Pressure Controlled Inverse Ratio Ventilation in Severe Adult Respiratory Failure

R. Steven Tharratt, M.D.;†
Roblee P. Allen, M.D., F.C.C.P.;‡
and Timothy E. Albertson, M.D., Ph.D., F.C.C.P.§

Thirty-one patients with severe respiratory failure who were failing volume controlled conventional ratio ventilation were placed on pressure controlled inverse ratio ventilation (PC-IRV) for a total of 4,426 patient-hours. The PC-IRV resulted in a reduction of minute ventilation from 22±1.0 L/min (mean ± SEM) to 15±0.7 L/min. Peak inspiratory pressure (PIP) was reduced from 66±2.3 cm H₂O to 46±1.6 cm H₂O and positive end expiratory pressures (PEEP) from 15±1.0 cm H₂O to 2.5±0.5 cm H₂O. Mean airway pressure increased from 30±1.7 cm H₂O to 38±1.7 cm H₂O. Oxygenation (PaO₂) improved from 68±4.0 mm Hg to 80±4.5 mm Hg. The PaCO₂ and arterial pH were not significantly changed. There were no significant changes in mean hemodynamic pressures. A lung compromise index (FiO₂×PIP/10/PaO₂) retrospectively distinguished between successful and unsuccessful PC-IRV episodes. These data suggest that PC-IRV can be successfully and safely implemented in critically ill patients with severe respiratory failure over prolonged periods of time resulting in significant improvement in oxygenation at lower minute volume, peak airway pressure and PEEP requirements. (Chest 1988; 94:755-62)

The management of patients with respiratory failure resulting from the adult respiratory distress syndrome (ARDS) continues to present many clinical challenges and controversies. The mortality rates of approximately 50 percent from ARDS have changed little since the initial description by Ashbaugh et al,¹ despite the use of continuous positive pressure ventilation, and positive end-expiratory pressure (PEEP). The newer techniques of high frequency ventilation and extracorporeal membrane oxygenation have also proven disappointing in increasing survival.² ³ In the last five years, new mechanical ventilatory approaches have been introduced that, through advances in biomedical engineering, allow manipulation of many of the ventilatory parameters not before changeable. Despite these advances in technology, little is known about the clinical utility of many of these new ventilatory modes or their impact on the management of patients with severe ARDS that cannot be supported by "conventional" ventilatory support.

One of these "newer" modes of ventilation is pressure controlled inverse ratio ventilation (PC-IRV). This ventilation mode, which reverses the conventional inspiratory:expiratory (I:E) ratio,⁴ has been reported to achieve higher oxygenation while maintaining ventilation at lower peak airway pressures. Pressure control is used to change the inspiratory flow pattern from a square wave to a rapid exponentially decaying curve and to safely allow initiation of the subsequent breath prior to expiratory flow reaching zero (Fig 1). The use of pressure control ventilation also prevents overinflation that could result from fixed volume control ventilation. The PC-IRV is thought to recruit closed alveolar units in a more homogeneous manner than

---

*From the Division of Pulmonary and Critical Care Medicine. The University of California, Davis Medical Center, Sacramento. Presented in part at the 53rd Annual Scientific Assembly, American College of Chest Physicians, Atlanta, October 26-30, 1987.
†Senior Fellow in Pulmonary-Critical Care Medicine.
‡Assistant Clinical Professor of Medicine.
§Associate Professor of Medicine.

Manuscript received October 12; revision accepted February 10. Reprint requests: Dr. Tharratt, Division of Pulmonary Medicine, 4301 X Street, Sacramento 95817

---

**FIGURE 1.** Comparison of flow-time curves VC-CRV and PC-IRV. Note that airflow at end expiration in PC-IRV approximates 15 percent of peak expiratory airflow INSE; inspiration; EXP, expiration.
volume controlled ventilation with conventional ratios (VC-CRV). 4

Despite encouraging studies with PC-IRV in infants
with respiratory distress syndrome of the newborn, 5,6
few studies have reported the usefulness or potential
clinical role of PC-IRV in the management of adults
with ARDS. Published studies reporting on the utility
of PC-IRV in adults have included case reports, 7,8 brief
reports, 9,10 and studies in which detailed measurements
were taken only for a short period of time. 10-12 Prior to
the initiation of a prospective study to identify a
patient population that might benefit from PC-IRV, we
retrospectively analyzed our experience with PC-IRV
in patients with severe ARDS who were failing volume
controlled conventional ratio ventilation (VC-CRV).
We report here our initial experiences with 31 patients.

METHODS

Thirty three patients identified from Respiratory Therapy
department records were placed on PC-IRV at the University
of California, Davis Medical Center between July 1985 and December
1986. One medical record could not be located and one patient
never was placed on PC-IRV although the equipment was set up at
bedside. The remaining 31 patients who underwent 35 episodes
of PC-IRV comprise the study group (Table 1). Two patients did not
tolerate the attempt to institute PC-IRV leaving 29 patients and 33
PC-IRV episodes for analysis.

