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REVIEW ARTICLE

Accuracy of stroke volume variation in predicting fluid responsiveness: a systematic review and meta-analysis

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Abstract
Purpose Stroke volume variation (SVV) appears to be a good predictor of fluid responsiveness in critically ill patients. However, a wide range of its predictive values has been reported in recent years. We therefore undertook a systematic review and meta-analysis of clinical trials that investigated the diagnostic value of SVV in predicting fluid responsiveness.
Methods Clinical investigations were identified from several sources, including MEDLINE, EMBASE, WANFANG, and CENTRAL. Original articles investigating the diagnostic value of SVV in predicting fluid responsiveness were considered to be eligible. Participants included critically ill patients in the intensive care unit (ICU) or operating room (OR) who require hemodynamic monitoring.
Results A total of 568 patients from 23 studies were included in our final analysis. Baseline SVV was correlated to fluid responsiveness with a pooled correlation coefficient of 0.718. Across all settings, we found a diagnostic odds ratio of 18.4 for SVV to predict fluid responsiveness at a sensitivity of 0.81 and specificity of 0.80. The SVV was of diagnostic value for fluid responsiveness in OR or ICU patients monitored with the PiCCO or the FloTrac/Vigileo system, and in patients ventilated with tidal volume greater than 8 ml/kg.
Conclusions SVV is of diagnostic value in predicting fluid responsiveness in various settings.

Keywords Meta-analysis · Stroke volume variation · Fluid responsiveness

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Introduction

Volume expansion is the most important therapeutic intervention in the management of circulatory failure [1, 2]. However, in some clinical situations, excessive fluid infusion may cause peripheral and pulmonary edema, thereby compromising vascular perfusion and oxygen delivery [3, 4]. Thus, the optimization of intravascular volume could be of particular interest for clinicians. The optimization can be achieved by finding predictors of fluid responsiveness. In past decades, many hemodynamic parameters such as central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), right ventricular end-diastolic volume (RVEDV), and right ventricular end-diastolic volume (LVEDV) have been extensively studied, but these parameters were found to have moderate or even no predictive value in predicting fluid responsiveness [5–7]. In contrast to these static parameters, dynamic parameters have emerged as promising predictors in recent years, and many investigations have been carried out to establish their diagnostic accuracy in predicting fluid responsiveness [8–11].

Stroke volume variation (SVV) is one of the most extensively investigated dynamic parameters. To our best knowledge, one systematic review [12] was carried out 2 years ago that investigated the diagnostic accuracy of dynamic variables including systolic pressure variation,

pulse pressure variation, and SVV. However, subgroups were not fully addressed because of the limited number of included studies. More recently, many additional new studies have been published, and the body of evidence requires updating. Thus, we performed a systematic review and meta-analysis of observational studies to establish the diagnostic accuracy of SVV in predicting fluid responsiveness. We hypothesized that SVV is of diagnostic value, both overall and across a range of subgroups.

Methods

Data sources and searching strategy

We followed the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines for the performance of meta-analysis of observational cohort studies [13]. Databases of MEDLINE, EMBASE, WANFANG, and CENTRAL were searched from inception to January 2011 to identify relevant articles or abstracts. There was no language restriction on the search. Terms used in our search included SVV and fluid responsiveness. The bibliographies of all relevant articles were reviewed manually to identify additional relevant articles.

Study inclusion and data extraction

Two reviewers independently performed the process of study selection. Clinical studies investigating the value of SVV in predicting fluid responsiveness were included. Studies conducted in patients with spontaneous breathing were excluded; articles of animal or experimental studies, reviews, and editorials were also excluded.

Data were abstracted on study design, sample size, clinical settings, patient population, tidal volume, methods used for hemodynamic monitoring, types of fluid, definition of fluid responsiveness, correlation coefficients, area under the receiver-operating characteristic curve (AUC), and specificity and sensitivity, as well as the number of patients who were responsive to fluid challenge. Quality assessment was performed for each included study according to the QUADAS document [14].

Statistical analysis

The correlation coefficients were pooled according to a fixed-effect model [15]. The effect sizes (correlation coefficients) were first converted into standard normal metrics (using Fisher's r-to-Z transformation), and a weighted average of these transformed scores was then calculated. The AUCs were pooled by a weighted average of areas from individual studies [16]. Meta-analysis of diagnostic accuracy was performed using a hierarchical bivariate generalized linear mixed model, and the computation was carried out using Stata program METANDI (Stata/SE 10.0 for Windows) [17]. Based on this model, the pooled sensitivity and specificity, diagnostic odds ratio, and relevant 95% confidence interval (CI) were obtained. Because of the heterogeneity and small sample sizes of included studies, publication bias of included studies was not assessed with funnel plot [18]. Heterogeneity was quantitatively assessed by using Cochran's Q. Subgroups were defined a priori, restricted to patients in the operating room (OR), ventilated with tidal volumes >8 ml/kg, with hemodynamic monitoring with PiCCO or Vigileo system.

