Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature*

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Objectives: **A systematic review of the literature to determine the ability of dynamic changes in arterial waveform-derived variables to predict fluid responsiveness and compare these with static indices of fluid responsiveness. The assessment of a patient's intravascular volume is one of the most difficult tasks in critical care medicine. Conventional static hemodynamic variables have proven unreliable as predictors of volume responsiveness. Dynamic changes in systolic pressure, pulse pressure, and stroke volume in patients undergoing mechanical ventilation have emerged as useful techniques to assess volume responsiveness.**

Data Sources: **MEDLINE, EMBASE, Cochrane Register of Controlled Trials and citation review of relevant primary and review articles.**

Study Selection: **Clinical studies that evaluated the association between stroke volume variation, pulse pressure variation, and/or stroke volume variation and the change in stroke volume/cardiac index after a fluid or positive end-expiratory pressure challenge.**

Data Extraction and Synthesis: **Data were abstracted on study design, study size, study setting, patient population, and the correlation coefficient and/or receiver operating characteristic between the baseline systolic pressure variation, stroke volume variation, and/or pulse pressure variation and the change in stroke index/cardiac index after a fluid challenge. When reported, the receiver operating characteristic of the central venous pressure, global end-diastolic volume index, and left ventricular end-diastolic area index were also recorded. Meta-analytic techniques were used to summarize the data. Twenty-nine studies (which enrolled 685 patients) met our inclusion criteria. Overall, 56% of patients responded to a fluid challenge. The pooled correlation coefficients between the baseline pulse pressure variation, stroke volume variation, systolic pressure variation, and the change in stroke/cardiac index were 0.78, 0.72, and 0.72, respectively. The area under the receiver operating characteristic curves were 0.94, 0.84, and 0.86, respectively, compared with 0.55 for the central venous pressure, 0.56 for the global end-diastolic volume index, and 0.64 for the left ventricular end-diastolic area index. The mean threshold values were 12.5 ± 1.6% for the pulse pressure variation and 11.6 ± 1.9% for the stroke volume variation. The sensitivity, specificity, and diagnostic odds ratio were 0.89, 0.88, and 59.86 for the pulse pressure variation and 0.82, 0.86, and 27.34 for the stroke volume variation, respectively.**

Conclusions: **Dynamic changes of arterial waveform-derived variables during mechanical ventilation are highly accurate in predicting volume responsiveness in critically ill patients with an accuracy greater than that of traditional static indices of volume responsiveness. This technique, however, is limited to patients who receive controlled ventilation and who are not breathing spontaneously. (Crit Care Med 2009; 37:2642–2647)**

KEY WORDS: arterial waveform; pulse pressure variation; stroke volume variation; pulse contour analysis; heart-lung interactions; fluid responsiveness; preload; stroke volume; fluid therapy; hemodynamic monitoring; critical care; systematic review; meta-analysis

The assessment of intravascular volume is one of the most difficult tasks in clinical medicine. This evaluation is usually made by a review of the patient's skin turgor, blood pressure, pulse rate, urine output, chest examination, and chest radiograph. These clinical signs are, however, notoriously unreliable. Similarly, the central venous pressure (CVP) and pulmonary artery occlusion pressure poorly predict the hemodynamic response to a fluid challenge (1–4). Consequently clinicians have evaluated other techniques for assessing intravascular volume, including the inferior vena caval diameter as measured by echocardiography (5), right ventricular end-diastolic volume index as measured with a modified pulmonary artery catheter (6), left ventricular end-diastolic area index (LVEDAI) as measured by echocardiography (7), and the global end-diastolic volume index (GEDVI) as determined by transpulmonary thermodilution (8, 9). However, the experience with these more sophisticated static indices of intravascular volume have been uniformly disappointing (3).