Patients were placed on PC-IRV at the request of their attending
physicians who had judged that the patient was failing VC-CRV. All
29 patients had severe ARDS as manifested by diffuse pulmonary
infiltrates on chest roentgenograms, arterial hypoxemia (PaO2 F60
mm Hg) despite supplemental oxygen, pulmonary artery capillary
wedge pressures (PACW) less than 30 cm H2O (uncorrected for
PEEP), and decreased thoracic compliance. All patients had peak
inspiratory pressures (PIP) greater than 40 cm H2O and either
PEEP greater than 15 cm H2O (19 PC-IRV placements), or FIO2
greater than 0.8 (20 PC-IRV placements) for at least two hours prior
to institution of PC-IRV. Sixteen PC-IRV placements occurred in
patients who manifested these severe abnormalities in all three
parameters (FIO2, PEEP and PIP). Hemodynamic monitoring
deVICES were placed at the discretion of the attending physicians
with the majority of patients having right heart catheters. All
patients had indwelling arterial catheters.

A PC-IRV episode was defined as a period of time greater than
one hour during which the I:E ratio of the ventilator in pressure
controlled mode was greater than 1:1. Two patients had two PC-
IRV episodes and one patient had three episodes of PC-IRV during
their hospital course. All multiple PC-IRV placements were sepa-

