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REVIEWPAPER

Accuracy of pleth variability index to predict fluid responsiveness in mechanically ventilated patients: a systematic review and meta-analysis

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Abstract To systemically evaluate the accuracy of pleth variability index to predict fluid responsiveness in mechanically ventilated patients. A literature search of PUBMED, OVID, CBM, CNKI and Wanfang Data for clinical studies in which the accuracy of pleth variability index to predict fluid responsiveness was performed (last update 5 April 2015). Related journals were also searched manually. Two reviewers independently assessed trial quality according to the modified QUADAS items. Heterogeneous studies and meta-analysis were conducted by Meta-Disc 1.4 software. A subgroup analysis in the operating room (OR) and in intensive care unit (ICU) was also performed. Differences between subgroups were analyzed using the interaction test. A total of 18 studies involving 665 subjects were included. The pooled area under the receiver operating characteristic curve (AUC) to predict fluid responsiveness in mechanically ventilated patients was 0.88 [95 % confidence interval (CI) 0.84–0.91]. The pooled sensitivity and specificity were 0.73 (95 % CI 0.68–0.78) and 0.82 (95 % CI 0.77–0.86), respectively. No heterogeneity was found within studies nor between studies. And there was no significant heterogeneity within each subgroup. No statistical differences were found between OR subgroup and ICU subgroup in the AUC [0.89 (95 % CI 0.85–0.92) versus 0.90 (95 % CI 0.82–0.94); $P = 0.97$], and in the specificity [0.84 (95 % CI 0.75–0.86) vs. 0.84 (95 % CI 0.75–0.91); $P = 1.00$]. Sensitivity was higher in the OR subgroup than the ICU subgroup [0.84 (95 % CI 0.78–0.88) vs. 0.56 (95 % CI 0.47–0.64); $P = 0.00004$]. The pleth variability index has a reasonable ability to predict fluid responsiveness.

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Keywords Pleth variability index · Fluid responsiveness · Meta-analysis · Sensitivity · Specificity · AUC

1 Introduction

Intravenous fluid is very important to improve hemodynamics of perioperative and critically ill patients. Before fluid infusion, evaluating volume status by monitoring some objective indicators to predict fluid responsiveness can ensure the fluid therapy reasonable and effective, avoiding excessive fluid infusion. Assessment of fluid responsiveness, described as the ability of the circulation to increase cardiac output in response to volume expansion, is essential to guide fluid therapy and optimize preload. Dynamic indicators relying on cardiopulmonary interactions in mechanically ventilated patients, such as pulse pressure variation (PPV), systolic pressure variation, and stroke volume variation (SVV), consistently have been shown to be more accurate than static indicators in predicting fluid or preload responsiveness [1–5]. More recently, interest has focused on the availability of pleth variability index (PVI), which is a dynamic variable that automatically and continuously measures the respiratory variations in the pulse oximeter waveform amplitude [6]. PVI has also been suggested to be an effective dynamic indicator of fluid responsiveness. Different from other invasive dynamic indices, PVI provides clinicians with a numerical value noninvasively, automatically, and continuously [7, 14, 25]. PVI is calculated on the basis of PI. The PI value is generated by pulse oximetry and the scale of absoption of red and infrared light. Division of pulsatile fraction (AC, caused by blood flow) and non-pulsatile fraction (DC, effected by skin and other tissues) of the red and infrared light is summarized by the following formular:

PI = (AC/DC) × 100(%). PVI reflects measurements of ventilation induced respiratory changes in PI over a constant period of time and is calculated as follows: $PVI = [(PI_{max} - PI_{min})/PI_{max}] \times 100(\%)$ [26].

Several studies demonstrated that PVI was accurate, sensitive and had high application value in predicting fluid responsiveness [9–16, 18–25], but they were not very convictive because the sample size of these studies was small. Fischer et al. [15] reported that PVI was unable to predict fluid responsiveness in the cardiac surgical setting. A recent study reported that PVI did not predict fluid responsiveness preoperatively, and it had moderate predictive value postoperatively in patients with aortic stenosis [12]. Besides, it was reported that the use of vasoactive drugs and nociceptive stimuli affected the accuracy [8, 17]. The systematic review reported here was conducted to assess the accuracy of PVI in predicting fluid responsiveness in both the operating room (OR) and intensive care unit (ICU).

