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Effect of prone position without volume expansion on pulse pressure variation in spinal surgery : a prospective observational study

H. Jabbour (*), M. Abou Haidar (*), K. Jabbour (*), A. Abi Lutfallah (*), H. Abou Zeid (*), I. Ghanem (**), N. Naccache (*), E. Ayoub (*)

Abstract : *Background :* Pulse pressure variation (PPV) is a predictor of fluid responsiveness in supine patients under mechanical ventilation. Its use has also been validated in the prone position. The aim of this study was to assess changes in PPV induced by prone position in patients undergoing spinal surgery.

Methods : Ninety-six patients aged 12 to 75 years, scheduled for elective spinal surgery were included. Patients were excluded if they had clinical signs related to any organ failure, or if they required vasoactive drugs and/or volume expansion during the early stages of anesthesia. Patients received a standardized anesthesia protocol. Fluid expansion was not allowed from induction until 10 minutes after positioning. Hemodynamic measurements recorded before the induction of anesthesia (T0) included : arterial pressure (systolic (SAP) diastolic (DAP) and mean (MAP)) and heart rate (HR). Radial artery was cannulated after intubation and measurements, as well as PPV, were noted in supine position (T1). Patients were then placed in prone position hemodynamics and PPV measurements were repeated (T2).

Results : Forty-eight patients completed the study. Anesthesia induction induced a significant decrease in SAP, DAP, and MAP with no effect on HR. Prone position did not induce any significant changes in SAP, MAP, DAP, and HR. A significant difference was found between PPV values in supine (Mean=10.5, SD=4.5) and prone positions (Mean=15.2, SD=7.1) ; t=-4.15 ($p<0.001$). The mean increase in PPV was 4.7%.

Conclusion : Prone position without prior volume expansion induces a significant increase in PPV prior to any modification in arterial blood pressure and heart rate.

Keywords : Hemodynamics ; Prone position ; spine ; pulse pressure ; monitoring ; fluid response

Introduction

Perioperative fluid therapy, aiming to optimize cardiac output and tissue perfusion is an essential part of the management of surgical patients during anesthesia (1). Perioperative hypovolemia, as well as fluid overload, can have negative effects on patient morbidity and mortality during and after surgery (2). Hypovolemia can lead to inadequate tissue perfusion, causing shock and organ dysfunction. Hypervolemia can lead to cardiopulmonary dysfunction and interstitial edema, increasing the risk of postoperative complications and longer recovery" (2). Goal-directed fluid therapy using dynamic indices, based on heart-lung interactions, is now the standard in the management of fluid balance during surgery and especially in high-risk patients (3). On the other hand, mean arterial pressure, heart rate, and central venous pressure do not precisely reflect intravascular status (4, 5). Pulse pressure variation (PPV) is an accurate predictor of fluid responsiveness and is widely used in hemodynamic optimization in the perioperative setting (6). PPV aims to predict an increase in cardiac output induced by volume expansion before a fluid challenge is performed (4). It has been shown that PPV-based fluid management, is associated with a significant decrease in post-surgical morbidity and length of stay (7).

The principles behind the use of PPV are based on the fact that intermittent positive-pressure ventilation induces cyclic changes in intrathoracic blood volumes, and consequently, modifies the loading conditions of the left and right ventricles (8, 9). These changes in stroke volume are greater when the ventricles are operating at a preload dependent

Hicham Jabbour, MD, PhD; Marc Abou Haidar, MD; Khalil Jabbour, MD; Antoine Abi Lutfallah; Hicham Abou Zeid, MD; Ismat Ghanem, MD, PhD; Nicole Naccache; Eliane Ayoub.

(*) Department of Anesthesia and Critical Care, Hotel Dieu de France, Saint Joseph University, Beirut, Lebanon.

(**) Department of Orthopedic Surgery, Hotel Dieu de France, Saint Joseph University, Beirut, Lebanon.

Corresponding author : Marc Abou Haidar, SAM building 2 Third floor, deek el mehdi, Metn, Lebanon. POBOX 1205. Phone : +961 70438320.

