Effects of Pressure-controlled with Different I:E Ratios Versus Volume-controlled Ventilation on Respiratory Mechanics, Gas Exchange, and Hemodynamics in Patients with Adult Respiratory Distress Syndrome

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Background: Pressure-controlled (PCV) and pressure-controlled inverse ratio ventilation (PCIRV) have been proposed instead of volume-controlled conventional ratio ventilation (VC) with positive end-expiratory pressure (PEEP) for patients with adult respiratory distress syndrome (ARDS). The advantages advocated with the use of PCIRV are to decrease airway pressures and to improve gas exchange. However, most studies did not compare PCIRV and VC while keeping both the level of ventilation and end-expiratory alveolar pressure (total-PEEP) constant.

Methods: Nine patients with moderate to severe ARDS (lung injury score 2.83 ± 0.18) had their lungs ventilated with VC, PCV with a conventional ratio (I:E 1:2; PC 1/2), and PCIRV (I: E 2:1 and 3:1; PC 2/1 and PC 3/1, respectively). Ventilator settings were adjusted to keep tidal volume, respiratory rate, Fio2, and total-PEEP constant in every mode. With each mode, a complete set of ventilatory, hemodynamic, and gas exchange parameters was obtained after 30 min.

Results: In PC 3/1, the data obtained could not be strictly compared to the other modes because total-PEEP was higher despite external-PEEP being set at zero. For the other modes (VC, PC 1/2, and PC 2/1), despite differences in peak airway pressures, no difference was noted for end-inspiratory and end-expiratory static airway pressures (which better reflect alveolar pressures) nor for lung and respiratory system compliance. Arterial oxygenation deteriorated slightly with PC 2/1 despite a higher mean airway pressure, whereas alveolar ventilation tended to be slightly, but not significantly, improved (lower PaCO2). A decrease in systolic and mean arterial pressure also was observed with PC 2/1 without other significant hemodynamic change.

Conclusions: In this prospective controlled study, no short-term beneficial effect of PCV or PCIRV could be demonstrated over conventional VC with PEEP in patients with ARDS. (Key words: Lung; adult respiratory distress syndrome; ARDS. Ventilation, mechanical: inverse ratio ventilation; PCIRV; positive end-expiratory pressure, intrinsic; pressure-controlled.)

SINCE adult respiratory distress syndrome (ARDS) was described more than two decades ago by Ashbaugh et al.,1 different ventilatory strategies have been proposed to restore arterial oxygenation and alveolar ventilation. The conventional approach consists of delivering volume-controlled ventilation with positive end-expiratory pressure (PEEP). Recent experimental data have demonstrated that mechanical ventilation with high volume and high pressure can cause further damage to the injured lung.2,3 New ventilatory strategies are now proposed to reduce ventilation-related lung injury and the duration of mechanical ventilation.

Pressure-controlled inverse ratio ventilation (PCIRV) is a ventilatory alternative that is claimed to improve gas exchange at lower peak airway pressure (Ppeak), thereby limiting lung damage. However, Ppeak is a poor reflection of alveolar pressure and of the related risk...
Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex (M/F)</th>
<th>Age (yr)</th>
<th>Diagnosis</th>
<th>SAPS</th>
<th>Duration of Ventilation (days)</th>
<th>PEEP (cmH2O)</th>
<th>Cns (ml/cmH2O)</th>
<th>LIS</th>
<th>Outcome (S/D)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>36</td>
<td>Bone marrow transplant</td>
<td>8</td>
<td>4</td>
<td>213</td>
<td>10</td>
<td>33</td>
<td>2.5</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>54</td>
<td>Septicemia</td>
<td>10</td>
<td>10</td>
<td>220</td>
<td>12</td>
<td>21</td>
<td>3.0</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>44</td>
<td>Viral pneumonia, AIDS</td>
<td>11</td>
<td>15</td>
<td>101</td>
<td>12</td>
<td>20</td>
<td>3.0</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>76</td>
<td>Carcinomatous lymphangitis</td>
<td>11</td>
<td>3</td>
<td>153</td>
<td>19</td>
<td>3</td>
<td>3.0</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>62</td>
<td>Cerebral hemorrhage, Pneumonia</td>
<td>19</td>
<td>4</td>
<td>186</td>
<td>10</td>
<td>19</td>
<td>2.75</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>30</td>
<td>Bone marrow transplant</td>
<td>9</td>
<td>12</td>
<td>214</td>
<td>15</td>
<td>45</td>
<td>2.75</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>27</td>
<td>Pneumonia</td>
<td>12</td>
<td>6</td>
<td>139</td>
<td>12</td>
<td>27</td>
<td>2.75</td>
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<tr>
<td>8</td>
<td>F</td>
<td>22</td>
<td>Tuberculosis</td>
<td>9</td>
<td>16</td>
<td>135</td>
<td>10</td>
<td>26</td>
<td>2.75</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>65</td>
<td>Septic shock</td>
<td>32</td>
<td>2</td>
<td>61</td>
<td>10</td>
<td>31</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Mean ± SD 46.2 ± 19.0 13.4 ± 7.7 7.9 ± 5.1 158 ± 55.2 11.2 ± 1.7 26.7 ± 6.5 2.83 ± 0.18 2/7

