의학석사 학위논문

Effect of Ventilatory Parameters on the Measurement of Arterial pressure-derived Stroke Volume Variation in Mechanically Ventilated Surgical Patients

기계환기 하 수술 중인 환자에서 인공호흡기 매개변수가 동맥압 유래 일회박출량변이 측정에 미치는 영향

2023년 2월

서울대학교 대학원
의학과 마취통증의학전공
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이 논문을 의학석사 학위논문으로 제출함

2022년 10월

서울대학교 대학원

의학과 마취통증의학전공

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박동녘의 석사 학위논문을 인준함

2023년 1월

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국문초록

현대 수술에서 적용되는 폐 보호 환기법 및 복강경 수술법의 도입으로 다양해진 수술 중 환자 체위로 인해, 수액 요법의 효율적인 지표로 알려져 있는 일회박출량변이 (stroke volume variation, SVV)의 적용 가치가 낮아지고 있다. 이는 기계환기 중인 환자에서 인공호흡기 매개변수의 변화가 일회박출량변이에 영향을 줌에 따라 해당 수치를 잘못 해석할 가능성이 발생하기 때문이다. 본 연구에서는 수술 중 인공호흡기의 동적 매개변수가 일회박출량변이에 끼치는 영향을 정량적으로 분석하고자 하였다.

비심장수술을 받는 환자의 인구 통계학적 정보 및 신체 계측치, 수술 중 활력 징후 및 인공호흡기 매개변수를 후향적으로 수집하여 선형 혼합 효과 분석 (linear mixed effect analyses)을 시행하였다. 이를 통해 일회박출량변이가 최고 흡기압 (peak inspiratory pressure), 호기말 양압 (positive end-expiratory pressure), 예측 체중 당 일회 호흡량 (tidal volume per kg of predicted body weight), 폐유순도 (lung compliance)와 같은 고정효과 독립변수의 영향을 받음을 보였다. 또한 일회 박출량 (stroke volume)이 교란 변수로 고려되었으며, 임의 효과를 설명하기 위해 임의절편 모델 (random intercept model)이 채택되었다.

비심장수술을 받은 694명의 환자로부터 148,732개의 data points를 분석하였고, 일회 박출량 값을 조정한 뒤 분석된 모든 인공호흡기 매개변수가 일회박출량변이와 유의미한 연관이 있음을 보였다. 이 가운데 최고 흡기압 (marginal R^2 = 0.08, conditional R^2 = 0.76) 이 가장 큰 예측력을 나타냈다.

본 논문의 결과에 따르면 인공호흡기 매개변수의 변화와 일회박출량변이 사이의 상관관계가 나타났으나, 일회박출량변이의 해석 시 인공호

흡기 매개변수의 변화가 일회박출량변이에 미치는 영향은 제한적인 것으로 나타났다. 나아가 일회박출량변이의 예측력을 높인 모형 수립을 위해 수술 중 수액 투여, 실혈, 환자의 혈관 내 용적 상태 등을 분석에 포함한 전향적 연구의 필요성이 제기된다.

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주요어 : 선형혼합효과모형, 일회박출량변이, 수술, 인공호흡기 매개변수

학 번 : 2020-26482

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1. Introduction

Changes in arterial pressure contours according to the respiratory cycle in mechanically ventilated patients are measured as systolic pressure variation (SPV), pulse pressure variation (PPV), and stroke volume variation (SVV). These parameters are useful dynamic indices of cardiac preload. SPV >10%, PPV >13%, and SVV >10% have been used as objective and sensitive indicators of volume responder.[1 2] These dynamic indices are useful in guiding goal-directed therapy to reduce complications from unnecessary fluid administration and improve the patient's prognosis.[3]

However, it is questionable whether the criteria values of dynamic indices presented in the past are still accurate today. It is known that the SVV is properly measured when a tidal volume (TV) of at least 8 mL kg^{-1} is applied,[4] but the current lung protective ventilatory strategy in operating rooms adopts a TV of <6 mL kg^{-1},[5 6] resulting in small changes in intrathoracic pressure and consequently reduced SVV values.[2 7–9] Furthermore, since laparoscopic surgery is widely practiced, varying intraabdominal pressure and operative position cause dynamic changes in intrathoracic pressure, airway compliance, and cardiac preload, making interpretation of the SVV more difficult.

We hypothesized that if the effects of dynamic ventilatory parameters on SVV could be quantitatively assessed, the SVV value would be interpreted more appropriately by observing changes in ventilatory parameters during surgery. Therefore, the primary goal of this study was to investigate the relationship between dynamic ventilatory parameters and SVV using linear mixed effects analysis.

2. Methods

2.1 Case selection

Data were retrieved from the data registry that collects intraoperative monitoring data of surgical patients in our institution. The registry was approved by our institutional review board (H-1408-101-605) and registered on a clinical trial registration site (ClinicalTrial.gov, NCT02914444). The retrospective use of registry data for the current study was approved by the institutional review board (H-1702-008-828). Data collection was performed in accordance with relevant guidelines and regulations of the committee. The need for written informed consent was waived owing to anonymity of the data. Adult patients who underwent non-cardiac surgeries under arterial pressure-derived cardiac output (APCO) monitoring between June 2016 and December 2016 were enrolled. Paediatric patients (age <18 years), one-lung ventilation cases were excluded from the study. Patients with preoperative atrial fibrillation which limits analysis of SVV were excluded because APCO monitoring was not applied to all of them.

