Assessment of Fluid Responsiveness in Prone Neurosurgical Patients Undergoing Protective Ventilation: Role of Dynamic Indices, Tidal Volume Challenge, and End-Expiratory Occlusion Test

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BACKGROUND: In patients in the prone position, the reliability of pulse pressure variation and stroke volume variation (PPV and SVV) and the use of functional hemodynamic tests to predict fluid responsiveness have not previously been established. Perioperatively, in this setting, optimizing fluid management can be challenging, and fluid overload is associated with both intraoperative and postoperative complications. We designed this study to assess the sensitivity and specificity of baseline PPV and SVV, the tidal volume (V_T) challenge (V_TC) and the end-expiratory occlusion test (EEOT) in predicting fluid responsiveness during elective spinal surgery.

METHODS: The study protocol was started during a period of intraoperative hemodynamic stability after prone positioning and before the administration of any vasopressor: (1) at baseline, the controlled ventilation was set at 6 mL/kg of predicted body weight (PBW) (T_0); (2) patients underwent the first EEOT ($EEOT_6$) by interrupting the mechanical ventilation for 30 seconds; (3) the ventilation was set again at 6 mL/kg PBW for 1 minute (T_1); (4) the V_TC was applied by increasing the V_T up to 8 mL/kg PBW for 1 minute; (5) the ventilation was kept at 8 mL/kg PBW for 1 minute (T_2); (6) a second EEOT ($EEOT_8$) was performed; (7) the V_T was reduced back to 6 mL/kg PBW for 1 minute (T_3); (8) a fluid challenge of 250 mL of Ringer's solution was infused over 10 minutes. After each step, a complete set of hemodynamic measurements was recorded.

RESULTS: Neither PPV and SVV values recorded at T_3 nor the $EEOT_6$ or the $EEOT_8$ predicted fluid responsiveness. The change in PPV after V_TC application predicted fluid responsiveness with an area under the curve of 0.96 (95% confidence interval, 0.87–1.00), showing a sensitivity of 95.2% and a specificity of 94.7%, using a cutoff increase of 12.2%. The change in SVV after V_TC application predicted fluid responsiveness with an area under the curve 0.96 (95% confidence interval, 0.89–1.00) showing a sensitivity of 95.2% and a specificity of 94.7%, using a cutoff increase of 8.0%. A linear correlation between stroke volume index changes after fluid challenge administration and the changes in PPV and SVV after V_TC application was observed ($r = 0.71$; $P < .0001$ and $r = 0.68$; $P < .0001$, respectively).

CONCLUSIONS: In prone elective neurosurgical patients, the baseline values of PPV and SVV and the EEOT fail to predict fluid responsiveness, while the V_TC is a very reliable functional hemodynamic test and could be helpful in guiding intraoperative fluid therapy. (Anesth Analg XXX;XXX:00–00)

KEY POINTS

- **Question:** Can the functional hemodynamic tests be applied to patients undergoing elective neurosurgery in the prone position?
- **Findings:** The tidal volume challenge reliably predicted fluid responsiveness while the end-expiratory occlusion test did not.
- **Meaning:** Functional hemodynamic assessment could help in assessing volume status and preventing inappropriate fluid administration.

GLOSSARY

ANOVA = analysis of variance; **ARDS** = acute respiratory distress syndrome; **AUC** = area under the ROC curve; **BIS** = bispectral index; **CI** = cardiac index; **EEOT** = end-expiratory occlusion test; **FC** = fluid challenge; **GOLD** = Global Initiative for Chronic Obstructive Lung Disease; **HR** = heart rate; **IVC** = inferior vena cava; **MAP** = mean arterial pressure; **PBW** = predicted body weight; **PPV** = pulse pressure variation; **ROC** = receiver operating characteristic; **SAP** = systolic arterial pressure; **SD** = standard deviation; **SV** = stroke volume; **SVI** = stroke volume index; **SVV** = stroke volume variation; **V_T** = tidal volume; **V_TC** = tidal volume challenge

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Prone positioning is commonly required to allow surgical access to the posterior head, neck, and spine during neurosurgery.[1]

An intraoperative fluid management strategy aimed at avoiding fluid overload is key to reducing perioperative complications. Fluid tends to accumulate in dependent areas of the body[1] and prone position is associated with anatomical obstruction of venous drainage.[1] These factors can lead to an increase in edema of structures within the head and neck, causing macroglossia and oropharyngeal swelling, and potentially difficulty with the surgical field.[1]

However, fluid management can be challenging due to the hemodynamic effects of prone positioning.[1] A key factor is the compression of the inferior vena cava (IVC).[2,3] As a consequence, venous return from the lower trunk and, in turn, stroke volume (SV) is decreased.[1,4,5] Moreover, these changes can cause venous congestion in the back, because the vertebral column venous plexus is an alternative route for the blood to return to the right heart, and a consequent increase in surgical bleeding,[1] which can be reduced by optimizing intraoperative fluid management and applying a pressure-controlled ventilation strategy.[6]

The dynamic indices of fluid responsiveness, such as pulse pressure variation (PPV) and stroke volume variation (SVV), are often used intraoperatively to optimize preload.[7] Because prone positioning affects heart-lung interactions by changing the chest wall compliance and the transmission of intrathoracic pressure to the vessels and to the heart,[1,5,8] the reliability of these indexes could be impaired. The use of PPV and SVV in surgical patients in the prone position is limited to a few small-sized research studies.[9,10]

Fluid responsiveness in the operating room can also be assessed by means of functional hemodynamic tests.[7] Among them, the end-expiratory occlusion test (EEOT) is obtained by measuring the effect on SV and cardiac output of interrupting positive pressure ventilation for a defined number of seconds,[11] whereas the "tidal volume challenge" (V_TC) consists of the assessment of changes in PPV and SVV following an increase in the tidal volume (V_T) for 1 minute from 6 to 8 mL/kg.[12]

No study has previously evaluated the feasibility and reliability of these dynamic tests to assess preload dependence during prone positioning in the operating room. We therefore designed this study (1) to assess the reliability of the tidal volume (V_T)C and of the EEOT in predicting fluid responsiveness and (2) to compare these tests to baseline PPV and SVV.