SAPS = simplified acute physiology score; Cns = total respiratory system static compliance; LIS = lung injury score; S = survived; D = died.

of barotrauma when the flow pattern is modified.\(^4,5\) PCIRV frequently is used in the management of patients with ARDS, despite an incomplete understanding of its ventilatory and hemodynamic effects and of its potential complications. As far as we know, the efficacy of PCIRV in improving gas exchange, arterial oxygenation, and carbon dioxide elimination has not been assessed carefully by controlled studies. Most importantly, PCIRV was not often compared with the conventional approach, volume-controlled conventional ratio ventilation (VC), at comparable levels of ventilation and end-expiratory alveolar pressure. This last point is critical, because decreasing the expiratory time with inverse ratio ventilation (IRV) induces dynamic hyperinflation. Thus, the total end-expiratory alveolar pressure (total-PEEP) generated both by external- and intrinsic-PEEP has to be measured to compare different ventilatory modes in the same conditions. Many existing data on PCIRV are either retrospective\(^6-8\) or uncontrolled case reports.\(^9\) In some of these reports, the effect of sedation and paralysis instituted when starting PCIRV was not controlled.\(^5,7\) East et al. prospectively compared PCIRV to VC, but their study was not designed to keep tidal volume ($V_T$), minute ventilation ($V_E$), and total-PEEP constant.\(^10\) Cole et al. found no difference in gas exchange when comparing the effects of IRV and external-PEEP at the same end-expiratory lung volume and constant minute ventilation.\(^11\) However, they used volume-controlled ventilation, and end-expiratory alveolar pressure was not measured. Data on the efficacy of PCIRV in reducing complications and improving outcome are also lacking. Because PCIRV has serious limitations, including variable $V_E$ with changes in characteristic of the patients' respiratory system, the need for monitoring intrinsic-PEEP with the risk of undetected high level of total-PEEP, hemodynamic disturbance, and discomfort requiring heavy sedation and/or paralysis, the use of this mode of ventilation should be based on clear demonstration of its efficacy.

Therefore we prospectively studied the respiratory mechanic, hemodynamic, and gas exchange parameters when comparing pressure-controlled ventilation (PCV) with VC, and when comparing PCV with different I:E ratios in a controlled protocol at a constant level of ventilation and total-PEEP in patients with ARDS.

