Comparison of stroke volume variation with pulse pressure variation as a diagnostic indicator of fluid responsiveness in mechanically ventilated critically ill patients

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ABSTRACT

الأهداف: مقارنة دقة التشخيص لاختلاف حجم المخ وضغط النبض في الدراسات التي تدرس هذه الصفات في نفس مجتمع المرضى.

الطريقة: أجري بحث بمكتبة قواعد البيانات ومحرك قوقل. تم اختبار خصائص منحنيات المشغل المتلقي وتلخيصها وتخطيط هذا المنحنى.

النتائج: أجريت الدراسة خلال الفترة من يناير حتى يوليو 2013م. من خلال 19 دراسة نشرت خلال الفترة من 2005م و 2013م ظهرت درجة دقة تشخيص عالية في كلا من SVV و PPV في توقع استجابة السائل، والحساسية والخصوصية في كلا من المؤشرات المراقبة أعلاه، 80% في المجموعة المتنوعة المكونة من أكثر من 700 مريض، 55% مريض استجاب لتطور السائلي. كانت القيم التالية جنباً إلى جنب مع فترة الثقة 95%: SVV – حساسية (59–93%) 82، والنوعية (62–95%) 84، والحساسية 84 (62–95%)، والنوعية (58–94%) 83. أما المنطقة أسفل المنحنى فبلغت SVV (0.79–0.89) 0.84 و (0.84–0.92) PPV 0.88.

خاتمة: أظهر كلا من SVV و PPV درجة عالية من دقة التشخيص في تنبؤ نجاح أو فشل تطور السائل في المرضى الذين يعنون من عدم انتظام الدورة الدموية.

Objectives: To compare the diagnostic accuracy of stroke volume variation (SVV) and pulse pressure variation (PPV) in studies that examined both parameters in the same patient population.

Methods: Literature search was conducted in PubMed, EMBASE, CINAHL, and Google Scholar. Receiver operator characteristic (ROC) curves were examined, and summary ROC curves were plotted.

Results: The study was conducted from January to July 2013 in The Second Affiliated Hospital of Fujian Medical University, Quanzhou, Fujian, China. The meta-analysis of 19 studies published during the years 2005 and 2013 revealed a high degree of diagnostic accuracy of both SVV and PPV in predicting fluid responsiveness. The sensitivity and specificity of both the parameters were observed above 80% in a heterogeneous group of over 850 patients of which 55% responded to fluid challenge. The following values along with 95% confidence interval were noticed: SVV - sensitivity 82 (59-93%) and specificity 84 (62-95%), PPV - sensitivity 84 (62-95%) and specificity 83 (58-94%). Area under the curve values obtained in the pooled analysis were 0.84 (0.79-0.89) for SVV, and 0.88 (0.84-0.92) for PPV.

Conclusions: Both SVV and PPV exhibit a high degree of diagnostic accuracy in predicting the success or failure of a fluid challenge in hemodynamically unstable critically ill patients under controlled mechanical ventilation.

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Optimization in monitoring of patient's hemodynamic, ventilatory, thermoregulatory, nutritive, and metabolic indicators plays a pivotal role in disease management and the survival of the critically ill patients. Hemodynamic monitoring aims at maintenance of optimized tissue oxygenation and nutrition to avoid hypoxia and organ failure.[1] In critical situations, prediction of fluid responsiveness in hemodynamically unstable patients remains a major issue to guess whether the volume expansion will increase patient's cardiac output (CO) or not, so that

hypovolemic conditions or overloading can be avoided. Functional hemodynamic monitoring is the study of dynamic interactions of hemodynamic indicators upon a definable perturbation.[2]

Clinical practice and research has identified both static and dynamic measures of fluid responsiveness in volume expansion management. Static hemodynamic indicators such as central venous pressure, left ventricular end-diastolic volume, right ventricular end-diastolic volume, pulmonary artery occlusion pressure, and so forth, are found to have less diagnostic value in discriminating responders from non-responders to a fluid challenge as compared with dynamic parameters such as the stroke volume variation (SVV) and pulse pressure variation (PPV), both of which measure positive mechanical pressure ventilation based parameters at the heart and lung interface involving respiratory-induced changes in arterial pulse pressure in mechanically ventilated patients.[3] If a patient exhibits wider range in stroke volume or its derived parameters then it can be reliably predicted that a fluid challenge will be effective and safe.

Based on the heart-lung interactions, SVV is a functional hemodynamic variable, which manifests ventilation-induced changes in left ventricular preload that result in oscillations in left ventricular stroke volume and arterial pressure. Oscillations in intrathoracic pressure cause a reduced venous return and a decreased stroke volume following inspiration, and then a restoration of preload and stroke volume after expiration. The inspiratory decrease in stroke volume lessens left ventricular preload after a phase lag of 2-3 heart beats because of the long transit time in the lungs.[4,5] These changes are theoretically more pronounced in hypovolemia, as in such a condition the left ventricular function conforms to the ascending part of the Frank-Starling curve, which depicts the relationship between ventricular preload and stroke volume. For the accurate measurement of these indicators, the patient must be on controlled mechanical ventilation with a tidal volume of 8-15 ml/kg.[6,7]

At present, very few studies on goal-directed therapy guided by SVV/PPV are available in the literature.[8,9] However, a number of research studies are

published to report the diagnostic accuracy of SVV and PPV.[10-31] Most researchers studied these predictors in observational studies of small populations of patients; this provides impetus for a meta-analysis of these indices to evaluate them systematically as there is no study to meta-analyze the diagnostic accuracy of SVV and PPV in the same patient population. This study was designed to systematically review the diagnostic accuracy data generated from studies that measured both SVV and PPV in the same patient population by meta-analyzing the last 10 year data involving measurement of SVV and PPV in various conditions in mechanically ventilated patients.

