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REVIEW

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Accuracy of plethysmographic indices as predictors of fluid responsiveness in mechanically ventilated adults: a systematic review and meta-analysis

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Abstract *Purpose:* To systematically review the accuracy of the variation in pulse oxymetry plethysmographic waveform amplitude (ΔPOP) and the Pleth Variability Index (PVI) as predictors of fluid responsiveness in mechanically ventilated adults. *Methods:* MEDLINE, Scopus and the Cochrane Database of Systematic Reviews were screened for clinical studies in which the accuracy of ΔPOP/PVI in predicting the hemodynamic response to a subsequent fluid bolus had been investigated. Random-effects meta-analysis was used to summarize the results. Data were stratified according to the amount of fluid bolus (large vs. small) and to the study index (ΔPOP vs. PVI). *Results:* Ten studies in 233 patients were included in this meta-analysis. All patients were in normal sinus rhythm. The pooled area under the receiver operating characteristic curve (AUC) for identification of fluid responders was 0.85 [95 % confidence interval (CI) 0.79–0.92]. Pooled sensitivity and specificity were 0.80 (95 % CI 0.74–0.85) and 0.76 (0.68–0.82), respectively. No heterogeneity was found within studies with the same amount of fluid bolus, nor between studies on ΔPOP and those on PVI. The AUC was significantly larger in studies with a large bolus amount than in those with a small bolus [0.92 (95 % CI 0.87–0.96) vs. 0.70 (0.62–0.79); $p < 0.0001$]. Sensitivity and specificity were also higher in studies with a large bolus [0.84 (95 % CI 0.77–0.90) vs. 0.72 (0.60–0.82) (small bolus), $p = 0.08$ and 0.86 (95 % CI 0.75–0.93) vs. 0.68 (0.56–0.77) (small bolus), $p = 0.02$], respectively. *Conclusions:* Based on our meta-analysis, we conclude that ΔPOP and PVI are equally effective for predicting fluid responsiveness in ventilated adult patients in sinus rhythm. Prediction is more accurate when a large fluid bolus is administered.

Keywords Fluid responsiveness · Plethysmography · Hemodynamics · Mechanical ventilation

Introduction

Assessment of fluid responsiveness, i.e., the ability of patients to increase cardiac output in response to an infusion of fluids, is essential to guide fluid resuscitation and optimize preload. Dynamic indices, which measure the cardiovascular response to a controlled variation in preload [1], have been proven to predict fluid responsiveness far better than static measures of preload, such as central venous pressure (CVP) [2, 3].

Arterial waveform derived dynamic indices, such as pulse pressure variation (PPV) [4], systolic pressure variation (SPV) [5], and stroke volume variation (SVV) [6], have become increasingly popular as predictors of fluid

responsiveness in patients undergoing mechanical ventilation. Those indices indirectly measure the beat-to-beat variations in either left ventricle stroke volume (SV) or its surrogates induced by positive pressure ventilation and are based on the analysis of the arterial blood pressure waveform, recorded invasively via an intra-arterial catheter.

The analysis of the pulse oximetry waveform was postulated more than 10 years ago as a non-invasive alternative to assess blood volume status in mechanically ventilated patients [7]. Recent advances in digital signal processing combined with improvements in pulse oximetry technology have led to the development of plethysmographic dynamic indices based on the analysis of the respiratory variations in the plethysmographic waveform recorded transcutaneously by the pulse oximeter [8]. The systematic review reported here was conducted to assess the accuracy of plethysmographic dynamic indices in predicting fluid responsiveness of mechanically ventilated adult patients in both the intensive care and perioperative settings.

Materials and methods

Data reported in this review are in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [9].

Description of investigated indices

Plethysmographic indices of fluid responsiveness include the respiratory variation in pulse oximetry plethysmographic waveform amplitude (ΔPOP) and the pleth variability index (PVI). Both ΔPOP and PVI are obtained by continuous analysis of the raw pulse oximeter signal. ΔPOP is calculated as $(POP_{max} - POP_{min})/[(POP_{max} + POP_{min}) \times 0.5]$, where POP_{max} and POP_{min} represent the maximal and the minimal amplitude, respectively, of the plethysmographic waveform over one respiratory cycle [10]. PVI is calculated as $[(PI_{max} - PI_{min})/PI_{max}] \times 100$, where PI_{max} and PI_{min} represent the maximal and the minimal value, respectively, of the plethysmographic perfusion index (PI) over one respiratory cycle [11, 12]. PI is the ratio between pulsatile and nonpulsatile infrared light absorption from the pulse oximeter, and it is physiologically equivalent to the amplitude of the plethysmographic waveform [13].