Volume expansion is usually considered the first line of therapy in hemodynamically unstable patients (10). However, clinical studies have reproducibly demonstrated that only about 50% of unstable critically ill patients will actually respond to a fluid challenge (1, 3). Furthermore, recent data suggested that a patient's cumulative fluid balance, as well as the strategy used to guide fluid management, may affect outcome (11–15). Fundamentally the only reason to give a patient a fluid challenge is to increase stroke volume (SV) and cardiac output (CO) (3). This assumes that the patient is on the ascending portion of the Frank-Starling curve and has "recruitable" CO. Once the

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left ventricle is functioning near the "flat" part of the Frank-Starling curve, fluid loading has little effect on CO and only serves to increase tissue edema and promote tissue dysoxia. It is therefore crucial during the resuscitative phase of all critically ill patients to determine whether the patient is responsive to fluid or not; this determines the optimal strategy of increasing CO and oxygen delivery (16).

Over the last decade, a number of studies have been reported which have used heart-lung interactions during mechanical ventilation to assess fluid responsiveness. Specifically, the systolic pressure variation (SPV) and the pulse pressure variation (PPV) derived from analysis of the arterial waveform and the stroke volume variation (SVV) derived from pulse contour analysis have been shown to be predictive of fluid responsiveness (3). The goal of this systematic review was to evaluate the accuracy of SPV, PPV, and SVV in predicting fluid responsiveness and to compare these variables to the static hemodynamic variables, which have been used to assess intravascular volume.

METHODS

Identification of Trials

Our aim was to identify all relevant clinical studies that evaluated the ability of the SPV, PPV, or SVV (dynamic variables) to predict the change in stroke volume index (SVI) or cardiac index (CI) after a fluid challenge in patients undergoing mechanical ventilation. We restricted this analysis to human adults; however, there was no restriction as to the type of patient or the setting where the study was performed. We excluded studies that used pressure-support ventilation or ventilatory modes that generated a tidal volume of <7 mL/kg. We used a multiple method approach to identify relevant studies for this review. All authors searched independently the National Library of Medicine's MEDLINE database for relevant studies in any language published from 1966 to November 2008, using the following Medical Subject Headings and keywords: pulse contour analysis, or systolic pressure variation, or SVV, or PPV, and fluid therapy or fluid responsiveness. In addition, we searched EMBASE and the Cochrane Database of Systematic Reviews. Bibliographies of all selected articles and review articles that included information on hemodynamic monitoring were reviewed for other relevant articles. This search strategy was done iteratively, until no new potential citations were found on review of the reference lists of retrieved articles. We performed this meta-analysis according to the guidelines proposed by the QUOROM group (17).

Study Selection and Data Extraction

Only studies that reported the correlation coefficient or receiver operating characteristic between the SPV, PPV, or SVV and change in SVI/CI after a fluid challenge were included in this analysis. Data on all dynamic variables were recorded in those studies that reported more than one variable. All authors independently abstracted data from all studies, using a standardized form. Data were abstracted on study design, study size, study setting, patient population (operating room [OR] or intensive care unit [ICU]), tidal volumes used, the correlation coefficients and area under the receiver operating characteristic curve (AUC), the percentage of patients responding to a fluid challenge as well as the baseline PPV/SVV in the fluid responders and nonresponders.

The fixed effects model, using Comprehensive Meta-analysis 2.0 (Biostat, Englewood, NJ), was used to determine the pooled AUC and correlation coefficients as well as the statistical difference between subgroups (18, 19). Subgroup analysis was performed, using OR-surgery/ICU as a moderating variable. Summary effects estimates are presented with 95% confidence intervals. We calculated the Cochran Q statistic to test for statistical heterogeneity. Values of Q significantly >0 ($p < .1$) were considered evidence of heterogeneity. The SVV/PPV between the responders and nonresponders were compared using Student's t test. When data were available to calculate the true positive, true negative, false positive, and false negative, we calculated the pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio, using a bivariate binomial mixed model (Stata Intercooled 10, Stata, College Station, TX).