Types of surgery included biliary/pancreas surgery, breast surgery, colorectal surgery, gastric surgery, hepatic surgery, transplantation, thyroid surgery, and vascular surgery.

2.2 Anesthesia

Patients arrived at the operating room without premedication. Electrocardiogram, pulse oximetry, and non-invasive blood pressure monitors were applied to the patients. During the study period, volatile anesthesia or total intravenous anesthesia with target-controlled infusion was randomly conducted. Propofol 1–1.5 mg kg^{-1} and fentanyl 50–100 mcg were administered for anesthesia induction in volatile anesthesia. Anesthesia induction in total intravenous anesthesia was conducted with target effect-site concentrations of propofol and remifentanil at 3.5–4.5 mcg mL^{-1} and 4–6 ng mL^{-1}, respectively. After loss of consciousness, rocuronium 0.9–1.2 mg $kg^{-1}$was administered and the trachea was intubated. Tube sizes with internal diameters of 7.5 mm and 7.0 mm were uniformly applied to male and female patients, respectively. Mechanical ventilation was initiated with a TV of 6 mL per kg of predicted body weight and a respiratory rate of 13 min^{-1}, then adjusted according to the surgical process and patient's status. Application of positive end-expiratory pressure (PEEP) was at the anesthesiologist's discretion during surgery, but an inspiratory pause of 10%, the default setting of the anesthesia machine, was uniformly applied. Anesthesia was maintained with sevoflurane or desflurane in air, or propofol and remifentanil infusions. Intermittent bolus of rocuronium was administered to maintain muscle relaxation. The radial artery was cannulated with 20 G intravenous catheter after induction of anesthesia. The arterial catheter was connected to the APCO monitor (EV1000™clinical platform, Edwards Lifesciences, Irvine, CA, USA) to continuously measure SVV throughout the operation. The arterial catheter was removed in the postanesthesia care unit.

2.3 Data collection

Age, sex, weight, height, operation name, and anesthesia duration were retrieved from the registry data. Vital signs data in the registry were recorded from the data communication ports of patient monitor (Solar™8000 with Tram module, GE healthcare, Wauwatosa, WI, USA), anesthesia machine (Primus®, Drägerwerk AG & Co. KGaA, Lübeck, Germany), and APCO monitor using the Vital Recorder program, a free tool for recording of high-resolution time-synchronized physiologic data from multiple anesthesia devices (available from the website, https://vitaldb.net[10]; accessed April 23, 2017). Among the recorded data, the following parameters were retrieved for analysis: heart rate, respiratory rate, set inspiratory TV, peak inspiratory pressure (Ppeak), positive end-expiratory pressure (PEEP), airway compliance, stroke volume (SV), and SVV.

Data from patient monitor and anesthesia machine were originally recorded at 2-second intervals; however, data collected every 60 seconds were used to match the update interval of SVV measurements. After visual data inspection and outlier analysis, the following data were considered invalid and excluded from the analysis: unusual values such as Ppeak = 0 cmH_2O or >40 cmH_2O, Pplat = 0 cmH_2O or >40 cmH_2O, and SVV >40%; and heart rate to respiratory rate ratio ≤3.6, which is known as a significant confounder of SVV measurements.[10] After removing invalid data points, a case with less than 30 data points was additionally excluded from the analysis.

2.4 Statistical analysis

Linear mixed effects analyses were performed using the modeling dataset to determine the relationship between ventilatory parameters and SVV. The fixed effect variables included age, sex, weight, BMI, ventilatory parameters, and SV. The ventilatory parameters included pressure (Ppeak, and PEEP), volume (TV per kg of predicted body weight), and compliance variables. The SV was also a presumed fixed effect variable because it is a surrogate indicator of left ventricular preload as well as cardiac contractility, and is known to be closely related to the SVV.[12] Since we assumed that the SVV has varying baseline values among individuals, a random intercept model was chosen to describe the random effect. The SVV was a dependent outcome of the mixed effects model. The mixed effect modeling was sequentially conducted as univariable and multivariable analyses. First, univariable models with age, sex, weight, BMI, SV or one of the ventilatory parameters as a sole fixed effect variable were tested. Multivariable modeling was then conducted using SV and one of the four ventilatory parameters as fixed effect variables to evaluate the predictive power of the ventilatory parameter after adjusting the SV and random effects. The mixed effects models were fitted using the maximum likelihood method. The predictive power of model was expressed as the marginal R^2, the percentage of the response variable variation that is explained by the fixed effect or population prediction model, and the conditional R^2, the coefficient of determination of the mixed effects or individual prediction model.[13]

Statistical analysis was performed using MedCalc (version17.0, MedCalc Software bvba, Mariakerke, Belgium). The linear mixed effects analysis was performed using R program (version 3.3.2, The R foundation) with lme4 version 1.1-12 and piecewiseSEM version 1.2.1 packages. A *P*-value <0.05 was considered significant.

3. Results

A total of 6338 cases in our data registry were screened. The enrolment and exclusion are described in Fig.1. The final analysis included 694 cases with 148,732 data points. The characteristics of the subjects are summarized in Table 1. The distribution of each ventilatory parameter and the distribution of stroke volume variation in the specific value of ventilatory parameters are shown as box-and-whisker diagram in Fig. 2.

