Arterial pulse pressure variation with mechanical ventilation

Jean-Louis TEBOU1 (jean-louis.teboul@aphp.fr)

Xavier MONNET1 (xavier.monnet@aphp.fr)

Denis CHEMLA2 (denis.chemla@aphp.fr)

Frédéric MICHARD3 (frederic.michard@bluewin.ch)

Departments and institutions:
1- Medical Intensive Care Unit, Bicetre Hospital, Paris-South University Hospitals, Inserm UMR_S999, Paris-South University, Le Kremlin-Bicêtre, France
2- Department of Physiology, Bicetre hospital, Paris-South University Hospitals, Inserm UMR_S999, Paris-South University, Le Kremlin-Bicêtre, France
3- MiCo, Chemin de Chapallaz 4, Denens, Switzerland

Corresponding author:
Prof. Jean-Louis TEBOU1
Service de réanimation médicale
Hôpital de Bicêtre
78, rue du Général Leclerc
94 270 Le Kremlin-Bicêtre
France

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Abstract

Fluid administration leads to a significant increase in cardiac output in only half of the intensive care unit patients. This led to the concept of assessing fluid responsiveness before infusing fluid. Pulse pressure variation, which quantifies the changes in arterial pulse pressure during mechanical ventilation, is one of the dynamic variables which can predict fluid responsiveness. The underlying hypothesis is that large respiratory changes in left ventricular stroke volume, and thus pulse pressure, occur in cases of biventricular preload responsiveness. Several studies showed that pulse pressure variation accurately predicts fluid responsiveness when patients are under controlled mechanical ventilation. Nevertheless, in many conditions encountered in the intensive care unit, the interpretation of pulse pressure variation is unreliable (spontaneous breathing, cardiac arrhythmias) or doubtful (low tidal volume). To overcome some of these limitations, it has been proposed to evaluate the dynamic response of pulse pressure variation using simple tests such as the tidal volume challenge. The applicability of pulse pressure variation is higher in the operating room setting, where fluid strategies based on pulse pressure variation improve postoperative outcomes. In medical critically ill patients, though no randomized controlled trial has compared a pulse pressure variation-based fluid management with standard care, the Surviving Sepsis Campaign guidelines recommend using fluid responsiveness indices, including pulse pressure variation, whenever applicable. In conclusion, pulse pressure variation is useful to manage fluid therapy, in specific conditions where it is reliable. The kinetics of pulse pressure variation during diagnostic or therapeutic tests also is helpful for fluid management.
Abstract word count

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Key words

Fluid responsiveness, cardiac preload, heart-lung interactions, cardiac output
Introduction

Hemodynamic resuscitation of patients with circulatory failure was most often guided by variables provided by the pulmonary artery catheter until the mid-90’s. Since that time, the use of the pulmonary artery catheter has declined dramatically (1). The factors that contributed to this decline are multiple, including the publication of randomized controlled trials that showed either no benefit (2) or even deleterious effects (3) of strategies aimed at maximizing oxygen delivery in the intensive care unit (ICU) patients. Moreover, a multicenter non-randomized clinical study showed an increased mortality associated with pulmonary artery catheterization (4), although subsequent randomized controlled trials did not confirm these findings (5, 6). These findings eventually contributed 1) to move away from the concept of maximization of oxygen delivery to the concept of individualization of the therapeutic strategy, and 2) to developing novel and less invasive alternatives to pulmonary artery catheterization (7).

Twenty years ago: emergence of the concept of fluid responsiveness and its bedside assessment

The concept of prediction of fluid responsiveness has emerged in the context of individualization of hemodynamic therapy and occupies a major place in guiding resuscitation of ICU patients today (8, 9). Fluid responsiveness is generally defined as the ability of the heart to increase its stroke volume or cardiac output in response to a fluid bolus (10). Physiologically, fluid responsiveness implies that both ventricles are preload responsive, i.e., they operate on the steep part of the curve plotted the respective stroke
volume vs. preload relationship (Frank-Starling mechanism) (Figure 1). A systematic review of the literature reported that fluid responsiveness is present in only 50% of the ICU patients in whom a decision for fluid administration fluid was made by the treating physician (10). However, one cannot exclude a higher percentage if only patients in shock are considered. Nevertheless, given that fluid overload may cause harm to ICU patients (11), particularly to fluid non-responders (12), it is important to detect fluid responsiveness before administering any fluid.