Email : marc.abouhaidar1@gmail.com
marc.abouhaidar@net.usj.edu.lb

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state, on the steep portion of the Frank Starling curve (8). PPV is the marker, with the largest amount of evidence, that can predict the response of cardiac output to volume expansion (10). The median threshold level for PPV to predict fluid responsiveness in a recent meta-analysis was 12% (interquartile range 10 to 13%). Studies reported a sensitivity of 0.88 and a specificity of 0.89 (11). However, the use of PPV has its limitations, as certain conditions can lead to false interpretations of PPV values. Spontaneous breathing, cardiac arrhythmias, increased intra-abdominal pressure, and right ventricular failure are conditions that generate false positive PPV values ; whereas an open chest, a high respiratory rate (HR/RR<3.6), a low tidal volume, and a decreased chest compliance will produce false negative results (10). PPV is also influenced by factors that affect arterial tone but remains the best among other dynamic indices to predict fluid responsiveness in patients receiving vasopressors (12). Recently an approach using the gray zone (PPV values, between 9% and 13%, for which fluid responsiveness cannot be reliably predicted), instead of a single threshold value for conducting goal-directed therapy has been found to improve fluid management of patients undergoing surgery (6).

Hemodynamic management during spinal surgery is largely affected by intraoperative bleeding as well as the surgical position (13, 14). Spinal surgery requires patients to be placed in the prone position, which is shown to decrease cardiac output and chest compliance as well as causing inferior vena cava obstruction by increasing intra-abdominal pressure (13, 15). These factors can impact heart-lung interactions and therefore have significant effects on PPV. Additionally, static indices such as central venous pressure and pulmonary artery occlusion pressure do not correlate with right and left ventricular end-diastolic volumes in the prone position (14). PPV is shown to be valid in the prone position, (16, 17) but studies show conflicting results regarding the change in its value.

We hypothesized that the prone position, without previous volume expansion, increases the value of PPV.

The aim of this prospective observational study is to determine the exact influence of prone positioning on PPV while excluding confusion factors (false positioning, abdominal compression, external stimulation, and fluid challenges), that may influence fluid status and hemodynamics.

Methods

Patients and hemodynamic monitoring

This manuscript adheres to the applicable STROBE guidelines. Approval was secured from the Institutional review board : Université Saint-Joseph Centre Universitaire d'Ethique, (Tfem/2016/04). Written informed consent was obtained from all subjects, a legal surrogate, the parents, or legal guardians for minor subjects. Ninety-six patients, aged between 12 and 75 years and scheduled for elective spinal surgery between April 2016-January 2017, were included in this mono-center, prospective observational study.

Exclusion criteria were : age superior to 75 years, uncontrolled arterial hypertension, arrhythmias (Atrial fibrillation, frequent ventricular extra-systoles, or any abnormal rhythm), left ventricular ejection fraction <50%, valvular heart disease, BMI > 35kg m^{-2} or < 15kg m^{-2}, advanced lung disease, and fever, defined by a central body temperature >38.2 °C. Preoperative anesthesia consultation helped collect medical information regarding the use of medications such as beta-blockers, angiotensin receptor blockers (ARB), angiotensin conversion enzyme (ACE) inhibitors, and calcium channel blockers (CCB). Patients requiring vasoactive drugs and or volume expansion during the first 10 minutes of prone position were secondarily excluded. The lower threshold of mean arterial pressure (MAP) before administration of vasoactive drugs and or fluid expansion was 65 mmHg. The upper threshold for MAP before administration of anti-hypertensive agents was 120 mmHg. All patients were on an empty stomach and no volume expansion was applied before surgery.

Upon arrival in the operating room, a three-lead ECG, a noninvasive arterial pressure monitoring, and a pulse oximetry were installed. All patients had an Entropy measurement and neuromuscular monitoring. Hemodynamic parameters : systolic arterial pressure (SAP), diastolic arterial pressure (DAP), MAP, heart rate (HR), and blood oxygen saturation (SaO2), were recorded while patients were in the supine position, before induction of anesthesia, at time **T0**.