RESULTS

The initial search strategy generated 68 citations; of these, 38 citations were excluded due to study design, including studies that investigated the dynamic changes in aortic blood flow, (7, 20–22) studied patients with an open chest during cardiac surgery, (23) used pressure-support ventilation or volume-controlled ventilation with a tidal volume of <7 mL/kg, (24, 25); and five citations were excluded as they did not report an outcome variable of interest (26–30). An additional four studies were identified from the bibliographies of the selected articles and review articles. The 29 studies included in the meta-analysis enrolled a total of 685 patients with an average of 23 patients per study (31–59). These studies are summarized in Table 1. Eight studies reported the SPV, 22 the PPV, and 12 the SVV. The predictive value of the CVP was reported in 18 studies, the GEDVI in three studies, and the LVEDAI in five studies. Nine studies were performed in ICU patients and 20 studies were conducted in the OR or immediately after surgery. Reuter and colleagues stratified their patients into two groups according to the patients' preoperative ejection fraction (<35% and >50%); these two populations were analyzed separately (37). Of the 20 OR/surgical studies, 15 studies were performed in patients undergoing cardiac surgery with five studies being performed after induction of anesthesia and ten studies after surgery. The outcome variable was the CI in 12 studies, the SVI in nine studies, the SV in three studies, the CO in two studies with one study not reporting the end point used. A responder was generally defined as a patient whose SVI (or CI) was ≥15% after a single (or multiple) fluid challenge(s); however, Berkenstadt et al (34) used an increase of 5% whereas Hofer et al used a threshold of 25% (42, 58).

Overall, 56% of the patients included in this review responded to a fluid challenge. The pooled correlation coefficients between the baseline PPV, SVV, SPV and the change in SVI/CI were 0.78, 0.72, and 0.72, respectively. The AUCs were 0.94, 0.84, and 0.86, respectively, compared with 0.55 for the CVP, 0.56 for the GEDVI, and 0.64 for the LVEDAI (Table 2). The AUC for the PPV was significantly greater than that for either the SPV or the SVV ($p < .001$) and the AUC for the SPV/SVV was significantly greater than that for the LVEDAI, GEDVI, and CVP ($p < .001$). The PPV was reported in six of the ICU studies and 12 of the OR/surgery studies. The AUC was 0.95 (95% confidence interval, 0.93–0.96) for the ICU patients and 0.93 (95% confidence interval, 0.92–0.94) for the OR/surgery patients (not significant). The Q statistic was not significant for any of the pooled correlation and AUC statistics. The mean threshold values were 12.5 ± 1.6% for the PPV and 11.6 ± 1.9% for the SVV. The baseline PPV was 16.6 ± 2.9% in the responders compared with 7.1 ± 1.5 in the nonresponders ($p < .001$). The baseline SVV was 15.3 ± 3.4% in the responders as compared with 8.4 ± 1.9% in nonresponders ($p < .001$). Data were

Table 1. Characteristics and findings with pooled results (95% confidence interval) of studies included in meta-analysis

