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Use of 'tidal volume challenge' to improve the reliability of pulse pressure variation

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Abstract

This article is one of ten reviews selected from the Annual Update in Intensive Care and Emergency Medicine 2017. Other selected articles can be found online at http://ccforum.com/series/annualupdate2017. Further information about the Annual Update in Intensive Care and Emergency Medicine is available from http://www.springer.com/series/8901.

Keywords: Tidal volume challenge, Pulse pressure variation, Fluid responsiveness, Preload responsiveness, Functional hemodynamic monitoring

Background

Fluid loading is usually the first step in the resuscitation of patients with acute circulatory failure. Fluid responsiveness is defined as the ability of the left ventricle to increase its stroke volume in response to fluid administration [1]. Fluids are administered with the aim of increasing cardiac output and oxygen delivery. Thus giving fluid is not beneficial if cardiac output does not increase. According to the Frank-Starling principle, increasing preload increases the left ventricular (LV) stroke volume if the ventricle is functioning on the steep portion of the Frank-Starling curve. Once the left ventricle is functioning on the flat portion of the curve, further fluid loading has little effect on the stroke volume. In a normal heart, both ventricles generally operate on the steep portion of the Frank-Starling curve and the patient is fluid responsive, unless large fluid volumes have already been administered (Fig. 1). In this case, the ventricles may operate on the flat part of the curve (Fig. 1). A failing heart operates on the flat portion of the curve, except for very low preload values and thus the same increase in cardiac preload induced by volume expansion may result in a negligible increase in stroke volume (Fig. 1).

Studies have shown that only about 50% of unstable critically ill patients will actually respond positively to a fluid challenge [1]. Uncorrected hypovolemia may result in inappropriate administration of vasopressor infusions, which may in turn affect tissue oxygenation, leading to organ dysfunction and death [2, 3]. On the other hand, excessive fluid loading is associated with increased complications, mortality and duration of intensive care unit (ICU) stay [4, 5]. Thus, it is important to identify fluid responders to know who can benefit from fluid administration and to avoid fluid overload in those who are not fluid responsive. However, identifying which patients will respond to volume expansion presents a daily challenge in ICUs today.

Dynamic changes in arterial waveform-derived variables during mechanical ventilation, such as systolic pressure variation (SPV), pulse pressure variation (PPV) and stroke volume variation (SVV), have proven to be superior to traditionally used static indices, such as central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP), to predict fluid responsiveness [1, 6–8]. Of these indices, PPV and SVV are commonly used in clinical practice, with PPV being more reliable and having a higher level of evidence [7, 9, 10].

Heart-lung interactions during mechanical ventilation: physiological principles underlying PPV and SVV

The PPV is calculated as the difference between the maximal and the minimal pulse pressure value over one ventilator cycle divided by their average value [6]. It can be automatically calculated by newer hemodynamic monitors. The SVV is derived from the arterial pressure waveform analysis and is automatically calculated by calibrated and uncalibrated pulse contour analysis cardiac output monitors. The principle mechanisms underlying how these parameters work are based on heart-lung interactions during mechanical ventilation [11].

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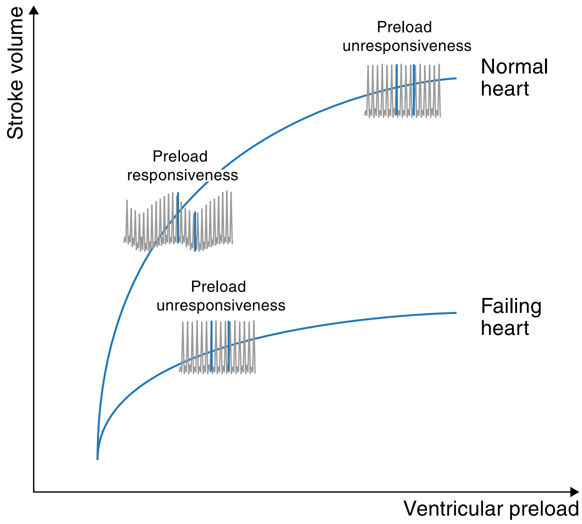

Fig. 1 Frank-Starling curves in a normal and failing heart. The same increase in cardiac preload induced by volume expansion may result in a significant increase (*normal heart*) or a negligible increase (*failing heart*) in stroke volume, depending upon the shape of the curve