Methods. *Literature search.* A comprehensive literature search was made in several electronic databases including MEDLINE, EMBASE, SCOPUS, CINAHL, and Google Scholar for research publications, which appeared in medical journals during the period (2003 to 2013). The MeSH terms used were stroke volume variation, SVV, pulse pressure variation, PPV, fluid responsiveness, diagnostic accuracy, prediction, fluid responders, fluid non-responders, hemodynamic, and response cutoffs with most logical combinations. The literature research, identification, and selection of potential studies, evaluation of relevant data, and exploration of corroborations were carried by 2 reviewers independently. Afterwards both the researchers mutually decided on the inclusion and exclusion of studies for meta-analysis by following respective criteria. The study was conducted from January to July 2013 in The Second Affiliated Hospital of Fujian Medical University, Quanzhou, Fujian, China.

Inclusion and exclusion criteria. Inclusion criteria of this meta-analysis were research studies that: a) measured both SVV and PPV simultaneously regardless of medical condition or cut-off values used, b) mentioned area under curve (AUC), receiver operator characteristics (ROC), sensitivity and specificity data for both SVV and PPV, and c) measured both SVV and PPV in the same patient population. Exclusion criteria were: a) studies which reported either SVV or PPV values but not both, b) studies which mentioned PPV/SVV ratio values (Ea_{dyn}) rather than individual SVV and PPV values, c) studies which evaluated SVV and PPV in infants/neonates.

Quality assessment. The QUADAS tool was used to assess the quality of included studies. This 14-item questionnaire assesses the quality of a research paper reporting diagnostic accuracy under one of 3 possible answers (yes, no, unclear) for each item. For

user's guidance, every item has been discussed by the developers of the tool.[32] This tool does not attempt to yield quality scores.

Data extraction and analysis. The researchers also independently extracted data from selected studies and stored them in Excel files. Data were collected regarding the patients' demographic, pathological, and clinical features, response to a fluid challenge, ROC (sensitivity and specificity), AUC values, correlation coefficients with other indicators, and relevant parameters, cutoffs for evaluation of fluid responsiveness, and measuring device(s).

Statistical analysis. For the statistical analyses, a 2x2 contingency table (true positives, false positives, false negatives, and true negatives) was first reconstructed by using sensitivity and specificity data provided by the authors of individual studies and applying it to the respective group total. Later, these reconstructed data were used to compute sensitivity/specificity with 95% confidence intervals (CI), diagnostic odds ratio (DOR), positive likelihood ratio, and negative likelihood ratio. Pooled DOR values of SVV and PPV were compared via t-test. For plotting summary ROC (SROC) curve for both the parameters, the Data and Analyses module of RevMan version 5.2 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark) was used for the diagnostic accuracy meta-analysis. For this, logits of the true positive rate and false positive rate are first calculated and then a scatter plot (linear) is created to generate values of the slope and intercept and then true positive rate and false positive rate values are re-transformed.[33] Weights of individual studies for the analysis are determined by the inverse variance of the log of DOR with a 95% CI, which unifies sensitivity and specificity values and then a summary was achieved to represent the accuracy of the test against a reference standard. For the assessment of publication bias, a visual examination of the funnel plots was made. For the evaluation of between study heterogeneity, the graphical method (forest plots) and statistical method (Q statistics) were used.

Results. The search recognized 19 studies published during the last 10 years, which examined the diagnostic accuracy of SVV and PPV simultaneously.[13-31] A flowchart of the search process and selection of studies is presented in **Figure 1**. Generally, the quality of these research studies as assessed by the QUADAS was good when the tool items were assessed by keeping in view the focus and inclusion criteria of this review. With regards to spectrum bias, selection criteria clarity, appropriation

of reference standard, description of index test from the point of replication, and the interpretation of index test in the light of standard reference, almost all studies conformed to good quality standards. However, the majority of studies did not explain withdrawals. Characteristics of the included studies are presented in **Table 1**. The overall population size was 865 patients suffering from circulatory failure under several conditions (**Figure 2**). In these studies, volume expansion was carried out with 250-500 ml fluid in the form of solutions of saline albumin / hydroxyethyl starch / dextran / synthetic colloid in varied concentrations. which were loaded in 5-30 minutes. The tidal volume of the patients was 8-10 ml/kg, except for one study[28] in which the value given was 6.5 (4.9-8.7) ml/kg.

