Optimal Mean Airway Pressure during High-frequency Oscillation

Predicted by the Pressure-Volume Curve

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Background: A number of groups have recommended setting positive end-expiratory pressure during conventional mechanical ventilation in adults at 2 cm H_2O above the lower corner pressure (P_{CL}) of the inspiratory pressure–volume (P-V) curve of the respiratory system. No equivalent recommendations for the setting of the mean airway pressure (P_{aw}) during high-frequency oscillation (HFO) exist. The authors questioned if the P_{aw} resulting in the best oxygenation without hemodynamic compromise during HFO is related to the static P-V curve in a large animal model of acute respiratory distress syndrome.

Methods: Saline lung lavage was performed in seven sheep (28 ± 5 kg, mean ± SD) until the arterial oxygen partial pressure/fraction of inspired oxygen ratio decreased to 85 ± 27 mmHg at a positive end-expiratory pressure of 5 cm H_2O (initial injury). The P_{CL} (20 ± 1 cm H_2O) on the inflation limb and the point of maximum curvature change (PMC; 26 ± 1 cm H_2O) on the deflation limb of the static P-V curve were determined. The sheep were subjected to four 1-h cycles of HFO at different levels of P_{aw} (P_{CL} + 2, + 6, + 10, + 14 cm H_2O), applied in random order. Each cycle was preceded by a recruitment maneuver at a sustained P_{aw} of 50 cm H_2O for 60 s.

Results: High-frequency oscillation with a P_{aw} of 6 cm H_2O above P_{CL} (P_{aw} + 6) resulted in a significant improvement in oxygenation (P < 0.01 vs. initial injury). No further improvement in oxygenation was observed with higher P_{aw}, but cardiac output decreased, pulmonary vascular resistance increased, and oxygen delivery decreased at P_{aw} greater than P_{CL} + 6. The PMC on the deflation limb of the P-V curve was equal to the P_{CL} + 6 (r = 0.77, P < 0.05).

Conclusion: In this model of acute respiratory distress syndrome, optimal P_{aw} during HFO is equal to P_{CL} + 6, which correlates with the PMC.

Materials and Methods

The following protocol was approved by the Subcommittee on Research Animal Care of the Massachusetts General Hospital. Animals were managed according to the Guiding Principles in the Care and Use of Animals of the National Institutes of Health.

Anesthesia and Instrumentation

Eight fasted Dorset sheep (28 ± 5 kg) were orotracheally intubated (Hi-Lo Jet Tracheal Tube, 9.0-mm ID; Mallinckrodt Laboratories Ltd., Athlone, Ireland) during halothane mask anesthesia. To ensure gastric drainage, a nasogastric tube (151-14, 14-French; Mallinckrodt Laboratories Ltd.) was also inserted. The external jugular vein was then cannulated, and an 8-French sheath introducer (Avanti+; Cordis, Miami, FL) was inserted using the Seldinger technique. After line placement, the anesthetic was switched to total intravenous anesthesia with a loading dose of 10 mg/kg pentobarbital, 3 mg/kg ketamine, and 0.1 mg/kg pancuronium followed by contin-
Fig. 1. Schematic providing details of the experimental protocol and the time line for each experiment. HFO = high-frequency oscillation; RM = recruitment maneuver; BL = baseline pressure measurements; CMV = conventional mechanical ventilation; $P_{aw}$ = mean airway pressure.

Experimental Protocol

After a stabilization period of 60 min, baseline measurements, including pulmonary gas exchange, hemodynamics, and a static inflation and deflation P-V curve of the respiratory system were obtained. Severe lung injury was then produced by bilateral lung lavage with 30-mL/kg instillations of isotonic saline warmed to 39°C. After establishing intravenous anesthesia, surgical cannulation of the femoral artery was performed, and a pulmonary artery catheter (Model 131HF7; Baxter Healthcare Corp., Irvine, CA) was inserted via the 8-French sheath introducer. Maintenance of intravascular volume was achieved by infusion of lactated Ringer solution (20 ml·kg$^{-1}$·h$^{-1}$). A heating blanket was used to maintain core temperature of 39°C. Basic ventilator settings (NPB 7200ae ventilator; Nellcor-Puritan-Bennett, Carlsbad, CA) were volume control at a respiratory rate of 15 breaths/min, tidal volume of 12 mL/kg, inspiratory to expiratory ratio of 1:2 with an inspiratory plateau time of 0.7 s, fraction of inspired oxygen ($F(IO_2)$) of 1.0, and positive end-expiratory pressure (PEEP) of 5 cm H$_2$O. The respiratory rate was adjusted to achieve normoventilation (arterial carbon dioxide partial pressure = 35–45 mmHg) at baseline.

Hemodynamics. Systemic arterial pressure, pulmonary artery pressure, and central venous pressure were monitored using pressure transducers (Model 1280C; Hewlett Packard, Waltham, MA) with the zero level at mid-thorax in the supine position. Pulmonary artery wedge pressure and central venous pressure were measured at end expiration. Cardiac output was measured in triplicate by thermodilution technique (Cardiac Output Computer 9520A; American Edwards Laboratory, Irvine, CA).

