Clinical Use of Respiratory Changes in Arterial Pulse Pressure to Monitor the Hemodynamic Effects of PEEP

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In ventilated patients with acute lung injury (ALI) we investigated whether respiratory changes in arterial pulse pressure (ΔPP) could be related to the effects of PEEP and fluid loading (FL) on cardiac index (CI). Measurements were performed before and after application of a PEEP (10 cm H2O) in 14 patients. When the PEEP-induced decrease in CI was >10% (six patients), measurements were also performed after FL. Maximal (PPmax) and minimal (PPmin) values of pulse pressure were determined over one respiratory cycle and ΔPP was calculated: ΔPP (%) = 100 × [(PPmax – PPmin)/((PPmax + PPmin)/2)]. PEEP decreased CI from 4.2 ± 1.1 to 3.8 ± 1.3 L/min/m² (p < 0.01) and increased ΔPP from 9 ± 7 to 16 ± 13% (p < 0.01). The PEEP-induced changes in CI correlated with ΔPP on ZEEP (r = –0.91, p < 0.001) and with the PEEP-induced increase in ΔPP (r = –0.79, p < 0.001). FL increased CI from 3.5 ± 1.1 to 4.2 ± 0.9 L/min/m² (p < 0.05) and decreased ΔPP from 27 ± 13 to 14 ± 9% (p < 0.05). The FL-induced changes in CI correlated with ΔPP before FL (r = 0.97, p < 0.01) and with the FL-induced decrease in ΔPP (r = –0.85, p < 0.05). In ventilated patients with ALI, ΔPP may be useful in predicting and assessing the hemodynamic effects of PEEP and FL. Michaud F, Chemla D, Richard C, Wysocki M, Pinsky MR, Lecarpentier Y, Teboul J-L. Clinical use of respiratory changes in arterial pulse pressure to monitor the hemodynamic effects of PEEP.


In ventilated patients with acute lung injury (ALI), positive end-expiratory pressure (PEEP) may improve pulmonary gas exchange. However, it may also decrease cardiac output and thus offset the expected benefits in terms of oxygen delivery. The PEEP-induced decrease in cardiac output is assumed to be mainly due to a decrease in systemic venous return secondary to the increased pleural pressure (1–3). Impairment of right ventricular (RV) ejection related to increased transpulmonary pressure (i.e., alveolar minus pleural pressure) could also play a role in some patients (4, 5). The adverse hemodynamic effects of PEEP are not easily predictable in clinical practice, although they have been shown to be more likely to occur in patients with low left ventricular (LV) filling pressure (6–8).

Mechanical ventilation induces cyclic changes in LV stroke volume (SV) characterized by a lower LV SV during expiration than during insufflation (9–12). This respiratory pattern is mainly explained by the expiratory decrease in LV filling that followed after a delay (caused by the long pulmonary transit time of blood) the decrease in RV SV occurring during insufflation (10). The inspiratory decrease in RV SV has been shown to result essentially from a decrease in RV filling caused by the effects of increased pleural pressure on systemic venous return (9) and from transient impairment of RV ejection related to increased transpulmonary pressure on pulmonary circulation (13, 14).

Interestingly, the decrease in mean cardiac output induced by PEEP and the decrease in RV SV induced by mechanical insufflation share the same mechanisms, i.e., the negative effects of increased pleural pressure on RV filling and of increased transpulmonary pressure on RV ejection. Thus, it is reasonable to expect that the magnitude of the expiratory decrease in LV SV would correlate with the PEEP-induced decrease in mean cardiac output.

Finally, the negative effects of increased pleural pressure on RV filling should be more pronounced in patients with low cardiac preload (15, 16). Thus, the beneficial effect of fluid loading on cardiac output might be expected to correlate with the magnitude of the inspiratory decrease in RV SV and hence of the expiratory decrease in LV SV before fluid loading.

Aortic pulse pressure is directly proportional to LV SV and inversely related to aortic capacitance (17). Respiratory changes in peripheral pulse pressure (ΔPP) during mechanical ventilation have been shown to closely reflect the variations in LV SV during the respiratory cycle (10). Thus, the aim of our study was to examine the relationships between ΔPP and the hemodynamic effects of PEEP and fluid loading in ventilated pa-
tients with ALI. We hypothesized that the higher the ΔPP on ZEEP, the higher the PEEP-induced decrease in cardiac output. In patients who received fluid while on PEEP, we also hypothesized that the higher the ΔPP before fluid loading, the higher the fluid-loading-induced increase in cardiac output.

