

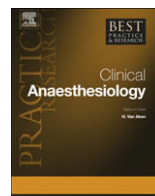


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Monitoring fluid therapy

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Hypovolaemia is a common cause of circulatory failure in the perioperative period. However, only 50% of critically ill patients respond to volume expansion with an adequate increase in cardiac output. Therefore, in daily clinical practice it is still a challenge to assess each subject's individual position on the Starling curve in order to optimize cardiac preload and avoid deleterious fluid overload. Recently, systolic pressure variation, stroke volume variation, and pulse pressure variation have been introduced as dynamic variables of fluid responsiveness which reflect ventilation-induced cyclic changes in left ventricular stroke volume. The concept of fluid responsiveness has been recognized for more than 20 years, and several studies have shown the superiority of these dynamic variables compared to static filling pressures. However, the usefulness of dynamic variables in critically ill patients is limited by several factors that the clinician needs to know for proper interpretation.

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Introduction

Only 50% of critically ill patients still have some cardiac preload reserve and will respond to volume expansion by a significant increase in cardiac output.¹ This emphasizes the need for accurate determination of preload variables and for reliable predictors of fluid responsiveness to avoid ineffective or deleterious fluid loading. Numerous experimental and clinical studies have clearly demonstrated that static variables, such as central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP),

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reflecting cardiac filling pressures, cannot adequately indicate changes in preload or reliably predict fluid responsiveness. According to the Frank-Starling relationship, left-ventricular preload is defined as the myocardial fibre length at the end of diastole. Therefore, left ventricular end-diastolic volume obtained by echocardiography, or global end-diastolic volume (GEDV) obtained by transpulmonary thermodilution, as static volumetric surrogates of left-ventricular preload, should be more accurate variables of preload and of fluid responsiveness. However, studies have yielded conflicting results about the usefulness of end-diastolic volume measured by echocardiography or GEDV obtained by transpulmonary thermodilution to differentiate between patients who will benefit from fluid resuscitation and patients who will not.^{2–8} Today, an increasing number of publications has underlined the superiority of dynamic variables of fluid responsiveness – such as systolic pressure variation (SPV), pulse pressure variation (PPV), stroke volume variation (SVV), plethysmographic waveform variations (Δ POP) and other variables which are based on the concept of heart–lung interaction – compared to static variables in the decision-making process of whether the patient needs fluids or not.^{9–16} The traditional clinical approach to test whether the patient adequately responds to a volume load by performing repeated fluid challenges may have deleterious effects in the case of reduced right and/or left ventricular function and increased pulmonary permeability.¹⁷ The basic principle of the dynamic approach is based on an intermittently decreased venous return to the right heart during a mechanical ventilatory cycle due to an increased intrathoracic pressure. Dynamic variables of fluid responsiveness have been extensively evaluated in different clinical scenarios, and threshold values for SPV, PPV and SVV have been defined to help the clinician in making the decision about whether the patient needs fluids or not. However, there are still some questions regarding indications and limitations before these dynamic variables of fluid responsiveness may be routinely used in daily clinical practice.

Static variables of preload and fluid (Table 1) responsiveness

Cardiac filling pressures

Numerous investigations have shown that cardiac filling pressures such as CVP and PAOP are not suitable to accurately reflect changes in preload.^{18,19} However, although they are not reliable predictors of fluid responsiveness^{1,18,20–23}, they are still considered the gold standard for guiding fluid therapy in patients with sepsis and septic shock.²⁴ There are several physiological reasons potentially explaining why cardiac filling pressures fail to be reliable predictors of fluid responsiveness. First, the Frank-Starling curve determining the ventricular preload/stroke volume relationship in every individual patient is not static, but changes in the shape of the individual curve (rightward/leftward shift) in response to impaired or enhanced left ventricular function may occur. In this respect, a given value of preload can be associated with fluid responsiveness (steep part of the Starling curve) in the case of normal cardiac function, or with the absence of fluid responsiveness in the case of a failing heart (flat part of the Starling curve) (Fig. 1). Furthermore, filling pressures are highly dependent on left-ventricular compliance²⁵ that is frequently altered in critically ill patients. As left-ventricular compliance may vary rapidly, changes in the relationship between filling pressure and end-diastolic volume may equally occur. Consequently, the relationship between cardiac filling pressures and end-diastolic volumes is curvilinear and may vary between individuals. Neither absolute values of filling

Table 1
Static haemodynamic variables.

