

## “UTILITY OF STROKE VOLUME VARIATION AS A PREDICTOR OF FLUID RESPONSIVENESS USING THIRD GENERATION VIGILEO DEVICE IN PATIENTS UNDERGOING BRAIN SURGERY”

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### ABSTRACT

#### Background

Assessment of Stroke volume variation (SVV) using minimally invasive devices in mechanically ventilated patients has been in use for several years to guide fluid administration. This study was designed to assess the utility of SVV derived from arterial pulse contour analysis, using FloTrac/Vigileo system to predict fluid status in patients scheduled for brain surgery.

#### Method

We studied 60 adult patients undergoing brain surgery. After a 5min period of stable hemodynamic parameters post-intubation, each patient received successive volume loading steps(VLS), of 200ml lactated Ringer's solution (LR), until the increase in SV(stroke volume) was <10%. Blood pressure(BP), Heart rate(HR), SV and SVV were measured before and after each VLS. We measured the optimal preload augmentation required for each patient by the number of VLS after which SV increase was <10%.

#### Results

There was a statistically significant difference in base line BP and SVV but not in HR between responsive and nonresponsive patients to first VLS. Except for HR, all the measured hemodynamic variables before first VLS showed significant correlation with change in SV after the first VLS. Receiver operating characteristic (ROC) analysis showed a larger area under the curve(AUC) of 0.758 for SVV compared to other measured variables. The median number of VLS administered were 2 per patient equating to a mean  $\pm$ SD of 368 $\pm$ 176 ml of crystalloid as the optimal preoperative infusion volume.

#### Conclusions

SVV obtained with 3rd generation Vigileo device is a better predictor of preload responsiveness when compared to BP and HR.

**KEYWORDS:** Stroke Volume Variation, Volume Loading Steps, Neurosurgery, Vigileo Device

### INTRODUCTION

Surgical outcome in patients scheduled for correction of intracranial pathology relies on maintenance of adequate cerebral perfusion during the intra-operative period. Many factors like preoperative fasting, general anaesthetics, diuretics, diabetes insipidus and intra-operative blood loss compromise the hemodynamic stability in the above subset of patients<sup>1</sup>.

Fluid optimisation is a double edged sword with organ hypo-perfusion, ischemia and increased use of vasopressors if uncorrected and prolonged Intensive care unit stay and compromised patient outcome if over corrected<sup>2,3</sup>.

Static indices like Central venous pressure(CVP), Pulmonary capillary wedge pressure(PCWP) and left ventricular end diastolic area which were traditionally used to guide fluid management were shown to be poor predictors of fluid responsiveness<sup>2,4,5</sup>. On the other hand, dynamic indices which monitor the change in stroke volume (SV) during mechanical ventilation have consistently been demonstrated to be better predictors of fluid responsiveness<sup>2,6,7,8</sup>. Stroke volume variation (SVV) derived from pulse contour analysis is a dynamic monitoring modality and is a reliable predictor of fluid responsiveness<sup>2,3,6,7,8</sup>.

SV and SVV are automatically and continuously displayed by the Vigileo device without need for external calibration. Various studies have analysed the accuracy of older generations of this device to assess SVV in different subsets of patients<sup>5,7</sup>. However, utility of Vigileo device in neurosurgery has not been fully evaluated.

The aim of our study was to evaluate the efficacy of SVV measured by Vigileo device as an essential index of preload responsiveness and thus the reliability of Vigileo device in assessing fluid status of the patient. We also aimed to determine the number of volume loading steps (VLS) required to achieve fluid optimisation.

## METHODS

### Study Population

After obtaining an ethics committee approval and written informed consent, 60 patients aged 20 -70 yrs of ASA physical status 1 or 2, undergoing craniotomy for an intracranial tumour removal or clipping of an aneurysm over a period of 8 months from October 2012 to May 2013 were enrolled in this prospective study. Exclusion criteria were documented coronary or peripheral arterial disease, pulmonary disease and cardiac arrhythmias.

