

Review

Using heart–lung interactions to assess fluid responsiveness during mechanical ventilation

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Abstract

According to the Frank–Starling relationship, a patient is a ‘responder’ to volume expansion only if both ventricles are preload dependent. Mechanical ventilation induces cyclic changes in left ventricular (LV) stroke volume, which are mainly related to the expiratory decrease in LV preload due to the inspiratory decrease in right ventricular (RV) filling and ejection. In the present review, we detail the mechanisms by which mechanical ventilation should result in greater cyclic changes in LV stroke volume when both ventricles are ‘preload dependent’. We also address recent clinical data demonstrating that respiratory changes in arterial pulse (or systolic) pressure and in Doppler aortic velocity (as surrogates of respiratory changes in LV stroke volume) can be used to detect biventricular preload dependence, and hence fluid responsiveness in critically ill patients.

Keywords: acute circulatory failure, arterial pressure, fluid responsiveness, left ventricular stroke volume, mechanical ventilation, pleural pressure, preload, pulse pressure

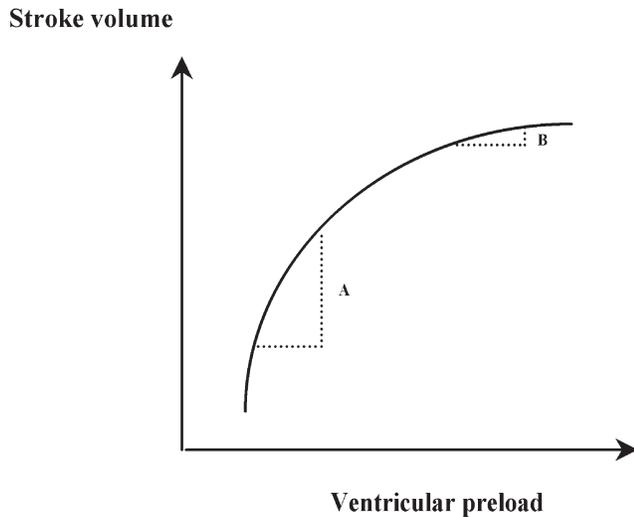
Introduction

Volume expansion is a frequently used therapy in critically ill patients with acute circulatory failure. The expected haemodynamic benefit of volume expansion is an increase in LV stroke volume, and hence in cardiac output. The relationship described by Frank and Starling between preload and stroke volume is not linear, but rather is curvilinear (Fig. 1). Thus, an increase in preload will induce a significant increase in stroke volume only if the ventricle operates on the ascending portion of the relationship (condition of ventricular preload dependence). In contrast, if the ventricle operates on the flat portion of the curve, a similar increase

in preload will not induce any significant change in stroke volume (condition of preload independence). Therefore, a patient is a ‘responder’ to volume expansion only if both ventricles operate on the ascending portion of the Frank–Starling curve (biventricular preload dependence). In contrast, if one of the ventricle or both ventricles operate on the flat portion of the curves, then the patient is a ‘non-responder’ (ie his/her cardiac output will not increase significantly in response to volume expansion).

In normal physiological conditions, both ventricles operate on the ascending portion of the Frank–Starling curve [1].

Figure 1



Schematic representation of Frank–Starling relationship between ventricular preload and stroke volume. A given change in preload induces a larger change in stroke volume when the ventricle operates on the ascending portion of the relationship (A, condition of preload dependence) than when it operates on the flat portion of the curve (B, condition of preload independence).

This mechanism provides a functional reserve (preload reserve) to the heart in situations of acute stress [1]. In normal individuals, increase in preload was reported [2] to result in a significant change in stroke volume. In contrast, analysis of the literature indicates that, in patients with acute circulatory failure, the mean rate of responders to volume expansion is only around 50% (Table 1). This finding emphasizes the need for predictive factors of volume expansion efficacy in order to select patients who could benefit from volume expansion and to avoid ineffective or even deleterious fluid therapy (worsening of pulmonary oedema, haemodilution, etc) in ‘nonresponder’ patients, in whom inotropic and/or vasopressor support should preferentially be used.

How to predict fluid responsiveness in critically ill patients?

In many patients with acute circulatory failure, a positive response to fluid therapy can be observed despite the lack of clinical and biological indicators of hypovolaemia. Therefore, bedside indicators of RV or LV preload are usually used when deciding whether to give fluid.

A recent postal survey performed in Germany [3] showed that central venous pressure and pulmonary artery occlusion pressure are used, respectively, by 93 and 58% of intensive care unit physicians in the decision-making process regarding volume expansion. However, many clinical studies have emphasized the poor value of right atrial pressure [4–7] and pulmonary artery occlusion pressure

Table 1

Number and rate of responder (R) and nonresponder patients (NR) to volume expansion in critically ill patients

Reference	R/NR (% R)	Criteria for response
[4]	20/8 (71)	Increase in SV >0%
[5]	26/15 (63)	Increase in CI >0%
[10]	26/29 (40)	Increase in CI >20%
[11]	20/16 (56)	Increase in SV >10%
[8]	21/14 (60)	Increase in SV >15%
[9]	16/24 (40)	Increase in SV >20%
[7]	16/24 (40)	Increase in CI >15%

CI, cardiac index; SV, stroke volume.