Author	Year	n	Patient	Dynamic Variable			Fluid Challenge	TV (mL/kg)	Device	Cardiac End Point
				SPV	PPV	SVV				
Tavernier (31)	1998	15	ICU-sepsis	Y	N	N	500 mL HES	8–11	PAC	SVI
Michard (32)	1999	14	ICU-ARDS	N	Y	N	10 PEEP[c]	7–12	PAC	CI
Michard (33)	2000	40	ICU-sepsis	Y	Y	N	500 mL HES	8–12	PAC	CI
Berkenstadt (34)	2001	15	Neurosurg[a]	N	N	Y	100 mL HES[b]	10	PiCCO[e]	SV
Reuter (35)	2002	20	Post C.Surg	Y	N	Y	20 mL × BMI gelatin	—	PiCCO	SVI
Reuter (36)	2002	20	Post C.Surg	N	N	Y	20 mL × BMI gelatin	13–15	PiCCO	CI
Reuter (37)	2003	12	Post C.Surg-a	N	N	Y	10 mL × BMI HES[b]	10	PiCCO	SVI
		14	Post C.Surg-b				10 mL × BMI HES[b]	10	PiCCO	SVI
Bendjelid (38)	2004	16	Post C.Surg	Y	Y	N	10 PEEP[c]	8–10	PAC	SVI
Rex (39)	2004	14	Post C.Surg	N	N	Y	Trendelenburg	8	PiCCO	SVI
Kramer (40)	2004	21	Post C.Surg	Y	Y	N	500 mL blood	8–10	PAC	CO
Marx (41)	2004	10	ICU-sepsis	N	N	Y	500 mL HES	8–10	PiCCO	—
Hofer (42)	2005	35	Post C.Surg	N	Y	Y	10 mL/kg HES	10	PiCCO	SVI
Preisman (43)	2005	18	Post C.Surg	Y	Y	Y	250 mL gelatin × 2	PCV	PiCCO	SVI
De Backer (44)[d]	2005	27	ICU-mixed	N	Y	N	1000 mL CR/500 HES	8–10	PAC	CI
Wiesenack (45)	2005	20	C.Surg[a]	N	Y	Y	7 mL/kg HES	7	PiCCO/PAC	SVI
Feissel (46)	2005	20	ICU-sepsis	N	Y	N	8 mL/kg HES	8–10	TTE	CI
Solus-Biguenet (47)	2006	8	Hepatic surgery	N	Y	N	250 mL gelatin[b]	8–10	PAC	SVI
Charron (48)	2006	21	ICU-mixed	N	Y	N	100 mL HES	8–10	TEE	SV
Natalini (49)	2006	22	ICU-mixed	Y	Y	N	500 mL HES	8	PAC	CI
Wyffels (50)	2007	32	Post C.Surg	N	Y	N	500 mL HES	8–10	PAC	CI
Feissel (51)	2007	23	ICU-sepsis	N	Y	N	8 mL/kg HES	8–10	TEE	CI
Lee (52)	2007	20	Neurosurg[a]	N	Y	N	7 mL/kg HES	10	Esophageal Doppler	SVI
Cannesson (53)	2007	25	C.Surg[a]	N	Y	N	500 mL HES	8–10	PAC	CI
Cannesson (54)	2008	25	C.Surg[a]	N	Y	N	500 mL HES	8–10	PAC	CI
Auler (55)	2008	59	Post C.Surg	N	Y	N	20 mL/kg LR	8	PAC	CO
Belloni (56)	2008	19	C.Surg[a]	Y	Y	Y	7 mL/kg HES	8	LiDCO[f]/PAC	CI
Cannesson (57)	2008	25	C.Surg[a]	N	Y	N	500 mL HES	8–10	PAC	CI
Hofer (58)	2008	40	Post CABG	N	Y	Y	Trendelenburg	8–10	FloTrac[g]/PiCCO	SV
Biasis (59)	2008	35	Liver transplant	N	Y	Y	Albumin 20 mL × BMI	8–10	FloTrac/TEE	CO

CI, cardiac index; TV, tidal volume; ICU, intensive care unit; HES, hydroxy-ethyl starch; C.Surg, cardiac surgery; PCV, pressure-controlled ventilation; PAC, pulmonary artery catheter; TTE, transthoracic echocardiography; CR, crystalloid; SVI, stroke volume index; SV, stroke volume; BMI, body mass index; C.Surg-a, ejection fraction <35%; C.Surg-b, ejection fraction >50%; PEEP, positive end-expiratory pressure; TEE, transesophageal echocardiography; CABG, coronary artery bypass graft; ARDS, acute respiratory distress syndrome; SPV, systolic pressure variation; PPV, pulse pressure variation; SVV, stroke volume variation.

[a]After induction of anesthesia; [b]repeated until patient nonresponder; [c]PEEP used to decrease venous return; [d]subgroup with TV >8 mL/kg; [e]Pulsion Medical Systems, Munich, Germany; [f]LidCO, London, UK; [g]Edwards Lifesciences, Irvine, CA.