All patients received the same standardized protocol of general anesthesia. Propofol Target controlled infusion (Propofol Lipuro 1% BBraun, Mode : Schnider Effect, CE= Effect-site concentration), CE= 6 mcg at induction then reduced to CE=3mcg. Sufentanil 0.1-0.2 mcg/kg IV bolus. A dose of rocuronium 0.6 mg/kg IV was used to facilitate tracheal intubation.

Lungs were ventilated with a tidal volume of 8ml/kg of the ideal body weight, a I :E ratio of 1:2, at a rate of 12/min, PEEP was set at 4 cm H2O. Anesthesia was maintained with a propofol concentration effect CE 2-4 mcg depending on hemodynamics and Entropy status.

Afterward, a catheter was inserted in either the left or right radial artery (Plastimed catheter 3F 1mm by 4cm) for invasive and continuous monitoring of arterial pressure. The pressure transducer was zeroed at the phlebostatic axis (fourth intercostal space midway between anterior and posterior chest wall). The arterial pressure waveform was displayed in real-time on the monitor (GE Healthcare Avance CS2). Pulse pressure was defined as the difference between systolic and diastolic arterial pressure. Both maximal and minimal pulse pressures were measured over the same respiratory cycle. PPV was automatically calculated and averages of PPV over four respiratory cycles were calculated.

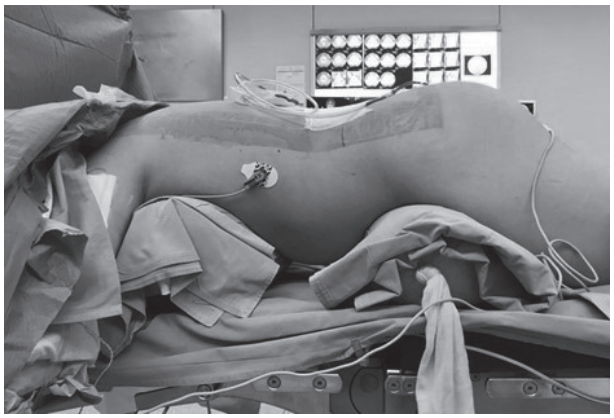

Fig. 1. – Prone positioning system.

Stimulation of patients was avoided, and all measurements were made after verification of neuromuscular blockade, post-tetanic count (PTC) <15. Fluid expansion was not allowed at any time from induction till 10 minutes after prone position.