Table I—Clinical Features and Course of Patients Placed on PC-IRV

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age-Sex</th>
<th>Conditions Leading to Respiratory Failure</th>
<th>Time to PC-IRV</th>
<th>Time on PC-IRV</th>
<th>Successful</th>
<th>Hospitalization (Days/Survived)</th>
<th>Subgroup</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12 F</td>
<td>Auto accid. C-5 quadruparesis</td>
<td>102</td>
<td>115</td>
<td>Yes</td>
<td>28-Y es</td>
<td>Surgical</td>
</tr>
<tr>
<td>2</td>
<td>33 M</td>
<td>Intentional gasoline ingestion</td>
<td>228</td>
<td>358</td>
<td>Yes</td>
<td>56-Y es</td>
<td>Medical</td>
</tr>
<tr>
<td>3</td>
<td>72 M</td>
<td>Auto accident with blunt trauma</td>
<td>109</td>
<td>23</td>
<td>Yes</td>
<td>14-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>4</td>
<td>60 M</td>
<td>Stab wounds to chest and abdomen</td>
<td>206</td>
<td>23</td>
<td>Yes</td>
<td>56-Y es</td>
<td>Surgical</td>
</tr>
<tr>
<td>5</td>
<td>30 M</td>
<td>Auto accid. 80% full thickness burns</td>
<td>208</td>
<td>36</td>
<td>No</td>
<td>11-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>6</td>
<td>33 F</td>
<td>Motorcycle accid. lower ext fracture</td>
<td>496</td>
<td>96</td>
<td>No</td>
<td>23-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>7</td>
<td>38 M</td>
<td>Penile cellulitis</td>
<td>643</td>
<td>1056</td>
<td>No</td>
<td>72-No</td>
<td>Medical</td>
</tr>
<tr>
<td>8</td>
<td>74 M</td>
<td>Stab wounds to chest</td>
<td>348</td>
<td>462</td>
<td>Yes</td>
<td>90-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>9</td>
<td>22 M</td>
<td>Heroin ingestion</td>
<td>7</td>
<td>36</td>
<td>Yes</td>
<td>6-Y es</td>
<td>Medical</td>
</tr>
<tr>
<td>10</td>
<td>24 M</td>
<td>Auto accid. with blunt trauma</td>
<td>20</td>
<td>30</td>
<td>Yes</td>
<td>6-Y es</td>
<td>Surgical</td>
</tr>
<tr>
<td>10-2</td>
<td></td>
<td></td>
<td>123</td>
<td>23</td>
<td>No</td>
<td>6-No</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>40 M</td>
<td>Blunt abdominal trauma</td>
<td>454</td>
<td>31</td>
<td>No</td>
<td>10-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>12</td>
<td>25 F</td>
<td>Motorcycle accident multiple fractures</td>
<td>112</td>
<td>27</td>
<td>No</td>
<td>16-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>13</td>
<td>60 M</td>
<td>E coli sepsis</td>
<td>373</td>
<td>18</td>
<td>Yes</td>
<td>24-No</td>
<td>Medical</td>
</tr>
<tr>
<td>14-1</td>
<td>53 M</td>
<td>Perforated duodenal ulcer</td>
<td>6</td>
<td>47</td>
<td>Yes</td>
<td>6-Y es</td>
<td>Surgical</td>
</tr>
<tr>
<td>14-2</td>
<td></td>
<td></td>
<td>63</td>
<td>150</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14-3</td>
<td></td>
<td></td>
<td>528</td>
<td>354</td>
<td>No</td>
<td>36-No</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>57 M</td>
<td>Auto accid. multiple trauma</td>
<td>23</td>
<td>44</td>
<td>Yes</td>
<td>43-Y es</td>
<td>Surgical</td>
</tr>
<tr>
<td>16</td>
<td>45 M</td>
<td>20% full and partial thickness burns</td>
<td>365</td>
<td>35</td>
<td>No</td>
<td>16-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>17</td>
<td>39 M</td>
<td>Stab wound to chest</td>
<td>259</td>
<td>184</td>
<td>No</td>
<td>23-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>18</td>
<td>19 F</td>
<td>Lupus cerebritis and aspiration</td>
<td>986</td>
<td>22</td>
<td>No</td>
<td>43-No</td>
<td>Medical</td>
</tr>
<tr>
<td>19</td>
<td>30 M</td>
<td>Auto accident with multiple trauma</td>
<td>552</td>
<td>343</td>
<td>Yes</td>
<td>96-Y es</td>
<td>Surgical</td>
</tr>
<tr>
<td>20</td>
<td>24 M</td>
<td>70% full thickness burn</td>
<td>26</td>
<td>44</td>
<td>No</td>
<td>12-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>21</td>
<td>18 F</td>
<td>Auto accid. 23 weeks pregnant</td>
<td>344</td>
<td>56</td>
<td>No</td>
<td>12-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>22</td>
<td>23 F</td>
<td>Pneumonia</td>
<td>82</td>
<td>Unsuccessful</td>
<td>PC-IRV attempt</td>
<td>4-No</td>
<td>Medical</td>
</tr>
<tr>
<td>23</td>
<td>65 M</td>
<td>Legionella sepsis</td>
<td>29</td>
<td>51</td>
<td>No</td>
<td>4-No</td>
<td>Medical</td>
</tr>
<tr>
<td>24-1</td>
<td>42 M</td>
<td>Orthotrophic liver transplant</td>
<td>118</td>
<td>67</td>
<td>Yes</td>
<td>6-Y es</td>
<td>Surgical</td>
</tr>
<tr>
<td>24-2</td>
<td></td>
<td></td>
<td>250</td>
<td>18</td>
<td>No</td>
<td>12-No</td>
<td>Medical</td>
</tr>
<tr>
<td>25</td>
<td>33 M</td>
<td>Hodgkins disease</td>
<td>298</td>
<td>17</td>
<td>No</td>
<td>13-No</td>
<td>Medical</td>
</tr>
<tr>
<td>26</td>
<td>49 M</td>
<td>Pancreatitis</td>
<td>422</td>
<td>5</td>
<td>Yes</td>
<td>72-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>27</td>
<td>42 M</td>
<td>Closed head injury 25% burns</td>
<td>104</td>
<td>140</td>
<td>No</td>
<td>10-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>28</td>
<td>30 M</td>
<td>Orthotrophic liver transplant</td>
<td>246</td>
<td>7</td>
<td>No</td>
<td>11-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>29</td>
<td>32 M</td>
<td>Auto accid. with blunt trauma</td>
<td>52</td>
<td>63</td>
<td>Yes</td>
<td>6-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>30</td>
<td>33 M</td>
<td>Pancreatitis</td>
<td>13</td>
<td>6</td>
<td>No</td>
<td>1-No</td>
<td>Surgical</td>
</tr>
<tr>
<td>31</td>
<td>18 M</td>
<td>90% full thickness burns</td>
<td>8</td>
<td>Unsuccessful</td>
<td>PC-IRV attempt</td>
<td>25-No</td>
<td>Surgical</td>
</tr>
</tbody>
</table>
rated by a minimum of 48 hours except for one episode separated by 12 hours.

A successful PC-IRV episode was defined as patient survival during PC-IRV and for 24 hours after resumption of conventional volume controlled ventilation or pressure controlled ventilation with I:E ratios no greater than 1:1. An unsuccessful PC-IRV episode was defined as death from any cause while on PC-IRV or within 24 hours after discontinuance of PC-IRV. An unsuccessful PC-IRV placement attempt was further defined as a patient who remained on PC-IRV for less than one hour due to respiratory and/or hemodynamic instability. Barotrauma was defined as any pneumothorax that required placement of a thoracostomy tube while the patient was on PC-IRV. Time to institution of PC-IRV was calculated in hours from admission to the initiation of any inspiratory:expiratory ratio greater than 1:1. Time on PC-IRV was defined as the period of time the I:E ratio was greater than 1:1. Figure 2 shows a graphic representation of the course of PC-IRV in this study. The oxygen index was calculated as PaO₂/FIO₂ (mm Hg). Total thoracic compliance was estimated as [inspired tidal volume/PIP-PEEP], a lung compromise index (LCI) was calculated as (FIO₂/PIP/PaO₂). All data before and after institution of PC-IRV are reported as mean ± standard error of the mean. Statistical significance was determined with Student's t-test (paired for before and after PC-IRV calculations) or the Wilcoxon signed-rank test at the p = 0.05 level. The oxygen index, estimated thoracic compliance, and the LCI were additionally analyzed at one hour, six hours, 12 hours, 24 hours after institution of PC-IRV and at conversion to VC-CRV or death by the multiple analysis of variance (ANOVA) with repeated measures.