### Anaesthetic Technique

All patients received oral alprazolam 0.25 mg the night before surgery. Following placement of standard monitors, intravenous and radial arterial (20 G) access were established and the patients were started on an infusion of Ringer's lactate at the rate of 10 ml/hr using an infusion pump. Following glycopyrrolate 0.05mg/Kg, anaesthesia was induced with 0.04 mg/Kg midazolam, 2µg/Kg fentanyl and 2mg/Kg propofol. Endotracheal intubation was facilitated with 0.1 mg/kg of Vecuronium bromide and mechanical ventilation was set with a tidal volume of 8ml/Kg and respiratory frequency was adjusted to achieve an end tidal CO<sub>2</sub> of 32–35 mm Hg. Sevoflurane in a mixture of oxygen(33%) and nitrous oxide (76%) was used for anaesthetic maintenance.

### Hemodynamic Monitoring

Flotrac sensor kit was used to connect radial arterial access to the Vigileo device and to the invasive blood pressure monitor. The Vigileo device uses a novel algorithm based on the relationship of arterial pulse pressure with stroke volume.  $SV = K \times \text{pulsatility}$  where K is a constant quantifying arterial compliance and vascular resistance and is derived from patient characteristics (gender, age, height and weight) according to the method described by Langewouters<sup>9</sup> and also from pressure waveform characteristics (eg., skewness and kurtosis of individual waves)<sup>8,10,11,12</sup>. This calibration constant is recalibrated every minute in newer versions of the Vigileo device. Pulsatility depends on the standard deviation of

arterial pressure wave over a 20-s interval<sup>8,10,11,12</sup>. The algorithm of third generation Vigileo device allows for broader patient monitoring through expanded patient algorithm database. This database informs the algorithm to recognize and adjust for hyperdynamic and vasodilated patient conditions.

Vigileo version 3.06 used in this study is also adjusted for certain arrhythmias. SVV is calculated from percentage changes in SV during mechanical ventilation and is continuously displayed by the Vigileo device. Beat to beat variation of SV in the preceding 20sec is used to calculate SVV as,  $SVV (\%) = (SV_{max} - SV_{min}) / SV_{mean}$ . Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), HR, SV and SVV were continuously measured.

### Experimental Protocol

Baseline BP, HR, SV and SVV were documented 5min after intubation to eliminate the bias of intubation response. A VLS of 200ml of lactated Ringer's solution (LR) was performed over 3 min and hemodynamic variables were recorded 1min after each step. Patients were documented as responsive and nonresponsive if increase in SV was  $\geq 10\%$  or  $< 10\%$  respectively after the first VLS. All the responsive patients received successive VLS till a non responsive VLS was observed followed by a confirmatory VLS to calculate the optimum preload value. However the final confirmatory VLS is not included in the calculation of optimum preload. Placement of cranial pins and surgical incision were deferred until the completion of the experimental protocol.

### Statistical Analysis

All hemodynamic variables were analysed as continuous variables and expressed as mean  $\pm$ SD. The data was analysed using MED CAL C statistical package version 12.7.5. Unpaired student's t test was used to analyse hemodynamic variables in responders and non responders. Karl Pearson's correlation was used to assess the relationship between change in SV after the first VLS and pre VLS value of each hemodynamic variable. Receiver operating characteristic (ROC) curves were generated for SBP, DBP, MAP, SVV and HR to analyse the ability of each hemodynamic variable in predicting responsiveness or non responsiveness to the first VLS. The method of De Long et al was used to compare ROC curves<sup>13</sup>. We calculated and compared the AUC for each variable. The area under ROC ranges between 0 and 1 where 1 implies a perfect performance, 0 implies no correlation and 0.5 implies that the screening measure is no better than a chance<sup>1</sup>. Bootstrap percentile method was used to calculate 95% confidence interval(CI) for the area under the ROC curve. We determined the optimal cut-off point which maximizes sensitivity and specificity for SVV to predict fluid responsiveness and calculated the positive and negative predictive values for SVV. Multiple regression analysis was also done to estimate the better predictor among the measured variables. The median number of VLS administered, which were the number of VLS needed for fluid optimisation was also analysed.

