Temporary increase in tidal volume to improve the reliability of dynamic preload indices during robot-assisted laparoscopic surgery in the Trendelenburg position with lung-protective ventilation

CURRENT STATUS: ACCEPTED

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DOI:
10.21203/rs.2.10452/v1

SUBJECT AREAS
Anesthesiology & Pain Medicine

KEYWORDS
Pulse pressure variation, stroke volume variation, fluid responsiveness, pneumoperitoneum, Trendelenburg position
Abstract

Background: Pulse pressure variation (PPV) and stroke volume variation (SVV) induced by mechanical ventilation are widely used as predictors of fluid responsiveness. However, the reliability of these dynamic preload indices is controversial under pneumoperitoneum. In addition, the usefulness of these indices is being called into question with the increasing adoption of lung-protective ventilation using low tidal volume (VT) in surgical patients. We investigated whether increasing tidal volume (VT) from 6 to 8 ml/kg can improve the predictive power of PPV and SVV during pneumoperitoneum. Methods: We performed a prospective observational study in patients undergoing robot-assisted laparoscopic surgery in the Trendelenburg position under lung-protective ventilation. PPV, SVV, and the stroke volume index (SVI) were measured at a VT of 6 mL/kg and 3 minutes after increasing the VT to 8 mL/kg. The VT was reduced to 6 mL/kg, and measurements were performed before and 5 minutes after volume expansion (infusing 6% hydroxyethyl starch 6 ml/kg over 10 minutes). Fluid responsiveness was defined as ≥ 15% increase in the SVI.

Results: Twenty-four of the 38 patients enrolled in the study were responders. In the receiver operating characteristic curve analysis, the augmented PPV and SVV associated with a temporary increase in VT from 6 to 8 ml/kg improved the predictability of fluid responsiveness, with area under the curve (AUC) values of 0.85 (95% confidence interval (CI), 0.70–0.95, P < 0.0001) and 0.77 (95% CI 0.61–0.89, P = 0.0003), compared to PPV and SVV values (as measured by VT) of 6 ml/kg. The absolute change in PPV and SVV values obtained by transiently increasing VT also predicted fluid responsiveness, with AUC values of 0.95 (95% CI 0.83–0.99, P < 0.0001) and 0.76 (95% CI 0.60–0.89, P = 0.0006).

Conclusions: Augmented PPV and SVV values, and absolute changes therein obtained by increasing VT from 6 to 8 ml/kg, predicted fluid responsiveness with high sensitivity and specificity in our surgical population.
Background

Robot-assisted laparoscopic surgery is increasingly performed due to its many advantages over open surgery, including minimal tissue trauma, fewer surgical complications, and earlier postoperative recovery [1]. However, while pneumoperitoneum is essential for adequate exposure in robot-assisted laparoscopic surgery, it has been associated with increased morbidity such as reduced renal blood flow (RBF) and post-operative renal dysfunction [2, 3]. As the level of hydration required to maintain RBF under pneumoperitoneum depends on the baseline volume status [4], an adequate assessment of intravascular volume and optimal fluid management are important [5].

Dynamic preload indices such as pulse pressure variation (PPV) and stroke volume variation (SVV), are generally accepted as accurate indicators of fluid responsiveness during surgery and in the intensive care unit [6, 7]. To optimize surgical conditions, robot-assisted laparoscopic surgery requires pneumoperitoneum and the Trendelenburg position, which have been shown to significantly alter respiratory mechanics [8]. As dynamic preload indices are generated by cyclic transmission of airway pressure to the pleural and pericardial spaces under positive ventilation, their reliability can be affected under these conditions. Several studies have highlighted the effect of intra-abdominal pressure (IAP) on the accuracy and cut-off values of these indices [9-13]. In addition, as the application of lung-protective ventilation using low tidal volume ($V_T$) with positive end expiratory pressure (PEEP) is gradually increasing in surgical patients [14-16], the usefulness of these indices during robot-assisted laparoscopic surgery has been questioned.

It has been clearly shown that the values of dynamic indices are significantly correlated with the magnitude of $V_T$ [17, 18]. Min et al. [19] reported that augmentation of PPV and
SVV via a temporary increase in $V_T$ from 8 to 12 ml/kg improved their predictive power in mechanically ventilated patients during surgery. Another recent study reported that on increasing $V_T$ from 6 to 8 ml/kg, augmented PPV and SVV, as well as their absolute changes, predicted fluid responsiveness with high sensitivity and specificity, even in critically ill patients receiving low $V_T$ [20]. Therefore, the aim of the current study was to investigate whether increasing $V_T$ from 6 to 8 ml/kg would improve the predictive power of PPV and SVV in patients undergoing robot-assisted laparoscopic surgery in the Trendelenburg position under lung-protective ventilation. We also assessed the ability of absolute changes in PPV and SVV values induced by a temporary increase in $V_T$ from 6 to 8 ml/kg to predict fluid responsiveness.