[4,5,7–9] in predicting volume expansion efficacy. Indeed, in most studies, the mean baseline value of right atrial pressure and of pulmonary artery occlusion pressure was not significantly different between responders and nonresponders to volume expansion [4–8,10] (Table 2). Even when a significant difference was reported [9], a marked overlap of individual baseline values was observed, so that no threshold value could help to discriminate responder and nonresponder patients. Other bedside indicators of preload, such as the RV end-diastolic volume (evaluated by thermodilution) and the LV end-diastolic area (measured by echocardiography) have also been tested as predictors of fluid responsiveness. Unfortunately, these parameters were not found to be able to differentiate accurately between responder and nonresponder patients before fluid infusion was given (Table 2) [5,6,8,9,11].

All of these findings may be explained as follows. The right atrial and pulmonary artery occlusion pressures do not always reflect transmural pressures in patients with external or intrinsic positive end-expiratory pressure (PEEP) [12,13]. Pulmonary artery occlusion pressure is not always a good indicator of LV preload, in particular in patients with a decreased LV compliance [14]. Measurement of RV end-diastolic volume by thermodilution is influenced by tricuspid regurgitation [15], which is frequently encountered in critically ill patients with pulmonary hypertension. LV end-diastolic area is not always a good indicator of the LV end-diastolic volume, and hence of the LV preload [16]. RV dilatation may offset any beneficial haemodynamic effect of volume expansion, even in case of a low LV preload [17]. Finally, the preload-induced changes in stroke volume depend also on contractility and afterload. For example, a given value of preload can be associated with preload dependence in normal hearts or with preload independence in failing hearts (Fig. 2). Therefore, assessment of preload is of poor value in predicting fluid responsiveness in critically ill patients.

Table 2

Mean values of right atrial pressure (RAP), pulmonary artery occlusion pressure (PAOP) and right ventricular end-diastolic volume index (RVEDVI) before volume expansion in responder and nonresponder patients to volume expansion

Reference	Responder	Nonresponder	P
RAP (mmHg)			
[4]	5 ± 1	5 ± 2	NS
[5]	9 ± 4	8 ± 4	NS
[6]	7 ± 2	6 ± 3	NS
[7]	9 ± 3	9 ± 4	NS
PAOP (mmHg)			
[4]	8 ± 1	7 ± 2	NS
[5]	10 ± 4	10 ± 3	NS
[10]	16 ± 6	15 ± 5	NS
[8]	10 ± 4	12 ± 3	NS
[9]	12 ± 2	16 ± 3	<0.01
[7]	10 ± 3	11 ± 2	NS
RVEDVI (ml/m²)			
[4]	143 ± 19	134 ± 26	NS
[5]	104 ± 27	117 ± 46	NS
[10]	80 ± 28	109 ± 33	<0.05
[6]*	177 ± 31	159 ± 33	NS
[11]	105 ± 31	119 ± 33	NS

Values are expressed as mean ± standard deviation. *Right ventricular end-diastolic volume (ml).

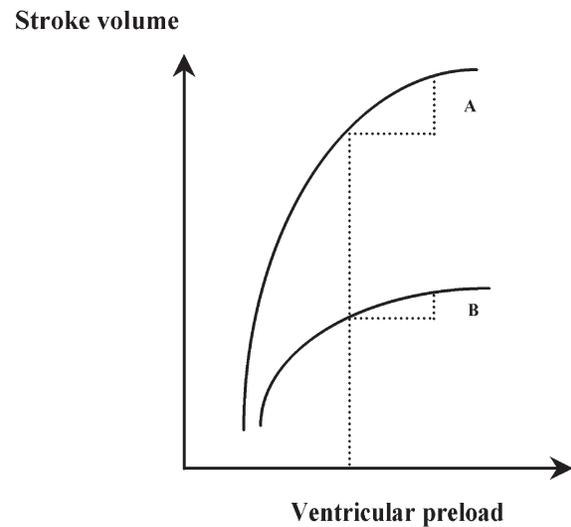
Respiratory changes in right atrial pressure in spontaneously breathing patients

In patients with significant spontaneous breathing activity, the respiratory changes in right atrial pressure have been proposed to differentiate patients whose hearts are functioning on the flat part of the cardiac function curve from those who still have volume reserves and are on the ascending part of the curve [18,19]. Patients who had no fall in the right atrial pressure with an inspiratory effort that was sufficient to lower the pulmonary artery occlusion pressure by 2 mmHg were proposed to be on the flat part of their cardiac function curve [18]. Indeed, in 13 out of the 14 patients in whom no fall in right atrial pressure was observed, cardiac output did not increase with volume challenges. In contrast, in 16 out of the 19 patients in whom the right atrial pressure decreased by more than 1 mmHg during inspiration, cardiac output increased by more than 250 ml/min in response to volume therapy [18]. Unfortunately, many patients in the intensive care unit do not have adequate inspiratory effort, and therefore do not have sufficient fall in pleural pressure to use this test to predict fluid responsiveness [19].