The use of mixed effects modeling was proved to be appropriate since random effects were substantial and measurable in all tested univariable and multivariable models. In the univariable analyses, age, sex, weight and BMI were not significant (Table 2). The ventilatory parameters were significant but their small marginal R^2 values suggested that they are weak predictors of the SVV in the general population. The SV showed the largest R^2 value among univariable parameters, and had a slope estimate of -0.1, which means that every mL change of the SV negatively affects the SVV change by 0.1% as SVV.

In the multivariable analyses, all ventilatory parameters remained significant after adjusting for the effect of SV (Table 3). Pressure parameter (Ppeak) showed the largest marginal R^2 (0.08), suggesting that the SVV change during surgery can be best predicted by Ppeak in the general population, after adjusting for SV values. The conditional R^2 value of the Ppeak models was 0.76, suggesting that the predictive power of these models can be enhanced within individuals by calculating individual baseline SVV and adjusting the individual intercept of the regression equation.

To schematically illustrate the effect of ventilatory parameters on SVV after adjusting for SV, data were divided according to low (<60 mL), normal (60–100 mL), and high (>100 mL) SV categories, and linear regression plots were drawn within each SV category (Fig. 3). The regression plots of the ventilatory parameters showed significant slopes when adjusted for the SV values.

4. Discussion

Contrary to the previous studies, this study extensively and quantitatively assessed the effect of dynamic ventilatory parameters during surgery on SVV using a large intraoperative dataset. We confirmed that ventilatory parameters affect SVV after adjusting for SV. The most powerful predictors of SVV change were pressure parameters such as Ppeak, which increased the SVV value by 0.3 per 1 cmH_2O increase.

The operating room setting is generally known to be ideal for accurate measurements of the dynamic preload indices compared with the intensive care unit (ICU) environment.[7] However, the lung protective ventilatory strategy that is widely used to enhance outcomes of intermediate- and high-risk surgical patients has made the dynamic indices less valuable due to misreading of SVV and PPV.[6] Lansdorp and colleagues[14] reported that SPV, PPV, and SVV are less predictive in routine cardiac surgery due to frequent low TV and cardiac arrhythmia, and the diversity of calculation methods. Many review studies have also referred to various confounding factors affecting SVV values as limitations of SVV use.[1 4 7–9 15] These factors include TV,[14 16–23] SV,[12 20 21 24] Ppeak,[25 26] PEEP,[27–29] compliance,[15 20 23 30 31] heart rate to respiratory rate ratio,[10 24] surgical position,[32 33] pleural pressure,[34] arrhythmia,[14] and increased pulmonary artery pressure.[35] However, these previous studies only identified the presence of various confounding factors that affect SVV. The current study was successful in extensively and quantitatively evaluating the effect of dynamic ventilatory parameters during surgery on SVV.

In the current study, SV was considered to be a significant confounding factor because an inversely semi-logarithmic relationship between SV and SVV was identified in a recent arithmetical analysis.[12] A negative relationship between blood pressure and SVV was also observed in cardiac surgery patients.[21] Our study assumed a linear relationship between the two parameters because simple linear curves fitted better than semi-log curves in our explorative analysis. We speculate that this is because most of our measurements were on the inclining portion rather than on the plateau of the Frank-Starling curve. In the mixed effects model, SV is a highly explanatory parameter that can account for as much as 30% of the SVV value, suggesting that the effect of ventilatory parameters on SVV changes can be properly evaluated only after adjusting for the SV value.

Since the widespread use of lung protective ventilation, the TV has been the most studied parameter for its effect on SVV. In animal[16 24] and clinical[17 19] experiments, SVV was positively correlated with TV. Studies have found that lung protective ventilation reduced the diagnostic power of PPV and SVV in predicting volume responsiveness in ICU patients[22] and one-lung ventilated surgical patients.[36] Dynamic indices were reliable only when the TV was larger than 8 mL per body weight.[18] The positive linear relationship between TV and SVV is evident by the slope estimate of 0.4 in the current study. However, since the range of TV used in routine clinical practice is not as wide as in the designed experimental environment, the effect of various TV on SVV is the smallest among our tested ventilatory parameters: the SVV in lung protective ventilation can be generally interpreted as approximately 1% lower SVV than the SVV in conventional ventilation. On the other hand, a decrease in TV results in an increase in respiratory rate for maintaining normocarbia. In order to measure the SVV correctly, the respiratory rate must be greater than 5,[24] however, the heart rate to respiratory rate ratio should be more than 3.6 at the same time.[37]

Several studies regarding the effect of compliance on the SVV have been performed in the acute respiratory distress syndrome and acute lung injury settings.[15 30 31] In general, we cannot rule out fluid responsiveness even with reduced SVV in the situation of reduced pulmonary compliance combined with low TV. However, compliance changes in surgical patients are mainly caused by extra-pulmonary causes such as surgical positioning and application of pneumoperitoneum. In animal experiments, applying chest and abdominal binders[20] and inducing intra-abdominal hypertension[31] resulted in a significant increase in SVV with increasing TV. Similarly, our study results showed a significant negative relationship between compliance and SVV during surgery. However, despite the large predictive power over other ventilatory parameters, the compliance parameter is less practical because several parameters, including Ppeak, PEEP, and TV, need to be measured for calculation of compliance.

