

# BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email [info.bmjopen@bmj.com](mailto:info.bmjopen@bmj.com)

# BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-051112
Article Type:	Original research
Date Submitted by the Author:	11-Mar-2021
Complete List of Authors:	Huan, Sheng; Nanjing Second Hospital, Ji, Yihao; Nanjing University of Traditional Chinese Medicine, Department of Critical Medicine; The Second Hospital of Nanjing, Department of Critical Medicine Yin, Guoping
Keywords:	Thoracic surgery < SURGERY, Cardiac surgery < SURGERY, Anaesthesia in cardiology < ANAESTHETICS

SCHOLARONE™  
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1  
2  
3 **Stroke volume variation for predicting responsiveness to fluid therapy in**  
4 **patients undergoing cardiac and thoracic surgery: A systematic review and**  
5 **meta-analysis**  
6  
7  
8  
9

10 **Sheng Huan<sup>1,2</sup>, Yihao Ji<sup>1,3</sup>, Guoping Yin<sup>2\*</sup>**

11  
12 **1** Second Clinical Medical College, Nanjing University of Traditional Chinese Medicine,  
13 Nanjing, Jangsu, China

14 **2** Department of Anesthesiology, The Second Hospital of Nanjing, Nanjing, Jangsu, China

15 **3** Department of Critical Medicine, The Second Hospital of Nanjing, Nanjing, Jangsu, China

16 \* [yinguoping0304@hotmail.com](mailto:yinguoping0304@hotmail.com)(GY)  
17  
18  
19  
20  
21  
22

23 **Abstract**

24  
25 **Objectives:** To study the utility of stroke volume variation (SVV) in predicting  
26 responsiveness to fluid therapy of patients undergoing cardiac and thoracic surgery.  
27  
28

29  
30 **Methods:** We searched PubMed, Cochrane Library, EMBASE, and Web of Science  
31 database (updated to August 9, 2020) for relevant trials. We used random-effects  
32 model to pool value of sensitivity, specificity, and diagnostic odds ratio (DOR) with  
33 95% CI. The area under the curve (AUC) of receiver operating characteristic (ROC)  
34 was calculated. Quality of the studies was assessed with the QUADAS-2.  
35  
36  
37  
38  
39  
40  
41

42 **Results:** Among the 20 relevant studies, data from 854 patients accepting  
43 mechanical ventilation were included in our systematic review. The AUC of ROC was  
44 0.73 (95% CI 0.69–0.77) in the thoracic surgery group, 0.80 (95% CI 0.76–0.83) in  
45 the cardiac surgery group and 0.89(95% CI 0.86–0.92) in cardiac intensive care unit  
46 (ICU) group. Subgroup analysis showed that in thoracic surgery, high tidal volume  
47 (VT) (AUC = 0.81) and non-positive end-expiratory pressure (PEEP) (AUC = 0.74)  
48 indicated good responsiveness while in cardiac surgery, non-PEEP (AUC = 0.78) was  
49 appropriate. Small volume infusion (AUC = 0.76) was suitable for heart surgery, but  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 large volume infusion (AUC = 0.88) and FloTrac/Vigileo (AUC = 0.80) were suitable  
4  
5 for thoracic surgery.  
6  
7

8 **Conclusion:** SVV is a reliable measurement parameter for patients undergoing  
9  
10 cardiac and thoracic surgery. Nevertheless, technical and clinical variables may affect  
11  
12 the predictive value.  
13  
14

15 **Keywords:** Stroke volume variation; Fluid responsiveness; Thoracic surgery; Cardiac  
16  
17 surgery; Meta-analysis  
18  
19

### 20 21 **Strengths and limitations of this study:** 22

- 23  
24 • QUADAS-2 scale in Review Manager 5.3 was used to assess the quality of our  
25  
26 included studies finding that most of them are of high quality.  
27  
28
- 29 • Three different analyzing software were used to compare the predictive value of  
30  
31 SVV in different condition and most of their results were consistent, showing high  
32  
33 credibility of the conclusion of our meta-analysis.  
34  
35
- 36 • Although meta regression analysis, sensitivity analysis and subgroup analysis  
37  
38 were conformed, heterogeneity existed in the overall dataset and in most  
39  
40 subgroups, which made comparison across trials difficult.  
41  
42
- 43 • Most cardiac surgery included in our research were related to coronary artery,  
44  
45 which made our conclusions not applicable to all kinds of cardiac surgery.  
46  
47  
48

### 49 50 **Background** 51

52  
53 Fluid therapy is important for maintaining a stable internal environment during  
54  
55 thoracic and cardiac surgery **【1】** . According to Frank Starling's curve **【2】** , the  
56  
57 preload of the ventricle is proportional to the cardiac output (CO) in the upcurve.  
58  
59 However, if the preload increases in the flat section of the curve, fluid therapy would  
60

1  
2  
3 not yield the desired effect and it could even result in cardiac overload and tissue  
4 oedema 【3, 4】. To more accurately predict the blood volume and preload of the  
5 ventricle during the perioperative period, goal-directed fluid therapy was suggested.  
6  
7  
8  
9

10 Anaesthetists previously tended to use some traditional hemodynamic indicators  
11 such as central venous pressure (CVP), pulmonary artery diastolic pressure (PADP)  
12 and cardiac index (CI) to predict fluid responsiveness 【5】. It could guide the  
13 regulation of CO but was of limited utility in reflecting ventricular preload. SVV as a  
14 predictive parameter has gained importance since the last decade 【6, 7】.  
15  
16  
17  
18  
19  
20  
21  
22

23 SVV reflects the variation of stroke volume (SV) in 30 seconds and was considered  
24 a reliable parameter under the condition of closed chest 【8】. It reflects the effect  
25 of respiratory movement on venous return. During inspiration, the increase in  
26 intrapulmonary pressure significantly decreases the negative intrapleural pressure,  
27 thereby decreasing venous return and CO. During expiration, the opposite changes  
28 occur 【9】. Toyoda et al 【6】 reported a curvilinear relationship between the  
29 right ventricular end-diastolic volume index (RVEDVI) and SVV. The regression curve  
30 accorded better with SVV than with CVP or PADP, showing its reliable prediction  
31 performance. In addition, SVV could distinguish several thresholds of RVEDVI more  
32 accurately.  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45

46 Although transoesophageal echocardiography (TEE), serving as a gold standard,  
47 had indisputable advantages in diagnosing ventricular preload and guiding fluid  
48 therapy, its practicability and availability as a commonly used technique were still  
49 limited 【10】. Therefore, SVV offers a good middle ground between conventional  
50 indicators and TEE.  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 Despite many studies conducted to determine whether SVV could be reliably  
4 applied to predict fluid responsiveness in cardiac and thoracic surgery patients 【11–  
5 30】 , there has been no consensus. Several previous systematic reviews have  
6 evaluated the reliability of SVV in predicting the outcome of common surgical  
7 operations in children and adults, but no large-sample study has been conducted to  
8 evaluate the utility of SVV in cardiac and thoracic surgery. Therefore, this study was  
9 conducted to address the issue.  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19

## 20 **METHODS**

21  
22  
23 The meta-analysis was performed according to the Preferred Reporting Items for  
24 Systematic Reviews and Meta-Analyses (PRISMA) statement issued in 2009 【31】 .  
25  
26  
27

### 28 **Description of investigated indices**

29  
30  
31 SVV is the ratio of the difference between the maximum and the minimum of the  
32 SV and the mean of the SV during 30 seconds as follows:  $(SV_{\max} - SV_{\min}) / SV_{\text{mean}}$ .  
33  
34  
35

### 36 **Search strategy**

37  
38  
39 We searched PubMed, Web of Science, EMBASE, and the Cochrane Library  
40 database for relevant literature by using searching terms such as SVV, stroke volume  
41 variation, responsiveness, and predict. The initial search was conducted on May 9,  
42 2020 with a language restriction of English.  
43  
44  
45  
46  
47  
48

49 The search string used was: ((SVV) OR (stroke volume variation)) AND  
50 (((((predictor) OR (prediction)) OR (predict)) OR (evolution)) OR (responsiveness)).  
51  
52  
53

### 54 **Eligibility criterial**

55  
56  
57 We included diagnostic trials evaluating the accuracy and effectiveness of SVV in  
58 predicting fluid responsiveness in the operating room (OR) and ICU. We excluded  
59  
60

1  
2  
3 review articles, commentaries, conference reports and research papers on animal or  
4  
5 in vitro experimental studies. In addition, we also excluded studies in which the  
6  
7 subjects were children or patients with spontaneous breathing, sepsis, shock, or  
8  
9 arrhythmia.  
10

### 11 12 **Data extraction**

13  
14  
15  
16 The basic characteristics and primary outcomes of each article were independently  
17  
18 extracted by two authors (Sheng Huan and Yihao Ji). The characteristics included  
19  
20 last name of the first author, publication year, number of patients, position, VT, PEEP,  
21  
22 and timing of manoeuvre. The outcomes included TP, FP, TN, FN, sensitivity,  
23  
24 specificity, best cut-off (%), AUC, and correlation coefficient. When there were  
25  
26 insufficient or missing data, one author (Sheng Huan) contacted the corresponding  
27  
28 author to of the included article to obtain the necessary data.  
29  
30

### 31 32 **Quality assessment**

33  
34  
35 Two authors (Sheng Huan and Yihao Ji) independently assessed the quality of the  
36  
37 included articles using the QUADAS-2 scale in Review Manager 5.3(Cochrane Library,  
38  
39 Oxford, UK) 【32】. Disagreements or discrepancies were resolved by discussion  
40  
41 with the third author (Guoping Yin). Publication bias was checked using Deeks'  
42  
43 Funnel Plot Asymmetry Test 【33】.  
44  
45  
46  
47

### 48 49 **Statistical treatment**

50  
51 The Stata software (version 14.0) was used for basic calculations. When the  
52  
53 number of included studies within some subgroups was less than four, not meeting  
54  
55 the minimum requirements of Stata, we used Review Manager (version 5.3) and R  
56  
57 software (version 3.6.3) to analyse data in these subgroups. For comparing the AUC,  
58  
59  
60



1  
2  
3 the Review Manager could only display the summary receiver operating  
4 characteristics (SROC).  
5  
6

7  
8 We used correlation (Mixed Model) of Stata to evaluate whether a threshold effect  
9 existed. When the correlation was positive and its P value was  $>0.05$ , no threshold  
10 effect was considered to exist. We then used a random-effects model to calculate  
11 pooled sensitivity, specificity and AUC with 95% CI. Statistical heterogeneity was  
12 estimated using the Cochrane Q and  $I^2$  tests 【34】 , and it was considered to be  
13 present when  $I^2 > 50\%$  or  $P < 0.05$ . In such cases, meta-regression analysis,  
14 sensitivity analysis, and subgroup analysis were used to determine the sources of  
15 heterogeneity.  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

## 26 27 **Patient and public involvement**

28  
29 Patient and public involvement is not applicable for this meta-analysis.  
30  
31

## 32 33 **RESULTS**

### 34 35 **Outcome of literature search and study characteristics**

36  
37 Of the 1371 related articles, 903 articles remained after eliminating duplicates.  
38  
39 Then, we excluded 834 articles because they were case reports, review articles,  
40 articles related to animal experiments or other irrelevant studies. Among the  
41 remaining  
42  
43  
44  
45  
46  
47  
48  
49 69 articles, 14 studies repeated the same content, two studies were not published in  
50 English, and data of our interest could not be obtained for 33 articles. Finally, 20  
51 articles were included in our meta-analysis (Fig.1).  
52  
53  
54

55  
56 The 20 articles included 854 patients. The main kinds of monitoring systems were  
57 FloTrac/Vigileo system and PiCCO system. Geerts et al 【28】 used pulmonary  
58  
59  
60

1  
2  
3 artery catheter insertion to measure thermodilution CO and CVP. Kang et al 【29】  
4  
5 used Swan-Ganz and NICOM monitors to detect SV and calculate SVV. We defined  
6  
7  $VT < 8 \text{ ml/kg}$  as “low VT” and  $VT \geq 8 \text{ ml/kg}$  as “high VT”; absence of PEEP or  
8  
9 PEEP  $< 5 \text{ mmHg}$  was considered non-PEEP. When the infusion volume was set above  
10  
11 5 ml/kg or 250 ml, we considered the study to involve a large bolus group. If not, it  
12  
13 was considered a small bolus group. Some patients in the same study accepted fluid  
14  
15 challenge with two different systems 【27】 or accepted different methods of TV  
16  
17 ventilation 【12,17】. We included all such methods and systems in our  
18  
19 meta-analysis. The basic characteristics of our included studies are presented in  
20  
21 Table 1 and Table 2.  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

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	$\Delta SVI > 25\%$	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	$\Delta CI > 15\%$	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	$\Delta CI > 10\%$	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	$\Delta CI > 10\%$	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	$\Delta CI > 10\%$	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

										surg ery	after finishing fluid loading.
Suehiro 2010	Lobectomy	30	$\Delta CI$ > 25%	500ml colliod	Yes	FloTr ac-Vi gileo syste m	5	8	later al posit ion	thor acos copy	Hemodynamic variables were measured before and after volume loading.
Suehiro 2011	Lobectomy	37	$\Delta CI$ > 15%	500ml colliod	No(6 ) Yes(8)	FloTr ac-Vi gileo syste m	5	6(OL V)  8(OL V)	later al posit ion	thor acos copy	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	$\Delta SVI$ > 12%	500ml colliod	Yes	FloTr ac-Vi gileo syste m	5	10	NA	NA	All hemodynamic data were assessed before sternotomy to maintain consistency of the closed thorax.
Monten ij 2016	coronary artery bypass grafting	22	$\Delta CO$ > 15%	7 mL/kg  crystall oid	NO	FloTr ac-Vi gileo syste m	5-10	8	NA	NA	Between induction of anaesthesia and incision, volume loading was performed in 15 min.
Broch 2011	GABG	81	$\Delta SVI$ > 12%	PLR	Yes	PiCC O	5	8	NA	NA	Measurements were performed after induction of anesthesia before surgery.
Broch 2012	CABG	92	$\Delta SVI$ > 15%	PLR	Yes	PiCC O	5	8	NA	NA	Measurements were performed after induction of anesthesia before surgery.
Hofer 2005	Off-Pump GABG	40	$\Delta SVI$ > 25%	10 mL/kg 6% hydroxy ethyl starch solution	Yes	PiCC O	0	10	NA	NA	prior to any surgical intervention, volume replacement was performed
Preisma n	CABG	18	SVI > 15%	250ml colliod	NO	TEE,P iCCO	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	$\Delta CI > 10\%$	4 mL/kg colloid	Yes	PiCC O	5	8	NA	NA		Directly after completion of cardiac surgery and thoracic closure
Cannesson 2009	coronary artery bypass grafting	25	$\Delta CI > 15\%$	500ml colloid	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	$\Delta CI > 15\%$	500ml colloid	No	PiCC O 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	PiCC O 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	$\Delta CO > 7\%$	passive leg raising (PLR).	Yes	pulmonary artery catheter insertion	5	8-10	NA	NA		NA
Kang 2014	ICU C	54	$\Delta CO > 7\%$	PLR	Yes	Swan-Ganz NICOM	5	10	NA	NA		NA

