

CARDIOVASCULAR

Validation of pulse pressure variation and corrected flow time as predictors of fluid responsiveness in patients in the prone position

S.-Y. Yang¹, J.-K. Shim², Y. Song², S.-J. Seo² and Y.-L. Kwak^{2,3*}

¹ Department of Anaesthesiology and Pain Medicine, Chung-Ang University College of Medicine, Seoul, Republic of Korea

² Department of Anaesthesiology and Pain Medicine, Anaesthesia and Pain Research Institute, Yonsei University Health System, 50 Yonsei-ro, Seodaemun-Gu, Seoul 120-752, Republic of Korea

³ Severance Biomedical Science Institute, Yonsei University College of Medicine, Seoul, Republic of Korea

* Corresponding author. E-mail: ylkwak@yuhs.ac

Editor's key points

- Pulse pressure variability, corrected flow time, and other derived indices can predict cardiovascular responses to i.v. fluids.
- This study investigated the accuracy of pulse pressure variability and corrected flow time during surgery in the prone position.
- Both predicted fluid responsiveness whether the patient was prone or supine.
- More data are needed to confirm these findings.

Background. The aim of this prospective trial was to investigate the ability of pulse pressure variation (PPV) and corrected flow time (FTc) to predict fluid responsiveness in the prone position.

Methods. Forty-four patients undergoing lumbar spine surgery in the prone position on a Wilson frame were prospectively studied. PPV and FTc were measured before and after a colloid bolus (6 ml kg⁻¹) both in the supine and in the prone positions. Fluid responsiveness was defined as an increase in the stroke volume index of $\geq 10\%$ as measured by oesophageal Doppler.

Results. In the supine position, 26 patients were responders and the areas under the curve (AUC) of the receiver-operator characteristic (ROC) curves of PPV and FTc were 0.935 [95% confidence interval (CI): 0.870–0.999, $P < 0.001$] and 0.822 (95% CI: 0.682–0.961, $P < 0.001$), respectively. The optimal cut-off PPV and FTc values were 15% (sensitivity 73%, specificity 94%) and 358 ms (sensitivity 88%, specificity 78%), respectively. In the prone position, 34 patients were responders and the AUCs of PPV and FTc were 0.969 (95% CI: 0.912–1.000, $P < 0.001$) and 0.846 (95% CI: 0.706–0.985, $P = 0.001$), respectively. The optimal cut-off PPV and FTc values were 14% (sensitivity 97%, specificity 90%) and 331 ms (sensitivity 77%, specificity 90%), respectively.

Conclusions. While the predictability of PPV was significantly higher than that of FTc in the prone position, both variables showed high predictability and remained as useful indices for guiding fluid therapy in prone patients with minimal alterations in their optimal cut-off values to predict fluid responsiveness.

Clinical trial registration. URL: <http://www.clinicaltrials.gov/ct2/show/NCT01646359?term=NCT01646359&rank=1> and unique identification number NCT01646359.

Keywords: fluids, i.v.; heart, cardiac output; monitoring, arterial pressure; position, prone

Accepted for publication: 12 October 2012

Adequate fluid therapy to optimize cardiac output is an essential part of anaesthetic management, yet is challenging because of the lack of appropriate indices. While invasively monitored cardiac filling pressures fail to predict fluid responsiveness,¹ increasing evidence suggests that less invasive dynamic indices such as pulse pressure variation (PPV) and stroke volume variation (SVV), which are derived from the arterial pressure waveform, may be more useful.^{2–3} Although less robust than PPV or SVV, the corrected flow time (FTc) measured non-invasively by oesophageal Doppler (OED) has

also been shown to be useful for intraoperative volume optimization.^{4–5}

PPV and SVV are based on the heart–lung interaction and reflect cyclic changes in stroke volume induced by mechanical ventilation in the closed-chest condition.⁶ Therefore, their ability to predict fluid responsiveness can be affected by factors that influence the arterial tone or the compliance of the respiratory system.^{7–9} FTc also can be influenced by changes in the systemic vascular resistance.¹⁰

Patients are placed in the prone position for many surgical procedures, including spine surgeries. Depending on the positioning system, the prone position induces increases in abdominal pressure, pulmonary and systemic vascular resistance, and a decrease in respiratory compliance;¹¹ all of these factors could influence the predictability and/or cut-off values of PPV, SVV, and FTc. However, the studies aimed at validating these indices of preload have mostly been performed with patients in the supine position; little data are available regarding the validity of these indices in patients in the prone position.

The aim of this prospective trial was to investigate the ability of PPV and FTc to predict fluid responsiveness in patients undergoing posterior lumbar spinal fusion using the Wilson frame.

Methods

Patients

After approval of the institutional review board and receiving informed consent from all patients, 44 patients undergoing elective posterior lumbar spinal fusion were studied in a university hospital setting. This study was registered with ClinicalTrials.gov (Ref: NCT01646359). Exclusion criteria were patients with a BMI >30 or <15 kg m⁻², valvular heart disease, left ventricular ejection fraction <50%, a history of lung disease, preoperative arrhythmia, and contraindications to OED monitoring probe insertion (i.e. oesophageal stent, carcinoma of the oesophagus or pharynx, previous oesophageal surgery, oesophageal stricture, oesophageal varices, pharyngeal pouch, and severe coagulopathy) (Fig. 1). Screening echocardiography was performed in patients who showed abnormal findings on preoperative evaluation (cardiac murmur, electrocardiogram, chest X-ray) to ensure the absence of valvular heart disease or ventricular dysfunction.