Results

Searching results and study characteristics

The search initially yielded 94 articles, of which 68 were excluded on the basis of abstract or title because they were laboratory studies, review articles, animal studies, or other irrelevant studies. Of the remaining articles, one was concerned with patients with spontaneous breathing [19], and one was aimed to explore the influence of airway driving pressure on the dynamic parameters as a predictor of fluid responsiveness [20]; both of these were excluded. A short communication [21] enrolled the same cohort of patients as in another original article and thus it was excluded. As a result, a total of 23 articles [22–44] were included in our systematic review (Fig. 1).

The 23 studies included a total of 568 patients. The characteristics of these studies were summarized in Table 1. Fourteen studies [22, 23, 25–28, 31, 34, 36, 38–41, 44] were performed in the operating room (OR) under general anesthesia, and 8 [24, 29, 30, 32, 33, 35, 42, 43] were performed in the intensive care unit (ICU). Patients in the latter setting were heterogeneous, including those after cardiac surgery, with severe sepsis and acute respiratory failure. All studies generally excluded patients with significant cardiac or pulmonary dysfunctions; however, the specific inclusion and exclusion criteria varied across these studies. The tidal volumes were mostly equal to or more than 8–10 ml/kg, with exceptions in five studies [30, 33, 40, 43, 44] using low tidal volume (<8 ml/kg). These studies were carried out across the globe, representing the international experience from nine countries. Strategies of fluid challenge were varied across the studies. Hydroxyethyl starch was used in 13 studies [22, 23, 27, 28, 31–33, 38–40, 42–44] for volume expansion, hetastarch was used in 3 studies [25, 26, 36], albumin was used in 1 study [24], and body position maneuvers to increase venous return were used in 3 studies [29, 37, 41]. Devices

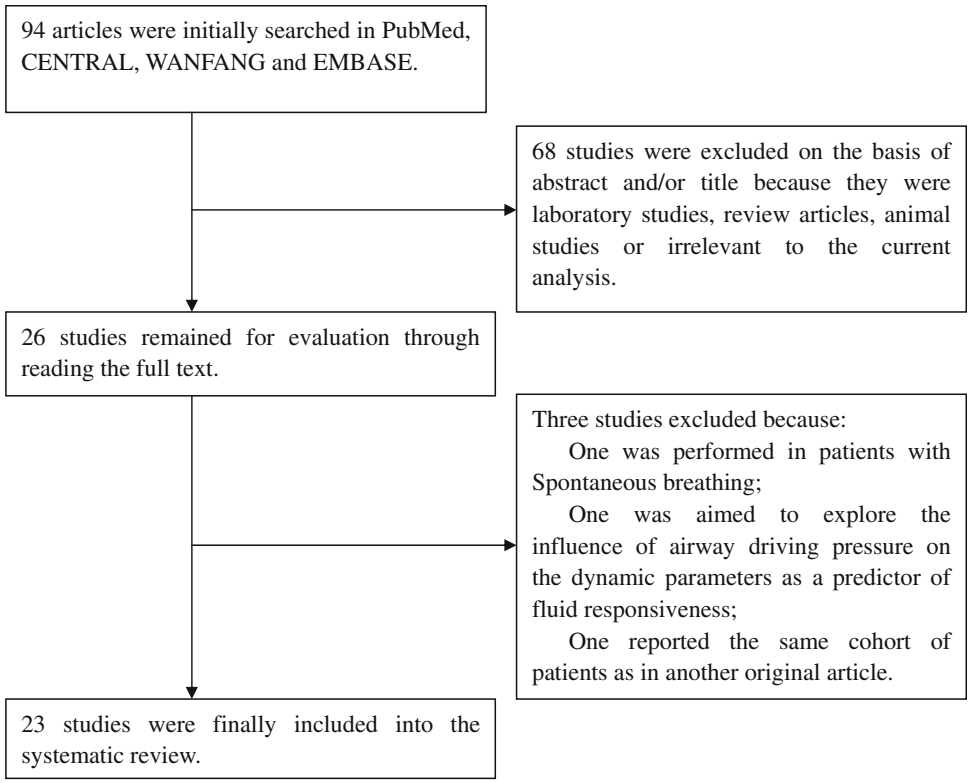

Fig. 1 Flow chart of study selection

were different across the studies, with 13 studies [23, 28–30, 33–37, 39, 40, 42, 43] using the PiCCO system and 8 studies [24–27, 29, 31, 38, 44] using the FloTrac/Vigileo system. The definition of fluid responsiveness varied across these studies, ranging from 5% to 25% increases from the baseline.