Respiratory changes in LV stroke volume in mechanically ventilated patients

In mechanically ventilated patients, the magnitude of the respiratory changes in LV stroke volume can be used to assess fluid responsiveness. Intermittent positive-pressure

Figure 2

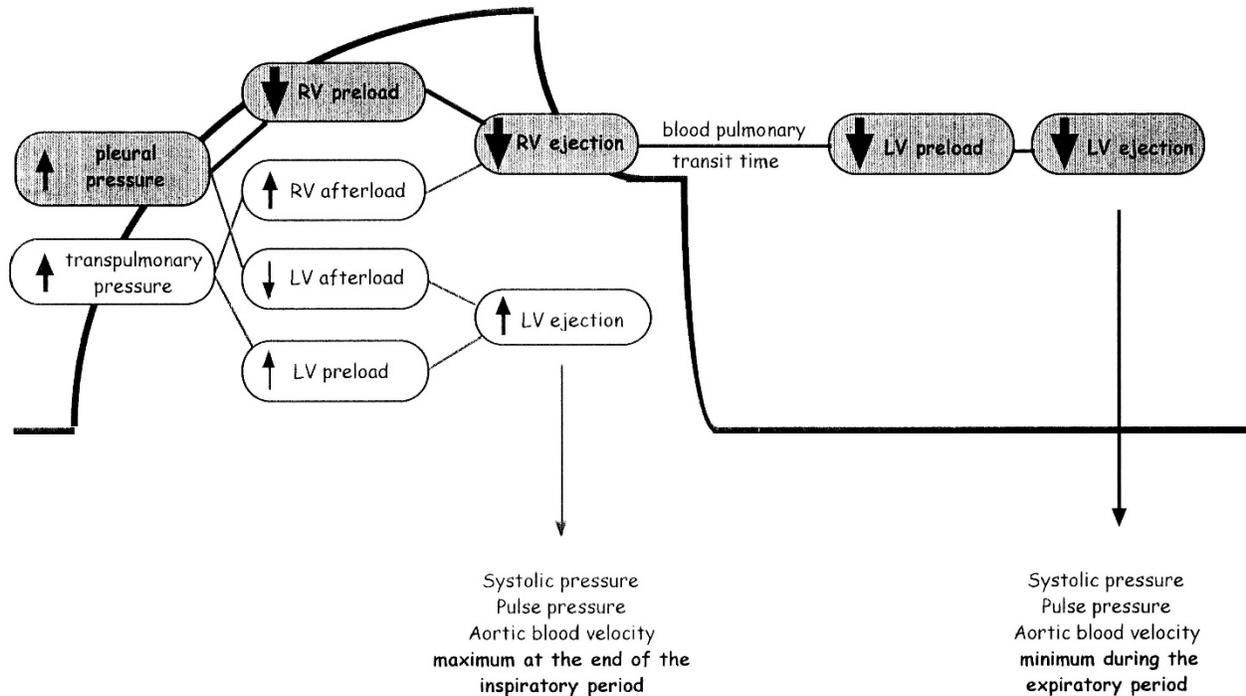


Schematic representation of Frank–Starling relationships between ventricular preload and stroke volume in a normal heart (A) and in a failing heart (B). A given value of preload can be associated with preload dependence in a normal heart or with preload independence in a failing heart.

ventilation induces cyclic changes in the loading conditions of right and left ventricles (Fig. 3). Mechanical insufflation decreases preload and increases afterload of the right ventricle [20,21,22]. The RV preload reduction is due to the decrease in the venous return pressure gradient that is related to the inspiratory increase in pleural pressure [20]. The increase in RV afterload is related to the inspiratory increase in transpulmonary pressure (alveolar minus pleural pressure) [22]. The reduction in RV preload and the increase in RV afterload both lead to a decrease in RV stroke volume, which is therefore at its minimum at the end of the inspiratory period [23]. The inspiratory impairment in venous return is assumed to be the main mechanism of the inspiratory reduction in RV ejection [24]. The inspiratory reduction in RV ejection leads to a decrease in LV filling after a phase lag of two to three heart beats because of the long blood pulmonary transit time [25]. Thus, the LV preload reduction may induce a decrease in LV stroke volume, which is at its minimum during the expiratory period [23].

Two other mechanisms may also occur: mechanical insufflation may induce a squeezing of blood out of alveolar vessels, and thus transiently increase LV preload [26]; and the inspiratory increase in pleural pressure may decrease LV afterload and thus facilitate LV ejection [27,28] (Fig. 3). The first mechanism in hypervolaemic conditions and the second mechanism in case of LV systolic dysfunction may induce a slight increase in LV stroke volume during the inspiratory period. However, experimental data suggest that

Figure 3



Haemodynamic effects of mechanical insufflation. The LV stroke volume is maximum at the end of the inspiratory period and minimum two to three heart beats later (ie during the expiratory period). The cyclic changes in LV stroke volume are mainly related to the expiratory decrease in LV preload due to the inspiratory decrease in RV filling and output.

these two mechanisms are only minor determinants of the respiratory changes in LV stroke volume, even in the cases of hypervolaemia [29,30] and LV dysfunction [29,31].

In summary, intermittent positive-pressure ventilation induces cyclic changes in LV stroke volume (maximum during the inspiratory period and minimum during the expiratory period), which are mainly related to the expiratory decrease in LV preload due to the inspiratory decrease in RV filling and ejection (Fig. 3).

Interestingly, the cyclic changes in RV preload induced by mechanical ventilation should result in greater cyclic changes in RV stroke volume when the right ventricle operates on the steep rather than on the flat portion of the Frank–Starling curve [17,32]. The cyclic changes in RV stroke volume, and hence in LV preload, should also result in greater cyclic changes in LV stroke volume when the left ventricle operates on the ascending portion of the Frank–Starling curve [17,32]. Thus, the magnitude of the respiratory changes in LV stroke volume should be an indicator of biventricular preload dependence [33].