Method of Placing Patients on PC-IRV

Once the decision was made to employ PC-IRV, the patient was placed on a ventilator (Siemens Servo 900C) functioning in volume controlled ventilation mode. An end-tidal CO₂ monitor was placed in the ventilator circuit and a pulse oximeter placed on a digit of the patient. Rapid shifts in these parameters were often observed and carefully monitored during conversion to, and stabilization on PC-IRV. An oscilloscope for observing the ventilator flow patterns was connected to the output jack on the ventilator. All monitors were stabilized and their accuracy confirmed with an arterial blood gas determination prior to conversion to PC-IRV. All patients had continuous monitoring of arterial blood pressure. All patients were sedated with appropriate doses of benzodiazepines and/or narcotics and paralyzed with nondepolarizing neuromuscular blocking agents (pancuronium bromide or vecuronium bromide). Neuromuscular blockade was continued for the duration of PC-IRV in all of the patients.

An estimate of the required inspiratory pressure was made prior to conversion to PC-IRV by subtracting PEEP from the PIP required to give a tidal volume of 15 to 20 ml/kg on volume control ventilation. The patient was then converted from volume control mode to pressure control mode at an inspiratory:expiratory ratio of 2:1 (an inspiratory time of 67 percent, and an expiratory hold time of 33 percent) while simultaneously reducing the PEEP to one half of its initial value. The PEEP was then rapidly reduced to low levels (0 to 2 cm H₂O). The inspiratory pressure was readjusted to provide exhaled tidal volumes of 15 to 20 ml/kg (the required pressure usually fell during the first hour on PC-IRV). The respiratory rate was adjusted in such a fashion that zero expiratory flow was not reached prior to the triggering of the next breath (expiratory flow rate 5 to 15 percent of peak flow) utilizing the flow curve on the oscilloscope. Gas exchange as measured by carbon dioxide retention was maintained by further adjustments in the respiratory rate.

If improvement in arterial oxygen saturation was not observed in 10 to 15 minutes, an attempt was made to increase the l:E ratio to increments to 4:1. This was followed by small incremental increases in PEEP to levels of 4 to 8 cm H₂O if necessary to improve oxygenation. Carbon dioxide retention was treated either by reducing the respiratory rate to allow more expiratory time or by reducing PEEP to increase the pressure gradient for expiratory gas flow. A smooth transition to PC-IRV usually required one to two respiratory therapists, a nurse, and a physician trained in PC-IRV in attendance at the bedside during the conversion, and stabilization period of approximately one hour.

Results

Table 1 summarizes the demographic characteristics of our study population. The average age was 38 ± 3.2 years (range 12 to 74). There was a significant difference in ages between male (42 ± 8.4 years) and female subjects (22 ± 2.6 years). The patients were divided into medical and surgical subgroups on the basis of admitting diagnosis and the service that had primary responsibility for their care. There was no significant difference between subgroups with respect to average time to institution of PC-IRV (medical 330 ± 119 hours, surgical 207 ± 127 hours), or time on PC-IRV (medical 216 ± 127 hours, surgical 99 ± 24 hours). The frequency of successful PC-IRV episodes, unsuccessful PC-IRV episodes, and survival from hospitalization were also not significantly different in the medical and surgical subgroups. The length of hospitalization and intensive care stay was significantly different between hospital survivors and nonsurvivors (survivors 51.2 ± 11 days, nonsurvivors 20.6 ± 4.3 days p = 0.01 by Wilcoxon). The total time spent on PC-IRV was not significantly different between the survivors and nonsurvivors (survivors 136 ± 87 hours, nonsurvivors 132 ± 31 hours). The time to institution of PC-IRV also was not different between the two groups (survivors 162 ± 188 hours, nonsurvivors 269 ± 235 hours). The study group together accounted for 4,426 patient-hours (185 patient-days) of experience with PC-IRV.

Figure 2. Study flowchart.
AIRWAY PRESSURES
VC-CRV AND PC-IRV

BLOOD GAS PARAMETERS
VC-CRV AND PC-IRV

Figure 3. Comparison of airway pressures and blood gas parameters between PC-IRV and VC-CRV. Values expressed as mean ± SEM significance values determined by paired Student’s t-test.

