

CARDIOVASCULAR

Comparison of an automated respiratory systolic variation test with dynamic preload indicators to predict fluid responsiveness after major surgery

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Editor's key points

- The automated respiratory systolic variation test (RSVT) is a new device to determine fluid responsiveness.
- This study compared automated RSVT with methods using stroke volume variation and pulse pressure variation.
- The RSVT was reproducible and was at least as accurate as the other devices.
- The study was relatively small and further work is needed to confirm these findings.

Background. Predicting the response of cardiac output to volume administration remains an ongoing clinical challenge. The objective of our study was to compare the ability to predict volume responsiveness of various functional measures of cardiac preload. These included pulse pressure variation (PPV), stroke volume variation (SVV), and the recently launched automated respiratory systolic variation test (RSVT) in patients after major surgery.

Methods. In this prospective study, 24 mechanically ventilated patients after major surgery were enrolled. Three consecutive volume loading steps consisting of 300 ml 6% hydroxyethylstarch 130/0.4 were performed and cardiac index (CI) was assessed by transpulmonary thermodilution. Volume responsiveness was considered as positive if CI increased by >10%.

Results. In total 72 volume loading steps were analysed, of which 41 showed a positive volume response. Receiver operating characteristic (ROC) curve analysis revealed an area under the curve (AUC) of 0.70 for PPV, 0.72 for SVV and 0.77 for RSVT. Areas under the curves of all variables did not differ significantly from each other ($P>0.05$). Suggested cut-off values were 9.9% for SVV, 10.1% for PPV, and 19.7° for RSVT as calculated by the Youden Index.

Conclusion. In predicting fluid responsiveness the new automated RSVT appears to be as accurate as established dynamic indicators of preload PPV and SVV in patients after major surgery. The automated RSVT is clinically easy to use and may be useful in guiding fluid therapy in ventilated patients.

Keywords: dynamic haemodynamic monitoring; heart–lung interaction; volume responsiveness

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As cardiac preload is an essential determinant of cardiac output (CO) the question of volume responsiveness remains a main challenge in perioperative and intensive care medicine. Optimizing CO has been shown to improve patient outcome by reducing hypoperfusion in hypovolaemic and haemodynamically unstable patients.^{1–3} Nevertheless, unnecessary volume loading in terms of not leading to a further increase of CO may cause not only pulmonary or intestinal oedema but also myocardial deterioration resulting in acute heart failure and organ insufficiency.^{4–5} Many studies have shown the limitations of pressure-based indicators of preload, like central venous pressure (CVP) or pulmonary artery occlusion pressure (PAOP), in properly predicting volume responsiveness,^{6–7} interest has focused on functional measures of cardiac preload. These are based on heart–lung interactions

and quantify the respiratory-induced variations in arterial pulse pressure variation (PPV) or stroke volume variation (SVV). Prerequisites for the use of these variables are an arterial catheter, the need for a regular cardiac rhythm and controlled mechanical ventilation.⁸ Nonetheless the use of functional haemodynamic measures still has certain inbuilt limitations, such as the influence of tidal volume and pulmonary and chest wall compliance.^{9–12} Therefore, to eliminate at least the dependency on tidal volume, the respiratory systolic variation test (RSVT) was introduced.^{13–14} The RSVT quantifies the decrease in systolic pressure in response to a standardized manoeuvre consisting of three consecutive mechanical breaths with increasing airway pressure. The main advantage of RSVT is that it is independent of certain tidal volumes.^{13–15} In contrast to established measures like PPV and SVV, the RSVT does not

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include the maximal increase of stroke volume in the beginning of inspiration (delta-up), which is not related to volume responsiveness. RSVT only takes into account the slope created by the lowest systolic values, showing its independence to the delta-up component.^{16–18} Recent data from our group have shown in an experimental study that the RSVT predicts volume responsiveness at least as accurate as SVV and PPV and might even have the potential to exceed SVV and PPV.¹⁵

However, so far only limited clinical data for the application of RSVT have been published. Especially no data regarding the performance and feasibility of the new automated and standardized RSVT software, embedded in last generation ventilators, exist. Hence, the aim of this study was to evaluate the ability and applicability of the recently introduced RSVT software (Dräger Medical, Lübeck, Germany) to predict volume responsiveness in a heterogenous patient population after major surgery and to compare its performance with PPV, and SVV.