2 Materials and methods

2.1 Inclusion criteria

1. All published cohort or randomised controlled studies evaluating the ability of PVI to predict the changes in cardiac output or cardiac index, stroke volume or stroke volume index, or pulse pressure variation occurring after a fluid challenge. 2. Responders to fluid challenge: the change in CO or CI, SV or SVI, or PPV was greater than threshold value. Nonresponders to fluid challenge: the change in CO or CI, SV or SVI, or PPV was less than threshold value. 3. Only studies that reported either the sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) of PVI in identifying fluid responders, and studies that the complete fourfold table of diagnostic test could be obtained were included.

2.2 Exclusion criteria

1. Studies that lack the check of gold standard test. 2. Review, case report or comment.

2.3 Literature search

Two researchers independently searched the PUBMED, OVID, CBM, CNKI and Wanfang Data (last update 5 April 2015), using the following keywords: (pleth OR plethysmographic OR plethysmography) AND (variation OR variability) AND (index OR indexes OR indices). The reference lists of all retrieved articles were checked to identify relevant studies.

2.4 Data extraction and quality assessment

Two reviewers examined and extracted the study characteristics and outcomes independently using a predesigned data abstraction form. The following data were extracted from each study: first author, published year, study setting, type of patient, study size, ventilation mode, amout of fluid challenge, definition of responsiveness, true positive, false positive, false negative, true negative, best threshold, sensitivity, specificity, and AUC. Quality assessment was made independently by two authors using the QUADAS scale, which is a tool developed specifically for assessing the quality of studies on diagnostic accuracy. The disagreement was resolved by discussion, if it still could not be resolved, then the third part would get involved [27]. Each item include "Yes", "No", "Unclear". "Yes" indicated satisfying this item, "No" indicated not satisfying this item or not being mentioned, "Unclear" indicated partly satisfying or information insufficient.

2.5 Evaluation indicator of the diagnostic efficiency

Pooled sensitivity, pooled specificity, pooled positive likelihood, pooled negative likelihood, their 95 % CI (credibility interval) and the SROC (summary receiver operating characteristics) were analysed. The AUC (area under the receiver operating characteristic curve) and Q* index were calculated.

2.6 Statistical treatment

Data were checked and entered into Meta-DiSc (version 1.4) for statistical analysis. The heterogeneity in diagnostic test was caused by threshold effect and non-threshold effect. The threshold effect was checked by calculating the spearman correlation coefficient. The non-threshold effect was checked by calculating the Cochrane-Q value of the DOR (diagnostic odds ratio). Heterogeneity was quantified by I^2 index, with $I^2 < 25$ % suggesting low heterogeneity, $25\ \% < I^2 < 50\ \%$ suggesting moderate heterogeneity, and $I^2 > 50$ % suggesting significant heterogeneity [28]. A subgroup analysis in intensive care unit and in the operating room was performed. Differences between subgroups were analyzed using the interaction test [29].

3 Results

3.1 Study selection

The initial literature search yielded a total of 374 studies, of which 323 were excluded after examining the titles and abstracts because they were duplicates of studies that were

already included in this review, irrelevant studies or review articles. After a detailed review of the remaining 51 studies, 33 studies were excluded because they did not provide relevant data on outcomes of interest of this study. 7 were excluded for using PVI to predict accuracy of preload change, 2 for using PVI to predict hypotension or hypovolaemia, 4 for using PVI to guide fluid management, 6 for investigating the index of POP but not PVI, 1 for investigating the effect of hypercapnia on PVI, 2 for investigating the effect of nerve blocking on PVI, 1 for investigating the effect of norepinephrine on PVI, 3 for investigating the effect of pain stimulation related to surgery on PVI, 1 for investigating the reference range of PVI in newborns, 4 for comparing PVI with other static volume monitoring indices, and 2 for lacking complete data. A total of 18 studies involving 665 patients or fluid challenges met the selection criteria and were subject to meta-analysis [9–26]. The inclusion and exclusion of the studies for this meta analysis are described in Fig. 1.