Measures of cardiac preload, such as central venous pressure (CVP) are of poor utility to predict fluid responsiveness (13). A given value of cardiac preload can be associated with either fluid responsiveness or fluid unresponsiveness depending on the shape of the Frank-Starling curve (Figure 1). There is a large variability in the shape of the Frank-Starling curve among individuals, mainly related to differences in cardiac contractility.

A more valuable method for predicting fluid responsiveness is to estimate the slope of the Frank-Starling curve by measuring the short-term changes in stroke volume (or in its surrogates) in response to a brief change in cardiac preload. The classical fluid challenge (infusing a small volume of fluid within a short time) involves fluid administration, with potential harm in the subset of fluid non-responders, especially when the test is repeated frequently. Thus, dynamic tests, which challenge the Frank-Starling relationship without the need for any fluid infusion, have become very popular. Quantification of the respiratory variation of stroke volume has emerged in the late 90’s as a practical application of the theoretical heart-lung interactions principles described in the 80’s by experts in cardiovascular and respiratory physiology (14-16). The physiological background is that mechanical ventilation induces cyclic changes in loading conditions of both ventricles (14-17) (Figure 2).
Insufflation decreases the right ventricular (RV) preload as a consequence of the decrease in venous return due to the inspiratory increase in intrathoracic pressure. Insufflation generally increases the RV afterload as a consequence of the inspiratory increase in transpulmonary pressure (18), in particular when West’s zone 2 conditions - when alveolar pressure becomes higher than the pulmonary venous pressure - are extended (19). As a result, the RV stroke volume is minimal at the end of insufflation (15, 18). It is generally assumed that the inspiratory reduction in venous return is the predominant mechanism, especially if the right ventricle operates on the steep part of the Frank-Starling curve (RV preload responsiveness). The inspiratory decrease in the RV stroke volume leads to a decrease in the left ventricular (LV) filling after a phase lag of two to four heart beats due to the blood pulmonary transit time. This generally occurs during expiration (17). In cases of LV preload responsiveness, the decrease in LV preload eventually results in a decrease in the LV stroke volume, which is thus minimal during expiration. From these physiological principles, it has been postulated that during mechanical ventilation, large changes in LV stroke volume should occur in cases of biventricular preload responsiveness, whereas no change in LV stroke volume should occur if at least one ventricle is preload unresponsive (17). Numerous studies have consistently demonstrated that the magnitude of respiratory variation of stroke volume predicts fluid responsiveness with great accuracy in mechanically ventilated patients (12, 20, 21).

**Pulse pressure variation: a valuable index to predict fluid responsiveness in patients receiving mechanical ventilation**

Among all the indices of fluid responsiveness, pulse pressure variation (PPV) has been one of the most studied and the most used in clinical practice.
Aortic pulse pressure (systolic pressure minus diastolic pressure) is directly proportional to LV stroke volume and inversely related to aortic compliance (22). We postulated that PPV reflects the respiratory changes in stroke volume and thus, should serve to assess fluid responsiveness (23, 24), assuming that the arterial compliance does not change over the respiratory cycle, a hypothesis confirmed experimentally (25). One of the advantages of using PPV rather than systolic pressure variation (SPV), which had been previously evaluated (26, 27), is that pulse pressure, which is a differential pressure, is less directly influenced by the cyclic changes in intrathoracic pressure than systolic pressure. Accordingly, we showed that PPV was a better predictor of fluid responsiveness than SPV (24). Importantly, in this study conducted in septic shock patients, PPV was a far better predictor of fluid responsiveness than cardiac filling pressures. We defined fluid responsiveness by an increase in thermodilution-derived cardiac output by more than 15% in response to a fluid bolus (500 mL colloid infused over 30 min) (24). Further studies in different clinical settings confirmed the utility of PPV as a reliable predictor of fluid responsiveness in patients ventilated with a tidal volume (V₉) of at least 8 mL/kg (19, 20) provided that they have no spontaneous breathing activity and/or cardiac arrhythmias (28). In a meta-analysis including 22 studies and 807 patients, PPV predicted fluid responsiveness with an area under the receiving operating characteristic (AUROC) curve of 0.94 and a threshold of 12% (20). It is noteworthy that in the studies included, fluid responsiveness was defined using either one of the following techniques: thermodilution, transpulmonary thermodilution, pulse contour analysis, or esophageal Doppler (20).