Table 2. Ability of dynamic and static hemodynamic variables to predict volume responsiveness: pooled data with 95% confidence intervals

	Correlation (r)	AUC
PPV	.78 (.74–.82)	0.94 (0.93–0.95)
SPV	.72 (.65–.77)	0.86 (0.82–0.90)
SVV	.72 (.66–.78)	0.84 (0.78–0.88)
LVEDAI	—	0.64 (0.53–0.74)
GEDVI	—	0.56 (0.37–0.67)
CVP	.13 (−.01–.28)	0.55 (0.48–0.62)

AUC, area under the curve; PPV, pulse pressure variation; SPV, systolic pressure variation; SVV, stroke volume variation; LVEDAI, left ventricular end-diastolic area index (derived from transesophageal echocardiography); GEDVI, global end-diastolic volume index (derived from transpulmonary thermodilution); CVP, central venous pressure.

available for calculations of the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio in 14 studies that reported the PPV and five that reported the SVV. The pooled performance estimates for these studies are listed in Table 3 and the standardized receiver operating characteristic curve for the PPV is displayed in Figure 1.

DISCUSSION

This meta-analysis has demonstrated that the dynamic changes in arterial waveform-derived variables (i.e., SPV, PPV, and SVV) measured during volume-controlled mechanical ventilation can predict with a high degree of accuracy those patients who are likely to respond to a fluid challenge as well as the degree to which the SV (and CO) is likely to increase. With remarkable consistency, these studies reported a diagnostic threshold of between 11% and 13% with a very high sensitivity and specificity. The diagnostic accuracy of these variables (receiver operating characteristic of 0.84–0.94 with a diagnostic odds ratio of 59.86 and 27.34) is better than any variable reported to date (3), and significantly better than the CVP, GEDVI, and LVEDAI reported in this study. The diagnostic accuracy (AUC) of the PPV was significantly greater ($p < .001$) than that for either the SPV or the SVV. The reason for this finding is not entirely clear from our study. However, it may be related to the fact that a number of assumptions are made in the calculation of the SV (by pulse contour analysis) and that most of the studies that measured the SPV did this manually; these factors may lead to errors in the calculation of both the SVV and SPV. The PPV is, however, usually measured directly from the arterial pressure tracing, using advanced digital software. These data suggest that the PPV may be the preferred arterial waveform-derived variable for hemodynamic monitoring.

In normal physiologic conditions, both ventricles operate on the ascending portion of the Frank-Starling curve (60). This mechanism provides a functional re-

Table 3. Pooled performance estimates (with 95% confidence intervals) from the studies where the true/false positive/negative results could be calculated

Parameter	PPV (n = 14)	SVV (n = 5)
ROC area	0.94 (0.92–0.96)	0.84 (0.81–0.87)
Sensitivity	0.89 (0.82–0.94)	0.82 (0.75–0.98)
Specificity	0.88 (0.81–0.92)	0.86 (0.77–0.92)
Positive likelihood ratio	7.26 (4.46–11.80)	5.77 (3.43–9.72)
Negative likelihood ratio	0.12 (0.07–0.21)	0.21 (0.15–0.30)
Diagnostic odds ratio	59.86 (23.88–150.05)	27.34 (13.46–55.53)

PPV, pulse pressure variation; SVV, stroke volume variation; ROC, receiver operating characteristic.