METHODS

The protocol was approved by the institutional review board for human subjects (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale, Cochin Hospital), and written informed consent was obtained from all the patients’ next of kin.

Patients

We studied 14 mechanically ventilated patients in whom ALI was diagnosed. This group consisted of 10 men and four women 37 to 83 yr of age (mean age, 58 ± 16 yr).

Inclusion criteria were as follows: (1) A LI defined by the combination of recent bilateral pulmonary infiltrates on chest radiograph, a PaO2/FIO2 ratio < 300 mm Hg, and a pulmonary artery occlusion pressure (Ppao) below 18 mm Hg; (2) all patients had to be instrumented with indwelling arterial (radial or femoral) and pulmonary artery catheters; (3) all patients had to be hemodynamically stable, as defined by a variation in heart rate, blood pressure, and CI of less than 10% over the 15-min period before starting the protocol. Patients were excluded if they had arrhythmias or any contraindication to the use of PEEP.

Hemodynamic Measurements

Patients were studied while supine, and zero pressure was measured at the midaxillary line. Right atrial pressure (PRA) and Ppao were recorded throughout the respiratory cycle and measured at end-expiration. Cardiac output was calculated as the mean of five measurements obtained by injecting 10 ml of dextrose solution randomly during the respiratory cycle. The CI was calculated as the ratio of cardiac output to body surface area.

Arterial Pressure Variations

We used the analog output from the monitor (H - P Monitor M 1092A; Hewlett-Packard, Les Ulis, France) via an A — T — D converter to record the arterial pressure and airway pressure curves over at least 10 breaths simultaneously onto a computer (Toshiba 3200 SX). Recording was performed at a sampling rate of 500 Hz using customized acquisition software. Pulse pressure (PP) was calculated on a beat-to-beat basis as the difference between systolic and diastolic arterial pressure. Maximal PP (PPmax) and minimal PP (PPmin) values were determined over a single respiratory cycle. To assess the respiratory changes in PP, the percent change in PP was calculated as:

\[ \text{ΔPP} \% = 100 \times \frac{(\text{PPmax } - \text{PPmin})}{(\text{PPmax } + \text{PPmin})/2}\]

An example of our data and their analysis is shown in Figure 1.

Respiratory Measurements

Airway pressures were measured by using a pressure transducer (Uniphys 43-600; Baxter Edwards Crit Care, Irvine, CA) connected close to the proximal end of the endotracheal tube. Plateau airway pressure (Pplat) was measured after an end-inspiratory (2 s) occlusion. Tidal volume (Vt) was measured by means of the ventilator transducer. The static compliance of the respiratory system (Crst.rs) was calculated as follows: Crst.rs = Vt/(Pplat − PEEP).

Study Protocol

All patients were sedated and mechanically ventilated in a volume-controlled mode with an I/E ratio of one-half to one-third. Six patients were therapeutically paralyzed according to the attending physician. In three of the eight remaining patients, spontaneous breathing activity was detected by visual inspection of the airway pressure curve. To ensure that ΔPP reflected only the effects of positive pressure ventilation, these three patients were temporarily paralyzed. Measurements were performed in duplicate, first during 0 cm H2O PEEP (ZEEP) and then 15 min after the addition of 10 cm H2O PEEP (PEEP). In patients in whom PEEP induced a decrease in CI of at least 10%, fluid loading using 500 ml H2O was performed over 30 min and a third set of hemodynamic measurements was then obtained. Except for PEEP, ventilatory settings and dosages of inotropic and vasopressor drugs were held constant.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Cause of ALI</th>
<th>Age (yr)</th>
<th>LIS</th>
<th>Pao2/Fio2 (mm Hg)</th>
<th>Crst.rs (ml/cm H2O)</th>
<th>Vt (ml/kg)</th>
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<td>71</td>
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<td>192</td>
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<td>256</td>
<td>31</td>
<td>10</td>
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</table>

Definition of abbreviations: ALI = acute lung injury; Crst.rs = static compliance of the respiratory system; LIS = Lung Injury Score; Vt = tidal volume.
Statistical Analysis
Results were expressed as means $\pm$ standard deviation. The effects of PEEP and fluid loading were assessed using Wilcoxon’s nonparametric rank sum test (18). Correlations were tested using Spearman’s rank test. A $p$ value less than 0.05 was considered statistically significant.