The calculation of ΔPOP is usually made offline, while PVI is automatically calculated by a commercial pulse oximeter (Masimo Radical 7®; Masimo Corp, Irvine, CA) so that it can be measured and continuously monitored at the bedside.

Study eligibility criteria

We considered for inclusion all clinical trials investigating the ability of ΔPOP or PVI to predict the change in cardiac index, SV, or the SV index occurring after a fluid challenge in mechanically ventilated adult patients. Only studies that reported either the sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) of ΔPOP/PVI in identifying fluid responders, or the correlation coefficient (r) between baseline ΔPOP/PVI values and subsequent changes in cardiac output after the fluid bolus were included.

Only full-text articles published in English in indexed journals were included. No publication date or publication status restrictions were imposed.

Data sources and search strategy

Two authors independently performed a search in MEDLINE, Scopus, and the Cochrane Database of Systematic Reviews using the following keywords: "fluid" OR "preload" OR "volume responsiveness"; "cardiovascular monitoring"; "fluid challenge"; "functional hemodynamic monitoring"; "dynamic indices OR indexes"; "delta POP"; "pleth index"; "plethysmographic waveform". The search was iterated until 31 January 2012.

The automatic alert system of MEDLINE was used to identify additional studies published during the process of data extraction and analysis. References of included papers were reviewed to identify other studies of interest.

Data collection and data items

Data extraction was performed by two authors independently using a standardized form. Data were abstracted on study setting, type of ventilation, cardiac rhythm, open- versus closed-chest condition, type and amount of fluid infused, number of fluid boluses administered, definition of responders, percentage of responders, mean value of ΔPOP/PVI in responders and in non-responders, correlation coefficient (Spearman or Pearson), AUC, best threshold, sensitivity, and specificity. When reported data were not sufficient to perform the planned statistical analysis, the first authors of the articles were contacted to acquire missing information.

Assessment of quality in individual studies

Quality assessment was made independently by two authors using the QUADAS scale [14], which is a tool developed specifically for assessing the quality of studies on diagnostic accuracy. Each study was scored from 0 to 14 on a 14-item evaluation sheet.

Summary measures and synthesis of results

Comprehensive Meta-Analysis® software ver. 2.2 (Biostat, Englewood, NJ: www.meta-analysis.com) was used to calculate the pooled values of AUC, the correlation coefficient r, and the difference between mean baseline values of ΔPOP/PVI in responders and in non-responders. Using MetaDISC®, ver. 1.4, a dedicated software for the meta-analysis of test accuracy data [15], we calculated the pooled values of sensitivity and specificity of ΔPOP/PVI in the included studies.

All values were reported as point estimate with 95 % confidence intervals (CI).

Heterogeneity and risk of bias across studies

A random-effects model was used to perform our meta-analysis. Heterogeneity was assessed using the Q and I^2 tests. The results were considered to be significant when $p < 0.1$ or $I^2 > 50$ %.

In order to investigate the potential causes of heterogeneity, the study sample was stratified according to the amount of fluid bolus administered [large (500 ml or 7–8 ml/kg) vs. small (250 ml)] and to the plethysmographic index used (ΔPOP vs. PVI). Differences between subgroups were analyzed using the interaction test [16].

Results

Study selection

The initial dataset included 1,100 hits from MEDLINE and 1,604 hits from Scopus. No items were identified from the Cochrane Database of Systematic Reviews. After the removal of duplications and screening, 42 studies were considered for further analysis. Among these, 21 studies investigated plethysmographic indices but did not evaluate the prediction of fluid responsiveness, while 11 studies evaluated the prediction of fluid responsiveness but did not fulfil our inclusion criteria. The remaining ten studies [11, 12, 17–24] were ultimately included in our meta-analysis (Fig. 1). Excluded studies with details on the reasons for their exclusion are listed in Electronic Supplementary Material (ESM) 1.