Classification	Variable	Monitoring
Filling pressures	Right atrial pressure or central venous pressure Pulmonary artery occlusion pressure	Central venous catheter Pulmonary artery catheter
Volumetric variables	Right/left ventricular end- diastolic volume/area Right ventricular end- diastolic volume/continuous end-diastolic volume Intrathoracic blood volume Global end-diastolic volume	Echocardiography Volumetric pulmonary artery catheter PiCCO device PiCCO device

PiCCO, Pulse Contour Cardiac Output monitoring system.

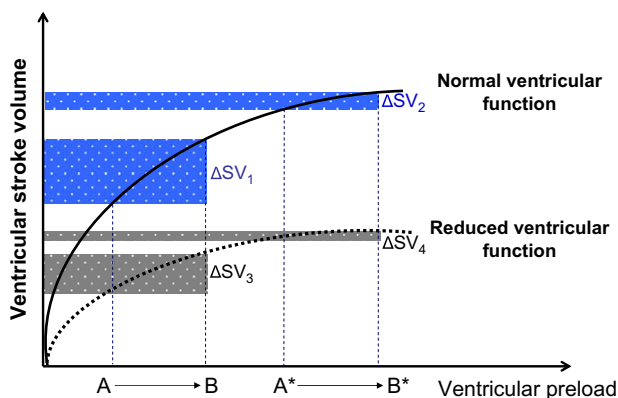


Fig. 1. The Frank-Starling curve representing the non-linear relationship between ventricular preload and ventricular stroke volume (straight curve = normal ventricular function; dashed curve = reduced ventricular function). If the heart is operating on the steep part of the Starling curve, an increase in preload is associated with a relevant increase in stroke volume (preload dependency, ΔSV_1). In contrast, if the heart is operating on the flat part of the Starling curve the same magnitude of change in preload after volume administration (from A^* to B^*) does not increase SV (preload independency, ΔSV_2). This relationship is strongly affected by cardiac function. In contrast to a normal ventricular function, the same increase in preload will not induce a relevant change in stroke volume in case of reduced left ventricular function (ΔSV_3 and ΔSV_4).

pressures nor changes in filling pressures are associated with a specific end-diastolic volume or its changes.²⁶ Moreover, critically ill patients often require positive-pressure ventilation, which affects intrathoracic pressure and pericardial pressure oppositely to spontaneous breathing. The increase in intrathoracic pressure is accompanied by an increase in pericardial pressure and secondarily by an increase in cardiac filling pressures, suggesting an inappropriate and potentially detrimental therapy.

To summarize, static cardiac filling pressures, although still recommended to guide fluid therapy, are not appropriate to assess intravascular volume status, and moreover are not reliable predictors of fluid responsiveness.^{24,27}

Static volumetric variables

Left ventricular end-diastolic volume obtained by echocardiography

Preload is defined as the myocardial fibre length at end diastole. Therefore, an ideal clinical correlate should be left ventricular end-diastolic volume. In the last two decades, trans-oesophageal echocardiography (TOE) has attracted increasing interest in this respect.²⁸ TOE provides rapid visualization of left ventricular function and dimensions. Consequently, left ventricular end-diastolic volume obtained by TOE has been introduced as a clinical variable to assess preload. Several studies have shown that TOE reliably reflects changes in preload in different experimental and clinical settings.^{29–33} However, it has been shown repeatedly that left ventricular end-diastolic area and/or left ventricular end-diastolic volume obtained by TOE fail to predict fluid responsiveness.^{5,7,34} Although echocardiography can provide an excellent estimate of preload, one fundamental limitation using TOE in daily clinical routine is the need for costly equipment and training. Also, TOE is not suitable for monitoring patients continuously for a long period of time.³⁵

Global end-diastolic volume obtained by transpulmonary thermodilution

Some years ago a new monitoring device, the PiCCO system (Pulsion Medical System, Munich, Germany), was introduced into clinical practice. The PiCCO provides both an alternative method for intermittently assessing cardiac output using the transpulmonary thermodilution technique and a measure of continuous cardiac output based on pulse contour analysis.³⁶ Moreover, this monitoring system offers the possibility of assessing GEDV as a static volumetric variable of preload using the mathematical analysis of the transpulmonary thermodilution curve.^{35,37–41} This technique requires the central venous injection of an ice-cold saline bolus followed by the calculation of the mean transit time (MTt) of the thermal indicator