**Methods and Materials**

**Patients**

We conducted a prospective study to compare VC to PCV with various I:E ratios in nine patients with moderate to severe ARDS and whose lungs were being mechanically ventilated. Inclusion criteria were: (1) diffuse bilateral infiltrates and a compatible medical etiology for ARDS, (2) lung injury score\(^12\) > 2.5, (3) pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg, and (4) total respiratory system compliance ≤ 50 ml/cmH2O. Patients were not included if they had hemodynamic instability or if they had any contra-indication to the use of PEEP. Patients' characteristics are listed in table 1. At the time of the study, all patients' lungs were ventilated in VC with PEEP ranging between 8 and 15 cmH2O. The protocol was approved by the ethical research Committee of University Paris XII, and written informed consent was obtained from the family of each patient.
Measurements
Airflow was measured with a heated Fleisch no. 2 pneumotachograph connected to a differential pressure transducer (Validyne MP45, ±2 cmH₂O) and inserted between the tracheal tube and the Y-piece of the ventilator. Respiratory rate (RR), Vₜ, and Vₑ were obtained from the flow signal. Airway pressure (Paw) was measured at the external end of the tracheal tube with a differential pressure transducer (Validyne MP45, ±100 cmH₂O). Elastic recoil pressure of the respiratory system was measured at end-inspiration (Pplat) and at end-expiration (total-PEEP) after a 2-s occlusion by depressing the inspiratory or the expiratory hold button on the ventilator. During PCIRV, flow reached zero before the end of the inspiratory period. Thus, Pplat was measured during occlusion 2 s after flow reached zero. Pleural pressure variations were estimated from esophageal pressure (Pes) variations recorded using a balloon catheter positioned in the lower third of the esophagus and connected to a differential pressure transducer (Sensym SDX001, ±70 cmH₂O). The Pes transducer was calibrated to zero after a 10-s disconnection of the patient from the ventilator. Total respiratory system compliance (Cₐ) and lung compliance (Cₜ) were calculated with the following equations, respectively:

\[ C_R = \frac{V_T}{P_{plat} - \text{total-PEEP}} \]

\[ C_L = \frac{V_T}{(P_{plat} - \text{PES}) - (\text{total-PEEP} - \text{PES})} \]

where Pes and Pes represent end-inspiratory and end-expiratory Pes respectively. Airflow, Paw, and Pes measurements were sampled over 30 s, recorded, and processed with a PC microcomputer.

Every patient had a radial artery catheter and a pulmonary artery catheter in place. Systemic arterial pressure, pulmonary artery pressure (PAP), right atrial pressure (RAP), and PCWP were recorded at end-expiration. Transmural PAP, RAP, and PCWP were obtained by subtracting Pes from end-expiratory PAP, RAP, and PCWP, respectively. Cardiac output was measured by the thermodilution technique, and the results of five measurements taken randomly through the respiratory cycle were averaged. Arterial and mixed venous blood were sampled for measurement of Pao₂, Paco₂, and hemoglobin concentration, and for measurement of Sao₂ and Svo₂ by oximetry (ABL 30, Radiometer, Copenhagen). Arterial and mixed venous oxygen content, oxygen delivery (DO₂), and venous admixture (Qva/Qs) were calculated with the usual formulas. Expired gases were collected from the ventilator outlet in a Douglas bag over 1 min for measurement of mixed expired carbon dioxide (PecO₂), and physiologic dead space (Vd/Vₜ) was calculated according to the Bohr equation:

\[ \frac{V_d}{V_t} = \frac{P_{aco} - P_{ecO}_2}{P_{aco}} \]

A correction factor was introduced to take into account the dilution of PecO₂ due to gas compression in the ventilator tubing.

Protocol
Patients were studied in the recumbent position. They were sedated with phenoperidine and flunitrazepam infusions and paralyzed with a vecuronium infusion. The attending physician was always present, and usual patient care was continued during the study period. Patients’ lungs were ventilated with a Siemens Servo 900C ventilator at a RR of 20 min⁻¹ and a constant FiO₂ throughout the study period. The patients were first studied during VC (25% inspiratory time, 10% pause) with constant inspiratory flow. They were then randomized to receive either pressure-controlled conventional ratio (I:E 1:2) ventilation (PC 1/2: 25% inspiratory time, 10% pause) or pressure-controlled inverse ratio (I:E 2:1) ventilation (PC 2/1: 67% inspiratory time, 0% pause). VC was then re instituted, after which the lungs were ventilated in the mode they had not yet received (PC 1/2 or PC 2/1). Finally, I:E ratio was increased to 3:1 in the pressure-controlled mode (PC 3/1). At the end of the study, the ventilatory mode requested by each patient’s attending physician was reestablished. For each patient, Vₜ, Vₑ, and total-PEEP were held constant in every mode of ventilation throughout the study by setting appropriately the ventilatory pressure and external-PEEP in the pressure-controlled modes. PC 3/1 was not delivered in random order (as PC 1/2 and PC 2/1) and was always the last mode delivered in the study period. We anticipated that dynamic hyperinflation and total-PEEP might be greater than with the other modes studied, and that some patients might not tolerate the hemodynamic effects associated with this mode of ventilation. After a 30-min stabilization period in every mode, ventilatory and respiratory mechanic parameters were measured in triplicate, a complete set of hemodynamic parameters.
was obtained, arterial and mixed venous blood were sampled, and expiratory gases were collected.