Methods

After approval by the Ethics Committee of the Hamburg Medical Board (Aerztekammer Hamburg) and personal written informed consent 24 patients undergoing major surgery were included in this prospective clinical study. Inclusion criteria were age >18 yr, controlled mechanical ventilation in the postoperative setting, the necessity of invasive arterial-pressure monitoring and central venous catheterization defined by our standard clinical procedures. Excluded were patients with a history of lung surgery or pneumothorax, cardiac arrhythmias, history of renal failure or severe renal insufficiency (serum creatinine >1.5 mg dl⁻¹) and the presence of contraindications for femoral artery catheterization.

Monitoring

Before surgery, patients were fasted overnight and premedication of 7.5 mg midazolam was administered orally 30 min before induction of anaesthesia. All patients were monitored with ECG, pulse oximetry and non-invasive arterial pressure. For the assessment of CVP an 8 Fr triple-lumen central venous catheter (B. Braun, Melsungen, Germany) was inserted into the internal jugular vein. Further, a 5 Fr thermistor-tipped femoral artery catheter (PV2025 L20, Pulsioath, Pulsion Medical Systems, Munich, Germany) was inserted into the femoral artery.

Anaesthesia

Anaesthesia was induced by i.v. injection of sufentanil 0.3 µg kg⁻¹, propofol 3 mg kg⁻¹, and rocuronium 0.6 mg kg⁻¹ and was maintained using a continuous infusion of propofol 4 mg kg⁻¹ min⁻¹ and sufentanil 0.2 µg kg⁻¹ h⁻¹. Tracheal intubation was performed using a cuffed tracheal tube. Controlled mechanical ventilation was performed in a pressure-controlled mode using tidal volumes of 8 ml kg⁻¹ and a positive end-expiratory pressure of 5 cm H₂O. Inspiration to expiration ratio was 1:2. End-expiratory P_{CO₂} was maintained at 5–6 kPa by adjusting respiratory rate. The amount of fluid intake and output was similar in all patients; crystalloid (Ringer's lactate)/colloid (6% hydroxyethyl starch 130/0.4) ratio was

kept 3:1, transfusion threshold was defined at a haemoglobin of 7 g dl⁻¹. To maintain a mean arterial pressure (MAP) within the range of 70–90 mm Hg, consistent with our standard operating procedure, norepinephrine was continuously applied intravenously via an infusion pump as required.

Measurements

Respiratory systolic variation test

For the first time we tested an automatically performed RSVT in a clinical setting. The software included in the ventilator (Evita XL, Drägermedical, Lübeck, Germany) controls the application of this standardized manoeuvre. After initiation of the RSVT the ventilator administers three consecutive pressure-controlled mechanical breaths of gradually increasing pressure (10–20–30 cm H₂O).^{13 15} The airway pressure and the arterial pressure wave form are analysed by the RSVT software simultaneously. The minimum systolic arterial pressure value after each mechanical breathing cycle is plotted against the corresponding airway pressure. The slope of this line (RSVT angle in degrees) is calculated from the first and third point by the following formula:

$$\text{RSVT slope} = \left(\frac{P_{\text{arterial1}} - P_{\text{arterial3}}}{P_{\text{insp_mean3}} - P_{\text{insp_mean1}}} \right)$$

where $P_{\text{arterial1}}$ is the minimum systolic pressure during the first breathing cycle, $P_{\text{arterial3}}$ is the minimum systolic pressure during the third breathing cycle, $P_{\text{insp_mean1}}$ is the mean airway pressure during the first breathing cycle, $P_{\text{insp_mean3}}$ is the mean airway pressure during the third breathing cycle, and thereafter RSVT angle is calculated as: RSVT angle = atan (RSVT slope).

The software algorithm defines the threshold for the beginning of inspiration at airway pressures at 1.5 cm H₂O above positive end-expiratory pressure (PEEP) and at the threshold for the end of inspiration at 1.0 cm H₂O above PEEP. The changed order of indices given in the formula assures positive values. A screenshot is presented in Figure 1. In our study protocol, at each point of measurement three RSVT manoeuvres (each consisting of three respiratory cycles) were performed and the mean of three valid measurements was calculated.

Pulse contour analysis and thermodilution

Online pulse contour analysis was carried out using the PiCCO monitoring system (PiCCO 2, Pulsion Medical Systems, Munich, Germany). Transpulmonary thermodilution measurements were performed with each point of measurement consisting of three sequential central venous injections of 10 ml cold saline solution (<8°C) randomly administered throughout the respiratory cycle. Measurements were accepted for statistical analysis if none of the three values differed by >10% from the mean of those three measurements.