3.2 Quality assessment results

The quality assessment results of the 18 included studies are described in Table 1. All studies provided clear selection criteria, details of index test and reference standard, and the reference standard was independent of the index test in all the included studies. Spectrum bias, condition progression bias, partial or differential verification bias, confounding bias, clinical review bias were not apparent. It was not clear that whether the index test results were interpreted without knowledge of the results of the reference standard or not, and whether the reference standard results interpreted without knowledge of the results of the index test or not. All the included studies described the execution of the index test and the reference standard in sufficient detail to permit replication of the test. All the studies reported the uninterpretable/intermediate test results, and explained the withdrawals from the study.

3.3 Study characteristics

The characteristics of the 18 included studies are summarized in Table 2. Of the 18 included studies, 17 were published in English and 1 in Chinese [24]. Of the 18 studies, 13 were conducted in the operation room [10, 11, 13, 14, 16, 18–22, 24–26] while 5 were conducted in the intensive care unit [9, 12, 15, 17, 23], and 16 were conducted on adults while 2 were conducted on children. All patients were in closed chest conditions, had normal sinus rhythm, and mechanical ventilated. In 2 studies [9, 21], different sites of measurements of PVI (finger, ear, forehead) were investigated. In order to maintain homogeneity with all other studies, only results obtained from the finger probe were included in the pooled analysis. 7 studies used a change in cardiac index (△CI) [9, 15, 17, 18, 21, 24, 26], 1 used a change in cardiac output (△CO) [23], 7 used a change in stroke volume index (△SVI) [10, 11, 14, 16, 19, 22, 25], 2 used a change in stroke volume (△SV) [9, 20], and 1 used a change in pulse pressure variation (△PPV) [13]. These reference standards were all used in reflecting responses of cardiac output to treatment clinically and were considered appropriate as a reference standard for the outcome of interest.

3.4 Results of included studies

The results of the included studies are reported in Table 3. A total of 18 studies involving 665 patients or fluid challenges met the selection criteria and were subject to meta-analysis [9–26]. The sample size of the included studies varied between 20 and 97. The best threshold for identification of responders ranged between 8 and 20 %. In 1 study [16] multiple fluid challenges were administered to a single patient and the results used fluid challenge not patient as the statistical unit. 1 study [12] evaluated fluid responsiveness before and after valve replacement respectively and their results indicated that arterial pressure-based dynamic variables, such as PPV and SVV, had limited potential to guide fluid therapy in patients with aortic stenosis and their ability to guide fluid therapy after aortic valve replacement seemed better. Arterial pressure-based dynamic variables PPV is our gold standard to distinguish between responders and nonresponders to fluid challenge, so we excluded the preperative data and just included the postoperative data.

3.5 Meta analysis results from all pooled studies and subgroup studies

For all pooled studies, the spearman correlation coefficient was 0.279 ($P = 0.262$), and the Cochrane-Q of the DOR was 15.77 ($P = 0.542$, $I^2 = 0.0$ %). For the OR subgroup and ICU subgroup, the spearman correlation coefficient were −0.044 ($P = 0.886$) and 0.300 ($P = 0.624$), respectively; the Cochrane-Q of the DOR were 7.2 ($P = 0.844$, $I^2 = 0.0$ %) and 7.54 ($P = 0.110$, $I^2 = 46.9$ %), respectively. There was no heterogeneity within studies nor between studies and there was no significant heterogeneity within each subgroup. So a fixed-effect model was used to perform our meta-analysis.