After the patients arrived at the operating theatre, pulse oximetry, three-lead ECG, and non-invasive arterial pressure monitoring were applied. Anaesthesia was induced with propofol (1.5–2.5 mg kg⁻¹) and remifentanyl (0.5–1 µg kg⁻¹), and tracheal intubation was facilitated with rocuronium (0.9 mg kg⁻¹). Patients' lungs were ventilated with a tidal volume of 10 ml kg⁻¹ of the ideal body weight, an I:E ratio of 1:1.9 in 50% oxygen with air without PEEP. After the last measurement of the assessed variables, tidal volume was reduced to 8 ml kg⁻¹ of the ideal body weight. Anaesthesia was maintained with continuous infusion of remifentanyl (0.05–0.2 µg kg⁻¹ min⁻¹) and sevoflurane (1.5%–2.5%) to maintain the bispectral index score between 40 and 60. After tracheal intubation, a radial artery cannula was inserted and the pressure transducer was zeroed at the mid-axillary level to ambient pressure. An OED probe (Cardio Q®; Deltex, Brighton, UK) was also inserted into the oesophagus and positioned ~35–40 cm from the teeth.

Arterial pressure waveforms were monitored through Philips Intelivue MP70 monitors (Intelivue MP70, Philips Medical Systems, Suresnes, France). PPV_{auto} was displayed in real time

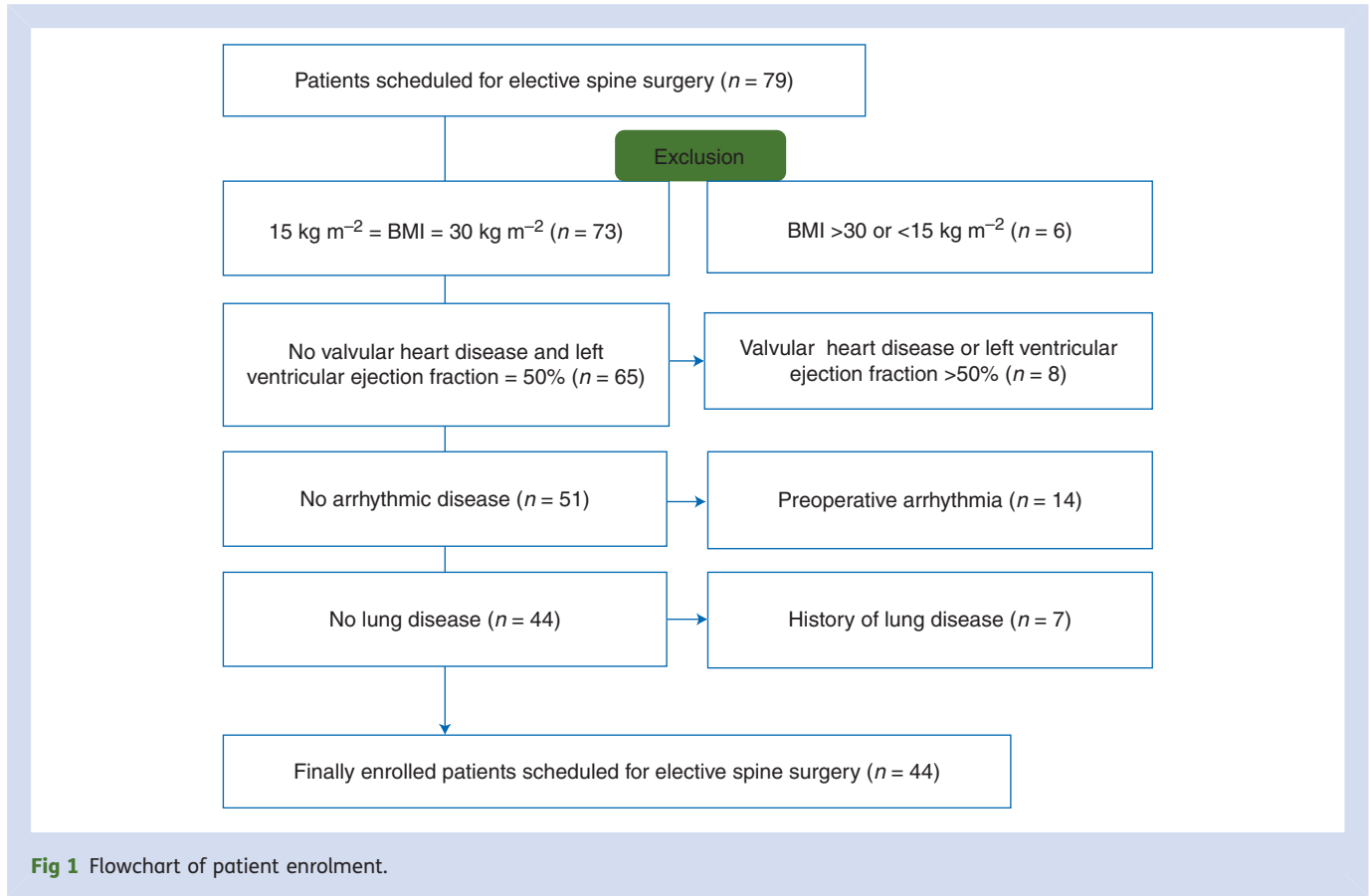
on the monitor and PPV_{auto} was determined from the arterial pressure waveform alone without airway pressure acquisition. PPV_{auto} is calculated by automatic detection algorithms, kernel smoothing, and rank-order filters based on seven consecutive steps (beat minima detection, beat maxima detection, beat mean calculation, pulse amplitude pressure, envelope estimation, pulse amplitude pressure estimation, and PPV estimation).¹² Averages of PPV_{auto} over four cycles of 8 s are calculated and displayed on the monitor.

