

# Effect of pneumoperitoneum on dynamic variables of fluid responsiveness (Delta PP and PVI) during Trendelenburg position

## ABSTRACT

**Background and Aims:** Pulse pressure variation ( $\Delta$ PP) is considered as one of the best predictors of fluid responsiveness in patients under mechanical ventilation. Pleth Variability Index (PVI) has been proposed as a noninvasive alternative. However, pneumoperitoneum has been recently suggested as a limitation to their interpretation. The aim of this study was to compare changes in  $\Delta$ PP and PVI related to autotransfusion associated with a Trendelenburg maneuver before and during pneumoperitoneum.

**Methods:** 50 patients undergoing elective abdominal laparoscopic surgery were enrolled in this prospective observational study. All patients were equipped with an invasive radial artery catheter and a PVI probe. After obtaining a stable signal with both  $\Delta$ PP and PVI, baseline values were recorded, before and after head-down tilts of 10°, with or without abdominal insufflation (10-12 mmHg). All measurements were made before any fluid challenge under standardized anaesthesia, while patients were paralyzed and mechanically ventilated with 8 mL/kg tidal volume.

**Results:** Changes in  $\Delta$ PP and PVI associated with the Trendelenburg maneuver before and after insufflation of the pneumoperitoneum were significantly different ( $P < 0.001$ ). In baseline conditions, the Trendelenburg maneuver was associated with a significant decrease in heart rate while mean arterial pressure remained unchanged. Both  $\Delta$ PP and PVI decreased. After insufflation of the pneumoperitoneum, the Trendelenburg maneuver was associated with a significant decrease in heart rate and  $\Delta$ PP and an increase in mean arterial pressure while PVI remained unchanged.

**Conclusion:** Pneumoperitoneum did not alter the response of  $\Delta$ PP to autotransfusion associated with the Trendelenburg maneuver, which was not the case for the PVI. This latter decreased during Trendelenburg maneuver performed alone and remained unchanged during Trendelenburg maneuver performed after insufflation of the pneumoperitoneum.

**Key words:** Dynamic variables; fluid responsiveness; pneumoperitoneum; Trendelenburg position

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## Introduction

Fluid therapy during the perioperative period remains a major challenge for anesthesiologists. A goal-directed approach is essential to maintain patients neither too wet nor too dry and to avoid complications associated with either hypovolemia or hypervolemia.<sup>[1]</sup>

Among the various monitoring able to predict fluid responsiveness, dynamic parameters derived from respiratory variations of blood pressure curves and those derived from pulse oximetry<sup>[2,3]</sup> have been found more accurate than static parameters such as central venous pressure.<sup>[4]</sup> Among dynamic parameters derived from respiratory variations of blood pressure curves, DeltaPP ( $\Delta$ PP) has been shown as the gold standard in many studies.<sup>[5,6]</sup>  $\Delta$ PP corresponds to the variation of pulse pressure during one respiratory cycle according to the formula “ $(PP_{max} - PP_{min}) / ((PP_{max} + PP_{min}) / 2)$ ”. As the  $\Delta$ PP needs an arterial cannulation, some authors developed completely non-invasive monitoring of dynamic variables of fluid responsiveness. Among those, pleth variability index (PVI) is obtained with the pulse oximetry curve on the Masimo Radical7 Set (Masimo Corp., Irvine, CA, USA), and is defined by the formula “ $((PI_{max} - PI_{min}) / PI_{max} \times 100\%)$ ”, where PI is the ratio expressed in % between the pulsed absorption infrared signal and the continuous absorption signal. According to a recent meta-analysis, PVI has a reasonable ability to predict fluid responsiveness in mechanically ventilated patients.<sup>[7]</sup>

Surprisingly, few studies have evaluated the ability of these dynamic parameters to predict fluid responsiveness during laparoscopic surgery.<sup>[8-10]</sup> The aim of this prospective observational trial was to explore the effects of pneumoperitoneum on  $\Delta$ PP and PVI during a modification of the patient position. This was obtained by a transient head-down tilt of 10° (Trendelenburg maneuver), leading to an increased preload, which is reversed when patient is tilted back to the horizontal line, so that this position allows the patient to act as his own control.<sup>[11]</sup>

## Methods

This study was a single-center, prospective trial carried out in the adult operating theatre of the university affiliated Brugmann Hospital, in Brussels. After obtaining written informed consent and local ethics committee approval (N°CE/201134, provided by the Ethical Committee of CHU Brugmann Hospital, Brussels, Belgium (Chairperson Valsamis Joseph) on 20 April 2011), 50 adult patients ASA I-II scheduled for elective abdominal laparoscopic surgery lasting