The computerized automated monitoring systems utilized in these studies to monitor SVV and PPV included FloTrac/vigileo, PiCCO (pulse counter cardiac output), PiCCOplus, LiDCO (lithium diluted cardiac output), Vigilance, PRAM (pressure recording analytical method), and TEE (transesophageal echocardiography). Some studies also used more than one device to study a variable or both (SVV/PPV), and some studies also examined changing body position from supine to prone or Trendelenburg, passive leg raising, and 30° head up/down. Cardiac end point as indicators of fluid responsiveness against which SVV and PPV were evaluated were cardiac output (CO), cardiac index (CI), stroke volume (SV), and stroke volume index
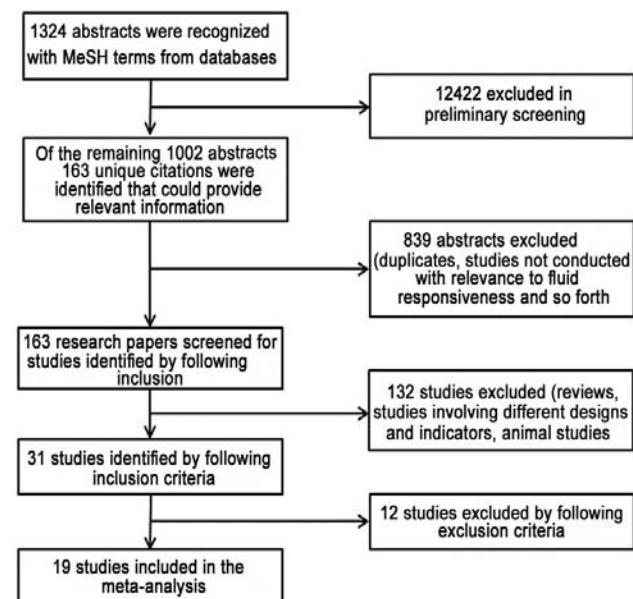

Figure 1 - Flow chart of the literature search process and study selection.

Table 1 - Characteristics of the included studies.

Study	Patients/conditions	Fluid challenge/body position	Tidal volume	Device used	Hemodynamic end point	SVV/PPV thresholds
Biais et al 2008[13]	40/liver transplantation	20 ml 4% albumin X BMI/supine	8-10 ml/kg	FloTrac/Vigileo	≥15% CO	>10%/>12%
Biais et al 2010[14]	30/scoliosis surgery	500 ml of 6% HES/supine, prone	≥8 ml/kg	FloTrac/Vigileo	≥15% CO	14%/15%
Biais et al 2012[15]	35/polytraumatism, septic shock, vascular surgery,	500 ml of saline/NA	8-9 ml/kg	PRAM	≥15% SV	12.6%/10%
Broch et al 2011[16]	81/CABG	NA/PLR, supine	8-9 ml/kg	PiCCOplus	SVI	>12%/>11%
Broch et al 2012[17]	92/CABG	NA/PLR, supine	8-9 ml/kg	PiCCOplus	>15% SVI	>11%/>11%
Cannenson et al 2009[18]	25/CABG	500 mL hetastarch/NA	8-10 ml/kg	FloTrac/Vigileo	≥15% CI	>10%/>10%
Cecconi et al 2012[19]	31/ICU surgical patients	250 mL colloid over 5 minutes/NA	8 ml/kg	LiDCO	≥15% SV	>12.5%/>13%
Derichard et al 2009[20]	11/gastrointestinal or vascular surgery	200-500 mL/NA	8-10 ml/kg	FloTrac/Vigileo	>10% SVI	>12%/>13%
Hofer et al 2005[21]	40/CABG	6% HES (10 mL/kg bw) for 20 minutes/NA	10 ml/kg	PiCCO plus	>25% SVI	>12.5%/>15.4%
Hofer et al 2008[22]	40/CABG	NA/30° head-up to 30° head-down	8-10 ml/kg	PiCCO plus and FloTrac	>25% SV	12.1%/13. 5%
Khwannimit and Bhurayanontachai, 2012[23]	42/septic shock	500 ml of 6% HES in 30 minutes/NA	≥8 ml/kg	FloTrac/Vigileo	≥15% SVI	10%/12%
Kim et al 2010[24]	52/liver transplantation	Preload parameter studied/NA	8-10 ml/kg	Vigilance	≥20% CO	10%/12%
Liu et al 2013[25]	20/intra-abdominal hypertension	6% HES (0.4 mL/kg/minutes in 15-20 minutes	8-10 ml/kg	FloTrac/Vigileo	>10% SV	10.5%/10.5%
Monge Garcia et al 2009[26]	38/general ICU	500 ml synthetic colloid/supine	8-10 ml/kg	FloTrac/Vigileo	29% SVI	>11%/>10%
Monnet et al 2012[27]	47/septic shock, drug poisoning, hypovolemia	500 ml saline in 30 minutes/supine, PLR	8.5±2.1 ml/kg	PiCCO	≥15% CI	14%/11%
Monnet et al 2013[28]	42/norepinephrine treated critically ill patients	500 ml saline in 30 minutes/NA	<8 ml/kg	PiCCO	≥15% CI	10%/11%
Nordstrom et al 2013[29]	20/colorectal surgery	200 ml of 6% HES/dextran 60 solutions	6.5 (4.9-8.7) ml/kg	LiDCO/TEE	≥10% SV	8.5%/8.5%
Preisman et al 2005[30]	18/CABG	250 ml of colloid solution in 5-7 minutes	8-12 ml/kg	TEE, PiCCO,	>15% SV	11.5%/9.4%
Wacharasint et al 2012[31]	20/septic shock					11%/12%