**Methods**

**Study design and patient population**

This prospective observational study was approved by the institutional review board of Hallym University Kangnam Sacred Heart Hospital (approval number: 2017-09-003). From March to June 2018, adult patients undergoing robot-assisted laparoscopic surgery with pneumoperitoneum in the Trendelenburg position were enrolled after obtaining their written informed consent. The trial was registered prior to patient enrollment at ClinicalTrials.gov (NCT03467711). Reporting of data was done in accordance with the STROBE guideline for observational trials [21]. Exclusion criteria were body mass index (BMI) > 30 or < 15 kg/m$^2$, preoperative arrhythmia, moderate to severe valvular heart disease, preoperative left ventricular ejection fraction < 40%, right ventricular dysfunction, intracardiac shunt, 1-second forced expiratory volume < 60% of predicted value, moderate to severe renal or liver disease, new-onset arrhythmia after anesthesia induction, and contraindications for oesophageal Doppler monitor (ODM) probe insertion.
(i.e., oesophageal stent, carcinoma of the esophagus or pharynx, previous oesophageal surgery, oesophageal stricture, oesophageal varices, pharyngeal pouch, and severe coagulopathy). During surgery, all patients were placed in the 25° Trendelenburg position, and pneumoperitoneum was achieved by continuous carbon dioxide insufflation maintaining an IAP of 15 mmHg.

Anesthetic technique

After the patients arrived at the operating room, pulse oximetry, three-lead electrocardiography (ECG), and non-invasive arterial pressure monitoring were applied. Anesthesia was induced with propofol (1.5–2.5 mg/kg) and remifentanil (0.05–0.15 μg/kg/min), and tracheal intubation was facilitated with rocuronium (0.8 mg/kg). The patient’s lungs were mechanically ventilated with a mixture of oxygen in air, with an inspired oxygen fraction of 0.5 using the volume-controlled mode. $V_T$ was adjusted to 6 ml/kg predicted body weight (PBW, determined as $x + 0.91[\text{height (in cm)} - 152.4]$, where $x = 50$ for males and $x = 45.5$ for females) [22]. The PEEP of 5 cm H$_2$O was applied without inspiratory pause. Respiratory rate was adjusted to maintain an end-tidal carbon dioxide tension between 35 and 40 mmHg. The inspiratory to expiratory ratio was set to 1:2. Peak inspiratory airway pressure (PIP) and compliance of the respiratory system (Crs) were recorded from the anesthesia machine (Datex-Ohmeda Avance CS$^2$ Anesthesia Machine; GE Healthcare, Helsinki, Finland). Anesthesia was maintained with continuous infusion of remifentanil (0.02–0.2 μg/kg/min) and sevoflurane (1.5–2.5 vol%) to maintain a bispectral index between 40 and 60.

Hemodynamic monitoring

After induction of anesthesia, a radial arterial catheter and ODM probe (CardioQ; Deltex Medical, Chichester, UK) were inserted. Both were connected to the CardioQ-ODM+ (Deltex
The ODM probe was positioned to obtain the optimum signal for descending aorta blood velocity. Stroke volume index (SVI), and peak velocity (PV) were measured continuously and displayed, and their mean values were calculated over 10 s. After zeroing the arterial transducer, a flush test was performed to ensure that the arterial pressure measurement system was critically damped. The arterial pulse pressure wave was simultaneously monitored through the patient monitor (CARESCAPE Monitor B850; GE Healthcare) and CardioQ-ODM+ monitor using a serial cable. The patient monitor displayed the automatically calculated PPV in real time using the algorithms described previously [23].

\[
PPV (\%) = \left( \frac{PP_{\text{max}} - PP_{\text{min}}}{PP_{\text{mean}}} \right) \times 100
\]

where \(PP_{\text{max}}\) and \(PP_{\text{min}}\) represent the maximum and minimum arterial pulse pressure (PP), and \(PP_{\text{mean}}\) is the mean arterial PP.

The CardioQ-ODM+ monitor combines ODM with pulse pressure wave analysis to measure SVI. It uses ODM-derived SVI for initial and periodic calibrations, and then continuously calculates pulse pressure wave analysis-derived SVI using the Liljestrand-Zander formula [24]. By continuous beat detection and analysis, the SV, SVI, and SVV were displayed continuously in a separate pressure-based data window as a column of values. SVV were obtained as described previously, regardless of the respiratory cycle [25].

\[
SVV (\%) = \left( \frac{SV_{\text{max}} - SV_{\text{min}}}{SV_{\text{mean}}} \right) \times 100
\]

where \(SV_{\text{min}}\) and \(SV_{\text{max}}\) are the minimum and maximum SV values over one respiratory cycle, respectively.