Quality assessment

Quality assessment was performed according to the QUADAS document (Table 2). The proportion of male subjects in three studies [27, 34, 42] was more than 80%, and a spectrum bias might be introduced for them. Eligibility criteria were sufficiently described in most studies, except for five studies [27, 30, 33, 35, 36]. The reference standard employed in the studies is the increase in cardiac output (CO) or stroke volume (SV); both were regarded as appropriate. Because the measurement of cardiac performance was taken immediately after fluid challenge, there was no disease progression bias for all studies. There was no partial or differential verification bias in all studies. Detailed descriptions of index and reference tests were provided in most studies, except for the study by He-Mei et al. [27]. No studies reported uninterpretable/intermediate test results. Missing or incomplete data were reported in two studies [28, 30], but no further details were given.

Evidence synthesis

The correlation coefficients were reported in 17 studies (Table 1). As the value reported by Wiesenack et al. [39] was extremely low, we excluded it in the meta-analysis. Hofer et al. [29] reported two sets of data. Thus, a total of 17 sets of data were available for meta-analysis. The pooled correlation coefficient was 0.718. The Cochran's Q was 26.3, indicating unremarkable heterogeneity across the studies.

In Table 3, true-positive, false-positive, false-negative, true-negative, paired sensitivity and specificity, and cutoff values of individual studies are listed for SVV to predict fluid responsiveness. A total number of 12 studies have complete quantitative data for meta-analysis of diagnostic accuracy. In Table 4, the pooled diagnostic accuracies of all settings and in various subgroups are listed. Across all settings, we found a diagnostic odds ratio (DOR) of 18.4 for SVV to predict fluid responsiveness at sensitivity of 0.81 and specificity of 0.80 (Fig. 2). Subgroup analysis showed some variability in DOR and area under the curve for the receiver-operating characteristic (AUC-ROC) values. The SVV was of diagnostic value for fluid responsiveness in OR and ICU, in patients monitored with the PiCCO or FloTrac/Vigileo system, and in patients ventilated with tidal volume >8 ml/kg. The pooled AUC across

Table 1 Characteristics of included studies

Reference	Setting or study population	Patient characteristics or exclusion criteria	Sample size	Age (years)	Man (%)	Tidal volume (ml/kg)	Fluid challenge	Device (software version if available)	Distinguish between responders and nonresponders	Correlation coefficient (r)[a]	Country of origin
Belloni et al. [22]	OR-C. Surg	EF > 40%; patients with valvular, right ventricular dysfunction, or arrhythmia were excluded	19	66.64 ± 7.1	63.2	8	7 ml/kg hydroxyethyl starch	LiDCOplus system	>15% increase in CI	0.779	Italy
Berkenstadt et al. [23]	OR-Brain surgery	Without significant cardiac or respiratory disease	15	55 ± 15	40.0	10	100 ml 6% hydroxyethylstarch	PiCCOplus system	>5% increase in SV	0.722	Israel
Biais et al. [24]	ICU- Post liver transplantation	Without hypoxia, hydrostatic pulmonary edema, arrhythmia, significant aortic or mitral valvulopathy, intracardiac shunt, spontaneous breathing activity, or unsatisfactory cardiac echogenicity	35	51 ± 11	65.7	8–10	20 ml × BMI 4% albumin	FloTrac/ Vigileo system (1.07)	>15% increase in CO	0.849	France
Biais et al. [25]	OR-Scoliosis surgery	Excluded if age <18 years, arrhythmias, BMI >40 or <15 kg/m2, valvular heart disease, LVEF < 50%, or a history of lung disease	27	48 (18–74)	29.6	8–10	500 ml hetastarch 6%	FloTrac/ Vigileo system (1.14)	>15% increase in CO	0.8	France
Cannesson et al. [26]	OR-C. Surg	Without cardiac arrhythmias or intracardiac shunt	25	67 ± 9	80	8–10	500 ml hetastarch 6%	FloTrac/ Vigileo system (1.10)	>15% increase in CI	–	France
He-mei et al. [27]	OR-Abdo. Surg	Without significant cardiac or pulmonary diseases	48	50–60	100	8	2 ml/kg 6% hydroxyethyl starch	FloTrac/ Vigileo system	–	–[b]	China
Hofer et al. [28]	OR-C. Surg	Exclusion criteria were dysrhythmias, EF < 40%, valvular heart disease, intracardiac shunts, pulmonary artery hypertension, or severe peripheral vascular obstructive disease	35	62 ± 7	–	10	10 ml/kg 6% hydroxyethyl starch solution	PiCCOplus system (5.2.2)	>25% increase in SVI	0.606	Switzerland