Intermittent positive-pressure ventilation produces cyclic changes in the loading conditions of both the ventricles. The intrathoracic and transpulmonary pressures increase during inspiration leading to variable changes in the loading conditions of both the ventricles. Increase in intrathoracic pressures during mechanical insufflation decreases venous return and in turn decreases the right ventricular (RV) preload, whereas an increase in transpulmonary pressure increases RV afterload resulting in decreased RV stroke volume, which will be at its lowest at the end of inspiration [11–16]. At the same time, an increase in the intrathoracic and transpulmonary pressures results in decreased LV afterload and a transient increase in LV preload due to squeezing out of alveolar blood, leading to increased LV stroke volume, which will be at its maximum at the end of inspiration [11]. The reduction in RV stroke volume during inspiration leads to decreased LV filling after a lag period of two to three heart beats due to the pulmonary transit time [17]. This leads to decreased LV stroke volume, which will be its lowest during expiration.

Thus, intermittent positive-pressure ventilation produces cyclic changes in LV stroke volume, which is maximum during inspiration and lowest during expiration. The magnitude of change in LV stroke volume, or of its surrogates, such as pulse pressure, will be magnified when the patient is preload-dependent. Therefore, a high PPV value should be associated with preload responsiveness and a low PPV value with preload unresponsiveness (Fig. 1). A threshold value greater than 12–13% has been reported to be highly predictive of volume responsiveness [7, 9, 10].

Comparison of dynamic changes of arterial waveform-derived variables during mechanical ventilation (SPV, PPV and SVV)

Since the earliest studies about PPV and SVV [6, 17], both indices have been consistently shown to be reliable predictors of fluid responsiveness. The first systematic review by Marik et al. [7] comparing PPV, SPV and SVV for prediction of fluid responsiveness in mechanically ventilated patients showed that the (AUROC) curves were 0.94, 0.84, and 0.86, respectively. The AUROC for PPV was significantly greater than that for either the SPV or the SVV ($p < 0.001$). Another meta-analysis [9] comparing SVV and PPV as diagnostic indicators of fluid responsiveness in mechanically ventilated critically ill patients showed AUROC values of 0.84 for SVV and 0.88 for PPV. A recent meta-analysis [10] that included only ICU patients ventilated with tidal volumes > 8 ml/kg, showed that PPV predicted fluid responsiveness accurately with an AUC of 0.94. A comparison of the predictive value of variables used to determine fluid responsiveness in these three systematic reviews [7, 9, 10] is given in Table 1. Among PPV, SVV and SPV, PPV has been most extensively studied and is more reliable.

Limitations with the use of PPV to predict fluid responsiveness

The PPV works on heart-lung interactions and has several limitations for use in predicting fluid responsiveness, which are enumerated in Table 2. Recent studies [18–20] have questioned the applicability of PPV and SVV in the ICU. Tests like passive leg raising (PLR) [21–23] and end-expiratory occlusion [24–26] can reliably predict fluid responsiveness and have been proposed as alternatives to be performed in these situations. PLR can help overcome most of the limitations of PPV. However, it requires continuous cardiac output monitoring and cannot be used in patients with neurotrauma or those requiring immobilization [27, 28]. The end-expiratory occlusion test is not suitable for patients who are not intubated, whereas PLR can be reliably used in these patients. A mini-fluid challenge [29] may also be used as an alternative to PPV, but requires a very precise technique for monitoring cardiac output. Using respiratory variations in the diameters of the superior [30] and inferior [31] vena cavae diameter obtained from transesophageal or transthoracic echocardiography to predict fluid responsiveness share the same limitations as PPV, except that they can be used in patients with cardiac arrhythmias. Although alternative tests have been proposed, few attempts have been made to improve the reliability of PPV itself in situations where it is currently not recommended for use [32].