Study protocol

After surgery anaesthesia was maintained with infusions of propofol (4 mg kg⁻¹ h⁻¹) and sufentanil (0.1 µg kg⁻¹ h⁻¹). After an initial time for equilibration of 30 min baseline

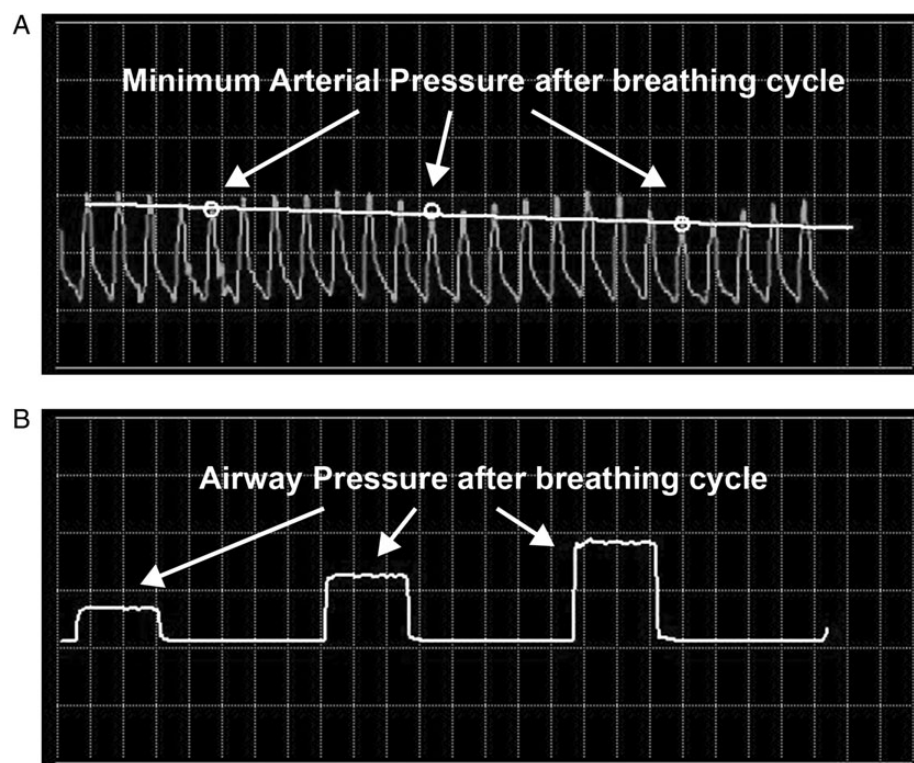


Fig 1 Screenshot of the RSVT manoeuvre. In (A) the automated definition of minimum systolic arterial pressures after each mechanical breathing cycle and the defined slope are shown. In (B) the corresponding three consecutively applied mechanical breaths of 10, 20, and 30 cm H₂O are depicted.

measurements were performed. Three consecutive volume loading steps each consisting of 300 ml 6% hydroxyethylstarch 130/0.4 were performed in order to assess volume responsiveness. Haemodynamic measurements followed each volume loading step after an equilibration period of 5 min. All patients were continuously monitored for any signs of acute volume overload. A sudden decrease of CI, a decrease of AP and an increase of CVP were defined as criteria to end further volume load and exclude the patient from further measurements.

Statistical analysis

Data were analysed using SigmaStat for Windows 3.5 (Systat Software, Inc., San Jose, CA, USA). Normal distribution of all data was tested using the Kolmogorov–Smirnov test with Lilliefors' correction. Normally distributed variables were expressed as mean (SD), otherwise as median (25–75 interquartile ranges). Normally distributed data were analysed with a one-way analysis of variance (ANOVA) for repeated measurements; non-normally distributed data were analysed with Friedman repeated measures ANOVA on ranks. *Post hoc* testing was performed using the Tukey's test. The assessment of tested variables to predict a positive volume response was performed by generating receiver operating characteristic (ROC) curves. ROC curves were compared statistically by the method of DeLong and colleagues.¹⁹ Threshold values were assessed determining values that yielded the greatest

sensitivity and specificity by calculating the Youden Index.²⁰ The response to volume administration was considered positive if CI increased by at least 10% (criterion value). A *P*-value of <0.05 was considered as statistically significant.

Results

Twenty-four patients (13 females and 11 males) were included in the study (Table 1). Haemodynamic data and their changes throughout the experimental protocol at baseline and after each volume loading step are given in Table 2.