All values were averages of at least three consecutive measurements acquired over 30 s. An independent investigator who was trained in maneuvering the ODM probe but was not
involved in the present study assessed ODM and all other variables during the study. ODM is routinely used to monitor surgical patients in our center and shows good inter-observer reliability [12].

**Study protocol**

Fig. 1. shows a schematic representation of the protocol, which was initiated at least 1 hour after increasing IAP to 15 mmHg, and after stabilization of hemodynamic parameters, defined as changes in mean arterial pressure (MAP) < 10% during 5 minutes. In addition, to minimize acute changes in IAP and sympathetic tone due to ongoing surgery [26, 27], which could confound the effects of fluid challenge, the study protocol was performed with little or no surgical stimulation (absence of cautery and instrumentation of intra-abdominal structures).

We first measured the hemodynamic response to a temporary increase in VT from 6 to 8 ml/kg, and then performed volume expansion (VE) to assess the subsequent changes in SVI. The first set of measurements, including (HR), MAP, SVI, PV, PIP, Cfs, PPV with 6 ml/kg PBW VT ventilation (PPV6), and SVV with 6 ml/kg PBW VT ventilation (SVV6), were recorded at baseline (T1, base 1). After the baseline measurement, VT was increased from 6 to 8 ml/kg PBW for 3 minutes. During the last minute of high VT ventilation, measurements of the above-mentioned hemodynamic and respiratory variables, including PPV with 8 ml/kg PBW VT ventilation (PPV8) and SVV with 8 ml/kg PBW VT ventilation (SVV8), were again recorded (T2). The changes in PPV and SVV values induced by a temporary increase in VT from 6 to 8 ml/kg (ΔPPV6-8 and ΔSVV6-8) were calculated as follows:

\[ ΔPPV_{6-8} = PPV_8 - PPV_6, \]

\[ ΔSVV_{6-8} = SVV_8 - SVV_6. \]

After the VT was returned to 6 ml/kg PBW and all of the hemodynamic variables had
returned to baseline values (variations < 10%), VE was performed for 10 minutes using an infusion of 6% hydroxyethyl starch (HES 130/0.4, Volulyte; Fresenius Kabi, Stans, Switzerland) 6 ml/kg PBW. Two sets of measurements (HR, MAP, SVI, PV, PIP, Crs, PPV, and SVV) were performed before (T3, base 2) and 5 minutes after VE (T4) [28, 29]. Percentage differences in ODM-derived SVIs before and after VE were used as principal indicators of fluid responsiveness. Patients were classified as responders to VE if they showed an increase in SVI ≥ 15% and as non-responders if they showed an increase < 15% [30, 31]. The changes in SVV and PPV values after VE (ΔPPV_{VE} and ΔSVV_{VE}) were calculated as follows:

\[ \Delta \text{PPV}_{\text{VE}} = \text{PPV} (T4) - \text{PPV} (\text{base 2}, T3), \]

\[ \Delta \text{SVV}_{\text{VE}} = \text{SVV} (T4) - \text{SVV} (\text{base 2}, T3). \]

**Statistical analysis**

MedCalc for Windows (ver. 15.6.1; MedCalc Software, Ostend, Belgium) was used to calculate sample size. The sample size was determined using the difference between the area under the curve (AUC) of 0.75 (alternative hypothesis that PPV \_8 can predict fluid responsiveness after VE) and 0.5 (null hypothesis). At least 38 patients were required to detect an AUC difference of 0.25 with a type I error of 0.05 and a desired power of 0.80, assuming equal numbers of responders and non-responders. With the expectation of a 10% dropout rate, 42 patients were enrolled in the study.

The normality of the continuous data was tested with the Shapiro–Wilk test. Data are presented as the mean (SD), median [interquartile range (IQR)], or number of patients (%). Student’s t-test or the Mann-Whitney U test for continuous variables, and the chi-square test for categorical data, were used to compare patient characteristics between responders and non-responders. The hemodynamic parameters were compared between
responders and non-responders using the Mann–Whitney U-test or t-test, as appropriate. The effects of the temporary increase in $V_T$ from 6 to 8 ml/kg and VE on hemodynamic parameters were assessed using the paired t-test or the Wilcoxon signed-rank sum test after the normality test. A Bonferroni-adjusted $P$-value (normal $P$-value multiplied by the number of outcomes being tested) was used to control for multiple comparisons.