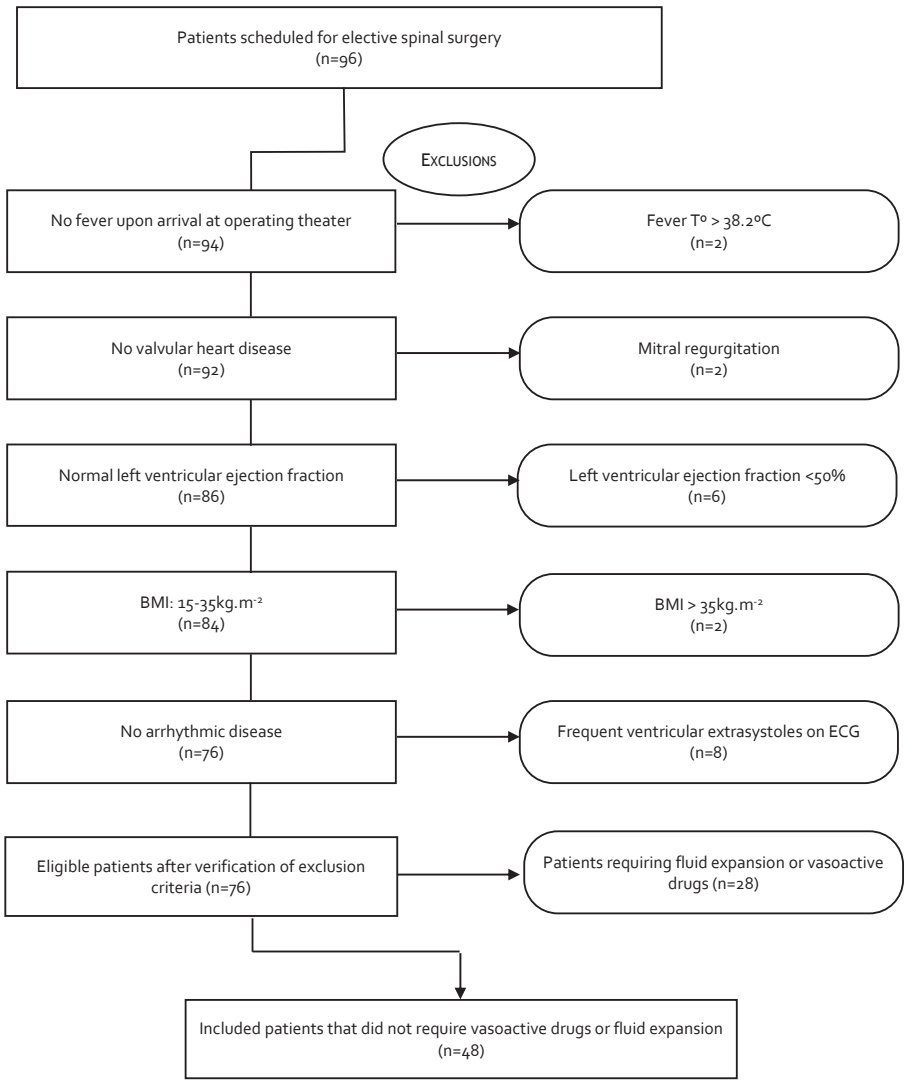

Fig. 2. – Flowchart of patient enrolment. BMI : body mass index.

Hemodynamic data recordings were obtained while patients had an entropy value between 40 and 60.

The second measurement of hemodynamics and PPV were made in the supine position while avoiding any stimulation for 10 minutes at time **T1**.

Patients were then turned into the prone position using two pads at the level of the anterior superior iliac spine to support the pelvis, and a single rectangular bolster to support the chest to allow the abdomen to hang free. The lower body and legs were free no extrinsic compression was applied. (Figure 1) Ten minutes after prone positioning, without fluid expansion, hemodynamics and PPV measurements were repeated at time **T2** after verification that PTC was <15**.**

Table I

Characteristics of the subjects. Variables are presented as mean (SD) and Numbers (%)

Characteristics	
Number of patients	48
Age (yr)	41 (25)
Weight (kg)	66 (15)
Height (cm)	165 (8)
BMI (kg m^{-2})	24 (5)
DAP (mmHg)	75 (8)
SAP (mmHg)	124 (21)
HR (beats/min)	83 (14)
ASA classification I	24 (50%)
ASA classification II	24 (50%)
ASA classification III	0 (0%)
Sex female/male	38(79%)/10(20%)
Diabetes	6 (12.5%)
Hypertension	6 (12.5%)
Use of ACE inhibitors or ARB	2 (4.2%)
Use of CCB	1 (2%)
Use of beta-blockers	5 (10.4%)

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Macintosh, version 20 (IBM Corp., Armonk, N.Y., USA). Hemodynamics were expressed as mean (SD : Standard deviation) and analyzed as continuous variables. Normality and homogeneity of variance tests were performed by application of Levene statistics to all the data.

Repeated ANOVA measures (one-way within-subjects) compared the effect of anesthesia induction and prone positioning on hemodynamic variables (SAP, DAP, MAP, HR, SaO2) measured at T0, T1, and T2. A p-value < 0.05 was considered statistically significant. The variables that demonstrated a difference between the groups (T0, T1, T2) were analyzed by a post hoc test to provide specific information on which means are significantly different from each other. A Bonferroni adjusted p-value (dividing the error rate by the number of tests) was applied in the comparison between different measure times. A paired t-test was used to compare the values of PPV between supine and prone position (T1 and T2), with a confidence interval of 95%, a statistically significant difference was considered for a p-value <0.05.