Initially, PPV was manually determined as the ratio of the difference between the maximal and minimal values of pulse pressure over the mean of these two values and
expressed as a percentage (Figure 3) (23). Today, most hemodynamic monitors allow automatic calculation of PPV with continuous display of its value in real time (29). Some monitors estimate the stroke volume using proprietary algorithms based on analysis of the arterial pressure waveform analysis (30). They also calculate and display stroke volume variation (SVV), which has been assumed to reflect the respiratory variation of stroke volume in patients receiving mechanical ventilation (31). In a meta-analysis, SVV predicted fluid responsiveness with greater accuracy than markers of cardiac preload in mechanically ventilated patients (19). However, SVV was significantly less accurate than PPV (AUROC curve: 0.84 vs. 0.94, respectively) (19). The results are not surprising since the calculation of PPV is prone to fewer errors than the more complex computation of SVV. Another advantage of PPV over SVV is that it requires a simple arterial catheter for its determination.

Non-invasive devices measuring the respiratory changes in various hemodynamic signals can also be used to predict fluid responsiveness during mechanical ventilation. The PPV measured using a finger blood pressure device (volume clamp method) was as reliable as the invasively obtained PPV to predict fluid responsiveness in the operating room (OR) (32) as well as in the ICU (33) settings. The respiratory changes in the amplitude of the plethysmographic signal predict fluid responsiveness with acceptable accuracy (34, 35), except in patients receiving norepinephrine (36, 37). The respiratory changes in ultrasound variables such as the velocity time-integral (VTI) of the LV outflow track (echocardiography) (38), the aortic blood flow (esophageal Doppler) (39), the diameter of the inferior (40) or superior vena cava (41) and the diameter of the internal jugular vein (42) have been shown to be acceptable predictors of fluid responsiveness, although they have been less studied and less validated compared to PPV. Overall, this confirms the theoretical basis that heart-lung interactions during mechanical ventilation can be judiciously used for predicting fluid
responsiveness. Non-invasive fluid responsiveness indices, as described above, can be useful when an arterial cannulation is not performed. In addition, echocardiography is recommended to be performed as soon as possible, as it is the preferred modality to initially evaluate the type of shock (8).

**Pulse pressure variation in specific clinical situations: what are the limitations? How to overcome them?**

Several conditions listed in Table 1, limit the interpretation of PPV (27). It is thus important to discuss the utility of PPV in some specific settings.

**PPV and acute respiratory distress syndrome (ARDS)**

At least, two factors limit the use of PPV in ARDS: low tidal volume ($V_T$) ventilation and low lung compliance (43).

1) Low $V_T$ ventilation is recommended in patients with ARDS (9). Under these conditions, respiratory changes in intrathoracic pressure might be insufficient to produce significant changes in preload. Accordingly, it was reported that in the case of $V_T \geq 8 \text{ mL/kg}$, PPV accurately predicted fluid responsiveness (AUROC curve: 0.89 with a threshold value of 12%) whereas the prediction was weaker (AUROC curve: 0.70 with a threshold value of 8%) when $V_T$ was $<8 \text{ mL/kg}$ (44). Nevertheless, during low $V_T$ ventilation, three important issues need to be highlighted. Firstly, a high PPV (e.g. $>12\%$) still suggests fluid responsiveness. Secondly, a low PPV cannot rule out fluid responsiveness. Thirdly, to overcome the difficult interpretation of low PPV, it has been suggested to measure the response of PPV to a transient (less than one minute) increase in $V_T$ (45). Myatra et al confirmed that PPV poorly predicts fluid responsiveness at 6 mL/kg $V_T$ (AUROC curve: 0.69) (46). After $V_T$ was increased
to 8 mL/kg, PPV predicted more reliably the hemodynamic response to fluid infusion, documented at 6 mL/kg (AUROC curve: 0.91) (46). Interestingly, an increase in the absolute value of PPV ≥3.5% during the V\textsubscript{T} challenge, predicted fluid responsiveness with excellent accuracy (AUROC curve: 0.99) (46). Another way to overcome the limitation of using PPV in case of low V\textsubscript{T} is to divide PPV by the respiratory changes in esophageal pressure (AUROC curve: 0.94 with vs. 0.78 without adjustment) (47). The disadvantage of using this index is the need for an esophageal probe.