Pressure parameters have not been extensively investigated compared with volume and compliance parameters. The sole effect of

PEEP has been tested in mechanically ventilated ICU patients,[29] demonstrating that the SVV linearly increases with increasing PEEP in volume responders, irrespective of the amount of TV. In current study, such a linear relationship between PEEP and SVV was shown but very weak because cases were not confined to volume responders, and the PEEP level was negligible in our daily practice. The positive relationship between Ppeak and SVV has been previously demonstrated in an animal experiment[26] and paediatric patients.[25] The Pplat has been tested in combination with PEEP as an driving pressure (Pplat-PEEP), which can adjust the PPV threshold values in volume responders.[28 38] The current study identified that the Ppeak is the most reliable ventilatory predictors of the SVV in surgical patients possibly due to their direct effect on pulmonary capillaries. Thses findings suggest that Ppeak may be the most useful ventilatory predictor because it has the greatest predictive power and can be easily assessed from most anesthesia machines.

There are several limitations of the current study. First, time-series data of volume status, fluid administration, and bleeding, which are important factors affecting SVV, were not included in the fixed effect variables, owing to the limitations of retrospective data collection. However, the effects of these factors were considered to be included in the SV parameter and random effects, making the ventilatory parameter significant and consistent. Second, the actual threshold of SVV after controlling the ventilatory parameter cannot be defined in the current study. The identification of threshold values in lung protective ventilation in combination with various surgical settings requires prospective trials. Third, the predictive power of the models was small in the fixed effect/general population model. Using categorical variables or involving hypovolemic patients only may have increased the explanatory power of the model as in the previous studies. However, the study is meaningful in that it showed a quantitative association between dynamic ventilatory parameters and SVV during surgery.

In conclusion, the change in SVV during surgery is linearly proportional to the changes in ventilatory parameters; the SVV has a positive relationship with pressure and volume parameters, and a negative relationship with compliance. However, the effects of ventilatory parameters change on SVV look limited because prediction power of the sole parameter on SVV was weak. In addition, prospective trials that evaluate the SVV threshold may be required in association with ventilatory parameter changes during surgery.

Table 1. Characteristics of subjects (n = 694)

Variable	
Number of data points	208 [123-298]
Age	60 [51-69]
Sex (male/female)	430/264
Height (cm)	163.9 [157.9-169.8]
Weight (kg)	60.85 [53.25-68.75]
Predicted body weight (kg)	59.4 [51.1-65.7]
Body mass index (kg m^{-2})	22.8 [20.5-25.0]
Heart rate (min^{-1})	74 [65-85]
Respiratory rate (min^{-1})	13 [15-16]
Set tidal volume (mL)	400 [350-440]
Peak inspiratory pressure (cmH_2O)	14 [12-18]
Positive end-expiratory pressure (cmH_2O)	0 [0-0]
Compliance (mL cmH_2O^{-1})	33 [27-40]
Tidal volume per kg of predicted body weight (mL kg^{-1})	6.6 [6.2-7.3]

Data are expressed as median [interquartile range(IQR)]

Table 2. Univariable linear mixed effects models to predict stroke volume variation during surgery (n = 694, n of measurement = 148,732)

Model	Fixed effects					Random effects		Marginal R^2	Conditional R^2
	Slope			Intercept		Intercept SD	Residual SD		
	Estimate	SE	P-value	Estimate	SE				
Age (years)	0.0	0.0	0.807	10.0	0.6	3.6	4.0	0.00	0.45
Sex (male)	0.4	0.3	0.184	10.0	0.2	3.6	4.0	0.00	0.45
Weight (kg)	0.0	0.0	0.118	9.1	0.7	3.6	4.0	0.00	0.45
BMI(kg m^{-2})	0.1	0.0	0.142	8.9	0.9	3.6	4.0	0.00	0.45
SV (mL)	-0.1	0.0	<0.001	20.3	0.2	3.8	3.5	0.30	0.68
Ppeak (cmH_2O)	0.5	0.0	<0.001	3.0	0.1	3.5	3.8	0.15	0.53
PEEP (cmH_2O)	0.2	0.0	<0.001	10.0	0.1	3.6	4.0	0.01	0.45
Compliance (mL cmH_2O^{-1})	-0.2	0.0	<0.001	16.5	0.1	3.5	3.9	0.11	0.52
TV per kg of PBW (mL kg^{-1})	0.5	0.0	<0.001	6.8	0.3	3.6	4.0	0.01	0.45