Statistical analysis
Data are expressed as mean ± SD. The data obtained from the two trials in VC were first compared to detect any variation over time. Since there was no such effect, all patients were analyzed as a sole group whatever the mode (PC 1/2 or PC 2/1) they had received first. Statistical analysis was done by two-way analysis of variance to separate the ventilatory mode effect from the patient effect. Two-by-two comparisons were done with Scheffe’s test. A probability level less than 0.05 was considered significant. Statistical analysis first compared VC, PC 1/2, PC 2/1, and PC 3/1. Because total-PEEP in PC 3/1 was statistically greater than in the other modes, subsequent analysis compared only PC 1/2 and PC 2/1 with VC.

Results
Nine patients with moderate to severe ARDS related to various medical etiologies were studied (table 1). The severity of the lung injury was supported by the mean lung injury score of 2.83 ± 0.18 and the 78% mortality. Mean simplified acute physiology score was 13.4 ± 7.7. In each of these patients, the trachea was intubated and the lungs ventilated because of a direct pulmonary injury. However, only one (patient 3) died of refractory respiratory insufficiency, and patient 5 died of a tension pneumothorax nine days after the study while ventilated in VC. All others died with multiple system organ failure, or refractory shock (Patient 9).

Ventilatory parameters associated with the different ventilatory modes are reported in table 2. In all modes, RR, Vt, and Ve were comparable. Mean total-PEEP was also the same in VC, PC 1/2, and PC 2/1, but was higher in PC 3/1 (P < 0.05) although external-PEEP had been set to zero. Thus subsequent statistical analysis compared only VC, PC 1/2, and PC 2/1. Ppeak was lower in PC 1/2 and lowest in PC 2/1, while mean airway pressure (Pmean) was increased in PC 2/1. However, static airway pressures (Pplat and total-PEEP) and static compliances (Crs and Cst) were not different within these three modes. To ascertain that the same level of total-PEEP corresponded to the same level of lung volume over functional residual capacity (FRC) in VC, PC 1/2, and PC 2/1, we measured end-expiratory lung volume over FRC by passive spirometry in one patient. Blood gas, ventilatory, and hemodynamic parameters are reported in table 3. Effects on oxygenation with PC 1/2 and PC 2/1 in individual patients are reported in figure 1. PaO₂ and SaO₂ were slightly but significantly lower in PC 2/1, but venous admixture (Qva/Qt) was not statistically different. Systolic and mean arterial pressure (SAP and MAP, respectively) were lower in PC 2/1. Other hemodynamic parameters were not statistically different. Alveolar ventilation (assessed from PaCO₂ at the same Ve) tended to be slightly but not significantly more efficient in PC 2/1. Vd/VT was unchanged. Trial in PC 3/1 resulted in a higher level of total-PEEP than in other modes and was associated with hemodynamic compromise in four patients (decrease in SAP more than 15%) which imposed to terminate the PC 3/1 trial early. No other adverse effect or complication occurred during the study period.

Discussion
The objective of this study was to compare in a controlled protocol the effects of PCV with and without IRV on respiratory mechanics, cardiovascular function, and gas exchange with those of VC at the same level of ventilation (RR, Vt, Ve) and total-PEEP. This could be achieved with PC 1/2 and PC 2/1. However, PC 3/1 frequently was associated with levels of total-PEEP higher than in other modalities and had to be ended early several times because of adverse hemodynamic changes. When ventilation and total-PEEP were maintained constant, no difference in respiratory mechanic and hemodynamic parameters were observed. However, the main finding of this study was that PCV with or without IRV (1:1 E 2:1) was comparable to VC, regarding gas exchange efficiency. This refutes the common opinion that PCIRV may be superior to conventional ventilation in most patients with ARDS.