### RESULTS

The demographic characteristics of the 60 patients enrolled in the study is given in Table 1. No patient had cardiac rhythm disturbances during the study period. Seven patients who were administered vasopressors and/ or additional fluids other than VLS, due to drop in MAP below 60mmHg during the study period were excluded from the study. Out of 53 patients included in the study, there were 6 patients with intracerebral aneurysm and 47 with cerebral tumour. Patients responsive and non responsive to first VLS differed significantly in Pre VLS value of SBP(P value $<0.05$ ), DBP(P value $<0.05$ ), MAP(P value $<0.05$ ) and SVV(P value $<0.00001$ ) but not the HR. SVV was significantly higher in

responders(17±6) than non responders(10±5). The P value for SVV was statistically highly significant when compared to other variables (Table 2). Significant correlation was found between the change in SV after first VLS and the pre VLS values of SBP (P value<0.0164), DBP(P value<0.0049), MAP(P value<0.0058)and SVV(P value<0.0012). No Significant correlation was found between change in SV and HR (Table 3).

The area (±SE) under the ROC curve was 0.582± 0.079 (95 % CI:0.439-0.716) for SBP, 0.610± 0.0794 (95% CI:0.466-0.741) for DBP, 0.592±0.0789 (95% CI:0.449-0.752) for MAP, 0.527±0.0829(95 % CI:0.385-0.666) for HR and 0.758± 0.0660 (95 % CI:0.621 to 0.865) for SVV. Only the area under the curve for SVV was statistically significant when compared to other variables with a P value <0.0001(Table 4, Figure 1). The optimum threshold value for SVV given by ROC analysis was 13%.

Thus, if a patient had a SVV value of more than 13%, he/she was very likely to be responsive to a subsequent volume load by increasing the SV by more than 10% with a sensitivity of 58.1% and specificity of 86.4% with a positive predictive value of 85.7 and a negative predictive value of 59.4. Only the AUC for SVV was statistically significant when compared to other variables with a P value <0.0001. Multiple logistic regression analysis was done which showed SVV to be the most reliable variable among other measured hemodynamic variables. Only SVV before volume loading was statistically significant predictor of SV> 10% after fluid loading (P value 0.0026) (Table 5).

Patients responsive to first VLS received successive VLS till a non responsive VLS was reached to calculate the optimum preload volume. All patients received a total of 98 VLS. 76 VLS were followed by a SV increase ≥10% and 22 VLS were followed by a SV increase < 10%. The median number of VLS administered were 2 per patient equating to a mean ±SD requirement of 368±176 ml of crystalloid per patient as the optimal preoperative infusion volume.

## DISCUSSIONS

Our study demonstrates the ability of SVV using Vigileo device to predict fluid responsiveness in patients scheduled for elective brain surgery. SVV by Vigileo device is a better predictor of fluid responsiveness than BP and HR.

There is lack of clarity regarding the hemodynamic parameter that best predicts volume status of a patient. Dynamic tests of volume responsiveness which rely on heart-lung interaction in mechanically ventilated patients are superior to static variables<sup>2,6,14</sup>. Mechanical ventilation induced cyclic changes in venacaval, pulmonary and aortic blood flows were first reported by Morgan et al<sup>15</sup>. The basic idea of giving a volume load relies on the fact that if a volume load does not increase the SV of the patient, it serves no benefit to the patient. Instead it could be harmful. Administration of preload increases the SV till the left ventricle reaches the flat part of Frank Starling curve. No further increase in SV occurs thereafter due to maximum overlap between actin-myosin myofibrils<sup>2,6</sup>. SVV greater than 12% to 13% has been reported to be highly predictive of volume responsiveness with a remarkable consistency<sup>2</sup>. Arrhythmias and spontaneous breathing activity and variation in tidal volume of a mechanical breath will lead to misinterpretations of the respiratory variations in stroke volume. A linear relationship was found between tidal volume and SVV by Reuter and his colleagues<sup>2</sup>.