De Waal 2009	ICU (Coronary artery bypass grafting)(open chest)	22	$\Delta$ SVI > 12%	7 mL/kg colloid	Yes	PiCC O	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	trials number	State					Revman	R	
		AUC	Sensitivity	Specificity	DOR	Youden index	Result	AUC	Youden

									index
<b>Thoracic surgery</b>	<b>9</b>	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			
<b>Cardiac surgery</b>	<b>8</b>	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
<b>ICU after cardiac surgery</b>	<b>6</b>	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

1  
2  
3 Our study revealed that SVV had excellent predictive performance in monitoring  
4 patients accepting cardiac surgery in OR and ICU and had good predictive  
5 performance in patients accepting thoracic surgery with one-lung ventilation (OLV).  
6  
7 In addition, we found that some operation aspects such as ventilation mode,  
8 rehydration mode, timing of intervention, and operation type can significantly affect  
9 the performance of SVV, which may also be the reason for the overall heterogeneity  
10 in our study.  
11  
12  
13  
14  
15  
16  
17  
18

## 19 **Ventilation**

20  
21  
22 Protective ventilation, defined as low TV, low inhaled oxygen (FIO<sub>2</sub>), and PEEP  
23 have recently been widely advocated in OLV. However, our meta-analysis found that  
24 it may negatively affect SVV monitoring. Ventilation volume rather than airway  
25 pressure is the key factor determining pleural pressure and right ventricular afterload  
26  
27 **【35】** . When TV decreased, the Frank starling curve of the left ventricle markedly  
28 moved to the right, making the variation in systolic pressure insignificant. Low TV  
29 would not cause any significant variation in SV especially under conditions of low  
30 blood volume **【17】** .  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40

41 Alvarado et al **【36】** found that low PEEP (0–10 mmHg) had no significant effect  
42 on cardiac preload because most of the pressure generated by the ventilator would  
43 be released to the atmosphere **【16】** , whereas high PEEP (10–15 mmHg) would  
44 mistakenly indicate blood volume **【37】** . This phenomenon would become more  
45 evident in OLV, in agreement with our result. However, another meta-analysis  
46 reported an opposite conclusion that the AUC of SVV is not affected by PEEP levels  
47 or driving pressures **【36】** , which may be explained by the difference between OLV  
48 and normal ventilation. It suggests that the effect of respiratory pressure and VT on  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 SVV depends primarily on the degree to which these variables transmitted to the  
4  
5 pulmonary circulation, rather than absolute value.  
6  
7

## 8 **Intervention**

10  
11 Fluid therapy with large bolus showed better reliability in thoracic surgery, whereas  
12  
13 small bolus fluid therapy was more used useful in cardiac surgery, and this could be  
14  
15 because patients undergoing cardiac surgery usually have cardiac dysfunction and  
16  
17 cannot tolerate a large bolus during in a short period, whereas thoracic surgery  
18  
19 patients often exhibit heavy bleeding. Regarding the type of fluid, the colloid rather  
20  
21 than crystalloid type can quickly compensate for fluid loss to achieve satisfactory CO  
22  
23 **【8】** and significantly increase RVEDVI **【38】** . By transfer of approximately 300  
24  
25 ml of venous blood from the lower body toward the right heart, PLR was often used  
26  
27 in the ICU to mimic a fluid challenge, which agreed with our result that PLR suited  
28  
29 ICU patients and fluid therapy suited OR patients **【29】** . Interestingly, Ma found  
30  
31 that PLR may replace fluid challenge as a more reliable intervention in protection  
32  
33 ventilation patients during cardiac surgery **【39】** .  
34  
35  
36  
37  
38

## 39 **Monitoring device**

40  
41  
42 The FloTrac/Vigileo system was better in thoracic surgery but was contradictory in  
43  
44 cardiac surgery. It has lower thresholds than the PiCCO system and could predict the  
45  
46 insufficiency of blood volume earlier and with greater sensitivity even if the wave of  
47  
48 hemodynamic status remained weak or unchanged in OLV **【27】** . In addition, it  
49  
50 requires no calibration and is considered to be less affected by arterial compliance  
51  
52 and elasticity **【40】** . However, misestimation of blood volume is possible when a  
53  
54 rapid wave of CO occurs **【41】** .  
55  
56  
57  
58  
59  
60

1  
2  
3 The PiCCO system can be used only after correction for low-temperature saline,  
4 and it is difficult to continuously calibrate the system during surgery in cases of  
5 heavy bleeding 【42】 . Its latest version incorporates adapted vascular compliance  
6 measurement from every 10 minutes to every minute based on a modification  
7 algorithm 【43】 . Wiesenack et al 【44】 reported a significant correlation  
8 between baseline SVV and changes of SVI after updating the algorithm of PiCCO  
9 system, which was opposite to their previous negative result that linear regression  
10 analysis between SVV and changes of SVI did not reveal a significant relationship.  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21

### 22 **Cardiac insufficiency and arrhythmia**

23  
24  
25 Although our analysis did not include studies with arrhythmia patients, wide pulse  
26 pressure has been considered to seriously affect SVV prediction 【18】 . Similarly, in  
27 shock patients with circulatory failure, the diagnostic value of SVV was greatly limited  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65  
66  
67  
68  
69  
70  
71  
72  
73  
74  
75  
76  
77  
78  
79  
80  
81  
82  
83  
84  
85  
86  
87  
88  
89  
90  
91  
92  
93  
94  
95  
96  
97  
98  
99  
100  
101  
102  
103  
104  
105  
106  
107  
108  
109  
110  
111  
112  
113  
114  
115  
116  
117  
118  
119  
120  
121  
122  
123  
124  
125  
126  
127  
128  
129  
130  
131  
132  
133  
134  
135  
136  
137  
138  
139  
140  
141  
142  
143  
144  
145  
146  
147  
148  
149  
150  
151  
152  
153  
154  
155  
156  
157  
158  
159  
160  
161  
162  
163  
164  
165  
166  
167  
168  
169  
170  
171  
172  
173  
174  
175  
176  
177  
178  
179  
180  
181  
182  
183  
184  
185  
186  
187  
188  
189  
190  
191  
192  
193  
194  
195  
196  
197  
198  
199  
200  
201  
202  
203  
204  
205  
206  
207  
208  
209  
210  
211  
212  
213  
214  
215  
216  
217  
218  
219  
220  
221  
222  
223  
224  
225  
226  
227  
228  
229  
230  
231  
232  
233  
234  
235  
236  
237  
238  
239  
240  
241  
242  
243  
244  
245  
246  
247  
248  
249  
250  
251  
252  
253  
254  
255  
256  
257  
258  
259  
260  
261  
262  
263  
264  
265  
266  
267  
268  
269  
270  
271  
272  
273  
274  
275  
276  
277  
278  
279  
280  
281  
282  
283  
284  
285  
286  
287  
288  
289  
290  
291  
292  
293  
294  
295  
296  
297  
298  
299  
300  
301  
302  
303  
304  
305  
306  
307  
308  
309  
310  
311  
312  
313  
314  
315  
316  
317  
318  
319  
320  
321  
322  
323  
324  
325  
326  
327  
328  
329  
330  
331  
332  
333  
334  
335  
336  
337  
338  
339  
340  
341  
342  
343  
344  
345  
346  
347  
348  
349  
350  
351  
352  
353  
354  
355  
356  
357  
358  
359  
360  
361  
362  
363  
364  
365  
366  
367  
368  
369  
370  
371  
372  
373  
374  
375  
376  
377  
378  
379  
380  
381  
382  
383  
384  
385  
386  
387  
388  
389  
390  
391  
392  
393  
394  
395  
396  
397  
398  
399  
400  
401  
402  
403  
404  
405  
406  
407  
408  
409  
410  
411  
412  
413  
414  
415  
416  
417  
418  
419  
420  
421  
422  
423  
424  
425  
426  
427  
428  
429  
430  
431  
432  
433  
434  
435  
436  
437  
438  
439  
440  
441  
442  
443  
444  
445  
446  
447  
448  
449  
450  
451  
452  
453  
454  
455  
456  
457  
458  
459  
460  
461  
462  
463  
464  
465  
466  
467  
468  
469  
470  
471  
472  
473  
474  
475  
476  
477  
478  
479  
480  
481  
482  
483  
484  
485  
486  
487  
488  
489  
490  
491  
492  
493  
494  
495  
496  
497  
498  
499  
500  
501  
502  
503  
504  
505  
506  
507  
508  
509  
510  
511  
512  
513  
514  
515  
516  
517  
518  
519  
520  
521  
522  
523  
524  
525  
526  
527  
528  
529  
530  
531  
532  
533  
534  
535  
536  
537  
538  
539  
540  
541  
542  
543  
544  
545  
546  
547  
548  
549  
550  
551  
552  
553  
554  
555  
556  
557  
558  
559  
560  
561  
562  
563  
564  
565  
566  
567  
568  
569  
570  
571  
572  
573  
574  
575  
576  
577  
578  
579  
580  
581  
582  
583  
584  
585  
586  
587  
588  
589  
590  
591  
592  
593  
594  
595  
596  
597  
598  
599  
600  
601  
602  
603  
604  
605  
606  
607  
608  
609  
610  
611  
612  
613  
614  
615  
616  
617  
618  
619  
620  
621  
622  
623  
624  
625  
626  
627  
628  
629  
630  
631  
632  
633  
634  
635  
636  
637  
638  
639  
640  
641  
642  
643  
644  
645  
646  
647  
648  
649  
650  
651  
652  
653  
654  
655  
656  
657  
658  
659  
660  
661  
662  
663  
664  
665  
666  
667  
668  
669  
670  
671  
672  
673  
674  
675  
676  
677  
678  
679  
680  
681  
682  
683  
684  
685  
686  
687  
688  
689  
690  
691  
692  
693  
694  
695  
696  
697  
698  
699  
700  
701  
702  
703  
704  
705  
706  
707  
708  
709  
710  
711  
712  
713  
714  
715  
716  
717  
718  
719  
720  
721  
722  
723  
724  
725  
726  
727  
728  
729  
730  
731  
732  
733  
734  
735  
736  
737  
738  
739  
740  
741  
742  
743  
744  
745  
746  
747  
748  
749  
750  
751  
752  
753  
754  
755  
756  
757  
758  
759  
760  
761  
762  
763  
764  
765  
766  
767  
768  
769  
770  
771  
772  
773  
774  
775  
776  
777  
778  
779  
780  
781  
782  
783  
784  
785  
786  
787  
788  
789  
790  
791  
792  
793  
794  
795  
796  
797  
798  
799  
800  
801  
802  
803  
804  
805  
806  
807  
808  
809  
810  
811  
812  
813  
814  
815  
816  
817  
818  
819  
820  
821  
822  
823  
824  
825  
826  
827  
828  
829  
830  
831  
832  
833  
834  
835  
836  
837  
838  
839  
840  
841  
842  
843  
844  
845  
846  
847  
848  
849  
850  
851  
852  
853  
854  
855  
856  
857  
858  
859  
860  
861  
862  
863  
864  
865  
866  
867  
868  
869  
870  
871  
872  
873  
874  
875  
876  
877  
878  
879  
880  
881  
882  
883  
884  
885  
886  
887  
888  
889  
890  
891  
892  
893  
894  
895  
896  
897  
898  
899  
900  
901  
902  
903  
904  
905  
906  
907  
908  
909  
910  
911  
912  
913  
914  
915  
916  
917  
918  
919  
920  
921  
922  
923  
924  
925  
926  
927  
928  
929  
930  
931  
932  
933  
934  
935  
936  
937  
938  
939  
940  
941  
942  
943  
944  
945  
946  
947  
948  
949  
950  
951  
952  
953  
954  
955  
956  
957  
958  
959  
960  
961  
962  
963  
964  
965  
966  
967  
968  
969  
970  
971  
972  
973  
974  
975  
976  
977  
978  
979  
980  
981  
982  
983  
984  
985  
986  
987  
988  
989  
990  
991  
992  
993  
994  
995  
996  
997  
998  
999  
1000

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 ( $50\% \geq EF \geq 30\%$ ) 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】 .

### 54 **Others**

55  
56  
57 Previous studies have shown that SVV is suitable for laparoscopic surgery in  
58 different positions such as supine, lateral decubitus, or prone positions. However,  
59  
60

1  
2  
3 thoracoscopy creates a continuous intrathoracic pressure, which compresses the  
4  
5 mediastinum and contralateral lung, further reducing lung compliance 【49,35】 .  
6  
7  
8 Due to the small sample size, our results have limited power in judging preference  
9  
10 between thoracoscopy and thoracotomy. Moreover, we found that the supine  
11  
12 position is more suitable than the lateral position to monitor SVV.  
13  
14

15 Opening the chest cavity would increase the aortic impedance and decrease  
16  
17 venous return, strongly affecting the correlation between SV and pulse pressure  
18  
19 【23】 . SVV correlated with the ventricular preload when the pericardium is closed  
20  
21 【30,50】 . Our results showed that SVV monitoring after cardiac surgery had a  
22  
23 better predictive value than that before cardiac surgery, which may result from cure  
24  
25 of cardiac dysfunction. Interestingly, Kang et al 【11】 found that SVV also has  
26  
27 good diagnostic value during lung recruitment manoeuvre.  
28  
29  
30

31  
32 More than vasoactive drugs affecting CO calculation, the classification criteria  
33  
34 between responders and non-responders, system error, and thresholds were  
35  
36 apparently potential factors influencing the predictive value of SVV.  
37  
38

### 39 **Limitations and strengths**

40  
41  
42 Our meta-analysis has some limitations. First, heterogeneity existed in the overall  
43  
44 dataset and in most subgroups, so our conclusion should be interpreted with caution.  
45  
46 Second, the best cut-off value of our included articles was too wide, ranging from  
47  
48 3.5 to 13.5. Physicians should refer to the related articles when choosing the  
49  
50 appropriate cut-off value. Third, we did not discuss the effect of vasoactive drugs on  
51  
52 SVV because of lack of relevant data. Fourth, most studies on cardiac surgery  
53  
54 patients involved coronary artery surgery, which prevents us from applying our  
55  
56  
57  
58  
59  
60

1  
2  
3 conclusions to all cardiac surgery types. Therefore, multicentre and large-sample  
4  
5 studies should be performed.  
6  
7

8  
9 There are also several strengths in our research. First, this is the first diagnostic  
10  
11 meta-analysis studying the utility of SVV in predicting responsiveness to fluid therapy  
12  
13 of patients undergoing cardiac and thoracic surgery. Second, most of our included  
14  
15 studies are of high quality. Third, we used three different software to compare the  
16  
17 predictive value of SVV between subgroups, so our results have high credibility.  
18  
19