BMI - body mass index, CABG - coronary artery bypass grafting, CI - cardiac index, CO - cardiac output, HES - hydroxyethyl starch, ICU - intensive care unit, LiDCO - lithium dilution cardiac output, PiCCO - pulse counter cardiac output, PLR - passive leg raising, PPV - pulse pressure variation, PRAM - pressure recording analytical method, SV - stroke volume, SVI - stroke volume index, SVV - strike volume variation, TEE - transesophageal echocardiography
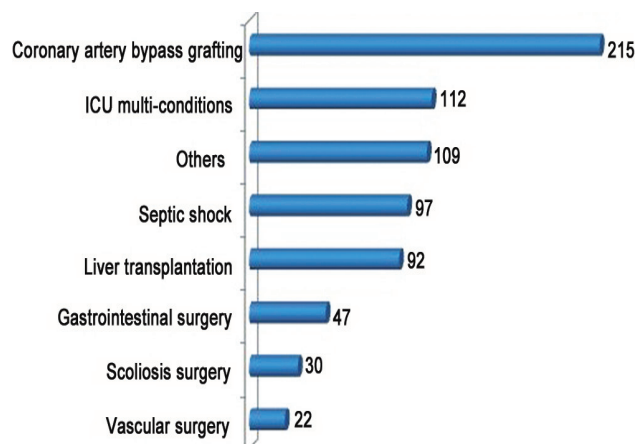
Figure 2 - Medical conditions of patients in the included studies. ICU - intensive care unit

(SVI). Threshold values used to discriminate between responders and non-responders to a fluid challenge were 8.5-14% for the SVV, and 8.5-15.4% for the PPV.

This meta-analysis has resulted in the generation of very similar summary ROC curves for both SVV and PPV with an area under the ROC curve represented above 80% sensitivity and specificity (**Figure 3**) where PPV attained a slightly superior position indicative of its better performance in predicting fluid responsiveness. There was no significant difference between SVV and PPV when pooled values of DOR were compared (*p*=0.44). Overall DOR values along with 95% CI for SVV and PPV were 64 (22-106) and 93 (33-153). Between-study heterogeneity was low (Cochran's Q

Figure 3 - Summary receiver operator curve (SROC) curves for stroke volume variation (SVV) and pulse pressure variation (PPV) depicting a great similarity between the diagnostic accuracy of these indicators of fluid responsiveness (*p*=0.44; diagnostic odds ratio SVV versus PPV). Dotted lines connecting a pair represent a single study outcome.