The pooled diagnostic accuracy of PVI to predict fluid responsiveness from all studies and different subgroups of studies are described in Table 4. The pooled sensitivity of the included 18 studies was 0.73 (95 % CI 0.68–0.78), the pooled specificity was 0.82 (95 % CI 0.77–0.86), the pooled positive likelihood was 4.16 (95 % CI 3.22–5.38),

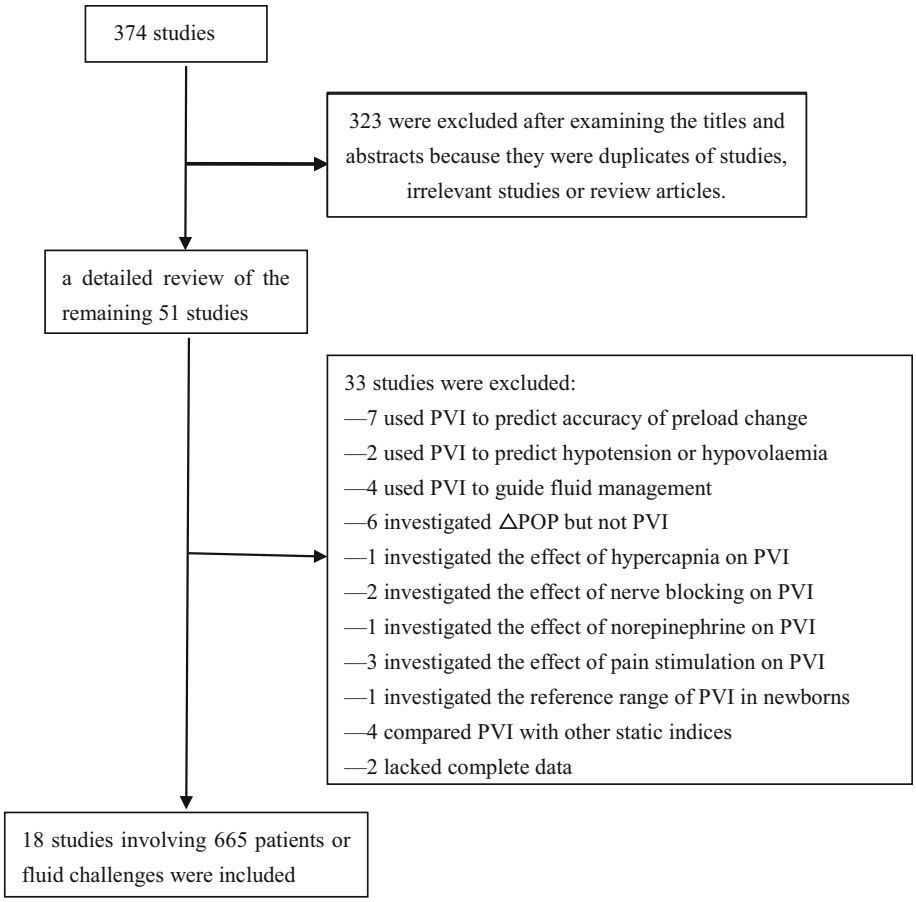

Fig. 1 Flowchart showing study inclusion and exclusion

pooled negative likelihood was 0.30 (95 % CI 0.24–0.36), the area under the summary ROC curve (AUC) was 0.88 (95 % CI 0.84–0.91) and Q* index was 0.8071. No statistical differences were found between the operating room (OR) subgroup and the intensive care unit (ICU) subgroup in the AUC [0.89 (95 % CI 0.85–0.92) vs. 0.90 (95 % CI 0.82–0.94); $P = 0.97$], and in the specificity [0.84 (95 % CI 0.75–0.86) vs. 0.84 (95 % CI 0.75–0.91); $P = 1.00$]. Sensitivity was higher in the OR subgroup than the ICU subgroup [0.84 (95 % CI 0.78–0.88) vs. 0.56 (95 % CI 0.47–0.64); $P = 0.00004$].