## 20 **CONCLUSION**

21  
22  
23 SVV had excellent predictive performance in patients accepting cardiac surgery in  
24  
25 OR and ICU and had good predictive performance in patients accepting thoracic  
26  
27 surgery with OLV. Colloid infusion, high VT ( $\geq 8$ ), and non-PEEP ventilation can  
28  
29 effectively improve the accuracy of SVV in both thoracic and cardiac surgery. PLR  
30  
31 was more suitable for ICU, whereas fluid challenge is more appropriate for OR. When  
32  
33 performing fluid challenge, a large bolus in thoracic surgery and a small bolus in  
34  
35 cardiac surgery were the preferred options. To monitor SVV, the FloTrac/Vigileo  
36  
37 system was better than the PiCCO system in thoracic surgery.  
38  
39

## 40 **Acknowledgments**

41  
42  
43 The authors would like to thank all the researchers of the included articles for their  
44  
45 data. We appreciate the help from Wordvice company for revising the language in  
46  
47 this manuscript.  
48  
49

## 50 **REFERENCES**

51  
52  
53  
54  
55 1. Navarro LH, Bloomstone JA, Auler JO, Jr., et al. Perioperative fluid therapy: a  
56  
57 statement from the international Fluid Optimization Group. Perioperative medicine  
58  
59  
60

1  
2  
3 (London, England) 2015;4:3. doi: 10.1186/s13741-015-0014-z [published Online  
4  
5 First: 2015/04/22]

6  
7 2. Ribarič S, Kordaš M. Simulation of the Frank-Starling Law of the Heart.  
8  
9 Computational and mathematical methods in medicine 2012;2012:267834. doi:  
10  
11 10.1155/2012/267834 [published Online First: 2012/12/18]

12  
13 3. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment  
14  
15 of severe sepsis and septic shock. N Engl J Med 2001;345(19):1368-77. doi:  
16  
17 10.1056/NEJMoa010307 [published Online First: 2002/01/17]

18  
19 4. Kirov MY, Kuzkov VV, Molnar Z. Perioperative haemodynamic therapy. Current  
20  
21 opinion in critical care 2010;16(4):384-92. doi: 10.1097/MCC.0b013e32833ab81e  
22  
23 [published Online First: 2010/05/29]

24  
25 5. Redondo FJ, Padilla D, Villarejo P, et al. The Global End-Diastolic Volume (GEDV)  
26  
27 Could Be More Appropriate to Fluid Management Than Central Venous Pressure (CVP)  
28  
29 During Closed Hyperthermic Intrabdominal Chemotherapy with CO(2) Circulation.  
30  
31 Journal of investigative surgery : the official journal of the Academy of Surgical  
32  
33 Research 2018;31(4):321-27. doi: 10.1080/08941939.2017.1325543 [published  
34  
35 Online First: 2017/05/31]

36  
37 6. Toyoda D, Fukuda M, Iwasaki R, et al. The comparison between stroke volume  
38  
39 variation and filling pressure as an estimate of right ventricular preload in patients  
40  
41 undergoing renal transplantation. Journal of anesthesia 2015;29(1):40-46. doi:  
42  
43 10.1007/s00540-014-1870-2

44  
45 7. Sahutoglu C, Turksal E, Kocabas S, et al. Influence of stroke volume variation on  
46  
47 fluid treatment and postoperative complications in thoracic surgery. Therapeutics and  
48  
49 clinical risk management 2018;14:575-81. doi: 10.2147/tcrm.S154093 [published  
50  
51 Online First: 2018/03/30]



- 1  
2  
3 8. Verheij J, van Lingen A, Beishuizen A, et al. Cardiac response is greater for colloid  
4 than saline fluid loading after cardiac or vascular surgery. *Intensive care medicine*  
5 2006;32(7):1030-8. doi: 10.1007/s00134-006-0195-5 [published Online First:  
6 2006/06/23]  
7  
8  
9  
10  
11  
12 9. Michard F, Teboul JL. Using heart-lung interactions to assess fluid responsiveness  
13 during mechanical ventilation. *Critical care (London, England)* 2000;4(5):282-9. doi:  
14 10.1186/cc710 [published Online First: 2000/11/30]  
15  
16  
17  
18 10. Reuter DA, Kirchner A, Felbinger TW, et al. Usefulness of left ventricular stroke  
19 volume variation to assess fluid responsiveness in patients with reduced cardiac  
20 function. *Critical care medicine* 2003;31(5):1399-404. doi:  
21 10.1097/01.Ccm.0000059442.37548.E1 [published Online First: 2003/05/29]  
22  
23  
24  
25  
26  
27 11. Kang WS, Oh CS, Park C, et al. Diagnosis Accuracy of Mean Arterial Pressure  
28 Variation during a Lung Recruitment Maneuver to Predict Fluid Responsiveness in  
29 Thoracic Surgery with One-Lung Ventilation. *BioMed research international*  
30 2016;2016:3623710. doi: 10.1155/2016/3623710 [published Online First:  
31 2016/11/08]  
32  
33  
34  
35  
36  
37  
38 12. Fu Q, Duan M, Zhao F, et al. Evaluation of stroke volume variation and pulse  
39 pressure variation as predictors of fluid responsiveness in patients undergoing  
40 protective one-lung ventilation. *Drug discoveries & therapeutics* 2015;9(4):296-302.  
41 doi: 10.5582/ddt.2015.01046 [published Online First: 2015/09/16]  
42  
43  
44  
45  
46  
47 13. Fu Q, Zhao F, Mi W, et al. Stroke volume variation fail to predict fluid  
48 responsiveness in patients undergoing pulmonary lobectomy with one-lung  
49 ventilation using thoracotomy. *Bioscience trends* 2014;8(1):59-63. doi:  
50 10.5582/bst.8.59 [published Online First: 2014/03/22]  
51  
52  
53  
54  
55  
56 14. Miñana A, Parra MJ, Carbonell J, et al. Validation study of the dynamic  
57 parameters of pulse wave in pulmonary resection surgery. *Revista española de*  
58  
59  
60

1  
2  
3 anesthesiologia y reanimacion 2020;67(2):55-62. doi: 10.1016/j.redar.2019.10.007

4  
5 [published Online First: 2020/01/01]

6  
7 15. Jeong DM, Ahn HJ, Park HW, et al. Stroke Volume Variation and Pulse Pressure  
8  
9 Variation Are Not Useful for Predicting Fluid Responsiveness in Thoracic Surgery.

10  
11 Anesthesia and analgesia 2017;125(4):1158-65. doi:

12  
13 10.1213/ane.0000000000002056 [published Online First: 2017/05/16]

14  
15 16. Suehiro K, Okutani R. Stroke volume variation as a predictor of fluid

16  
17 responsiveness in patients undergoing one-lung ventilation. Journal of cardiothoracic  
18  
19 and vascular anesthesia 2010;24(5):772-5. doi: 10.1053/j.jvca.2010.03.014

20  
21 [published Online First: 2010/07/20]

22  
23 17. Suehiro K, Okutani R. Influence of tidal volume for stroke volume variation to  
24  
25 predict fluid responsiveness in patients undergoing one-lung ventilation. Journal of

26  
27 anesthesia 2011;25(5):777-80. doi: 10.1007/s00540-011-1200-x [published Online  
28  
29 First: 2011/07/12]

30  
31 18. Kim SY, Song Y, Shim JK, et al. Effect of pulse pressure on the predictability of  
32  
33 stroke volume variation for fluid responsiveness in patients with coronary disease.

34  
35 Journal of critical care 2013;28(3):318.e1-7. doi: 10.1016/j.jcrc.2012.09.011

36  
37 [published Online First: 2012/11/06]

38  
39 19. Montenij LJ, Sonneveld JP, Nierich AP, et al. Diagnostic accuracy of stroke  
40  
41 volume variation measured with uncalibrated arterial waveform analysis for the  
42  
43 prediction of fluid responsiveness in patients with impaired left ventricular function: a  
44  
45 prospective, observational study. Journal of clinical monitoring and computing

46  
47 2016;30(4):481-6. doi: 10.1007/s10877-015-9743-2 [published Online First:

48  
49 2015/08/01]

50  
51 20. Broch O, Bein B, Gruenewald M, et al. Accuracy of the pleth variability index to  
52  
53 predict fluid responsiveness depends on the perfusion index. Acta anaesthesiologica

1  
2  
3 Scandinavica 2011;55(6):686-93. doi: 10.1111/j.1399-6576.2011.02435.x [published  
4  
5 Online First: 2011/04/13]

6  
7  
8 21. Broch O, Renner J, Gruenewald M, et al. Variation of left ventricular outflow tract  
9  
10 velocity and global end-diastolic volume index reliably predict fluid responsiveness in  
11  
12 cardiac surgery patients. Journal of critical care 2012;27(3):325.e7-13. doi:  
13  
14 10.1016/j.jcrc.2011.07.073 [published Online First: 2011/08/23]

15  
16 22. Hofer CK, Müller SM, Furrer L, et al. Stroke volume and pulse pressure variation  
17  
18 for prediction of fluid responsiveness in patients undergoing off-pump coronary  
19  
20 artery bypass grafting. Chest 2005;128(2):848-54. doi: 10.1378/chest.128.2.848  
21  
22 [published Online First: 2005/08/16]

23  
24 23. Preisman S, Kogan S, Berkenstadt H, et al. Predicting fluid responsiveness in  
25  
26 patients undergoing cardiac surgery: functional haemodynamic parameters including  
27  
28 the Respiratory Systolic Variation Test and static preload indicators. British journal of  
29  
30 anaesthesia 2005;95(6):746-55. doi: 10.1093/bja/aei262 [published Online First:  
31  
32 2005/11/16]

33  
34 24. Haas S, Eichhorn V, Hasbach T, et al. Goal-directed fluid therapy using stroke  
35  
36 volume variation does not result in pulmonary fluid overload in thoracic surgery  
37  
38 requiring one-lung ventilation. Critical care research and practice 2012;2012:687018.  
39  
40 doi: 10.1155/2012/687018 [published Online First: 2012/07/11]

41  
42 25. Cannesson M, Musard H, Desebbe O, et al. The ability of stroke volume  
43  
44 variations obtained with Vigileo/FloTrac system to monitor fluid responsiveness in  
45  
46 mechanically ventilated patients. Anesthesia and analgesia 2009;108(2):513-7. doi:  
47  
48 10.1213/ane.0b013e318192a36b [published Online First: 2009/01/20]

49  
50 26. Fischer MO, Coucoravas J, Truong J, et al. Assessment of changes in cardiac  
51  
52 index and fluid responsiveness: a comparison of Nexfin and transpulmonary  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 thermodilution. *Acta anaesthesiologica Scandinavica* 2013;57(6):704-12. doi:  
4 10.1111/aas.12108 [published Online First: 2013/03/26]  
5  
6  
7 27. Hofer CK, Senn A, Weibel L, et al. Assessment of stroke volume variation for  
8 prediction of fluid responsiveness using the modified FloTrac and PiCCOplus system.  
9  
10 *Critical care (London, England)* 2008;12(3):R82. doi: 10.1186/cc6933 [published  
11  
12 Online First: 2008/06/24]  
13  
14  
15  
16 28. Cherpanath TGV, Hirsch A, Geerts BF, et al. Predicting Fluid Responsiveness by  
17 Passive Leg Raising: A Systematic Review and Meta-Analysis of 23 Clinical Trials.  
18  
19 *Critical care medicine* 2016;44(5):981-91. doi: 10.1097/ccm.0000000000001556  
20  
21  
22  
23 29. Kang WS, Kim SH, Kim SY, et al. The influence of positive end-expiratory  
24 pressure on stroke volume variation in patients undergoing cardiac surgery: an  
25 observational study. *The Journal of thoracic and cardiovascular surgery*  
26  
27 2014;148(6):3139-45. doi: 10.1016/j.jtcvs.2014.07.103 [published Online First:  
28  
29 2014/09/17]  
30  
31  
32  
33 30. de Waal EE, Rex S, Kruitwagen CL, et al. Dynamic preload indicators fail to  
34 predict fluid responsiveness in open-chest conditions. *Critical care medicine*  
35  
36 2009;37(2):510-5. doi: 10.1097/CCM.0b013e3181958bf7 [published Online First:  
37  
38 2008/12/31]  
39  
40  
41  
42 31. Moher D, Liberati A, Tetzlaff J, et al. Reprint--preferred reporting items for  
43 systematic reviews and meta-analyses: the PRISMA statement. *Phys Ther*  
44  
45 2009;89(9):873-80. [published Online First: 2009/09/03]  
46  
47  
48  
49 32. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the  
50 quality assessment of diagnostic accuracy studies. *Ann Intern Med*  
51  
52 2011;155(8):529-36. doi: 10.7326/0003-4819-155-8-201110180-00009 [published  
53  
54 Online First: 2011/10/19]  
55  
56  
57  
58  
59  
60