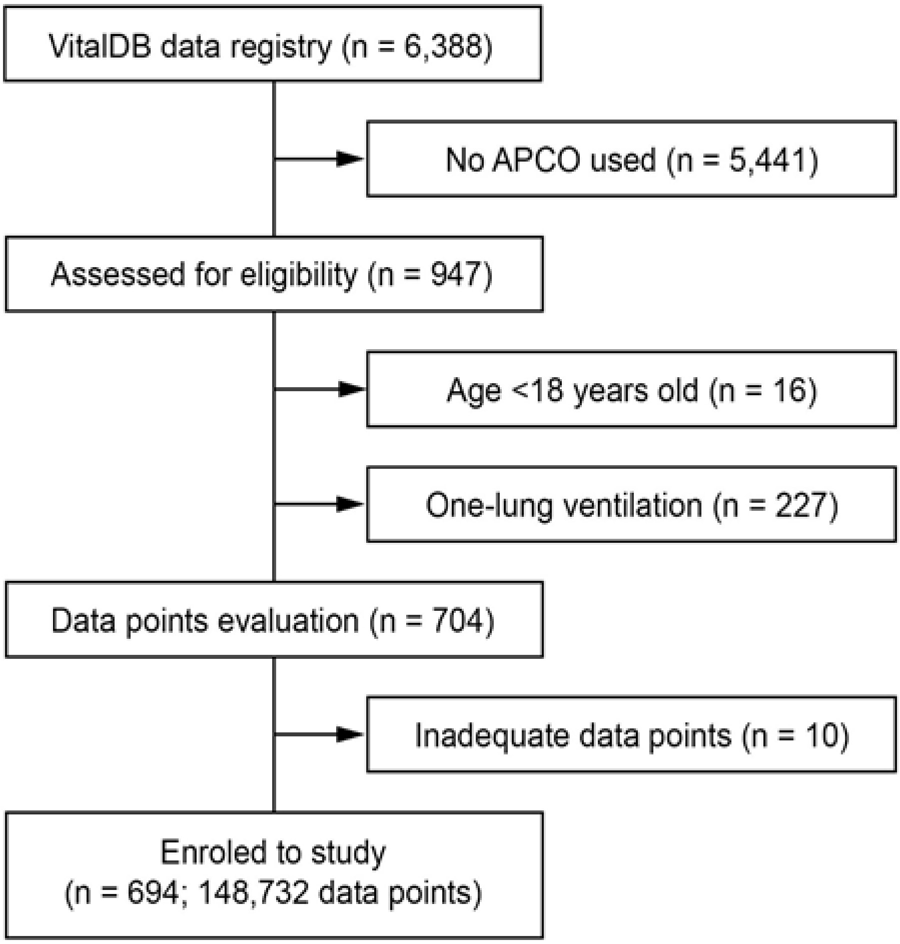
Abbreviations: BMI = body mass index, SV = stroke volume, PEEP = positive end-expiratory pressure, Ppeak = peak inspiratory pressure, TV = tidal volume, PBW = predicted body weight, SE = standard error, SD= standard deviation

Table 3. Nested linear mixed effect models to predict stroke volume variation during surgery (n = 694, n of measurement = 148,732, n of stroke volume measurement by subject = 28,515)

Model	Fixed effects					Random effects			Marginal R^2	Conditional R^2
	Slope			Intercept		SV SD	Subject SD	Residual SD		
	Estimate	SE	P-value	Estimate	SE					
Ppeak (cmH_2O)	0.3	0.0	<0.001	5.0	0.1	3.3	3.2	2.8	0.08	0.76
PEEP (cmH_2O)	0.1	0.0	<0.001	10.1	0.1	3.5	3.4	2.8	0.00	0.76
Compliance ($mL\ cmH_2O^{-1}$)	-0.2	0.0	<0.001	15.1	0.1	3.3	3.3	2.8	0.06	0.76
TV per kg of PBW ($mL\ kg^{-1}$)	0.4	0.0	<0.001	7.6	0.2	3.5	3.3	2.8	0.00	0.74

Abbreviations: SV = stroke volume, SE = standard error, SD= standard deviation, Ppeak = peak inspiratory pressure, PEEP = positive end-expiratory pressure, TV = tidal volume, PBW = predicted body weight

Figure 1. Flow diagram



Abbreviations: APCO = arterial pressure-derived cardiac output

Figure 2. Distribution of ventilatory parameters (horizontal boxes) and SVV in each value of ventilatory parameters (vertical boxes)