4 Discussion

The results of our meta-analysis showed that the pooled sensitivity of the included 18 studies was 0.77 (95 % CI 0.68–0.78), the pooled specificity was 0.82 (95 % CI 0.77–0.86), indicating that PVI had high value in predicting fluid responsiveness. The pooled AUC in our study was 0.88 and Q* index was 0.8071, indicating that PVI was a good index to predict fluid responsiveness, and there was no heterogeneity between studies ($I^2 = 0.0$ %). No statistical differences were found between OR subgroup and ICU subgroup in the AUC [0.89 (95 %CI 0.85–0.92) vs. 0.90 (95 % CI 0.82–0.94); $P = 0.97$], and in the specificity [0.84 (95 % CI 0.75–0.86) vs. 0.84 (95 % CI 0.75–0.91); $P = 1.00$]. While sensitivity was significantly higher in the OR subgroup than the ICU subgroup [0.84 (95 % CI 0.78–0.88) vs. 0.56 (95 %CI 0.47–0.64); $P = 0.00004$]. The following two reasons may explain this difference. First, patients in IUC are critically ill and most of them have lower perfusion. Peripheral hypoperfusion with impaired blood flow results in a decreased PI because of a stable constant part of the plethysmographic signal contributed by skin and other tissues [34, 36]. Broch et al. [33] demonstrated that low PI may impact the accuracy of PVI to reliably predict fluid responsiveness and PVI reliably predicted fluid responsiveness only in higher perfusion states indicated by a PI > 4 %. Second, many patients in ICU are treated with vasoactive drugs such as norepinephrine (NE), which modify vascular tone. PVI measurements are influenced by vascular tone that may affect its pulsatile absorption component [36, 42, 43]. The amplitude of the pulse oximetry plethysmographic waveform is influenced by changes in vascular tone from all tissue compartments present in the fingertip, and vasoconstriction narrows the amplitude of the waveform. Thus, patients who require NE had potentially a different

Table 1 Quality assessment

Item	Proportion of included studies (%)		
	Yes	No	Unclear
1. Was the spectrum of patients representative of the patients who will receive the test in practice ?	100		
2. Were selection criteria clearly described?	100		
3. Is the reference standard likely to correctly classify the target condition?	100		
4. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?(condition progression bias)	100		
5. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?(partial verification bias)	100		
6. Did patients receive the same reference standard regardless of the index test result? (differential verification bias)	100		
7. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)? (confounding bias)	100		
8. Was the execution of the index test described in sufficient detail to permit replication of the test?	100		
9. Was the execution of the reference standard described in sufficient detail to permit its?	100		
10. Were the index test results interpreted without knowledge of the results of the reference standard?			100
11. Were the reference standard results interpreted without knowledge of the results of the index test?			100
12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice? (clinical review bias)	100		
13. Were uninterpretable/intermediate test results reported?	100		
14. Were withdrawals from the study explained?	100		

vasomotor tone and this may affect PVI in a different manner [39]. The clinical studies of PVI are still limited, and some practical problems in the clinical application still remain to be solved.

4.1 Firstly, applicable objects

PVI is more suitable for mechanical ventilated patients without irregular heart rhythm, open chest, right ventricular failure or increased intra-abdominal pressure [30]. The reasons may be as follows: PVI is the dynamic parameter that relies on cardiopulmonary interactions. PVI can predict fluid responsiveness accurately from the premise that the change of intrathoracic pressure is evident enough and the cardiopulmonary interactions is stable in different respiratory cycles. So the dynamic parameters of cardiopulmonary interactions such as PVI are more suitable for mechanical ventilated patients not spontaneously breathing patients. But it is worth mentioning that Keller et al. researched [31] the ability of PVI to detect hemodynamic changes in spontaneously breathing volunteers and showed that PVI could detect hemodynamic changes in spontaneously breathing volunteers but it was a weak predictor of fluid responsiveness in this setting. However, the hemodynamic changes were induced by passive leg raising but not fluid challenge, therefore this study was excluded from our meta-analysis.