The relations between percentage changes in SVI after VE and hemodynamic parameters before VE ($PPV_6$, $PPV_8$, $\Delta PPV_{6-8}$, $SVV_6$, $SVV_8$, and $\Delta SVV_{6-8}$) were assessed using Spearman’s rank correlation. The relationship between the percentage changes in SVI after and the changes in PPV and SVV after VE ($\Delta PPV_{VE}$ and $\Delta SVV_{VE}$) were also assessed using Spearman’s rank correlation analysis. The intraclass correlation between the SVI, PPV, and SVV measurements at the two baseline steps (T1 and T3) was measured using random-effects models [32].

To test the abilities of dynamic preload indices to predict fluid responsiveness, the AUCs of receiver operating characteristic (ROC) curves were calculated and compared using the DeLong method. Briefly, the general interpretations of a test according to the value of the AUC of the ROC were as follows: AUC = 0.5, no better than chance, a useless test with no prediction possible; AUC = 0.6–0.69, a test with a poor predictive capability; AUC = 0.7–0.79, a fair test; AUC = 0.8–0.89, a test with good predictive capability; AUC = 0.9–0.99, an excellent test; AUC = 1.0, a perfect test with the best possible prediction. An optimal threshold value was determined for each variable to maximize the Youden index (sensitivity + specificity – 1). Statistical analyses were performed using MedCalc (ver. 15.6.1) and SPSS software (ver. 24.0; IBM Corp., Armonk, NY, USA). In all analyses, $P < 0.05$ was taken to indicate statistical significance.

Results
Patient characteristics

Of the 49 patients included in the initial screen, 42 fulfilled the inclusion criteria and were enrolled in the study. Four patients were excluded; one developed intraoperative subcutaneous emphysema and required a ventilator mode change, one had severe hypotension during VE and required vasopressor support, one developed paroxysmal atrial fibrillation during surgery, and the remaining patient’s arterial pressure measurement system was critically damped. Among the 38 patients included in the final analysis, 24 patients (63%) were responders and 14 (37%) were non-responders (Fig. 2). There were no significant differences in age, PBW, or BMI between responders and non-responders, whereas the surgery type and sex distribution differed between the two groups (Table 1).

The intraclass correlation between the SVI, PPV, and SVV measurements at the two baseline steps (T1 and T3) were 0.98 [95% confidence interval (CI), 0.96–0.99], 0.96 (95% CI, 0.92–0.98), and 0.81 (95% CI, 0.64–0.90), respectively.

Effects of increased $V_T$ and VE on hemodynamic and respiratory variables

At baseline, with 6 ml/kg PBW $V_T$ ventilation, no significant differences were found in any hemodynamic variables, including $PPV_6$ and $SVV_6$, between responders and non-responders. After increasing $V_T$ to 8 ml/kg PBW, MAP decreased and PPV and SVV increased significantly only in responders, resulting in significant differences in MAP, $PPV_8$, and $SVV_8$ between responders and non-responders. Baseline PIP and Crs were comparable between the two groups and increased significantly after the temporary increase in $V_T$ from 6 to 8 ml/kg in responders and non-responders (Table 2).

Significant changes in PIP, Crs, SVI, and PPV were induced in responders and non-responders after VE, while significant decreases in HR and SVV were induced only in
responders. (Table 2).

**Relationships between changes in PPV and SVV induced by VE and percentage changes in SVI induced by VE**

PPV\textsubscript{VE} and ΔSVV\textsubscript{VE} were significantly correlated with VE-induced percentage changes in SVI (r = −0.61 [95% CI −0.78 to −0.36], P < 0.001; r = −0.44 [95% CI −0.67 to −0.14], P = 0.006, respectively) (Fig. 3), indicating the ability of these variables to track changes in SVI induced by VE during pneumoperitoneum.

**Prediction of fluid responsiveness**

In the ROC curve analysis, PPV\textsubscript{6} showed poor ability to predict fluid responsiveness, with an AUC of 0.69 (95% CI 0.52–0.83, P = 0.036), but PPV\textsubscript{8} showed good ability, with an AUC of 0.85 (95% CI 0.70–0.95, P < 0.0001). SVV\textsubscript{6} was not predictive of fluid responsiveness, but SVV\textsubscript{8} showed fair predictive ability, with an AUC of 0.77 (95% CI 0.61–0.89). The optimal threshold values of PPV\textsubscript{8} and SVV\textsubscript{8} were 7% [sensitivity 79% (95% CI 58–93); specificity 79% (95% CI 49–95)] and 5% [sensitivity 67% (95% CI 45–84); specificity 79% (95% CI 49–95)], respectively (Table 3). The AUCs for PPV\textsubscript{8} and SVV\textsubscript{8} were significantly larger than those for PPV\textsubscript{6} (P < 0.001) and SVV\textsubscript{6} (P = 0.0007), respectively. No significant differences were found between the AUCs for PPV\textsubscript{6} and SVV\textsubscript{6} (P = 0.182) or between those for PPV\textsubscript{8} and SVV\textsubscript{8} (P = 0.245) (Fig. 4).