The position of the OED probe was confirmed by continuously measuring the blood flow velocity in the descending thoracic aorta to find the optimum peak velocity and waveform signal. After positioning, the cardiac index (CI), stroke volume index (SVI), and FTc were continuously measured and displayed. The position of the OED probe was adjusted as necessary before each set of data collection to maintain optimum peak velocity and waveform.

Fifteen minutes after induction of anaesthesia with the patient in a supine position (T1), heart rate (HR), mean arterial pressure (MAP), CI, SVI, PPV_{auto}, FTc, and peak and mean airway pressure were measured. The dynamic and static compliance of the respiratory system were calculated (C_{dyn}=tidal volume/ peak pressure, C_{sts}=tidal volume/ plateau pressure). Thereafter, 6% hydroxyethyl starch solution (HES 130/0.4; Voluven®; Fresenius Kabi, Stans, Switzerland) per 6 ml kg⁻¹ of the ideal body weight was loaded for 10 min. Five minutes after completion of fluid loading (T2), the same variables listed above were measured and recorded. After all measurements, patients were turned to the prone position using a Wilson frame. Fifteen minutes after prone positioning (T3), the same haemodynamic and respiratory variables were measured, and surgery was started. During the operation, a second set of fluid loading was performed as decided by the attending anaesthesiologist, and haemodynamic and respiratory variables were collected before (T4) and 5 min after fluid loading (T5). All measurements were collected in a haemodynamically steady state without the use of vasoactive drugs. An independent investigator who was trained in manoeuvring the OED probe who was not involved in the current study assessed OED and all other variables during the study.

Statistical analysis

Statistical analysis was performed using SPSS 18.0 software (SPSS Inc., Chicago, IL, USA). All haemodynamic data were analysed as continuous variables and are expressed as mean (SD). A sample size of 44 patients achieves 82% power to detect a difference of 0.2 between the area under the curve (AUC) of the receiver-operator characteristic (ROC) curve under the null hypothesis of 0.7 and an AUC under the alternative hypothesis of 0.9 using a two-sided t-test at a significance level of 0.05. The χ^2 test was used to compare the types of operations between responders and non-responders. A Bonferroni-adjusted *P*-value (the normal *P*-value multiplied by the number of outcomes being tested) was applied to the comparisons of the



variables between T1 and T2, T2 and T3, and T3 and T4. The correlation between changes in SVI and initial haemodynamic variables was assessed using Pearson's correlation. Percentage differences in OED-derived SVIs before and after fluid challenge were used as principle indicators of fluid responsiveness. Patients were classified as responders to fluid loading if they showed an increase in SVI $\geq 10\%$, and as non-responders if they showed an increase of $<10\%$. To evaluate the abilities of PPV_{auto} and FTc to predict fluid responsiveness, the AUC of the ROC curves of the responders (AUC=0.5: no better than chance, no prediction possible; AUC=1.0: best possible prediction) were calculated and compared using the Hanley–McNeil test. $P < 0.05$ was considered statistically significant.

Results

Forty-four patients were included in the study (Fig. 1, Table 1).

In the supine position, fluid loading significantly increased SVI, while it decreased HR and PPV_{auto}. The remaining variables did not change after fluid loading. When the patients were turned to the prone position, PPV_{auto} increased significantly while FTc decreased significantly. The dynamic compliance and static compliance of the respiratory system were significantly reduced in the prone position compared with the supine position. There were no significant changes in HR, MAP, CI, or SVI between the supine and prone positions. In the prone position, MAP, CI, SVI, and FTc were

Table 1 Patients' characteristics. Age is expressed as mean (range). Other data are expressed as mean (sd) or number of patients. BMI, body mass index

Characteristics	
Age (yr)	56 (20–76)
Sex (male/female)	21/ 23
Height (cm)	164 (10)
Weight (kg)	63 (9)
BMI (kg m ⁻²)	23 (2)
ASA classification (I/II/III)	(22/22/0)
Hypertension/diabetes/stroke	16/5/2
Duration of surgery (min)	198 (84)
Levels operated (1/2/3/4)	7/12/14/1
Fluid administration (ml)	2612 (1354)
Blood loss (ml)	1055 (1002)

significantly increased after fluid loading, whereas PPV_{auto} was significantly decreased. The compliance of the respiratory system did not change after fluid loading in either the supine or the prone position (Table 2).