- 1  
2  
3 33. Stuck AE, Rubenstein LZ, Wieland D. Bias in meta-analysis detected by a simple,  
4 graphical test. Asymmetry detected in funnel plot was probably due to true  
5 heterogeneity. *BMJ* 1998;316(7129):469; author reply 70-1. [published Online First:  
6 1998/03/11]  
7  
8  
9  
10  
11 34. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat*  
12 *Med* 2002;21(11):1539-58. doi: 10.1002/sim.1186 [published Online First:  
13 2002/07/12]  
14  
15  
16  
17 35. Romand JA, Shi W, Pinsky MR. Cardiopulmonary effects of positive pressure  
18 ventilation during acute lung injury. *Chest* 1995;108(4):1041-8. doi:  
19 10.1378/chest.108.4.1041 [published Online First: 1995/10/01]  
20  
21  
22  
23 36. Alvarado Sánchez JI, Caicedo Ruiz JD, Diaztagle Fernández JJ, et al. Predictors of  
24 fluid responsiveness in critically ill patients mechanically ventilated at low tidal  
25 volumes: systematic review and meta-analysis. *Annals of intensive care*  
26 2021;11(1):28. doi: 10.1186/s13613-021-00817-5 [published Online First:  
27 2021/02/09]  
28  
29  
30  
31 37. Kubitz JC, Annecke T, Kemming GI, et al. The influence of positive  
32 end-expiratory pressure on stroke volume variation and central blood volume during  
33 open and closed chest conditions. *European journal of cardio-thoracic surgery* :  
34 official journal of the European Association for Cardio-thoracic Surgery  
35 2006;30(1):90-5. doi: 10.1016/j.ejcts.2006.04.008 [published Online First:  
36 2006/05/26]  
37  
38  
39  
40  
41 38. Kanda H, Hirasaki Y, Iida T, et al. Effect of fluid loading with normal saline and 6%  
42 hydroxyethyl starch on stroke volume variability and left ventricular volume.  
43 *International journal of general medicine* 2015;8:319-24. doi: 10.2147/ijgm.S89939  
44 [published Online First: 2015/10/23]  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 39. Ma GG, Tu GW, Zheng JL, et al. Changes in Stroke Volume Variation Induced by  
4 Passive Leg Raising to Predict Fluid Responsiveness in Cardiac Surgical Patients With  
5 Protective Ventilation. *Journal of cardiothoracic and vascular anesthesia*  
6  
7  
8  
9 2020;34(6):1526-33. doi: 10.1053/j.jvca.2019.10.002 [published Online First:  
10  
11 2019/11/23]
- 12  
13  
14 40. Manecke GR, Jr., Auger WR. Cardiac output determination from the arterial  
15 pressure wave: clinical testing of a novel algorithm that does not require calibration.  
16  
17  
18  
19 *Journal of cardiothoracic and vascular anesthesia* 2007;21(1):3-7. doi:  
20  
21 10.1053/j.jvca.2006.08.004 [published Online First: 2007/02/10]
- 22  
23 41. Kanazawa M, Fukuyama H, Kinefuchi Y, et al. Relationship between  
24 aortic-to-radial arterial pressure gradient after cardiopulmonary bypass and changes  
25 in arterial elasticity. *Anesthesiology* 2003;99(1):48-53. doi:  
26  
27  
28  
29 10.1097/00000542-200307000-00011 [published Online First: 2003/06/27]
- 30  
31 42. Cottis R, Magee N, Higgins DJ. Haemodynamic monitoring with pulse-induced  
32 contour cardiac output (PiCCO) in critical care. *Intensive & critical care nursing*  
33  
34  
35  
36 2003;19(5):301-7. doi: 10.1016/s0964-3397(03)00063-6 [published Online First:  
37  
38 2003/10/01]
- 39  
40 43. Button D, Weibel L, Reuthebuch O, et al. Clinical evaluation of the FloTrac/Vigileo  
41 system and two established continuous cardiac output monitoring devices in patients  
42 undergoing cardiac surgery. *British journal of anaesthesia* 2007;99(3):329-36. doi:  
43  
44  
45  
46 10.1093/bja/aem188 [published Online First: 2007/07/17]
- 47  
48  
49 44. Wiesenack C, Fiegl C, Keyser A, et al. Assessment of fluid responsiveness in  
50 mechanically ventilated cardiac surgical patients. *European journal of*  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60 *anaesthesiology* 2005;22(9):658-65. doi: 10.1017/s0265021505001092 [published  
Online First: 2005/09/17]

- 1  
2  
3 45. Angappan S, Parida S, Vasudevan A, et al. The comparison of stroke volume  
4 variation with central venous pressure in predicting fluid responsiveness in septic  
5 patients with acute circulatory failure. *Indian journal of critical care medicine* :  
6 peer-reviewed, official publication of Indian Society of Critical Care Medicine  
7  
8  
9  
10  
11  
12 2015;19(7):394-400. doi: 10.4103/0972-5229.160278 [published Online First:  
13  
14 2015/07/17]
- 15  
16 46. Cannesson M, Tran NP, Cho M, et al. Predicting fluid responsiveness with stroke  
17 volume variation despite multiple extrasystoles. *Critical care medicine*  
18  
19  
20 2012;40(1):193-8. doi: 10.1097/CCM.0b013e31822ea119 [published Online First:  
21  
22 2011/09/20]
- 23  
24 47. Jardin F. Cyclic changes in arterial pressure during mechanical ventilation.  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60
47. Jardin F. Cyclic changes in arterial pressure during mechanical ventilation.  
*Intensive care medicine* 2004;30(6):1047-50. doi: 10.1007/s00134-004-2254-0  
[published Online First: 2004/03/31]
48. Mahjoub Y, Lorne E, Micaux Y, et al. Accuracy of automated continuous  
calculation of pulse pressure variation in critically ill patients. *Intensive care medicine*  
2011;37(2):360-1. doi: 10.1007/s00134-010-2064-5 [published Online First:  
2010/10/21]
49. Kim HK, Pinsky MR. Effect of tidal volume, sampling duration, and cardiac  
contractility on pulse pressure and stroke volume variation during positive-pressure  
ventilation. *Critical care medicine* 2008;36(10):2858-62. doi:  
10.1097/CCM.0b013e3181865aea [published Online First: 2008/09/04]
50. Rex S, Schälte G, Schroth S, et al. Limitations of arterial pulse pressure variation  
and left ventricular stroke volume variation in estimating cardiac pre-load during  
open heart surgery. *Acta anaesthesiologica Scandinavica* 2007;51(9):1258-67. doi:  
10.1111/j.1399-6576.2007.01423.x [published Online First: 2007/08/24]

1  
2  
3  
4  
5  
6  
7  
8 **Contributors:** SH and GY conceived and designed the meta-analysis; SH and YJ  
9  
10 searched the literature; SH and YJ analysed the data; SH and YJ contributed analysis  
11  
12 tools; SH wrote the paper; SH and GY revised the manuscript.  
13  
14

15  
16 **Funding:** The authors have not declared a specific grant for this research from any  
17  
18 funding agency in the public, commercial or not-for-profit sectors.  
19  
20

21  
22  
23 **Competing interests:** None declared.  
24  
25

26  
27 **Data availability statement:** All data relevant to the study are included in the  
28  
29 article or uploaded as online supplemental information. No additional data available.  
30  
31

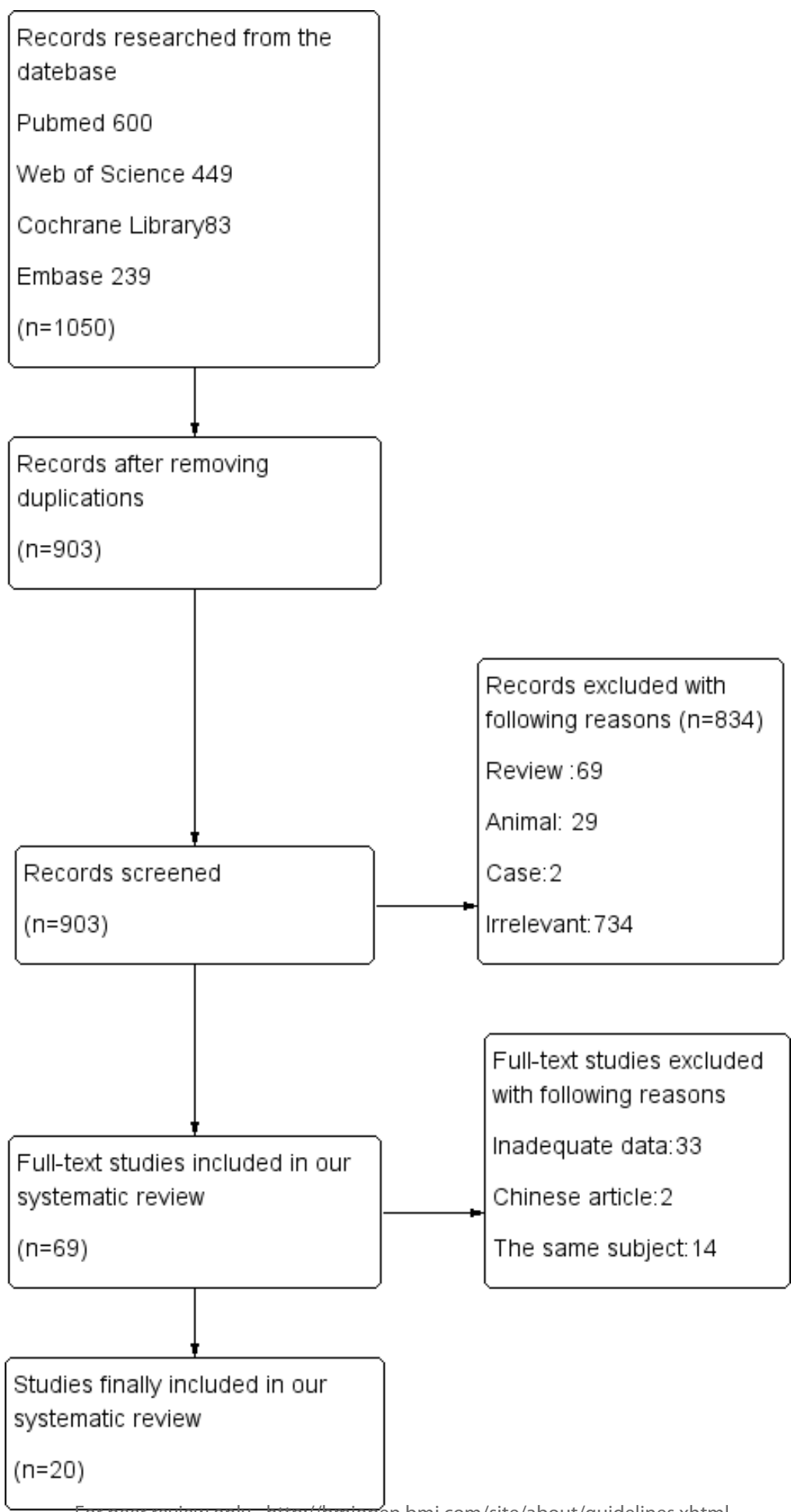
32  
33  
34 **Fig. 1** The search, included and exclusion of the literature  
35

36  
37 **Fig. 2** The result of quality assessment of the included articles (overview)  
38

39  
40 **Fig. 3** The result of quality assessment of each articles  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

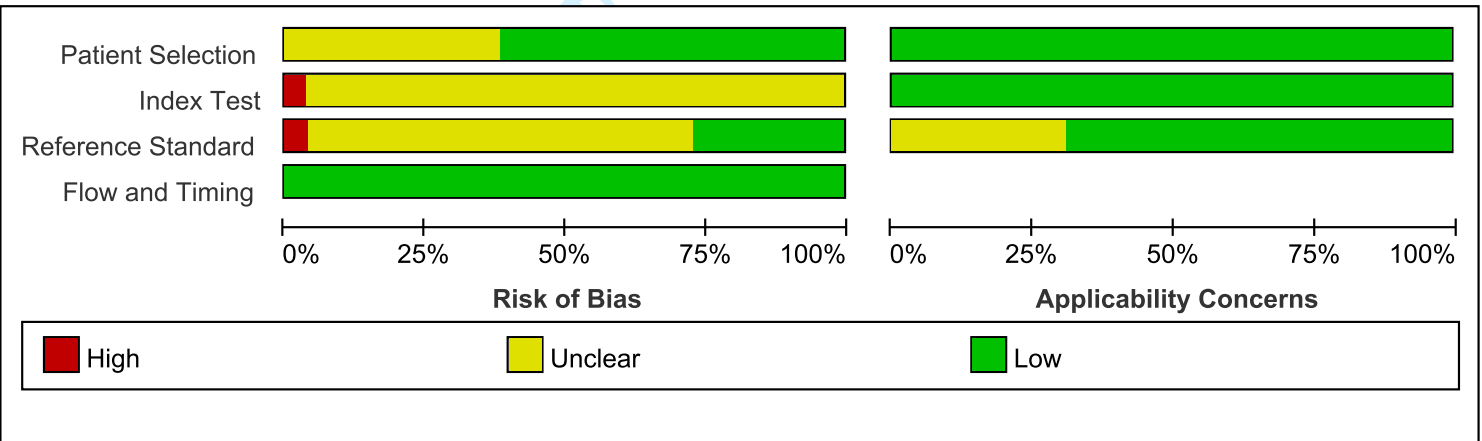


1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only



only

	<u>Risk of Bias</u>				<u>Applicability Concerns</u>		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
1							
2							
3							
4							
5							
6							
7							
8							
9	Belloni 2008	+	-	-	+	+	+
10							
11	Broch 2011	?	?	?	+	+	+
12							
13	Broch 2012	?	?	?	+	+	+
14							
15	Cannesson 2009	+	?	?	+	+	+
16							
17	De Waal 2009	+	?	?	+	+	+
18							
19	Fischer 2013	+	?	?	+	+	+
20							
21	Fu 2014	+	?	?	+	+	+
22							
23	Fu 2015	+	?	?	+	+	+
24							
25	Geerts 2011	+	?	?	+	+	+
26							
27	Haas 2012	+	?	?	+	+	+
28							
29	Hofer 2005	+	?	+	+	+	?
30							
31	Hofer 2008	+	?	+	+	+	?
32							
33	Jeony 2017	+	?	?	+	+	+
34							
35	Kang 2014	+	?	?	+	+	+
36							
37	Kang 2016	+	?	?	+	+	?
38							
39	Kim 2013	+	?	+	+	+	+
40							
41	Kobayashi 2009	+	?	?	+	+	?
42							
43	Miñana 2020	+	?	?	+	+	+
44							
45	Montenij 2016	?	?	?	+	+	+
46							
47	Presiman 2005	?	?	+	+	+	+
48							
49	Reuter 2002	?	?	+	+	+	+
50							
51	Reuter 2003	?	?	+	+	+	+
52							
53	Rex 2007	?	?	+	+	+	?
54							
55	Suehiro 2010	?	?	?	+	+	?
56							
57	Suehiro 2011	?	?	?	+	+	?
58							
59	Wyffels 2010	?	?	?	+	+	?
60							



High



Unclear



Low



# PRISMA 2009 Checklist

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Page 1 ( <b>Title</b> )
<b>ABSTRACT</b>			
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 ( <b>Abstract</b> )
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 1 , 2 ( <b>Background</b> )
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 1 , 2 ( <b>Background</b> )
<b>METHODS</b>			
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 ( <b>Methods</b> )
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 ( <b>Eligibility criterial</b> )
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 ( <b>Search strategy</b> )
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Page 4 ( <b>Search strategy</b> )
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 ( <b>Data Extraction</b> )
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 ( <b>Data Extraction</b> )
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 ( <b>Data</b> )



# PRISMA 2009 Checklist

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

			<b>Extraction)</b>
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 <b>(Quality assessment)</b>
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Page 5 <b>(Statistical treatment)</b>
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> ) for each meta-analysis.	Page 5 <b>(Statistical treatment)</b>

Page 1 of 2

<b>Section/topic</b>	<b>#</b>	<b>Checklist item</b>	<b>Reported on page #</b>
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 <b>(Statistical treatment)</b>
<b>RESULTS</b>			
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 <b>(Identification of eligible studies characteristics of the studies , Fig. 1)</b>
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 <b>(Characteristics of the studies, Table 1, 2 )</b>
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 <b>(Assessment of study quality and publication</b>



# PRISMA 2009 Checklist

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

			<b>bias)</b>
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 <b>(Outcome of literature search and study characteristics)</b>
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Page 14 <b>(Results of our meta-analysis, Comparison between subgroups)</b>
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Page 6 <b>(Assessment of study quality and publication bias, Table 4)</b>
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Page 13, 14 <b>(Heterogeneity )</b>
<b>DISCUSSION</b>			
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 <b>(Discussion )</b>
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 <b>(Limitations)</b>
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page 20 <b>(Conclusions)</b>
<b>FUNDING</b>			
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.	<b>N/A</b>

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

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>  
For more information, visit: [www.prisma-statement.org](http://www.prisma-statement.org)



# PRISMA 2009 Checklist

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- 24
- 25
- 26
- 27
- 28
- 29
- 30
- 31
- 32
- 33
- 34
- 35
- 36
- 37
- 38
- 39
- 40
- 41
- 42
- 43
- 44
- 45
- 46
- 47

For peer review only

# BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-051112.R1
Article Type:	Original research
Date Submitted by the Author:	09-Nov-2021
Complete List of Authors:	Huan, Sheng; Nanjing Second Hospital; Nanjing University of Traditional Chinese Medicine Dai, Jin; Nanjing Second Hospital Song, Shilian; Nanjing Second Hospital Zhu, Guining; Nanjing Second Hospital Ji, Yihao; Nanjing University of Traditional Chinese Medicine; The Second Hospital of Nanjing Yin, Guoping; Nanjing Second Hospital; Nanjing Medical University
<b>Primary Subject Heading</b>:	Anaesthesia
Secondary Subject Heading:	Anaesthesia, Cardiovascular medicine, Surgery
Keywords:	Thoracic surgery < SURGERY, Cardiac surgery < SURGERY, Anaesthesia in cardiology < ANAESTHETICS, ANAESTHETICS

SCHOLARONE™  
Manuscripts





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

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

Sheng Huan<sup>1,2</sup>, Jin Dai<sup>1,2</sup>, Shilian Song<sup>1,2</sup>, Guining Zhu<sup>1,2</sup>, Yihao Ji<sup>1,3</sup>, Guoping Yin<sup>2\*</sup>

1 Nanjing University of Traditional Chinese Medicine, Nanjing, Jangsu, China

2 Department of Anesthesiology, The Second Hospital of Nanjing, Nanjing, Jangsu, China

3 Department of Critical Medicine, The Second Hospital of Nanjing, Nanjing, Jangsu, China

## Correspondence to

Guoping Yin;

Postal address: Department of Anesthesiology, The Second Hospital of Nanjing, 1-1Zhongfu Road, Nanjing, Jiangsu, China.