Table 1 Comparison of predictive value of variables used to determine fluid responsiveness in mechanically ventilated patients in three systematic reviews

Systematic review/metaanalysis	Publication year	Types of studies	Patient type	Variable	AUC (95% confidence interval)
Marik et al. [7]	2009	29 studies 685 patients variable tidal volume	ICU and OR patients	PPV	0.94 (0.93–0.95)
				SPV	0.86 (0.82–0.90)
				SVV	0.84 (0.78–0.88)
				LVEDA	0.64 (0.53–0.74)
				GEDV	0.56 (0.37–0.67)
				CVP	0.55 (0.48–0.62)
Hong et al. [9]	2014	19 studies 850 patients variable tidal volume	Only ICU patients	PPV	0.88 (0.84–0.92)
				SVV	0.84 (0.79–0.89)
Yang and Du [10]	2014	22 studies 807 patients tidal volume > 8 ml/kg	Only ICU patients	PPV	0.94 (0.91–0.95)

AUC area under the curve, *ICU* intensive care unit, *OR* operating room, *PPV* pulse pressure variation, *SPV* systolic pressure variation, *SVV* stroke volume variation, *LVEDA* left ventricular end-diastolic area, *GEDV* global end-diastolic volume, *CVP* central venous pressure

Using a 'tidal volume challenge' to overcome the limitations associated with PPV during low tidal volume ventilation

Several studies have shown that PPV does not reliably predict fluid responsiveness during low tidal volume ventilation [25, 33–37]. De Backer et al. [33] showed that PPV was a reliable predictor of fluid responsiveness, provided that the tidal volume was at least 8 ml/kg predicted body weight (PBW). During low tidal volume ventilation, PPV may indicate a non-responsive status even in responders as the tidal volume might be insufficient to produce a significant change in the intrathoracic pressure [38, 39]. However, Freitas et al. [40] showed that PPV was a reliable marker of fluid responsiveness in septic patients with acute respiratory distress syndrome (ARDS) during low tidal volume ventilation using a lower cut-off value of 6.5%.

Among the limitations with use of PPV during controlled mechanical ventilation in the ICU, the use of low tidal volume is the most common. Today the indications for use of low tidal volume in ICU are expanding [41, 42]. Two multicenter studies [18, 19] showed that the number of ICU patients in whom PPV was suitable for use was very low, with as many as 72–87% of the patients on controlled mechanical ventilation being unsuitable for use of this parameter, because of the use of low tidal volume ventilation. Two recent studies [43, 44] that used the 'gray zone' approach to investigate the clinical value of PPV, included several patients ventilated with low tidal volume. Biais et al. [44], in a subgroup analysis, showed that the gray zone was larger in patients ventilated with a low tidal volume than in patients with a tidal volume of at least 8 ml/kg PBW. These studies may mislead one to conclude that PPV has limited clinical value [32].

Table 2 Limitations with the use of pulse pressure variation (PPV) to predict fluid responsiveness

	Limitations	Mechanisms for failure	Type of error
1	Spontaneous breathing activity	Irregular variations in intrathoracic pressure and thus the variation in stroke volume cannot correlate with preload dependency	False positive (may occasionally be false negative depending on the type of breathing)
2	Cardiac arrhythmias	The variation in stroke volume is related more to the irregularity in diastole than to the heart-lung interactions	False positive
3	Mechanical ventilation using low tidal volume (<8 ml/kg)	The small variations in intrathoracic pressure due to the low tidal volume are insufficient to produce significant changes in the intrathoracic pressure	False negative
4	Low lung compliance	The transmission of changes in alveolar pressure to the intrathoracic structures is attenuated	False negative
5	Open thorax	No change in intrathoracic pressure during the respiratory cycle	False negative
6	Increased intra-abdominal pressure	Threshold values of PPV will be elevated	False positive
7	Low HR/RR ratio < 3.6 (severe bradycardia or high frequency ventilation)	If the RR is very high, the number of cardiac cycles per respiratory cycle may be too low to allow variation in stroke volume	False negative

HR heart rate, *RR* respiratory rate

The ‘tidal volume challenge’ is a novel test proposed to improve the reliability of PPV during low tidal volume ventilation [45]. The test involves transiently increasing tidal volume from 6 ml/kg PBW to 8 ml/kg PBW for one minute and observing the change in PPV (ΔPPV_{6-8}) from baseline (PPV_6) to that at 8 ml/kg PBW (PPV_8). In a recent study testing the tidal volume challenge [45], 30 sets of measurements were recorded in 20 patients with acute circulatory failure receiving low tidal volume ventilation using volume assist-control ventilation and without spontaneous breathing activity. Fluid responsiveness was defined as an increase in thermodilution cardiac output > 15% after giving a fluid bolus after reducing tidal volume back to 6 m/kg PBW. As expected, the PPV_6 could not predict fluid responsiveness, with an AUROC of 0.69. Importantly, there was a significant increase in PPV (ΔPPV_{6-8}), following the tidal volume challenge only in fluid responders. The ΔPPV_{6-8} discriminated responders from non-responders with an AUROC of 0.99 (sensitivity 94% and specificity 100%) with a cut off value of 3.5% [45]. The tidal volume challenge thus improved the reliability of PPV in predicting fluid responsiveness in patients receiving low tidal volume ventilation. Similar results were also seen using SVV (ΔSVV_{6-8}) obtained from a pulse contour analysis cardiac output device with an AUROC of 0.97 (sensitivity 88% and specificity 100%) with a cut off value of 2.5% [45]. The change in PPV after giving a fluid bolus (ΔPPV_{fb}) also accurately confirmed fluid responsiveness with an AUROC of 0.98 (sensitivity 94% and specificity 100%) with a cut off value of 1.5%.