Twenty-six patients were responders in the supine position. SVI and FTc were significantly increased, and HR and PPV_{auto} were significantly decreased in responders. In the non-responders, no significant changes in the measured variables were observed, except for a reduction in PPV_{auto}.

Table 2 Changes in variables before and after fluid loading and positioning change. Data are expressed as mean (sd). T1, supine position before fluid loading; T2, supine position after fluid loading; T3, 15 min after prone positioning; T4, prone position before fluid loading; T5, prone position after fluid loading; HR, heart rate; MAP, mean arterial pressure; CI, cardiac index; SVI, stroke volume index; PPV, pulse pressure variation; FTc, corrected flow time; Ppeak, peak airway pressure; Pplat, plateau pressure, Cdyn, dynamic compliance of the respiratory system; Cstat, static compliance of the respiratory system. * $P < 0.05$ compared with T1; $^{\dagger}P < 0.05$ compared with T2. $^{\ddagger}P < 0.05$ compared with T4; P -values were adjusted using the Bonferroni correction

	T1	T2	T3	T4	T5
HR (beats min ⁻¹)	80 (12)	73 (10)*	72 (9)	66 (9)	66 (9)
MAP (mm Hg)	78 (14)	78 (11)	78 (11)	71 (8)	77 (10) [‡]
CI (litre min ⁻¹ m ⁻²)	2.9 (0.8)	3.2 (0.9)	3.0 (0.9)	2.5 (0.6)	3.0 (0.7) [‡]
SVI (litre min ⁻¹ m ⁻²)	37 (9)	43 (10)*	42 (11)	38 (9)	45 (10) [‡]
PPV (%)	14 (5)	7 (3)*	9 (3) [†]	16 (4)	10 (4) [‡]
FTc (ms)	353 (57)	384 (61)	350 (39) [†]	323 (38)	367 (32) [‡]
Ppeak (cm H ₂ O)	14 (3)	14 (3)	16 (3) [†]	18 (2)	18 (3)
Pplat (cm H ₂ O)	13 (3)	14 (3)	16 (3) [†]	17 (3)	17 (3)
Cdyn (ml cm H ₂ O ⁻¹)	45 (13)	44 (12)	37 (8) [†]	34 (7)	34 (7)
Cstat (ml cm H ₂ O ⁻¹)	48 (13)	48 (13)	39 (8) [†]	36 (8)	35 (7)

Table 3 Changes in haemodynamic variables after fluid loading in responders and non-responders in the supine position. Data are expressed as mean (sd). * $P < 0.05$ compared with before fluid loading. $^{\dagger}P < 0.05$ compared with baseline values (before fluid loading) in responders. HR, heart rate; MAP, mean arterial pressure; CI, cardiac index; SVI, stroke volume index; PPV, pulse pressure variation; FTc, corrected flow time

	Responders (n = 26)		Non-responders (n = 18)	
	Before	After	Before	After
HR (beats min ⁻¹)	83 (11)	74 (9)*	76 (12) [†]	72 (11)
MAP (mm Hg)	77 (15)	76 (13)	79 (12)	80 (9)
CI (litre min ⁻¹ m ⁻²)	2.9 (0.8)	3.3 (1)	3.0 (0.8)	3.0 (0.8)
SVI (litre min ⁻¹ m ⁻²)	35 (10)	45 (11)*	40 (8)	41 (8)
PPV (%)	17 (4)	8 (3)*	10 (2) [†]	5 (2)*
FTc (ms)	329 (38)	372 (42)*	387 (64) [†]	401 (79)
Fluid administration (ml)	2429 (1459)		2867 (1186)	
Blood loss (ml)	1024 (1042)		1097 (971)	

Baseline HR and PPV_{auto} were significantly greater and FTc was significantly shorter in the responders than in the non-responders (Table 3, Fig. 2).

In the prone position, 34 patients were responders after fluid loading. MAP, CI, SVI, and FTc were significantly increased and PPV_{auto} was significantly decreased in responders. In the non-responders, only PPV_{auto} was significantly decreased after fluid loading. Baseline PPV_{auto} was significantly greater and SVI and FTc were significantly lower in responders than in non-responders (Table 4, Fig. 2).

The degree of change in SVI after fluid loading was directly related to baseline PPV_{auto} and inversely related to baseline FTc, while it was not associated with baseline HR and MAP in either the supine or the prone position (Table 5).

In the supine position, the AUCs of the ROC curves of PPV_{auto} and FTc were 0.935 (95% CI: 0.870–0.999, $P < 0.001$) and 0.822 (95% CI: 0.682–0.961, $P < 0.001$), respectively. The optimal cut-off values of PPV_{auto} and FTc were 15% (sensitivity 73%, specificity 94%) and 358 ms (sensitivity 88%, specificity 78%), respectively (Fig. 3A). In the

prone position, the AUCs of PPV_{auto} and FTc were 0.969 (95% CI: 0.912–1.000, $P < 0.001$) and 0.846 (95% CI: 0.706–0.985, $P = 0.001$), respectively. The optimal cut-off values of PPV_{auto} and FTc were 14% (sensitivity 97%, specificity 90%) and 331 ms (sensitivity 77%, specificity 90%), respectively (Fig. 3B). There were no significant differences in the AUCs of the ROC curves of PPV_{auto} and FTc between the supine and prone positions ($P = 0.434$ and 0.811 , respectively). There was a trend for the AUC of the ROC curve of PPV_{auto} to be larger than that of FTc in the supine position ($P = 0.097$); this difference became significant in the prone position ($P = 0.014$).