2) Low lung compliance and low compliance of the respiratory system (Crs = V\textsubscript{T} /driving pressure), which are characteristics of ARDS, can also result in misleading interpretation of PPV by reducing the transmission of airway pressure to the intrathoracic structures (43). Although the chest wall compliance is generally reduced, the resultant effect is a decrease in that airway pressure transmission as illustrated by the correlation between Crs and the airway pressure transmission found in a previous study (48). It has been shown that when Crs was >30 mL/cm\textsubscript{H}\textsubscript{2}O, PPV predicted fluid responsiveness accurately (AUROC curve: 0.98), whereas when Crs was ≤30 mL/cm\textsubscript{H}\textsubscript{2}O, the prediction was poor (AUROC curve: 0.69) essentially due to a high rate of false negatives (49). Interestingly, among fluid responders, there was a subset of patients ventilated with a V\textsubscript{T} <8 mL/kg, a Crs >30 mL/cm\textsubscript{H}\textsubscript{2}O and a high PPV and another subset with a V\textsubscript{T} >8 mL/kg, a Crs ≤30 mL/cm\textsubscript{H}\textsubscript{2}O, and a low PPV (5% on average), suggesting that the decreased Crs might play a more important role than the low V\textsubscript{T} in the poor predictive value of PPV (49).

Other factors limit the interpretation of PPV in ARDS. Persistent breathing activity during mechanical ventilation is common as it is currently recommended to minimize the use of sedative agents and to allow the patient to partially use his/her respiratory muscles (9),
although this issue is still a matter of debate (50). In such cases, PPV cannot predict fluid responsiveness (51), since the respiratory changes in intrathoracic pressure are irregular, either in rate or in amplitude. In case of low Vt controlled-ventilation, a high respiratory rate may be needed. In such a case, the decrease in LV filling secondary to the insufflation-induced decrease in RV stroke volume, might occur at insufflation and not at expiration, resulting in low PPV even in cases of fluid responsiveness. A clinical study showed that PPV cannot be interpreted reliably when the heart rate/respiratory rate ratio is lower than 3.6 (52). Prone positioning is often used in severe ARDS patients. One clinical study reported a poor predictive value of PPV during prone positioning in ARDS patients (53), probably due to the low V\textsubscript{T} ventilation and the low lung compliance. Finally, the level of positive end-expiratory pressure (PEEP) should not affect the predictive value of PPV. Indeed, PEEP increases the mean airway pressure but does not change the cyclic variation in airway pressure during a mechanical breath, which is the main determinant of PPV. Some publications that showed a good predictive value for PPV during mechanical ventilation included patients receiving PEEP (23, 24, 33, 41, 54). Interestingly, PPV can also be used to predict the hemodynamic effects of PEEP (23). We speculated that a high PPV in ARDS patients was linked to the presence of biventricular preload-dependence and that a significant decrease in cardiac output with PEEP should occur only in patients with biventricular preload-dependence. Accordingly, we showed that the higher the PPV before applying PEEP, the more pronounced was the decrease in cardiac output with PEEP (23).

**PPV and right ventricular dysfunction**

It has been suggested that RV dysfunction could result in false positive values of PPV (i.e. high PPV despite fluid unresponsiveness) due to the predominant effect of mechanical
insufflation on the RV afterload through the compression of intra-alveolar microvessels by the transpulmonary pressure. As a failing and dilated right ventricle is more sensitive to its afterload than to its preload, the decrease in RV stroke volume during insufflation would be more related to RV afterload-dependence than to RV preload-dependence. Two clinical studies reported high PPV values (>12%) despite fluid unresponsiveness in the context of RV dysfunction (55, 56). However, in these studies, the tidal volume was greater than 8 mL/kg, and one cannot exclude an attenuation of the phenomenon of RV afterload-dependence during low V\textsubscript{T} ventilation. Additionally, in these studies, which were performed before the publication of international guidelines (57), the way RV function was assessed can be debated.

