 2)
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	Page 7, 8 (**Heterogeneity**)
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	Page 10, 11, 12, 13 (**Discussion**)
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	Page 13 (**Limitations**)
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	Page 13 (**Conclusions**)
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	**N/A**

Adapted From: McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163.

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