Discussion

In the current prospective study, we found that both FTc and PPV_{auto} were accurate predictors of fluid responsiveness in patients in the supine position and the prone position using a Wilson frame. The corresponding cut-off values that provided the greatest sum of sensitivity and specificity showed

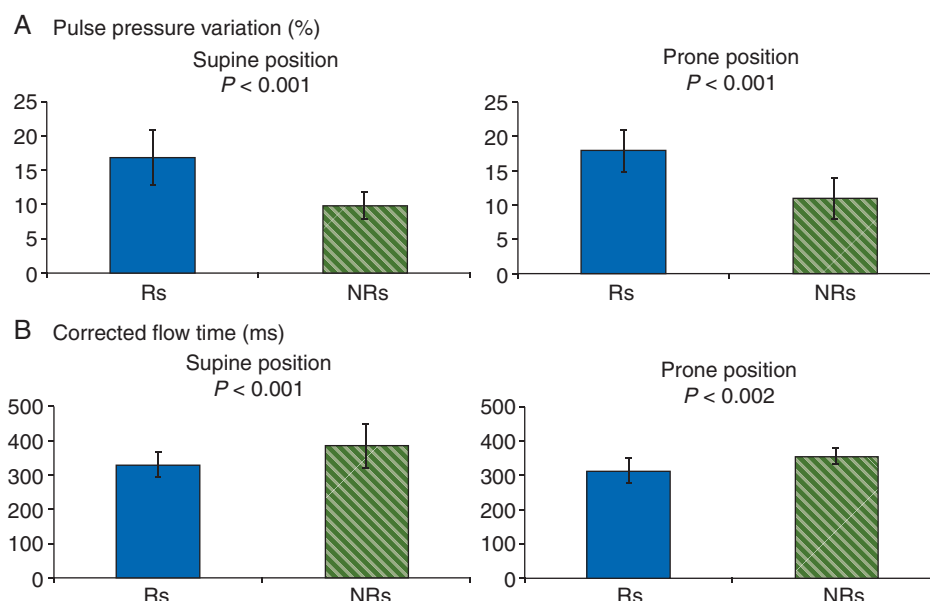


Fig 2 Mean, SD values of PPV (A) and corrected flow time (B) before fluid loading in responders (Rs) and non-responders (NRs) in the supine position and the prone position. In both the supine and the prone positions, PPV was significantly higher and corrected flow time was significantly lower in the Rs compared with the NRs.

Table 4 Changes in haemodynamic variables after fluid loading in responders and non-responders in the prone position. Data are expressed as mean (SD). * $P < 0.05$ compared with before fluid loading. † $P < 0.05$ compared with baseline values (before fluid loading) in responders. HR, heart rate; MAP, mean arterial pressure; CI, cardiac index; SVI, stroke volume index; PPV, pulse pressure variation; FTc, corrected flow time

	Responders (n = 34)		Non-responders (n = 10)	
	Before	After	Before	After
HR (beats min ⁻¹)	68 (8)	68 (10)	62 (9)	63 (7)
MAP (mm Hg)	71 (8)	76 (10)*	73 (9)	81 (10)
CI (litre min ⁻¹ m ⁻²)	2.4 (0.6)	3.0 (0.8)*	2.8 (0.6)	2.9 (0.6)
SVI (litre min ⁻¹ m ⁻²)	36 (9)	44 (10)*	45 (6)†	46 (8)
PPV (%)	18 (3)	11 (3)*	11 (3)†	6 (2)*
FTc (ms)	313 (37)	367 (34)*	355 (23)†	365 (26)
Fluid administration (ml)	2727 (1412)		2235 (1124)	
Blood loss (ml)	115 (1074)		735 (661)	

minimal alterations in the prone position. Intraoperative optimization of cardiac output using volume expansion has been shown to reduce the length of hospital stay, the incidence of critical care admission, and mortality after surgery, while inappropriate fluid administration might be harmful.^{13 14} Therefore, appropriate indices to guide fluid therapy are essential for effective haemodynamic management during the perioperative period. Unfortunately, however, commonly used static indicators of fluid responsiveness, such as central venous pressure and pulmonary artery occlusion pressure, are not accurate predictors of the effects of fluid administration.