4.2 Secondly, site of measurement

The site of measurement could affect the accuracy of PVI. Fischer et al. [9] demonstrated that Cephalic sites (namely the ear and the forehead), which are less sensitive to increased vasomotor tone, could be more appropriate in critically ill and/or high-risk surgical patients. Shelley et al. [32] reported that using cephalic sensors is expected to significantly improve the PVI signal quality while simultaneously decreasing the background noise. Moreover, the respiratory signal in the pulse oximeter waveform could be more than 10 times higher in the cephalic region when compared with the digital one. Desgranges et al. demonstrated [21] that the three sites of measurement (forehead and ear finger) of PVI were able to predict fluid responsiveness with the best site being the forehead, then the ear and finger; however, there was no statistical difference between these three areas. They supported the use of PVI in the cephalic region when the finger is inaccessible or during

Table 2 Characteristics of the included studies

Study	Year	Setting	Type of patient	Size	Ventilation mode	Fluid challenge	Definition of responsiveness
Fischer [9]	2014	ICU	Adult—postoperative, cardiac surgery	50	Mechanical	Colloids 500 ml	ΔCI > 15 %
Siswojo [10]	2014	OR	Adult—noncardiac surgery	29	Mechanical	Colloids 500 ml	ΔSVI > 10 %
Xu [11]	2014	OR	Adult—upper abdominal operation	26	Mechanical	Crystalloids 2 ml/h kg	ΔSVI > 10 %
Hoiseth [12]	2014	ICU	Adult—postoperative, aortic stenosis surgery	28	Mechanical	Ringer's acetate 500 ml or HES 250 ml or PRBC 250 ml or plasma 250 ml	ΔSV > 15 %
Lu [13]	2014	OR	Adult—abdominal surgery	30	Mechanical	10 mL 50 % glucose	PPV > 11 %
Vos [14]	2013	OR	Adult—hepatic resection	30	Mechanical	15 ml/kg colloids or crystalloids	ΔSVI > 20 %
Fischer [15]	2013	ICU	Adult—postoperative, cardiac surgery	80	Mechanical	Colloids 500 ml	ΔCI > 15 %
Julien [16]	2013	OR	Children—noncardiac surgery	97	Mechanical	Crystalloids 10 ml/kg	ΔSVI > 15 %
Monnet [17]	2013	ICU	Adult—circulatory insufficiency	35	Mechanical	Crystalloids 500 ml	ΔCI ≥ 15 %
Haas [18]	2012	OR	Adult— cardiac surgery	22	Mechanical	Colloids 4 ml/kg	ΔCI > 10 %
Fu [19]	2012	OR	Adult—retroperitoneal surgery	51	Mechanical	Colloids 8 ml/kg	ΔSVI ≥ 10 %
Hood [20]	2011	OR	Adult—colorectal surgery	25	Mechanical	Colloids 500 ml	ΔSV > 10 %
Desgranges [21]	2011	OR	Adult—cardiac surgery	28	Mechanical	Colloids 500 ml	ΔCI > 15 %
Renner [22]	2011	OR	Children—congenital heart surgery	27	Mechanical	Colloids 10 ml/kg	ΔSVI ≥ 15 %
Loupec [23]	2011	ICU	Adult—circulatory insufficiency	40	Mechanical	Colloids 500 ml	ΔCO ≥ 15 %
Cai [24]	2010	OR	Adult—general surgery	25	Mechanical	Colloids 7 ml/kg	ΔCI ≥ 15 %
Zimmermann [25]	2010	OR	Adult—general surgery	20	Mechanical	Colloids 7 ml/kg	ΔSVI ≥ 15 %
Cannesson [26]	2008	OR	Adult—CABG	25	Mechanical	Colloids 500 ml	ΔCI ≥ 15 %

ICU intensive care unit, *OR* operating room, *CI* cardiac index, *CO* cardiac output, *PPV* pulse pressure variation, *SVI* stroke volume index, *SV* stroke volume

states of low peripheral perfusion. Now the most common site of measurement is the finger because of its simple operation. We suggest that PVI monitoring probably should move from digital to cephalic sites when necessary.