Prediction of volume responsiveness

A total of 72 volume loading steps were administered and analysed, thereof 41 (57%) presenting with a positive response in CI to fluid loading. The areas under the ROC curve (AUC) for an increase in CI >10% of all investigated parameters were significantly larger than 0.5. In detail, the AUC for PPV was 0.70 [95% confidence intervals (CIs) 0.21–0.85], for SVV 0.72 (95% CIs 0.21–0.85) and for RSVT angle 0.77 (95% CI 0.55–0.80). There were no statistical differences in AUC values between tests and variables (Fig. 2).

According to ROC analysis for this study, the following threshold values for a prediction of volume responsiveness can be proposed: PPV >10.1% (sensitivity 61.0%; specificity 80.7%; and Youden Index 41.6), SVV >9.9% (sensitivity

63.4%; specificity 74.2%; and Youden Index 0.38) RSVT angle $>19.7^\circ$ (sensitivity 78.1%; specificity 67.7%; and Youden Index 0.46). Figure 3A–C presents dot histograms of the respective variables, representing the individual test value before volume loading.

Discussion

This study is the first demonstration of the feasibility of an automated RSVT—consisting of a linkage between ventilator and monitor—to predict volume responsiveness in patients after major surgery. One of the main findings of our study is that the standardized, automated RSVT is easy to use and provides good reproducibility. Further, the RSVT is a reliable predictor of volume responsiveness in ventilated patients in an every day clinical scenario after major surgery with a remarkable fluid turnover. Our results demonstrate no significant difference in sensitivity and specificity in the prediction of volume responsiveness for RSVT in comparison with the well-established parameters SVV and PPV.

The rationale for volume loading is to increase cardiac preload and thereby cardiac output resulting in improved organ perfusion and clinical outcome.⁴ There is convincing evidence, that in mechanically ventilated patients dynamic haemodynamic parameters quantifying heart–lung interactions are superior to barometric indicators of cardiac preload

in their ability to predict fluid responsiveness.^{6,7} The definition of a 10% increase of CI as positive volume response to volume administration was chosen as this cut-off is widely used and has been published in several previous publications.^{21–23} Undoubtedly, reliable prediction of volume responsiveness and differentiation between patients whose CI will increase after fluid administration (responders) and those who have already reached the flat part of the cardiac function curve, are of tremendous importance for guidance of volume therapy and clinical outcome in critically ill patients. Especially, as unnecessary fluid administration may be harmful by aggravating pulmonary and tissue oedema or causing myocardial deterioration and thereby worsen clinical outcome.^{2,5}

Even though SVV, PPV, and RSVT are useful in determination of fluid responsiveness their use is limited by the prerequisite of a mechanically ventilated patient without cardiac arrhythmias. The required tidal volume for a reliable SVV and PPV is reported to be at least 8 ml kg^{−1} and hence higher than

Table 1 Patient characteristics of the study population. BMI, body mass index. Data are presented as mean (SD) or median (range)

Age (yr)	61 (25–81)
Height (cm)	170 (10)
Weight (kg)	85 (27)
BMI (kg m ^{−2})	29 (8)
Gender	Female: 13 Male: 11
Operation time (min)	252 (94)
Type of surgery	Liver resection (15) Spinal (3) Gastrectomy (2) Colon (2) Gynaecological (2)

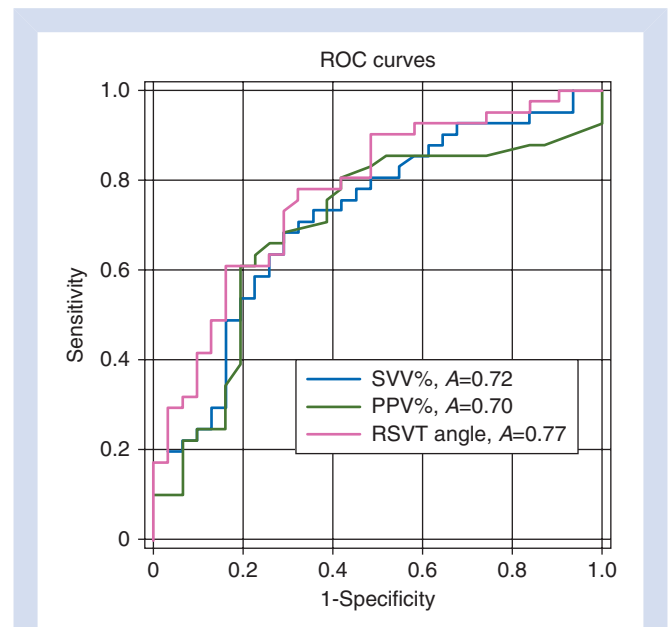


Fig 2 ROC curves for PPV, SVV, and angle of RSVT. A, area under the receiver operating characteristic curve.