METHODS

Patients

This study was approved by the Institutional Review Board of the University Hospital "Maggiore della Carità" of Novara, Italy (approval number CE 192/17), and informed written consent was obtained from all subjects participating in the trial. The trial was registered at https://www.anzctr.org.au (ACTRN12618000682246; Principal Investigator: Antonio Messina, Date of registration last approval: April 26, 2018) and conducted in the operating rooms of neurosurgery at the University Hospital of Novara, Italy, from January 2018 to July 2018.

All consecutive adult neurosurgical patients (age >18 years) scheduled for elective spinal surgery and requiring invasive arterial monitoring and not requiring neurophysiologic monitoring (which could affect arterial waveform signals) were considered eligible to participate. The exclusion criteria were (1) chronic cardiac arrhythmia; (2) depressed left (<30% of ejection fraction) or right (tricuspid annular plane systolic excursion <16 mm) ventricular function; (3) body mass index >30 kg/m^2; (4) chronic obstructive pulmonary disease classified as Global Initiative for Chronic Obstructive Lung Disease (GOLD) scale ≥2; (5) preexisting use of β-blocking agents; (6) a persistent poor-quality arterial signal in the prone position.

Perioperative Management

Standard intraoperative monitoring including heart rate (HR), peripheral oxygen saturations, continuous electrocardiography, and noninvasive blood pressure monitoring was used for all patients. General anesthesia was induced, after preoxygenation, with propofol, remifentanil, and rocuronium (0.6 mg/kg), and maintained with propofol (1.5–3.0 mg·kg^{-1}·hour^{-1}) or sevoflurane (1%–2%) plus remifentanil (0.1–0.5 μg/kg/min) to maintain a bispectral index (BIS monitor, Medtronic, Brooklyn Park, MN) target of 40–60 throughout the surgical time. Neuromuscular blockade was maintained throughout the operating time by using intermittent boluses of rocuronium 0.10 mg/kg every 40–50 minutes. Intraoperatively, all patients received maintenance fluid of Ringer's solution at 4 mL·kg^{-1}·hour^{-1} and were ventilated using a FLOW-I C40 ventilator (Maquet Critical Care, Solna, Sweden) in volume-control mode with the following settings: V_T of 6 mL/kg of the predicted body weight (PBW); positive end-expiratory pressure set between 3 and 6 cm H_2O to achieve and maintain a peripheral oxygen saturation ≥96%; respiratory rate set to achieve and maintain an end-tidal carbon dioxide concentration between 30 and 35 mm Hg. The PBW (kg) was calculated according to the acute respiratory distress syndrome (ARDS) Network PBW equation (http://www.ardsnet.org/tools.shtml). The positive end-expiratory pressure was kept constant during the study period. Invasive blood pressure monitoring was obtained by inserting a 20-G cannula into the radial artery. Using a Y cable, the arterial pressure signal was transmitted to both the operating room monitor (Mindray BeneView T8; Soma Technology, Inc, Bloomfield, CT) and the MostCare device (Vytech Health, Padua, Italy). Patients were then turned to the prone position using the Wilson frame.[1] The type of bed used was the same for all the patients. After positioning the patient and zeroing the arterial signal, the arterial waveform was checked for quality by means of a square-wave test and optimized in the case of the occurrence of under- or overdamping.[13,14]

Hemodynamic Monitoring

The MostCare calculates the SV according to the O. Frank equation: SV = A_{sys}/Z_{tot}, where A_{sys} is the area under the

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systolic part of the arterial pressure waveform and Z_{tot} is the systemic vascular impedance. The MostCare works with a sampling rate of 1.000 points (P/t) per second analyzing both the systolic and the diastolic parts of the arterial waveform signal to accurately assess the position of the dicrotic notch (systolic component) and the systemic vascular impedance. This latter variable is calculated by analyzing the profile of the "points of instability'" generated by the mechanical interaction (ie, pressure/time changes) between forward (due to cardiac systole) and backward pressure waves (coming from the peripheral vessels), defining a patient-specific profile for each arterial waveform.[14,15] The MostCare directly measures the systolic, diastolic, mean, dicrotic pressure, and PPV from the arterial pressure waveform and it calculates the SVV by assessing the changes in SV over time. All the indexed values, including SV index (SVI) and cardiac index (CI), are calculated using the patient's anthropometric measurements. The default setting, as indicated by the manufacturer, of the MostCare is to average all the hemodynamic measurements obtained during a 30-second period. Each set of measurements (including systolic and mean arterial pressures [SAP and MAP], HR, SVI, CI, PPV, and SVV) was exported into a dedicated Excel (Microsoft, Redwood, MS) spreadsheet for further analysis.