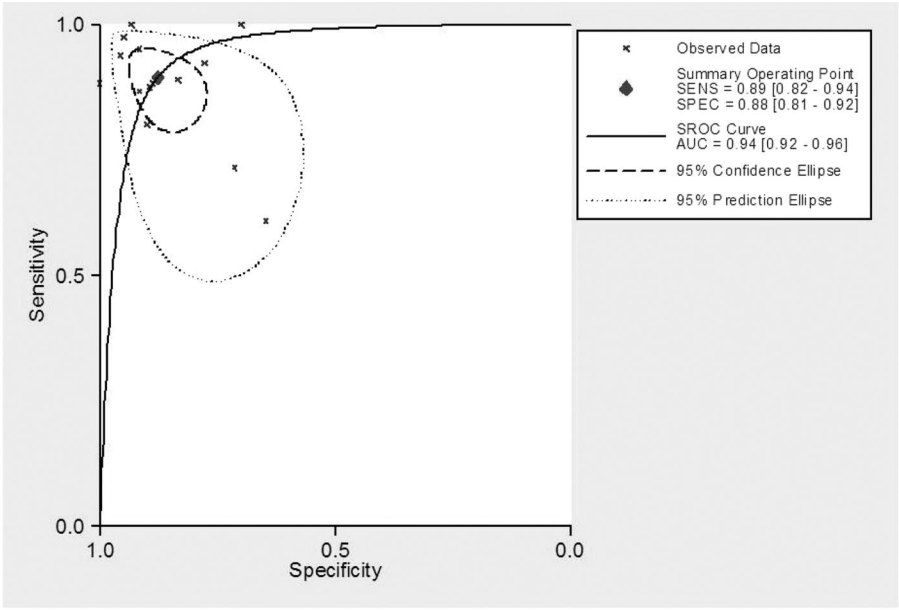

Figure 1. Standardized receiver operating characteristic (*SROC*) curve with confidence and predictive ellipses for the 14 studies that allowed abstraction of the true/false positive/negative values for the ability of the pulse pressure variation to predict volume responsiveness. *SENS*, sensitivity; *SPEC*, specificity; *AUC*, area under the curve.

serve (preload reserve) to the heart in situations of acute stress. In normal individuals, an increase in preload (volume loading) is associated with a significant increase in SV (61). In contrast, analysis of the literature indicated that, in critically ill patients, only about 50% of patients respond to volume expansion (1). This finding suggests the need for predictive factors of volume expansion efficacy to select patients who could benefit from volume expansion and avoid ineffective fluid therapy in "nonresponders" in whom inotropic and/or vasopressor support should preferentially be used (62). Previous studies have demonstrated that the CVP (right atrial pressure), pulmonary artery occlusion pressure, and right ventricular end-diastolic volume index obtained from hemodynamic monitoring do not predict volume responsiveness (1, 2, 62).

The principles underlying the SPV, PPV, and SVV are based on simple physiology. Intermittent positive-pressure ventilation induces cyclic changes in the loading conditions of the left and right ventricles. Mechanical insufflation decreases preload and increases afterload of the right ventricle (RV). The RV preload reduction is due to the decrease in the venous return pressure gradient that is related to the inspiratory increase in pleural pressure (62). The increase in RV afterload is related to the inspiratory increase in transpulmonary pressure (62). The reduction in RV preload and increase in RV afterload both lead to a decrease in RV SV, which is at a minimum at the end of the inspiratory period. The inspiratory reduction in RV ejection leads to a decrease in left ventricle (LV) filling after a phase lag of two or three heart beats because of the long blood pulmonary transit time (62). Thus, the LV preload reduction may induce a decrease in LV SV, which is at its minimum during the expiratory period. The cyclic changes in RV and LV SV are greater when the ventricles operate on the steep rather than the flat portion of the Frank-Starling curve. Therefore, the magnitude of the respiratory change in LV SV is an indicator of biventricular preload dependence (62).

The respiratory variation in vena caval diameter (63, 64) and SV (65) as measured by echocardiography have been used to predict fluid responsiveness; however, they do not perform as well as PPV/SVV and are not conducive to minute-to-minute monitoring. In addition, although the GEDVI and intrathoracic blood volume as determined by transpulmonary thermodilution adequately reflect preload status, they seem to be unreliable predictors of volume responsiveness (36, 42, 45). Even assessment of LVEDI by echocardiography is not necessarily a good predictor of fluid responsiveness (7, 31, 39, 42, 47, 52, 56). These data suggest that currently the SPV, PPV, and SVV are the most accurate predictors of volume responsiveness in critically ill patients.