RESULTS
The main characteristics of the 14 patients studied are listed in Table 1. Our patients had no history of heart failure, and CI during ZEEP ranged from 2.9 to 7.0 L/min/m$^2$. A II patients exhibited maximal PP during insufflation and minimal PP during the expiratory period. The effects of PEEP on the hemodynamic parameters are presented in Table 2.

On ZEEP, $\Delta$PP correlated both with $P_{\text{RA}}$ ($r = -0.62$, $p < 0.05$) and with $P_{\text{pao}}$ ($r = -0.64$, $p < 0.05$). However, $\Delta$PP on ZEEP did not correlate with $V_{\text{R}}$ and $C_{\text{rs}}$.

PEEP induced a decrease in CI from $4.2 \pm 1.1$ to $3.8 \pm 1.3$ L/min/m$^2$ ($p < 0.01$) and an increase in $\Delta$PP from $9 \pm 7$ to $16 \pm 13$% ($p < 0.01$). The PEEP-induced changes in CI correlated both with $\Delta$PP on ZEEP ($r = -0.91$, $p < 0.001$) and with the PEEP-induced changes in $\Delta$PP ($r = -0.79$, $p < 0.001$) (Figure 2). The PEEP-induced changes in CI also correlated with $P_{\text{pao}}$ on ZEEP ($r = 0.75$, $p < 0.01$) but were not significantly correlated with $P_{\text{RA}}$ on ZEEP ($r = 0.48$, $p = 0.08$).

Six patients demonstrated a decrease in CI $> 10\%$ with the application of PEEP. In these patients, fluid loading increased CI from $3.5 \pm 1.1$ to $4.2 \pm 0.9$ L/min/m$^2$ ($p < 0.05$) and decreased $\Delta$PP from $27 \pm 13$ to $14 \pm 9$% ($p < 0.05$). The fluid-loading-induced changes in CI correlated with $\Delta$PP on PEEP before volume expansion ($r = 0.97$, $p < 0.01$) and with the fluid-loading-induced changes in $\Delta$PP ($r = -0.85$, $p < 0.05$) (Figure 3).

DISCUSSION
Our results demonstrate strong relationships between $\Delta$PP and the effects of both PEEP and fluid loading on cardiac output in ventilated patients with ALI.

All of our patients exhibited a maximal PP during mechanical insufflation and a minimal PP at expiration. These findings are consistent with the respiratory pattern of arterial pulse pressure previously described in animal and clinical studies during positive pressure ventilation (9–12, 19–26). The respiratory changes in PP have been shown related to the cyclic changes in LVSV that followed after a delay the respiratory changes in RVSV (10). At insufflation, RVSV is minimal because of the negative effects both of increased pleural pressure on RV filling (9) and of increased transpulmonary pressure on RV ejection (13, 14). In conventional ventilatory conditions, this should result in a minimal LVSV during expiration because of the phase lag between RV output and LV filling caused by the long blood pulmonary transit time (9, 10, 21). Other mechanisms might also contribute to the increase in LVSV at insufflation, particularly in patients with congestive heart failure: (1) a further LV filling caused by squeezing of blood out of alveolar vessels (20, 27), and (2) a decrease in LV afterload caused by the increased pleural pressure (11, 28).

In fact, the main mechanisms that induce the inspiratory decrease in RVSV and hence the expiratory decrease in LVSV are identical to those whereby PEEP decreases mean cardiac output. Accordingly, we found a strong correlation between $P_{\text{pao}}$ and the expiratory decrease in LVSV $> 10\%$ with the application of PEEP. In these patients, fluid loading increased CI from $3.5 \pm 1.1$ to $4.2 \pm 0.9$ L/min/m$^2$ ($p < 0.05$) and decreased $\Delta$PP from $27 \pm 13$ to $14 \pm 9$% ($p < 0.05$). The fluid-loading-induced changes in CI correlated with $\Delta$PP on PEEP before volume expansion ($r = 0.97$, $p < 0.01$) and with the fluid-loading-induced changes in $\Delta$PP ($r = -0.85$, $p < 0.05$) (Figure 3).