Respiratory changes in systolic pressure

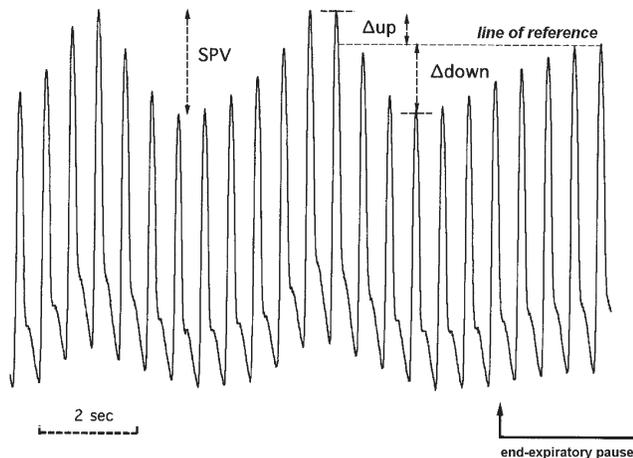
Because LV stroke volume is a major determinant of systolic arterial pressure, analysis of respiratory changes in

systolic pressure has been proposed to assess the respiratory changes in LV stroke volume during mechanical ventilation. In 1983, Coyle *et al* [34] proposed that the respiratory changes in systolic pressure could be analyzed by calculating the difference between the maximal and the minimal value of systolic pressure over a single respiratory cycle (Fig. 4). This difference was called 'systolic pressure variation' (SPV) and was divided into two components (Δ_{up} and Δ_{down}). These two components are calculated using a reference systolic pressure, which is the systolic pressure measured during an end-expiratory pause.

Δ_{up} is the difference between the maximal value of systolic pressure over a single respiratory cycle and the reference systolic pressure. It reflects the inspiratory increase in systolic pressure, which results either from increase in LV stroke volume related to the increase in LV preload (squeezing of blood out of alveolar vessels) or a decrease in LV afterload, or both; or an increase in extramural aortic pressure related to the rise in pleural pressure.

Δ_{down} is the difference between the reference systolic pressure and the minimal value of systolic pressure over a single respiratory cycle. It reflects the expiratory decrease in LV preload and stroke volume related to the inspiratory decrease in RV stroke volume (see above).

Figure 4



Respiratory changes in systolic pressure in a mechanically ventilated patient. The difference between the maximal and minimal value of systolic pressure over a single respiratory cycle is called SPV (for Systolic Pressure Variation). The reference systolic pressure is measured during an end-expiratory pause (line of reference) and SPV is divided in two components: Δ_{up} and Δ_{down} . Δ_{up} is the difference between the maximal and the reference systolic pressure. Δ_{down} is the difference between the reference and the minimal systolic pressure. Adapted with permission [33].

In mechanically ventilated dogs, Perel and coworkers [29–31,35–37] demonstrated the following. First, in normo- or hypovolaemic conditions, Δ_{down} is the main component of SPV [35–37]. Second, haemorrhage increases SPV and Δ_{down} [35–37]. Third, the amount of blood loss is closely correlated with SPV and Δ_{down} [35]. Fourth, volume expansion decreases SPV and Δ_{down} [35–37]. Finally, LV dysfunction [29,31] and hypervolaemia [29,30] increase Δ_{up} , but decrease Δ_{down} and SPV such that, in this setting, SPV is minimal and Δ_{up} is the main component of SPV.

In mechanically ventilated patients, haemorrhage has also been shown to increase SPV and Δ_{down} [38], whereas volume expansion has been shown to decrease SPV and Δ_{down} [38,39]. More interestingly, Coriat *et al* [39] reported a significant relationship between Δ_{down} before fluid infusion and the increase in cardiac index in response to volume expansion in patients after aortic surgery. Therefore, Δ_{down} can be considered as an indicator of fluid responsiveness, because the higher Δ_{down} before volume expansion, the greater the increase in cardiac index in response to fluid infusion. This finding has been recently confirmed by Tavernier *et al* [8] in patients with sepsis-induced hypotension. In that study, a Δ_{down} threshold value of 5 mmHg allowed prediction of volume expansion efficacy (defined as an increase in stroke volume $\geq 15\%$), with positive and negative predictive values of 95 and 93%, respectively. Also, the baseline value of Δ_{down} was

significantly correlated with the volume expansion-induced increase in stroke volume ($r = 0.76$).

However, the respiratory changes in systolic pressure result from changes in transmural pressure (mainly related to changes in LV stroke volume) and also from changes in extramural pressure (ie from changes in pleural pressure) [40]. Therefore, respiratory changes in systolic pressure may be observed despite no variation in LV stroke volume. In this regard, Denault *et al* [41] recently demonstrated, in anaesthetized cardiac surgery patients, that changes in systolic pressure may reflect changes in airway pressure and pleural pressure better than they reflect concomitant changes in LV haemodynamics.

