

To evaluate the ability of svv obtained by vigileo-flo tracdevice to predict fluid responsiveness in mechanicallyventilated patients and to correlate it to calculated ivcdistensibility index

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Abstract

Background: Respiratory variations in arterial pulse pressure (APP) are accurate predictors of fluid responsiveness in mechanically ventilated patients. **Aim and Objective:** To evaluate the ability of SVV obtained by the vigileo-flo trac device to predict fluid responsiveness in mechanically ventilated patients and to correlate it to the calculated ivc distensibility index. **Method and material:** We conducted a prospective study on 36 septic shock patients. SVV, PPV, and other hemodynamic data were recorded before and after the fluid administration of 500 ml of 6% hydroxyethyl starch. Responders were defined as patients with an increase in stroke volume index of at least 15% after fluid loading. **Results:** The correlation between baseline SVV and PPV was strong ($P < 0.001$). Twenty (55.56%) patients were classified as responders to fluid administration. The hemodynamic variables in responders and nonresponders are shown in Table 2. Volume infusion produced an increase in MAP, CVP, SVI, CI, and DO2I. In contrast, the intravenous fluid significantly decreased HR, SVRI, SVV, and PPV. Both baseline SVV and PPV were significantly higher in responders than in nonresponders, 14.75 ± 1.37 vs. $8.4 \pm 0.72\%$ and 16.7 ± 2.23 vs. 8.7 ± 0.8 , respectively ($P < 0.013$ for both). **Conclusion:** In patients in passively ventilated septic shock with a regular cardiac rhythm and a tidal volume of at least 8 ml kg^{-1} , the SVV, obtained by FloTrac/Vigileo, and the automated PPV, obtained by the IntelliVue MP monitor, performed similarly well in terms of anticipating fluid responsiveness.

Keyword: IGILEO-FLO TRAC DEVICE, SVV, SVV

Introduction

Fluid resuscitation and fluid challenge remain the first-line modality in the management of circulatory shock, including septic shock. Even the latest sepsis guideline recommends fluid resuscitation with at least 30 mL/kg of IV crystalloid within the first 3 hours [1]. Fluid challenge is intended mainly to increase cardiac output (CO) and consequently to improve tissue perfusion and oxygen delivery. However, in most critically ill patients where there is an increase in capillary permeability, there is a narrow therapeutic window for fluid resuscitation, beyond

which it might cause more harm than good. Septic shock is the most common cause of morbidity and mortality in critically ill patients. Relative and absolute hypovolemia due to vasodilatation, increased microvascular permeability, and capillary leakage may facilitate the development of organ failure. Fluid administration is essential for restoring and optimizing cardiac output (CO) and organ perfusion. Early and aggressive fluid resuscitation is one of the cornerstones of management in septic shock patients,¹ and previous studies have shown that about 50% of severe sepsis and septic shock patients respond beneficially to fluid loading (fluid responsiveness). [2-3]. In contrast, in about half of the patients, fluid administration can induce deleterious pulmonary edema, compromising microvascular perfusion and oxygen delivery. Several studies on sepsis have shown that a positive cumulative fluid balance is associated with a high mortality rate. [4-6] Hence, an accurate and reliable technique to guide fluid resuscitation is required. Currently, none of the routinely used static variables of cardiac preload, such as central venous pressure (CVP), [2, 3, 7], pulmonary artery occlusion pressure, [8-9], or global end-diastolic volume index [10-11], reliably predict fluid responsiveness. On the contrary, dynamic indicators derived from the arterial pressure waveform, such as stroke volume variation (SVV) [12-13] and pulse pressure variation (PPV) [14-15], can be used to assess fluid responsiveness in mechanically ventilated patients.