Study characteristics

The characteristics of the ten included studies are summarized in Table 1. Six studies investigated ΔPOP [17, 19, 20, 22–24], three studies investigated PVI [12, 18, 21], and one study investigated both ΔPOP and PVI [11]. Since in this last study both indices were recorded in the same patient population at the same time, we included only data on PVI in the pooled analysis to avoid duplication of the sample size. The administered fluid bolus was large in seven studies and small in two studies. In one study [21], large and small fluid boluses were given to the same patient population at two different clinical times. The results from these two interventions were reported separately. In one study [18], 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.

In four studies [20–23] multiple fluid boluses were administered to a single patient and the results reported using bolus—and not patient—as the statistical unit. We followed the same criteria in our meta-analysis.

Three studies [19, 22, 24] were carried out in general or post-surgical intensive care units (ICUs), while seven studies [11, 12, 17, 18, 20, 21, 23] were carried out in operating room during abdominal or cardiac surgery. All patients were in closed chest conditions, had normal sinus rhythm, and were ventilated in controlled mode with the tidal volume ranging from 7 to 10 ml/kg.

Results of included studies

The results from the included studies are reported in Table 2. A total of 365 fluid boluses (214 large, 151 small) were administered to 233 patients (range 8–32 patients per study). The mean responder rate was 62.3 ± 14.0 %. The best threshold for the identification of responders ranged between 9.5 and 15 %.

Pooled values for AUC, sensitivity, and specificity in all studies were 0.85 (95 % CI 0.79–0.92), 0.80 (95 % CI 0.74–0.85), and 0.76 (95 % CI 0.68–0.82), respectively. The pooled r was 0.58 (95 % CI 0.43–0.70; $p < 0.001$), and the pooled difference between baseline values of ΔPOP/PVI in responders and in non-responders was 9.1 % (95 % CI 6.3–11.9 %, $p < 0.0001$).

Heterogeneity and subgroup analysis

The median quality (QUADAS) score was 12 (range 12–13). Since study quality was uniformly good, a sensitivity analysis was not performed [25].

A significant heterogeneity within the ten studies was found for AUC and sensitivity ($I^2 = 72.9$ %, $p < 0.0001$ and $I^2 = 46.8$ %, $p = 0.043$, respectively; Table 3). Following stratification according to the amount of fluid bolus (large vs. small), no heterogeneity was found within each subgroup. Specificity was significantly higher in the subgroup receiving a large bolus than in that receiving the small bolus [0.86 (95 % CI 0.75–0.93) vs. 0.68 (95 % CI 0.56–0.77), respectively; $p = 0.02$]. Sensitivity was also