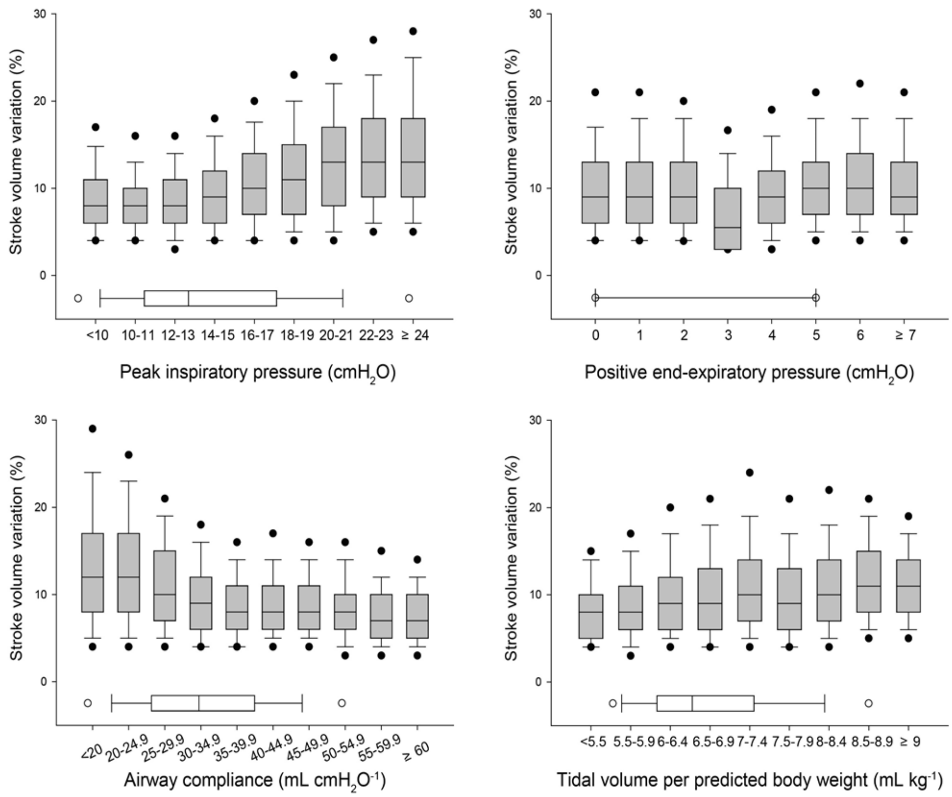
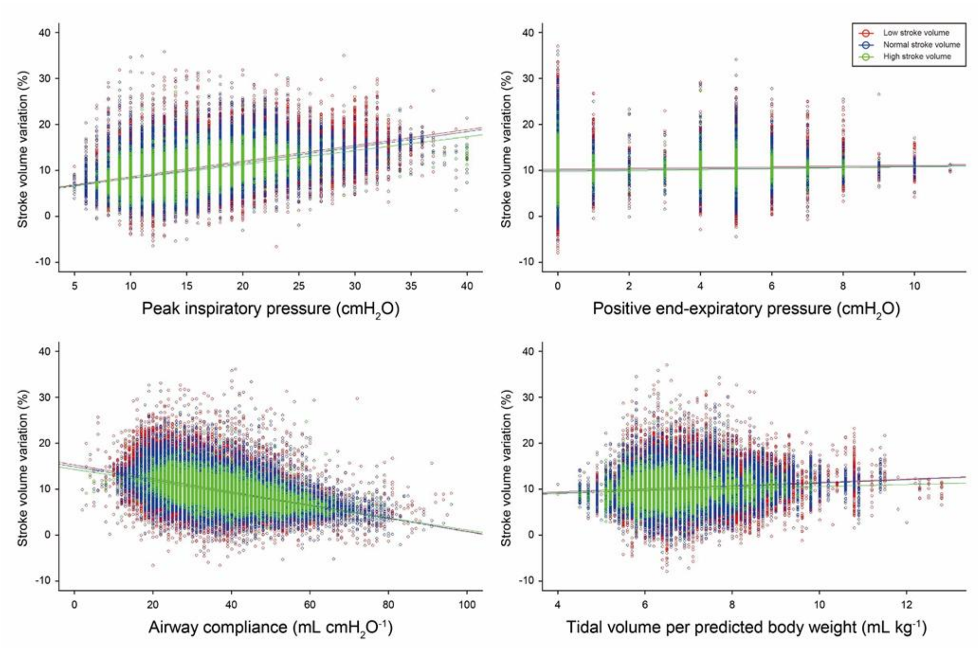


Figure 3. Effect of ventilatory parameters on stroke volume variation after adjusting for stroke volume



Scatter plots are drawn after controlling individual random effects. Linear regression plots between stroke volume variation and ventilatory parameter are illustrated according to the stroke volume values such as low (<60 mL), normal (60–100 mL), and high (>100 mL) stroke volume categories. The regression plots of the ventilatory parameters show significant slopes except for those of the positive end-expiratory pressure.

References

1. Hofer CK, Cannesson M. Monitoring fluid responsiveness. *Acta Anaesthesiol Taiwan* [Internet] 2011; **49**: 59–65 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21729812

2. Roberson RS. Respiratory variation and cardiopulmonary interactions. *Best Pract Res Clin Anaesthesiol* [Internet] Elsevier Ltd; 2014; **28**: 407–18 Available from: http://dx.doi.org/10.1016/j.bpa.2014.09.001

3. Salzwedel C, Puig J, Carstens A, et al. Perioperative goal-directed hemodynamic therapy based on radial arterial pulse pressure variation and continuous cardiac index trending reduces postoperative complications after major abdominal surgery: a multi-center, prospective, randomized study. *Crit Care* [Internet] Critical Care; 2013; **17**: R191 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24010849

4. Ouattara A, Dewitte A, Rozé H. Intraoperative management of heart-lung interactions: 'from hypothetical prediction to improved titration'. *Ann Fr Anesth Reanim* [Internet] 2014; **33**: 476–9 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25127853

5. Wanderer JP, Blum JM, Ehrenfeld JM. Intraoperative Low-Tidal-Volume Ventilation. *N Engl J Med* [Internet] 2013; **369**: 1861–3 Available from: http://www.nejm.org/doi/abs/10.1056/NEJMc1310006

6. Futier E, Constantin J-M, Paugam-Burtz C, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. *N*

Engl J Med [Internet] 2013; **369**: 428–37 Available from: http://www.ncbi.nlm.nih.gov/pubmed/23902482