A

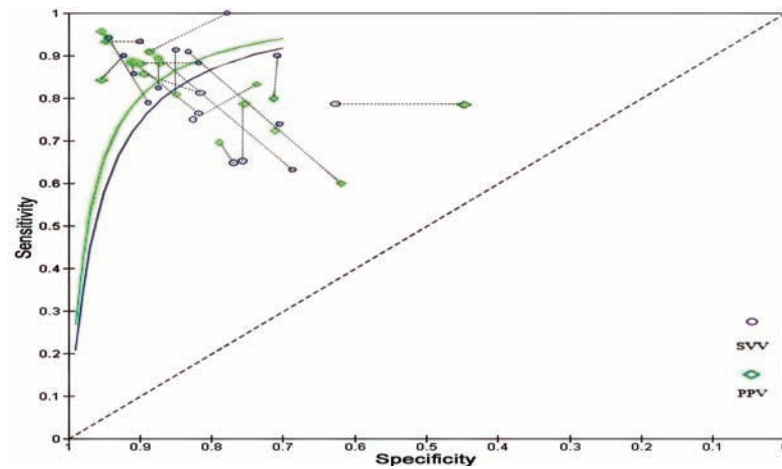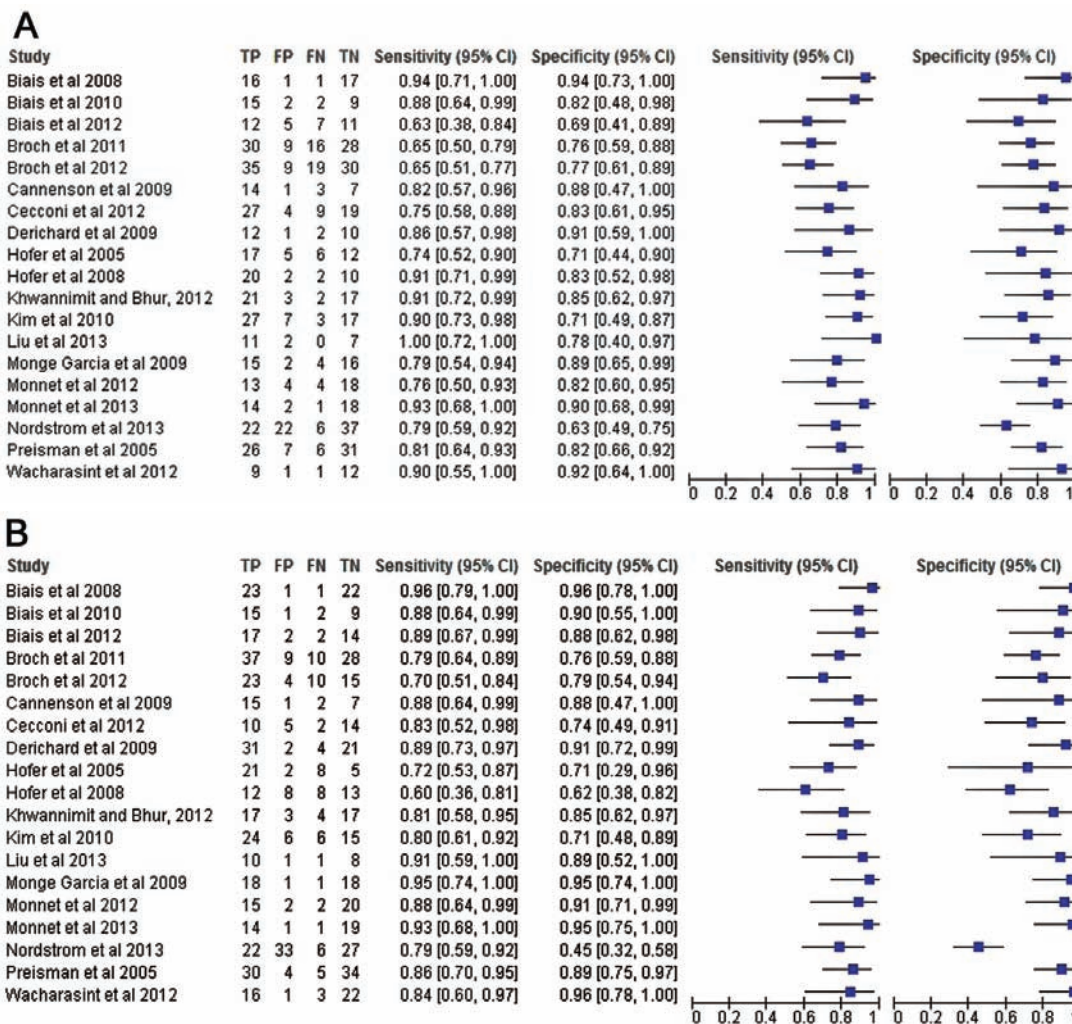| Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Biais et al 2008	16	1	1	17	0.94 [0.71, 1.00]	0.94 [0.73, 1.00]
Biais et al 2010	15	2	2	9	0.88 [0.64, 0.99]	0.82 [0.48, 0.98]
Biais et al 2012	12	5	7	11	0.63 [0.38, 0.84]	0.69 [0.41, 0.89]
Broch et al 2011	30	9	16	28	0.65 [0.50, 0.79]	0.76 [0.59, 0.88]
Broch et al 2012	35	9	19	30	0.65 [0.51, 0.77]	0.77 [0.61, 0.89]
Cannenson et al 2009	14	1	3	7	0.82 [0.57, 0.96]	0.88 [0.47, 1.00]
Cecconi et al 2012	27	4	9	19	0.75 [0.58, 0.88]	0.83 [0.61, 0.95]
Derichard et al 2009	12	1	2	10	0.86 [0.57, 0.98]	0.91 [0.59, 1.00]
Hofer et al 2005	17	5	6	12	0.74 [0.52, 0.90]	0.71 [0.44, 0.90]
Hofer et al 2008	20	2	2	10	0.91 [0.71, 0.99]	0.83 [0.52, 0.98]
Khwannimit and Bhur, 2012	21	3	2	17	0.91 [0.72, 0.99]	0.85 [0.62, 0.97]
Kim et al 2010	27	7	3	17	0.90 [0.73, 0.98]	0.71 [0.49, 0.87]
Liu et al 2013	11	2	0	7	1.00 [0.72, 1.00]	0.78 [0.40, 0.97]
Monge Garcia et al 2009	15	2	4	16	0.79 [0.54, 0.94]	0.89 [0.65, 0.99]
Monnet et al 2012	13	4	4	18	0.76 [0.50, 0.93]	0.82 [0.60, 0.95]
Monnet et al 2013	14	2	1	18	0.93 [0.68, 1.00]	0.90 [0.68, 0.99]
Nordstrom et al 2013	22	22	6	37	0.79 [0.59, 0.92]	0.63 [0.49, 0.75]
Preisman et al 2005	26	7	6	31	0.81 [0.64, 0.93]	0.82 [0.66, 0.92]
Wacharasint et al 2012	9	1	1	12	0.90 [0.55, 1.00]	0.92 [0.64, 1.00]

B

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Biais et al 2008	23	1	1	22	0.96 [0.79, 1.00]	0.96 [0.78, 1.00]
Biais et al 2010	15	1	2	9	0.88 [0.64, 0.99]	0.90 [0.55, 1.00]
Biais et al 2012	17	2	2	14	0.89 [0.67, 0.99]	0.88 [0.62, 0.98]
Broch et al 2011	37	9	10	28	0.79 [0.64, 0.89]	0.76 [0.59, 0.88]
Broch et al 2012	23	4	10	15	0.70 [0.51, 0.84]	0.79 [0.54, 0.94]
Cannenson et al 2009	15	1	2	7	0.88 [0.64, 0.99]	0.88 [0.47, 1.00]
Cecconi et al 2012	10	5	2	14	0.83 [0.52, 0.98]	0.74 [0.49, 0.91]
Derichard et al 2009	31	2	4	21	0.89 [0.73, 0.97]	0.91 [0.72, 0.99]
Hofer et al 2005	21	2	8	5	0.72 [0.53, 0.87]	0.71 [0.29, 0.96]
Hofer et al 2008	12	8	8	13	0.60 [0.36, 0.81]	0.62 [0.38, 0.82]
Khwannimit and Bhur, 2012	17	3	4	17	0.81 [0.58, 0.95]	0.85 [0.62, 0.97]
Kim et al 2010	24	6	6	15	0.80 [0.61, 0.92]	0.71 [0.48, 0.89]
Liu et al 2013	10	1	1	8	0.91 [0.59, 1.00]	0.89 [0.52, 1.00]
Monge Garcia et al 2009	18	1	1	18	0.95 [0.74, 1.00]	0.95 [0.74, 1.00]
Monnet et al 2012	15	2	2	20	0.88 [0.64, 0.99]	0.91 [0.71, 0.99]
Monnet et al 2013	14	1	1	19	0.93 [0.68, 1.00]	0.95 [0.75, 1.00]
Nordstrom et al 2013	22	33	6	27	0.79 [0.59, 0.92]	0.45 [0.32, 0.58]
Preisman et al 2005	30	4	5	34	0.86 [0.70, 0.95]	0.89 [0.75, 0.97]
Wacharasint et al 2012	16	1	3	22	0.84 [0.60, 0.97]	0.96 [0.78, 1.00]