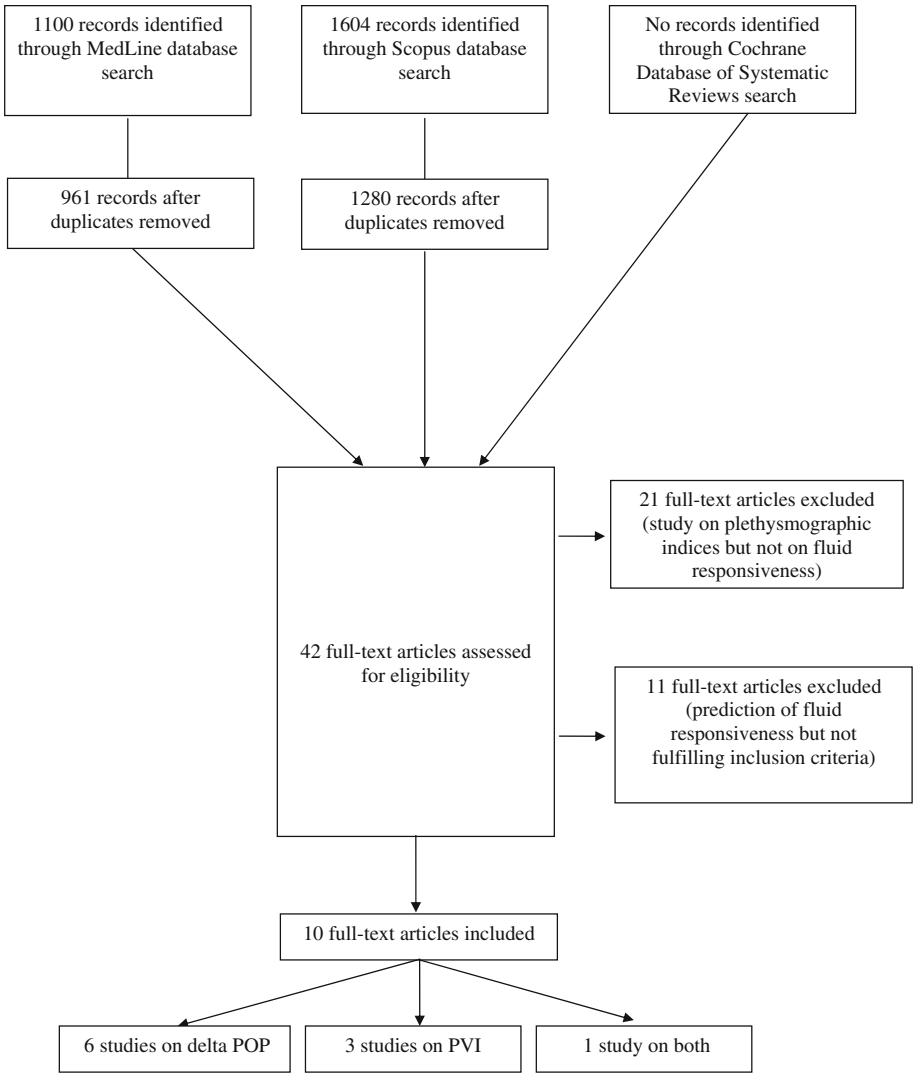

Fig. 1 Selection process for the inclusion of studies in the meta-analysis. *POP* Pulse oximetry plethysmographic waveform amplitude, *PVI* Pleth Variability Index

higher—although not significantly—in the subgroup receiving the large bolus [0.84 (95 % CI 0.77–0.90) vs. 0.72 (95 % CI 0.60–0.82), respectively; $p = 0.08$).

Heterogeneity according to study index (ΔPOP vs. PVI) was also investigated. The analysis was restricted to the seven studies with large fluid bolus, for reasons of sample size. No heterogeneity was found between studies on ΔPOP and those on PVI (Table 3).

Discussion

The results of our meta-analysis show that in adult patients with normal sinus rhythm receiving controlled mechanical ventilation, plethysmographic indices are an accurate tool for predicting the response to a subsequent fluid challenge of 500 ml or 7–8 ml/kg, while they are less accurate in predicting the response to a fluid challenge of 250 ml.

Plethysmographic indices and arterial waveform-derived indices of fluid responsiveness are physiologically related. The plethysmographic curve represents the pulsatile variation over the cardiac cycle in the amount of infrared light absorbed by hemoglobin in the capillaries of the explored tissue. The amount of absorbed light is proportional to the amount of blood in the capillary bed, which in turn is proportional to the amplitude of the arterial pulse [26, 27]. Variation in the amplitude of the arterial pulse—such as that induced by mechanical ventilation—therefore should result in a proportional variation in the amplitude of the plethysmographic curve [7, 28]. Cannesson et al. [29] found a strong correlation ($r^2 = 0.83$, $p < 0.001$) between PPV and the variations in POP in 22 sedated patients under mechanical ventilation. Similarly, a significant correlation between SPV and the