Table 2 Haemodynamic data throughout the experimental protocol. M1, baseline measurement in hypovolemia; M2, measurement after the first volume loading step; M3, measurement after the second volume loading step; M4, measurement after the third volume loading step; MAP, mean arterial pressure; HR, heart rate; CI, cardiac index; SVV, stroke volume variation; PPV, pulse pressure variation; RSVT, respiratory systolic variation test. *Representing statistically significant change in comparison with previous time of measurement

	M1	M2	M3	M4
MAP (mm Hg)	67.7 (13.1)	75.5 (11.1)	85.8 (11.9)*	92.2 (16.4)
HR (min ^{−1})	71.2 (12.0)	69.2 (10.9)	70.5 (11.8)	73.5 (13.8)
CI (litre min ^{−1} m ^{−2})	2.6 (0.7)	3.0 (0.7)	3.4 (0.7)	3.7 (0.8)
SVV (%)	16.1 (9.0)	7.2 (5.6; 14.6)*	5.3 (3.7; 11.0)	6.4 (5.1)
PPV (%)	14.4 (9.0)	11.1 (6.6)	8.5 (4.8)*	7.4 (4.0)
RSVT angle (°)	37.5 (21.9; 42.9)	25.6 (13.9)*	14.7 (7.7; 20.2)	7.4 (4.6; 11.9)

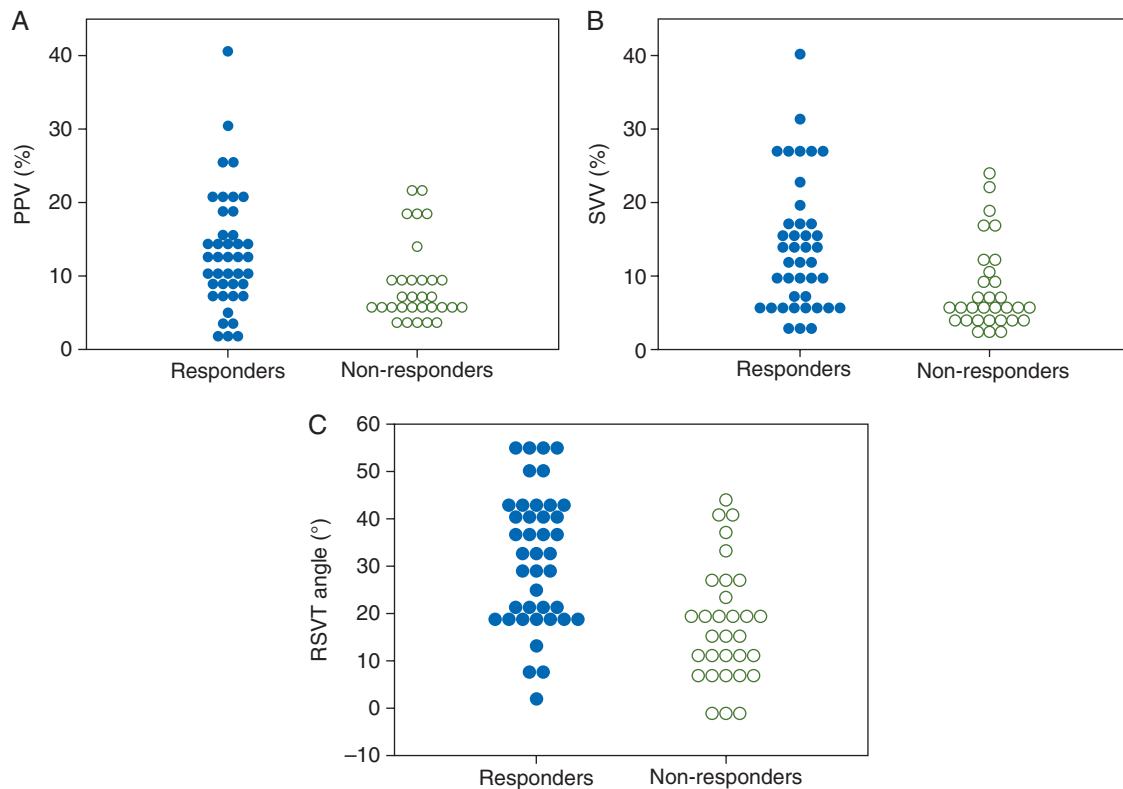


Fig 3 Dot histograms for prediction of volume responsiveness. Values of the respective variables before volume loading are presented. Closed circles: values where a positive volume response was detected; open circles: values where a negative volume response was detected. (A) PPV. (B) SVV. (C) RSVT.