ΔPPV\textsubscript{6,8} showed excellent predictive capability for fluid responsiveness with an AUC of 0.95 (95% CI 0.83–0.99, P < 0.0001). ΔPPV\textsubscript{6,8} > 1% identified responders with sensitivity of 92% (95% CI 73–99) and specificity of 86% (95% CI 57–98). ΔSVV\textsubscript{6,8} could also predict fluid responsiveness but showed only fair predictive capability, with an AUC of 0.76 (0.60–
0.89). The $\Delta SVV_{6.8} > 2\%$ identified responders with a sensitivity 46% (95% CI 26–67) and specificity of 100% (95% CI 77–100) (Table 4).

**Discussion**

In this study on patients undergoing robot-assisted laparoscopic surgery in the Trendelenburg position under lung-protective ventilation, we demonstrated that augmentation of PPV and SVV via a temporary increase in $V_T$, from 6 to 8 ml/kg, improved the predictability of fluid responsiveness compared to PPV and SVV measured with a $V_T$ of 6 ml/kg. The optimal thresholds of augmented PPV and SVV were $> 7\%$ and $5\%$, respectively. This study also showed that the absolute change in PPV and SVV values obtained by transiently increasing $V_T$ ($\Delta PPV_{6.8}$ and $\Delta SVV_{6.8}$) can predict fluid responsiveness in these populations. The optimal thresholds of $\Delta PPV_{6.8}$ and $\Delta SVV_{6.8}$ were $> 1\%$ and $> 2\%$, respectively.

Several studies have demonstrated that a temporary increase in $V_T$ directly augments the values of these dynamic indices and their capacity to predict fluid responsiveness [19, 33]. Our study also demonstrated that a temporary increase in $V_T$ from 6 to 8 ml/kg improved the predictive power of PPV and SVV values, even in patients with elevated IAP. Because PPV and SVV values are augmented in fluid responders, but not in non-responders, the absolute changes in the PPV and SVV values induced by increased $V_T$ could also be used to predict fluid responsiveness with high sensitivity and specificity, which is consistent with a study by Myatra et al. [20]. Moreover, changes in PPV values induced by VE were significantly correlated with percentage changes in SVI induced by VE (Fig. 3), showing the ability of this variable to track changes in SV induced by VE during pneumoperitoneum. Thus, observing changes in PPV values during an increase in $V_T$ and VE can help predict and confirm fluid responsiveness when continuous cardiac output
monitoring is unavailable.

Our study showed discordant results versus those of previous studies regarding the capacity of dynamic preload indices to predict fluid responsiveness during increased IAP [9-13]. In our study, PPV and SVV predicted fluid responsiveness at a $V_T$ value of 8 ml/kg.

Hoiseth et al. demonstrated that PPV and SVV values at a $V_T$ of 8 ml/kg had a relatively poor capacity to predict fluid responsiveness during laparoscopy [12]. This discrepancy can be explained by those researchers not controlling clinical factors, such as blood loss, use of vasopressors, or changes in ventilator settings, which may have altered PPV values independent of the preload condition, whereas we performed VE under controlled clinical conditions with little or no surgical stimulation. Unlike our study, Renner et al. reported that increasing IAP abolished the ability of SVV values, but not PPV values, to predict fluid responsiveness [10]. Increased IAP leads to increased systemic vascular resistance (SVR) by activation of antidiuretic hormones and the sympathetic and renin-angiotensin-aldosterone systems [34]. However, the validity of the SV monitor used in Renner et al.’s study was influenced by SVR [35, 36], whereas the CardioQ-ODM+ monitor used in our study calculates pulse pressure wave analysis-derived SV based on the Liljestrand-Zander formula, which has been reported to estimate SV accurately even during arterial load changes [24, 37].