Table 1 Characteristics of included studies

References (first author)	Index	Setting	Type of patients/surgery	Ventilation mode	Tidal volume (ml/kg)	Fluid bolus	Definition of responders	QUADAS score [14]
Natalini [22]	ΔPOP	ICU	Shock, various etiologies	Volume control	8 ± 2	Colloids 500 ml (large)	ΔCI >15 %	13
Solus-Biguenet [23]	ΔPOP	OR	Hepatic surgery	Volume control	8–10	Colloids 250 ml (small)	ΔSVI >10 %	13
Cannesson [17]	ΔPOP	OR	Cardiac surgery	Volume control	8–10	Colloids 500 ml (large)	ΔCI >15 %	12
Feissel [19]	ΔPOP	ICU	Septic shock	Volume control	8–10	Colloids 8 ml/kg (large)	ΔCI >15 %	13
Wyffels [24]	ΔPOP	ICU	Postoperative, cardiac surgery	Volume control	8–10	Colloids 500 ml (large)	ΔCI >15 %	12
Hoiseth [20]	ΔPOP	OR	Abdominal surgery	Volume control	8	Colloids 250 ml (small)	ΔSV >15 %	13
Cannesson [11]	ΔPOP PVI	OR	Cardiac surgery	Volume control	8–10	Colloids 500 ml (large)	ΔCI >15 %	12
Zimmermann [12]	PVI	OR	Abdominal surgery	Volume control	7	Colloids 7 ml/kg (large)	ΔSVI >15 %	12
Desgranges [18]	PVI	OR	Cardiac surgery	Volume control	8	Colloids 500 ml (large)	ΔCI >15 %	12
			Low-risk colorectal surgery (pre-incision)	Volume control	8–10	Colloids 500 ml (large)	ΔSV >15 %	12
Hood [21]	PVI	OR	Low-risk colorectal surgery (intra-operative)	Volume control		Colloids 250 ml (small)		

ΔCI/ΔSV/ΔSVI Increase in cardiac index/stroke volume/stroke volume index after fluid infusion, respectively, *ΔPOP* respiratory variation in pulse oximetry plethysmographic waveform amplitude, *ICU* intensive care unit, *OR* operating room, *PVI* pleth variability index

variations in plethysmographic waveform peaks during controlled ventilation has been demonstrated in patients during general anaesthesia [7, 30].

In our meta-analysis, the predictive value of plethysmographic indices in studies using a large fluid challenge was comparable to that of arterial waveform-derived indices. The pooled AUC of ΔPOP/PVI in those studies was 0.92 (95 % CI 0.87–0.96). In comparison, in a meta-analysis from Marik et al. [2], in which almost all included studies had been made using a large fluid challenge, the pooled AUC for PPV, SVV and SPV were 0.94 (95 % CI 0.93–0.95), 0.84 (95 % CI 0.78–0.88), and 0.86 (95 % CI 0.82–0.90), respectively. However, the correlation coefficient of plethysmographic indices in our meta-analysis was lower than that of arterial waveform-derived indices. In fact, the pooled *r* between the baseline value of ΔPOP/PVI and the following increase in cardiac output in studies with a large bolus was 0.66 (95 % CI 0.54–0.75), while in the above-mentioned meta-analysis from Marik et al. [2] the corresponding pooled *r* for PPV, SVV and SPV were 0.78 (95 % CI 0.74–0.82), 0.72 (95 % CI 0.66–0.78), and 0.72 ((95 % CI 0.65–0.77), respectively. A higher correlation coefficient *r* for PPV versus ΔPOP was also demonstrated in a prospective study from Feissel et al. [19] which directly compared ΔPOP with PPV in mechanically ventilated adults. These data suggest that while plethysmographic indices are as accurate as arterial waveform-derived indices in identifying fluid responders, they are less accurate in predicting the magnitude of cardiac output increase after the fluid challenge.

Arterial waveform-derived indices are not reliable in patients with spontaneous breathing or arrhythmias [31]. In these conditions, plethysmographic indices, which share the same physiological basis of arterial waveform-derived indices, are expected to lose their predictive ability as well. We are not aware of any study on plethysmographic indices made in arrhythmic patients. However, we identified two studies that enrolled a total of 51 spontaneously breathing healthy volunteers in sinus rhythm. One of those studies was made using ΔPOP [32] and the other using PVI [33]. The pooled AUC and specificity in these two studies were only 0.70 ((95 % CI 0.56–0.84) and 0.60 (95 % CI 0.38–0.78), respectively. These data confirm that plethysmographic indices have probably a limited value in patients with spontaneously breathing activity in whom passive leg raising-induced changes in cardiac output [34] should rather be used to predict fluid responsiveness.

