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## ORIGINAL LABORATORY RESEARCH

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# EFFECT OF LOW TIDAL VOLUME VENTILATION ON DYNAMIC PRELOAD PARAMETERS DURING GRADED HEMORRHAGE AND RETRANSFUSION: AN ANIMAL MODEL

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### Abstract

**Background:** Dynamic preload parameters as systolic pressure variation (SPV) and stroke volume variation (SVV) are established monitoring tools for volume responsiveness during critical care therapy. The impact of ventilator settings on SPV/SVV is still under research.

**Methods:** We studied the impact of two different ventilator settings (low tidal volume ventilation (LTVV) (6ml/kg bodyweight) and normal tidal volume ventilation (NTVV) (12ml/kg bodyweight)) on SPV/SVV-measurements during graded hemorrhage (-15% and -30% blood volume) and retransfusion of the blood in an animal model.

**Results:** Cardiac output decreased significantly during volume depletion compared to baseline. Dynamic preload parameters increased during graded hemorrhage both during LTVV and NTVV. Changes in dynamic preload parameters show a tidal volume dependency: During NTVV values of SVV and SPV were higher and differed significantly from values obtained during LTVV.

**Conclusions:** The cardiac volume responsiveness in critical care is a surrogate of intravascular volume status and positive intrathoracic pressure induced by mechanical ventilation. Dynamic preload parameters are more sensitive monitoring tools for ventilation-induced changes in volume responsiveness than static preload parameters. The use of SPV/SVV for calculation of volume responsiveness depends on comparable ventilator settings during the measurements.

**Keywords:** Hemodynamic monitoring; Fluid management; Systolic pressure variation (SPV); Pulse pressure variation (PPV); Stroke volume variation (SVV); Ventilation

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## Introduction

Static preload parameters like central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) are unreliable markers of intravascular volume state in ICU patients. Therefore dynamic preload parameters (systolic pressure variation (SPV), pulse pressure variation (PPV), and stroke volume variation (SVV)) have been established as parameters for evaluating intravascular fluid balances and volume responsiveness.<sup>1-5</sup> However, the question to what extent dynamic preload parameters are influenced by tidal volume and fluid load is still a matter of discussion.

Our study was conducted to measure the impact of mechanical ventilation on SPV and SVV during graded hemorrhage and retransfusion using low tidal volume ventilation (LTVV) (6ml/kg) compared with normal tidal volume ventilation (NTVV) (12ml/kg) which is still used in many intensive care facilities.<sup>6</sup>

## Methods

With approval of the regional Governmental Animal Care Office, eight female German Landrace pigs (26-32kg) were anesthetized with propofol (2-3mg/kg i.v.) and rocuronium (1.2mg/kg i.v.) to facilitate oral intubation. NTVV using an ICU respirator (Evita 2, Draeger, Luebeck, Germany) was adapted by adjusting respiratory frequency to ensure normocarbida ( $\text{PaCO}_2$  4,1-4,7kPa). PEEP was set to zero. Anesthesia was maintained with propofol (30-60mg/kg/h) and remifentanyl (15-30 $\mu\text{g}$ /kg/h).

For measurements of pulmonary capillary wedge pressure (PCWP) and mean pulmonary artery pressure a 7F pulmonary artery catheter (Baxter, Irvine, USA) was introduced into the pulmonary artery. A central venous catheter was advanced into the superior vena cava. For analyzing arterial pressure waveform, cardiac output (CO), and stroke volume variation (SVV), a 4F fibreoptic thermistor catheter (Pulsicath, Pulsion medical systems, Munich, Germany) was positioned into the abdominal aorta. Thermodilution curves were analysed using a PiCCO® Plus monitor (Pulsion medical systems, Munich, Germany). CO data were collected by means of a PiCCO®-Plus

System calculating the mean of three consecutive measurements of 10ml iced saline 0.9% injected into the central venous catheter.

Via a serial port the arterial pressure curve was transmitted to a notebook computer. Using a custom-made software a computerized online analysis of the systolic pressure variation was realized (GJB Datentechnik, Ilmenau, Germany). Beside SPV a calculation of the delta up/ delta down component of the SPV was possible once the system was calibrated by implementing a 10 sec interval of apnea. Systolic pressure variation was calculated during a 30sec interval by dividing it into four parts of 7.5 sec each. The highest and the lowest systolic pressure during each time window were determined. The mean value of the maximum systolic pressures of all time windows (7.5 sec) was subtracted from the systolic arterial pressure during apnea to calculate the delta up/ delta down component.

After a 30 min of steady state, four study steps were undertaken:

**Phase 1:** Hemodynamic parameters at baseline (normovolaemia) were collected with NTVV and LTVV. Respiratory frequency was adapted to ensure normocarbida. The equilibration time after changing the tidal volume was 10min before performing the next measurements.

**Phase 2:** Animals were bled through the arterial catheter by 15% of their estimated blood volume (calculated as 7% of body weight) within 10min followed by a 5min interval for hemodynamic stabilization. Hemodynamic measurements at both ventilator settings were done as at baseline.

**Phase 3:** Animals were bled by another 15% of their estimated blood volume, (i.e. total volume depletion 30%) within 10min followed by a 5min interval for hemodynamic stabilization. Measurements and modification of respiratory parameters were done as at baseline.

**Phase 4:** The pigs were re-transfused the shed blood within 10min. Hemodynamic measurements and modification of respiratory parameters were done as at baseline.

At the end of the experiment the animals were euthanized.