Recently, several new software applications and algorithms have been developed to automatically and continuously calculate these indices. A new device for noncalibrated pulse contour analysis (FloTrac/Vigileo; Edwards Lifescience, Irvine, California, USA) can be used for automatic and continuous CO monitoring. [16] The screen of this device continuously displays the SVV, which is the percentage variation of stroke volume (SV) over a floating period. Previous studies have shown that the SVV obtained by FloTrac/Vigileo could be successfully used for predicting fluid responsiveness in surgical patients [11, 13], with the suggestion that this approach could improve postoperative outcomes. [17] A recently developed automated and continuous measurement of variation in arterial pulse pressure (automated PPV) uses an IntelliVue MP monitor (Philips Medical Systems, Boeblingen, Germany). [18-19]

Cannesson et al. [12] found that there was strong agreement between the automated and manual PPV in terms of fluid responsiveness, particularly in coronary artery bypass graft (CABG) patients. Measurements obtained by one specific device or method cannot be applied to indices from other devices and may result in differences in the threshold value of fluid responsiveness. Therefore, the specific validation of an automated index is needed before clinical use. The aim of this study was to evaluate the ability of SVV obtained by the vigileo-flo trac device to predict fluid responsiveness in mechanically ventilated patients and to correlate it to the calculated ivc distensibility index.

Methods

This prospective study was conducted in the Medical Intensive Care Unit of Saifee Hospital, Mumbai, India. It was approved by the Institutional Ethics Committee, and

informed written consent was obtained from the next of kin of each patient. The inclusion criteria were as follows: having septic shock as defined by the International Sepsis Definitions Conference, [20] being on mechanical ventilation with a tidal volume of at least 8 ml kg⁻¹ without any spontaneous breathing efforts as detected by continuous airway pressure and flow monitoring on the ventilator screen, and having a clinical requirement for a rapid volume challenge according to the attending physician.

The physician's decision was based on the presence of clinical signs of acute circulatory failure [mean arterial pressure (MAP) <65 mmHg, urine output <0.5 ml kg⁻¹ h⁻¹, tachycardia, and skin mottling] and on the absence of any contraindication to a fluid challenge, including life-threatening hypoxaemia and/or evidence of volume overload by physical examination or chest radiograph. Patients were excluded if their chest radiographs were compatible with acute pulmonary oedema, cardiac arrhythmia (atrial fibrillation or frequent premature beats), severe peripheral vascular disease, and left ventricular ejection fraction less than 40%.

Stroke volume variation obtained by FloTrac/Vigileo

A FloTrac sensor kit was connected to the arterial line and coupled to the Vigileo monitor (software version 03.01). The system was zeroed to ambient pressure at the phlebostatic axis, and measurement was initiated. The FloTrac analyzed the arterial pressure waveform 100 times per second over 20s. The SV was based on the contribution of pulse pressure relative to the SV, which is the proportion of pulse pressure to the standard deviation of arterial pulse pressure (APsd). The device calculated SV as $APsd \times K_{hi} (\chi)$, where χ compensates for differences in vascular compliance and resistance derived from a multivariate regression model. This system allowed for real-time adjustments to changing vascular tone with a recalculation of χ every minute. The CO was calculated from $SV \times \text{heart rate (HR)}$, and SVV used the following equation: $SVV (\%) = \frac{1}{4} (SV_{max} - SV_{min}) / SV_{mean}$. SV_{max} , SV_{min} , and SV_{mean} were determined by this system over a 20-second window. The hemodynamic data were set to display continuously in 1-min intervals on the Vigileo monitor. The mean values of the three determinations before and after the completion of volume loading were recorded for statistical analysis.

Automated pulse pressure variation by an IntelliVue MP monitor

The automated PPV was displayed in real-time as a percentage by a Philips IntelliVue MP70 monitor (Philips Medical Systems). The algorithm is commercially available and has been described by Aboy et al. 26. It allows PPV determination from the arterial pressure waveform alone, with no need for airway pressure acquisition. This method is based on an automatic detection algorithm, kernel smoothing, and rank-order filters involving seven consecutive steps (beat minimal detection, beat maximum detection, beat mean calculation, pulse amplitude pressure, envelope estimation, pulse amplitude pressure estimation, and PPV estimation). PPV was calculated and averaged over four cycles of 8s. The mean values of the three determinations before and within 3 minutes after the completion of volume loading were recorded for statistical analysis.

