Simplified Method to Measure Respiratory-Related Changes in Arterial Pulse Pressure in Patients Receiving Mechanical Ventilation*

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Study objectives: Measuring respiratory-related changes in arterial pulse pressure is useful to guide fluid expansion in hemodynamically compromised patients. In the absence of automation, this can be uneasy in clinical practice. The objective of this study was to test an alternative approach (expiratory pause) that should be easier to apply.

Design: Prospective observational study comparing two measurement methods of a biological variable.

Patients: Seventeen patients receiving mechanical ventilation without spontaneous respiratory activity, with an arterial indwelling catheter, exhibiting respiratory-related fluctuations in arterial pressure.

Setting: Ten-bed respiratory ICU in a 2,000-bed university hospital.

Intervention: Analysis of clinically gathered data without specific experimental intervention.

Measurements: Determinations of the change in arterial pulse pressure observed during ventilatory cycling (ΔPp,dyn) [“dynamic”] and change in arterial pulse pressure observed during expiratory pauses (ΔPp,stat) [“static”] were performed to assess respiratory mechanics, and comparison of the two sets of data (correlation, Bland and Altman, Passing and Bablok regression).

Results: ΔPp,dyn and ΔPp,stat were strongly correlated (R = 0.964; 95% confidence interval, 0.917 to 0.987; p < 0.0001), with a good level of agreement (mean difference, 0.016; lower limit of agreement, −0.087; upper limit, 0.120) and no systematic difference.

Conclusion: Measuring respiratory-related ΔPp,stat provides data that seem interchangeable with ΔPp,dyn, providing an easy means to routinely obtain this information.

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Key words: arterial pressure; critical care; fluid expansion; heart-lung interactions; hemodynamics; ICUs; mechanical ventilation; monitoring

Abbreviations: CI = confidence interval; ΔPp,dyn = change in arterial pulse pressure observed during ventilatory cycling; ΔPp,stat = change in arterial pulse pressure observed during expiratory pauses; Ppmax = maximal pulse pressure; Ppmin = minimal pulse pressure

In the presence of hemodynamic instability, the therapeutic strategy closely depends on the underlying mechanism. Fluid expansion is appropriate to increase cardiac output only if the left ventricle preload is insufficient, namely if the left ventricle operates on the leftward part of its curvilinear pressure-volume relationship. Identifying this situation is therefore of the utmost clinical relevance. Mechanical ventilation with intermittent positive pressure induces major changes in cardiac function.

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One of the easily identifiable expressions is the presence of cyclical changes in arterial pulse. These changes result from a sequence of events following the rise in alveolar pressure associated with mechanical insufflation. At the beginning of inspiration, the rise in alveolar pressure boosts the pulmonary capillary blood into the left ventricle, producing a sudden preload increase and an immediate increase in stroke volume. Thus, inspiration is first associated with an increase in arterial pressure, above its reference value (“Δ-up” phenomenon). However, the positive alveolar pressure tends to impair the venous return to the right ventricle and concomitantly increases the impedance to its ejection. The capillary bed can thus not be immediately refilled. This, in turn, has a negative impact on left ventricular filling that is transiently impaired. This occurs later during inspiration or at the onset of expiration because at least one or two unpaired right ventricular strokes are needed to fill the pulmonary vascular bed again. As a result, a drop in left ventricular stroke output occurs and arterial pressure decreases below its reference value (“Δ-down” phenomenon). These changes are amplified if the left ventricle operates on the curvilinear portion of its pressure-volume relationship. Respiratory-related changes in arterial pressure, if they are of excessive magnitude, are a sign of insufficient left ventricular preload, and can justify a decision of volume expansion. Because pulse pressure is directly proportional to left ventricular stroke volume, it is particularly interesting to focus on. In sedated patients receiving mechanical ventilation with sepsis-related circulatory failure, Michard et al showed that respiratory-related changes in pulse pressure predicted much better a positive effect of fluid expansion on cardiac output after right atrial pressure or pulmonary artery occlusion pressure. In this study, the magnitude of the respiratory changes in pulse pressure was correlated with the magnitude of the volume expansion-induced changes in cardiac output. Many clinical data currently support this approach, but methodologic traps and technical difficulties still limit its use in daily clinical practice. Fluctuations glanced at on an arterial pressure trace are not sufficient to ascertain pulse pressure variability, because mechanical insufflation can provoke cyclical variations of diastolic and systolic pressures concomitantly. Pulse pressure must thus be carefully computed, but automation is not yet available. Isolated extrasystoles can be difficult to detect within a fluctuating arterial pressure tracing, particularly in the presence of tachycardia. The simultaneous display of a respiratory signal and of an arterial pressure trace is not always available. Even when it is the case, detecting ventilatory efforts from the patients (that modify the significance of respiratory-related changes in arterial pressure) can be uneasy during ventilatory cycling.