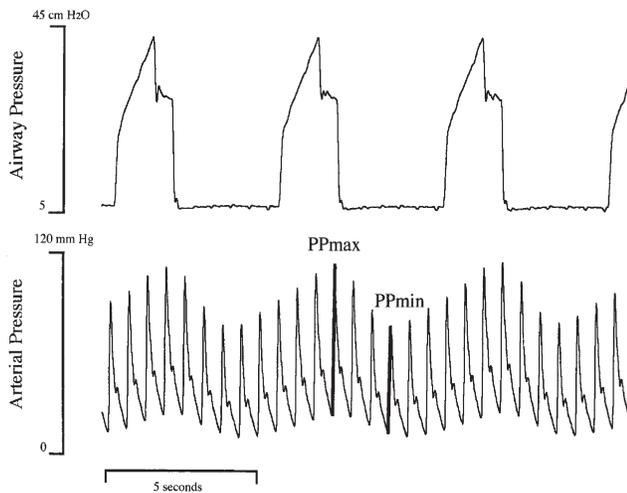
Respiratory changes in pulse pressure

The pulse pressure (defined as the difference between the systolic and the diastolic pressure) is directly proportional to LV stroke volume and inversely related to arterial compliance [42]. The pulse pressure is not directly influenced by the cyclic changes in pleural pressure, because the increase in pleural pressure induced by mechanical insufflation affect both diastolic and systolic pressures. In this regard, the respiratory changes in LV stroke volume have been shown to be reflected by changes in peripheral pulse pressure during the respiratory cycle [23]. Therefore, it was recently proposed that fluid responsiveness may be assessed by calculating the respiratory changes in pulse pressure (ΔPP) as follows:

$$\Delta PP (\%) = 100 \times \frac{(PP_{max} - PP_{min})}{(PP_{max} + PP_{min})/2}$$

where PP_{max} and PP_{min} are the maximal and minimal values of pulse pressure over a single respiratory cycle, respectively (Fig. 5).

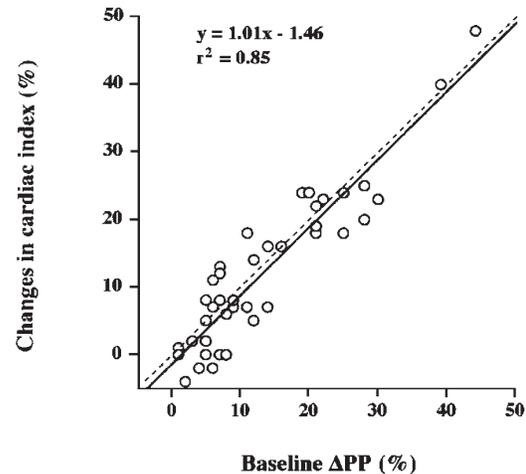
In 40 patients with acute circulatory failure related to sepsis, Michard *et al* [7] demonstrated the following. First, ΔPP accurately predicted the haemodynamic effects of volume expansion; a threshold value of 13% allowed discrimination between responder (defined as patients who experienced an increase in cardiac index $\geq 15\%$ in response to volume expansion) and nonresponder patients with a sensitivity and a specificity of 94 and 96%, respectively. Second, the baseline value of ΔPP was closely correlated with the percentage increase in cardiac index in response to volume expansion; the higher ΔPP was before volume expansion, the greater the increase in cardiac index (Fig. 6). Third, ΔPP was a more reliable indicator of fluid responsiveness than were the respiratory changes in systolic pressure. Finally, the decrease in ΔPP induced by volume expansion was correlated with the increase in cardiac index, such that changes in ΔPP could be used to assess the haemodynamic effects of volume expansion.

Figure 5

Respiratory changes in airway and arterial pressures in a mechanically ventilated patient. The pulse pressure (systolic minus diastolic pressure) is maximal (PPmax) at the end of the inspiratory period and minimal (PPmin) three heart beats later (ie during the expiratory period). The respiratory changes in pulse pressure (Δ PP) are calculated as the difference between PPmax and PPmin, divided by the mean of the two values, and expressed as a percentage (see text for details). Adapted with permission [33].

In summary, calculation of Δ PP may be of particular help in the decision-making process regarding whether to institute volume expansion. Indeed, if Δ PP is low (<13%), then a beneficial haemodynamic effect of volume expansion is very unlikely, and inotropes or vasoactives drugs should be proposed in order to improve haemodynamics. In contrast, if Δ PP is high (>13%), then a significant increase in cardiac index in response to fluid infusion is very likely. However, the decision regarding whether to institute volume expansion must take into account the risk of fluid therapy (worsening in gas exchange), and a decrease in the mean airway pressure (ie a decrease in tidal volume or in PEEP) is an alternative therapeutic approach in this instance.

Interestingly, the assessment of cardiac preload dependence is not only useful in predicting volume expansion efficacy, but also in predicting the haemodynamic effects of any therapy that induces changes in cardiac preload conditions. In this regard, Δ PP has been shown to be useful in monitoring the haemodynamic effects of PEEP in mechanically ventilated patients with acute lung injury. Indeed, the decrease in mean cardiac output induced by PEEP and the decrease in RV stroke volume induced by mechanical insufflation share the same mechanisms (ie the negative effects of increased pleural pressure on RV filling and of increased transpulmonary pressure on RV afterload). Thus, the magnitude of the expiratory decrease in LV stroke volume would correlate with the PEEP-induced decrease in mean cardiac output.

Figure 6

Relationship between the respiratory changes in pulse pressure before volume expansion (Baseline Δ PP) and the volume expansion-induced changes in cardiac index (y-axis) in 40 septic patients with acute circulatory failure. The higher Δ PP is before volume expansion, the more marked the increase in cardiac index induced by volume expansion. Adapted with permission [7].