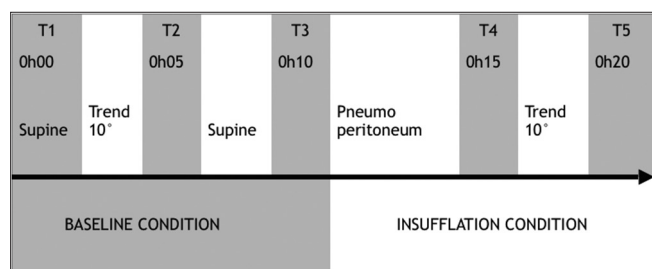
at least one hour were studied between 2011 and 2013. This study was registered on Clinicaltrials.gov (identifier: NCT02709252).

Exclusion criteria were patients under 18 years, ASA score III-IV, with a Body Mass Index  $>40$  kg.m<sup>-2</sup>, supraventricular arrhythmias, low ejection fraction  $<25\%$ , peripheral vascular and severe respiratory disease, and end stage renal failure (creatinine clearance  $<30$  ml/min). Patients were fasting from midnight and received alprazolam (0.25 to 1 mg per os) as a premedication one hour before induction of the general anesthesia. On arrival in the operating room, the patients received standard monitoring that included 3-lead electrocardiogram, non-invasive blood pressure, and inspiratory and expiratory gas concentrations. In addition, for the purpose of the study, Entropy (GE Healthcare, Chalfont St Giles, United Kingdom) was placed on the forehead.

On the contralateral arm, an 18G catheter was inserted in a peripheral vein. An infusion of Ringer Lactate at a rate of 2 mL kg<sup>-1</sup> hour<sup>-1</sup> was started. On the same hand, the probe of a Masimo Radical7 Set pulse oximeter (Masimo Corp., Irvine, CA, USA) was set on the ring finger and covered from ambient light. Preoxygenation was performed with 100% O<sub>2</sub> given through a facemask for 3 minutes to achieve SpO<sub>2</sub>  $>99\%$ . General anaesthesia was induced with propofol 1 to 2 mg kg<sup>-1</sup>, and rocuronium 0.5 mg kg<sup>-1</sup>. Sufentanil was administered on a target controlled infusion mode (TCI), based on the Gepts model (Alaris PK syringe pump, CardinalHealth, Rolle, Switzerland) to maintain an effect concentration of 0.2 ng mL<sup>-1</sup>. After intubation of the trachea (oro-tracheal tube size of 7.5 if woman, 8.0 if man), the lungs were ventilated on a volume-controlled mode with a tidal volume of 8 mL kg<sup>-1</sup> (ideal weight of the patient), a PEEP of 4 mmHg and an I/E ratio of 1:2 (Dräger Zeus, Drägerwerk AG and Co. KGaA, Lübeck, Germany). Ventilary conditions were adapted through changes in respiratory rate to maintain end expiratory partial pressure of carbon dioxide level between 35 to 40 mmHg.

Maintenance of anaesthesia was performed with TCI sufentanil set at 0.2 ng mL<sup>-1</sup> and with sevoflurane. End tidal fraction of Sevoflurane was adapted to maintain a State Entropy value between 40 and 60. The use of N<sub>2</sub>O, clonidine and ketamine was not allowed.

Thereafter, a 20-G radial artery catheter was placed on the same side as the Masimo with  $\Delta$ PP displayed on the IntelliVue (MP5 monitoring (Philips Healthcare, Best, Netherlands)).  $\Delta$ PP and PVI were directly acquired respectively



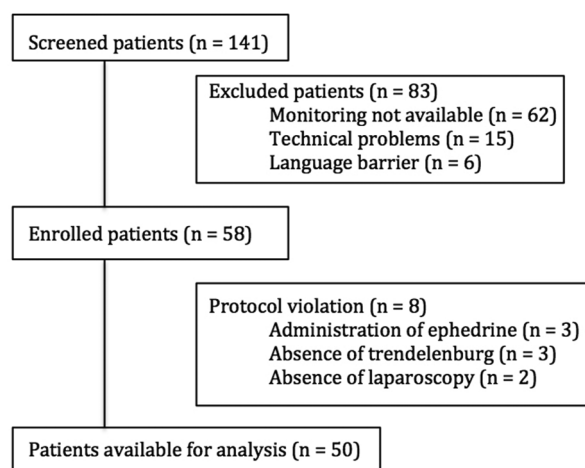
**Figure 1: Study Protocol.** T1: Baseline condition = starting time with the patient supine. T2: 5 minutes after a Trendelenburg maneuver. T3: 5 minutes after the patient is tilted back to the horizontal position. T4: Insufflation condition = 5 minutes after insufflation of the pneumoperitoneum with the patient supine. T5: 5 minutes after a Trendelenburg maneuver

on the screen of the Philips IntelliVue (MP5 and on the screen of the Masimo Radical7 Set) and heart rate and mean arterial pressure were recorded manually from the screen of the monitor.