Results

Among the 96 patients initially enrolled in the study, 20 presented one or more exclusion criteria and were therefore eliminated. Additional 28 patients were excluded for requiring vasoactive drugs or fluid expansion. (Figure 2). Forty-eight patients fulfilled inclusion criteria and completed the study.

Hemodynamic variables at different times and comparisons are shown in Table 2.

Variations in hemodynamics SAP, DAP, MAP, HR, SaO2 :

No statistically significant variability was observed between the HR and SaO2 at different times

Table II

Hemodynamic Variables at different time points and comparison of respective means.

	T0	T1	T2	Overall p value
SAP (mmHg)	131.04 (24.28) *	107.43 (26.67) **	97.13 (13.72)	0.001
DAP (mmHg)	74.52 (11.92) *	61.13 (13.50) **	58.91 (9.08)	0.001
MAP (mmHg)	94.91 (15.23) *	75.78 (16.56)**	73.69 (11.49)	0.001
HR (bpm)	82.52 (14.99)	75.52 (16.24)	73.65 (17.10)	0.219
SaO2 (%)	98.39 (1.37)	99.26 (0.54)	97.26 (6.91)	0.204

Values are mean (SD). T0, supine position before anesthesia. T1, supine position after intubation. T2, prone position. SAP, systolic arterial pressure. DAP, diastolic arterial pressure. MAP, mean arterial pressure. HR, heart rate. SaO2, arterial oxygen saturation. bpm, beats per minute. * p<0.005 compared with T1, ** p<0.005 compared with T2. P-value adjusted using Bonferroni correction

(CI 95% and alfa 0.05). SAP, DAP, MAP, showed significant changes between T0 and T1 or T2.

Comparison between T0 and T1 showed that anesthesia induction induced a marked decrease in SAP ($p<0.005$), DAP ($p<0.001$), and MAP ($p<0.001$) with no effect on HR and SaO2. The difference was still present when T0 and T2 were compared with a decrease in the SAP ($p<0.001$), DAP ($p<0.001$), and MAP ($p<0.001$). When pressures were compared between supine and prone position after anesthesia no difference was observed. Prone positioning did not have a significant effect on the hemodynamic variables measured.

Effect of prone position on PPV

Analysis of differences between PPV means at T1 and T2 was done using a paired t-test. A significant difference was found between PPV values in supine (Mean=10.5%, SD=4.5) and prone position (Mean=15.2%, SD=7.1) ; $t = -4.15$ ($p<0.001$). The mean increase in PPV after prone positioning was found to be 4.7% (95% confidence interval, 2.3 to 6.9 ; $P<0.001$)

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Discussion

This study shows that the prone position during spinal surgery induces a significant increase in PPV before any change in arterial blood pressure and heart rate occurs. Yang et al. (16) and Biais et al. (17), have validated the use of PPV as an accurate predictor of fluid responsiveness to hemodynamic variations in the supine position. Yan et al also confirmed that a responder in the supine position will remain a responder in the prone position (16).

However, both studies did not produce the same results regarding the changed cut-off value for PPV to predict a positive fluid response in the prone position. Biais et al reported a cut-off value of 11% in supine and 15% in the prone position, compared to 15% in supine and 14% in the prone position for Yan et al. This difference can be attributed to multiples factors. In fact, both studies did not use the same method of positioning on the operating table. Biais et al used four supports, two pelvic and two thoracic pads. Yang et al used a Wilson frame for the prone position. The Wilson frame is known to induce more hemodynamic changes, mainly by reducing cardiac output (18). One of the best methods to reduce hemodynamic changes due to positioning and external compression, is to use a chest bolster and two pelvic pads under the anterior superior iliac spine (15). This was the method used in our study. In addition, both studies used a fluid challenge in supine and prone positions. The fluid challenge can alter PPV after changing positions since volume loading in a non-hypovolemic patient induces vasodilatation, thus altering arterial elastance (19). In this case PPV in prone position would be altered by the previous fluid challenge and would not be the result of hemodynamic changes induced by the change in positioning.