7. Guerin L, Monnet X, Teboul J-L. Monitoring volume and fluid responsiveness: from static to dynamic indicators. *Best Pract Res Clin Anaesthesiol* [Internet] Elsevier Ltd; 2013; **27**: 177–85 Available from: http://dx.doi.org/10.1016/j.bpa.2013.06.002

8. Perel A, Pizov R, Cotev S. Respiratory variations in the arterial pressure during mechanical ventilation reflect volume status and fluid responsiveness. *Intensive Care Med* [Internet] 2014; **40**: 798–807 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24737260

9. Pinsky MR. Functional Hemodynamic Monitoring. *Crit Care Clin* [Internet] 2015; **31**: 89–111 Available from: http://www.ncbi.nlm.nih.gov/pubmed/20402989

10. H-C Lee, Y Park, SB Yoon, SM Yang, D Park, C Jung. VitalDB, a high-fidelity multi-parameter vital signs database in surgical patients. *Scientific Data* 2022; **9**: Article number: 279 Available from: https://www.nature.com/articles/s41597-022-01411-5

11. De Backer D, Taccone FS, Holsten R, Ibrahimi F, Vincent J-L. Influence of respiratory rate on stroke volume variation in mechanically ventilated patients. *Anesthesiology* [Internet] 2009; **110**: 1092–7 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19352152

12. Sawa T, Kinoshita M, Kainuma A, et al. Effective evaluation of arterial pulse waveform analysis by two-dimensional stroke volume variation-stroke volume index plots. *J Clin Monit Comput* [Internet] Springer Netherlands; 2016; **v**: 1–15 Available from: http://www.ncbi.nlm.nih.gov/pubmed/27492429

13. Nakagawa S, Schielzeth H. A general and simple method for obtaining R 2 from generalized linear mixed-effects models. O'Hara RB, editor. *Methods Ecol Evol* [Internet] 2013; **4**: 133–42 Available from: http://www.ncbi.nlm.nih.gov/pubmed/11165473

14. Lansdorp B, Lemson J, van Putten MJAM, de Keijzer A, van der Hoeven JG, Pickkers P. Dynamic indices do not predict volume responsiveness in routine clinical practice. *Br J Anaesth* [Internet] 2012; **108**: 395–401 Available from: http://www.ncbi.nlm.nih.gov/pubmed/22185905

15. Teboul J. Pulse pressure variation and ARDS. *Ed MINERVA MEDICA* 2013; **79**: 398–407

16. Szold a, Pizov R, Segal E, Perel A. The effect of tidal volume and intravascular volume state on systolic pressure variation in ventilated dogs. *Intensive Care Med* [Internet] 1989; **15**: 368–71 Available from: http://www.ncbi.nlm.nih.gov/pubmed/2681312

17. Reuter D a, Bayerlein J, Goepfert MSG, et al. Influence of tidal volume on left ventricular stroke volume variation measured by pulse contour analysis in mechanically ventilated patients. *Intensive Care Med* [Internet] 2003; **29**: 476–80 Available from: http://www.ncbi.nlm.nih.gov/pubmed/12579420

18. De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent J-L. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. *Intensive Care Med* [Internet] 2005; **31**: 517–23 Available from: http://www.ncbi.nlm.nih.gov/pubmed/15754196

19. Charron C, Fessenmeyer C, Cosson C, et al. The influence of tidal volume on the dynamic variables of fluid responsiveness in critically

ill patients. *Anesth Analg* [Internet] 2006; **102**: 1511–7 Available from: http://www.ncbi.nlm.nih.gov/pubmed/16632835

20. 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* [Internet] 2011; **37**: 1672–9 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21739340

21. Sakka SG, Becher L, Kozieras J, van Hout N. Effects of changes in blood pressure and airway pressures on parameters of fluid responsiveness. *Eur J Anaesthesiol* [Internet] 2009; **26**: 322–7 Available from: http://www.ncbi.nlm.nih.gov/pubmed/19401662

22. Lakhal K, Ehrmann S, Benzekri-Lefèvre D, et al. Respiratory pulse pressure variation fails to predict fluid responsiveness in acute respiratory distress syndrome. *Crit Care* [Internet] 2011; **15**: R85 Available from: http://ccforum.biomedcentral.com/articles/10.1186/cc10083

23. Díaz F, Erranz B, Donoso A, Salomon T, Cruces P. Influence of tidal volume on pulse pressure variation and stroke volume variation during experimental intra-abdominal hypertension. *BMC Anesthesiol* [Internet] BMC Anesthesiology; 2015; **15**: 127 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26395001%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4579832

24. 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* [Internet] 2008; **36**: 2858–62 Available from: http://www.ncbi.nlm.nih.gov/pubmed/18766112

25. Kang W-S, Kim JY, Woo NS, Yoon TG. The influence of different mechanical ventilator settings of peak inspiratory pressure on stroke volume variation in pediatric cardiac surgery patients. *Korean J Anesthesiol* [Internet] 2014; **66**: 358–63 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24910727

26. Kawazoe Y, Nakashima T, Iseri T, et al. The impact of inspiratory pressure on stroke volume variation and the evaluation of indexing stroke volume variation to inspiratory pressure under various preload conditions in experimental animals. *J Anesth* [Internet] Springer Japan; 2015; **29**: 515–21 Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4543412&tool=pmcentrez&rendertype=abstract