recommended tidal volumes for protective ventilation in critically ill patients.^{24–27} The RSVT has the main advantage of being independent of a given tidal volume.²⁸ RSVT showed promising results in an animal model and in patients undergoing heart and major vascular surgery.^{13–15} To our knowledge, up to now, there are no data evaluating the use of an automated RSVT in patients after major abdominal and spine surgery. High values of RSVT angle represent a strong decrease in systolic arterial pressure during elevation of intra-thoracic pressure and identify the patient to be in the volume responsive part of the Frank–Starling curve. In patients showing adequate cardiac preload the decrease in arterial pressure under RSVT and consequently the RSVT angle will be small. A heart with satisfactory ventricular filling will not be influenced as much by the increasing intra-thoracic pressures during the RSVT as without a sufficient filling. Therefore, additional volume administration in the circumstance of a low RSVT will not increase stroke volume any more. Our study provides a direct comparison of the RSVT with other dynamic parameters of preload that are derived from ventilator induced variations in the arterial pressure and stroke volume regarding their ability to predict an increase in CO after volume loading. Comparing the AUC for SVV, PPV, and RSVT no statistically significant differences were found. Therefore, we consider the RSVT manoeuvre a useful alternative in clinical practice for guiding fluid therapy in a

perioperative or intensive care setting. What is more, in clinical practice there is a large percentage of patients monitored by an arterial line, which however is not connected to an advanced haemodynamic monitoring device that enables quantification of PPV or SVV. In this situation, when the main interest is evaluation of volume responsiveness, the RSVT—if integrated in the software of the ventilator—is an easily available and easily executed method to determine the individual's position on the Frank–Starling curve. The RSVT does not require connecting the patient to further monitoring devices or even placing a special arterial or central venous catheter. Another aspect is that RSVT will in all likelihood remain usable in patients with some mild spontaneous breathing activity. However, requirement is that the patient is able to tolerate the execution of the RSVT without intervening between the breaths of the ventilator.

The automated RSVT defines the three lowest systolic arterial pressures after each breathing cycle. For the calculation of the slope, the first and the third point are used as presented in the formula in the Methods section. Two points of measurements are as accurate in calculating the slope by linear regression as three points, because the middle number is not necessary to define the slope. The minimum systolic arterial pressure after the second breathing cycle is also defined and highlighted for visualization in order to make visual control

and detection of artifacts easier. These include spontaneous breathing efforts or irregular heart beats potentially resulting in invalid calculations. If the defined points differ substantially from the regression line this helps the user to detect the necessity to repeat the RSVT. The pressures applied for execution of RSVT were set as previously described in the literature. Whether other pressure settings may result in differing results or whether certain patient groups require specific settings for optimal results currently is still being investigated. With the user friendly integration of the software in the ventilator the RSVT can be easily performed. Results are calculated online and presented on screen as RSVT angle. As stated before, RSVT has the advantage of being independent of setting certain required tidal volumes. This holds the advantage that the RSVT also can be executed and also valid when the patient is ventilated applying protective ventilation with reduced tidal volumes, like patients suffering from ARDS.^{29–31} Nonetheless, to date this remains hypothetical and cannot be proved in our study. However, not only tidal volume but also lung and chest wall compliance are important influencing factors for dynamic preload variables and lately there is increasing evidence that these variables are less reliable in the injured lung with decreased compliance and consequently limited intra-thoracic transmission of the airway pressure.^{10 11 32} In patients requiring high PEEP levels theoretically peak airway pressures could easily be driven over recommended limits when the RSVT manoeuvre comes on top of PEEP. Therefore, the user needs to be aware of possible lung barotraumas. However pressures of RSVT will not exaggerate pressures that often are recommended for recruitment manoeuvres.^{33 34} Another aspect is that the RSVT might be more reliable in patients with compromised cardiac function. The reason for this is that RSVT—unlike SVV and PPV—does not consider the maximal increase of stroke volume in the beginning of inspiration (delta-up component) for its calculation, which is not related to volume responsiveness.¹⁴ Nonetheless, the application of RSVT like other dynamic variables based on quantification of heart–lung interactions is limited to mechanically ventilated patients.