Higher PPV and SVV cut-off values for determining fluid responsiveness might be expected in our study population, because pneumoperitoneum decreases chest wall compliance, which increases the variation in pleural pressure associated with an increase in dynamic indices [38]. However, the PPV and SVV cutoff values in our study were not as high as in previous studies [9, 10]. These results can be explained by two main factors: the application of small to moderate increases in IAP (10-15 mmHg) and a steep Trendelenburg position. The cardiopulmonary interactions that are altered during
pneumoperitoneum depend on the level of IAP [21]. Indeed, previous animal studies have reported that IAP elevations > 20 mm Hg progressively increase the values of dynamic preload indices independent of volume status [10, 11], while a lower IAP (10–15 mmHg) in the surgical setting does not modify the cut-off values [9, 12, 13]. Because the extent of the increase in SV during head-down tilt was unchanged by pneumoperitoneum [12], adding a steep Trendelenburg position to pneumoperitoneum may induce an increase in SV and could have contributed to a lower cutoff value than under pneumoperitoneum alone.

The optimal thresholds of ΔPPV_{6-8} and ΔSVV_{6-8} for discriminating fluid responsiveness were lower than those reported by Myatra et al. (>3.5% and 2.5%, respectively) [20]. There are several possible explanations for this discrepancy. Pneumoperitoneum and the Trendelenburg position significantly worsen respiratory mechanics by shifting the diaphragm cranially and facilitating transmission of abdominal weight to the lung parenchyma [8]. The extent to which Crs was increased by the temporary increase in \( V_T \) from 6 to 8 ml/kg was lower in our study than in that by Myatra et al. (1 vs. 7 ml/cmH{2}O).

As the extent of airway pressure transmission to the pleural space is decreased according to the degree of Crs [39], it can be assumed that pneumoperitoneum and the Trendelenburg position restricted the increase in Crs, and the increased \( V_T \) induced a smaller variation in pleural pressure, resulting in smaller absolute changes in PPV and SVV values. In addition, the hemodynamic characteristics of the patients differed between the two studies; Myatra et al. studied critically ill patients with acute circulatory failure who were tachycardic (mean HR > 130), whereas our study population consisted of patients with no clinical signs of shock who had a normal HR. As a decrease in HR can decrease the PPV [40, 41], the higher baseline preload reserve in our patients would also have
contributed to the less profound changes in PPV and SVV values.

This study had several limitations. First, the study population consisted of only a small number of highly selected patients receiving robot-assisted laparoscopic surgery in the Trendelenburg position. As the IAP was maintained at 15 mmHg, our results cannot be extrapolated to different IAP values. Our results require validation in a larger and more heterogeneous population. Second, ODM was used to track changes in SVI and measure the effects of preload changes. When IAP is increased, blood flow may be redistributed from the descending aorta to vessels leaving the aortic arch.[42] This may contribute to falsely reduced SVI, as ODM measures blood flow in the descending aorta. However, the trending ability of ODM to monitor changes in SVI during patient management is well established.[43, 44] Therefore, we assumed that the trending ability of ODM was unaffected by pneumoperitoneum once established. Third, there were sex differences between the responders and non-responders, which may have been due to differences in types of surgery based on sex, resulting in different hemodynamic status at the start of the study protocol. However, we considered it unlikely that this difference would have affected our primary outcome in predicting the fluid response during robot-assisted laparoscopic surgery in the Trendelenburg position because the IAP and angle of Trendelenburg position during surgery were constant in all patients.

Conclusions

In conclusion, in this study of patients undergoing robot-assisted laparoscopic surgery in the Trendelenburg position under lung-protective ventilation, augmentation of PPV and SVV through a temporary increase in V_T (from 6 to 8 ml/kg) led to good predictability of fluid responsiveness. This study also implied that observing the magnitude of PPV and SVV augmented by increasing V_T could serve as a functional test to predict fluid
responsiveness.

List Of Abbreviations

AUC: area under the curve; BMI: body mass index; CI: confidence interval; Crs: compliance of the respiratory system; ECG: electrocardiography; HR: heart rate; IAP: intra-abdominal pressure; MAP: mean arterial pressure; ODM: oesophageal Doppler monitor; PBW: predicted body weight; PEEP: positive end expiratory pressure; PIP: Peak inspiratory airway pressure; PPV: pulse pressure variation; PP: pulse pressure; PV: peak velocity; RBF: renal blood flow; SVI: stroke volume index; SVV: stroke volume variation; VE: volume expansion; 

\( V_T \): tidal volume

Declarations

Ethics approval and consent to participate

This study was performed according to the Declaration of Helsinki after the approval of Institutional Review Board of Hallym University Kangnam Sacred Heart Hospital (2017-09-003). Written informed consent was obtained from the enrolled patients before surgery.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to the regulation of Institutional Review Board, but are available from the corresponding author after getting permission from IRB for sharing the dataset on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research was supported by the Hallym University Research Fund, 40074 (HURF-2017-
The funding body had no influence on study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Authors’ contributions**

J-HJ: concept/design, data collection, drafting article, approval of article. R-KC: concept/design, critical revision of article, approval of article. H-CB: data collection, critical revision of article, approval of article. M-HC: data collection, critical revision of article, approval of article. J-SH: data collection, critical revision of article, approval of article. Y-GL: data analysis/interpretation, critical revision of article, approval of article. S-HP: data analysis/interpretation, critical revision of article, approval of article. All authors read and approved the final manuscript.