27. Huang C-C, Fu J-Y, Hu H-C, et al. Prediction of fluid responsiveness in acute respiratory distress syndrome patients ventilated with low tidal volume and high positive end-expiratory pressure. *Crit Care Med* [Internet] 2008; **36**: 2810–6 Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00003246-200810000-00015%5Cnpapers3://publication/doi/10.1097/CCM.0b013e318186b74e

28. 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. *Appl Physiol Intensive Care Med 1 Physiol Notes - Tech Notes - Semin Stud Intensive Care, Third Ed* 2012; 217–24

29. Kang W-S, Kim S-H, Kim SY, Oh C-S, Lee S-A, Kim J-S. The influence of positive end-expiratory pressure on stroke volume variation in patients undergoing cardiac surgery: an observational

study. *J Thorac Cardiovasc Surg* [Internet] Elsevier Inc.; 2014; **148**: 3139–45 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25224551

30. Monnet X, Bleibtreu A, Ferré A, et al. Passive leg-raising and end-expiratory occlusion tests perform better than pulse pressure variation in patients with low respiratory system compliance. *Crit Care Med* [Internet] 2012; **40**: 152–7 Available from: http://www.ncbi.nlm.nih.gov/pubmed/21926581

31. Erranz B, Díaz F, Donoso A, et al. Decreased lung compliance increases preload dynamic tests in a pediatric acute lung injury model. *Rev Chil Pediatr* [Internet] Sociedad Chilena de Pediatría; 2015; **86**: 404–9 Available from: http://dx.doi.org/10.1016/j.rchipe.2015.06.023

32. Min JH, Lee SE, Lee HS, et al. The correlation between the Trendelenburg position and the stroke volume variation. *Korean J Anesthesiol* [Internet] 2014; **67**: 378–83 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25558337

33. Mathis MR, Schechtman SA, Engoren MC, et al. Arterial Pressure Variation in Elective Noncardiac Surgery: Identifying Reference Distributions and Modifying Factors. *Anesthesiology* [Internet] 2017; **126**: 249–59 Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00000542-201702000-00015%0Ahttp://www.ncbi.nlm.nih.gov/pubmed/27906705%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5243154

34. Liu Y, Wei L, Li G, Yu X, Li G, Li Y. Pulse Pressure Variation Adjusted by Respiratory Changes in Pleural Pressure, Rather Than by Tidal Volume, Reliably Predicts Fluid Responsiveness in Patients With

Acute Respiratory Distress Syndrome. *Crit Care Med* [Internet] 2016; **44**: 342–51 Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00003246-900000000-97146%5Cnhttp://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00003246-201602000-00013%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/26457754

35. Daudel F, Tüller D, Krähenbühl S, Jakob SM, Takala J. Pulse pressure variation and volume responsiveness during acutely increased pulmonary artery pressure: an experimental study. *Crit Care* [Internet] 2010; **14**: R122 Available from: http://www.ncbi.nlm.nih.gov/pubmed/20576099

36. Fu Q, Duan M, Zhao F, Mi W. Evaluation of stroke volume variation and pulse pressure variation as predictors of fluid responsiveness in patients undergoing protective one-lung ventilation. *Drug Discov Ther* [Internet] 2015; **9**: 296–302 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26370528

37. De Backer D, Scolletta S. Why do pulse pressure variations fail to predict the response to fluids in acute respiratory distress syndrome patients ventilated with low tidal volume? *Crit Care* [Internet] 2011; **15**: 150 Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3219368&tool=pmcentrez&rendertype=abstract

38. Vallée F, Richard JCM, Mari A, et al. Pulse pressure variations adjusted by alveolar driving pressure to assess fluid responsiveness. *Intensive Care Med* 2009; **35**: 1004–10

Abstract

Effect of Ventilatory Parameters on the Measurement of Arterial pressure-derived Stroke Volume Variation in Mechanically Ventilated Surgical Patients

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Background: Stroke volume variation (SVV), a useful guide of fluid administration, has become less valuable in recent surgery because lung protective ventilation and surgical positioning result in substantial changes in ventilatory parameters and misreading of SVV values. The aim of this study was to quantitatively assess the effect of dynamic ventilatory parameters during surgery on SVV.

Methods: Intraoperative data of non-cardiac surgical patients were retrospectively collected. Linear mixed effects analyses were performed using a modeling dataset. SVV was a dependent outcome and independent fixed effect variables included peak inspiratory pressure, positive end-expiratory pressure, tidal volume per kg of predicted body weight, and airway compliance. Stroke volume was considered a confounding factor. A random intercept model was chosen to describe the random effect. The final models were externally validated using a validation dataset.

Results: Analysis included 694 non-cardiac patients with 148,732 data points. All ventilatory parameters were significantly correlated with SVV after adjusting for stroke volume (*P* <0.001). The peak inspiratory pressure showed the largest predictive power (marginal R^2=0.08 and conditional R^2=0.76).

Conclusion: Change in SVV during surgery is linearly proportional to the changes in ventilatory parameters. The effects of ventilatory parameters change on SVV looks limited because the predictive ability of the sole parameter on SVV was weak. In addition, prospective trials that evaluate the SVV threshold may be required in association with ventilatory parameter changes during surgery.

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keywords : Linear mixed effects analysis, Stroke volume variation, Surgery, Ventilatory parameters.

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