The study protocol is detailed on Figure 1. After obtaining a stable signal with both  $\Delta$ PP and PVI (defined by obtaining a stable value for at least one minute), baseline values were recorded, together with heart rate and mean arterial pressure with the patient supine (T1 - Baseline condition). The surgical table was then tilted down to achieve a Trendelenburg position of 10° and the different parameters were recorded 5 minutes thereafter (T2 - Baseline condition). An electronic goniometer was used to reach the 10° head-down tilt position. Patients were then tilted back to the horizontal position and the different parameters were recorded 5 minutes after (T3). Then, the patient’s abdomen was inflated with carbon dioxide through a Veress needle to an intra-abdominal pressure of 10-12 mmHg. After 5 minutes, new measurements were done supine (T4 - Insufflation condition). Finally, the patient was tilted head-down again, and measurements were made after 5 minutes in the Trendelenburg position (T5 - Insufflation condition). All these measurements were made before any fluid challenge and under unchanged anaesthetic conditions.

A mixed model was performed to assess the influence of Trendelenburg maneuver and insufflation conditions on heart rate and mean arterial pressure. After a Box-Cox transformation of the response variable ( $\exp^{0.2551471}$ ), a mixed model, using a maximum likelihood estimation, with no imposition of the correlation structure, was performed to compare  $\Delta$ PP and PVI values in baseline and insufflation conditions.

Data were presented as means  $\pm$  standard deviation. A  $P < 0.05$  was considered significant. Statistical analysis was performed with the R Software 3.0.1. (R Foundation, Vienna, Austria).



**Figure 2: Flow Chart**

**Table 1 : Demographic Characteristics of the Patients**

Patient characteristics (n=50)	
Age (years)	46 $\pm$ 13
Weight (kg)	68 $\pm$ 16
Height (cm)	165 $\pm$ 8
BMI (kg.m <sup>2</sup> )	25 $\pm$ 5
ASA physical status I/II, n (%)	25/25 (50/50)
Female gender, n (%)	48 (96)
Anti hypertensive treatment, n (%)	11 (22)
Antecedent of abdominal surgery, n (%)	26 (52)
Type of surgery (n)	
LAVH	25
Salpingectomy/Ovariectomy	13
Colectomy or Rectosigmoidectomy	5
Rectopexy	2
Gastric and biliary tract surgery	1
Surrenalectomy	1
Other	3

Data are mean  $\pm$  SD. ASA, American Society of Anesthesiologists. BMI, Body Mass Index. LAVH, Laparoscopic Assisted Vaginal Hysterectomy.

## Results

Inclusion of patients is described on Figure 2. 141 patients were assessed for eligibility since October 2011. 83 patients were excluded because of not meeting inclusion criteria or declining to participate. 58 patients were enrolled, but we noticed 8 protocol violations (three administration of ephedrine and 5 absence of Trendelenburg or insufflation of the pneumoperitoneum on demand of the surgeon), so that 50 patients were finally available for analysis. Table 1 presents the demographic characteristics of our patients. The majority of the patients were women.

In baseline conditions, the Trendelenburg maneuver was associated with a significant decrease in heart rate while mean arterial pressure remained unchanged. Insufflation of

the pneumoperitoneum was associated with a significant decrease in heart rate, and a significant increase in mean arterial pressure (T4 versus T1, Table 2). In insufflation condition, the Trendelenburg maneuver was associated with a significant decrease in heart rate and a significant increase in mean arterial pressure. Mean airway pressure remained unchanged during the Trendelenburg maneuver in both conditions.

The Trendelenburg maneuver was associated with a significant decrease of the  $\Delta PP$  in both baseline and insufflation conditions [Table and Figure 3]. It was associated with a significant decrease of the PVI only during baseline condition, while PVI did not change during the insufflation condition [Table and Figure 3]. The main finding of our study is that the response of  $\Delta PP$  and of PVI to the Trendelenburg maneuver with or without insufflation of the pneumoperitoneum is significantly different (Table 3,  $P < 0.001$ ).