The main limitation of this study is its short-term nature. Each ventilatory mode was administered for a 30-min period, at the end of which measurements were done. It has been shown that alveolar recruitment does not occur immediately with the addition of PEEP but necessitates several breathing cycles before reaching a plateau in lung volume. However, these lung volume changes as well as the hemodynamic and gas exchange changes usually are completed within a few minutes, which is consistent with the time schedule of the protocol. However, a progressive effect over a longer time period cannot be excluded, and we cannot draw
any conclusion on a possible "time-dependent" beneficial effect of PCIRV as suggested by some authors.6,21 It must be stated that our sample may not be representative of all patients with ARDS. Five patients (1, 4, 5, 7, and 9) were studied during the early phase of ARDS, whereas the others could be considered to be in the late phase at the time of the study. Although some differences in response to PEEP and to IRV could have been expected between these two subgroups, no difference in response to PCV or PCIRV was noted on an individual basis (fig. 1). Finally we cannot exclude that different effects of PCIRV could be found in more severely hypoxemic patients who cannot be adequately ventilated with VC. Nevertheless, our results suggest

Table 2. Ventilatory and Respiratory Mechanic Parameters

<table>
<thead>
<tr>
<th></th>
<th>VC</th>
<th>PC 1/2</th>
<th>PC 2/1</th>
<th>PC 3/1</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR (min⁻¹)</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>VT (ml)</td>
<td>614 ± 89</td>
<td>612 ± 89</td>
<td>620 ± 77</td>
<td>617 ± 87</td>
</tr>
<tr>
<td>V̇e (l/min)</td>
<td>12.2 ± 1.8</td>
<td>12.1 ± 1.8</td>
<td>12.3 ± 1.5</td>
<td>12.2 ± 1.7</td>
</tr>
<tr>
<td>Airway pressures (cmH₂O)</td>
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<td></td>
</tr>
<tr>
<td>P₀peak</td>
<td>51 ± 9</td>
<td>45 ± 8*</td>
<td>39 ± 8*</td>
<td>43 ± 9</td>
</tr>
<tr>
<td>Pₘ₀</td>
<td>36 ± 8</td>
<td>36 ± 7</td>
<td>35 ± 7</td>
<td>40 ± 9</td>
</tr>
<tr>
<td>Pₘ₀</td>
<td>21 ± 2</td>
<td>22 ± 3</td>
<td>27 ± 5*</td>
<td>31 ± 7</td>
</tr>
<tr>
<td>Total-PEEP</td>
<td>12 ± 2</td>
<td>12 ± 1</td>
<td>12 ± 1</td>
<td>14 ± 3†</td>
</tr>
<tr>
<td>Static compliances (ml/cmH₂O)</td>
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<tr>
<td>RS</td>
<td>28 ± 10</td>
<td>28 ± 9</td>
<td>29 ± 9</td>
<td>26 ± 9</td>
</tr>
<tr>
<td>Lung</td>
<td>38 ± 16</td>
<td>39 ± 17</td>
<td>40 ± 15</td>
<td>35 ± 14</td>
</tr>
</tbody>
</table>

VC = volume-controlled conventional ratio (1:2) ventilation; PC 1/2 = pressure-controlled conventional ratio (1:2) ventilation; PC 2/1 = pressure-controlled inverse ratio (2:1) ventilation; RS = respiratory system. Data are expressed as mean ± SD. Except for total-PEEP, statistical analysis compares only PC 1/2 and PC 2/1 with VC (see text.

* P < 0.001; † P < 0.05 (PC 3/1 vs. all others).
that, in these conditions, PCIRV should be tried with great caution.

In this study, Ppeak was reduced with PCV, especially with IRV. This was achieved because of the decreasing inspiratory flow pattern with PCV, and the increased inspiratory time with IRV. With IRV, the same volume of gas can be insufflated in the lungs at a slower rate, thereby decreasing the resistive component of dynamic airway pressure, a large part of which is due to tracheal tube resistance.4 However, static airway pressure (Pplat) was not modified with PCV or PCIRV compared to VC. Similar Pplat values suggest that true distal Ppeak were similar in all modes and that PCIRV did not produce any significant alveolar recruitment. Given the small number of patients in our study (n = 9), a failure to detect a real difference (type II statistical error) cannot be excluded.22 However, our findings are not unexpected, because the same Vt was insufflated in the lungs with the three different modes of ventilation. Peak transalveolar pressure was not reduced, and Gs and Gk were not changed. These data suggest that, within the conditions of the study (fixed Vt and total-PEEP), the ability of PCV or PCIRV to reduce pulmonary barotrauma and alveolar injury is questionable. It is known that, in severe ARDS, only a small portion of the injured lungs receives most of the ventilation and a large part of the effect of PEEP.23–25 Reduction of Pplat and peak transalveolar pressure probably would be more relevant and can be achieved by decreasing Vt and/or total-PEEP rather than by changing the flow pattern. A different distribution of ventilation could be expected using different flow patterns, with the theoretical risk of regional hyperinflation. However, no change in Qva/Qo was observed among the different modes, indirectly suggesting that this effect, if present, was small.