Figure 3 summarizes the ventilatory and blood gas changes that occurred immediately surrounding institution of PC-IRV. There was a significant reduction in PIP and PEEP together with a significant increase in mean airway pressure (Paw). The PaO₂ and PaO₂/FIO₂ were both significantly improved, and there was no significant change in PaCO₂. Minute ventilation decreased from 22 ± 1.0 L/min to 15 ± 0.7 L/min (p<0.001). There was no significant change in arterial pH (7.33 ± 0.01 to 7.36 ± 0.01).

There was no significant difference in any of the ventilatory or blood gas parameters between the successful and unsuccessful PC-IRV groups prior to institution of PC-IRV (Table 2).

Table 2—Ventilatory Parameters Before Institution of PC-IRV: Successful and Unsuccessful PC-IRV Episodes

<table>
<thead>
<tr>
<th></th>
<th>V̇E (L/min)</th>
<th>PIP (cmH₂O)</th>
<th>Paw (cmH₂O)</th>
<th>PEEP (cmH₂O)</th>
<th>PaO₂ (mm Hg)</th>
<th>PaCO₂ (mm Hg)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful</td>
<td>21 ± 1.4</td>
<td>62 ± 3.0</td>
<td>29 ± 1.7</td>
<td>14 ± 1.5</td>
<td>92 ± 11</td>
<td>71 ± 6.4</td>
<td>41 ± 2.0</td>
</tr>
<tr>
<td>episodes</td>
<td>n = 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unsuccessful</td>
<td>23 ± 1.6</td>
<td>64 ± 6.8</td>
<td>32 ± 2.4</td>
<td>15 ± 1.7</td>
<td>90 ± 11</td>
<td>65 ± 4.7</td>
<td>47 ± 1.6</td>
</tr>
<tr>
<td>episodes</td>
<td>n = 18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All differences not significant

Table 3 summarizes the calculated ventilatory parameters of oxygen index, estimated static compliance, and the lung compromise index before, after, and at six hours, 12 hours, 24 hours after institution of PC-IRV and the final value before death or return to VC-CRV. Only patients who survived for 24 hours were included in these analyses (n=12 for both the successful and unsuccessful PC-IRV groups). A significant difference (p≤0.001) in the LCI was seen at all times after institution of PC-IRV (F₅,₂₅ = 21) despite no significant differences in the LCI at the time of placement on PC-IRV between the successful and unsuccessful episodes (Fig 4). There was also a significant difference (p≤0.05) in the oxygen index at all times after institution of PC-IRV (F₅,₂₅ = 5.5). There was no significant difference in the estimated thoracic compliance between successful and unsuccessful episodes after institution of PC-IRV.

There was no significant difference in mean arterial pressure (85 ± 3.0 to 87 ± 3.0 mm Hg), mean pulmonary artery pressure (38 ± 2.0 to 36 ± 2.3 mm Hg), and pulmonary artery capillary wedge pressure (19 ± 1.2 to 17 ± 1.4 mm Hg) before and after institution of PC-IRV or during return from PC-IRV to VC-CRV for all subjects. Cardiac output as measured by thermodilution methods varied dramatically in individual patients depending on the part of the ventilatory cycle that the indicator injection occurred. Since the timing of the injection could not be retrieved from the charts, no comment on any significant differences in cardiac output can be made. Adequate data concerning mixed venous oxygen saturations was not available to allow conclusions to be made on the effects of PC-IRV on oxygen transport.

There were eight incidences of pneumothorax while on PC-IRV (Table 4). The number of pneumothoraces roughly paralleled the distribution of time at each of the PC-IRV ratios.

There were two attempts to institute PC-IRV that were not tolerated. The first patient was a 23-year-old black woman with severe ARDS from a presumed viral etiology. Ventilator settings prior to the attempt at PC-IRV were minute volume of 21.2 L/min, PIP of 74 cm H₂O, PEEP of 24 cm H₂O, and FIo₂ of 1. These parameters yielded an arterial PaO₂ of 80 mm Hg, PaCO₂ of 41 mm Hg, and pH of 7.4. Hemodynamic...
parameters included a mean arterial pressure of 115 mm Hg, heart rate of 131, mean pulmonary artery pressure of 37 mm Hg, and a pulmonary artery capillary wedge pressure of 14 mm Hg. Cardiac output was 5.42 L/min. Institution of PC-IRV with an I:E ratio of 2:1 resulted in prompt oxygen desaturation to 79 percent, this desaturation worsened to 77 percent despite increasing the I:E ratio to 4:1, and the addition of 8 cm H₂O of PEEP. At that point, mean arterial pressures declined to 60 mm Hg, and the patient was returned to conventional ratio volume control ventilation. After an infusion of 1,000 ml of saline, with PEEP settings of 32 cm H₂O, PIP of 93 cm H₂O and a PaO₂ of 52 mm Hg, another attempt to institute PC-IRV was made. Immediate oxygen desaturations to 78 percent were again observed with the conversion to PC-IRV. The VC-CRV was continued, and the patient died approximately four hours later from refractory hypoxemia and respiratory acidosis.