(detection of the downstream changes in temperature) which represents the weighted mean passage of all indicator particles between injection (central venous) and detection points (distal aorta). The product of CO and MTT is the volume of distribution of the thermal indicator, the so called intrathoracic thermal volume (ITTV), which theoretically represents to the sum of intrathoracic blood volume (ITBV) and extravascular lung water (EVLW). The product of CO and the exponential down-slope time of the thermodilution curve is the pulmonary thermal volume (PTV), which is composed of pulmonary blood volume and EVLW. GEDV is the difference between ITTV and PTV and is supposed to be the sum of the right and left heart end-diastolic volumes (Fig. 2). Today, several investigations in both adults and infants are available which highlight the clinical significance of GEDV as an indicator of preload and potentially as a variable to predict fluid responsiveness with acceptable sensitivity and specificity.^{5,40,42,43} In a recent study in pigs during haemorrhage, Nirmalan et al were able to show that the algorithm used in this study for estimation of GEDV was robust even during extreme loading conditions.⁴⁴ However, to our knowledge, GEDV has not been compared so far to standard methods assessing heart volumes, e.g. magnetic resonance imaging (MRI). Another important issue relates to the possibility of mathematical coupling between GEDV and CO, since both variables are derived from the same thermodilution curve.⁴⁵ In a recent investigation, however, McLuckie et al have shown that the MTT of an indicator may change independently of changes in CO⁴⁶, a finding supported by a study performed in patients during minimal invasive coronary artery bypass grafting.⁴⁷ In contrast to dynamic variables of fluid responsiveness, the application of GEDV, as a volumetric variable based on transpulmonary thermodilution technique, is not limited by spontaneous breathing efforts.⁴⁸ As a large percentage of patients in the intensive care unit cannot be monitored by dynamic variables of fluid responsiveness due to spontaneous breathing, GEDV may be particularly useful under these circumstances. From all variables studied so far, only GEDV was able to reflect both actual preload and fluid responsiveness, a fact that puts GEDV in a unique position for guidance of fluid administration.

Dynamic variables of fluid responsiveness

The basic principle of a dynamic approach to elucidate the individual Frank-Starling curve at the bedside is to induce a cyclic change in cardiac preload induced by mechanical ventilation. Positive pressure ventilation intermittently decreases right ventricular end-diastolic volume and consequently decreases left ventricular preload in response to a reduction in venous return.⁴⁹ Observing and analysing the resulting effects on stroke volume or its surrogates, such as pulse pressure or systolic pressure, is the main concept of what is today known as functional haemodynamic monitoring.

The concept of respiratory variation of haemodynamic variables such as systolic pressure (SP), pulse pressure (PP), stroke volume (SV) and the plethysmographic waveform has led to the development and

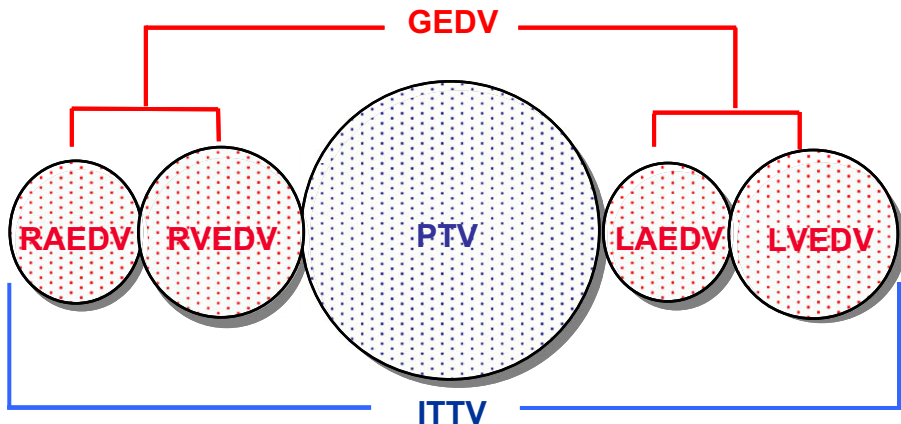


Fig. 2. Schematic diagram of the relevant intrathoracic fluid compartments and their derivation. RAEDV, right atrial end-diastolic volume; RVEDV, right ventricular end-diastolic volume; PTV, pulmonary thermal volume; LAEDV, left atrial end-diastolic volume; LVEDV, left ventricular end-diastolic volume; GEDV, global end-diastolic volume; ITTV, intrathoracic thermal volume.

availability of several techniques, allowing for example real-time SV monitoring based on pulse contour analysis.