Experimental Protocol

All patients were studied immediately after induction of anesthesia and after a 3-minute period of hemodynamic stability with no changes in anesthetic protocol and no intravascular volume expansion. Baseline hemodynamic measurements were obtained and then followed by an IV intravascular volume expansion consisting of 500 mL of hetastarch 6%, given over 10 min. Hemodynamic measurements were performed within 3 minutes after intravascular volume expansion. SVV was determined in real time, and Δ PP was determined *post hoc* based upon recorded waveforms. Cardiac arrhythmias were absent during hemodynamic readings. The ventilator setting and dosage of vasopressors were all kept constant during the study period.

Statistical analysis

Continuous variables were assessed for normal distribution (Kolmogorov-Smirnov test for normality). All data were presented as mean \pm SD unless otherwise specified. The comparisons of hemodynamic data before and after volume expansion were assessed using the paired Student's t-test, and the comparisons between responders and nonresponders were assessed using the two-sample Student's t-test. Responders were defined as patients with an increase in SVI of at least 15% after fluid administration. Receiver operating characteristic (ROC) curves were generated for SVV and PPV by varying the discriminative threshold, and areas under the ROC curves (AUC) with a 95% confidence interval were calculated and compared. The threshold values for SVV and PPV were determined by considering the values that yielded the greatest sensitivity and specificity for predicting fluid responsiveness. The correlation between SVV and PPV and between the baseline values of each variable and the SVI response to volume infusion was determined using Pearson's linear correlation coefficient. A P value less than 0.05 was considered statistically significant. All data were analyzed using SPSS version 23. A calculated sample size of 36 patients was considered necessary to detect a 5% (SD $\frac{1}{4}$ 5%) difference in SVV and PPV between fluid responders and nonresponders (α 0.05 and power $\frac{1}{4}$ 0.9).

Observation and Results

36 patients were enrolled in this study. 33 of them were sedated with morphine and midazolam, and only three received vecuronium during the study period. All patients received norepinephrine, which was supplemented with dopamine. Baseline patient characteristics are shown in Table 1. 28 (77.78%) patients were studied within 24 hours after the onset of septic shock. The arterial line was inserted in either the radial artery (77.78%) or the femoral artery (22.22%).

Table No. 1: Baseline clinical characteristics

Variable	Frequency (Mean \pm SD)	%
Age (years)	(53.61 \pm 5.99)	
Sex (male)	21	58.33
Height (cm)	(161.3 \pm 5.86)	
weight (kg)	(61.88 \pm 6.42)	
BSA (m ²)	(1.57 \pm 0.26)	
Community-acquired infection,	23	66.66

number . of patients (%)		
	Respiratory tract	20 55.56
	Gastrointestinal tract	6 16.67
Site of infection, number . of patients (%)	Primary bacteraemia	6 16.67
	Bone and joint	2 5.56
	Skin and soft tissue	1 2.78
	Urinary tract	1 2.78
Haemoculture positive		15 41.67
Norepinephrine, number . of patients, dose (mg kg¹ min¹)		36 (0.26±0.07) 100
Dopamine, number . of patients, dose (mg kg¹ min¹)		(8.16±0.5)
APACHE II score		(26.83±1.56)
SOFA score		(9.53±0.27)
ICU mortality, number . of patients (%)		21 58.33
ICU length of stay (days)		(7.75±0.73)

(Note: APACHE, acute physiology and chronic health evaluation; BSA, body surface area; SOFA, sequential organ failure assessment.)