Therefore, because during an expiratory pause there is a restoration of left ventricular filling that leads to a stabilization of arterial pressure, we set out to compare the respiratory-related change in arterial pulse pressure measured during ventilatory cycling \( \Delta Pp,dy \) (“dynamic”) with the change in arterial pulse pressure observed during expiratory pauses \( \Delta Pp,stat \) (“static”). Indeed, it seemed to us that if the two methods yielded interchangeable results, the static procedure could alleviate some of the practical drawbacks of the dynamic procedure.

### Materials and Methods

#### Patients

Seventeen patients receiving mechanical ventilation were studied (20 pairs of measurements points) [Table 1]. Criteria for inclusion were as follows: (1) the presence of an indwelling radial or arterial catheter placed after the decision of the physician in charge of the patient; (2) controlled mechanical ventilation without spontaneous respiratory activity (complete absence of patient-triggered ventilatory cycle, linear inspiratory pressure-time relationship without changes in shape from breath to breath, and pressure trace absolutely still during the expiratory pauses); (3) absence of arrhythmia; and (4) absence of massive pleural effusion and of chest tubes. Because the study was purely observational (analysis of data gathered during routine procedures, complete absence of intervention interfering with the clinical management) informed consent was not required.

#### Measurements

The ECG from standard chest leads, arterial pressure from the pressure transducer connected to the arterial line of the patient, and airway pressure and ventilatory flows from the pressure transducers of the mechanical ventilator were recorded simultaneously. All the patients received ventilation with Siemens Servo 900C or 900D ventilators (Siemens Elena; Solna, Sweden). Paper tracings were obtained from a high-precision thermic printer hooked to the analog output of the monitor (Siemens Sirecust 1200 series; Siemens; St-Ouen, France), running at a constant paper speed of 50 mm/s. Systolic and diastolic arterial pressures were measured on a beat-to-beat basis by a single investigator who repeated the readings twice at a minimal interval of 1 day. They were checked by a second investigator in a blinded manner. Pulse pressure was calculated as the difference between systolic and diastolic pressures.

### Dynamic Measurements

Dynamic measurements were performed over randomly selected respiratory cycles, after verifying that the hemodynamic state of the patient was reasonably stable (change in systolic arterial pressure and cardiac frequency not exceeding 15% of average values for at least 10 min, absence of change in the rate of infusion of catecholamines for at least 10 min, and 10 min interval after the end of a volume expansion procedure). The magnitude of the \( \Delta Pp,dy \) was defined as the difference between the maximal pulse pressure \( (Pp_{\text{max}}) \) value and the minimal pulse pressure \( (Pp_{\text{min}}) \) value over this respiratory cycle, and was normalized according to the method proposed by Michard et al:

\[
\Delta Pp,dy = \frac{(Pp_{\text{max}} - Pp_{\text{min}})}{\text{sys.}}
\]
Each data point in the analysis corresponds to the average of two \(Pp_{\text{max}} + Pp_{\text{min}}/2\) determinations over nonconsecutive respiratory cycles. All the dynamic measurements were performed immediately before the static measurements (see below).