### Statistical analysis

Values are expressed as mean  $\pm$  standard error (SEM). One-way analysis of variance was performed for repeated measurements. A p-value of 0,05 was considered to be statistically significant.

### Results

All animals completed the protocol. During volume depletion  $225 \pm 13$ ml (-15%) and  $450 \pm 20$ ml (-30%) of blood were removed and retransfused.

Each step caused a significant decrease in CO, MAP, CVP and PCWP compared to the preceding step. Dynamic parameters (SPV, SPVdown, SVV) significantly increased during graded hemorrhage. Ventilation at different tidal volumes caused significant changes in dynamic parameters but not in CO, MAP, CVP, and PCWP (Table 1).

For systolic pressure variation and SPVdown the mean values at baseline during NTVV were higher than at baseline and even at graded hemorrhage during LTVV. During retransfusion CO always increased by more than 15%. Dynamic preload parameters decreased significantly during LTVV. During NTVV the changes in SPV, SPVdown and SVV were more pronounced.

Static preload parameters showed a significant increase during retransfusion that was not significantly affected by the applied tidal volume.

### Discussion

Our study demonstrates significant changes of dynamic preload parameters during graded hemorrhage both during LTVV and NTVV. CO was significantly decreased during volume depletion compared to baseline as a result of a clinically relevant blood loss. The changes in dynamic preload parameters show

a tidal volume dependency. During NTVV values of SVV, SPV, SPVdown were higher and differed significantly from values obtained during LTVV.<sup>7</sup>

After graded hemorrhage (-30% of intravascular fluid amount) all animals were volume responsive as demonstrated by the significant increase of cardiac output after retransfusion. During this phase the tendency to higher CO during LTVV compared to cardiac output using NTVV at same volume loading step was also seen. This is in contrast to older data that showed lower cardiac output during retransfusion using LTVV.<sup>8</sup>

Cardiac volume responsiveness is a surrogate of intravascular volume load as well as positive intrathoracic pressure induced by mechanical ventilation. Under certain circumstances the effect of positive pressure ventilation even seems to exceed the effect of changes in intravascular fluid load. Dynamic preload parameters are more sensitive to monitor these ventilation-induced changes in volume responsiveness than static preload parameters. Therefore, influence of mechanical ventilation on SPV/SVV cannot be interpreted as limitation of the parameters. However, the question to what extent both, intravascular fluid load and respiratory settings contribute to the volume responsiveness of a certain individual cannot be clearly differentiated.

### Conclusion

Our experiment demonstrates that the interpretation of changes in SPV/SVV as a marker of fluid responsiveness has to be done with a close look on the ventilator settings.<sup>9</sup> Changes of SPV/SVV should only be interpreted as marker of volume responsiveness if the ventilator settings during the measurements are comparable.<sup>10</sup>

**Financial disclosures:** None

**Conflicts of interest:** None

*Table 1*  
*Hemodynamic variables at baseline, during 15% and 30% volume depletion respectively and after retransfusion at two different tidal volumes (TV)*

	Normovolemia TV 6ml/kg	Normovolemia TV 12ml/kg	Volume depletion -15% TV 6ml/kg	Volume depletion -15% TV 12ml/kg	Volume depletion -30% TV 6ml/kg	Volume depletion -30% TV 12ml/kg	Retransfusion TV 6ml/kg	Retransfusion TV 12ml/kg
CO	4.21 ±0.26*	3.98 ±0.23*	3.69 ±0.21*	3.51 ±0.19*	2.96 ±0.22*	2.76 ±0.21*	3.87 ±0.29*	3.58 ±0.33*
MAP	67.50 ±4.54*	74.00 ±4.49*	59.88 ±4.57*	61.63 ±3.33*	50.88 ±4.75*	51.63 ±4.14*	57.71 ±5.77*	75.71 ±5.67*
PCWP	10.38 ±1.68*	10.88 ±1.99*	8.38 ±1.36*	8.13 ±1.33*	7.13 ±1.20*	6.75 ±1.23*	10.29 ±1.04*	10.14 ±0.98*
CVP	8.13 ±1.27*	8.88 ±1.60*	7.25 ±1.08*	6.88 ±1.00*	6.50 ±1.29*	6.00 ±1.08*	9.71 ±1.34*	9.00 ±1.38*
SPV	5.50 ±1.19**	9.01 ±1.09**	6.75 ±0.50**	12.15 ±1.20**	7.85 ±0.73**	19.51 ±1.74**	6.89 ±0.98**	9.68 ±1.19**
SPV <sub>dd</sub>	5.04 ±1.28**	7.16 ±1.10**	5.93 ±0.745**	11.01 ±1.22**	6.62 ±0.53**	16.88 ±1.21**	4.55 ±0.89**	8.06 ±1.10**
SVV	7.00 ±0.82**	7.87 ±1.09**	7.87 ±0.93**	12.62 ±1.70**	10.25 ±1.46**	16.62 ±2.06**	7.37 ±1.03**	13.37 ±1.98**
PIP	18.88 ±1.46*	23.63 ±1.97*	19.50 ±1.28*	24.50 ±1.66*	17.88 ±1.17*	23.38 ±1.05*	19.14 ±1.72*	23.43 ±1.27*
PAW	9.63 ±0.49*	15.38 ±1.22*	11.00 ±0.82*	16.63 ±1.25*	9.75 ±0.52*	16.13 ±1.09*	10.00 ±0.65*	17.00 ±1.27*

\* significant changes during fluid load

\*\* significant changes at different tidal volumes

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