Systolic pressure variation

The arterial systolic pressure variation (the difference between maximal and minimal systolic arterial pressure values during one mechanical breath) and its Δ_{down} component ($\Delta_{\text{down}} = \text{apnoeic} - \text{minimum systolic blood pressure}$) have been shown to be sensitive indicators of hypovolaemia.^{16,50} Using the systolic pressure during apnoea as a reference point or baseline, the increase in systolic pressure above baseline during the respiratory cycle has been defined as Δ_{up} , and the decrease in systolic pressure below baseline has been defined as the Δ_{down} component. The overall SPV is therefore the sum of Δ_{up} and Δ_{down} (Table 2, Fig. 3).

Pulse pressure variation and stroke volume variation

Today, several computerized monitoring systems allow online measurement of PPV and SVV. The algorithm used by the PiCCO system enables continuous calculation of SV by measuring the systolic portion of the aortic pressure waveform and dividing the area under the curve by the aortic impedance. Initially, the specific aortic impedance is determined by transpulmonary thermodilution.⁵¹ Based on the beat-to-beat measurement of pulse-contour-derived SV, SVV can be derived continuously from the mean values of four minimum and maximum SVs averaged during the previous 30 seconds (Table 2, Fig. 4). The respiratory variations of the arterial pulse pressure can be calculated accordingly (Table 2, Fig. 5).

Table 2
Dynamic variables of fluid responsiveness.

Variable	Description	Calculation	Monitoring
Delta down (Δ_{down})	Difference between systolic arterial pressure (SAP) in apnoea and at end-expiration (minimal value during one mechanical ventilatory cycle)	$SAP_{\text{apnoea}} - SAP_{\text{exp}}$	Invasive arterial pressure recordings and appropriate monitor
Delta up (Δ_{up})	Difference between maximal SAP value during mechanical ventilatory cycle and apnoeic SAP	$SAP_{\text{insp}} - SAP_{\text{apnoea}}$	Invasive arterial pressure recordings and appropriate monitor
Systolic pressure variation (SPV)	Systolic arterial pressure variation during one mechanical ventilatory cycle: sum of $\Delta_{\text{up}} + \Delta_{\text{down}}$	$SAP_{\text{insp}} - SAP_{\text{exp}}$	Invasive arterial pressure recordings and appropriate monitor
Pulse pressure variation (PPV)	Pulse pressure (PP) variation calculated from the mean values of four minimum and maximum SVs averaged during the previous 30 seconds	$\frac{PP_{\text{max}} - PP_{\text{min}}}{1/2(PP_{\text{max}} + PP_{\text{min}})} \times 100$	Invasive arterial pressure recordings and appropriate monitor (PiCCO®, LIDCO®)
Stroke volume variation (SVV)	Stroke volume (SV) variation calculated from the mean values of 4 minimum and maximum four SVs averaged during the previous 30 seconds	$\frac{SV_{\text{max}} - SV_{\text{min}}}{1/2(SV_{\text{max}} + SV_{\text{min}})} \times 100$	PiCCO®, LIDCO®
Variation in pulse oxymetric plethysmographic waveform (ΔPOP)	Pleth variability index (PVI) calculates the respiratory variations in the plethysmography waveform amplitude	$\frac{PI_{\text{max}} - PI_{\text{min}}}{PI_{\text{max}}}$	PVI, Masimo® Radical-7™
Peak aortic flow velocity variation (ΔV_{peak})	Peak aortic blood flow velocity variation (ΔV_{peak}) during one mechanical ventilatory cycle	$\frac{Vpk_{\text{max}} - Vpk_{\text{min}}}{1/2(Vpk_{\text{max}} + Vpk_{\text{min}})} \times 100$	Echocardiography

PiCCO, Pulse Contour Cardiac Output monitoring system.