Table 1 continued

Reference	Setting or study population	Patient characteristics or exclusion criteria	Sample size	Age (years)	Man (%)	Tidal volume (ml/kg)	Fluid challenge	Device (software version if available)	Distinguish between responders and nonresponders	Correlation coefficient (r)[a]	Country of origin
Hofer et al. [29]	ICU-post C. Surg	Exclusion criteria were EF < 40%, preoperative dysrhythmia, intracardiac shunt, pulmonary arterial hypertension, severe arterial occlusion disease and body weight <40 kg	40	66.5 ± 9.2	80	8–10	from 30° head-up to 30° head-down position	Vigileo (1.07) and PiCCOplus system (6.0.1)	>25% increase in SV	0.653 and 0.701[c]	Switzerland
Huang et al. [30]	ICU-ARDS	ARDS patients in early course of disease, with acute lung injury score >2.5	22	54 ± 17	72.7	6.4 ± 0.7	500 ml 10% pentastarch	PiCCOplus system (5.2.2)	>15% increase in CI	–	Taiwan
Lahner et al. [31]	OR-Abdo. Surg	Exclusion criteria were coronary or peripheral artery disease, severe pulmonary disease, arterial hypertension, diabetes mellitus, cardiac arrhythmias, coagulopathies, and infections	20	52.7 (25–77)	50	8	250 ml hydroxyethyl starch 130/0.4 6% or RLS	FloTrac/ Vigileo system (1.07)	>10% increase in SVI	–	Germany
Lei et al. [32]	ICU-Sepsis	Exclusion criteria were EF < 40%, dysrhythmia, hypoxia, pulmonary arterial hypertension	28	48.6 ± 20.5	67.9	8–10	250–500 ml 6% hydroxyethyl starch	Ultrasonic Cardiac Output Monitor	>12% increase in CI	–	China
Marx et al. [33]	Severe sepsis	Patients with a cardiac rhythm other than sinus rhythm were excluded	10	44–76	50	6–8	500 ml hydroxyethyl starch 10%	PiCCOplus system	–	0.64	United Kingdom
Preisman et al. [34]	OR-C. Surg	Exclusion criteria were femoral artery disease, significant arrhythmias, pulmonary disease, aortic aneurysms, oesophageal pathology, and patients undergoing repeated operations	18	66.2 (49–84)	88.9		250 ml colloid solution	PiCCOplus system	>15% increase in SVI	0.58	Israel

Table 1 continued

Reference	Setting or study population	Patient characteristics or exclusion criteria	Sample size	Age (years)	Man (%)	Tidal volume (ml/kg)	Fluid challenge	Device (software version if available)	Distinguish between responders and nonresponders	Correlation coefficient (r)[a]	Country of origin
Reuter et al. [35]	Post C. Surg	38% < EF < 89%; without occlusive peripheral artery disease	20	66 (48–78)	50	13–15	20 ml × BMI 3.5% oxypolygelatine	PiCCOplus system (4.1)	>15% increase in SVI	0.67	Germany
Reuter et al. [36]	OR-C. Surg	Patients underwent elective coronary artery bypass grafting	26	61 ± 10; 64 ± 7[d]	–	10	10 ml × BMI hetastarch 130 kD 6%	PiCCOplus system (4.12)	>5% increase in SVI	0.742	Germany
Rex et al. [37]	Post C. Surg	Exclusion criteria were emergency operations, occlusive peripheral arterial disease, intracardiac shunts, significant valvular heart disease, and EF < 30%	16	63 (45–84)	–	8	Anti-Trendelenburg position	PiCCOplus system (5.2.2)	–	0.61	Germany
Suehiro and Okutani [38]	OR-pulmonary lobectomy requiring one lung ventilation	Exclusion criteria were risk of hepatic/renal/ cardiac dysfunction and BMI > 35	30	–	–	8	500 ml 6% hydroxyethyl starch	FloTrac/ Vigileo system (1.14)	>25% increase in SVI	0.863	Japan
Wiesenack et al. [39]	OR-C. Surg	Exclusion criteria were valvular heart disease, intracardiac shunts, peripheral vascular disease, preoperative dysrhythmias, and EF < 50%	20	60 (43–73)	80	10	7 ml/kg 6% hydroxyethyl starch	PiCCOplus system	–	0.19	Germany
Wiesenack et al. [40]	OR-C. Surg	Exclusion critiera were valvular heart disease, intracardiac shunts, peripheral vascular disease, preoperative dysrhythmias and EF < 30%	20	66 (53–78)	80	7	7 ml/kg 6% hydroxyethyl starch	PiCCOplus system (5.2.2)	>20% increase in SVI	0.812	Germany
Wyffels et al. [41]	OR-C. Surg	Exclusion criteria were moderate to severe valve disease and the presence of intracardiac shunts	15	–	–	8–10	Leg elevation	PulseCO system	–	0.897	Belgium