The Vigileo device continuously displays SV, cardiac output(CO), cardiac index(CI), SVV and can derive Systemic vascular resistance and central venous haemoglobin saturation<sup>10</sup>. It is minimally invasive and does not require an external system for calibration in contrast to LiDCO system (LiDCO Limited, UK), requiring lithium dilution; the PiCCO system (Pulsion Medical System, Munich, Germany), requiring trans-pulmonary thermo-dilution; and Finapres Modelflow

system (Finapres Medical Systems, The Netherlands), requiring calibration with another means of CO measurement<sup>16</sup>. Vigileo algorithm and software are continuously being revised since 2005. We used the 3rd generation device (version 3.06) for our study.

In a study by De Waal and coworkers<sup>17</sup> in patients undergoing coronary artery bypass grafting, SVV failed to predict fluid responsiveness where in the software used was adapted to changes in vascular compliance at 10 min intervals, which was reduced to 1 min in subsequent generation devices. A study by Christoph K Hofe and coworkers, compared SVV using the FloTrac/Vigileo(version 1.07) and the PiCCOplus (6.01)systems and concluded that they exhibited similar performance in predicting fluid responsiveness<sup>8</sup>. In a study conducted in postoperative cardiac surgical patients R B P de Wilde and coworkers concluded SVV by Flotrac and LiDCO did not show similar results<sup>18</sup>.

A study by Maxime Cannesson and coworkers showed that SVV is a good predictor of fluid responsiveness and is a surrogate to continuous monitoring of respiratory variation in arterial pulse pressure<sup>5</sup>. Matthieu Biais and coworkers conducted a study in patients undergoing liver transplantation and concluded that SVV-FloTrac and SVV-Doppler measurements showed similar performance in terms of fluid responsiveness<sup>7</sup>. D. Lahner and coworkers compared SVV derived with FloTrac version 1.07 with TEE in patients undergoing major abdominal surgeries and concluded that SVV obtained with Vigileo device is not a reliable predictor of fluid responsiveness<sup>3</sup>. None of the above studies were done with the 3rd generation Vigileo device.

## STUDY LIMITATIONS

Our study was restricted to patients with ASA physical status 1&2 and therefore extrapolation of these results to other subset of patients needs further evaluation. We did not use a standard monitoring device like echocardiography to compare our findings. Other preload indices like CVP and PAOP were not analysed. Predictive value of SVV for fluid responsiveness in the intra operative period was not determined as the present study was focussed on fluid optimisation before the surgical incision. VLS was not tailored to the patient's weight which might have influenced the results.

## CONCLUSIONS

In conclusion, we believe that SVV obtained with 3rd generation Vigileo device is a better predictor of fluid responsiveness when compared to BP and HR in patients before brain surgery. However, further studies comparing it with other preload indices in various subsets of patient's are required to confirm its clinical utility.

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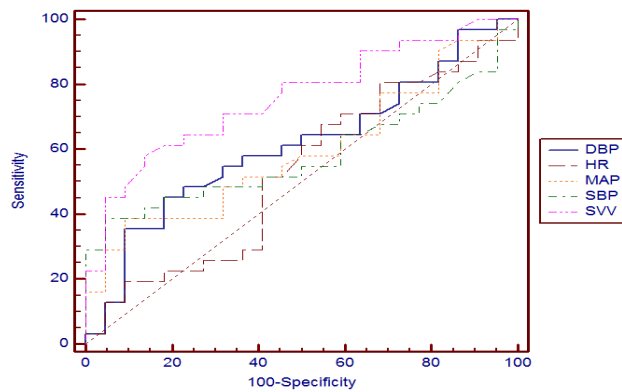
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**APPENDICES**