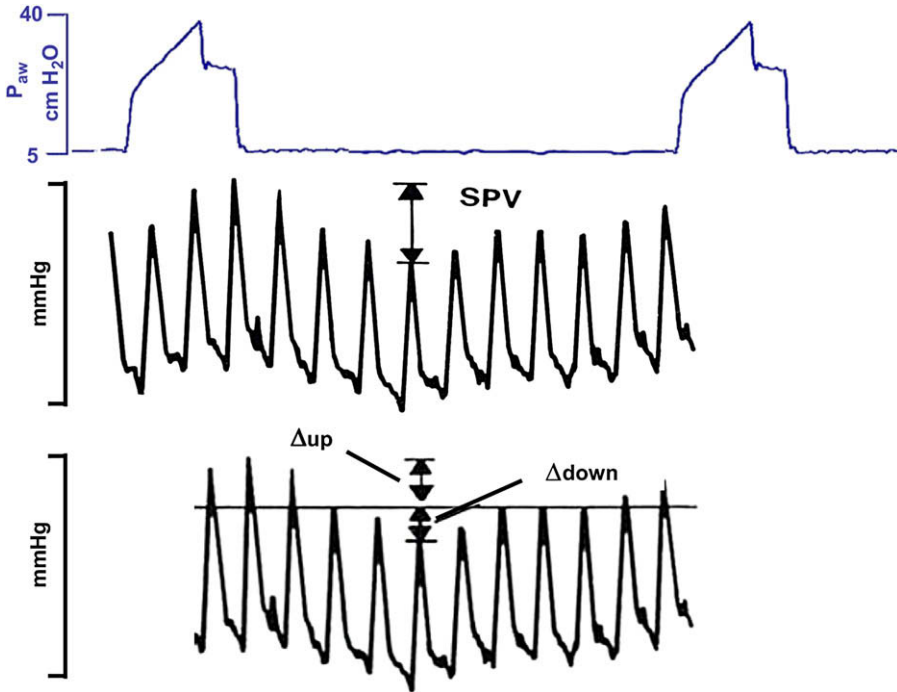


Fig. 3. The respiratory-cycle-induced changes in arterial systolic pressure. The reference line indicates apnoea and allows for measurement of the Δ_{up} and Δ_{down} component of systolic pressure variation. P_{aw} , positive airway pressure; SPV, systolic pressure variation.

All these dynamic variables have one common denominator: the higher the pre-infusion value, the more pronounced the increase in SV in response to fluid administration will be. Consequently, during the last 20 years dynamic variables have been investigated extensively in a number of clinical and experimental settings. However, all these investigations reported a wide variety of threshold values ranging from 9% to 17% with respect to PPV (Table 3). Although some monitoring systems have made most of the abovementioned variables available, they are still not widely used in daily clinical routine. There are potentially several factors contributing to this phenomenon. Most of the monitoring systems offer a continuous measurement of PPV and SVV over an arbitrarily chosen period of time, i.e. independent of synchronization with the respiratory cycle, which is in contrast to the more accurate calculation of dynamic variables induced by one single breath.^{52–54} Cannesson et al demonstrated in a recent investigation on 25 patients scheduled for coronary artery bypass grafting only a weak agreement between PPV measured automatically with PPV measured manually, yielding different

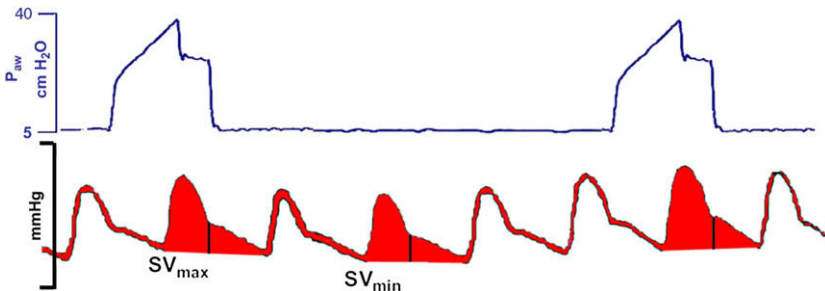


Fig. 4. The respiratory-cycle-induced changes in stroke volume (SV). The stroke volume variation is calculated between the maximal (SV_{max}) and minimal (SV_{min}) values of stroke volume. P_{aw} , positive airway pressure.