Study Protocol

The study protocol was started during a period of intraoperative hemodynamic stability as previously defined (ie, change in MAP of <10% during 5 minutes[16,17]), after prone positioning and before the administration of any vasopressor. The attending anesthetist also observed the curves displayed on the ventilator to ensure the absence of spontaneous breathing activity, then the arterial blood gases were measured. The study protocol (Figure 1) was the following: (1) at baseline (T_0), a set of measurements was recorded, (2) patients underwent the first EEOT by using the software function, "expiratory hold," on the FLOW-I C40 to interrupt mechanical ventilation for 30 seconds ($EEOT_6$); (3) after 1 minute, when all hemodynamic variables had returned to their baseline value, a second set of measurements was recorded (T_1); (4) the V_TC was applied by increasing the V_T up to 8 mL/kg PBW for 1 minute; (5) after 1 minute another set of baseline measurements was recorded (T_2); (6) a second EEOT ($EEOT_8$) was performed, as described above; (7) the V_T was reduced back to 6 mL/kg PBW (T_3) and a set of baseline measurements was recorded; (8) after 1 minute, a fluid challenge (FC) of 250 mL of Ringer's solution was infused over 10 minutes. A set of measurement was also recorded at the end of each test (EEOTs, V_TC, and FC). The attending anesthetist was allowed to interrupt the protocol at any stage for either hemodynamic instability or any other adverse effects requiring urgent treatment.

Statistical Analysis

The reliability of PPV, SVV, V_TC, and EEOT tests in predicting fluid responsiveness was assessed using a receiver operating characteristic (ROC) curve approach (95% confidence interval). ROC curves were constructed as follows: (1) for the averaged values of PPV and SVV recorded at T_0 before the application of the hemodynamic tests; (2) for the percentage change between the averaged values of PPV and SVV recorded at T_1 and the values of PPV and SVV recorded at the end of V_TC application (ΔPPV_{VTC} and ΔSVV_{VTC}, respectively); (3) for the percentage changes between the averaged values of SVI and CI recorded at T_0 and T_2 (for $EEOT_6$ and $EEOT_8$, respectively) and the values of SVI and CI recorded

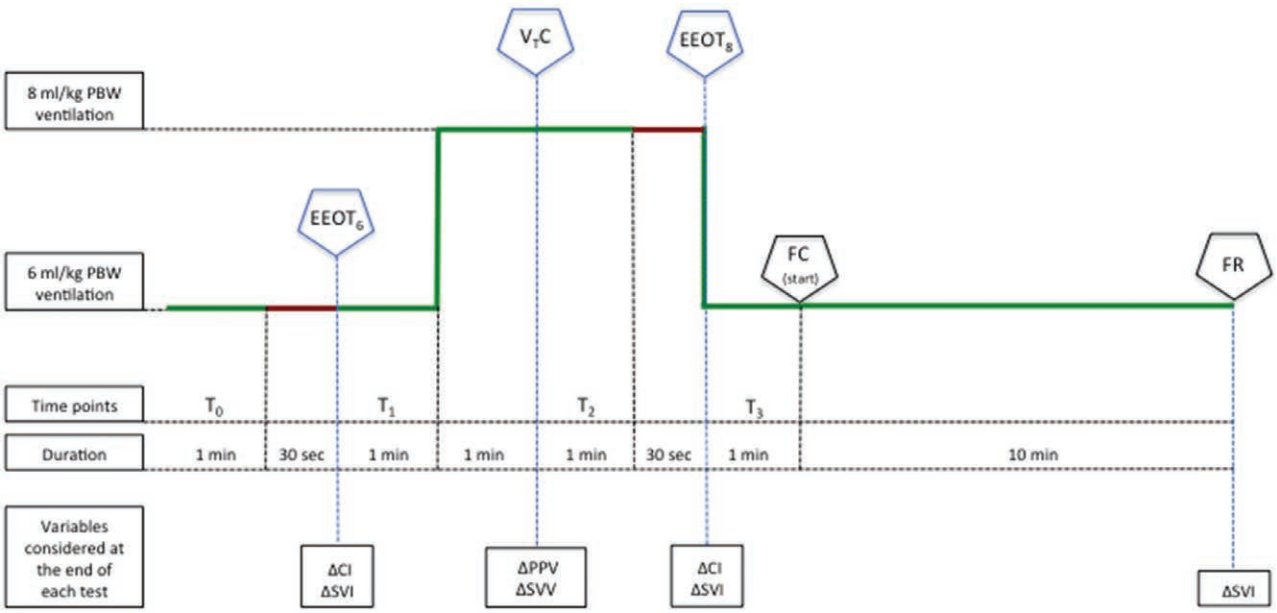

Figure 1. Study protocol (see text for further explanations). EEOTs were performed by interrupting mechanical ventilation (green line) for 30 s (red lines) and analyzing the changes in cardiac and stroke volume index with respect to T_0 (for $EEOT_6$) and T_3 (for $EEOT_8$). The V_TC was performed by increasing the tidal volume from 6 to 8 mL/kg PBW for 1 min (grey line) and analyzing the changes in pulse and stroke volume variations with respect to T_2. Fluid responsiveness was assessed 10 min after fluid challenge administration. CI indicates cardiac index; EEOT, end-expiratory occlusion test; FC, fluid challenge; FR, fluid responsiveness; PBW, predicted body weight; PPV, pulse pressure variation; SVI stroke volume index; SVV stroke volume variation; V_TC, tidal volume challenge.

at the end of each EEOT (ΔSVI and ΔCI, respectively). A patient was considered fluid responsive if FC administration increased SVI ≥10%[16,18] as compared to the averaged values of SVI recorded at T_3. Only the hemodynamic data obtained from the first FC administered to each patient was analyzed. Statistically significant ROC curves ($P < .05$) were compared using the DeLong test, the grey zone was determined by considering low and high cutoff values that included 90% of negative and positive FC responses, respectively.[16,19] Cutoff values for the ROC curves were chosen with the highest Youden index.