Figure 4 - Forest graphs representing the receiver operator curve values of: **A**) stroke volume variation; and **B**) pulse pressure variation of individual studies. TP - true positive, FP - false positive, FN - false negative, TN - true negative

= 10.5) enough to consider the study population as statistically homogeneous for applying appropriate AUC statistics.

The meta-analysis yielded the following values along with 95% confidence intervals: SVV - sensitivity 82 (59-93%), and specificity 84 (62-95%), PPV - sensitivity 84 (62-95%), and specificity 83 (58-94%). The AUC values obtained in the pooled analysis were 0.84 (0.79-0.89) for SVV, and 0.88 (0.84-0.92) for PPV. The positive likelihood ratio and negative likelihood ratios were 5.83 and 0.22 for SVV, and 8.43 and 0.21 for the PPV. Highest ROC values along with 95% CI of SVV in predicting fluid responsiveness have been noted as 94% (71-99%) sensitivity, and 94% (73-99%) specificity,[13] while lowest values are recorded as 63% (38-84%) sensitivity, and 69% (41-89%) specificity.[15] For PPV, the highest ROC values for predicting fluid responsiveness were 96% (79-99%) sensitivity, and 96% (78-99%) specificity,[13] while the lowest were 60% (38-82%) sensitivity, and 62% (36-81%) specificity[22] (**Figure** 4).

Discussion. In almost all clinical situations where circulatory failure is evident, volume expansion becomes vital, but when the excessive fluid infusion leads to peripheral/pulmonary edema, it causes impairment of vascular perfusion and oxygen delivery. To cope with such conditions, fluid volume expansion needs to be optimized by monitoring predictors of fluid responsiveness. Fluid responsiveness is defined as an increase in cardiac output by at least a specified degree following a measured bolus of a particular fluid in patients to be identified as responders, whereas other means to increase the cardiac output will be needed in non-responding patients, for example ≥15% in cardiac output in response to a 500 ml bolus fluid challenge.[2] In hemodynamically unstable patients, volume expansion is a prerequisite but the evidence suggests that only around 50% of such critically ill patients respond positively to a fluid challenge.[34] In the present analysis too, the percentage of responders has been observed at 55% and non-responders at 45%.

This meta-analysis has provided supporting evidence in favor of SVV and PPV for the prediction of fluid responsiveness in volume expansion by virtue of a high area under the ROC curve for both the variables observed herein. In a clinically heterogeneous patient population, achievement of very similar SROC curves for both the parameters with over 80% sensitivity and specificity suggests that these can be reliably utilized in clinical situations according to the circumstances.

Pooled DOR for SVV and PPV were 64 and 93 in this meta-analysis. The DOR combines the measures of sensitivity and specificity and accurately judges the performance of a test. For this, DOR not only becomes important for AUC analysis but also in comparative analyses. The intercept of ROC curve is determined by the logarithm of DOR of individual studies, and the slope determines its relationship with the positivity threshold.[35] No statistically significant difference (*p*=0.44) existed between SVV and PPV in this patient population when pooled DOR of both the variables were compared. A relative superiority of PPV over SVV as noted in the SROC curve in this study is compatible with a previous combination of these 2 indicators by Marik[34] who observed a significantly higher AUC value for PPV. These authors included studies on the basis of the correlation coefficient and ROC values between systolic pressure volume (SPV), PPV, or SVV. In this meta-analysis, we have considered only those studies that examined SVV and PPV in the same patient population.

Generally patients with arrhythmia, heart valve/ ventricular dysfunctions, hypoxemia, major lung dysfunctions, severe peripheral obstructive disease, severe arterial occlusion disease, pulmonary hypertension/ edema, aortic aneurysm, and spontaneous breathing were not included in the contributing studies of this meta-analysis. For SVV/PPV utilization as an indicator of fluid responsiveness, arrhythmia, right heart failure, patients' spontaneous breathing, and too small or large tidal volumes are among the most important contraindications.[4,6]

In hypovolemic conditions, left ventricular function is depicted by the ascending part of the Frank-Starling curve, and thus higher SVV can be observed. However, the slope of the Frank-Starling curve also depends on many factors including the ventricular contractility and impaired ventricular contractility results in increases in stroke volume due to an increase in preload.[36] Furthermore, the prediction of volume responsiveness by SVV/PPV, besides cardiac filling status, also depends on the changes in intrathoracic pressure in association with tidal volume, and accurate prediction by the SVV is associated with tidal volumes of 10-15 ml/kg.[5,6] Larger tidal volumes reduce compliance of the chest wall and air trapping may lead to exaggerated SVV values.[13]