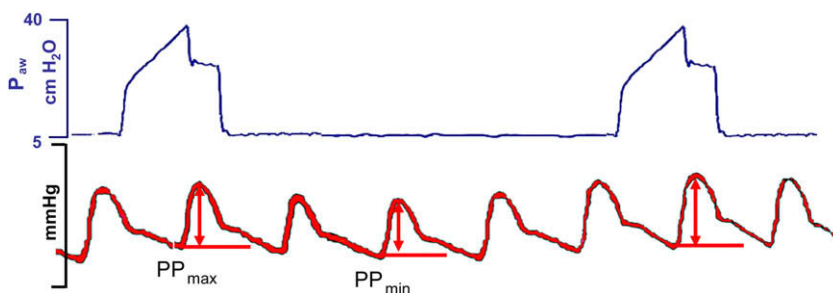


Fig. 5. The respiratory-cycle-induced changes in pulse pressure (PP). The pulse-pressure variation is calculated between the maximal (PP_{max}) and minimal (PP_{min}) values of pulse pressure. P_{aw}, positive airway pressure.

threshold values predicting fluid responsiveness (10% threshold value for the automatically measured PPV and 12% for the manually measured PPV).⁵³ Also, different threshold values were obtained in different clinical and experimental settings. Therefore, studies differed with respect to the fluid challenge performed⁵⁵ and the definition of responder and non-responder. The amount of fluid administered ranges from 100 mL in 60 s^{2,10} over one bolus of 500 mL^{50,56} up to 20 mL/kg over 20 minutes.⁵² Moreover, the defined percentage change in SV (Δ SV) or Δ CO/ Δ CI to qualify for being a responder due to a fluid challenge ranges from 5%^{10,57} through 12%⁵⁰ up to 25%.^{14,58} Although Δ SV is the most accurate target variable to discriminate between responders and non-responders, a number of studies based their results on percentage changes in CO and/or CI.^{56,59,60} Despite this uncertainty based on differing study designs and definitions, there are several confounders potentially influencing the performance of dynamic variables of fluid responsiveness. Recently, investigations yielded conflicting results regarding the application of dynamic variables during different tidal volumes applied^{2,12,61} during open-chest conditions^{62–64} in the presence of intra-abdominal hypertension (IAH)^{65,66}, during elevated positive end-expiratory pressure (PEEP)^{67–69} in the case of norepinephrine-treated haemorrhage⁷⁰ in paediatrics^{40,71}, and in the case of spontaneous breathing activity.^{48,72–74}

Table 3

Experimental and clinical studies investigating threshold values for pulse pressure variation (PPV) and stroke volume variation (SVV) predicting fluid responsiveness.

Reference	Year of publication	Clinical/experimental setting	Threshold values (%)
Michard et al ²²	2000	Septic patients on ICU	PPV: 13%
Berkenstadt et al ¹⁰	2001	Patients undergoing brain surgery	SVV: 9.5%
Reuter et al ⁵⁷	2003	Patients with reduced cardiac function	SVV: 9.5%
Kramer et al ⁵⁰	2004	Post-cardiac-surgery patients on ICU	PPV: 11%
Vieillard-Baron et al ⁵⁹	2004	Medical patients on ICU	PPV: 12%
Preisman et al ⁸⁴	2005	Post-coronary-artery-bypass surgery patients	PPV: 9%
De Backer et al ¹²	2005	Medical and post-surgery patients on ICU	PPV: 12%
Feissel et al ⁶⁰	2005	Medical and post-surgery patients on ICU	PPV: 17%
Hofer et al ⁵⁸	2005	Post-cardiac-surgery patients on ICU	PPV: 13.5% SVV: 12.5%
Cannesson et al ⁸⁵	2005	Post-coronary-artery-bypass surgery patients	PPV: 13%
Charron et al ²	2006	Post-surgery patients on ICU	PPV: 10%
Solus-Biguenet et al ⁸⁶	2006	Patients undergoing hepatic resection	PPV: 14%
Natalini et al ⁸⁷	2006	Medical and post-surgery patients on ICU	PPV: 15%
Feissel et al ⁸⁸	2007	Medical patients on ICU	PPV: 12%
Cannesson et al ¹¹	2007	Post-coronary-artery-bypass surgery patients	PPV: 11%
Renner et al ¹⁴	2008	Paediatric animal setting (pigs)	SVV: 9.5%
Renner et al ⁶⁶	2008	Experimental setting of intra-abdominal hypertension (IAH) (pigs)	SVV: 9.5% PPV: 11.5% (IAH) PPV: 20.5%

Effect of tidal volume on dynamic variables

Cyclic changes in left ventricular stroke volume induced by positive pressure ventilation are based on cyclic changes in intrathoracic pressure and in lung volume. Consequently, the higher the magnitude of tidal volume applied, the more pronounced should be the effect on dynamic variables of fluid responsiveness, independently of intravascular volume status. DeBacker et al demonstrated in a clinical trial the influence of different tidal volumes applied on PPV, and concluded that PPV is a reliable predictor of fluid responsiveness only when tidal volume is at least 8 mL/kg.¹² In an experimental investigation of acute haemorrhage and resuscitation, Renner et al showed that SVV also varied directly with different tidal volumes both during severe haemorrhage and after resuscitation.⁶¹ In a clinical study, Charron et al compared the effect of different tidal volumes on the cyclic changes in aortic velocity–time integrals obtained by echocardiography with the behaviour of PPV. Surprisingly, although both variables were good predictors of fluid responsiveness, the cyclic changes in aortic velocity–time integrals were clearly less influenced by different tidal volumes applied than PPV.