Table 1 continued

Reference	Setting or study population	Patient characteristics or exclusion criteria	Sample size	Age (years)	Man (%)	Tidal volume (ml/kg)	Fluid challenge	Device (software version if available)	Distinguish between responders and nonresponders	Correlation coefficient (r)[a]	Country of origin
Yu et al. [42]	Severe sepsis	Exclusion criteria were dysrhythmias, contraindications for PAC and MODS	17	82 ± 5	88.2	10	250–500 ml 6% hydroxyethyl starch	PiCCOplus system	>10% increase in CI	0.447	China
Zhang et al. [43]	Severe sepsis	Exclusion criteria were arrhythmia, valvular heart disease, pulmonary artery hypertension, tidal volume <6 ml/kg	42	56.5 ± 14.1	64.3	6–8	250 or 500 ml 6% hydroxyethyl starch	PiCCOplus system	>10% increase in SVI	–	China
Zimmermann et al. [44]	OR-Abdo. Surg	Exclusion criteria were valvular heart disease, intracardiac shunts, regional myocardial asynchrony, peripheral vascular disease, preoperative dysrhythmias and EF < 30%	20	53 ± 15.5	65	7	7 ml/kg 6% hydroxyethyl starch	FloTrac/ Vigileo system (1.14)	>15% increase in SVI	0.80	Germany

OR operation room, *EF* ejection fraction, *C. Surg* cardiac surgery, *ICU* intensive care unit, *Abdo. Surg* abdominal surgery, *ARDS* acute respiratory distress syndrome, *RLS* Ringer's lactate solution, *CO* cardiac output, *CI* cardiac index, *SV* stroke volume, *SVI* stroke volume index, *PAC* pulmonary artery catheter, *MODS* multiple organ dysfunction syndrome

[a] The correlation was between baseline stroke volume variation (SVV) and changes in cardiac endpoints (e.g., cardiac output, cardiac index, or stroke volume)

[b] The correlation was between SVV and the amount of fluid infusion; thus, the value is not extracted

[c] Values were for $SVV_{FloTrac}$ and SVV_{PiCCO}, respectively

[d] Patients were divided into study group (EF < 35%) and control group (EF > 50%)

Table 2 Quality assessment of included studies

Reference	Spectrum bias[a]	Eligibility criteria clearly defined	Appropriate reference standard	Disease progression bias[b]	Partial verification bias[c]	Differential verification bias[d]	Detailed description of index and reference tests	Uninterpretable/ intermediate test results reported
Belloni et al. [22]	No	Yes	Yes	No	No	No	Yes	No
Berkenstadt et al. [23]	No	Yes	Yes	No	No	No	Yes	No
Biais et al. [24]	No	Yes	Yes	No	No	No	Yes	No
Biais et al. [25]	No	Yes	Yes	No	No	No	Yes	No
Cannesson et al. [26]	No	Yes	Yes	No	No	No	Yes	No
He-mei et al. [27]	Yes	No	Yes	No	No	No	No	No
Hofer et al. [28]	No	Yes	Yes	No	No	No	Yes	No
Hofer et al. [29]	No	Yes	Yes	No	No	No	Yes	No
Huang et al. [30]	No	No	Yes	No	No	No	Yes	No
Lahner et al. [31]	No	Yes	Yes	No	No	No	Yes	No
Lei et al. [32]	No	Yes	Yes	No	No	No	Yes	No
Marx et al. [33]	No	No	Yes	No	No	No	Yes	No
Preisman et al. [34]	Yes	Yes	Yes	No	No	No	Yes	No
Reuter et al. [35]	No	No	Yes	No	No	No	Yes	No
Reuter et al. [36]	No	No	Yes	No	No	No	Yes	No
Rex et al. [37]	No	Yes	Yes	No	No	No	Yes	No
Suehiro and Okutani [38]	Yes	Yes	Yes	No	No	No	Yes	No
Wiesenack et al. [39]	No	Yes	Yes	No	No	No	Yes	No
Wiesenack et al. [40]	No	Yes	Yes	No	No	No	Yes	No
Wyffels et al. [41]	No	Yes	Yes	No	No	No	Yes	No
Yu et al. [42]	Yes	Yes	Yes	No	No	No	Yes	No
Zhang et al. [43]	No	Yes	Yes	No	No	No	Yes	No
Zimmermann et al. [44]	No	Yes	Yes	No	No	No	Yes	No