How to perform and interpret the tidal volume challenge

This test is performed to assess fluid responsiveness in patents in shock, ventilated using low tidal volume without spontaneous breathing activity. The PPV is noted from the bedside monitor at baseline (tidal volume 6 ml/kg PBW). The tidal volume is then transiently increased from 6 ml/kg PBW to 8 ml/kg PBW for one minute. The PPV is recorded at 8 ml/kg PBW and the tidal volume is reduced back to 6 ml/kg PBW. The ΔPPV_{6-8} after performing the tidal volume challenge is recorded. A ΔPPV_{6-8} greater than 3.5% predicts fluid responsiveness with high accuracy.

PPV is unreliable in patients with low lung compliance, especially in patients with ARDS [38]. In these patients, airway pressure transmission is reduced, such that the cyclic changes in intrathoracic pressure may be attenuated even with marked changes in alveolar pressure [46]. Monnet et al. [25] showed that the predictive value of PPV was related to the compliance of the respiratory system and if the compliance was < 30 ml/cmH_2O, PPV was less accurate in predicting fluid responsiveness. In our study, although the median compliance of the respiratory system was < 30 ml/cmH_2O (25 [23–33]) during low tidal volume ventilation, it increased to > 30 ml/cmH_2O (32 [24–40]) after the tidal volume challenge. Thus, the tidal volume challenge may help identify responders even when compliance of the respiratory system is low in patients receiving low tidal volume ventilation with recruitable lungs. This needs to be confirmed in an adequately powered study. Whether this approach will also work in patients who do not increase compliance of the respiratory system after giving a tidal volume challenge needs to be tested. Whether PPV will be reliable during spontaneous breathing attempts after giving a tidal volume challenge or in other situations where the use of PPV is limited also needs to be tested.

Advantages of using the tidal volume challenge

Use of a tidal volume challenge increases the reliability of PPV to predict fluid responsiveness during low tidal volume ventilation, which is now common practice in the ICU. It is a simple test that can be performed easily at the bedside. Importantly, observing the changes in PPV (obtained from a simple bedside hemodynamic monitor) during this test does not require a cardiac output monitor, making this test applicable even in resource-limited settings. The ΔPPV_{fb} accurately confirms fluid responsiveness. Thus, a combination of ΔPPV_{6-8} with ΔPPV_{fb} can help predict and thereafter confirm fluid responsiveness when continuous cardiac output monitoring is unavailable.

Limitations of the tidal volume challenge

The tidal volume challenge may not be able to overcome the other limitations associated with the use of PPV, such as spontaneous breathing, cardiac arrhythmias, open chest, and raised intra-abdominal pressure and needs to be evaluated in these settings. Alternative techniques, such as PLR or end-expiratory occlusion, when applicable, may be considered in these situations.

Conclusion

The PPV is a dynamic parameter that can be easily recorded from a bedside monitor and reliably predicts preload responsiveness. In addition, it does not require continuous cardiac output monitoring or any other tools or maneuvers to be performed. One of the major limitations with its use in patients receiving controlled mechanical ventilation is that it is unreliable during low tidal volume ventilation, which is now widely practiced in ICU patients. Discarding this useful parameter would, however, be like throwing the baby out with the bathwater. This major limitation can be easily overcome by using the ‘tidal volume challenge’ a simple bedside test, following which PPV can reliably predict fluid responsiveness. Whether this test may also have the potential to overcome other limitations associated with the use of PPV needs to be further studied. Alternative methods to assess preload responsiveness may be required to overcome the other limitations with the use of PPV.

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