Being based on non-invasive pulse oximetry, plethysmographic indices do not require arterial catheterization, and this allows a safer and faster assessment of fluid responsiveness as compared to arterial waveform derived indices. However, the quality of the plethysmographic signal is critically dependent on peripheral perfusion [35], which may be significantly reduced by factors such as hypothermia [36], low cardiac output [37], and drug-induced vasoconstriction. In particular, norepinephrine, by increasing the peripheral vascular tone, may reduce the pulsatile component of plethysmographic wave and therefore the accuracy of plethysmographic indices. Recent observational studies [38, 39] have in fact shown that the correlation between ΔPOP/PVI and PPV is significantly reduced in patients who are given norepinephrine. Finally, a study carried out on critical patients using Laser Doppler Flowmetry [39] revealed the presence of spontaneous cyclic peripheral vasomotor tone changes which may cause wide periodical oscillations of the peripheral plethysmographic signal recorded from the index finger. These oscillations overlap the respiratory variations in the plethysmographic signal

Table 2 Study results

References (first author)	Index	Number of patients/boluses	% Responders	Best threshold	*r*	AUC (SE)	Sensitivity	Specificity
Natalini [22]	ΔPOP	22/31	61.0	15.0	–	0.70 (0.094)	0.63	0.83
Solus-Biguenet [23]	ΔPOP	8/54	42.0	9.5	0.29	0.68 (0.071)	0.64	0.68
Cannesson [17]	ΔPOP	25/25	60.0	13.0	0.62	0.85 (0.081)	0.93	0.90
Feissel [19]	ΔPOP	23/28	64.0	14.0	0.70	0.94 (0.050)	0.94	0.80
Wyffels [24]	ΔPOP	32/32	62.5	11.8	0.65	0.89 (0.061)	0.90	0.83
Hoiseth [20]	ΔPOP	25/34	64.7	11.4	–	0.72 (0.082)	0.86	0.67
Cannesson [11]	ΔPOP[b]	25/25	64.0	12.0	0.69	0.94 (0.043)	0.87	0.89
	PVI	25/25	64.0	14.0	0.67	0.93 (0.051)	0.81	1.00
Zimmermann [12]	PVI	20/20	75.0	9.5	0.61	0.97 (0.033)	0.93	1.00
Desgranges [18]	PVI	28/28	68.0	12.0	–	0.84 (0.077)	0.74	0.67
Hood [21] (large bolus)	PVI	25/25	88.0	10.0	–	0.96 (0.031)	0.86	1.00
Hood [21] (small bolus)	PVI	25/63	36.5	10.0	–	0.71 (0.071)	0.65	0.67
Overall[a]		233/365	62.3 ± 14.0	9.5–15.0 (range)	0.58 [0.43–0.70]	0.85 [0.79–0.92]	0.80 [0.74–0.85]	0.76 [0.68–0.82]

AUC Area under the receiver operating characteristic curve, *SE* standard error, *CI* Confidence interval, *SE* standard error

[a] 95 % CI is presented in square brackets

[b] All values for ΔPOP from Cannesson [11] were not included in the pooling in order to avoid duplication of sample size

Table 3 Subgroup analysis and heterogeneity

Subgroup	AUC				Sensitivity				Specificity			
	Pooled value (95 % CI)	Heterogeneity			Pooled value (95 % CI)	Heterogeneity			Pooled value (95 % CI)	Heterogeneity		
		Within groups		Between groups		Within groups		Between groups		Within groups		Between groups
		I^2	*p*	*p*		I^2	*p*	*p*		I^2	*p*	*p*
All studies	0.85 (0.79–0.92)	72.9	<0.0001*		0.80 (0.74–0.85)	46.8	0.043		0.76 (0.68–0.8)]	33.2	0.133	
Large bolus	0.92 (0.87–0.96)	40.2	0.11		0.84 (0.77–0.90)	37.5	0.13		0.86 (0.75–0.93)	10.5	0.35	
Small bolus	0.70 (0.62–0.79)	0.0	0.93		0.72 (0.60–0.82)	44.4	0.17		0.68 (0.56–0.77)	0.0	1.00	
Large vs. small				<0.0001*				0.08				0.02*
ΔPOP	0.89 (0.82–0.96)	39.3	0.16		0.85 (0.76–0.92)	53.3	0.07		0.85 (0.72–0.93)	0.0	0.97	
PVI	0.95 (0.91–0.99)	0.0	0.41		0.83 (0.73–0.91)	0.0	0.45		0.89 (0.70–0.98)	58	0.07	
ΔPOP versus PVI[a]				0.13				0.76				0.70

AUC area under the ROC curve, *CI* confidence interval, *ΔPOP* variation in plethysmographic waveform amplitude, *PV* pleth variability index

* Results were considered to be significant when $p < 0.1$

[a] Only studies with large bolus were included

and may cause interferences whose removal requires appropriate signal processing [40, 41].