Regardless of the influencing factors, better patient outcomes have been reported after monitoring of fluid responsiveness in high-risk surgery patients in terms of postoperative outcomes and length of hospital stay.[9] The SVV and PPV can be valuable in patients under

controlled mechanical ventilation because varying tidal volume alters both SVV and PPV, and therefore deeply sedated or apneic patients with regular cardiac rhythm are more likely subjects to benefit from volume expansion interventions using these predictors. However, for spontaneously breathing patients, passive leg raising followed by use of SVV measurement is proposed to be an effective technique to predict response.[37]

This study is an important step towards the reduction of the methodological heterogeneity in assessing the strengths of dynamic indicators of fluid responsiveness. In future, further refinements of the results achieved in this study can be possible upon delimiting the study population to specific devices and techniques of SVV/PPV measurement. The same can also be useful if delimitation is based on the clinical conditions of the patients, as the present study represents a heterogeneous group of patients.

Among the foremost limitations of this study, utilization of different devices in measuring SVV and PPV in the individual studies may also have an impact on overall results as considerable data pertaining to comparisons of various devices is not yet available. From the point of view of precision in statistical judgment, population size of individual studies and overall population of this meta-analysis should also be considered as a precision limiting factor in the overall outcome. Several sources of data pertaining to SVV and PPV in predicting fluid responsiveness in the excluded as well as in a few included studies could not be utilized owing to the inclusion criteria of this meta-analysis.

In conclusion, the present meta-analysis strengthens the supporting evidence of the high diagnostic accuracy of SVV and PPV in predicting fluid responsiveness in critically ill mechanically ventilated patients by achieving over 80% sensitivity and specificity for both these dynamic indicators of fluid responsiveness. These indicators are based on heart-lung interactions during positive mechanical pressure ventilation and can be efficiently analyzed by modern electronic devices.

References

1. Kipnis E, Ramsingh D, Bhargava M, Dincer E, Cannesson M, Broccard A, et al. Monitoring in the intensive care. *Crit Care Res Pract* 2012; 2012: 473507.
2. Garcia X, Pinsky MR. Clinical applicability of functional hemodynamic monitoring. *Annals Intensive Care* 2011; 1: 35.
3. Auler JO Jr, Galas FR, Sundin MR, Hajjar LA. Arterial pulse pressure variation predicting fluid responsiveness in critically ill patients. *Shock* 2008; 30: 18-22.
4. Hofer CK, Cannesson M. Monitoring fluid responsiveness. *Acta Anaesthesiol Taiwan* 2011; 49: 59-65.
5. Benington S, Ferris P, Nirmalan M. Emerging trends in minimally invasive haemodynamic monitoring and optimization of fluid therapy. *Eur J Anaesthesiol* 2009; 26: 893-905.
6. Rex S, Brose S, Metzelder S, Huneke R, Schälte G, Autschbach R, et al. Prediction of fluid responsiveness in patients during cardiac surgery. *Br J Anaesth* 2004; 93: 782-788.
7. Cannesson M, Aboy M, Hofer CK, Rehman M. Pulse pressure variation: Where are we today? *J Clin Monit Comput* 2010; 25: 45-56.
8. Haas S, Eichhorn V, Hasbach T, Trepte C, Kutup A, Goetz AE, et al. Goal-directed fluid therapy using stroke volume variation does not result in pulmonary fluid overload in thoracic surgery requiring one-lung ventilation. *Crit Care Res Pract* 2012; 2012: 687018.
9. Lopes RL, Oliveira MA, Pereira VOS, Lemos IP, Auler JO Jr, Michard F. Goal directed fluid management based on pulse pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. *Crit Care* 2007; 11: R100.
10. Machare-Delgado E, Decaro M, Marik PE. Inferior vena cava variation compared to pulse contour analysis as predictors of fluid responsiveness: a prospective cohort study. *J Intensive Care Med* 2011; 26: 116-124.
11. Suehiro K, Okutani R. Stroke volume variation as a predictor of fluid responsiveness in patients undergoing one-lung ventilation. *J Cardiothorac Vasc Anesth* 2010; 24: 772-775.
12. Hofer CK, Muller SM, Furrer L, Klaghofer R, Genoni M, Zollinger A. Stroke volume and pulse pressure variation for prediction of fluid responsiveness in patients undergoing off-pump coronary artery bypass grafting. *Chest* 2005; 128: 848-854.
13. Biais M, Nouette-Gaulain K, Cottenceau V, Revel P, Sztark F. Uncalibrated pulse contour-derived stroke volume variation predicts fluid responsiveness in mechanically ventilated patients undergoing liver transplantation. *Br J Anaesth* 2008; 101: 761-768.
14. Biais M, Bernard O, Ha JC, Degryse C, Sztark F. Abilities of pulse pressure variations and stroke volume variations to predict fluid responsiveness in prone position during scoliosis surgery. *Br J Anaesth* 2010; 104: 407-413.
15. Biais M, Cottenceau V, Stecken L, Jean M, Ottolenghi L, Roullet S, et al. Evaluation of stroke volume variations obtained with the pressure recording analytic method. *Crit Care Med* 2012; 40: 1186-1191.
16. Broch O, Bein B, Gruenewald M, Hocker J, Schottler J, Meybohm P, et al. Accuracy of the pleth variability index to predict fluid responsiveness depends on the perfusion index. *Acta Anaesthesiol Scand* 2011; 55: 686-693.
17. Broch O, Renner J, Gruenewald M, Meybohm P, Höcker J, Schöttler J, et al. Variation of left ventricular outflow tract velocity and global end-diastolic volume index reliably predict fluid responsiveness in cardiac surgery patients. *J Crit Care* 2012; 27: e7-13.
18. Cannesson M, Musard H, Desebbe O, Boucau C, Simon R, Hénaine R, et al. The ability of stroke volume variations obtained with Vigileo/FloTrac system to monitor the fluid responsiveness in mechanically ventilated patients. *Anesth Analg* 2009; 108: 513-517.
19. Cecconi M, Monti G, Hamilton MA, Puntis M, Dawson D, Tuccillo ML, et al. Efficacy of functional hemodynamic parameters in predicting fluid responsiveness with pulse power analysis in surgical patients. *Minerva Anestesiol* 2012; 78: 527-533.