[a] This item is scored "No" if the spectrum of patients is representative of the patients who will receive the test in practice

[b] This item is scored "No" if the time period between reference standard and index test is short enough to be reasonably sure that the target condition does not change between the two sets

[c] This item is scored "No" if the whole sample or a random selection of the sample receives verification using a reference standard

[d] This item is scored "No" if all patients receives the same reference standard regardless of the index test result

Table 3 Paired sensitivity and specificity of individual studies for SVV to predict fluid responsiveness

Reference	No. of fluid challenges				SVV cutoff (%)	Sensitivity (95% CI) (%)	Specificity (%)	AUC-ROC (95% CI or ±SE)
	TP	FP	FN	TN				
Berkenstadt et al. [23]	55	5	15	65	9.5	78.6	93	0.870 (0.809–0.903)
Biais et al. [24]	16	1	1	17	10	94 (71–99)	94 (73–99)	0.95 (0.81–0.99)
Biais et al. [25]	14	1	2	10	9	88 (62–98)	91 (59–99)	0.932 (0.765–0.990)
Cannesson et al. [26]	14	1	3	7	10	82	88	0.871 ± 0.085
Hofer et al. [28]	16	4	5	10	12.5	74	71	0.823 (0.677–0.969)
Hofer et al. [29] (PiCCOplus)	20	4	3	13	12.1	87	76	0.858 (0.745–0.971)
Hofer et al. [29] (Vigileo)	21	3	2	14	9.6	91	83	0.824 (0.680–0.967)
Huang et al. [30]								0.606
Lahner et al. [31] (colloid + crystalloid)	40	9	12	6	8.5	77	43	0.51 (0.32–0.70)
Lahner et al. [31] (colloid)	13	2	7	4	8.5	65	67	0.58 (0.23–0.82)
Lahner et al. [31] (crystalloid)	27	7	5	2	8.5	85	25	0.44 (0.23–0.70)
Lei et al. [32]	11	3	2	12	15.5	84.6	80	0.836 (0.680–0.992)
Preisman et al. [34]	26	7	6	31	11.5	81	82	0.87 (0.79–0.96)
Reuter et al. [35]	–	–	–	–	–	–	–	0.83 (0.64–1.00)
Reuter et al. [36] (EF < 35%)	–	–	–	–	9.5	71	80	0.76 (0.59–0.96)
Reuter et al. [36] (EF > 50%)	–	–	–	–	9.5	79	85	0.88 (0.77–0.99)
Suehiro and Okutani [38]	12	1	3	14	10.5	82.4	92.3	0.900 (0.809–0.991)
Yu et al. [42]	–	–	–	–	11.5	71	67	0.672 (0.463–0.885)
Zhang et al. [43]	18	3	6	15	12	77	85	0.86 (0.734–0.989)
Zimmermann et al. [44]	15	1	0	4	11	100	80	0.993 (0.967–1.00)

SVV stroke volume variation, *TP* true positive, *FP* false positive, *FN* false negative, *TN* true negative, *EF* ejection fraction, *CI* confidence interval, *SE* standard error, *AUC-ROC* area under the curve for the receiver-operating characteristic

all settings was 0.93 (95% CI, 0.907–0.945). As this was disproportionally high, a sensitivity analysis by excluding the study by Zimmermann et al. [44] was performed, which showed an AUC of 0.84 (95% CI, 0.81–0.87).

Discussion

The number of studies included in our meta-analysis is twice that of the previous one (counting only studies reporting SVV) [12]. The results of this systemic review demonstrated that (1) the baseline SVV was correlated to the fluid responsiveness (changes in cardiac output or stroke volume) with pooled correlation coefficient of 0.718; and (2) SVV was able to predict fluid responsiveness across a wide spectrum of clinical settings, with a pooled diagnostic odds ratio of 18.4 (95% CI, 9.52–35.5) and an AUC of 0.94. Because the study by Zimmermann et al. [44] reported a large AUC value with an extremely narrow band, sensitivity analysis was performed by excluding this study, and a pooled AUC of 0.84 was obtained. A diagnostic tool with an AUC of 0.84 is considered to have good diagnostic accuracy. In clinical practice, SVV can be employed as a reliable predictor of fluid responsiveness in patients with controlled mechanical ventilation.