E-mail: yinguoping0304@hotmail.com

Telephone: ++86+13801585795

Fax numbers: 025-83626060

**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

1  
2  
3 system (AUC =0.80, Youden index =0.38) and large tidal volume (TV) (AUC =0.81,  
4 Youden index =0.48) in thoracic surgery, colloid (AUC =0.85, Youden index =0.55)  
5 and postoperation (AUC =0.85, Youden index =0.63) in cardiac surgery, passive leg  
6 raising (PLR) (AUC =0.90, Youden index =0.72) in cardiac ICU were reliable.  
7

8 **Conclusion:** SVV had good predictive performance in cardiac surgery or ICU after  
9 cardiac surgery and had fair predictive performance in thoracic surgery. Nevertheless,  
10 technical and clinical variables may affect the predictive value potentially.  
11

### 12 **Strengths and limitations of this study:**

- 14 • As far as we know, this is the first systematic review and meta-analysis  
15 discussing the predicative value of fluid responsiveness of SVV during thoracic  
16 and cardiac perioperation.
- 17 • We assessed the included studies with QUADAS-2 tool in Review Manager V.5.3  
18 to ensure their quality.
- 19 • Three different software (Stata V.14.0, Review Manager V.5.3, and R V.3.6.3)  
20 were used to compare the predictive value of SVV between different subgroups.  
21
- 22 • A limitation was the existence of overall heterogeneity among our included  
23 studies.
- 24 • We did not discuss whether the SVV is suitable for children in thoracic and  
25 cardiac surgery due to a lack of relevant studies.  
26  
27  
28  
29

### 30 **Introduction**

31  
32 Fluid therapy is the most important factor for maintaining a stable internal  
33 environment during perioperative period, especially in thoracic and cardiac surgery.<sup>1</sup>  
34 In recent years, more and more studies have showed that goal directed fluid therapy  
35 (GDFT) can provide individual treatment for patients, preventing perioperative  
36 patients from potentially hypovolemia or hypervolemia and reducing complications  
37 or mortality. According to Frank Starling's curve,<sup>2</sup> the preload of the ventricle is  
38 proportional to the cardiac output (CO) in the raising stage. However, if the preload  
39 reaches the platform stage, fluid therapy would not yield the desired effect but result  
40 in cardiac overload and tissue edema.<sup>3 4</sup> Therefore, it is urgent to find an effective  
41 method of hemodynamics monitoring sensitive to fluid responsiveness.  
42  
43

44  
45 Anaesthetists previously tended to use traditional hemodynamic indicators to  
46 monitor hemodynamics and predict fluid responsiveness, such as central venous  
47 pressure (CVP), pulmonary artery diastolic pressure (PADP), and cardiac index (CI).<sup>5</sup>  
48 However, it was of limited utility in reflecting actual ventricular preload, which may  
49 be affected by many non-cardiovascular factors. On the other hand, although  
50 transoesophageal echocardiography (TEE), serving as a gold standard of evaluating  
51 cardiac function, has indisputable advantages in monitoring ventricular preload and  
52 guiding fluid therapy, its complex manipulations and potential complications prevent  
53 it from being widely used in thoracic and cardiac surgery.<sup>6</sup> Stroke volume variation  
54 (SVV) offers a good middle ground between them, and combine their superiority and  
55 security during perioperative period.<sup>7</sup>  
56

57  
58 SVV means the variation of stroke volume (SV) in 30 seconds and was considered  
59 a reliable parameter under the condition of closed chest.<sup>8</sup> It reflects the effect of  
60 respiratory movement on venous return. During inspiration of mechanical ventilation,

1  
2  
3 the increase of intrapulmonary pressure significantly decreases the negative  
4 intrapleural pressure, thereby decreasing venous return and CO. During expiration,  
5 the opposite changes occur.<sup>9</sup> When the body has insufficient circulating blood  
6 volume, the variation of SV fluctuates obviously with the switching between  
7 inspiratory and expiration. Thus, the fluid responsiveness can be predicted according  
8 to SVV, so as to judge the condition of blood volume. Toyoda et al<sup>10</sup> reported a  
9 curvilinear relationship between the right ventricular end-diastolic volume index  
10 (RVEDVI) and SVV. They found the regression curve accorded better with SVV than  
11 with CVP or PADP, showing its reliable predictive value of RVEDI.  
12  
13

14 Several meta-analysis have synthesised present evidence and evaluated the  
15 reliability of SVV in common surgery of children and adults, but there was still no a  
16 systematic review discussing whether SVV could be applied for thoracic and cardiac  
17 surgery. Lots of trials have been conducted to investigate this issue.<sup>11-30</sup>  
18 Unfortunately, they haven't been able to reach a consensus so far. A series of  
19 studies proved good reliability of SVV in predicting fluid responsiveness during such  
20 surgery.<sup>11 16 18 20-22 24-25 27-30</sup> However, some other studies are not convincing due to  
21 different anesthesia and surgical strategy, such as model of mechanical ventilation,  
22 position, method of fluid therapy, moment of maneuvers, etc.<sup>12-15 17 19 23 26</sup> Fu et  
23 al<sup>12</sup> and Suehiro et al<sup>17</sup> reported that SVV was not suitable for thoracic surgery when a  
24 protection ventilation was conducted. Miñana et al<sup>15</sup> found that SVV successfully  
25 predicted fluid responsiveness only in thoracoscopy but not thoracotomy. Moreover,  
26 Fishcher et al<sup>26</sup> reported that SVV also could not give a good performance within the  
27 first 6 post-operative hours in cardiac ICU. There seems to be a great deal of debate  
28 about which anesthesia or surgical strategy SVV is more appropriate for in thoracic  
29 and cardiac surgery. However, no large-sample study has been conducted to  
30 evaluate the utility of SVV in such conditions and surgery. The purpose of this  
31 meta-analysis was to review relevant literatures and systematically evaluate the  
32 predictive value of SVV in such surgery, and provide evidence and guidance for the  
33 clinical application of SVV.  
34  
35  
36

## 37 **METHODS**

38  
39 The meta-analysis was performed according to the Preferred Reporting Items for  
40 Systematic Reviews and Meta-Analyses (PRISMA) statement issued in 2009.<sup>31</sup>  
41

### 42 **Description of investigated indices**

43  
44 SVV is the ratio of the difference between the maximum and the minimum of the SV  
45 and the mean of the SV during 30 seconds as follows:  $(SV_{\max} - SV_{\min}) / SV_{\text{mean}}$ .  
46

### 47 **Eligibility criterial**

48  
49 We included diagnostic trials evaluating the accuracy and effectiveness of SVV in  
50 predicting fluid responsiveness in the operating room (OR) and ICU. We excluded  
51 review articles, commentaries, case reports and research papers on animal or in vitro  
52 experimental studies. In addition, we also excluded studies of which the subjects  
53 were pregnant women or patients with spontaneous breathing, sepsis, shock, and  
54 arrhythmia.  
55

### 56 **Search strategy**

57  
58 We searched PubMed, Web of Science, EMBASE, and the Cochrane Library database  
59 for relevant literature by using searching terms such as SVV, stroke volume variation,  
60

1  
2  
3 responsiveness, and predict. The full search strategy was described in the online  
4 supplemental file. The initial search was conducted on August 9, 2020 with a  
5 language restriction of English.  
6

### 7 **Data extraction and quality assessment**

8  
9 Backgrounds and conclusions of the included literatures were screened  
10 independently by two authors, following the inclusion and exclusion criteria. Then,  
11 the full content was read in detail. Disagreements or discrepancies were resolved by  
12 discussion with the third author. The information was extracted from the included  
13 studies as follows: study characteristics (last name of the first author, publication  
14 year, sample number, operations, fluid therapy, reference standard, position, TV,  
15 positive end-expiratory pressure, endoscopy, and moments of manoeuvres) and  
16 outcome indicators (TP, FP, TN, FN, sensitivity, specificity, best cut-off, AUC, and  
17 correlation coefficient). When there were insufficient or missing data, one author  
18 contacted the corresponding author of the included article to obtain the necessary  
19 data.  
20  
21

22  
23 The quality of our included studies was assessed by two authors independently  
24 using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) in  
25 Review Manager 5.3(Cochrane Library, Oxford, UK).<sup>32</sup> QUADAS-2 mainly consists of  
26 four parts (case selection, trials to be evaluated, gold standard, case process and  
27 progress). All components would be assessed in terms of bias risk, and the first three  
28 components would also be assessed in terms of clinical. In addition, publication bias  
29 was also checked using Deeks' Funnel Plot Asymmetry Test in Stata V.14.0.<sup>33</sup> quality  
30 assessment was performed independently by two authors. Disagreements were  
31 reconciled through discussion until a consensus was reached.  
32

### 33 **Statistical treatment and Quality assessment**

34  
35 The Stata software V.14.0 was used for basic calculations. Subgroup analysis on  
36 primary outcomes stratified by intervention, TV, positive end-expiratory pressure  
37 (PEEP), position, endoscopy and moments of maneuvers was conducted. When the  
38 number of included studies within some subgroups was less than four, not meeting  
39 the minimum requirements of Stata V.14.0, we used Review Manager V.5.3 and R  
40 V.3.6.3 to process data in these subgroups. For comparing the AUC, the Review  
41 Manager V.5.3 could only display the summary receiver operating characteristics  
42 (SROC) and the R V.3.6.3 could only give the result of mean AUC. The operative  
43 performance is graduated as follows:  
44

- 45 o AUC 0.9-1 excellent operative performance
- 46 o AUC 0.8-0.9 good operative performance.
- 47 o AUC 0.7-0.8 fair operative performance.

48  
49  
50  
51 We used correlation (Mixed Model) of Stata to evaluate whether a threshold effect  
52 existed. When the correlation was positive and its P value was  $>0.05$ , no threshold  
53 effect was considered to exist. We then used a random-effects model to calculate  
54 pooled sensitivity, specificity and AUC with 95% CI. Statistical heterogeneity was  
55 estimated using the Cochrane Q and  $I^2$  tests,<sup>34</sup> and it was considered to be present  
56 when  $I^2 > 50\%$  or  $P < 0.05$ . In such cases, meta-regression analysis and sensitivity  
57 analysis were used to determine the sources of heterogeneity.  
58  
59

### 60 **Patient and public involvement**

1  
2  
3 Patient and public involvement is not applicable for this meta-analysis.  
4

## 5 **RESULTS**

### 7 **Outcome of literature search and study characteristics**

8  
9 Of the 795 related articles, 645 articles remained after eliminating duplicates. Then,  
10 we excluded 576 articles because they were case reports, review articles, articles  
11 related to animal experiments or other irrelevant studies. Among the remaining 69  
12 articles, 14 studies repeated the same content, two studies were not published in  
13 English, and data of our interest could not be obtained for 33 articles. Finally, 20  
14 articles were included in our meta-analysis (figure 1).  
15