In our study, all patients underwent the same standardized anesthesia protocol. The system used for prone positioning had the least reported negative effect on venous return and chest compliance (20). No patient received a fluid bolus before and during the times of measurements and no vasoactive drugs were used to prevent any alteration in PPV predictability (19). All patients were safely positioned and kept at rest for 10 minutes without any stimulation or fluid expansion to limit any external confusion factor that would alter PPV measurement. The mean 4.7% augmentation in PPV found in this study is therefore related to prone positioning only. The cause of the augmentation is multifactorial : the heart positioned at a slightly higher hydrostatic level than the lower limbs induces a decrease in venous return (18). On the other hand, all prone positions will induce a certain degree of abdominal compression that causes direct pressure on the inferior vena cava resulting in an additional decrease in venous return by venous pooling (20, 21). Also, pulmonary pressure increases as chest wall compliance drops, impeding venous return as well (18, 22).For the same degree of volume responsiveness, by decreasing chest wall compliance, PPV will increase. (22) The sum of these factors results in a state of preload dependence by relative hypovolemia, which was expressed in our study as an increase in PPV.

Induction of anesthesia induced a drop in arterial pressures due to the intrinsic effect of anesthetic agents (23) without any change in heart rate or SaO2. Prone position did not induce any significant changes in the same parameters in the absence of fluid expansion or the use of vasoactive drugs. Our study confirms that the only hemodynamic parameter to show an early change with the prone position is PPV, and may therefore be used as the most sensitive variable to reflect hemodynamic instability during spine surgery, before any change in other more known variables such as blood pressure and heart rate (3). Prone positioning of patients who are in the hemodynamic grey zone (PPV between 9 and 13% in supine position) could lead to a preload-dependent state

that would be an argument to support a preemptive volume expansion.

However certain limitations should be taken into consideration regarding the results of this study :

1. The small patient population and its heterogeneity.
2. We noted that some patients experienced a higher augmentation in the value of PPV after prone position. Probably, that these patients were already in the preload dependent state, and that the change of position resulted in a greater augmentation than what would be seen in patients in the preload independent state. A study that compares PPV augmentation in preload dependent, versus independent patients, is required to increase the validity of our results.
3. We did not measure pulmonary compliance nor arterial elastance in the selected patients. We cannot correlate changes of these variables with the augmentation of PPV in the prone position.
4. Our study had rather healthy patients, ASA I and II, if more vulnerable patients were involved the results could have been different.
5. In this study no measurements were made after T2. Therefore a drop in arterial pressures that could occur after PPV values were increased was not observed. It would be interesting to assess any time gap between the changes in PPV and arterial pressures.
6. Finally, a cut-off value was not determined in our study. In the supine position, it is estimated that a PPV of 10 to 15% with a mean of 12% can predict fluid responsiveness (24, 25).

The question raised is whether a PPV of 12% in the prone position can be used to predict a good response to a fluid challenge. A study that couples this protocol, with a measure of the cardiac output during a fluid challenge for patients with a PPV between 12 and 16% in prone position should be able to establish a correct cut-off value to guide fluid therapy in patients undergoing spinal surgery.

In conclusion, the prone position using one thoracic chest bolster with two pelvic pads under the anterior superior iliac spines without prior volume expansion induces a significant increase of 4.7% in PPV before any change in arterial blood pressure or heart rate.

Institutional review board approval

Université Saint-Joseph Centre Universitaire d'Ethique, B.P. 17-5208 Mar Mikhael Beyrouth 1104 2020, Liban. Phone : +961 1 421 000 ext 2335
Chair person : Michel Scheuer
Internal reference : Tfem/2016/04
Inclusion start/end : April 2016-January 2017.

Informed consent

Written informed consent was obtained from all subjects or legal guardians for minors < 18 years old.

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