Table No. 2: Haemodynamic Variables Before and After Fluid Expansion in Responders and Nonresponders

	Responders (n = 20)		P-value	Nonresponders (n-16)		P-value
	Before volume expansion	After volume expansion		Before volume expansion	After volume expansion	
Heart rate (bpm)	121.5±5.54	119.4±4.66	0.202	114.5±3.16	113.43±3.78	0.392
SBP (mmHg)	104.35±1.9	124.25±5.25	0.000	112.31±4.77	117.31±4.66	0.005
DBP (mmHg)	59.45±2.68	61.15±2.7	0.053	62.69±2.6	66.5±3.58	0.002
MAP (mmHg)	71.7±4.6	81.5±5.05	0.000	80.25±6.67	83.69±4.29	0.093

SVP							
(mmHg)	13.6±1.47	16.1±1.94	0.000	14.69±0.87	19.25±2.38	0.000	
SVI							
(ml beat ⁻¹ m ²)	29.25±2.88	38.4±2.52	0.000	36.75±4.14	37.63±2.13	0.456	
CI							
(l min ⁻¹ m ²)	3.85±0.79	4.6±0.75	0.004	4.44±0.73	4.81±0.75	0.984	
SVRI (dyne s ⁻¹ cm ⁵ m ²)	1435.2±20.36	1148.4±32.97	0.000	1428±9.87	1355.25±37.35	0.000	
DO2I (ml min ⁻¹ m ²)	443.25±15.87	552.35±49.39	0.000	529.5±67.1	545.1±59.04	0.49	
SVV (%)	14.75±1.37	7.6±0.88	0.00	8.4±0.72	7.25±0.93	0.00	
PPV (%)	16.7±2.13	8.25±1.07	0.00	8.7±0.8	7.8±1.1	0.013	

[Note: Bpm, beat per minute; CI, cardiac index; CVP, central venous pressure; DO2I, oxygen delivery index; MAP, mean arterial pressure; PPV, pulse pressure variation; SVI, stroke volume index; SVRI, systemic vascular resistance index; SVV, stroke volume variation]

The correlation between baseline SVV and PPV was strong ($P < 0.001$). Twenty (55.56%) patients were classified as responders to fluid administration. The hemodynamic variables in responders and nonresponders are shown in Table 2. Volume infusion produced an increase in MAP, CVP, SVI, CI, and DO2I. In contrast, the intravenous fluid significantly decreased HR, SVRI, SVV, and PPV. Both baseline SVV and PPV were significantly higher in responders than in nonresponders, 14.75±1.37 vs. 8.4±0.72% and 16.7±2.23 vs. 8.7±0.8, respectively ($P < 0.013$ for both).

Other baseline hemodynamic data were not different between responders and nonresponders. The amount of fluid resuscitation before enrollment in the study and within 24 h after study was not different between responders and nonresponders (2720±130.5 vs. 2792.5±138.7 ml and 5148±611.2 vs. 4781±814.2 ml, respectively). The AUC (95% confidence interval) of SVV and PPV was 0.000 (0.013–0.000) and 0.013, respectively. There was no difference between the AUC of SVV and PPV ($P = 0.68$). When the 33 patients with radial artery catheterization were selected, the results were statistically unchanged. The AUC (95% confidence interval) of SVV and PPV was 0.94 (0.862–1.00) and 0.933 (0.849–1.00), respectively.

The optimal threshold values for SVV and PPV were 10% (sensitivity 90.6% and specificity 83.2%) and 12% (sensitivity 80.52% and specificity 87%.5), respectively. There was a statistically significant positive linear correlation between baseline SVV

and PPV with percentage changes in SVI by volume loading ($P < 0.001$) and ($P < 0.001$), respectively. In the 23 patients with hypotension and preserved preload dependence, defined as the presence of SVV at least 10%, fluid administration induced at least a 15% increase in MAP in 12 (MAP responder). The baseline Eadyn was not different between MAP responders and MAP non-responders (9.8 ± 0.45 vs. 3.44 ± 2.38 , respectively).

Discussion

This study demonstrated that both the SVV measurement by FloTrac/Vigileo and the automated PPV obtained by IntelliVue MP70 can be used to predict fluid responsiveness in mechanically ventilated septic shock patients. This is the first study to validate fluid responsiveness in this group using novel continuous automated devices and the recently released version (third generation) of FloTrac/Vigileo software.