In 14 mechanically ventilated patients with acute lung injury [43] the following was demonstrated. First, Δ PP on zero end-expiratory pressure (ZEEP) was closely correlated with the PEEP-induced decrease in cardiac index; the higher Δ PP was on ZEEP, the greater the decrease in cardiac index when PEEP was applied (Fig. 7). Also, the increase in Δ PP induced by PEEP was correlated with the decrease in cardiac index, such that changes in Δ PP from ZEEP to PEEP could be used to assess the haemodynamic effects of PEEP without the need for a pulmonary artery catheter. Finally, when cardiac index decreased with PEEP, volume expansion induced an increase in cardiac index that was proportional to Δ PP before fluid infusion.

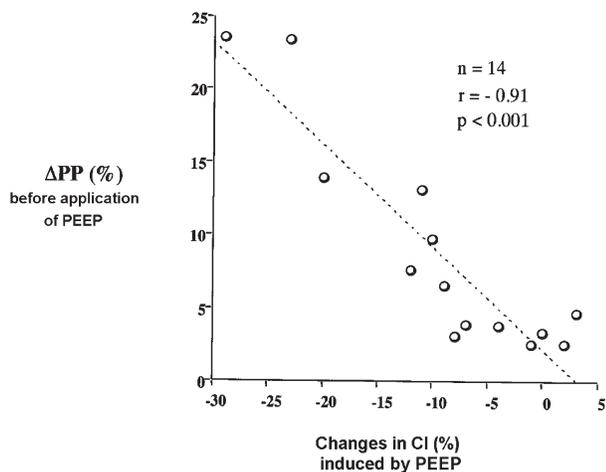
It is likely that analysis of the respiratory changes in LV stroke volume could also be useful to monitor the haemodynamic effects of ultrafiltration during dialysis or of any change in ventilatory parameters.

Limitations

Analysis of the respiratory changes in arterial pressure is not possible in patients with cardiac arrhythmias. Moreover, these parameters have been validated in sedated and mechanically ventilated patients. Therefore, whether the respiratory changes in LV stroke volume predict fluid responsiveness in nonsedated and in spontaneously breathing patients remains to be evaluated.

As mentioned above, the respiratory changes in LV stroke volume might also result from a decrease in LV afterload caused by the inspiratory increase in pleural pressure

Figure 7



Relationship between the respiratory changes in pulse pressure on ZEEP (y-axis) and the PEEP-induced changes in cardiac index (x-axis) in 14 ventilated patients with acute lung injury. The higher Δ PP is on ZEEP, the more marked the decrease in cardiac index induced by PEEP. Adapted with permission [43].

[21,28]. Thus, the respiratory changes in LV stroke volume could theoretically be an indicator of afterload dependence, rather than of preload dependence, for example in patients with congestive heart failure. In fact, it is unlikely that the inspiratory increase in LV stroke volume can be responsible for large variations in LV stroke volume and hence in arterial pressure, even in the case of LV dysfunction [29,31]. In animals, induction of an experimental cardiac dysfunction was showed to result in a decrease rather than an increase in systolic pressure variation [29,31].

Because the pulse pressure depends not only on stroke volume, but also on arterial compliance, large changes in pulse pressure could theoretically be observed despite small changes in LV stroke volume if arterial compliance is low (elderly patients with peripheral vascular disease). Similarly, small changes in pulse pressure could be observed despite large changes in LV stroke volume if arterial compliance is high (young patients without any vascular disease). In fact, a close relationship between baseline Δ PP and the changes in cardiac index induced by volume expansion was observed in a series of patients with a large range of ages and comorbidities [7], suggesting that the arterial compliance poorly affected the relationship between respiratory changes in LV stroke volume and Δ PP.

Noninvasive assessment of respiratory changes in LV stroke volume

Although less invasive than pulmonary artery catheterization, femoral or radial arterial catheterization remains an invasive procedure. Infrared photoplethysmography coupled with the volume clamp technique [44] allows a non-

invasive and continuous measurement of finger blood pressure, which has been shown to track changes in blood pressure accurately [45]. In mechanically ventilated patients, we recently found a close correlation and a good agreement between Δ PP measured from intra-arterial recordings and Δ PP measured noninvasively using the continuous measurement of finger blood pressure [46].

The respiratory changes in LV stroke volume can also be assessed noninvasively by Doppler echocardiography. Indeed, by assuming that aortic annulus diameter is constant over the respiratory cycle, the changes in aortic blood flow should reflect changes in LV stroke volume. Therefore, the respiratory changes in aortic blood velocity have also been proposed to assess fluid responsiveness in mechanically ventilated patients [47].

Whether other methods, such as beat-to-beat measurements of aortic blood flow by oesophageal Doppler or of stroke volume from the pulse contour analysis, may be used to assess the respiratory changes in LV stroke volume and hence cardiac preload dependence remains to be determined.

Conclusion

Right atrial and pulmonary artery occlusion pressures are still extensively used to decide whether to employ fluid therapy [3], although many clinical studies have emphasized the poor value of cardiac filling pressures in predicting volume expansion efficacy. In sedated and mechanically ventilated patients, analysis of the respiratory changes in LV stroke volume allows an accurate evaluation of cardiac preload dependence, and thus of fluid responsiveness. In the future, the assessment of respiratory changes in arterial pressure should be automated and displayed on a monitor, which may facilitate and possibly improve the cardiorespiratory management of mechanically ventilated patients.