The second patient was an 18-year-old white man with 90 percent total body surface area full thickness burns who was hypoxicemic (PaO₂ 54 mm Hg) on an FIO₂ of 1, with peak inspiratory pressures of 95 cm H₂O, PEEP of 30 cm H₂O, and a minute ventilation of 36 L/min. He was hypotensive with mean arterial pressures of 68 mm Hg and was receiving intravenous fluids at 600 ml/hr. The patient suffered a cardiac arrest (bradyarrhythmia) when pressure control was instituted prior to inversion of the inspiratory:expiratory ratios, and he failed to respond to resuscitation. It could not be determined if the cardiac arrest was secondary to the change made in the ventilator or if the two events were coincidental in this moribund patient.

**DISCUSSION**

Current management of ARDS utilizing mechanical ventilation, supplemental oxygen, and PEEP, has changed little over the last ten years. Limiting factors in this supportive therapy have included the development of normobaric oxygen toxicity, pulmonary barotrauma, and hemodynamic instability from the positive pressures employed.

The overall goal in treatment of ARDS has been to recruit and stabilize closed, potentially functional alveolar units while minimizing inhomogeneity of expansion, shear forces, and barotrauma. Ideally, this should be accomplished in such a way that keeps the FIO₂ to the minimum acceptable, allows for CO₂ excretion, an appropriate cardiac output, acceptable vascular pressures, and adequate oxygen transport. Clearly, all current modes of ventilatory therapy balance effects on ventilatory and hemodynamic parameters while trying to effect an overall improvement in

---

**Table 3—Calculated PC-IRV Indices Successful and Unsuccessful PC-IRV Episodes**

<table>
<thead>
<tr>
<th></th>
<th>Before PC-IRV</th>
<th>After PC-IRV</th>
<th>6 Hours</th>
<th>12 Hours</th>
<th>24 Hours</th>
<th>Last PC-IRV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen index (PaO₂/FIO₂)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful episodes n = 12</td>
<td>78±9.2</td>
<td>104±15</td>
<td>110±11</td>
<td>126±12</td>
<td>124±9.2</td>
<td>194±24</td>
</tr>
<tr>
<td>Unsuccessful episodes</td>
<td>111±16</td>
<td>115±23</td>
<td>97±14</td>
<td>96±17</td>
<td>93±16</td>
<td>90±17</td>
</tr>
<tr>
<td>Estimated thoracic compliance (Tidal volume/PIP-PEEP)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful episodes n = 12</td>
<td>24±1.8</td>
<td>24±1.9</td>
<td>22±2.2</td>
<td>26±3.2</td>
<td>27±3.4</td>
<td>29±2.9</td>
</tr>
<tr>
<td>Unsuccessful episodes</td>
<td>17±1.4</td>
<td>20±2.2</td>
<td>20±1.7</td>
<td>18±1.2</td>
<td>16±0.8</td>
<td></td>
</tr>
<tr>
<td>Lung compromise index (FIO₂-PIP-10 / PaO₂)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful episodes n = 12</td>
<td>8.9±1.8</td>
<td>4.2±0.8</td>
<td>4.3±0.6</td>
<td>3.6±0.4</td>
<td>2.5±0.4</td>
<td>2.6±0.7</td>
</tr>
<tr>
<td>Unsuccessful episodes</td>
<td>6.9±1.4</td>
<td>5.4±0.8</td>
<td>6.2±0.7</td>
<td>6.9±1.0</td>
<td>6.9±1.2</td>
<td>8.1±1.2</td>
</tr>
</tbody>
</table>

---

**Figure 4.** Time course of the lung compromise index between successful and unsuccessful PC-IRV episodes. Last is the last value before conversion to VC-CRV or death; n = 12 for both successful and unsuccessful PC-IRV episodes.

---

**Table 4—Relation of Barotrauma to PC-IRV**

<table>
<thead>
<tr>
<th>PC-IRV Ratio</th>
<th>No. of Pneumothoraces (%)</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.0:1</td>
<td>4/8 (50)</td>
<td>74</td>
</tr>
<tr>
<td>2.5:1</td>
<td>1/8 (12)</td>
<td>15</td>
</tr>
<tr>
<td>3.3:1</td>
<td>2/8 (25)</td>
<td>1</td>
</tr>
<tr>
<td>4.0:1</td>
<td>1/8 (12)</td>
<td>10</td>
</tr>
</tbody>
</table>

*Ratio = I:E ratio; % of total PC-IRV time spent at each I:E ratio.
Patients who underwent PC-IRV in this study had demonstrated a poor response to VC-IRV by manifesting continued arterial hypoxemia and/or elevated airway pressures. A wide range of medical and surgical conditions predisposed our patients to ARDS. In this study, PC-IRV generally was not utilized until several days into the patient's hospital course. This may have reflected progressive illness or complications of the initial injuries that led to worsening respiratory function.