### Discussion

Our results indicate that the pneumoperitoneum did not alter the response of  $\Delta PP$  to autotransfusion associated

with the Trendelenburg maneuver, although it blunts the response of the PVI, at least in the presence of baseline values of  $14 \pm 6\%$ .

There is some debate regarding the usefulness of dynamic parameters of fluid responsiveness during some particular situations such as laparoscopic surgery. On the one hand, in an observational study conducted on 100 patients, Macdonald and colleagues concluded that the predictive accuracy of the pulse pressure variation ( $\Delta PP$ ) for fluid responsiveness was insufficient to recommend it for routine clinical use during major gastrointestinal surgery.<sup>[12]</sup> On the other hand, Forget and colleagues reported that PVI monitoring during laparoscopic procedure improves fluid management<sup>[13]</sup> and reduces lactate levels.<sup>[14]</sup>

Actually, a few studies have evaluated the effects of a fluid loading maneuver on  $\Delta PP$  and PVI before and during the insufflation of a pneumoperitoneum. Chin and colleagues<sup>[10]</sup> recently demonstrated the ability of  $\Delta PP$  to predict fluid responsiveness in 42 patients undergoing robot-assisted laparoscopic prostatectomy requiring a steep Trendelenburg position of 35 degrees. In 45 patients undergoing laparoscopic cholecystectomy, Liu and colleagues<sup>[8]</sup> revealed that both

**Table 2: Effect of Trendelenburg maneuver and of insufflation on heart rate, mean arterial pressure and mean airway pressure**

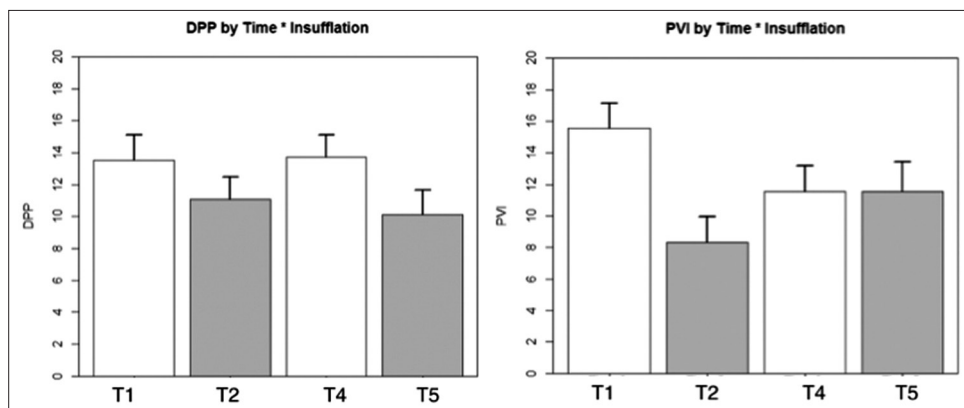
	T1	T2	T3	T4	T5	P Trend	P Insufflation	P Trend* Insufflation
HR	72±14	63±11	63±10	65±11	63±11	0.002	0.077	0.254
MAP	77±17	77±12	70±10	86±19	97±15	0.058	<0.001	0.088
Paw	17±3	18±4	17±4	23±5	24±5	0.002	<0.001	0.431

HR Heart Rate, MAP Mean, Paw Mean Airway Pressure,  $P < 0.050$  considered significant, Trend=Trendelenburg maneuver

**Table 3: Effect of Trendelenburg maneuver and of insufflation on DeltaPP and PVI**

	T1	T2	T3	T4	T5	P Insufflation	0.001
$\Delta PP$	15±6	12±4	15±5	14±5	11±5	P Trend*Insufflation	0.843
PVI	17±8	9±4	13±7	14±6	14±8	P Trend*Insufflation*Group	0.006

$\Delta PP$  Delta PP, PVI Pleth Variability Index,  $P < 0.050$  considered significant, Trend=Trendelenburg maneuver



**Figure 3: Effect of Trendelenburg maneuver and insufflation on  $\Delta PP$  and PVI.  $\Delta PP$  = Delta PP, PVI = Pleth Variability Index, T1: Starting time with the patient supine, T2: 5 minutes after a Trendelenburg maneuver, T4: 5 minutes after insufflation of the pneumoperitoneum with the patient supine, T5: 5 minutes after a Trendelenburg maneuver. Whiskers are standard deviation**