**Acknowledgements**

Not applicable

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Tables

Table 1. Patient Characteristics

|                          | Overall (N = 38) | Responders (n = 24) | Non-responders (n = 14) | P-value |
|--------------------------|------------------|---------------------|-------------------------|---------|
| Age, years (range)       | 49.5 (45–62.3)   | 56.5 (45.3–62.8)    | 47 (41–52.5)            | 0.058   |
| Sex (male/female)        | 17/21            | 14/10               | 3/11                    | 0.043   |
| Height, cm               | 162 ± 7.0        | 163.5 ± 7.2         | 161.5 ± 6.9             | 0.406   |
| Predicted body weight, kg | 57 ± 7.8         | 58.26 ± 8.0         | 54.8 ± 7.2              | 0.717   |
| Body mass index, kg/m2   | 24.4 ± 2.5       | 24.5 ± 2.2          | 24.2 ± 2.9              | 0.664   |
| Hypertension             | 9 (29)           | 6 (28.6)            | 3 (30)                  | 1.000   |
| Surgery type, n (%)      |                  |                     |                         | 0.102   |
| Radical prostatectomy    | 18 (47.4)        | 15 (62.5)           | 3 (21.4)                |         |
| Hysterectomy             | 14 (36.8)        | 6 (25)              | 8 (57.1)                |         |
| Myomectomy               | 6 (15.8)         | 3 (12.5)            | 3 (21.4)                |         |

Values are mean ± SD, median (IQR) or number (%).

Table 2. Hemodynamic and Respiratory Variables at Baseline, after the Tidal Volume Challenge, before Volume Expansion, and after Volume Expansion in Responders (n = 24) and Non-responders (n = 14)
|                      | T1 Base 1 (VT 6ml/kg) | T2 Increased VT (VT 8 ml/kg) | P1 Value | T3 Base 2 (VT 6ml/kg) | T4 After VE (VT 6ml/kg) | P2 Value |
|----------------------|-----------------------|-------------------------------|----------|-----------------------|-------------------------|----------|
| **HR (beats/min)**   |                       |                               |          |                       |                         |          |
| Responders           | 74 (68–86)            | 74 (68–85)                    | 0.492    | 75 (69–85)            | 73 (66–82)              | 0.012    |
| Non-responders       | 68 (65–77)            | 68 (65–77)                    | > 0.99   | 68 (63–75)            | 68 (64–77)              | > 0.99   |
| **MAP (mm Hg)**      |                       |                               |          |                       |                         |          |
| Responders           | 82 ± 10               | 79 ± 12                       | 0.036    | 80 ± 13               | 85 ± 11                 | 0.078    |
| Non-responders       | 91 ± 13               | 89 ± 11                       | > 0.99   | 87 ± 11               | 87 ±10                  | > 0.99   |
| **PIP (cm H2O)**     |                       |                               |          |                       |                         |          |
| Responders           | 26 ± 3                | 31 ± 4                        | < 0.001  | 26 ± 3                | 27 ± 3                  | < 0.001  |
| Non-responders       | 25 ± 3                | 30 ± 4                        | 0.006    | 25 ± 3                | 26 ± 3                  | 0.016    |
| **Crs (ml/cmH2O)**   |                       |                               |          |                       |                         |          |
| Responders           | 17 (14.3–19)          | 17 (15–19)                    | 0.018    | 16 (14–19)            | 15.5 (14–18)            | <0.001   |
| Non-responders       | 16.5 (13.8–18.3)      | 17 (14.8–18.3)                | 0.066    | 16 (13.8–17.3)        | 15 (13–17)              | 0.024    |
| **SVI (ml/min2)**    |                       |                               |          |                       |                         |          |
| Responders           | 41.5 ± 8.2            | 40.6 ± 8.9                    | > 0.99   | 40.2 ± 9.0            | 50.6 ± 10.9             | <0.001   |
| Non-responders       | 50.5 ± 15.2           | 52.2 ± 15.3                   | 0.864    | 52 ± 15.7             | 55.2 ± 16.8             | 0.018    |
| **PPV (%)**          |                       |                               |          |                       |                         |          |
| Responders           | 7 (5.3–8.8)           | 9 (8–13)*                     | <0.001   | 7.5 (5.3–9.8)*        | 3.5 (3–5)               | <0.001   |
| Non-responders       | 5.5 (3.8–6.5)         | 6 (3.8–7.3)                   | 0.132    | 5 (3.8–6)             | 3 (1.8–3.8)             | 0.006    |
| **SVV (%)**          |                       |                               |          |                       |                         |          |
| Responders           | 5 (4–6)               | 6.5 (4–9)*                    | <0.001   | 6 (4–7)*              | 4 (3–5)                 | 0.042    |
| Non-responders       | 5 (2.8–5)             | 4 (3–5.3)                     | > 0.99   | 4 (2.8–5)             | 4 (2.8–5)               | > 0.99   |