### Table 2
**EFFECTS OF PEEP ON HEMODYNAMIC PARAMETERS**

<table>
<thead>
<tr>
<th></th>
<th>ZEEP</th>
<th>PEEP</th>
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<tbody>
<tr>
<td>HR, beats/min</td>
<td>$114 \pm 16$</td>
<td>$117 \pm 17$</td>
</tr>
<tr>
<td>$P_{\text{a}}$, mm Hg</td>
<td>$81 \pm 12$</td>
<td>$73 \pm 14^\dagger$</td>
</tr>
<tr>
<td>$P_{\text{w}}$, mm Hg</td>
<td>$8 \pm 4$</td>
<td>$9 \pm 3^\dagger$</td>
</tr>
<tr>
<td>$P_{\text{Pa}}$, mm Hg</td>
<td>$24 \pm 6$</td>
<td>$26 \pm 5^\dagger$</td>
</tr>
<tr>
<td>$P_{\text{pao}}$, mm Hg</td>
<td>$9 \pm 4$</td>
<td>$12 \pm 3^\dagger$</td>
</tr>
<tr>
<td>CI, L/min/m$^2$</td>
<td>$4.2 \pm 1.1$</td>
<td>$3.8 \pm 1.3^\dagger$</td>
</tr>
<tr>
<td>$\Delta$PP, %</td>
<td>$9 \pm 7$</td>
<td>$16 \pm 13^\dagger$</td>
</tr>
</tbody>
</table>

*Definition of abbreviations: CI = cardiac index; HR = heart rate; $P_{\text{a}}$ = mean arterial pressure; $P_{\text{w}}$ = right atrial pressure; $P_{\text{Pa}}$ = mean pulmonary arterial pressure; $P_{\text{pao}}$ = pulmonary artery occlusion pressure; $\Delta$PP = respiratory changes in arterial pulse pressure.

* Values are means $\pm$ SD.
† $p < 0.05$.
‡ $p < 0.01$ PEEP versus ZEEP.

Figure 2. (Upper panel) Correlation between respiratory pulse pressure variations ($\Delta$PP) on ZEEP and the PEEP-induced changes in cardiac index (CI). (Lower panel) Correlation between PEEP-induced changes in $\Delta$PP ($\Delta$PP on PEEP – $\Delta$PP on ZEEP) and the PEEP-induced changes in CI.
lated with PRA and Ppao. Furthermore, in the six patients who
received fluid, the increase in CI correlated both with \( \Delta PP \) before fluid loading and with the fluid-loading-induced decrease in \( \Delta PP \). These findings suggest that \( \Delta PP \) may be useful for monitoring the hemodynamic effects of fluid loading.

No correlation was found between \( \Delta PP \) and tidal volume. This result could be due to the small range of \( V_T \) and to the fact that, in contrast to others studies (19, 23), we did not modify \( V_T \) throughout the study.

When our patients were transferred from ZEEP to PEEP, the changes in \( \Delta PP \) strongly correlated with the changes in CI. These results were in accordance with those of Pizov and colleagues (26) who found that systolic pressure variations in dogs increased mostly when cardiac output decreased with PEEP. In preload-sensitive subjects, it may be assumed that the further increase in pleural pressure with PEEP would have produced a greater decrease in both respiratory LVSV and mean cardiac output. However, because our study was not designed to elucidate why \( \Delta PP \) increased with PEEP, we cannot exclude the possibility that mechanisms affecting RV afterload may also have occurred: an additional increase in RV afterload during insufflation on PEEP, related to the extension of West’s Zone 1 or 2 (13) cannot be excluded. Conversely, PEEP-induced improvement in functional residual capacity and/or a decrease in hypoxic pulmonary vasoconstriction might have resulted in a lower RV afterload during insufflation on PEEP than on ZEEP.

It must be underlined that arrhythmias and spontaneous breathing activity may result in misleading interpretation of \( \Delta PP \). Finally, since our study concerned patients with ALI, the results cannot be extrapolated to patients with chronic respiratory disease or congestive heart failure.

In summary, our findings suggest that (1) \( \Delta PP \) could be used at the bedside to predict adverse hemodynamic effects of PEEP, (2) changes in \( \Delta PP \) from ZEEP to PEEP could be used to assess changes in CI that occur when PEEP is applied, (3) in patients with ALI ventilated with PEEP, \( \Delta PP \) and its changes induced by fluid may be helpful in predicting and assessing the effects of fluid loading on hemodynamics. Because the potential risk of using pulmonary artery catheters is currently a subject of debate (29), the use of \( \Delta PP \) to monitor hemodynamics in ventilated patients with ALI may be an attractive alternative approach.

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References

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