The distribution of variables was assessed using the D'Agostino-Pearson test. Data were expressed as the median with interquartile (IQR 25th–75th) range or mean ± standard deviation (SD) or proportions (percentage), as appropriate. Proportions were compared using the χ^2 test or the Fisher exact test while continuous variables were compared with Wilcoxon or Mann-Whitney tests, as appropriate. The hemodynamic values of responders and nonresponders from T_0 to T_3 were separately analyzed with a 1-way analysis of variance (ANOVA) for repeated measurements and Geisser-Greenhouse correction. Post hoc pairwise multiple comparisons analysis were performed using the Tukey test. Correlation between the percentage change in SVI after FC administration and the hemodynamic changes associated with V_TC (ΔPPV_{VTC} and ΔSVV_{VTC}) and EEOTs (ΔSVI and ΔCI) were determined by linear regression.

Because V_TC has not previously been studied in prone surgical patients, we predicted an area under the ROC curve (AUC) for V_TC of at least 0.75, which is the minimum threshold required for considering a diagnostic test accurate.[20] To calculate the sample size of the study, we compared this value to the null hypothesis (AUC = 0.50; ratio of sample sizes in negative/positive groups = 1) and generated a sample size of 38 patients (type I error of 5% and type II error of 20%).

Statistical analyses were conducted using GraphPad PRISM V6 (GraphPad Software Inc, San Diego, CA). For all comparisons, we considered P values <.05 to be significant.

RESULTS

In the enrollment period, 208 consecutive prone neurosurgical patients were screened and 61 considered eligible. However, 20 were excluded before and 1 after enrollment (Figure 2). Finally, 40 patients were analyzed. No adverse effects were described after EEOT or V_TC application, and the study protocol did not need to be interrupted for any of the enrolled patients. Demographic data, risk scores, comorbidities, surgical procedures, ventilatory variables at enrollment (Table 1), and hemodynamic measurements before FC (T_3) administration did not differ between responders (19 patients, 47.5%) and nonresponders (Table 2). The ANOVA of the hemodynamic values recorded at each step of the protocol was not statistically significant in the 2 populations,

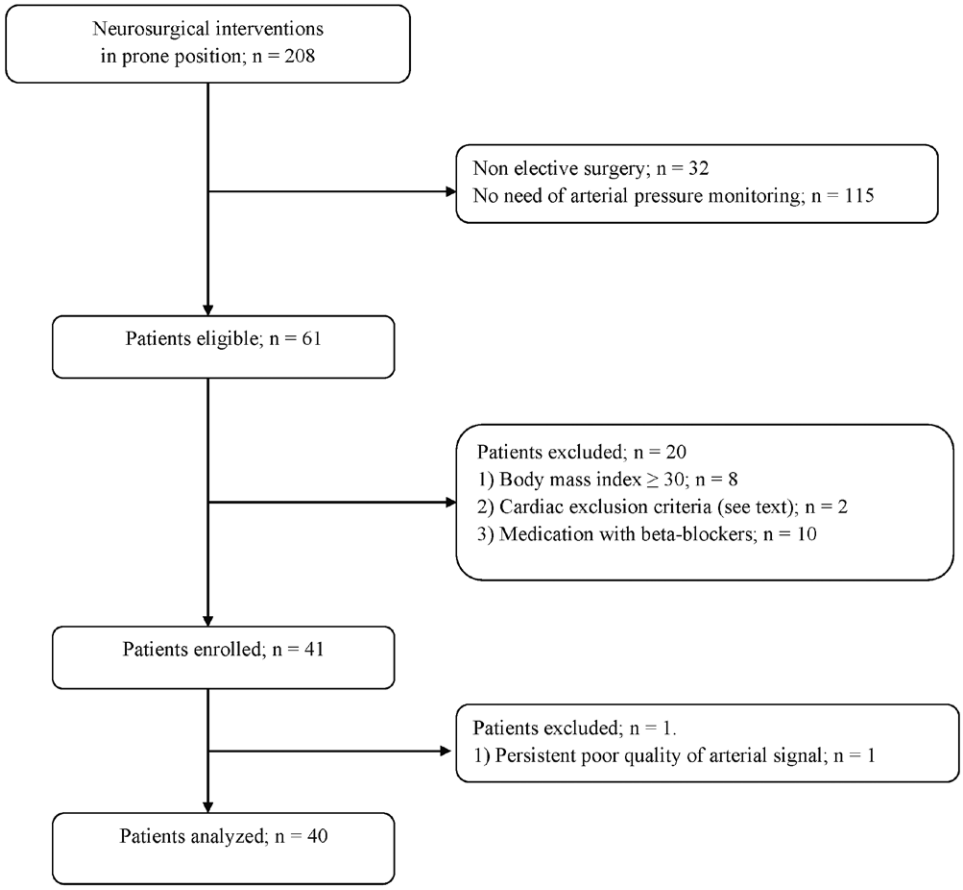

Figure 2. The flow of patients in the study.