Data are mean ± SD or median (IQR). Patients were considered responders if the stroke volume index increased by at least 15% after volume expansion (6% hydroxyethyl starch 6 ml/kg for 10 minutes). HR, heart rate; RR, respiratory rate; MAP, mean arterial pressure; PIP, peak inspiratory pressure; Crs, respiratory compliance; SVI, stroke volume index; PPV, pulse pressure variation; SVV, stroke volume variation; VT challenge, tidal volume challenge; VE, volume expansion. *P < 0.05 comparison between responders and non-
responders \((n = 14)\) at each time point; \(P1\)-values are for intragroup comparisons of values before \((T1)\) and after the tidal volume challenge \((T2)\); \(P2\)-values are for intragroup comparisons of values before \((T3)\) and after volume expansion \((T4)\); \(P\)-values were adjusted using the Bonferroni correction

### Table 3. Prediction of Fluid Responsiveness based on the ROC Curves of Various Indices

|       | AUC (95%CI) | \(P\)-value | Cut-off value,\% | Sensitivity (95% CI) | Specificity (95% CI) | (+) Predictive value (95% CI) | (-) Predictive value (95% CI) | (+) LR | (-) LR |
|-------|-------------|-------------|------------------|----------------------|----------------------|-------------------------------|-------------------------------|-------|-------|
| PPV6  | 0.69 (0.52–0.83) | 0.036       | > 6              | 54 (33–74)           | 79 (49–95)           | 81 (54–96)                    | 50 (28–72)                    | 2.53  | 0.58  |
| PPV8  | 0.85 (0.70–0.95) | < 0.0001    | > 7              | 79 (58–93)           | 79 (49–95)           | 86 (65–97)                    | 69 (41–89)                    | 3.69  | 0.27  |
| SSV6  | 0.56 (0.39–0.72) | 0.563       | -                | -                    | -                    | -                             | -                             | -     | -     |
| SSV8  | 0.77 (0.61–0.89) | 0.0003      | > 5              | 67 (45–84)           | 79 (49–95)           | 84 (60–97)                    | 58 (34–80)                    | 3.11  | 0.42  |
| \(\Delta PPV6\)-8 | 0.95 (0.83–0.99) | < 0.0001    | > 1              | 92 (73–99)           | 86 (57–98)           | 92 (73–99)                    | 86 (57–98)                    | 6.42  | 0.097 |
| \(\Delta SSV6\)-8 | 0.76 (0.60–0.89) | 0.0006      | > 2              | 46 (26–67)           | 100 (77–100)         | 100 (72–100)                  | 52 (32–71)                    | -     | 0.54  |

ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; LR, likelihood ratio; PPV6, pulse pressure variation during tidal volume at 6 ml/kg predicted body weight (PBW); SSV6, stroke volume variation during tidal volume at 6 ml/kg PBW; PPV8, pulse

**Figures**
Figure 1

Study protocol. Arrows indicate time points at which measurements were made.

PnP, pneumoperitoneum; VT, tidal volume; PBW, predicted body weight.
Figure 2

Study diagram.
Figure 3

Relationship between volume expansion-induced changes in pulse pressure variation and stroke volume variation and volume expansion-induced percentage changes in the stroke volume index (SVI). \( \Delta \text{PPV}_{VE} \), changes in pulse pressure variation after volume expansion; \( \Delta \text{SVVV}_{VE} \), changes in stroke volume variation after volume expansion.
Comparison of receive-operating characteristic curves of PPV6, PPV8, SVV6, and SVV8 to predict fluid responsiveness during robot-assisted laparoscopic surgery in the Trendelenburg position under lung-protective ventilation. PPV6, pulse pressure variation during tidal volume at 6 ml/kg predicted body weight (PBW); PPV8, pulse pressure variation during tidal volume at 8 ml/kg PBW; SVV6, stroke volume variation during tidal volume at 6 ml/kg predicted body weight (PBW); SVV8, stroke volume variation during tidal volume at 8 ml/kg PBW; area under the ROC curve appears in cartouche with 95% confidence interval.
Supplementary Files

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