In contrast to static variables, numerous studies have validated the usefulness of dynamic indices based on the heart-lung interaction for guiding volume resuscitation in patients

under mechanical ventilation. Values derived from respiratory changes in arterial pressure waveform, such as SVV and PPV, have been demonstrated to be able to predict fluid responsiveness in surgical or critically ill patients.^{2 3 15 16} In conjunction, efforts have also been made to validate the role of these variables as components of goal-directed therapies to improve patient outcomes.^{17 18} However, as these variables rely on the heart-lung interaction under mechanical ventilation, they can be influenced by factors such as increased abdominal pressure^{19–21} or reduced lung compliance.^{8 16}

FTc, although a static index, has been reported to predict fluid responsiveness in different surgical settings performed with patients in the supine position.^{5 22} OED-guided fluid therapy, including FTc, improved patients' recovery and

decreased postoperative hospital stay.^{4 23} FTc, however, is also inversely related to systemic vascular resistance. Therefore, numerous other conditions that affect the afterload can modify FTc.¹⁰

In current anaesthetic practice, numerous surgical procedures, including spinal surgeries, are performed with the patient in the prone position, which induces various physiological changes.^{11 24 25} The prone position increases abdominal pressure, which results in reduced venous return and lung compliance.²⁵ Theoretically, the resultant changes in right ventricular preload and afterload^{26 27} and the transmission of airway pressure to the intracardiac cavities can affect the reliability and cut-off values of SVV, PPV, and FTc for predicting fluid responsiveness.⁷ Indeed, altered cut-off values of SVV measured with FloTrac and PPV measured manually in the prone position have been reported.²⁸ Thus, the validity of each specific index of fluid responsiveness should not be extrapolated to surgical procedures in the prone position. As surgeries on the spine are often associated with a significant amount of blood loss requiring fluid resuscitation,

validation of indices that can guide preload optimization is of great clinical significance, while evidence in that regard is limited.

As our results indicate, PPV_{auto} and FTc demonstrated high predictability for fluid responsiveness in both the supine and the prone positions. Although without statistical significance, the AUC of the ROC curves of both PPV_{auto} and FTc were larger in the prone position than in the supine position. The optimal cut-off values of PPV_{auto} and FTc were both lower in the prone position vs the supine position, but without statistical significance. In the current study, all responders in the supine position were also responders in the prone position. The corresponding PPV_{auto} and FTc values of the non-responders in the supine position who became responders in the prone position were 10 (2)% and 394 (66) ms, respectively. Considering their optimal cut-off values to predict fluid responsiveness, these findings indicate that these patients were not on the steep portion of the Frank–Starling’s curve in the supine position, confirming the validity of the tested indices regardless of the patients’ position.

Similar results had been observed in a previous study that assessed the predictability of SVV measured by FloTrac and PPV measured manually in patients in the prone position; the authors reported that the ability of these variables to predict fluid responsiveness was retained in the prone position, but that the optimal cut-off values of SVV and PPV were both significantly higher in the prone position than in the supine position.²⁸ Although evidence is limited regarding the changes in the predictability and cut-off values of PPV and FTc in the prone position, it is reasonable to assume that the cut-off values would change for the following reasons: partial compression of the abdomen, reduced compliance of the respiratory system, and positioning of the

Table 5 The relationships between haemodynamic variables and changes in SVI in the supine and the prone positions. HR, heart rate; MAP, mean arterial pressure; PPV, pulse pressure variation; FTc, corrected flow time

	Supine		Prone	
	Rho	P-value	Rho	P-value
HR	0.34	0.023	0.2	0.195
MAP	−0.08	0.621	−0.23	0.131
PPV	0.72	<0.0001	0.66	<0.0001
FTc	−0.52	0.0003	−0.41	0.005

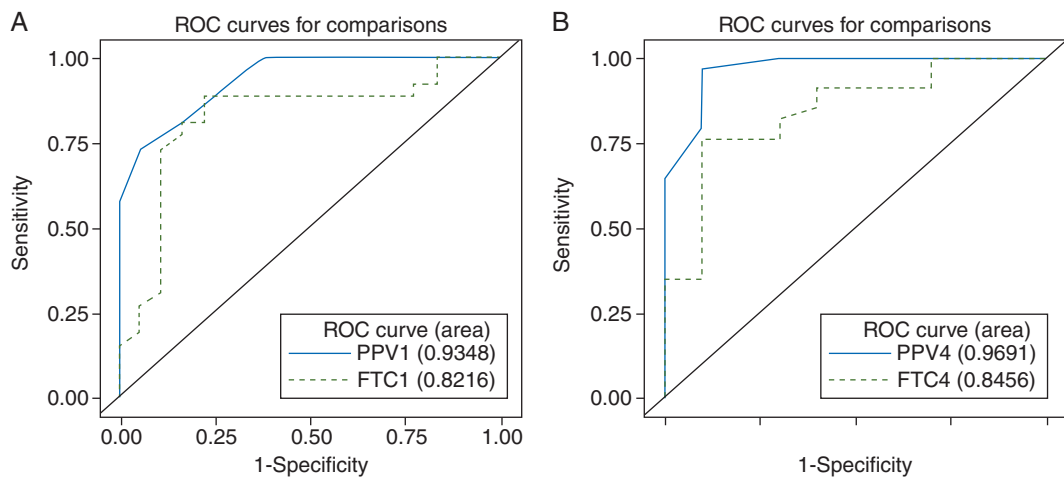


Fig 3 ROC curves of automated PPV (PPV_{auto}) and time-corrected aortic flow (FTc) of predictability for fluid responsiveness. (A) In the supine position, the AUC of PPV_{auto} was 0.935 (95% CI: 0.870–0.999) with a cut-off value of 15% (sensitivity 73% and specificity 94%) and the ACU of FTc was 0.822 (95% CI: 0.682–0.961) with a cut-off value of 358 ms (sensitivity 88% and specificity 78%). (B) In the prone position, the AUC of PPV_{auto} was 0.969 (95% CI: 0.912–1.000) with a cut-off value of 14% (sensitivity 97% and specificity 90%) and the AUC of FTc was 0.846 (95% CI: 0.706–0.985) with a cut-off value of 331 ms (sensitivity 77% and specificity 90%). CI, confidence interval.

limbs lower than the heart could reduce the venous return and increase afterload, thereby affecting the tested indices.