Table 1. Patients' Characteristics at Enrollment

	R (n = 19)	NR (n = 21)	Comparison Between R and NR (*P*)
General characteristics			
Age (y)	71 (59–76)	65 (47–71)	.10
Sex (M/F)	11/8	9/12	.90
Body mass index (kg/m^2)	26.6 (24.5–29.1)	26.7 (23.2–28.1)	.30
ASA physical status (I/II/III/IV) (n)	5/10/4/0	3/12/6/0	.61
NSQIP score for any complication (%)	6.0 (4.3–6.7)	5.6 (3.3–7.3)	.35
NSQIP score for serious complication (%)	5.4 (4.1–6.4)	4.6 (3.0–6.5)	.39
Duration of surgery (min)	180 (120–240)	240 (135–270)	.26
Preoperative hemoglobin (mg/dL)	13.8 (13.0–14.3)	13.2 (12.0–14.5)	.23
Preoperative creatinine (mg/dL)	0.8 (0.6–0.9)	0.7 (0.6–0.9)	.53
Lactate (mmol/L)	0.5 (0.5–0.7)	0.6 (0.4–0.8)	.86
Intraoperative urine output at T_0 (mL)	218 (131–252)	184 (143–264)	.81
Fluid administration at T_0 (mL)	350 (322–398)	354 (328–408)	.67
Ventilator settings			
pH	7.38 (7.34–7.43)	7.38 (7.36–7.44)	.70
Total PEEP (cm H_2O)	5 (5.0–5.5)	5 (5.0–5.0)	.95
V_T (mL)	390 (330–430)	380 (330–460)	.89
Total respiratory compliance 6 mL/kg VCV (mL/cm H_2O)	64 (57–72)	66 (56–72)	.70
Total respiratory compliance 8 mL/kg VCV (mL/cm H_2O)	62 (55–68)	63 (56–68)	.92
Driving pressure 6 mL/kg VCV (cm H_2O)	7 (7–9)	7 (6–9)	.94
Driving pressure 8 mL/kg VCV (cm H_2O)	8 (7–9)	7 (6–9)	.66
Pao_2/Fio_2 (mm Hg)	418 (318–498)	465 (307–530)	.43
pco_2 (mm Hg)	38.0 (34.9–43.7)	40.0 (37.5–42.3)	.70
RR (breaths/min)	16 (15–18)	16 (14–17)	.35
Chronic preoperative disease, n (%)			
Hypertension	15 (78.9)	17 (80.9)	.76
Coronary heart disease	2 (10.5)	3 (14.2)	.99
Cerebrovascular disease	1 (5.2)	2 (9.5)	.99
Diabetes mellitus	4 (21.0)	3 (14.2)	.98
Chronic kidney disease	2 (10.5)	3 (14.2)	.99
COPD/asthma	2 (10.5)	4 (19.0)	.66

Values are reported as absolute (%) or median (25th–75th interquartile range), as appropriate.

Abbreviations: ASA, American Society of Anesthesiologists Classification; COPD, chronic obstructive pulmonary disease; NR, nonresponders; NSQIP; national surgical quality improvement program; Pao_2/Fio_2, arterial Po_2/fraction of inspired oxygen; PEEP, positive end-expiratory pressure; R, responders; RR, respiratory rate; VCV, volume-controlled ventilation; V_T, tidal volume.

Table 2. Hemodynamic Parameters in the Study Period in Fluid Responders and Nonresponders

	T_0	T_1	T_2	T_3	Post-FC	*P* Value T_3 (R Versus NR)	*P* Value T_3 Versus Post-FC	ANOVA (*P*)
CI (L/min/m^2)								
R	2.3 (2.2–2.7)	2.4 (2.1–2.7)	2.4 (2.2–2.8)	2.2 (2.1–2.6)	2.5 (2.2–3.0)	.29	.001	.07
NR	2.6 (2.4–2.7)	2.5 (2.3–2.7)	2.5 (2.3–2.8)	2.6 (2.4–2.7)	2.5 (2.3–2.7)		.19	.30
SVI (mL/min/m^2)								
R	45 (33–47)	45 (33–48)	43 (35–49)	41 (32–46)	49 (37–54)	.66	<.0001	.001
NR	43 (34–48)	43 (34–48)	42 (35–48)	41 (32–48)	42 (33–47)		.47	.39
MAP (mm Hg)								
R	68 (60–76)	68 (60–75)	66 (62–74)	66 (56–71)	72 (64–79)	.83	.01	.21
NR	67 (59–75)	66 (59–76)	64 (58–76)	67 (58–75)	68 (57–73)		.28	.87
SAP (mm Hg)								
R	95 (86–108)	96 (87–109)	97 (90–111)	89 (77–97)	103 (94–110)	.72	.003	.06
NR	92 (82–106)	95 (82–108)	92 (80–107)	97 (79–108)	96 (82–106)		.41	.51
HR (beats/min)								
R	60 (52–70)	58 (53–70)	58 (53–70)	60 (50–69)	58 (49–69)	.47	.92	.99
NR	62 (56–70)	62 (56–70)	61 (56–69)	61 (57–69)	60 (46–69)		.40	.49
PPV (%)								
R	6.9 (4.8–11.2)	6.4 (5.0–9.8)	8.6 (5.3–12.2)	9.0 (3.7–12.6)	6.1 (4.2–8.0)	.11	.02	.32
NR	8.2 (6.5–13.2)	9.2 (6.3–13.0)	9.4 (7.4–13.3)	8.0 (6.0–12.1)	7.1 (5.2–10.9)		.14	.33
SVV (%)								
R	5.5 (3.1–9.8)	6.8 (4.4–7.9)	7.9 (4.4–7.9)	6.9 (5.2–9.0)	6.5 (3.8–13.0)	.26	.62	.14
NR	8.3 (6.5–13.2)	8.7 (6.1–10.2)	7.9 (5.6–10.8)	7.5 (4.7–12.2)	7.7 (4.7–11.4)		.63	.50