4.3 Thirdly, the best threshold

Results of the included studies assessing PVI as a predictor for fluid responsiveness demonstrated a high variability of the best threshold, ranging from 8 to 20 %. One reason for the high variability might be the different settings in which the studies have been performed (before and after cardiac surgery, major abdominal surgery and ICU patients) [18]. Another reason might be that PVI is affected more by external conditions such as low cardiac output, hypothermia, vasoactive drugs, and peripheral vascular disease [33]. This variability underlines that PVI has to be interpreted specific to the population group with potential confounding external factors in mind.

4.4 Fourthly, peripheral perfusion

The quality of the PVI signal is critically dependent on peripheral perfusion [33]. Several studies investigated the effects of low perfusion caused by hypothermia, vasoconstriction and hypotension on the accuracy of pulse oximetry [34–36]. Peripheral hypoperfusion (e.g. vasoconstriction) with impaired blood flow results in a decreased PI because of a stable constant part of the plethysmographic signal contributed by skin and other tissues [34, 36]. So far the pulse oximeter, which PVI is calculated from, is not able to determine whether the decreased PI was induced by the change of intrathoracic pressure or by the peripheral hypoperfusion. Therefore, any

Table 3 Results of the included studies

Author	Size	TP	FP	FN	TN	Best threshold (%)	Sensitivity	Specificity	AUC [95 % CI] (SD)
Fischer [9]	50	21	0	20	9	19	0.51	1.00	0.74 [0.60–0.86]
Siswojo [10]	29[a]	15	4	2	8	10.5	0.88	0.67	0.84 [0.69–0.99]
Xu [11]	23[b]	8	1	2	12	16	0.80	0.92	0.82[0.60–0.95]
Hoiseth [12]	28[c]	11	7	0	10	8	1.00	0.92	0.72 [0.52–0.87]
Lu [13]	30[d]	16	3	1	11	13	0.92	77.8	0.75[0.56–0.89]
Vos [14]	30	14	3	3	10	12	0.82	0.77	0.78[0.59–0.96]
Fischer [15]	80[e]	22	3	35	20	20.0	0.38	0.87	0.60 [0.48–0.71]
Julien [16]	97*	36	10	9	42	17.0	0.80	0.80	0.85[0.77–0.93]
Monnet [17]	35[f]	7	2	8	18	16.0	0.47	0.90	0.68 (0.09)
Haas [18]	22	4	2	0	16	16.0	1.00	0.89	0.95 (–)
Fu [19]	51[g]	24	4	7	16	13.5	0.77	0.80	0.79 [0.65–0.92]
Hood [20]	25	19	0	3	3	10.0	0.86	1.00	0.96 [0.88–1.00]
Desgranges [21]	28	14	3	5	6	12.0	0.74	0.67	0.84 [0.69–0.99]
Renner [22]	27	11	5	2	9	13.0	0.84	0.61	0.78 [0.61–0.88]
Loupec [23]	40[h]	20	2	1	17	17.0	0.95	0.91	0.88 [0.74–0.96]
Cai [24]	25	15	1	2	7	15.5	0.88	0.88	0.93 [0.83–1.04]
Zimmermann [25]	20	14	0	1	5	9.5	0.93	1.00	0.97 [0.91–1.00]
Cannesson [26]	25	13	0	3	9	14.0	0.81	1.00	0.93 [0.83–1.03]

TP true positive, *FP* false positive, *FN* false negative, *TN* true negative, *AUC* area under the receiver operating characteristic curve, *CI* confidence interval, *SD* standard deviation, *PVI,* plethysmographic variability index

* Multiple fluid challenges were administered to a single patient and the results used fluid challenge not patient as the statistical unit

[a] 1 patient was excluded from the study due to use of a vasopressor after the induction of anesthesia

[b] 3 patients were excluded because their blood pressure drop reached treatment standards after T8-9 gap epidural block

[c] 1 patient was excluded due to a profoundly dampened arterial waveform presumably because of a peripheral arterial stenosis

[d] 1 patient was excluded from the study due to a pre-injection blood glucose level over 9.0 mmol/L

[e] 7 patients were excluded—4 were excluded because PVI could not be obtained, and 3 for abnormalities in postoperative cardiac rhythm

[f] 7 patients were excluded because PVI could not be obtained

[g] 4 patients were excluded −3 for arrhythmia and 1 for obvious hemorrhage

[h] 5 patients were excluded because PVI could not be obtained

factors affecting the peripheral perfusion, namely the factors affecting PI, can influence the accuracy of PVI to predict fluid responsiveness.