References

1. Braunwald E, Sonnenblick EH, Ross J: **Mechanisms of cardiac contraction and relaxation**. In: *Heart Disease*. Edited by Braunwald E. Philadelphia: WB Saunders company; 1988:383-425.
2. Nixon JV, Murray RG, Leonard PD, Mitchell JH, Blomqvist CG: **Effect of large variations in preload on left ventricular performance characteristics in normal subjects**. *Circulation* 1982, **65**:698-703.
3. Boldt J, Lenz M, Kumle B, Papsdorf M: **Volume replacement strategies on intensive care units: results from a postal survey**. *Intensive Care Med* 1998, **24**:147-151.
4. Calvin JE, Driedger AA, Sibbald WJ: **The hemodynamic effect of rapid fluid infusion in critically ill patients**. *Surgery* 1981, **90**:61-76.
5. Reuse C, Vincent JL, Pinsky MR: **Measurements of right ventricular volumes during fluid challenge**. *Chest* 1990, **98**:1450-1454.
6. Squara P, Journois D, Estagnasié P, Wysocki M, Brusset A, Dreyfuss D, Teboul JL: **Elastic energy as an index of right ventricular filling**. *Chest* 1997, **111**:351-358.
7. Michard F, Boussat S, Chemla D, Anguel N, Mercat A, Lecarpentier Y, Richard C, Pinsky MR, Teboul JL: **Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure**. *Am J Respir Crit Care Med* 2000, **162**:134-138.