Our study has several limitations. First, the amount and type of fluid (300 ml 6% hydroxyethylstarch 130/0.4) that was used for volume loading was chosen arbitrarily and the amount of fluid was not individualized to the patient's body weight. Moreover, although volume loading was performed using 6% hydroxyethylstarch 130/0.4 which is reported to cause a greater cardiac response than crystalloids,³⁵ the amounts of volume administered were rather low and possibly are the reason why values for SVV and PPV in our study are slightly inferior to other results reported in the literature. We avoided a higher volume load in order to not cause harmful fluid overload and potential aggravation of pulmonary or tissue oedema and cardiac deterioration. Our measurements may be influenced to some extent by the use of vasopressors in our patient population. Most patients required moderate dosages of norepinephrine to maintain a mean arterial pressure >70 mm Hg. However, Kubitz and colleagues exemplarily showed for SVV that it is not affected by changes in cardiac afterload.³⁶

Although we cannot prove this for RSVT in our study we do hold the opinion that this is also true for other variables based on quantification of heart–lung interactions. To our knowledge, no such data exist for the accuracy of RSVT. Another aspect is, that our data were collected in patients after major surgery with remarkable fluid turnover. This probably does not exactly reflect the situation of suddenly changing haemodynamic circumstances, like acute loss of large amounts of blood, for example, because of surgery or trauma that may be present in the operating theatre. In contrast to SVV or PPV the RSVT does not provide continuous data. Nonetheless, if executed repeatedly during changing haemodynamic conditions the RSVT delivers equally reliable information as SVV or PPV for monitoring of cardiac preload and volume responsiveness.

In conclusion, our study showed promising results in a heterogenous patient population after major surgery with remarkable volume turnover. RSVT appears to be as accurate as PPV and SVV in the ability to predict volume responsiveness. Furthermore, the integration of automated and standardized RSVT is successfully interfacing the ventilator and the monitor, providing reliable on-line calculation of the RSVT and thereby making the test easy to execute in mechanically ventilated patients and feasible for monitoring purposes.

Authors' contributions

C.J.C.T.: study concept and design, acquisition and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, obtained funding, and study supervision. V.E.: study concept and design, acquisition and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, obtained funding, and study supervision. S.A.H.: acquisition and interpretation of data, critical revision of the manuscript for important intellectual content. K.S.: acquisition and interpretation of data, critical revision of the manuscript for important intellectual content. F.S.: study concept and design, acquisition and interpretation of data, and critical revision of the manuscript for important intellectual content. R.N.: critical revision of the manuscript for important intellectual content, and study supervision. A.E.G.: critical revision of the manuscript for important intellectual content, and study supervision. D.A.R.: study concept and design, drafting of the manuscript, critical revision of the manuscript for important intellectual content, obtained funding, and study supervision.

Declaration of interest

A.E.G. and D.A.R. are members of the Medical Advisory Board of Pulsion Medical Systems.