Another factor which could affect the accuracy of plethysmographic indices is their site of measurement. In a recent study from Desgranges et al. [18], the accuracy of PVI as a predictor of fluid responsiveness was higher when the probe was positioned on the forehead or earlobe, where the subcutaneous vasculature is relatively resistant to sympathetically mediated vasomotor tone changes [42]. This suggests that, contrary to the usual practice, the fingertip is not the preferred site of measurement for plethysmographic indices, especially in patients who are on vasoactive drugs.

An important technical limitation of plethysmographic indices is represented by filtering. Pulse oximeters have been primarily developed to detect the oxygen saturation signal rather than to detect ventilation-induced changes in pulsatile plethysmogram. In particular, adaptive digital filters, which dynamically change their filtering characteristics in response to a change in band noise, have been adopted to remove noise occurring within the pulse oximeter signal bandwidth. However, this continuous adjustment in filtering may result in changes in the pulse amplitude that interfere with those induced by mechanical ventilation [43]. We cannot exclude the possibility that the accuracy of the plethysmographic indices of fluid responsiveness as reported in our review could have been affected by filtering techniques. Moreover, the use of different filtering techniques in different devices may

have represented an undetected source of heterogeneity in our meta-analysis.

No difference in accuracy between PVI and ΔPOP was identified in our meta-analysis. Similarly, the only study conducted to date which has directly compared PVI with ΔPOP [11] did not find any significant difference between those two indices, whose reciprocal correlation coefficient *r* was high (0.92). In practical terms, however, PVI is more appropriate for monitoring purposes than ΔPOP since it is automatically and continuously displayed by a dedicated pulse oximeter with no need for off-line analysis.

Study limitations

Our study has a series of limitations. Firstly, only three of the ten studies included in our meta-analysis were conducted in ICUs, and one of these three studies included only postoperative patients. This scarcity of studies in this clinical setting reflects the limited evidence that is currently available on the use of plethysmographic indices in the ICU, which is not entirely surprising considering that many possible sources of interference, such as spontaneous breathing, arrhythmias, and peripheral hypoperfusion, are common in intensive care patients.

Secondly, in almost all studies included in our systematic review patients were ventilated using a tidal volume of $\geq$8 ml/kg; therefore, our results cannot be extrapolated to patients ventilated using lower tidal volumes. Both plethysmographic and arterial waveform-derived indices are based on the hemodynamic effects on preload caused by positive pressure ventilation. These heart–lung interactions are more likely to occur when higher rather than lower tidal volumes are used. According to a paper from de Backer et al. [44], a tidal volume of at least 8 ml/kg is required for a reliable prediction using arterial waveform-derived indices. We suppose the same applies to plethysmographic indices, but this hypothesis will require further studies to be confirmed.

Thirdly, we could not specifically assess whether plethysmographic indices are less reliable predictors of fluid responsiveness in patients who are given norepinephrine, since the use of norepinephrine was reported in only three studies [19, 20, 22] included in our meta-analysis. These studies were heterogeneous as regards the amount of fluid challenge, and in two of them norepinephrine was used in combination with other vasoactive drugs (dobutamine, dopamine, or epinephrine). Specifically designed studies will be needed to investigate the effects of norepinephrine or other vasopressors on the accuracy of plethysmographic indices.

Fourthly, our meta-analysis included only studies carried out on adults, so that its results cannot be directly extrapolated to the pediatric population. Although some studies on plethysmographic indices in children have been carried out (see ESM 1), evidence regarding their use at present is still insufficient to allow for a meta-analysis.

Conclusions

The results of our meta-analysis show that in mechanically ventilated adult patients in normal sinus rhythm, both ΔPOP and PVI are reliable predictors of responsiveness to a fluid infusion of at least 500 ml or 7–8 ml/kg, while they are less capable of predicting the response to smaller boluses. The applicability of plethysmographic indices in the ICU may be limited by potential interference from several factors, such as the use of low tidal volume ventilation, spontaneous breathing activity, arrhythmias, and the use of vasopressors.

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Conflicts of interest None.

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