Broch et al. [33] demonstrated that PVI was affected by many factors related to PI, and the accuracy with which PVI predicted fluid responsiveness was reduced at lower PI values. Peripheral vasoconstriction caused by vasoactive drugs, hypothermia or surgical stress response can, therefore, decrease the reliability of PVI. These may limit the use of PVI to guide fluid therapy during dynamic intraoperative conditions. So when the PVI is used to predict fluid responsiveness, we should consider if there are factors affecting peripheral perfusion, such as vascular disease, hypothermia, low CO, surgical stress response and drug-induced vasoconstriction [17, 37, 38]. In particular, norepinephrine, by increasing the peripheral vascular tone, may reduce the pulsatile component of plethysmographic wave and therefore the accuracy of PVI [39].

4.5 Fifthly, colloid administration

Vos et al. [40] found that PVI could predict fluid responsiveness comparable with that of dynamic preload variables such as stroke volume (SVV) and pulse pressure (PPV), but was unable to track changes induced by fluid administration. They supposed that colloid solution might influence the calculation of PVI by the Masimo Radical 7 device because they and Bergek et al. [41] previously reported that colloid solution might influence the accuracy of haemoglobin measurement by the Masimo Radical 7

Table 4 Meta analysis results from all pooled studies and subgroup studies

Setting (numbers of studies)	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	AUC [95 % CI]
PVI across all settings (n = 18)	0.73 (95 % CI 0.68–0.78)	0.82 (95 % CI 0.77–0.86)	4.16 (95 % CI 3.22–5.38)	0.30 (95 % CI 0.24–0.36)	0.88 (95 % CI 0.84–0.91)
PVI in OR (n = 13)	0.84 (95 % CI 0.78–0.88)	0.84 (95 % CI 0.75–0.86)	4.17 (95 % CI 3.09–5.62)	0.21 (95 % CI 0.16–0.29)	0.89 (95 % CI 0.85–0.92)
PVI in ICU (n = 5)	0.56 (95 % CI 0.47–0.64)	0.84 (95 % CI 0.75–0.91)	4.14 (95 % CI 2.49–6.89)	0.45 (95 % CI 0.36–0.57)	0.90 (95 % CI 0.82–0.94)

device. However, we have not found other studies researching on this issue. Further studies are needed to explore the effect of colloid administration on the accuracy of PVI in predicting fluid responsiveness.

Our systematic review has some limitations. Firstly, our meta-analysis included only mechanically ventilated patients, so that its results cannot be directly extrapolated to the whole population. Secondly, subgroup analysis on the amount of fluid challenge was not performed in our study. Thirdly, Hoiseth's study [12] which evaluated fluid responsiveness before and after valve replacement respectively indicated that arterial pressure-based dynamic variables, such as PPV and SVV, had limited potential to guide fluid therapy in patients with aortic stenosis and their ability to guide fluid therapy after aortic valve replacement seemed better. Arterial pressure-based dynamic variables PPV is our gold standard to distinguish between responders and non-responders to fluid challenge, so we excluded the preoperative data and just included the postoperative data. Therefore, selection bias probably existed.

5 Conclusion

The results of our meta-analysis show that in mechanically ventilated patients in normal sinus rhythm, PVI has a reasonable ability to predict fluid responsiveness. But the applicability of PVI may be limited by potential interference from several factors, such as spontaneous breathing activity, arrhythmia, and low peripheral perfusion.

Compliance with ethical standards

Conflict of interest The authors declare that they have no financial relationship with any organization and have no conflict of interest.

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