8. Tavernier B, Makhotine O, Lebuffe G, Dupont J, Scherpereel P: **Systolic pressure variation as a guide to fluid therapy in patients with sepsis-induced hypotension.** *Anesthesiology* 1998, **89**:1313–1321.
9. Tousignant CP, Walsh F, Mazer CD: **The use of transesophageal echocardiography for preload assessment in critically ill patients.** *Anesth Analg* 2000, **90**:351–355.
10. Diebel L, Wilson RF, Heins J, Larky H, Warsaw K, Wilson S: **End-diastolic volume versus pulmonary artery wedge pressure in evaluating cardiac preload in trauma patients.** *J Trauma* 1994, **37**:950–955.
11. Wagner JG, Leatherman JW: **Right ventricular end-diastolic volume as a predictor of the hemodynamic response to a fluid challenge.** *Chest* 1998, **113**:1048–1054.
12. Pinsky MR, Vincent JL, De Smet JM: **Estimating left ventricular filling pressure during positive end-expiratory pressure in humans.** *Am Rev Respir Dis* 1991, **143**:25–31.
13. Teboul JL, Pinsky MR, Mercat A, Anguel N, Bernardin G, Achard JM, Boulain T, Richard C: **Estimating cardiac filling pressure in mechanically ventilated patients with hyperinflation.** *Crit Care Med* 2000, in press.
14. Raper R, Sibbald WJ: **Misled by the wedge? The Swan-Ganz catheter and left ventricular preload.** *Chest* 1986, **89**:427–434.
15. Spinale FG, Mukherjee R, Tanaka R, Zile MR: **The effects of valvular regurgitation on thermodilution ejection fraction measurements.** *Chest* 1992, **101**:723–731.
16. Urbanowicz JH, Shaaban J, Cohen NH, Cahalan MK, Botvinick EH, Chatterjee K, Schiller NB, Dae MW, Matthay MA: **Comparison of transesophageal echocardiographic and scintigraphic estimates of left ventricular end-diastolic volume index and ejection fraction in patients following coronary artery bypass grafting.** *Anesthesiology* 1990, **72**:607–612.
17. Magder S: **The cardiovascular management of the critically ill patients.** In: *Applied Cardiovascular Physiology*. Edited by Pinsky MR. Berlin: Springer; 1997:28–35.
18. Magder S, Georgiadis G, Cheong T: **Respiratory variations in right atrial pressure predict the response to fluid challenge.** *J Crit Care* 1992, **7**:76–85.
19. Magder S, Lagonidis D: **Effectiveness of albumin versus normal saline as a test of volume responsiveness in post-cardiac surgery patients.** *J Crit Care* 1999, **14**:164–171.
20. Morgan BC, Martin WE, Hornbein TF, Crawford EW, Guntheroth WG: **Hemodynamic effects of intermittent positive pressure ventilation.** *Anesthesiology* 1966, **27**:584–590.
21. Jardin F, Delorme G, Hardy A, Auvert B, Beauchet A, Bourdarias JP: **Reevaluation of hemodynamic consequences of positive pressure ventilation: emphasis on cyclic right ventricular afterloading by mechanical lung inflation.** *Anesthesiology* 1990, **72**:966–970.
22. Permutt S, Wise RA, Brower RG: **How changes in pleural and alveolar pressure cause changes in afterload and preload.** In: *Heart-Lung Interactions in Health and Disease*. Edited by Scharf SM, Cassidy SS. New York: Marcel Dekker; 1989:243–250.
23. Jardin F, Farcot JC, Gueret P, Prost JF, Ozier Y, Bourdarias JP: **Cyclic changes in arterial pulse during respiratory support.** *Circulation* 1983, **68**:266–274.
24. Theres H, Binkau J, Laule M, Heinze R, Hundertmark J, Blobner M, Erhardt W, Baumann G, Stangl K: **Phase-related changes in right ventricular cardiac output under volume-controlled mechanical ventilation with positive end-expiratory pressure.** *Crit Care Med* 1999, **27**:953–958.
25. Scharf SM, Brown R, Saunders N, Green LH: **Hemodynamic effects of positive-pressure inflation.** *J Appl Physiol* 1980; **49**:124–131.
26. Brower R, Wise RA, Hassapoyannes C, Bronberger-Barnea B, Permutt S: **Effects of lung inflation on lung blood volume and pulmonary venous flow.** *J Appl Physiol* 1985, **58**:954–963.
27. Pinsky MR, Matuschak GM, Klain M: **Determinants of cardiac augmentation by elevations in intrathoracic pressure.** *J Appl Physiol* 1985, **58**:1189–1198.
28. Fessler HE, Brower RG, Wise RA, Permutt S: **Mechanism of reduced LV afterload by systolic and diastolic positive pleural pressure.** *J Appl Physiol* 1988, **65**:1244–1250.
29. Pizov R, Ya'ari Y, Perel A: **The arterial pressure waveform during acute ventricular failure and synchronized external chest compression.** *Anesth Analg* 1989, **68**:150–156.
30. Szold A, Pizov R, Segal E, Perel A: **The effect of tidal volume and intravascular volume state on systolic pressure variation in ventilated dogs.** *Intensive Care Med* 1989, **15**:368–371.
31. Pizov R, Cohen M, Weiss Y, Segal E, Cotev S, Perel A: **Positive end-expiratory pressure-induced hemodynamic changes are reflected in the arterial pressure waveform.** *Crit Care Med* 1996, **24**:1381–1387.
32. Guyton AC: *Textbook of Medical Physiology*, 8th edn. Philadelphia: WB Saunders; 1991.
33. Michard F and Teboul JL: **Respiratory changes in arterial pressure in mechanically ventilated patients.** In: *Yearbook of Intensive Care and Emergency Medicine*. Edited by Vincent JL. Berlin: Springer; 2000:696–704.
34. Coyle JP, Teplick RS, Long MC: **Respiratory variations in systemic arterial pressure as an indicator of volume status [abstract].** *Anesthesiology* 1983, **59**:A53.
35. Perel A, Pizov R, Cotev S: **Systolic blood pressure variation is a sensitive indicator of hypovolemia in ventilated dogs subjected to graded hemorrhage.** *Anesthesiology* 1987, **67**:498–502.
36. Pizov R, Ya'ari Y, Perel A: **Systolic pressure variation is greater during hemorrhage than during sodium nitroprusside-induced hypotension in ventilated dogs.** *Anesth Analg* 1988, **67**:170–174.
37. Preisman S, Pfeiffer U, Lieberman N, Perel A: **New monitors of intravascular volume: a comparison of arterial pressure waveform analysis and the intrathoracic blood volume.** *Intensive Care Med* 1997, **23**:651–657.
38. Alec Rooke G, Schwid HA, Shapira Y: **The effect of graded hemorrhage and intravascular volume replacement on systolic pressure variation in humans during mechanical and spontaneous ventilation.** *Anesth Analg* 1995, **80**:925–932.
39. Coriat P, Vrillon M, Perel A, Baron JF, Le Bret F, Saada M, Viars P: **A comparison of systolic blood pressure variations and echocardiographic estimates of end-diastolic left ventricular size in patients after aortic surgery.** *Anesth Analg* 1994, **78**:46–53.
40. Robotham JL, Cherry D, Mitzner W, Rabson JL, Lixfeld W, Bromberger-Barnea B: **A re-evaluation of the hemodynamic consequences of intermittent positive pressure ventilation.** *Crit Care Med* 1983, **11**:783–793.
41. Denault AY, Gasior TA, Gorcsan III J, Mandarino WA, Deneault LG, Pinsky MR: **Determinants of aortic pressure variation during positive-pressure ventilation in man.** *Chest* 1999, **116**:176–186.
42. Berne RM, Levy MN: *Physiology*, 4th edn. St Louis: Mosby; 1998.
43. Michard F, Chemla D, Richard C, Wysocki M, Pinsky MR, Lecarpentier Y, Teboul JL: **Clinical use of respiratory changes in arterial pulse pressure to monitor the hemodynamic effects of PEEP.** *Am J Respir Crit Care Med* 1999, **159**:935–939.
44. Penaz J: **Criteria for set point estimation in the volume clamp method of blood pressure measurement.** *Physiol Res* 1992, **41**:5–10.
45. Imholz BP, Wieling W, van Montfrans GA, Wesseling KH: **Fifteen years experience with finger arterial pressure monitoring: assessment of the technology.** *Cardiovasc Res* 1998, **38**:605–616.
46. Michard F, Mercat A, Chemla D, Richard C, Teboul JL: **Non invasive assessment of respiratory changes in arterial pulse pressure by infrared photoplethysmography in mechanically ventilated patients [abstract].** *Am J Respir Crit Care Med* 1999, **159**:A520.
47. Feissel M, Michard F, Mangin I, Ruyer O, Faller JP, Teboul JL: **Respiratory changes in aortic blood velocity as an indicator of fluid responsiveness in ventilated patients with septic shock.** *Chest* 2000, in press.

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