Mortality was specifically not utilized as an endpoint in our study. Mortality in patients with ARDS is in excess of 50 percent in a nonselected patient population, and as high as 92 percent in one study where the patients were selected for severe ARDS. Our study group is biased toward high mortality rates because these patients were selected for severe, often refractory ARDS. Further, the study size is small, without matched control subjects and our analysis retrospective making any mortality comparisons difficult. Consistent with previous reports on ARDS, a significant number of our patients died of nonrespiratory complications of their illnesses (renal failure, cardiac arrhythmias, or Gram-negative sepsis). The difference in hospital and intensive care stay between survivors and nonsurvivors probably reflects the concomitant illnesses in the survivors and time spent in rehabilitation as the total time spent on PC-IRV and the time to institution of PC-IRV was not significantly different between the two groups.

Significant decreases in minute ventilation ($V_T$), PIP, and PEEP occurred in patients placed on PC-IRV. Since no significant change occurred in PaCO$_2$, this implies some combination of a reduction in dead space to tidal volume ratio ($V_D/V_T$), an improvement in ventilation perfusion matching ($V_a/Q$) possibly secondary to more efficient recruitment of ventilation perfusion surface area, and/or improvement in shunt ($Q_s/Q_t$). No data on shunt fractions was available in our patients but other authors have reported decreases in $Q_s/Q_t$ with PC-IRV in both animal models and limited clinical series.

One mechanism by which PC-IRV is thought to exert its beneficial effect on $\text{PaO}_2/\text{FiO}_2$ is through increases in functional residual capacity (FRC). Increased FRC has also been postulated as a mechanism for the effects attributed to PEEP. Cole et al compared the effects of I:E ratios and PEEP on external end-expiratory volume (EEEV) as approximated by changes measured by respiratory inductance plethysmography. The EEEV was increased by PC-IRV an average of 1,200 ml. Similar changes in EEEV could be produced by an average of 12.8 cm H$_2$O of PEEP. However, improvement in oxygenation and ventilation could also be demonstrated by ratios of 1.1:1 and 1.7:1 that did not significantly change the EEEV. This may be due to the pattern of inspiratory gas flow which is a function of both the I:E ratio and pressure control mode. The PC-IRV produces an initially high inspiratory flow followed by a rapidly decelerating flow pattern compared to the constant flow pattern seen in volume controlled ventilation. (Fig 1). This decelerating flow pattern has been shown to produce an improvement in oxygenation in oleic acid injured canine lungs and in patients on intermittent positive pressure ventilation. An additional benefit from the flow pattern may occur through the lengthening of the expiratory time constant. High inspiratory flow rates have been shown to improve gas exchange and provide for a more even distribution of ventilation to lung units with long expiratory time constants. The increased time constant may augment the increase in FRC in a manner different from PEEP effects.

Another presumed benefit of PC-IRV is that the improvement seen in oxygenation occurs at significantly lower PIP and PEEP than VC-IRV. High airway pressures are associated with increased lung damage in both human and animal studies. High PIP is often cited as the major determinant of risk for barotrauma and may result in shear forces at the alveoli that are significant. The PC-IRV may reduce these shear forces by producing a more even inflation and stabilization of the terminal respiratory structures.

Early in our experience with PC-IRV, we adjusted ventilatory ratios and pressures based on clinical response. As our experience increased we searched for a numerical index that could objectively assist in guiding PC-IRV therapy. The lung compromise index reflects both the effectiveness of oxygenation and the effect of peak inspiratory pressures on the lung. This descriptive index retrospectively distinguished between successful and unsuccessful PC-IRV episodes in our patients. It is similar to the lung lesion index proposed by Lachmann et al except that a larger value implies increased lung compromise, both through the effects of peak airway pressure and inspired concentrations of oxygen. The possible predictive value of this index cannot be assessed from our retrospective data, but the LCI may serve as an objective measure together with other parameters of respiratory and hemodynamic status in accessing the response to PC-IRV.

The significant reductions in PIP and PEEP seen with PC-IRV were accompanied by a small but significant increase in Paw. The relation between Paw and oxygenation appears complex. Several investigators have suggested a role between mean airway pressure and oxygenation, while others have failed to find a relationship. It seems an oversimplification to directly attribute all the improvement in oxygenation
seen in our patients to the average 4 cmH₂O increase in Paw. Increasing the level of PEEP to produce a 4 cmH₂O increase in Paw alone in VC-CRV did not produce a similar increase in oxygenation.