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References

- Goepfert MS, Reuter DA, Akyol D, et al. Goal-directed fluid management reduces vasopressor and catecholamine use in cardiac surgery patients. *Intensive Care Med* 2007; **33**: 96–103
- Hamilton MA, Cecconi M, Rhodes A. A systematic review and meta-analysis on the use of preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. *Anesth Analg* 2011; **112**: 1392–402
- Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; **345**: 1368–77
- Bellamy MC. Wet, dry or something else? *Br J Anaesth* 2006; **97**: 755–7
- Boyd JH, Forbes J, Nakada TA, Walley KR, Russell JA. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. *Crit Care Med* 2011; **39**: 259–65
- Gelman S. Venous function and central venous pressure: a physiologic story. *Anesthesiology* 2008; **108**: 735–48
- Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest* 2008; **134**: 172–8
- Michard F. Volume management using dynamic parameters: the good, the bad, and the ugly. *Chest* 2005; **128**: 1902–3
- Monnet X, Bleibtreu A, Ferre 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* 2012; **40**: 152–7
- Lakhal K, Ehrmann S, Benzekri-Lefevre D, et al. Respiratory pulse pressure variation fails to predict fluid responsiveness in acute respiratory distress syndrome. *Crit Care* 2011; **15**: R85
- Mesquida J, Kim HK, Pinsky MR. Effect of tidal volume, intrathoracic pressure, and cardiac contractility on variations in pulse pressure, stroke volume, and intrathoracic blood volume. *Intensive Care Med* 2011; **37**: 1672–9
- Reuter DA, Bayerlein J, Goepfert MS, et al. Influence of tidal volume on left ventricular stroke volume variation measured by pulse contour analysis in mechanically ventilated patients. *Intensive Care Med* 2003; **29**: 476–80
- Perel A, Minkovich L, Preisman S, et al. Assessing fluid-responsiveness by a standardized ventilatory maneuver: the respiratory systolic variation test. *Anesth Analg* 2005; **100**: 942–5
- Preisman S, Kogan S, Berkenstadt H, Perel A. Predicting fluid responsiveness in patients undergoing cardiac surgery: functional haemodynamic parameters including the Respiratory Systolic Variation Test and static preload indicators. *Br J Anaesth* 2005; **95**: 746–55
- Eichhorn V, Trepte C, Richter HP, et al. Respiratory systolic variation test in acutely impaired cardiac function for predicting volume responsiveness in pigs. *Br J Anaesth* 2011; **106**: 659–64
- Pizov R, Ya'ari Y, Perel A. The arterial pressure waveform during acute ventricular failure and synchronized external chest compression. *Anesth Analg* 1989; **68**: 150–6
- Tavernier B, Makhotine O, Lebuffe G, Dupont J, Scherpereel P. Systolic pressure variation as a guide to fluid therapy in patients with sepsis-induced hypotension. *Anesthesiology* 1998; **89**: 1313–21
- Preisman S, DiSegni E, Vered Z, Perel A. Left ventricular preload and function during graded haemorrhage and retransfusion in pigs: analysis of arterial pressure waveform and correlation with echocardiography. *Br J Anaesth* 2002; **88**: 716–8
- DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988; **44**: 837–45
- Youden WJ. Index for rating diagnostic tests. *Cancer* 1950; **3**: 32–5
- Lahner D, Kabon B, Marschalek C, et al. Evaluation of stroke volume variation obtained by arterial pulse contour analysis to predict fluid responsiveness intraoperatively. *Br J Anaesth* 2009; **103**: 346–51
- Yu YH, Dai HW, Yan ML, et al. An evaluation of stroke volume variation as a predictor of fluid responsiveness in mechanically ventilated elderly patients with severe sepsis. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue* 2009; **21**: 463–5
- Zhang HM, Liu DW, Wang XT, et al. Stroke volume variation in the evaluation of fluid responsiveness in refractory septic shock. *Zhonghua Nei Ke Za Zhi* 2010; **49**: 610–3
- Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med* 2009; **37**: 2642–7
- De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. *Intensive Care Med* 2005; **31**: 517–23
- Vallee F, Richard JC, Mari A, et al. Pulse pressure variations adjusted by alveolar driving pressure to assess fluid responsiveness. *Intensive Care Med* 2009; **35**: 1004–10
- Zhang Z, Lu B, Sheng X, Jin N. Accuracy of stroke volume variation in predicting fluid responsiveness: a systematic review and meta-analysis. *J Anesth* 2011; **25**: 904–16
- Monnet X, Teboul JL. Invasive measures of left ventricular preload. *Curr Opin Crit Care* 2006; **12**: 235–40
- The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; **342**: 1301–8
- Needham DM, Colantuoni E, Mendez-Tellez PA, et al. Lung protective mechanical ventilation and two year survival in patients with acute lung injury: prospective cohort study. *BMJ* 2012; **344**: e2124
- Uttman L, Bitzen U, De Robertis E, et al. Protective ventilation in experimental acute respiratory distress syndrome after ventilator-induced lung injury: a randomized controlled trial. *Br J Anaesth* 2012; **109**: 584–94
- Jardin F, Genevray B, Brun-Ney D, Bourdarias JP. Influence of lung and chest wall compliances on transmission of airway pressure to the pleural space in critically ill patients. *Chest* 1985; **88**: 653–8
- Spieth PM, Gama de Abreu M. Lung recruitment in ARDS: we are still confused, but on a higher PEEP level. *Crit Care* 2012; **16**: 108
- de Matos GF, Stanzani F, Passos RH, et al. How large is the lung recruitability in early acute respiratory distress syndrome: a prospective case series of patients monitored by computed tomography. *Crit Care* 2012; **16**: R4
- Trof RJ, Sukul SP, Twisk JW, Girbes AR, Groeneveld AB. Greater cardiac response of colloid than saline fluid loading in septic and non-septic critically ill patients with clinical hypovolaemia. *Intensive Care Med* 2010; **36**: 697–701
- Kubitz JC, Annecke T, Forkl S, et al. Validation of pulse contour derived stroke volume variation during modifications of cardiac afterload. *Br J Anaesth* 2007; **98**: 591–7

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