The cardiovascular effects of mechanical ventilation are closely related to Pmean, through its effects on pleural pressure.26–28 Increasing the inspiratory time fraction with IRV may result in a significant increase in Pmean and may further impede venous return. Chan et al.27 reported a significant decrease in cardiac output with the institution of PCIRV when compared to PCV with an I:E ratio of 1:2. East et al.10 also reported a decrease in cardiac output with PCIRV compared to VC. In their study, total-PEEP was maintained constant, but Vt and Vd were both lower with PCIRV. At a comparable level of ventilation, cardiac output could have been decreased further. In the present study, compared to VC, no change in cardiac output was observed with PC 2/1 but it tended to decrease with PC 3/1. However, the small number of patients, the high variability of cardiac output measurements over the respiratory cycle, the low accuracy of the thermodilution technique, or the possibility of changes in tricuspid regurgitation induced by higher mean alveolar pressures may explain that we were not able to measure a small but significant decrease in cardiac output with PC 2/1 (type II statistical error).22 Although not reaching the level of significance, a trend toward an increase in arterial-tomixed venous oxygen content (C(a–v)O2) also was observed with PC 2/1 (P = 0.06). Because all patients were sedated and paralyzed, it is unlikely that oxygen consumption (V˙O2) changed during the study period and no change in calculated V˙O2 was observed. Again this could suggest a reduction in cardiac output. The significant decrease in SAP and MAP also suggested some hemodynamic effects of PCIRV (PC 2/1 and PC 3/1).

Arterial oxygenation has been reported to be improved with PCIRV.6–9 However, in this study, with total-PEEP being maintained constant when comparing PCIRV with VC, no improvement in oxygenation could be demonstrated. Moreover, mean PaO2 and SaO2 decreased with PC 2/1. Compared with VC, PaO2 was lower with PC 2/1 in six patients, higher in one, and not different in two (less than 5-mmHg difference; fig. 1). Despite a higher level of total-PEEP, arterial oxygenation with PC 3/1 was also lower than with VC. However, calculated Qva/Qo was not different. This decrease in arterial oxygenation can be better related to a lower mixed venous oxygen content, which, at a high pulmonary shunt fraction, can decrease arterial oxygenation. Lower mixed venous oxygen saturation and

Fig. 1 Change in oxygenation (PaO2) in individual patients with PC 1/2 and PC 2/1 compared with volume-controlled conventional ratio ventilation (VC).

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content may be explained by a likely depressing effect of IRV on cardiovascular function, although we were not able to detect a statistically significant change in cardiac output. Cardiovascular impairment probably accounted for the decrease in arterial oxygenation observed with PC 2/1.

Pmean, which should reflect mean alveolar pressure, has been suggested to be a major determinant of arterial oxygenation. The lengthening of inspiratory time with IRV increases Pmean. In the present study, no improvement in oxygenation and no decrease in \( \dot{Q}_{\text{VO}}/ \dot{Q}_{\text{T}} \) were observed with PC 2/1 compared with PC 1/2 and VC at the same level of total-PEEP, despite a Pmean significantly higher with PC 2/1. What is suggested here is that, when oxygenation was improved by increasing end-expiratory lung volume with PEEP, increasing Pmean had no further beneficial effect if total-PEEP is maintained constant. On the other hand, increasing Pmean may decrease oxygenation through cardiovascular impairment. East et al. also suggested that arterial oxygenation may be more closely related to total-PEEP and increase in FRC than to Pmean. Again, what is suggested here is that improvement in \( P_aO_2 \) with IRV reported in other studies should be interpreted cautiously when total-PEEP is not maintained constant. Also, no study has demonstrated that a lower total-PEEP can be used with PCIRV compared with VC, keeping Pmean constant.