Effect of open-chest conditions on dynamic variables

The effect of positive pressure ventilation on the cyclic changes in left ventricular preload is fundamentally influenced by the integrity of the chest. The cyclic changes in intrathoracic pressure should be decreased if the chest is opened, and consequently the effect on dynamic variables of fluid responsiveness should be less pronounced. This hypothesis is underlined by a few clinical and experimental investigations.^{62,63,75} Rex et al evaluated the effect of open-chest conditions in 45 patients undergoing coronary artery bypass grafting on the behaviour of PPV and SVV, and concluded that PPV and SVV may be misleading in predicting fluid responsiveness in open-chest conditions.⁶³ In contrast, Reuter et al demonstrated that PPV and SVV were able to predict fluid responsiveness in hypovolaemic patients under open-chest and open-pericardium conditions.⁶² Currently, the use of dynamic variables of fluid responsiveness to guide fluid therapy under open-chest conditions cannot be recommended.

Influence of intra-abdominal hypertension on dynamic variables

Intra-abdominal hypertension (IAH) is associated with a mechanical impairment of venous return as the result of inferior vena cava compression.⁷⁶ Consequently, dynamic variables of fluid responsiveness must also be altered in the presence of IAH. Duperett et al were the first to show in an experimental setting that SPV and PPV as well as inferior vena cava flow fluctuations were dependent on changes in intra-abdominal pressure which caused changes in pleural pressure swing. This dependency was more marked during hypovolaemia, indicating that dynamic variables are not solely related to intravascular volume but also to the presence of elevated intra-abdominal pressure.⁶⁵ In another experimental trial, Renner et al demonstrated that during IAH SVV failed to predict fluid responsiveness, whereas PPV and GEDV preserved their ability to be reliable predictors of fluid responsiveness. Interestingly, the threshold value for PPV before IAH (11.5%) increased to 20.5% after inducing IAH, whereas the threshold value for GEDV remained unchanged.⁶⁶ More studies are needed to investigate the influence of elevated intra-abdominal pressure on the performance of dynamic variables of fluid responsiveness before these variables can be recommended to reliably guide fluid therapy in critically ill patients with IAH.

Influence of elevated positive end-expiratory pressure on dynamic variables

Increasing PEEP primarily distends the lungs and increases intrathoracic pressure. Consequently, initially venous return is reduced, and this effect is more pronounced during hypovolaemia. It has been shown by Kubitz et al that increasing PEEP levels increased both PPV and SVV during closed- and open-chest conditions.⁷⁷ Lambert et al have shown in an animal investigation that the change in SV due to an increase in PEEP level might be an indicator of fluid responsiveness.⁶⁷ In a recent paediatric animal experiment of elevated PEEP level and changing loading conditions, it has been shown that SVV and

GEDV were sensitive and specific predictors of fluid responsiveness even during elevated PEEP levels, in contrast to PPV. However, the optimal threshold value for SVV to discriminate between responders (increase in SV >15%) and non-responders varied from 9.5% at PEEP 5 mmHg to 14% at PEEP 10 mmHg.⁶⁹ Again, GEDV was the only variable that yielded comparable threshold values at different PEEP levels.⁶⁹

Influence of norepinephrine on dynamic variables

It has been suggested that vasopressors might exert a direct effect on regional vascular capacitance, and that they would alter PPV and SPV and interfere with their ability to predict fluid responsiveness. Nouira et al investigated in an experimental setting of norepinephrine-treated haemorrhage the effect of norepinephrine on PPV and SPV.⁷⁰ They showed that norepinephrine induced a significant decrease in both PPV and SPV during haemorrhage, though they were not able to differentiate whether this effect was the consequence of a blood shift from unstressed to stressed volume or whether it was an effect of the vasopressor on the vascular tone, i.e. arterial elastance and compliance, that are both determinants of pulse pressure and systolic pressure. Recently, Sennoun and colleagues investigated the effects of early versus delayed use of norepinephrine in endotoxic shock.⁷⁸ They observed in endotoxin-treated rats that the early use of norepinephrine was associated with a significant decrease in PPV, although aortic blood flow (e.g. stroke volume) also decreased significantly. Additional investigations are needed to clarify the influence of vasoconstrictors administered in hypovolaemic patients on dynamic variables.