**PPV and congestive heart failure**

Few studies have addressed the issue of fluid responsiveness in patients with congestive heart failure probably because fluid administration is rarely indicated in such patients. In some studies, including patients with left ventricular dysfunction and in sinus rhythm, PPV (or SVV) was reported to predict fluid responsiveness with an acceptable accuracy (41, 58). However, the presence of cardiac arrhythmias is an obvious contraindication to use PPV since the variation of pulse pressure is mainly related to the irregularity of the cardiac diastole, irrespective of the respiratory cycle.

**PPV and intra-abdominal hypertension**

Experimental data suggest that PPV can still predict fluid responsiveness in cases of increased intra-abdominal pressure, but that the threshold value might be higher than in the case of normal abdominal pressure (59). However, the experimental conditions (acute rise of intra-abdominal pressure, very high values of intra-abdominal pressure achieved, high V\textsubscript{T}}
and low chest compliance) were far from those encountered in ICU patients. In a series of ventilated patients with acute liver failure, the authors concluded that PPV predicted fluid responsiveness, whereas the respiratory changes in VTI were not predictive (60).

**PPV in the general population of ICU patients**

An international observational study published in 2015 investigated in 2213 patients whether fluid responsiveness indices were used before performing fluid challenges (61). The CVP was the most used variable (576 cases) compared with PPV or SVV (176 cases) and passive leg raising (248 cases) (61). These practices are likely to evolve as the most recent version of the Surviving Sepsis Campaign guidelines suggests using dynamic indices of fluid responsiveness (including PPV when applicable) instead of CVP when hemodynamic reassessment is required after the initial fluid bolus (9).

Low VT ventilation is commonly used in non-ARDS critically ill patients, as illustrated by a study that enrolled 540 mechanically ventilated patients, the vast majority of whom received low VT (62). PPV as well as echocardiographic fluid responsiveness indices did not reliably predict fluid responsiveness (62). However, in this study, fluid responsiveness was identified by passive leg raising and not by fluid administration (62). Since passive leg raising was shown to be hemodynamically equivalent to 312 [250-350] mL fluid administration (63), there were likely a significant number of true 500-mL fluid responders rated non-responders using passive leg raising and some fluid non-responders classified as responders using passive leg raising (62). This may have resulted in higher rates of false positive, and to a lesser extent in higher rates of false negative cases of PPV (64) compared to studies that assessed fluid responsiveness using a real fluid administration.

The conditions under which the reliability of PPV is limited are quite common in the
ICU. As an example, in a prospective study that included ICU patients, who actually received fluid boluses, the incidence of cases where PPV could be used without limitation was 17% (65). This incidence may vary in function of the case mix and the ventilator settings. Another study showed that in cases of shock, the conditions of applicability of PPV were present in 39% of patients with sepsis and 53% of patients with trauma (66). Performance of VT challenge in cases of low VT ventilation should extend the conditions of PPV use.

**Pulse pressure variation and impact on outcome**

In surgical patients, there is strong evidence that both insufficient and excessive fluid administrations are associated with an increased rate of postoperative complications (67). Tailoring fluid administration to individual needs is recommended (68). Maintaining patients close to the inflection part of the Frank-Starling curve, i.e. maintaining PPV within the range 10-15%, should protect from the consequences of both hypovolemia and fluid overload (69). A meta-analysis of 14 randomized controlled trials concluded that the use of PPV or SVV to guide fluid management during and/or right after surgery was associated with a significant decrease in postoperative morbidity (70). However, due to heterogeneity and inconsistency among the assessed studies, further confirmation is needed.

In medical ICU patients, no outcome randomized controlled trial has yet compared PPV-based fluid management with standard care.

**Practical use of pulse pressure variation (Figure 4)**

Only when the patient has no spontaneous breathing activity and has a sinus rhythm, PPV should be considered for predicting fluid responsiveness.
In cases of high values (e.g. >13%), PPV should have a good predictive value even if \( V_T \) or Crs are low. In case of doubt about a false positive PPV (e.g., in the setting of RV dysfunction diagnosed by echocardiography), a passive leg raising test can be performed: a decrease in PPV during passive leg raising would suggest that the patient is actually fluid responsive, whereas a lack of decrease in PPV would suggest that the patient is not fluid responsive and that the high PPV value was a false positive.