Data are presented as median (25th–75th interquartile). R, n = 19; NR, n = 21. The series of ANOVA was performed by separately analyzing the 2 subgroups (R/NR) and considering the time-points (T_0, T_1, T_2, and T_3) as the independent variable. Wilcoxon or Mann-Whitney *U* tests have been used to compare the hemodynamic values of R and NR recorded at T_3, as appropriate.

Abbreviations: ANOVA, analyses of variance; CI, cardiac index; FC, fluid challenge; HR, heart rate; MAP, mean arterial pressure; NR, nonresponders; PPV, pulse pressure variation; R, responders; SAP, systolic arterial pressure; SVI, stroke volume index; SVV, stroke volume variation.

with the exception of SVI for responders ($P < .001$), in whom, SVI at T_3 was significantly lower than at both T_0 and T_1 (both $P < .05$) and T_2 ($P < .01$; Table 2).

Effect of FC Administration

As shown in Table 2 (T_3 versus post-FC comparison), in responders the FC significantly increased CI, SVI, SAP, and MAP, and decreased PPV, but did not affect SVV and HR. In nonresponders, FC administration did not change any of the recorded variables.

Assessment of Fluid Responsiveness

PPV and SVV values recorded at T_3 (before FC administration) (AUC = 0.69, $P = .10$ and AUC = 0.61, $P = .25$, respectively) and ΔCI and ΔSVI after $EEOT_6$ (AUC = 0.58, $P = .35$ and AUC = 0.64, $P = .14$, respectively) or after EEO_8 (AUC = 0.59, $P = .35$ and AUC = 0.65, $P = .11$, respectively) did not predict fluid responsiveness.

V_TC application increased PPV (from 6.4% [95% confidence interval, 5.0%–9.8%] to 8.5% [95% confidence interval, 5.0%–11.5%]; $P < .0001$) and SVV (from 6.8% [95% confidence interval, 4.4%–7.9%] to 8.1% [95% confidence interval, 6.2%–10.0%]; $P < .0001$) in responders and reduced PPV (from 9.2% [95% confidence interval, 6.4%–13.0%] to 8.9% [95% confidence interval, 6.1%–12.1%]; $P = .01$) and SVV (from 8.7% [95% confidence interval, 6.1%–10.2%] to 8.6% [95% confidence interval, 5.7%–9.6%]; $P = .002$) in nonresponders. The AUC of ΔPPV_{VTC} was 0.96 (95% confidence interval, 0.87–1.03; Youden index = 0.92) showing a sensitivity of 95.2% and a specificity of 94.7% for a best cutoff value of a 12.2% increase as compared to T_1 (Figure 3). The ΔPPV values of 2 enrolled patients (5.0%) were within the grey zone of the test, which ranged between 4% and 13%.

The AUC of ΔSVV_{VTC} was 0.96 (95% confidence interval, 0.89–1.02; Youden index = 0.92) showing a sensitivity of 95.2% and a specificity of 94.7% for a best cutoff value of an 8.0% increase as compared to T_1 (Figure 3). The ΔSVV value of 1 enrolled patient (2.5%) was within the grey zone of the test, which ranged between 3% and 11%. The ROC curves for ΔPPV_{VTC} and ΔSVV_{VTC} were not significantly different ($P = .75$).

Linear Correlation

A linear correlation between SVI change after FC administration and ΔPPV_{VTC} ($r = 0.71$; $P < .0001$) and ΔSVV_{VTC} ($r = 0.68$; $P < .0001$) was observed (Figure 4).

DISCUSSION

The number of patients undergoing elective spinal surgery has grown exponentially in recent years.[21–23] To the best of our knowledge, this study represents the first application of functional hemodynamic tests to predict fluid responsiveness in prone patients undergoing spinal surgery. The main finding of our study is that V_TC is an excellent predictor of fluid responsiveness in prone patients undergoing elective surgery, with a 12.2% and 8.0% increase from baseline for PPV and SVV, respectively, after the V_TC application. Secondarily, as expected, our findings show that baseline values of PPV and SVV are unreliable when a lung-protective ventilatory strategy is applied and that the EEOT performed at both 6 and 8 mL/kg PBW failed to predict fluid responsiveness, in this surgical setting.