There was a discrepancy between our study and that of Biais and colleagues²⁸ in the degree of change of the cut-off values of the preload indices in patients in the prone position. This could be because we used a Wilson frame to position the patients, whereas Biais and colleagues²⁸ used four pads (two chest and two pelvic supports). The degree of haemodynamic change may differ significantly according to the positioning system.¹¹ However, it is difficult to compare the possible differences in haemodynamic changes according to the positioning systems used in the current study and the study by Biais and colleagues, since a fluid bolus was administered in both studies in the supine position before turning to the prone position which may have masked the subsequent changes of the haemodynamic variables including CI in both studies. Secondly, increased intrathoracic pressure after reduced chest compliance after prone positioning is thought to impede venous return. Although the compliance of the respiratory system was significantly reduced in the current study in the prone position compared with the supine position, it was still preserved better than that reported by Biais and colleagues.²⁸ The highest peak airway pressure in the current study was <20 cm H₂O, which may not have been high enough to significantly impede venous return and increase right ventricular afterload, given that an airway driving pressure of 20 cm H₂O has been reported to be the threshold value above which the transmission of airway pressure to the intracardiac cavities is significantly affected.⁸ Thirdly, responders in our study were defined by an increase in SVI >10% after a fluid bolus, based on previous studies,^{2,5} whereas Biais and colleagues used an increase in cardiac output ≥15% to define responders. Because cardiac output is also determined by HR, defining responders by SVI could be argued to be more appropriate. However, different cut-off values based on different definitions yield different ROC curve analysis results. Furthermore, we used a fluid bolus volume of 6 ml kg⁻¹ colloid, while Biais and colleagues²⁸ used 500 ml of colloid. In most clinical situations, a fluid bolus of 200–300 ml is usually used first as a fluid challenge. However, in the absence of ventricular dysfunction, a larger fluid bolus is more likely to result in an increase in SV and so we used a colloid volume of 6 ml kg⁻¹. However, considering the mean weight of the patients in the current study, the fluid bolus would be less (~360 ml) compared with the 500 ml used in the study by Biais and colleagues.²⁸

Although not statistically significant, MAP was increased in the non-responders in the prone position after fluid challenge in the absence of an increase in CI and SVI. While the exact reason remains unclear, changes in the sympathetic tone (common during surgical procedures on the spine requiring retraction of the nerve roots) may have increased the systemic vascular resistance resulting in an increase in MAP without an increase in SVI.

A limitation of our study is that although cardiac output and stroke volume measured by OED have been shown to

correlate well with those measured by the thermodilution technique or a conductance catheter and aortic flow probe,^{29,30} OED assumes a fixed aortic area and a constant proportional descending aortic flow during systolic phase. These assumptions may be invalid if there are alterations in aortic geometry or sympathetic tone.

In conclusion, both PPV_{auto} and FTc were good predictors of fluid responsiveness in patients placed in the prone position using the Wilson frame with insignificant alterations in their cut-off values. While the predictability of PPV_{auto} was significantly higher than that of FTc in the prone position as assessed by the AUC of the ROC curve, both variables were accurate predictors of fluid responsiveness and could serve as useful indices to guide fluid therapy in prone patients.

Declaration of interest

None declared.

Funding

This work was supported by departmental sources only.

References

- 1 Kumar A, Anel R, Bunnell E, et al. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. *Crit Care Med* 2004; **32**: 691–9
- 2 Derichard A, Robin E, Tavernier B, et al. Automated pulse pressure and stroke volume variations from radial artery: evaluation during major abdominal surgery. *Br J Anaesth* 2009; **103**: 678–84
- 3 Biais M, Nouette-Gaulain K, Rouillet S, Quinart A, Revel P, Sztark F. A comparison of stroke volume variation measured by Vigileo/FloTrac system and aortic Doppler echocardiography. *Anesth Analg* 2009; **109**: 466–9
- 4 Wakeling HG, McFall MR, Jenkins CS, et al. Intraoperative oesophageal Doppler guided fluid management shortens post-operative hospital stay after major bowel surgery. *Br J Anaesth* 2005; **95**: 634–42
- 5 Lee JH, Kim JT, Yoon SZ, et al. Evaluation of corrected flow time in oesophageal Doppler as a predictor of fluid responsiveness. *Br J Anaesth* 2007; **99**: 343–8
- 6 Michard F. Changes in arterial pressure during mechanical ventilation. *Anesthesiology* 2005; **103**: 419–28; quiz 49–5
- 7 Reuter DA, Goresch T, Goepfert MS, Wildhirt SM, Kilger E, Goetz AE. Effects of mid-line thoracotomy on the interaction between mechanical ventilation and cardiac filling during cardiac surgery. *Br J Anaesth* 2004; **92**: 808–13
- 8 Muller L, Louart G, Bousquet PJ, et al. The influence of the airway driving pressure on pulsed pressure variation as a predictor of fluid responsiveness. *Intensive Care Med* 2010; **36**: 496–503
- 9 Kim HK, Pinsky MR. Effect of tidal volume, sampling duration, and cardiac contractility on pulse pressure and stroke volume variation during positive-pressure ventilation. *Crit Care Med* 2008; **36**: 2858–62
- 10 Singer M, Allen MJ, Webb AR, Bennett ED. Effects of alterations in left ventricular filling, contractility, and systemic vascular resistance on the ascending aortic blood velocity waveform of normal subjects. *Crit Care Med* 1991; **19**: 1138–45