In cases of low values (e.g. <9%), PPV has an excellent predictive value if \( V_T \) is at least 8 mL/kg and Crs >30 mL/kg. In patients with ARDS, interpretation is more difficult (false negative cases) due to low \( V_T \) ventilation or low Crs. As mentioned above, this is a good indication of performing a \( V_T \) challenge consisting of transiently increasing \( V_T \) (from 6 to 8 mL/kg) and measuring the absolute changes in PPV (45, 46).

Some authors described a “grey zone” for PPV (e.g. between 9 and 13%) where no conclusion can be drawn about fluid responsiveness, even when tidal volume is \( \geq 8 \text{mL/kg} \) (71). Challenging PPV following a transient increase in \( V_T \) from 8 to 12 mL/kg has been proposed to overcome this limitation (72).

Finally, PPV should not be interpreted in cases of cardiac arrhythmias and spontaneous breathing activity (Table 1; Figure 4). This latter condition includes: 1) patients who are intubated and ventilated with persistent respiratory efforts, 2) patients with non-invasive ventilation, and 3) patients with no mechanical ventilation, whether the expiration is active (73) or not. This is the right place for other dynamic tests of fluid responsiveness such as passive leg raising or end-expiratory occlusion tests (49).

Whatever the method used, the presence of fluid responsiveness, which is a physiological phenomenon, should not lead automatically to fluid administration. In reality, three
different situations should be distinguished:

- The decision to initiate fluid administration urgently at the early phase of shock should not be based on the presence of fluid responsiveness indices, especially in cases of septic shock (9), active bleeding or evident fluid losses.

- The decision to continue fluid infusion after initial fluid resuscitation is a different issue, except in cases of active bleeding or persistent fluid losses. Since not all patients are fluid responsive, predictors of fluid responsiveness, though required, represent only one element of the decision-making process (Figure 5). The decision to infuse fluids should be based on the presence of three elements: 1) signs of shock, 2) fluid responsiveness, and 3) limited risks of fluid overload. In cases where the risks of lung edema are not negligible, additional variables, such as extravascular lung water (74) or the presence of B-lines on lung ultrasound examination (75), are useful in making the appropriate decision. The decision to discontinue fluid administration should be based on the presence of only one of the following three elements: 1) either disappearance of signs of shock, 2) or appearance of fluid unresponsiveness, 3) or appearance of signs of pulmonary edema.

- In the OR setting, fluid therapy is not limited to the patients with shock. During high-risk surgery, the rationale of fluid administration is to optimize hemodynamics in order to prevent post-operative complications. As mentioned above, fluid strategies guided on PPV (or SVV) may result in improved outcomes (70).

Recently, it has been proposed to use the PPV/SVV ratio - called dynamic arterial elastance - to predict the blood pressure response to fluid administration. Two clinical studies (76, 77) suggested that a low PPV/SVV ratio predicts the absence of blood pressure response to fluid and hence would recommend the use of vasopressors. However, other studies have failed to replicate these results (78, 79). An experimental study (80) showed
that vasopressors decrease the PPV/SVV ratio, calling into question the recommendation to give vasopressors when the ratio is low. Some authors have reported that age is the main determinant of the PPV/SVV ratio, the ratio being higher in the elderly than in the younger patients (81). Thus, caution should be used in interpreting the PPV/SVV ratio as an indicator to initiate vasopressor therapy (82).

Conclusions

PPV is an easy to obtain but not always easy to use marker of fluid responsiveness. Ignoring its limitations could lead to serious misinterpretation. A survey showed that a large proportion of intensivists did not have complete knowledge of factors confounding the interpretation of PPV (83). This is clearly a plea for optimizing education.

PPV is applicable in mechanically ventilated patients with no spontaneous breathing and no arrhythmias. Its validity is indisputable in cases of ventilation with a $V_T \geq 8$ mL/kg, with minimally altered lung compliance, and with no RV failure and no intra-abdominal hypertension. Conditions for its optimum utilization are usually met in the OR, where fluid management strategies based on PPV (or SVV) monitoring have shown to reduce post-operative morbidity (70). Moreover, monitoring the dynamics of PPV is of interest since during fluid administration, the decrease in PPV inversely correlates with the increase in cardiac output (23, 24, 84). Non-invasive PPV monitoring tools should be increasingly used in the OR (85) provided that technological advancements would optimize their validity.