16 The 20 articles included 854 patients. The main kinds of monitoring systems were  
17 FloTrac/Vigileo system and PiCCO system. Geerts et al<sup>28</sup> used pulmonary artery  
18 catheter insertion to measure thermodilution CO and CVP. Kang et al<sup>29</sup> used  
19 Swan-Ganz and NICOM monitors to detect SV and calculate SVV. We defined TV < 8  
20 ml/kg as 'low TV' and TV  $\geq$  8 ml/kg as 'high TV'; absence of PEEP or PEEP < 5  
21 mmHg was considered non-PEEP. When the infusion volume was set above 5 ml/kg  
22 or 250 ml, we considered the study to involve a large bolus group. If not, it was  
23 considered a small bolus group. Some patients in the same study accepted fluid  
24 challenge with two different systems<sup>27</sup> or accepted different methods of TV  
25 ventilation.<sup>12 17</sup> We included both conditions of these studies in our meta-analysis.  
26 The basic characteristics of our included studies are presented in Table 1 and  
27 Supplementary Table1.  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Study	Year	Surgery	Number	Standard	Intervention	Result	Device	PEEP (mmHg)	TV ( ml/kg)	Position	Endosc ope	Moment of maneuver
1												
Thoracic surgery												
3 4 5	Kang et al <sup>11</sup> 2016	Pulmonary lobectomy	76	$\Delta$ SVI> 25%	10 ml/kg colloid	Yes	FloTrac-Vigil eo system	0	4	Supine	NO	After lung recruitment maneuver and thorax closure.
6 7 8	6 et al <sup>12</sup> 2015	Esophagect omy	24	$\Delta$ CI>15%	7 ml/kg colloid	No Yes	FloTrac-Vigil eo system	5	6 8	Lateral	YES	After the procedure of laparoscopic part.
9 10 11	9 et al <sup>13</sup> 2014	Pulmonary lobectomy	30	$\Delta$ CI>10%	8 ml/kg colloid	NO	PiCCO system	0	8	Lateral decubitus	NO	Before, and within 30s after volume expansion (VE) without stimulation.
11 12 13	Minana et al <sup>14</sup> 2020	open lung resection	76	$\Delta$ CI>10%	250ml crystalloids	NO	PiCCO system	5	6	lateral	NO	Once the patient had been placed lateral, with the chest open.
14 15 16	14 et al <sup>15</sup> 2017	Lung cancer surgery	79	$\Delta$ CI>10%	7 ml/kg colloid	No	FloTrac-Vigil eo system	5	6	Lateral	Disput e	15 minutes after the start of OLV, before and after finishing fluid loading.
17 18	Suehiro et al <sup>16</sup> 2010	Lobectomy	30	$\Delta$ CI>25%	500ml colloid	Yes	FloTrac-Vigil eo system	5	8	Lateral	YES	Before and after volume loading.
19 20 21	Sueniro et al <sup>17</sup> 2011	Lobectomy	37	$\Delta$ CI>15%	500ml colloid	No Yes	FloTrac-Vigil eo system	5	6 8	Lateral	YES	30 min after starting OLV.
Cardiac surgery												
23 24 25	Kim et al <sup>18</sup> 2013	Coronary surgery	33	$\Delta$ SVI> 12%	500ml colloid	Yes	FloTrac-Vigil eo system	5	10	NA	NA	Before sternotomy to maintain consistency of the closed thorax.
26 27 28	Mehenij et al <sup>19</sup> 2016	CABG	22	$\Delta$ CO>15%	7ml/kg crystalloid	NO	FloTrac-Vigil eo system	5-10	8	NA	NA	Between induction of anaesthesia and incision.
29 30	Broch et al <sup>20</sup> 2011 2011	CABG	81	$\Delta$ SVI> 12%	PLR	Yes	PiCCO system	5	8	NA	NA	After induction of anesthesia before surgery.
31 32 33	Broch et al <sup>21</sup> 2012	CABG	92	$\Delta$ SVI> 15%	PLR	Yes	PiCCO system	5	8	NA	NA	After induction of anesthesia before surgery.
34 35	Hoff et al <sup>22</sup> 2005	Off-Pump CABG	40	$\Delta$ SVI> 25%	10mL/kg colloid	Yes	PiCCO system	0	10	NA	NA	Prior to any surgical intervention or volume replacement.
36 37 38 39	Preisman et al <sup>23</sup> 2005	CABG	18	$\Delta$ 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.
40 41 42	Haas et al <sup>24</sup> 2012	Cardiac Surge	18	$\Delta$ CI>10%	4 mL/kg colloid	Yes	PiCCO system	5	8	NA	NA	After completion of cardiac surgery and thoracic closure.
43 44 45	Andersson et al <sup>25</sup> 2009 2009	CABG	25	$\Delta$ CI>15%	500ml colloid	Yes	FloTrac-Vigil eo system	0-2	8-10	NA	NA	After a 3 min period of hemodynamic stability.
ICU after cardiac surgery												
47 48 49	Hofner et al <sup>26</sup> 2013	ICU	37	$\Delta$ CI>15%	500ml colloid	No	PiCCO s	NA	NA	NA	NA	within the first 6 post-operative hours
50 51 52 53 54	Hofer et al <sup>27</sup> 2008	ICU	40	$\Delta$ SV>25%	PLR	Yes	PiCCO system FloTrac-Vigil eo system	5	8-10	NA	NA	After transfer of patients to the intensive care unit.

55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Geerts et al <sup>28</sup>	2011	ICU	20	ΔCO>7%	PLR	Yes	Pulmonary artery catheter	5	8-10	NA	NA	NA
Kang et al <sup>29</sup>	2014	ICU	54	ΔCO>7%	PLR	Yes	Swan-Ganz NICOM	5	10	NA	NA	NA
DeWaal et al <sup>30</sup>	2009	ICU	22	ΔSVI>12%	7ml/kg colloid	Yes	PiCCO system	5	8	NA	NA	After stabilization of the patients arriving 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<sup>2</sup> = 92%) and 15.791 (P < 0.001, I<sup>2</sup> = 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<sup>2</sup> = 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<sup>15</sup> 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 shown 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 calculate 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 system 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	Youden index
		AUC(95% CI)-ROC	Sensitivity(95% CI)	Specificity(95% CI)	DOR(95% CI)	Result of AUC comparison	AUC	Youden index
<b>Thoracic surgery</b>	<b>9</b>	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
Prone 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
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
<b>Cardiac surgery</b>	<b>8</b>	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

1  
2

3 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
4 Fluid challenge	2					Low	0.73	0.41
5 PLR	4					High	0.90	0.72

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

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 (FIO<sub>2</sub>), 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.<sup>35</sup> 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.<sup>17</sup> Alvarado et al<sup>36</sup> found that low PEEP (0–10 mmHg) had no significant effect on cardiac preload due to release of most

1  
2  
3 pressure generated from the ventilator to the atmosphere<sup>16</sup>, whereas high PEEP (10–  
4 15 mmHg) would mistakenly make SVV predict actual blood volume<sup>37</sup>. This  
5 phenomenon would become more evident in OLV, in agreement with our result.  
6 However, another study reported an opposite conclusion that SVV is not affected by  
7 PEEP or driving pressures<sup>36</sup>, which may be explained by the difference between OLV  
8 and normal ventilation. This suggests that the effect of respiratory pressure and TV  
9 on SVV depends primarily on the degree to which these variables transmitted to the  
10 pulmonary circulation, rather than absolute value. As far as our result were  
11 concerned, high TV without PEEP may be better recommended in thoracic surgery  
12 when SVV monitoring. This may also be the reason for the high accuracy of SVV in  
13 perioperative patients with cardiac surgery, because all patients received normal  
14 mechanical ventilation with 8 ml/kg TV and non-PEEP. However, it cannot be ignored  
15 that the use of non-protective ventilation during period of OLV may cause damage to  
16 the healthy lung. In total, the applicability of SVV in thoracic surgery is fair and  
17 limited.  
18  
19

20  
21 We found that fluid therapy with large bolus had better reliability of SVV in  
22 thoracic surgery, whereas small bolus fluid therapy was more recommended in  
23 cardiac surgery. Patients undergoing cardiac surgery usually have cardiac  
24 dysfunction, not tolerating a large bolus during in a short period, whereas in thoracic  
25 surgery patients often experience heavy bleeding and need large bolus of colloid to  
26 maintain body blood volume. Regarding the type of fluid, the colloid rather than  
27 crystalloid could quickly compensate for fluid loss to achieve satisfactory CO<sup>8</sup> and  
28 significantly increase RVEDVI.<sup>38</sup> Ma et al<sup>39</sup> found that PLR could replace fluid  
29 challenge as a more effective intervention in protection ventilation patients during  
30 cardiac surgery. By transfer of approximately 300 ml of venous blood from the lower  
31 body toward the right heart, PLR can mimic a fluid challenge and increase systemic  
32 filling pressure without influencing vascular resistance. However, our result showed  
33 that fluid challenge has larger AUC than PLR in cardiac surgery, and PLR was more  
34 suitable for ICU patients, especially those with cardiovascular dysfunction.<sup>29</sup> Precious  
35 systematic review has showed that the change of CO and pulse press induced by PLR  
36 can reliably predict the response of CO to volume expansion in adult patients with  
37 acute circulatory failure. The preload of right and left ventricles was increased to a  
38 sufficient extent to induce fluid responsiveness, having the same effect as the liquid  
39 challenge. PLR has been proposed by consensus conference of the European Society  
40 of Intensive Care Medicine for a long time and became a useful maneuver of predict  
41 fluid responsiveness in the high-risk patients.<sup>40 41</sup>  
42  
43  
44

45 As to monitoring device, FloTrac/Vigileo system was better recommended in  
46 thoracic surgery. It has lower thresholds than the PiCCO system and predicts the  
47 insufficiency of blood volume earlier with good sensitivity even if the wave of  
48 hemodynamic status remained weak in OLV.<sup>27</sup> In addition, it need no calibration and  
49 was less affected by arterial compliance and elasticity.<sup>42</sup> However, misestimation of  
50 blood volume may happen when a rapid wave of CO occurs.<sup>43</sup> The PiCCO system can  
51 be used only after correction for low-temperature saline, and it is difficult to  
52 continuously calibrate the system during surgery in cases of heavy bleeding.<sup>44</sup> It was  
53 reported that latest version of PiCCO system incorporates adapted vascular  
54 compliance measurement from every 10 minutes to every one minute based on a  
55 modification algorithm<sup>45</sup>, giving a more accurate result of SVV. Wiesenack et al<sup>46</sup>  
56 reported a significant correlation between baseline SVV and changes of SVI after  
57 updating the algorithm of PiCCO system, which was opposite to their previous  
58 negative result. Therefore, the version update of monitoring device may make SVV  
59 more and more suitable for difficulty conditions.  
60

1  
2  
3 Our analysis did not include studies with arrhythmia patients because it is reported  
4 that wide pulse pressure could seriously affect accuracy of SVV<sup>18</sup>. Similarly, in shock  
5 patients or patients with heart failure, the diagnostic value of SVV was greatly  
6 limited<sup>47</sup>. However, Cannesson et al<sup>48</sup> reported that a new SVV algorithm using  
7 multi-parameter signal recognition to reject ectopic beats could work well even in  
8 patients with arrhythmia. Heart failure could seriously decrease the ventricular  
9 output due to the increasing afterload during inspiration<sup>49</sup>. Right ventricular  
10 dysfunction would also lead to false positive prediction of preload<sup>50</sup>. Interestingly,  
11 some studies found that SVV applied in patients with slightly impaired LV function  
12 (50% $\geq$ EF $\geq$ 30%) still had good values.<sup>10 23</sup> This showed that SVV may have a  
13 potential value in predicting fluid responsiveness of patients with mild cardiac  
14 dysfunction. Moreover, we found monitoring after main operative manipulation had a  
15 better predictive value than that monitoring before that, which may result from  
16 partial cure of cardiac dysfunction.  
17  
18

19  
20 Previous studies have shown that SVV is suitable for laparoscopic surgery in  
21 different positions such as supine, lateral decubitus, or prone positions. However,  
22 thoracoscopy, different from other endoscopy, creates a continuous intrathoracic  
23 pressure, which compresses the mediastinum and contralateral lung and further  
24 reducing lung compliance.<sup>35 51</sup> Oppositely, opening the chest cavity would increase  
25 the aortic impedance and decrease venous return, strongly affecting the correlation  
26 between SV and pulse pressure.<sup>23</sup> Therefore, SVV correlated closely with the  
27 ventricular preload when the pericardium is closed.<sup>30 52</sup> Our result also showed supine  
28 position is better in thoracic surgery when monitoring with SVV. However, the  
29 applicability of SVV may be further limited because the lateral position is mostly used  
30 when thoracic surgery is in progress. Interestingly, Kang et al<sup>11</sup> found that SVV also  
31 has good diagnostic value during lung recruitment manoeuvre. This may prove that  
32 SVV was suitable for different time periods in surgery, not just during operative  
33 manipulation.  
34  
35

36  
37 Systolic pressure variation (SPV) and pulse pressure variation (PPV) are also widely  
38 used in guiding intraoperative fluid therapy. However, present studies suggested that  
39 SVV may be more applicable in patients with high-risk non cardiac surgery.<sup>53</sup> Some  
40 studies found correlation coefficients between baseline SVV with  $\Delta$ SVI were higher  
41 than PPV, and SPV with  $\Delta$ SVI. SV is derived from the arterial pressure waveform, and  
42 relies on the PulseCO algorithm. SPV and PPV, on the other hand, is based on  
43 absolute measures of arterial waveform analysis, which may not reflect true CO as  
44 accurately as former.<sup>54</sup>  
45

46  
47 As development of anesthesiology and surgery, number of patients accepting  
48 thoracic and cardiac surgical operations increased rapidly. Perioperative  
49 haemodynamic monitoring combined with GDFT has been demonstrated to usefully  
50 reduce mortality and cardiac dysfunction. More and more anaesthetists and surgeons  
51 are now aware of the importance of body fluid balance and cardiac perfusion during  
52 perioperative period. Despite this, the reliability of minimally invasive cardiac output  
53 monitoring indicator is not widely accepted, and a lack of consensus on monitoring  
54 method and device has done little to promote the popularization of GDFT, especially  
55 in undeveloped areas and grass-rooted hospital. There is increasing evidence that  
56 fluid therapy should be defined as 'the right amount of the right type at the right  
57 time', but this is hard to be perfectly performed. When a patient showed hypotension  
58 or pallor, it does not imply that this patient blindly needs large bolus of crystalloid or  
59 colloid infusion. The specific liquid therapy needs to be reasonably and individually  
60

1  
2  
3 analysed and chosen according to anesthetic management and surgical  
4 manipulation.  
5

6 The use of SVV monitoring for high-risk surgery was firstly put forward by the  
7 National Institute for Clinical Excellence (NICE) in the UK in 2012. During recent  
8 years, it is obvious that the popularization of SVV monitoring has been more  
9 prompted. However, whether these monitoring device and indicators accurately  
10 predict responsiveness of fluid therapy in high-risk patients and when the necessary  
11 fluid therapy is required are still not clear. More studies related with SVV in thoracic  
12 and cardiac surgical should be conducted.  
13

14 In view of authors, our study assisted rational decisionmaking and provide clinical  
15 consistency for the high-risk thoracic and cardiac patients in guiding fluid therapy  
16 and for this cohort the potential complication and complexity of minimally. SVV in  
17 perioperative period of thoracic and cardiac surgery may be justified.  
18  
19

## 20 21 22 **Limitations and strengths**

23 Our meta-analysis has some limitations. First, heterogeneity existed in the overall  
24 dataset and in most subgroups, so our conclusion should be interpreted with caution.  
25 Second, the best cut-off value of our included articles was too wide, ranging from  
26 3.5 to 13.5. Physicians and anesthesiologists should refer to the related articles when  
27 choosing the appropriate cut-off value. Third, we did not discuss the effect of  
28 vasoactive drugs on SVV because of lack of relevant data. Fourth, most studies on  
29 cardiac surgery patients involved coronary artery surgery, which prevents us from  
30 applying our conclusions to all cardiac surgery types. Therefore, multicentre and  
31 large-sample studies should be performed.  
32  
33

34 There are also several strengths in our research. First, this is the first diagnostic  
35 meta-analysis studying the reliability of SVV in predicting responsiveness to fluid  
36 therapy of patients undergoing cardiac and thoracic surgery. Second, most of our  
37 included studies are of high quality. Third, we used three different software to  
38 compare the predictive value of SVV between subgroups, so our results have a high  
39 credibility.  
40  
41