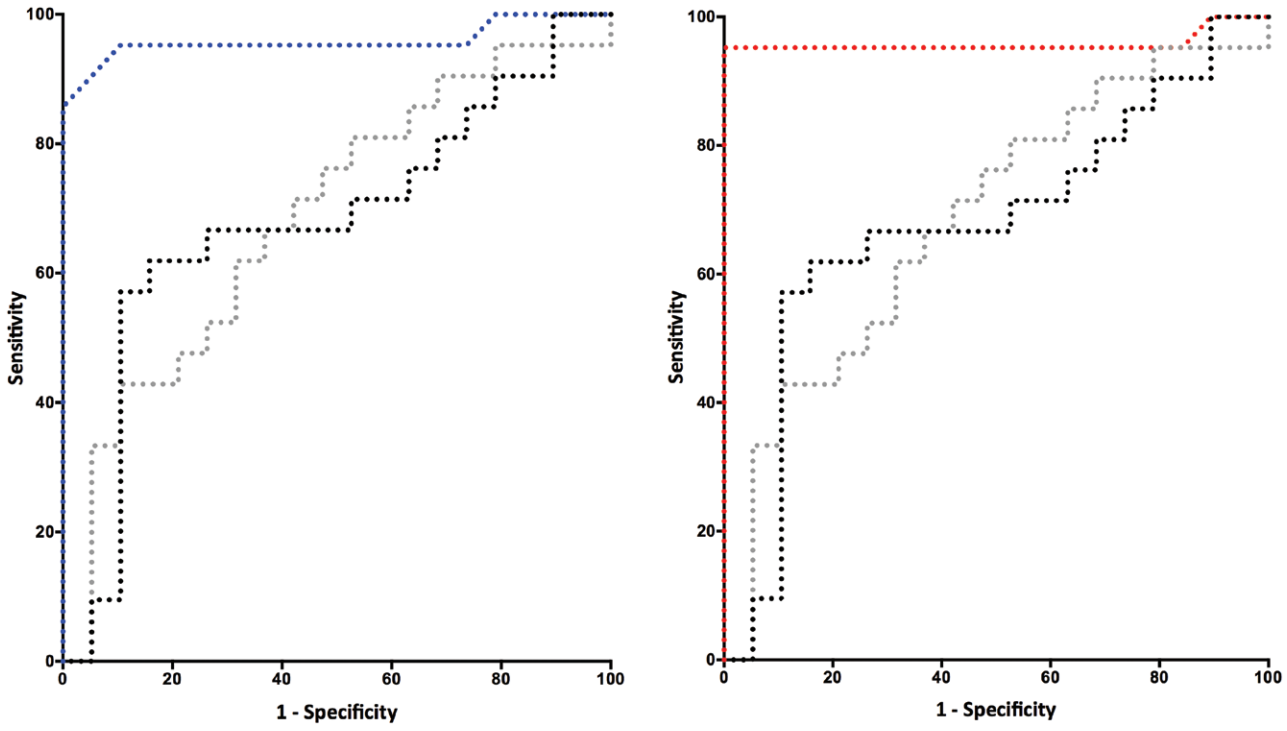

Figure 3. ROC curves of PPV and SVV variation after V_TC application (ΔPPV_{VTC} [blue line] and ΔSVV_{VTC} [red line]). The ROC curves of PPV (black line) and SVV (grey line) at T_3 are also reported in each figure (see text for further explanations). PPV indicates pulse pressure variation; ROC, receiver operating characteristics; SVV stroke volume variation; V_TC, tidal volume challenge.