Another putative advantage of PCIRV is to improve the efficiency of alveolar ventilation, resulting in a lower \( P_aCO_2 \) for the same \( \dot{V}_E \). This would allow to reduce \( \dot{V}_E \), hence the stress and the potential damage that mechanical ventilation imposes on the injured lung. In the present study, \( P_aCO_2 \) was not decreased significantly with PC 2/1, although a trend could be observed. As suggested by some authors, a small improvement in the efficiency of alveolar ventilation can be expected with PCIRV. However, the magnitude of this improvement was not sufficient to consider any clinically significant reduction in \( V_T \) or \( \dot{V}_E \).

To maintain the same level of total-PEEP (mean level 12 cmH\(_2\)O) during PCIRV as that during VC, appropriate reduction of external-PEEP on the ventilator was needed. However, when we attempted to increase the I:E ratio to 3:1, total-PEEP could be maintained at the same level in only four patients. In the five others, it increased by 20–50% despite external-PEEP set at zero on the ventilator. Pmean also markedly increased. PC 3/1 was associated with hemodynamic deterioration: decreased SAP and MAP, decreased cardiac output, and increased oxygen extraction (table 3). Pplat was increased and static compliance deteriorated (table 2), suggesting over-distention of alveolar units and increased risk of barotrauma and diffuse alveolar injury. The main determinant of dynamic hyperinflation and intrinsic-PEEP is expiratory time, not I:E ratio per se.

Therefore, considering a specific respiratory system with its compliance and its inspiratory and expiratory resistances, for a constant RR, intrinsic-PEEP and total-PEEP will increase with increasing inspiratory time fraction (increasing I:E ratio). Likewise, for a fixed inspiratory time fraction, intrinsic-PEEP and total-PEEP will increase with increasing RR. In the present study, at an RR of 20 min\(^{-1}\), expiratory times were 2.0, 1.0, and 0.75 s at I:E ratios of 1:2, 2:1, and 3:1, respectively. At this RR, with I:E ratio greater than 2:1, intrinsic-PEEP and total-PEEP may increase rapidly. Moreover, if ventilatory pressure is adjusted to keep \( V_T \) unchanged, peak transalveolar pressure also may rise to dangerous levels.

First reports on PCIRV were retrospective and claimed marked improvement in gas exchange at lower levels of external-PEEP compared with conventional ventilation. However, total-PEEP was not measured and a marked increase in end-expiratory alveolar pressure, and volume may have gone undetected. Cole et al. reported that IRV increases end-expiratory lung volume. Then the virtues of PCIRV were questioned, and it was suggested that the beneficial effect of PCIRV was related simply to intrinsic-PEEP and increase in total-PEEP. A major drawback of PCIRV is its complexity. Much closer monitoring and more frequent adjustments of ventilator settings are required. To overcome this problem, East et al. developed a computerized protocol for management of patients receiving PCIRV. PCIRV also imposes an unnatural breathing pattern, and patients require heavy sedation and paralysis. Despite these serious questions, no controlled study had compared PCIRV to conventional modes in the same conditions. Marini and Kelsen in a recent editorial emphasized the need of prospective controlled trials comparing PCIRV to conventional ventilation at fixed transalveolar pressures. To our knowledge, this is one of the first two studies with such characteristics. With a similar protocol, Mercat et al. recently reported similar findings about the effects on oxygenation of PCIRV in patients with ARDS. Although they did not assess the effects of PC 3/1, they even observed a significant reduction in cardiac output with PC 2/1.
Comparing in a short-term prospective study PCV with different I:E ratios with conventional VC while keeping total-PEEP, $V_b$, $V_t$, and RR constant, we could find no beneficial effect of PCV with or without IRV over conventional VC in patients with moderate to severe ARDS. Some authors have suggested that the beneficial effects of PCIV might be time-dependent.\(^{2,1}\) However, data supporting this clinical impression are lacking. We did not look at morbidity and mortality either, and we cannot draw any conclusion on outcome variables. These questions should be addressed in prospective randomized trials designed to compared PCIV with conventional ventilation at fixed peak and end-expiratory alveolar pressures and volumes.

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References

PRESSURE-VERSUS VOLUME-CONTROLLED VENTILATION IN ARDS


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