## 42 **CONCLUSION**

43  
44 SVV has good predictive performance in patients accepting cardiac surgery in OR  
45 and ICU, and has fair predictive performance in patients accepting thoracic surgery  
46 with OLV. Colloid infusion, high TV, and non-PEEP ventilation can effectively improve  
47 the accuracy of SVV in both thoracic and cardiac surgery. PLR was more suitable in  
48 ICU, whereas fluid challenge is more appropriate in OR. When performing fluid  
49 challenge, a large bolus in thoracic surgery and a small bolus in cardiac surgery were  
50 the preferred options. Regarding the monitoring device, the FloTrac/Vigileo system  
51 was better recommended than the PiCCO system during surgery.  
52  
53

54  
55  
56 **Acknowledgments** The authors would like to thank all the researchers of the  
57 included articles for their data. We appreciate the help from Wordvice company for  
58 revising the language in this manuscript.  
59  
60

**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.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**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

## REFERENCES

- [dataset] [1] Navarro LH, Bloomstone JA, Auler JO, Jr., et al. Perioperative fluid therapy: a statement from the international Fluid Optimization Group. *Perioperative medicine (London, England)* 2015;4:3. doi: 10.1186/s13741-015-0014-z
- [dataset] [2] Ribarič S, Kordaš M. Simulation of the Frank-Starling Law of the Heart. *Computational and mathematical methods in medicine* 2012;2012:267834. doi: 10.1155/2012/267834
- [dataset] [3] Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *The New England journal of medicine* 2001;345(19):1368-77. doi: 10.1056/NEJMoa010307
- [dataset] [4] Kirov MY, Kuzkov VV, Molnar Z. Perioperative haemodynamic therapy. *Current opinion in critical care* 2010;16(4):384-92. doi: 10.1097/MCC.0b013e32833ab81e
- [dataset] [5] Redondo FJ, Padilla D, Villarejo P, et al. The Global End-Diastolic Volume (GEDV) Could Be More Appropriate to Fluid Management Than Central Venous Pressure (CVP) During Closed Hyperthermic Intrabdominal Chemotherapy with CO<sub>2</sub> Circulation. *Journal of investigative surgery : the official journal of the Academy of Surgical Research* 2018;31(4):321-27. doi: 10.1080/08941939.2017.1325543

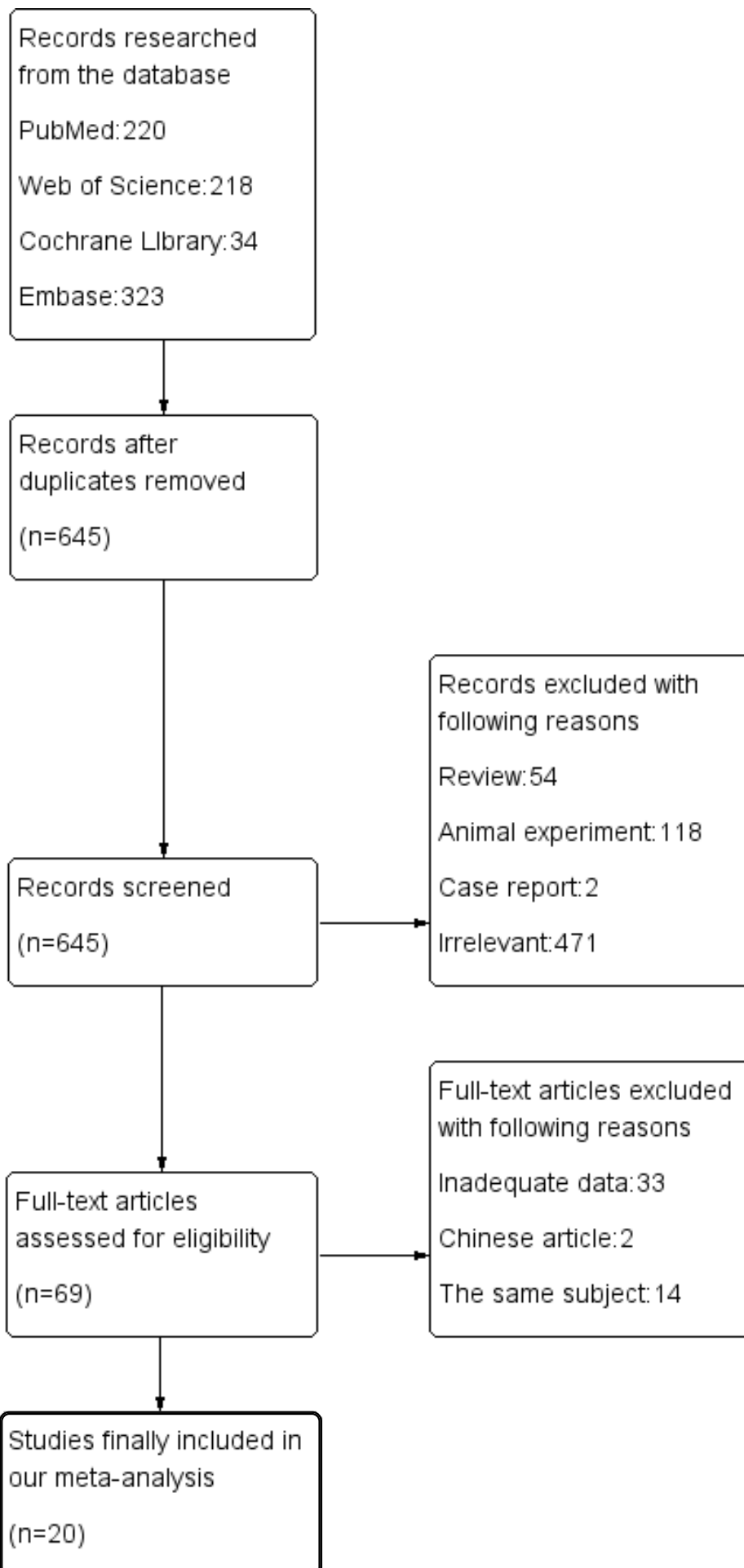
- 1  
2  
3 [dataset] [6] Reuter DA, Kirchner A, Felbinger TW, et al. Usefulness of left  
4 ventricular stroke volume variation to assess fluid responsiveness in patients with  
5 reduced cardiac function. *Critical care medicine* 2003;31(5):1399-404. doi:  
6 10.1097/01.Ccm.0000059442.37548.E1  
7  
8 [dataset] [7] Sahutoglu C, Turksal E, Kocabas S, et al. Influence of stroke volume  
9 variation on fluid treatment and postoperative complications in thoracic surgery.  
10 *Therapeutics and clinical risk management* 2018;14:575-81. doi:  
11 10.2147/tcrm.S154093  
12 [dataset] [8] Verheij J, van Lingen A, Beishuizen A, et al. Cardiac response is greater  
13 for colloid than saline fluid loading after cardiac or vascular surgery. *Intensive care*  
14 *medicine* 2006;32(7):1030-8. doi: 10.1007/s00134-006-0195-5  
15 [dataset] [9] Michard F, Teboul JL. Using heart-lung interactions to assess fluid  
16 responsiveness during mechanical ventilation. *Critical care (London, England)*  
17 2000;4(5):282-9. doi: 10.1186/cc710  
18 [dataset] [10] Toyoda D, Fukuda M, Iwasaki R, et al. The comparison between  
19 stroke volume variation and filling pressure as an estimate of right ventricular  
20 preload in patients undergoing renal transplantation. *J Anesth* 2015;29(1):40-6. doi:  
21 10.1007/s00540-014-1870-2  
22 [dataset] [11] Kang WS, Oh CS, Park C, et al. Diagnosis Accuracy of Mean Arterial  
23 Pressure Variation during a Lung Recruitment Maneuver to Predict Fluid  
24 Responsiveness in Thoracic Surgery with One-Lung Ventilation. *BioMed research*  
25 *international* 2016;2016:3623710. doi: 10.1155/2016/3623710  
26 [dataset] [12] Fu Q, Duan M, Zhao F, et al. Evaluation of stroke volume variation and  
27 pulse pressure variation as predictors of fluid responsiveness in patients undergoing  
28 protective one-lung ventilation. *Drug discoveries & therapeutics* 2015;9(4):296-302.  
29 doi: 10.5582/ddt.2015.01046  
30 [dataset] [13] Fu Q, Zhao F, Mi W, et al. Stroke volume variation fail to predict fluid  
31 responsiveness in patients undergoing pulmonary lobectomy with one-lung  
32 ventilation using thoracotomy. *Bioscience trends* 2014;8(1):59-63. doi:  
33 10.5582/bst.8.59  
34 [dataset] [14] Miñana A, Parra MJ, Carbonell J, et al. Validation study of the dynamic  
35 parameters of pulse wave in pulmonary resection surgery. *Revista espanola de*  
36 *anestesiologia y reanimacion* 2020;67(2):55-62. doi: 10.1016/j.redar.2019.10.007  
37 [dataset] [15] Jeong DM, Ahn HJ, Park HW, et al. Stroke Volume Variation and Pulse  
38 Pressure Variation Are Not Useful for Predicting Fluid Responsiveness in Thoracic  
39 Surgery. *Anesthesia and analgesia* 2017;125(4):1158-65. doi:  
40 10.1213/ane.0000000000002056  
41 [dataset] [16] Suehiro K, Okutani R. Stroke volume variation as a predictor of fluid  
42 responsiveness in patients undergoing one-lung ventilation. *Journal of cardiothoracic*  
43 *and vascular anesthesia* 2010;24(5):772-5. doi: 10.1053/j.jvca.2010.03.014  
44 [dataset] [17] Suehiro K, Okutani R. Influence of tidal volume for stroke volume  
45 variation to predict fluid responsiveness in patients undergoing one-lung ventilation.  
46 *Journal of anesthesia* 2011;25(5):777-80. doi: 10.1007/s00540-011-1200-x  
47 [dataset] [18] Kim SY, Song Y, Shim JK, et al. Effect of pulse pressure on the  
48 predictability of stroke volume variation for fluid responsiveness in patients with  
49 coronary disease. *Journal of critical care* 2013;28(3):318.e1-7. doi:  
50 10.1016/j.jcrc.2012.09.011  
51 [dataset] [19] Montenij LJ, Sonneveld JP, Nierich AP, et al. Diagnostic accuracy of  
52 stroke volume variation measured with uncalibrated arterial waveform analysis for  
53 the prediction of fluid responsiveness in patients with impaired left ventricular  
54 function: a prospective, observational study. *Journal of clinical monitoring and*  
55 *computing* 2016;30(4):481-6. doi: 10.1007/s10877-015-9743-2  
56  
57  
58  
59  
60



- 1  
2  
3 [dataset] [20] Broch O, Bein B, Gruenewald M, et al. Accuracy of the pleth variability  
4 index to predict fluid responsiveness depends on the perfusion index. *Acta*  
5 *anaesthesiologica Scandinavica* 2011;55(6):686-93. doi:  
6 10.1111/j.1399-6576.2011.02435.x  
7  
8 [dataset] [21] Broch O, Renner J, Gruenewald M, et al. Variation of left ventricular  
9 outflow tract velocity and global end-diastolic volume index reliably predict fluid  
10 responsiveness in cardiac surgery patients. *Journal of critical care*  
11 2012;27(3):325.e7-13. doi: 10.1016/j.jcrc.2011.07.073  
12 [dataset] [22] Hofer CK, Müller SM, Furrer L, et al. Stroke volume and pulse pressure  
13 variation for prediction of fluid responsiveness in patients undergoing off-pump  
14 coronary artery bypass grafting. *Chest* 2005;128(2):848-54. doi:  
15 10.1378/chest.128.2.848  
16 [dataset] [23] Preisman S, Kogan S, Berkenstadt H, et al. Predicting fluid  
17 responsiveness in patients undergoing cardiac surgery: functional haemodynamic  
18 parameters including the Respiratory Systolic Variation Test and static preload  
19 indicators. *British journal of anaesthesia* 2005;95(6):746-55. doi: 10.1093/bja/aei262  
20 [dataset] [24] Haas S, Eichhorn V, Hasbach T, et al. Goal-directed fluid therapy using  
21 stroke volume variation does not result in pulmonary fluid overload in thoracic  
22 surgery requiring one-lung ventilation. *Critical care research and practice*  
23 2012;2012:687018. doi: 10.1155/2012/687018  
24 [dataset] [25] Cannesson M, Musard H, Desebbe O, et al. The ability of stroke  
25 volume variations obtained with Vigileo/FloTrac system to monitor fluid  
26 responsiveness in mechanically ventilated patients. *Anesthesia and analgesia*  
27 2009;108(2):513-7. doi: 10.1213/ane.0b013e318192a36b  
28 [dataset] [26] Fischer MO, Coucoravas J, Truong J, et al. Assessment of changes in  
29 cardiac index and fluid responsiveness: a comparison of Nexfin and transpulmonary  
30 thermodilution. *Acta anaesthesiologica Scandinavica* 2013;57(6):704-12. doi:  
31 10.1111/aas.12108  
32 [dataset] [27] Hofer CK, Senn A, Weibel L, et al. Assessment of stroke volume  
33 variation for prediction of fluid responsiveness using the modified FloTrac and  
34 PiCCOplus system. *Critical care (London, England)* 2008;12(3):R82. doi:  
35 10.1186/cc6933  
36 [dataset] [28] Cherpanath TGV, Hirsch A, Geerts BF, et al. Predicting Fluid  
37 Responsiveness by Passive Leg Raising: A Systematic Review and Meta-Analysis of  
38 23 Clinical Trials. *Critical care medicine* 2016;44(5):981-91. doi:  
39 10.1097/ccm.0000000000001556  
40 [dataset] [29] Geerts BF, Aarts LP, Groeneveld AB, et al. Predicting cardiac output  
41 responses to passive leg raising by a PEEP-induced increase in central venous  
42 pressure, in cardiac surgery patients. *British journal of anaesthesia*  
43 2011;107(2):150-6. doi: 10.1093/bja/aer125  
44 [dataset] [30] de Waal EE, Rex S, Kruitwagen CL, et al. Dynamic preload indicators  
45 fail to predict fluid responsiveness in open-chest conditions. *Critical care medicine*  
46 2009;37(2):510-5. doi: 10.1097/CCM.0b013e3181958bf7  
47 [dataset] [31] Moher D, Liberati A, Tetzlaff J, et al. Reprint--preferred reporting  
48 items for systematic reviews and meta-analyses: the PRISMA statement. *Phys Ther*  
49 2009;89(9):873-80.  
50 [dataset] [32] Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool  
51 for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*  
52 2011;155(8):529-36. doi: 10.7326/0003-4819-155-8-201110180-00009  
53 [dataset] [33] Stuck AE, Rubenstein LZ, Wieland D. Bias in meta-analysis detected by  
54 a simple, graphical test. Asymmetry detected in funnel plot was probably due to true  
55 heterogeneity. *BMJ* 1998;316(7129):469; author reply 70-1.  
56  
57  
58  
59  
60