The logistics of maintaining PC-IRV were not as difficult as first anticipated. Neuromuscular blockade with sedation was successfully maintained for prolonged periods of time without apparent physical or psychologic harm. Survivors who underwent PC-IRV were largely amnestic for the period of time PC-IRV was maintained. No episode of mechanical or equipment failure occurred that compromised a patient’s oxygenation or ventilation status during this study. Prolonged paralysis is not without risks, and our lack of complications was partially due to continuous monitoring by experienced ICU staff. Patients were safely transported to radiology examinations and the operating rooms using a “transport module” consisting of a ventilator with a portable power supply and compressed oxygen and air tanks. Five fiberoptic bronchoscopies were performed on patients undergoing PC-IRV without changes in either hemodynamics or oxygenation. One female patient, 23 weeks pregnant and suffering from severe ARDS resulting from a fat embolism secondary to a femur fracture, underwent successful emergency cesarean section while on PC-IRV without changes in either hemodynamics or oxygenation.

The PC-IRV presents some theoretical advantages over other new ventilatory approaches. The equipment and technology required to implement PC-IRV is present or easily obtainable by most hospitals. Dedicated equipment to this ventilatory mode is not required, patients can be transported while on PC-IRV, and invasive vascular access is not required. It is important to prove prospectively the effectiveness and define the patient population that would benefit most from PC-IRV. We were unable to identify any subgroup from our small series that had disproportionate benefit or potential harm. Patients hypoxic on conventional ratio ventilation who have no other alternatives might benefit from a trial of PC-IRV.

These data show that PC-IRV can be successfully and safely implemented in critically ill patients with severe ARDS over prolonged periods of time. The PC-IRV resulted in significant improvement in oxygenation compared to VC-CRV with reduced peak airway pressures and PEEP requirements. These observations suggest that PC-IRV appears to complement VC-CRV in a subset of patients with severe ARDS; it does not replace VC-CRV. Additional studies are needed to prospectively compare PC-IRV and VC-CRV and to better define the clinical role of PC-IRV in ARDS. To extend Perel’s analogy, PC-IRV may prove to be a powerful motor car that allows the skillful physician to better maneuver on the often rocky road of ARDS.

ACKNOWLEDGMENT: The authors wish to thank Kathy Grace, RRT, RCP, Rusty Reid, RCF, Vance Wilson, RRT, RCP, Steve Kutler, RRT, RCP, and the respiratory therapists of the University of California Davis Medical Center intensive care units for their expert technical assistance in the management of the patients undergoing PC-IRV.

REFERENCES
Plan to Attend
55th Annual Scientific Assembly —
XVI World Congress on Diseases of the Chest

BOSTON 1989
ACCP

Boston • October 30–November 2, 1989

19 Modell HI, Cheney FW. Effects of inspiratory flow pattern on
gas exchange in normal and abnormal lungs. J Appl Physiol
1979; 42:1103-07
20 Al-Saad N, Bennett ED. Decelerating inspiratory flow wave-
form improves lung mechanics and gas exchange in patients on
intermittent positive-pressure ventilation. Intensive Care Med
1985; 11:69-75
21 Connors AF, McCaffree DR, Gray BA. Effect of inspiratory
flow rate on gas exchange during mechanical ventilation. Am Rev
Respir Dis 1981; 124:537-43
22 Lhghizadeh A, Renolds EOR. Pathogenesis of bronchopulmonary
dysplasia following hyaline membrane disease. Am J Pathol
1976:241-46
23 Kolobow T, Moretti MP, Fumagalli R, Mascheroni D, Prato F,
Chen V, et al. Severe impairment in lung function induced by
high peak airway pressure during mechanical ventilation. Am
Rev Respir Dis 1987; 135:312-15
24 Hughes JMB, Hoppin FG, Mead J. Effect of lung inflation on
bronchial length and diameter in excised lungs. J Appl Physiol
1972; 32:25-35
25 Bowe EA, Bowe RL, Klein EF, Buckwalter JA. CPAP vs PEEP:
mean airway pressure does not determine oxygenation. Anes-
thesiology 1983; 59:A106
26 Berman LS, Downs JB, Van Eeden A, Delhagen D. Inspiration:
expiration ratio: is mean airway pressure the difference?
Crit Care Med 1981; 9:775-77
27 Op de Coul AAW, Lambregts PCLA, Koeman J, Van Puyenbroek
MJE, Ter Laak NJ, Gabreels-Festen AAWM. Neuromuscular
complications in patients given pancuronium bromide during
artificial ventilation. Clin Neurol Neurosurg 1985; 87:17-22
28 Kupfer Y, Okrent DG, Twersky RA, Tessler S. Disuse atrophy
in a ventilated patient with status asthmaticus receiving neu-
29 Perel A. Newer ventilation modes—temptations and pitfalls.
Crit Care Med 1987; 15:707-09