PVI and stroke volume variation (Vigileo system, Edwards Lifesciences, Irvine, CA, USA) demonstrated rapid and correlative changes with increased intra-abdominal pressure resulting from the insufflation of a pneumoperitoneum. However, PVI appeared more sensitive to reflect changes in intra-abdominal pressure, with a more steep response compared to the one observed with the stroke volume variation. Hoiseth and colleagues<sup>[9]</sup> investigated the effects of the pneumoperitoneum on  $\Delta$ PP, PVI, SVV and respiratory variations in pulse oximetry plethysmography waveform amplitude ( $\Delta$ POP) in twenty adult patients undergoing abdominal surgery. They observed that the pneumoperitoneum did not modify the ability of  $\Delta$ PP to predict fluid responsiveness but altered the ability of PVI to predict it. The blunting effect of laparoscopy on the PVI and not on the  $\Delta$ PP, seen in this work, drives interesting physiological hypotheses. The possible effects of raising intra-abdominal pressure *per se* on thoracic compliance and intra thoracic pressure variations were poorly studied in the literature, except in animal models or in the specific situation of Intra Abdominal Hypertension Syndrome. The different response of  $\Delta$ PP and PVI to Trendelenburg maneuver during insufflation of pneumoperitoneum might be explained by a different effect of the carbon dioxide insufflation on both parameters. It is well known that the insufflation of carbon dioxide during the pneumoperitoneum may induce an increase in sympathetic activity.<sup>[15]</sup> The concomitant release of catecholamines is associated with an increase in PVI.<sup>[16,17]</sup> Hypercapnia may result from carbon dioxide insufflation and influence PVI.<sup>[18]</sup> However, in our study ventilatory conditions were adapted through changes in respiratory rate to maintain end expiratory partial pressure of carbon dioxide level between 35 to 40 mmHg. We observed an increase in the mean arterial pressure during insufflation of the pneumoperitoneum, which is consistent with an increase in sympathetic activity. An acute sympathetic stimulation may indeed affect differently  $\Delta$ PP and PVI, as  $\Delta$ PP is obtained with an arterial cannulation of the radial artery while PVI is obtained with a signal derived from the microcirculation on the finger.

The significant reduction of both  $\Delta$ PP and PVI values during the Trendelenburg maneuver performed before the insufflation of the pneumoperitoneum is consistent with a fluid responsiveness situation. In fact, the initial mean values of PVI ( $17 \pm 8$ ) and of  $\Delta$ PP ( $15 \pm 6$ ) were high, suggesting some degree of hypovolemia for the majority of the patients, in relationship with the induction of general anaesthesia. Some authors have also implicated the preoperative fasting in the development of some degree of hypovolemia before surgery.<sup>[19]</sup>

There are some methodological limitations to our study. Firstly, we did not measure other flow variables such as cardiac output or stroke volume to predict fluid responsiveness. Invasive procedures of pulmonary artery catheter did not seem to be ethical in this surgery. The measurement of cardiac output would be necessary to determine which of the two tools (PVI or  $\Delta$ PP) best depicts patient's fluid responsiveness.

Moreover, most of the patients were women free from cardiovascular disease. We may not extrapolate our results for patients with cardiovascular comorbidities or true cardiovascular compromise. However, in that particular condition, more invasive monitoring is usually necessary to assess dynamic preload and hemodynamic optimization. Our results have to be interpreted within the conditions of our study and could not be extrapolated to other clinical situations associated with lower or higher initial mean values of  $\Delta$ PP and PVI. This is in agreement with the usefulness of the PVI during laparoscopic surgery identified by Forget and colleagues.<sup>[13]</sup>

Secondly, the time interval between the different measurement points were always five minutes. However, it was an ethical necessity to keep prolongation of general anesthesia as short as possible.

Thirdly, the head-down tilt of  $10^\circ$  was used to mimic administration of fluids. Different levels of Trendelenburg position have been used by different authors. We used  $10^\circ$  because it corresponded to the level of Trendelenburg position in the study of Terai and colleagues,<sup>[11]</sup> which demonstrated that this position produced an autotransfusion effect to the same degree as did the  $60^\circ$  passive leg raising in normovolemic individuals. Moreover,  $10^\circ$  corresponded to the local habits of our surgeons for that type of surgery.

In conclusion, pneumoperitoneum modifies the PVI response to a Trendelenburg position of  $10^\circ$ . The fact that  $\Delta$ PP responds adequately to an auto transfusion challenge may indicate that it is still useful to guide fluid administration in patients undergoing laparoscopy.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest

Patrice Forget has received speaker fees from Masimo Corp. and was advisory board member for Masimo Corp. For the remaining authors, none were declared.

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