However, because our analysis did not include patients who were breathing spontaneously, the predictive value of SVV can only be validated in patients under controlled mechanical ventilation. Perner and Faber [19] found that, in patients who underwent pressure support ventilation, SVV did not discriminate between those who would or would not increase the cardiac index in response to a colloid challenge (AUC, 0.52). This limitation occurs because conditions of spontaneous breathing differ significantly from those under controlled ventilation, especially in the amplitude of intrathoracic pressure swing and the unpredictable nature of the tidal volume under spontaneous conditions [45, 46]. Thus, the judgment of fluid status of patients with spontaneous breathing is still challenging for clinicians and requires more experimental and clinical investigations.

Tidal volume is an important factor that influences the predictive value of dynamic parameters. One study demonstrated that pulse pressure variation was not predictive of fluid responsiveness when ventilated with low tidal volume [20]. Vistisen et al. [47] found that the predictive value of

Table 4 Pooled diagnostic accuracy of SVV in predicting fluid responsiveness

Setting [no. of studies (data sets)]	Sensitivity (95% CI)	Specificity (95% CI)	DOR (95% CI)	AUC-ROC (95% CI)[a]	Sensitivity analysis for AUC-ROC (95% CI)[b]	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Across all settings (12 [15])	0.81 (0.77–0.85)	0.80 (0.70–0.88)	18.4 (9.52–35.5)	0.93 (0.907–0.945)	0.84 (0.81–0.87)	4.19 (2.62–6.72)	0.23 (0.18–0.29)
In OR under general anesthesia (8 [10])	0.80 (0.75–0.84)	0.78 (0.61–0.89)	14.1 (5.84–34.3)	0.94 (0.92–0.96)	0.85 (0.82–0.88)	3.63 (1.90–6.93)	0.26 (0.19–0.35)
In ICU (4 [5])	0.86 (0.78–0.92)	0.84 (0.74–0.91)	28.3 (12.3–65.1)	0.85 (0.79–0.91)	NA	4.69 (2.90–7.57)	0.20 (0.12–0.32)
Patients ventilated with TV > 8 ml/kg (10 [13])	0.81 (0.77–0.85)	0.80 (0.68–0.89)	17.5 (8.44–36.5)	0.85 (0.82–0.88)	NA	4.09 (2.42–6.93)	0.23 (0.18–0.31)
Hemodynamic monitoring with PiCCO system (6 [6])	0.80 (0.72–0.85)	0.84 (0.75–0.91)	21.0 (10.7–41.5)	0.85 (0.81–0.89)	NA	5.09 (3.12–8.29)	0.24 (0.18–0.33)
Hemodynamic monitoring with Vigileo system (7 [9])	0.85 (0.78–0.90)	0.78 (0.58–0.91)	20.8 (6.09–71.2)	0.96 (0.94–0.98)	0.84 (0.79–0.89)	3.99 (1.80–8.83)	0.19 (0.11–0.32)

OR operating room, *ICU* intensive care unit, *DOR* diagnostic odds ratio, *TV* tidal volume, *CI* confidence interval, *AUC-ROC* area under the curve for the receiver-operating characteristic, *NA* not applicable

[a] AUC-ROC was estimated by weighted mean of AUC-ROC in individual studies

[b] Sensitivity analyses were performed by excluding the study by Zimmermann et al. [44]