Reuter et al and Preisman et al assessed the predictive accuracy of PPV/SVV after cardiac surgery in patients with reduced cardiac function (low ejection fraction) compared with patients with normal ventricular function (37, 43). Both these studies demonstrated that the performance of PPV/SVV was similar in patients with normal and impaired ventricular function. The appeal of using the PPV/SVV as a marker of volume responsiveness is that it dynamically predicts an individual patient's position on the Starling curve and this is independent of ventricular function and compliance as well as pulmonary pressures and mechanics. Furthermore, as demonstrated in our meta-analysis, there is a close relationship between the degree of respiratory variation of the SV/pulse pressure and the increase in SV. Therefore, the PPV/SVV can be used to guide decisions regarding volume resuscitation, monitor the effects of fluid therapy, and at the same time gauge the "degree of fullness" of the intravascular compartment.

It should be appreciated that both arrhythmias and spontaneous breathing activity will lead to misinterpretations of the respiratory variations in systolic pressure, SV, and pulse pressure. Furthermore, in all the studies included in our meta-analysis, patients were well sedated during the evaluation of these dynamic indices. Perner and Faber demonstrated

that SVV did not predict the response to a fluid challenge in patients who had septic shock and received pressure-support ventilation (24). Furthermore, for any specific preload condition, the PPV/SVV will vary according to the tidal volume. Reuter and colleagues demonstrated a linear relationship between tidal volume and SVV (25). De Backer and colleagues evaluated the influence of tidal volume on the ability of the PPV to predict fluid responsiveness (44). These authors reported that the PPV was a reliable predictor of fluid responsiveness only when the tidal volume was at least 8 mL/kg. This finding was confirmed in an animal model (anesthetized pigs) where SVV was not sensitive to acute changes in preload during ventilation with a tidal volume of 5 mL/kg (66). Huang and colleagues recently reported the use of PPV in predicting fluid responsiveness in patients with acute respiratory distress syndrome (67). These authors used pressure-controlled ventilation with a mean tidal volume of 6.4 mL/kg; the low tidal volume used in this study largely explains the inconsistencies in the results of this study. Most of the studies included in this meta-analysis used a tidal volume of between 8 and 10 mL/kg. For accuracy, reproducibility, and consistency, we therefore suggest that the tidal volume should be between 8 and 10 mL/kg ideal body weight before and after a fluid challenge.

Although the PPV/SVV is a clinically useful tool to predict fluid responsiveness (recruitable preload), it provides no information concerning ventricular function. A given preload can be associated with preload dependence in a normal heart or with preload independence in a failing heart. We therefore use bedside transthoracic echocardiography to assess global left and right ventricular function in all hemodynamically unstable ICU patients (68). We believe that the combination of PPV/SVV and bedside transthoracic echocardiography are the preferred tools to evaluate cardiac function in critically ill patients. Furthermore, the dynamic changes in aortic flow velocity and SV, as assessed by Doppler echocardiography, supplements the information obtained by dynamic changes in the arterial waveform-derived variables (7, 65).

In conclusion, by virtue of its simplicity, accuracy, and availability as a continuous monitoring tool, dynamic monitoring of pulse pressure/SV would seem to be the ideal method for the titration of fluid resuscitation in mechanically ventilated critically ill patients. However, additional studies are required to confirm these findings in general and in complex ICU patients. Furthermore, as no clinical parameter should be evaluated in isolation, the PPV/SVV should be interpreted in the context of the patients' diagnoses and comorbidities, together with a careful clinical evaluation, and appraisal of other parameters including the patients' hemodynamic profile, echocardiogram, chest radiograph, Pa_{O_2}/F_{IO_2}, urine output, renal function, and fluid balance.

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