**Static Measurements:** Static measurements were performed when expiratory pauses were decided by the clinician in charge of the patient to measure respiratory system compliance or monitor intrinsic positive expiratory pressure. According to standard procedures, the pauses were obtained by pressing the “end-expiratory pause” button of the ventilator, and maintained for 5 s. Each measurement was repeated twice, with a three- to six-respiratory cycle interval. The magnitude of the \(Pp_{\text{stat}}\) was defined as the difference between the \(Pp_{\text{min}}\) and \(Pp_{\text{max}}\) value observed during the period corresponding to the normal expiration followed by the 5-s pause. The same normalization formula as for the dynamic value was applied. Each data point in the analysis corresponds to the average of two \(Pp_{\text{stat}}\) determinations, except in cases where the routine procedure of respiratory mechanics assessment was not completed. In these cases, \(Pp_{\text{stat}}\) is taken from a single pause (n = 3).

**Data Analysis**

The statistical association between \(\Delta Pp_{\text{dyn}}\) and \(\Delta Pp_{\text{stat}}\) was expressed in terms of the Z coefficient of correlation with 95% confidence interval (CI). The agreement between the two methods was studied using a graphical analysis and the regression method described by Passing and Bablok. The data are expressed as mean ± SD.

**RESULTS**

Figure 1, top, A shows a caricatural example of respiratory-related changes in arterial pressure. Figure 1, bottom, B shows the course of arterial pressure with time during an end-expiratory pause. During a given expiratory pause, the minimum value of \(\Delta Pp_{\text{stat}}\) consistently corresponded to the first or second heart beat occurring after the beginning of the considered expiratory period (Fig 1, bottom, B). Stabilization was then achieved after the fourth or fifth heart beat.

![Figure 1. Caricatural example, in one patient, of the respiratory-related ΔPpDyn (top, A: top trace, arterial pressure (AP); bottom trace, ventilatory flow; no units indicated). The vertical bars indicate the pulse pressure values retained to compute ΔPpDyn. When an end-expiratory pause is performed (bottom, B: top trace, arterial pressure; bottom trace, ventilatory flow; no units indicated), both the diastolic and the pulse pressure stabilize after a few heart beats. The vertical bars indicate the pulse pressure values retained to compute ΔPpStat.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21997/ on 06/27/2017)
fifth heart beat, and consistently corresponded to the maximal $\Delta P_{p,stat}$ value. $\Delta P_{p,dyn}$ and $\Delta P_{p,stat}$ were strongly correlated ($R = 0.964; 95\% \text{ CI}, 0.917$ to $0.987; p < 0.0001$) [Fig 2]. The mean difference between $\Delta P_{p,dyn}$ and $\Delta P_{p,stat}$ was $0.016$, with a lower limit of agreement at $-0.087$ and an upper limit at $0.120$ according to the representation of Bland and Altman$^6$ (Fig 3, top, A). The $95\% \text{ CI}$ of the $\Delta P_{p,stat}$ vs $\Delta P_{p,dyn}$ regression intercept included zero and the $95\% \text{ CI}$ of the slope included one indicating the absence of systematic difference between the two techniques (Fig 3, bottom, B)$.^7$

**Discussion**

This study shows that the restoration of arterial pulse pressure that occurs during an expiratory interruption of mechanical ventilation can provide an adequate reflection of the cyclic changes observed during mechanical ventilation. What “adequate” means here is not unequivocal. The Bland and Altman$^6$ graphical approach to compare two methods of measurements of a given biological value does not tell if the agreement found between these two methods is “good” or not. This qualification depends on the error magnitude that is, arbitrarily, considered clinically acceptable. When looking at Figures 2, 3, it can be seen that for many of the 20 data points, the two methods yielded values very close to identity. This was the case when $\Delta P_{p,dyn}$ was above the 13% cut-off proposed by Michard et al,$^4$ as indicative of responsiveness to fluid expansion (13 measurements out of 20). This was also the case when $\Delta P_{p,dyn}$ was below this value; therefore, it seems to us reasonable to propose, from our results, that the two methods are likely to be interchangeable. It must be noted that with both approaches, the variations in arterial pressure are representative for changes induced by positive pressure ventilation (and thus possible indicator of the hemodynamic status) solely if there is no ventilatory muscle activity, which in most cases apply only to sedated patients.$^4$