In ICU patients, the conditions of applicability of PPV are more restricted. Nevertheless, some limitations of PPV interpretation can be overcome by performing tests that rely on the dynamics of PPV such as the $V_T$ challenge.
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Figure legends

Figure 1

Frank-Starling relationship, preload responsiveness and pulse pressure variation

When the heart is operating on the steep part of the Frank-Starling relationship (top), an increase in cardiac preload (from A to B) results in an increase in stroke volume (preload responsiveness). When the heart is operating on the plateau of the Frank-Starling relationship (bottom), the same increase in cardiac preload (from A to B) does not result in a significant increase in stroke volume (preload unresponsiveness). Importantly, a given value of cardiac preload (whatever is the way it is measured) before preload increase (A) cannot predict preload responsiveness / unresponsiveness, while pulse pressure variation is especially valuable for that purpose.

Figure 2

Mechanisms of heart-lung interactions explaining pulse pressure variation

Top: airway pressure tracing; bottom: arterial pressure tracing
LV: left ventricle, PP: pulse pressure, RV: right ventricle.
Adapted from ref #17 after permission

Figure 3

Calculation of pulse pressure variation from an arterial pressure curve

PP: pulse pressure, PPV: pulse pressure variation.

Figure 4

Practical use of pulse pressure variation

Crs: compliance of the respiratory system; IAH: intra-abdominal hypertension; PPV: pulse pressure variation; RV: right ventricular; V_{T}: tidal volume

Figure 5

Decision algorithm for fluid administration in the intensive care unit

PPV: pulse pressure variation
<table>
<thead>
<tr>
<th>Condition</th>
<th>Reliability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous breathing</td>
<td>False +</td>
</tr>
<tr>
<td>Cardiac arrhythmias</td>
<td>False +</td>
</tr>
<tr>
<td>Low Vt</td>
<td>False -</td>
</tr>
<tr>
<td>Low lung compliance</td>
<td>False -</td>
</tr>
<tr>
<td>Increased intra-abdominal pressure</td>
<td>False +</td>
</tr>
<tr>
<td>Very high respiratory rate (HR/RR&lt;3.6)</td>
<td>False -</td>
</tr>
<tr>
<td>Right ventricular dysfunction</td>
<td>False +</td>
</tr>
</tbody>
</table>

Vt: tidal volume, HR: heart rate, RR: respiratory rate
Figure 1

Stroke volume

Preload responsiveness

Preload unresponsiveness

High PPV

Low PPV

Cardiac preload

A B
$PPV = \frac{PP_{\text{max}} - PP_{\text{min}}}{(PP_{\text{max}} + PP_{\text{min}}) / 2}$
**Figure 4**

- **Fluid responsiveness** is likely if there is no RV failure* or IAH**.
- In case of any doubt, perform **Passive Leg Raising**:
  - decrease in PPV: fluid responsiveness is likely
  - no decrease in PPV: fluid responsiveness is unlikely

- **Mechanical ventilation with no spontaneous breathing and no cardiac arrhythmias**
  - Take PPV into account

- **Presence of spontaneous breathing or cardiac arrhythmias**
  - **Do not** take PPV into account
  - Consider other tests of fluid responsiveness

- **PPV > 13%**
  - Consider a $V_T$ challenge

- **9% < PPV ≤ 13%**
  - $V_T \geq 8 \text{ mL/kg}$ and $Crs > 30 \text{ mL/cmH}_2\text{O}$
  - Fluid responsiveness is unlikely

- **PPV ≤ 9%**
  - $V_T < 8 \text{ mL/kg}$ or $Crs \leq 30 \text{ mL/cmH}_2\text{O}$
  - Consider a $V_T$ challenge

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* detected by echocardiography
** detected by measuring intra-abdominal pressure
Figure 5

**Presence of shock**

- **Urgent fluid bolus**
  *especially in cases of sepsis, active bleeding, or evident fluid losses*

**Persistence of shock?**

- **No**
  - Stop fluid

- **Yes**
  - **Presence of fluid responsiveness?**
    - **Yes**
      - **Risks of fluid overload?**
        - **Yes**
          - Assess the **benefit/risk ratio** of continuing fluid infusion
            - **benefit > risk**
              - Continue fluid
            - **benefit < risk**
              - Stop fluid
        - **No**
          - Continue fluid
    - **No**
      - Stop fluid