- 11 Dharmavaram S, Jellish WS, Nockels RP, et al. Effect of prone positioning systems on hemodynamic and cardiac function during lumbar spine surgery: an echocardiographic study. *Spine (Phila Pa 1976)* 2006; **31**: 1388–93; discussion 94
- 12 Aboy M, McNamers J, Thong T, Phillips CR, Ellenby MS, Goldstein B. A novel algorithm to estimate the pulse pressure variation index deltaPP. *IEEE Trans Biomed Eng* 2004; **51**: 2198–203
- 13 Gan TJ, Soppitt A, Maroof M, et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. *Anesthesiology* 2002; **97**: 820–6
- 14 Sinclair S, James S, Singer M. Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: randomised controlled trial. *Br Med J* 1997; **315**: 909–12
- 15 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**: 64–9
- 16 Mesquida J, Kim HK, Pinsky MR. Effect of tidal volume, intrathoracic pressure, and cardiac contractility on variations in pulse pressure, stroke volume, and intrathoracic blood volume. *Intensive Care Med* 2011; **37**: 1672–9
- 17 Willars C, Dada A, Hughes T, Green D. Functional haemodynamic monitoring: the value of SVV as measured by the LiDCORapid in predicting fluid responsiveness in high risk vascular surgical patients. *Int J Surg* 2012; **10**: 148–52
- 18 Broch O, Bein B, Gruenewald M, et al. Accuracy of the pleth variability index to predict fluid responsiveness depends on the perfusion index. *Acta Anaesthesiol Scand* 2011; **55**: 686–93
- 19 Jacques D, Bendjelid K, Duperret S, Colling J, Piriou V, Viale JP. Pulse pressure variation and stroke volume variation during increased intra-abdominal pressure: an experimental study. *Crit Care* 2011; **15**: R33
- 20 Renner J, Gruenewald M, Quaden R, et al. Influence of increased intra-abdominal pressure on fluid responsiveness predicted by pulse pressure variation and stroke volume variation in a porcine model. *Crit Care Med* 2009; **37**: 650–8
- 21 Duperret S, Lhuillier F, Piriou V, et al. Increased intra-abdominal pressure affects respiratory variations in arterial pressure in normovolaemic and hypovolaemic mechanically ventilated healthy pigs. *Intensive Care Med* 2007; **33**: 163–71
- 22 Monnet X, Rienzo M, Osman D, et al. Esophageal Doppler monitoring predicts fluid responsiveness in critically ill ventilated patients. *Intensive Care Med* 2005; **31**: 1195–201
- 23 Abbas SM, Hill AG. Systematic review of the literature for the use of oesophageal Doppler monitor for fluid replacement in major abdominal surgery. *Anaesthesia* 2008; **63**: 44–51
- 24 Yokoyama M, Ueda W, Hirakawa M, Yamamoto H. Hemodynamic effect of the prone position during anesthesia. *Acta Anaesthesiol Scand* 1991; **35**: 741–4
- 25 Marks R, Silverman R, Fernandez R, Candiotti KA, Fu E. Does the systolic pressure variation change in the prone position? *J Clin Monit Comput* 2009; **23**: 279–82
- 26 Mahjoub Y, Pila C, Friggeri A, et al. Assessing fluid responsiveness in critically ill patients: false-positive pulse pressure variation is detected by Doppler echocardiographic evaluation of the right ventricle. *Crit Care Med* 2009; **37**: 2570–5
- 27 Vieillard-Baron A, Charron C. Preload responsiveness or right ventricular dysfunction? *Crit Care Med* 2009; **37**: 2662–3
- 28 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**: 407–13
- 29 Valtier B, Cholley BP, Belot JP, de la Coussaye JE, Mateo J, Payen DM. Noninvasive monitoring of cardiac output in critically ill patients using transesophageal Doppler. *Am J Respir Crit Care Med* 1998; **158**: 77–83
- 30 Gunn SR, Kim HK, Harrigan PW, Pinsky MR. Ability of pulse contour and esophageal Doppler to estimate rapid changes in stroke volume. *Intensive Care Med* 2006; **32**: 1537–46

Handling editor: J. P. Thompson