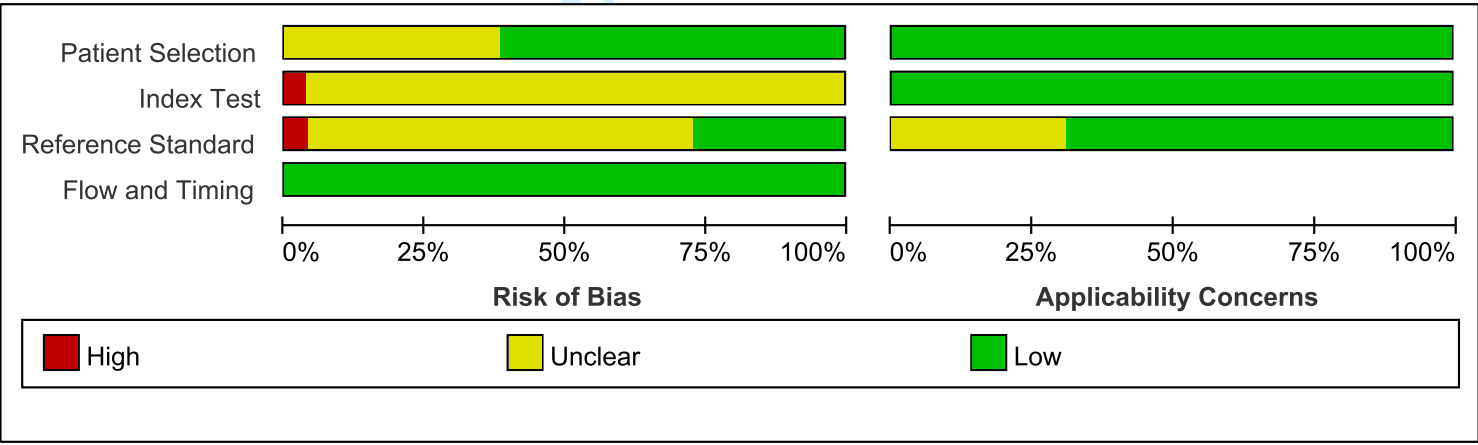
- 1  
2  
3 [dataset] [34] Higgins JP, Thompson SG. Quantifying heterogeneity in a  
4 meta-analysis. *Stat Med* 2002;21(11):1539-58. doi: 10.1002/sim.1186
- 5 [dataset] [35] Romand JA, Shi W, Pinsky MR. Cardiopulmonary effects of positive  
6 pressure ventilation during acute lung injury. *Chest* 1995;108(4):1041-8. doi:  
7 10.1378/chest.108.4.1041
- 8 [dataset] [36] Alvarado Sánchez JI, Caicedo Ruiz JD, Diaztagle Fernández JJ, et al.  
9 Predictors of fluid responsiveness in critically ill patients mechanically ventilated at  
10 low tidal volumes: systematic review and meta-analysis. *Annals of intensive care*  
11 2021;11(1):28. doi: 10.1186/s13613-021-00817-5
- 12 [dataset] [37] Kubitz JC, Annecke T, Kemming GI, et al. The influence of positive  
13 end-expiratory pressure on stroke volume variation and central blood volume during  
14 open and closed chest conditions. *European journal of cardio-thoracic surgery :  
15 official journal of the European Association for Cardio-thoracic Surgery*  
16 2006;30(1):90-5. doi: 10.1016/j.ejcts.2006.04.008
- 17 [dataset] [38] Kanda H, Hirasaki Y, Iida T, et al. Effect of fluid loading with normal  
18 saline and 6% hydroxyethyl starch on stroke volume variability and left ventricular  
19 volume. *International journal of general medicine* 2015;8:319-24. doi:  
20 10.2147/ijgm.S89939
- 21 [dataset] [39] Ma GG, Tu GW, Zheng JL, et al. Changes in Stroke Volume Variation  
22 Induced by Passive Leg Raising to Predict Fluid Responsiveness in Cardiac Surgical  
23 Patients With Protective Ventilation. *Journal of cardiothoracic and vascular  
24 anesthesia* 2020;34(6):1526-33. doi: 10.1053/j.jvca.2019.10.002
- 25 [dataset] [40] Cooke K, Sharvill R, Sondergaard S, et al. Volume responsiveness  
26 assessed by passive leg raising and a fluid challenge: a critical review focused on  
27 mean systemic filling pressure. *Anaesthesia* 2018;73(3):313-22. doi:  
28 10.1111/anae.14162
- 29 [dataset] [41] Monnet X, Marik P, Teboul J-L. Passive leg raising for predicting fluid  
30 responsiveness: a systematic review and meta-analysis. *Intensive care medicine*  
31 2016;42(12):1935-47. doi: 10.1007/s00134-015-4134-1
- 32 [dataset] [42] Manecke GR, Jr., Auger WR. Cardiac output determination from the  
33 arterial pressure wave: clinical testing of a novel algorithm that does not require  
34 calibration. *Journal of cardiothoracic and vascular anesthesia* 2007;21(1):3-7. doi:  
35 10.1053/j.jvca.2006.08.004
- 36 [dataset] [43] Kanazawa M, Fukuyama H, Kinefuchi Y, et al. Relationship between  
37 aortic-to-radial arterial pressure gradient after cardiopulmonary bypass and changes  
38 in arterial elasticity. *Anesthesiology* 2003;99(1):48-53. doi:  
39 10.1097/00000542-200307000-00011
- 40 [dataset] [44] Cottis R, Magee N, Higgins DJ. Haemodynamic monitoring with  
41 pulse-induced contour cardiac output (PiCCO) in critical care. *Intensive & critical care  
42 nursing* 2003;19(5):301-7. doi: 10.1016/s0964-3397(03)00063-6
- 43 [dataset] [45] Button D, Weibel L, Reuthebuch O, et al. Clinical evaluation of the  
44 FloTrac/Vigileo system and two established continuous cardiac output monitoring  
45 devices in patients undergoing cardiac surgery. *British journal of anaesthesia*  
46 2007;99(3):329-36. doi: 10.1093/bja/aem188
- 47 [dataset] [46] Wiesenack C, Fiegl C, Keyser A, et al. Assessment of fluid  
48 responsiveness in mechanically ventilated cardiac surgical patients. *European journal  
49 of anaesthesiology* 2005;22(9):658-65. doi: 10.1017/s0265021505001092
- 50 [dataset] [47] Angappan S, Parida S, Vasudevan A, et al. The comparison of stroke  
51 volume variation with central venous pressure in predicting fluid responsiveness in  
52 septic patients with acute circulatory failure. *Indian journal of critical care medicine :  
53 peer-reviewed, official publication of Indian Society of Critical Care Medicine*  
54 2015;19(7):394-400. doi: 10.4103/0972-5229.160278
- 55  
56  
57  
58  
59  
60

- 1  
2  
3 [dataset] [48] Cannesson M, Tran NP, Cho M, et al. Predicting fluid responsiveness  
4 with stroke volume variation despite multiple extrasystoles. *Critical care medicine*  
5 2012;40(1):193-8. doi: 10.1097/CCM.0b013e31822ea119  
6 [dataset] [49] Jardin F. Cyclic changes in arterial pressure during mechanical  
7 ventilation. *Intensive care medicine* 2004;30(6):1047-50. doi:  
8 10.1007/s00134-004-2254-0  
9 [dataset] [50] Mahjoub Y, Lorne E, Micaux Y, et al. Accuracy of automated  
10 continuous calculation of pulse pressure variation in critically ill patients. *Intensive*  
11 *care medicine* 2011;37(2):360-1. doi: 10.1007/s00134-010-2064-5  
12 [dataset] [51] Kim HK, Pinsky MR. Effect of tidal volume, sampling duration, and  
13 cardiac contractility on pulse pressure and stroke volume variation during  
14 positive-pressure ventilation. *Critical care medicine* 2008;36(10):2858-62. doi:  
15 10.1097/CCM.0b013e3181865aea  
16 [dataset] [52] Rex S, Schälte G, Schroth S, et al. Limitations of arterial pulse  
17 pressure variation and left ventricular stroke volume variation in estimating cardiac  
18 pre-load during open heart surgery. *Acta anaesthesiologica Scandinavica*  
19 2007;51(9):1258-67. doi: 10.1111/j.1399-6576.2007.01423.x  
20 [dataset] [53] Cooke K, Sharvill R, Sondergaard S, et al. Volume responsiveness  
21 assessed by passive leg raising and a fluid challenge: a critical review focused on  
22 mean systemic filling pressure. *Anaesthesia* 2018;73(3):313-22. doi:  
23 10.1111/anae.14162  
24 [dataset] [54] Monnet X, Marik P, Teboul J-L. Passive leg raising for predicting fluid  
25 responsiveness: a systematic review and meta-analysis. *Intensive care medicine*  
26 2016;42(12):1935-47. doi: 10.1007/s00134-015-4134-1  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

	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"))

218

**Cochrane**

(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

1  
2  
3 predictor\* OR Physiological NEXT Monitoring\* OR Monitoring, Physiologic\*) AND  
4 (fluid NEXT infusion\* OR fluid NEXT challenge\* OR fluid NEXT therapy\* OR passive  
5 NEXT leg NEXT raising\* OR reaction\* OR response\* OR responsiveness\*) AND  
6 (SVV\* OR stroke NEXT volume NEXT variation\* OR volume NEXT variation\* OR  
7 cardiac NEXT output NEXT variation\* OR stroke NEXT volume\*)  
8

9  
10 34  
11  
12

13 **Embase:**

14  
15 ("thoracic procedures\*" OR "thoracic operation\*" OR "chest surgery\*" OR "thoracic  
16 surgical procedures\*" OR "operation on chest\*" OR "major thoracic surgery\*" OR  
17 "Thoracic Surgery\*" OR "heart operation\*" OR "cardiac operations\*" OR "open heart  
18 surgery\*" OR "cardiac surgical procedures\*" OR "cardiac operation\*" OR "heart  
19 surgical\*" OR "Cardiac Surgical Procedures\*" OR "critical care unit\*" OR "intensive  
20 care\*" OR "intensive care unite\*" OR "intensive care unit\*" OR "Recovery Room\*"  
21 OR "Respiratory Care Units\*" OR "Intensive Care Units") AND ("evaluation\*" OR  
22 "predication\*" OR "predictor\*" OR "Physiological Monitoring\*" OR "Monitoring,  
23 Physiologic\*") AND ("fluid infusion\*" OR "fluid challenge\*" OR "fluid therapy\*" OR  
24 "passive leg raising\*" OR "reaction\*" OR "response\*" OR "responsiveness\*") AND  
25 ("SVV\*" OR "stroke volume variation\*" OR "volume variation\*" OR "cardiac output  
26 variation\*" OR "stroke volume\*")  
27  
28

29 323  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



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 et al <sup>11</sup>	2016	33	13	4	25	86.8	65.8	3.5	0.82	NA
Fu et al <sup>12</sup>	2015	8	6	4	6	66.7	50.0	8.5	0.77	0.41
Fu et al <sup>12</sup>	2015	8	3	2	7	80.0	70.0	8.5	0.78	0.68
Fu et al <sup>13</sup>	2014	8	5	8	9	50.0	64.0	NA	0.51	-0.17
Miñan et al <sup>14</sup>	2020	8	3	14	14	36.4	82.4	8.0	0.47	NA
Jeony et al <sup>15</sup>	2017	26	39	3	11	89.7	22.0	NA	0.53	NA
Suehiro et al <sup>16</sup>	2010	14	1	3	13	82.4	92.3	10.5	0.90	0.87
Suehiro et al <sup>16</sup>	2011	13	9	9	7	58.3	44.0	10.0	0.65	NA
Suehiro et al <sup>17</sup>	2011	18	4	5	8	85.7	66.7	10.5	0.78	NA
Cardiac surgery										
Kim et al <sup>18</sup>	2013	16	4	5	8	76.0	67.0	13.0	0.81	0.57

1											
2											
3	Monte										0.32
4	nij et	2016	5	4	4	9	56.0	69.0	10.0	0.70	
5	a <sup>19</sup>										
6											
7											
8	Broch										0.57
9	et al <sup>20</sup>	2011	30	9	16	28	65.0	76.0	12.0	0.72	
10											
11	Broch										0.62
12	et al <sup>21</sup>	2012	35	9	19	31	65.0	77.0	11.0	0.77	
13											
14											
15	Hofer										-0.66
16	et al <sup>22</sup>	2005	17	5	6	12	74.0	71.0	12.5	0.82	
17											
18											
19	Presi										0.58
20	man	2005	26	7	6	32	81.0.	82.0	NA	0.58	
21	et al <sup>23</sup>										
22											
23	Haas										NA
24	et al <sup>24</sup>	2012	4	5	0	13	100.0	72.2	11.0	0.87	
25											
26											
27	Cann										NA
28	esson	2009	14	1	3	7	82.0	88.0	10.0	0.87	
29	et al <sup>25</sup>										
30											
31											
32	ICU after										
33	cardiac										
34	surgery										
35											
36	Fisch										NA
37	er et	2013	8	1	19	9	30.0.	90.0	NA	0.50	
38	al <sup>26</sup>										
39											
40											
41	Hofer										0.70
42	et al <sup>27</sup>	2008	20	4	3	13	87.0	76.0	12.1	0.86	
43	(PiCC										
44	O)										
45											
46											
47	Hofer										0.65
48	et al <sup>27</sup>	2008	21	3	2	14	91.0	83.0	9.6	0.82	
49	(Vigil										
50	eo)										
51											
52											
53	Geert										0.67
54	s et	2011	7	0	3	10	70.0	100.0	7.3	0.90	
55	al <sup>28</sup>										
56											
57											
58	Kang										NA
59		2014	25	4	2	23	92.3	84.0	13.5	0.94	
60											

et al <sup>29</sup>										
De Waale t al <sup>30</sup>	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

For peer review only



# PRISMA-DTA Checklist

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
<b>TITLE / ABSTRACT</b>			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	Page 1 ( <b>Title</b> )
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	Page 1 , 2 ( <b>Abstract</b> )
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 2, 3 ( <b>Background</b> )
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 ( <b>Background</b> )
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 ( <b>Background</b> )
<b>METHODS</b>			
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 ( <b>Eligibility criterial</b> )
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 ( <b>Search strategy</b> )
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 ( <b>Search strategy</b> )
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 ( <b>Data Extraction</b> )
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 ( <b>Data Extraction</b> )
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 ( <b>Data Extraction</b> )



## PRISMA-DTA Checklist

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

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)

Page 1 of 2

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)
<b>RESULTS</b>			
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

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

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 <b>(Characteristics of the studies, Table 1)</b>
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	Page 8, 9,10 <b>(Comparison between subgroups, Table 2)</b>
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 <b>(Heterogeneity )</b>
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	Page 10, 11, 12, 13 <b>(Discussion)</b>
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 <b>(Limitations)</b>
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 <b>(Conclusions)</b>
<b>FUNDING</b>			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	<b>N/A</b>

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.

For more information, visit: [www.prisma-statement.org](http://www.prisma-statement.org).