**Figure 1: Receiver Operating Characteristic Curves for Diastolic Blood Pressure (DBP), Heart Rate (HR), Mean Arterial Pressure (MAP), Systolic Blood Pressure (SBP), Stroke Volume Variation (SVV) before Volume Loading as Predictors of Increase in Stroke Volume by >10% after Volume Loading. Only the Area for SVV was Significantly Different from That for Other Variables (p<0.0001)**

**Table 1: Demographic Data of 53 Patients Included in the Study**

Age(years)	43.96±13.96
Height(cms)	155.81±6.88
Weight(kgs)	59.51±12.53

Data presented as mean ± SD

**Table 2: Hemodynamic Variables in Responsive and Nonresponsive Patients before Volume Loading Step**

	Responsive <sup>a</sup>	Non Responsive <sup>b</sup>	Statistical Significance
SBP(mm Hg)	110±19	119±15	P<0.05
DBP(mm Hg)	68±9	73±11	P<0.05
MAP(mm Hg)	84±12	91±12	P<0.05
HR(beats/min)	85±16	82±17	NS
SVV(%)	17±6	10±5	P<0.00001

Data presented as mean ± SD

Volume load was in steps after anaesthesia and before brain surgery. Each step consisted of infusion of 200ml Ringer's lactate solution over 3 min. Responsive, defined as an increase in stroke volume of ≥ 10%. Non responsive, defined as an increase in stroke volume of < 10% after first volume loading step.

SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; SVV, stroke volume variation; NS, not statistically significantly different between the groups ( $P \geq 0.05$ ; unpaired student's t test).

**Table 3: Correlation of Hemodynamic Variables before Volume Loading with the Change in SV after Volume Loading in 53 Patients Scheduled for Brain Surgery**

Variable	Pearson's Correlation Coefficient	Statistical Significance
SBP	-0.3282	$P < 0.0164$
DBP	-0.4	$P < 0.0049$
MAP	-0.3742	$P < 0.0058$
HR	0.18	NS
SVV	0.4339	$P < 0.0012$

Significant correlation was found between change in SV after first volume loading step(VLS) and pre VLS values of SVV(positive correlation) and blood pressure(negative correlation).

SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; SVV, stroke volume variation; NS, not statistically significantly different between groups ( $P \geq 0.05$ )

**Table 4: Area under ROC Curve of Hemodynamic Variables of in 53 Patients Scheduled for Brain Surgery before Volume Loading as Predictors of Increase in Stroke Volume by >10% after Volume Loading. Only the Area for SVV was Significantly Different from That for Other Variables ( $p < 0.0001$ )**

Variable	AUC( $\pm$ SE)	Statistical Significance
SBP	0.582 $\pm$ 0.079	NS
DBP	0.610 $\pm$ 0.0794	NS
MAP	0.592 $\pm$ 0.0789	NS
HR	0.527 $\pm$ 0.0829	NS
SVV	0.758 $\pm$ 0.0660	$P < 0.0001$

ROC, Receiver Operating Curves; SE, standard error; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; SVV, stroke volume variation; NS, not statistically significantly different between groups ( $P \geq 0.05$ ). Only the area for SVV was significantly different from that for other variables ( $p < 0.0001$ ).

**Table 5: Multiple Regression Analysis of Hemodynamic Variables of in 53 Patients Scheduled for Brain Surgery before Volume Loading as Predictors of Increase in Stroke Volume by >10% after Volume Loading. Only SVV was Significantly Different from That for Other Variables ( $p = 0.0026$ )**

Variable	Coefficient	Standard Error	P
SBP	-0.073364	0.072026	0.3084
DBP	-0.22100	0.16759	0.1873
MAP	0.24340	0.20503	0.2352
HR	-0.016759	0.026394	0.5255
SVV	0.27499	0.091192	0.0026

Constant 0.8574

SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; SVV, stroke volume variation.. Only SVV before volume loading was statistically significant predictor of SV > 10% after fluid loading ( $P = 0.0026$ ).