Influence of spontaneous breathing activity on dynamic variables

One basic requirement for the assessment of dynamic variables of fluid responsiveness is positive pressure ventilation. Whether changes in intrathoracic pressure during spontaneous breathing and/or under positive pressure support ventilation might be insufficient to adequately modify loading conditions is still a matter of debate. In septic patients under pressure support ventilation, Perner et al were able to demonstrate that SVV could not accurately predict the response to a fluid load.⁴⁸ Heenen et al confirmed this observation for PPV and the inspiratory changes in right atrial pressure in a similar setting.⁷² Also, Soubrier et al demonstrated that PPV and SPV are less reliable to predict fluid responsiveness during spontaneous breathing.⁷⁴

Perioperative optimization of fluid therapy guided by dynamic variables

So far, only a few studies are available highlighting the impact of dynamic variables to optimize and guide fluid therapy. It has been shown repeatedly that maximizing SV by fluid loading during high-risk surgery decreases the incidence of postoperative complications and the length of stay in the ICU and in the hospital.^{79–81} Lopes et al were the first to show in a small number of patients undergoing high-risk surgery that monitoring and optimizing PPV by fluid loading improves outcome and decreases the length of stay in the hospital compared to an unspecific fluid management protocol.⁸² In another study on 80 patients scheduled for major abdominal surgery, Buettner et al analysed the effects of SPV-guided intraoperative fluid management on organ function and perfusion compared to routine care.⁸³ They found that in comparison with routine care, intraoperative SPV-guided treatment was associated with a slight increase in fluid administration whereas organ perfusion and function were similar.

Conclusion

In critically ill patients undergoing major surgery or on the ICU, fluid responsiveness is an important issue since the response to a volume load is difficult to predict by clinical examination, and fluid overload is associated with the risk of pulmonary oedema and heart failure. The approach of functional haemodynamic monitoring in patients receiving mechanical ventilation in the absence of cardiac arrhythmias currently is the best option to predict fluid responsiveness. However, there are several issues that have to be considered when interpreting the values

obtained, such as high tidal ventilation, elevated PEEP levels, presence of IAH, need for vasoconstrictors, and spontaneous breathing efforts. The wide range of threshold values defined for dynamic variables of fluid responsiveness is quite confusing and may discourage the clinician to use these variables. At present, dynamic variables of fluid responsiveness yield threshold values that depend both on variables adjusted by the physician (e.g. tidal volume) and on patient-related factors (e.g. IAH). More precise information regarding different clinically relevant pathologies is needed to gain insight into the behaviour of dynamic variables of fluid responsiveness in relation to the underlying pathology. Since the static, volumetric variable GEDV has been shown to be a robust and reliable variable to indicate changes in preload, and moreover to predict fluid responsiveness, we recommend involving GEDV in the decision-making process whether the patient needs fluid or not.

Practice points

- static filling pressures are not appropriate to assess intravascular volume status, and moreover are not reliable predictors of fluid responsiveness
- dynamic variables of fluid responsiveness are more reliable predictors of fluid responsiveness in the absence of cardiac arrhythmias and in patients receiving mechanical ventilation without any spontaneous breathing efforts
- the threshold values defined to discriminate between patients who will improve haemodynamically after a fluid load and those who will not may vary according to the underlying pathology, e.g. high tidal volume ventilation, elevated PEEP levels, increased intra-abdominal pressure, need for norepinephrine administration, or open-chest conditions
- the static, volumetric variable GEDV has been shown to be a robust and reliable variable to indicate changes in preload and moreover to predict fluid responsiveness; therefore, we recommend involving GEDV in the decision-making process whether the patient needs fluid or not

Research agenda

- monitoring systems are needed that can synchronize the measures of dynamic variables with the respiratory cycle
- future studies must more clearly define the influence of different pathologies on the threshold values of dynamic variables of fluid responsiveness
- randomized multicentre trials with appropriate numbers of patients are needed to investigate the superiority of dynamic variables over traditionally used variables for optimizing and guiding fluid therapy

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