Of note, the fact that the two measurements...
appear numerically and statistically interchangeable does not mean that they have the same pathophysiologic determinants. As described in the introduction, the changes in arterial pressure following a positive pressure inspiration include a Δ-up component (difference between the maximal value of systolic pressure during the ventilatory cycle, observed at the beginning of inspiration and the reference systolic pressure, determined during a 5-s expiratory pause) and a Δ-down component (difference between the reference systolic pressure and the minimal value of systolic pressure, observed during expiration). During an expiratory pause, the Δ-up component is absent by definition. The extramural vascular pressure does not vary, and the venous return prevailing conditions remain constant. It is therefore logical for left ventricular stroke volume to tend to be a stable value, which is necessary close to the maximal value observed during the respiratory cycle. The changes in pulse pressure observed correspond in the restoration of the filling volume of the left ventricle. We consistently observed such stabilization in our patients, after four or five cardiac cycles, and the comparison of the stabilized value with the Ppmax value measured during the preceding respiratory cycle did not show any statistically significant difference. As a result, ΔPp,stat should be close, pathophysiologically, to the Δ-down component. It can therefore be predicted that ΔPp,stat should be slightly smaller than ΔPp,dyn. Our data are in line with this prediction (clinical example in Figs 1, 2, and 3, bottom, B, where the slope of the relationship is < 1). This difference is not a problem regarding the clinical usefulness of the data. Indeed, Perel et al showed that Δ-down was the main component of variations in systolic pressure observed in dogs receiving mechanical ventilation, and that it was a very sensitive indicator of hypovolemia in this setting. They also established the link between Δ-down and insufficient ventricular preload by demonstrating that nitroprusside induced hypotension did not provoke changes of the same magnitude as in the case of hypovolemia. In man, Tavernier et al established in 15 patients with sepsis-related hypotension that Δ-down was a sensitive indicator of the response of cardiac output to volume infusion, and that its value in this context was superior to that of the simpler to measure systolic pressure variation. The Δ-up and Δ-down components have been described for systolic arterial pressure. Because systolic pressure depends on diastolic pressure, and because diastolic pressure may increase during mechanical insufflation (Fig 1, top, A) due to a rise in aortic extramural pressure, respiratory-related changes in systolic pressure may include a component not directly related to the left ventricular stroke volume. Studying respiratory-related variations in pulse pressure instead of respiratory-related variations in systolic pressure suppresses, in principle, the errors induced by the direct effects of pleural pressure on the respiratory-related variability of arterial pressure. In addition, the use of pulse pressure alleviates the difficulties and limitations of the measurement of the reference systolic pressure. Michard et al relied on this argument to promote the use of ΔPp,dyn, and indeed demonstrated that the clinical performance of this index to predict fluid responsiveness, expressed in terms of receiver-operating curves, was better than that of systolic pressure variation. Our approach combines the above-described advantages of the use of pulse pressure to an element of simplicity provided by the fact that the end-expiratory pause abolishes changes in alveolar pressure during the hemodynamic assessment.

In conclusion, we submit that, although ΔPp,stat and ΔPp,dyn do not correspond exactly to the same mechanism, their interchangeability should allow clinicians to use either technique in the decision-making process of fluid responsiveness in patients receiving mechanical ventilation exhibiting hemodynamic instability. In some cases, some can find the static approach easier to use because it can alleviate possible technical and methodologic limitations of the standard approach, and thus facilitate the routine gathering of the corresponding information until automatic monitoring algorithms become available.

REFERENCES

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