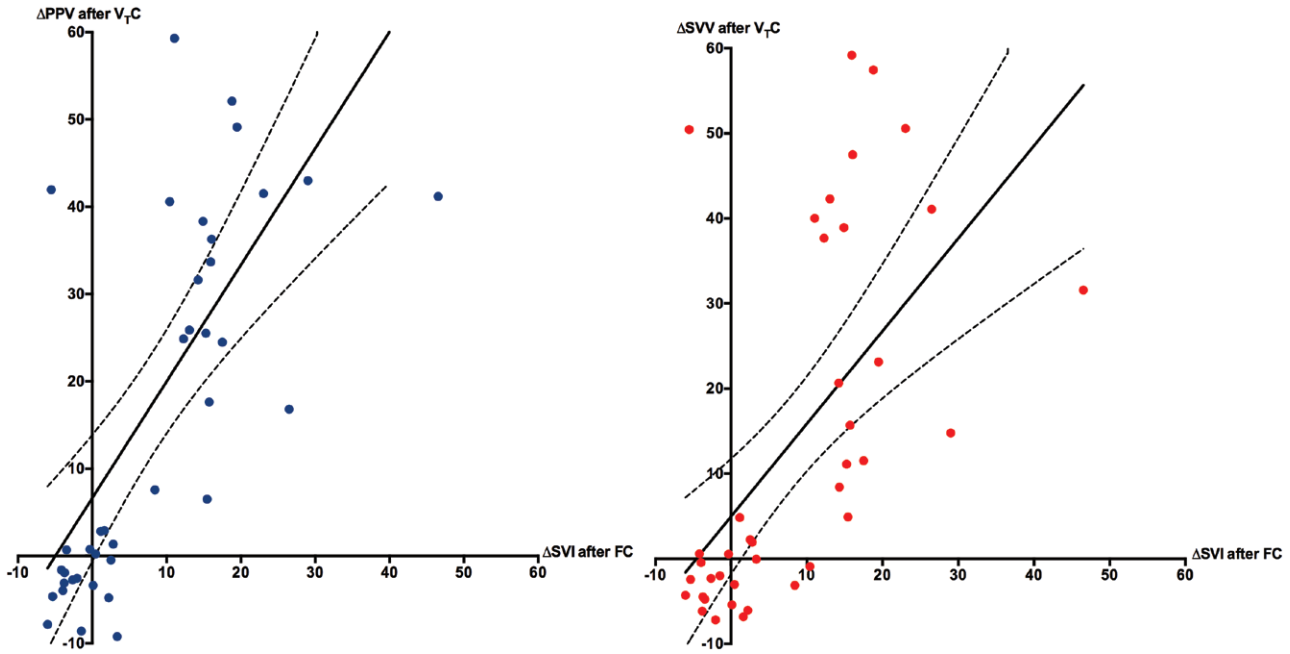

Figure 4. Relation between pulse and stroke volume variations after V_TC application (ΔPPV_{VTC} [r = 0.71] and ΔSVV_{VTC} [r = 0.68]) and the changes in stroke volume index (ΔSVI) after fluid challenge administration. PPV indicates pulse pressure variation; SVV stroke volume variation; V_TC, tidal volume challenge.

Perioperative blood pressure management is an important aspect of anesthetic care and the optimal approach to intraoperative fluid management remains a topic of debate.[24–28] These 2 points are closely related. Targeting intraoperative MAP is of key importance to reduce postoperative complications[29,30,31] and fluid administration should be guided by hemodynamic parameters, including functional hemodynamic tests, to prevent fluid overload,[32] which is associated with setting-specific complications during prone positioning, such as an increase in the orbital venous pressure and visual loss.[1]

In keeping with the findings of previous studies conducted in elective surgical patients, in our study, only about 50% of the enrolled patients responded to FC administration.[33] Baseline values of PPV and SVV were unable to predict preload dependence in the prone position.

In this study, the EEOT did not predict fluid responsiveness when performed in patients undergoing controlled mechanical ventilation with a V_T of either 6 or 8 mL/kg PBW. During an EEOT, the interruption to mechanical ventilation leads to an increase in venous return. This increased venous return causes an increase in SV from the preload-dependent right ventricle of volume responders and, in turn, the CI and SVI increase, to a greater extent than seen in nonresponders. However, previous studies evaluating the reliability of the EEOT during surgery demonstrated that the best threshold for discriminating fluid responsiveness is rather small, ranging between 4% and 6% of changes from baseline values for both CI and SVI.[11,16,34] Prone positioning reduces venous return mainly compressing the IVC and raising intra-abdominal pressure.[1,4,5] These effects could, in turn, dampen the changes in CI and SVI seen in response to the occlusion maneuver, meaning the changes are insufficient to discriminate between responders and nonresponders.

On the contrary, the sensitivity (95.2%) and specificity (94.7%) in predicting fluid responsiveness of both ΔPPV_{VTC} and ΔSVV_{VTC} were very high and the overall number of patients included within the grey zone very limited. Interestingly, the best thresholds for these variables (12.2% and 8.0% of increase from baseline, respectively) were lower than those first reported by Myatra et al[12] with a similar sensitivity and specificity, but for a 48% and 43% of increase in PPV and SVV, respectively, after the V_TC application. This finding could be related to differences in the extent of the hemodynamic effects of V_TC application in critically ill and elective surgical patients, due to differences in the heart-lung interactions among these populations.[35,36] In fact, a reduced respiratory system compliance, which is present in about 30% of critically ill patients,[36] affects the magnitude of the hemodynamic effect related to the transmission of the applied pressure to the great thoracic vessels and to the right heart. It also increases the baseline values of dynamic indexes.[9] Moreover, the prone position increases pulmonary vascular resistance and redistributes the pulmonary blood flow to dependent lung areas.[1] The correlation between the change in PPV and SVV after the V_TC application and the change in SVI after FC administration (Figure 4) suggests that prone positioning in surgical patients with normal respiratory compliance does not alter the complex interplay between volume status, the transmission of the applied pulmonary pressure to the heart, and the final effect on PPV and SVV, making the V_TC applicable in this setting. However, the cutoff value for this test is far from defined, because the comparability of the clinical research studies published so far is rather low.

Some limitations of this study should be acknowledged. First, in the present study, the EEOT has been applied by using a 30-second interruption, as previously described in surgical patients[7] and corresponding to the MostCare default

time-setting modality of averaging hemodynamic data. However, the EEOT was previously described in critically ill patients using a 15-second hold,[11,37,38] limiting the comparability of the results. Second, the duration of each step of the protocol (1 minute) could bias the results by introducing, to some extent, a carry-over effect. The ANOVA showed that the median SVI in the responder group before FC administration was lower than the SVI recorded at the other stages of the protocol. However, the impact of this finding seems to be more statistical than clinical (a median of 41 vs 43 or 45 mL/min/m^2). Third, the presence of artifacts in the arterial signal substantially influences the reliability of the MostCare. The data obtained in this study were from a center highly trained in the use of this device. Finally, we cannot exclude that the reproducibility of our results could be affected by the use of different prone positioning devices, which could influence the IVC compression and the respiratory system compliance somewhat differently from the Wilson frame.

CONCLUSIONS

In prone elective neurosurgical patients, the baseline values of PPV and SVV and the EEOT fail to predict fluid responsiveness, while the V_TC is a very reliable functional hemodynamic test and could be helpful in guiding intraoperative fluid therapy.

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Contribution: This author helped in the study design, in data interpretation, made critical revisions of the manuscript for important intellectual content and wrote the draft of the manuscript.
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