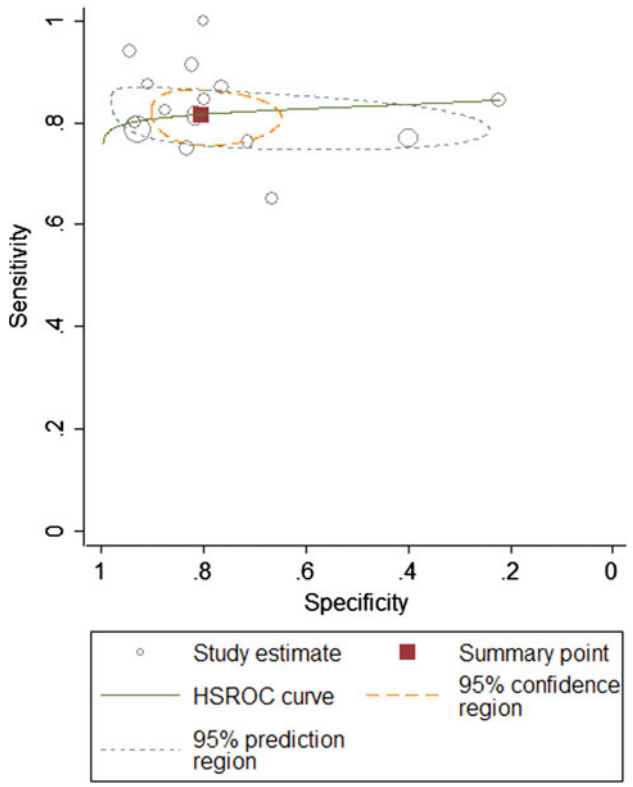

Fig. 2 Hierarchical summary receiver-operating characteristic (*HSROC*) plot of stroke volume variation to predict fluid responsiveness. Based on combined sensitivity and specificity weighted for sample size of each data set reflected by the size of the circles, showing average sensitivity and specificity estimate of the study results (*solid square*) and 95% confidence region around it. The 95% prediction region represents the confidence region for a forecast of the true sensitivity and specificity in a future study

dynamic parameters can be increased by indexing to tidal volume, that is, dynamic parameters increases proportionally to tidal volume. In our subgroup analysis restricting to studies with tidal volume >8 ml/kg, the predictive value of SVV was comparable to that across all settings. With respect to patients ventilated with low tidal volume (<8 ml/kg), only two sets of data are available, and the total sample size was 33. Thus, no definitive conclusion can be drawn in this subgroup of patients. Because low tidal volume ventilation has become the standard strategy in treating acute respiratory distress syndrome (ARDS) and its use will become more and more popular [48], extensive investigations on the value of SVV in patients ventilated with a small tidal volume is feasible. The subgroup analysis showed that the predictive value of SVV was much better in the ICU setting than in the OR setting, with the DOR of 28.3 versus 14.1. One reason for this observed phenomenon lies in the differences in volemic states between the two subgroups; that is, while patients who underwent elective surgery are usually in the euvolemic state, those in ICU setting are always hypovolemic and require large volume resuscitation. It is likely that SVV performs differently in predicting fluid responsiveness through the spectrum of euvolemia to hypovolemia.

Commercially available monitors used to estimate cardiac output include ultrasonic devices, LiDCOplus, PiCCOplus, and FloTrac/Vigileo systems. Most of the studies included in our analysis used PiCCOplus and FloTrac/Vigileo systems, and their effects on the diagnostic value of SVV mandate further discussion. These two techniques differ in the way they estimate aortic impedance. The PiCCO device

provides an estimate of the cardiac index through analysis of pulse contour, calibrated by transpulmonary thermodilution [49]. In contrast, the Vigileo device does not require external calibration because it estimates aortic impedance based on certain characteristics of the arterial pressure waveform and relevant demographic data [29]. Some studies in cardiac surgery patients suggested that PiCCO reliably measures cardiac index when compared with the pulmonary artery catheter-derived measurement [49, 50], whereas the reliability of the Vigileo has been questioned [51–53]. Our meta-analysis showed that the predictive value of SVV seemed slightly better when measured with PiCCO device than with the Vigileo device. No direct comparison between these two techniques has been performed.

The major limitation of the review is the small sample size in each individual study, which significantly compromised the quality of evidence. Further clinical investigations with larger sample sizes should be conducted to confirm the result. The sensitivity analyses showed large variations from the original results (Table 4), which is another drawback of the present study. The large variation can be explained by the study of Zimmermann et al. [44], to which great weight was assigned because of its large AUC value and narrow 95% CI. By excluding this study, we obtained an AUC-ROC of about 0.84, which is consistent with a previous meta-analysis [12]. Wiesenack et al. [39] reported an extremely low correlation coefficient (0.19, compared to an average of >0.7 in other studies). If such outlier is included in the meta-analysis, the combined result might be distorted. Additionally, this study only stated that SVV was not a good predictor of fluid responsiveness, but did not report the estimates of diagnostic accuracy such as sensitivity and specificity. Thus, it was not included in the meta-analysis.

In conclusion, SVV is a good predictor in patients ventilated with tidal volume of more than 8 ml/kg, whereas its predictive value in patients with low tidal volume ventilation remains to be investigated. The presence of spontaneous breathing compromises the predictive value of SVV. In addition, SVV cannot be used in situations such as cardiac arrhythmia, valvular heart disease, intracardiac shunts, peripheral vascular disease, and decreased ejection fraction.

Conflict of interest The authors declared that they have no conflict of interest.

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