20. Derichard A, Robin E, Tavernier B, Costecalde M, Fleyfel M, Onimus J, et al. Automated pulse pressure and stroke volume variations from radial artery: evaluation during major abdominal surgery. *Br J Anaesth* 2009; 103: 678-684.

21. Hofer CK, Müller SM, Furrer L, Klaghofer R, Genoni M, Zollinger A. Stroke volume and pulse pressure variation for prediction of fluid responsiveness in patients undergoing off-pump coronary artery bypass grafting. *Chest* 2005; 128: 848-854.

22. Hofer CK, Senn A, Weibel L, Zollinger A. Assessment of stroke volume variation for prediction of fluid responsiveness using the modified FloTrac and PiCCO plus system. *Crit Care* 2008; 12: R82.

23. Khwannimit B, Bhurayanontachai R. Prediction of fluid responsiveness in septic shock patients: comparing stroke volume variation by FloTrac/Vigileo and automated pulse pressure variation. *Eur J Anaesthesiol* 2012; 29: 64-69.

24. Kim YK, Shin WJ, Song JG, Jun IG, Kim HY, Seong SH, et al. Effect of right ventricular dysfunction on dynamic preload indices to predict a decrease in cardiac output after inferior vena cava clamping during liver transplantation. *Transplant Proc* 2010; 42: 2585-2589.

25. Liu X, Fu Q, Mi W, Liu H, Zhang H, Wang P. Pulse pressure variation and stroke volume variation predict fluid responsiveness in mechanically ventilated patients experiencing intra-abdominal hypertension. *BioSci Trends* 2013; 7: 101-108.

26. Monge García MI, Gil Cano A, Díaz Monrové JC. Brachial artery peak velocity variation to predict fluid responsiveness in mechanically ventilated patients. *Crit Care* 2009; 13: R142.

27. Monnet X, Dres M, Ferre A, Le Teuff G, Jozwiak M, Bleibtreu A, et al. Prediction of fluid responsiveness by a continuous non-invasive assessment of arterial pressure in critically ill patients: comparison with four other dynamic indices. *Br J Anaesth* 2012; 109: 330-338.

28. Monnet X, Guérin L, Jozwiak M, Bataille A, Julien F, Richard C, et al. Pleth variability index is a weak predictor of fluid responsiveness in patients receiving norepinephrine. *Br J Anaesth* 2013; 110: 207-213.

29. Nordström J, Hällsjö-Sander C, Shore R, Björne H. Stroke volume optimization in elective bowel surgery: a comparison between pulse power wave analysis (LiDCOrapid) and oesophageal Doppler (CardioQ). *Br J Anaesth* 2013; 110: 374-380.

30. Preisman S, Kogan S, Berkenstadt H, Perel A. Predicting fluid responsiveness in patients undergoing cardiac surgery: functional haemodynamic parameters including the Respiratory Systolic Variation Test and static preload indicators. *Br J Anaesth* 2005; 95: 746-755.

31. Wacharasint P, Lertamornpong A, Wattanathum A, Wongsa A. Predicting fluid responsiveness in septic shock patients by using 3 dynamic indices: is it all equally effective? *J Med Assoc Thai* 2012; 95: S149-156.

32. Whiting P, Rutjes AWS, Reitsma JB, Bossuyt PMM, Kleijnen J. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Method* 2003; 3: 25-36.

33. Jones C, Athanasiou T. Summary receiver operating characteristic curve analysis techniques in the evaluation of diagnostic tests. *Annals Thoracic Surgery* 2005; 79: 16-21.

34. Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature. *Crit Care Med* 2009; 37: 2642-2647.

35. Glas AS, Lijmer JG, Prins MH, Bonsel GJ, Bossuyt PM. The diagnostic odds ratio: a single indicator of test performance. *J Clin Epidemiol* 2003; 56: 1129-1135.

36. Michard F, Teboul J. Using heart-lung interactions to assess fluid responsiveness during mechanical ventilation. *Crit Care* 2000; 4: 282-289.

37. Cavallaro F, Sandroni C, Antonelli M. Functional hemodynamic monitoring and dynamic indices of fluid responsiveness. *Minerva Anestesiol* 2008; 74: 123-135.

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Al-Shafei AI, El-Gendy OA. Effects of Roselle on arterial pulse pressure and left ventricular hypertrophy in hypertensive patients. *Saudi Med J* 2013; 34: 1248-1254.

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Salih MA, Abdel-Gader AG, Al-Jarallah AA, Kentab AY, Al-Nasser MN. Outcome of stroke in Saudi children. *Saudi Med J* 2006; 27 Suppl 1: S91-S96.