Our results are in agreement with a recent study that evaluated and compared the SVV obtained by FloTrac/Vigileo and automated PPV, assessed with an IntelliVue monitor, during major abdominal surgery. Derichard et al. [15] found that these two devices performed similarly in terms of fluid responsiveness in hemodynamically unstable surgical patients. Previous studies have investigated the ability of the SVV obtained by FloTrac and Vigileo to predict fluid responsiveness in surgical patients. The results of our study are in accordance with recent studies affirming the value of SVV obtained by this device as an accurate predictor of fluid responsiveness, with an AUC range of 0.824 to 0.95. Automated PPV measurement correlates strongly with that obtained manually in predicting fluid responsiveness in pre-CABG patients, with best threshold values of 10% and 12%, respectively [12], and Derichard et al. [15] also reported that automated PPV obtained by an IntelliVue monitor correlated with manual PPV. Their optimal threshold value was 13% for both PPV methods.

Our results agree that the automated and continuous PPV from the IntelliVue MP monitor is able to predict fluid responsiveness using the algorithm proposed by Aboy et al. Our study showed that the discrimination and optimal threshold values of each variable were not statistically dependent on the site of arterial catheterization. Previous studies have shown that CO measurements via radial and femoral arteries using FloTrac and Vigileo were comparable. [21-22] This supports the use of the proprietary algorithm of the FloTrac/Vigileo to allow CO or SVV monitoring, irrespective of the signal detection site. SVV and PPV are shown to be good predictors of fluid responsiveness in various patient groups and devices. [12-13] However, the validation of these indices has not yet been confirmed in a large multicenter study. However, previous studies have shown that SVV25 or PPV33-guided fluid management can reduce postoperative complications. Further study is thus clearly needed to establish whether goal-directed fluid management based on SVV and PPV will result in improved outcomes in septic shock patients.

Dynamic indices of fluid responsiveness cannot be used in the settings of cardiac arrhythmias, spontaneous breathing activity, ventilation with low tidal volumes, right and left ventricular dysfunction, and open chest conditions. Potential users should be aware of these limitations before using them in clinical practice. Recently, Monge Garcia et al. [23] found that baseline Eadyn was significantly different between MAP

responders and MAP nonresponders and that a baseline Eadyn greater than 0.89 predicted a MAP increase after fluid loading. We failed to find a difference in baseline Eadyn between MAP responders and nonresponders, and it is possible that different methods for PPV measurement may be responsible for these conflicting results. Monge Garcia et al. measured PPV manually, in contrast to automated PPV in our study. Clearly, more evaluation is needed before Eadyn can be used in a clinical setting. One must take into account some of this study's shortcomings. First, inconsistent results have been observed from validation tests on the accuracy of CO acquired by FloTrac/Vigileo. Comparing this device to the pulse-induced continuous cardiac output system, recent research has shown that it is inaccurate for monitoring CO in septic shock. [24-25]

Some limitations of this study must be considered. First, validation studies on the accuracy of CO obtained by FloTrac and Vigileo have yielded conflicting results. Recent studies have demonstrated that this device does not accurately monitor CO in septic shock when compared with the pulse-induced continuous cardiac output system. [24-25] These studies, however, made use of the device's older software versions. According to De Backer et al. [26], FloTrac/Vigileo's third-generation software is more appropriate for treating septic shock than its second-generation counterpart and is also more accurate, precise, and less impacted by total systemic vascular resistance. FloTrac/Vigileo has been used in many prior studies to assess fluid responsiveness because of its ability to monitor changes in SV and CO caused by volume loading.[12,13,15,21] Secondly, a patient was classified as a responder if their SVI increased by at least 15% following fluid delivery; this could have an impact on the SVV and PPV threshold values. The ROC analysis's thresholds are influenced by various responder definitions.

Conclusion

Similar performance was shown in predicting fluid responsiveness in patients with septic shock who were on passive ventilation and had a regular heart rhythm, as evidenced by the SVV measurement performed by FloTrac/Vigileo and the automated PPV acquired by the IntelliVue MP70. Additional investigation is required to determine how these devices optimize care and what effect that has on individuals with septic shock.

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