Gas Exchange. Paired arterial and mixed venous blood samples were drawn and analyzed at each measurement point (Model 238; Ciba Corning Diagnostics Corp., Norwood, MA). Hemoglobin content and oxygen saturation were also measured (Model 282; Instrumentation Laboratory, Lexington, MA). The venous admixture ($Qs/Qt$) was calculated using the standard equation:

$$Qs/Qt = \frac{C_{CO_2} - C_{aO_2}}{C_{CO_2} - C_{vO_2}}$$

and the oxygenation index was calculated using the following formula:

$$OI = \frac{F(IO_2) \times P_{aw} \times 100}{P_{aO_2}}$$

Pulmonary Mechanics. Airway pressures proximal and distal to the endotracheal tube were monitored with precision pressure transducers (Model 45-32-871±100;
Validyne, Northridge, CA). All signals were amplified (Model 8805C, Hewlett Packard) and recorded at a sampling rate of 300 Hz per channel with an analog–digital conversion system (Windaq/200 v1.36; Dataq Instruments, Hartfield, PA). All devices were calibrated at the beginning of the experiment.

Static P-V curves of the respiratory system were obtained with a calibrated 2-l syringe (Model S2000; Hamilton, Reno, NV) using the method described by Harris et al.\textsuperscript{15} Stepwise inflations in increments of 50 ml up to a total volume of 200 ml followed by steps of 100 ml until the plateau airway pressure reached 45 cm H\textsubscript{2}O were performed while recording the corresponding airway pressure. On completion of the inspiratory limb, the syringe was disconnected and the sheep briefly ventilated. The syringe was then reconnected, the lungs were slowly inflated to the same volume reached at the end of the inspiratory limb, and then stepwise deflation was performed in four decrements of 50 ml, followed by steps of 100 ml, which established the deflation limb of the P-V curve. Volumes were adjusted to reflect body temperature pressure saturated conditions. The PCL was determined as the point of intersection between the slopes of the initial flat and subsequently steep and linear portions of the inflation limb of the P-V curve. The point of intersection between the steep, linear, and final flat portions of the inflation limb identified the PCU. The PMC was identified as the point of intersection between the slopes of the steep, linear, and final flat portions of the inflation limb identified the PCL. The PMC was identified as the point of intersection between the slopes of the initial flat and subsequently steep portions of the deflation limb of the P-V curve (fig. 2). P\textsubscript{CL}, P\textsubscript{CL}, and PMC were all determined by the manual application of tangents to the corresponding slopes of the P-V curve. Analysis was performed by the same trained investigator blinded to the outcome of the analysis. PCL, PCU, and PMC were clearly determined in all animals studied. To ensure a consistent lung volume history, three consecutive sighs with a tidal volume of 24 ml/kg, using the sigh function of the PB 7200, were applied before the P-V curve measurement.

Statistical Analysis

Experimental data are expressed as mean ± SD. One-way analysis of variance for repeated measures was used to compare data. Post hoc analysis was performed with the Scheffé test. The Pearson correlation coefficient was used to determine the relation between PCL and PMC. A statistics software package (Statistica v5.1; StatSoft Inc., Tulsa, OK) was used, and a P value of 0.05 was considered statistically significant.

Results

Data from seven of the eight sheep investigated were analyzed. One sheep died during establishment of lung injury because of intractable hypoxemia. Seven sheep (28 ± 5 kg) completed the 4-h protocol. No sheep died during the study period.

Lung Injury

The average number of lung lavages needed to establish lung injury was 3 ± 1. After establishment of lung injury, the arterial oxygen partial pressure/FIO\textsubscript{2} (P/F) ratio decreased (P < 0.01; fig. 3), Qs/Qt increased (P <
Pulmonary Gas Exchange

Baseline and postinjury (injury) blood gases, oxygenation index, and venous admixture (Qs/Qt) during conventional mechanical ventilation (PEEP = 5 cm H₂O, FIO₂ = 1.0) are listed in table 2 and figures 3 and 4. In all animals, ventilation and acid base balance were normal after injury, but the P/F ratio decreased to 85 ± 27 mmHg. With the application of HFO, normocapnia and acid base balance could be maintained with pressure amplitudes of 50–70 cm H₂O. The P/F ratio increased to a maximum at a Paw level of PCL + 6 (26 ± 1 cmH₂O) (P < 0.05 vs injury). Increasing Paw to levels of PCL + 10 (30 ± 1 cm H₂O) or PCL + 14 (34 ± 1 cm H₂O) did not further significantly improve the P/F ratio. At PCL + 14, the P/F ratio lost significance versus injury. On returning to baseline ventilation after 4 h of HFO (baseline 2), the P/F ratio decreased equivalent to that of injury. The calculated Qs/Qt showed significant improvement at PCL + 6, PCL + 10 and PCL + 14 versus injury (fig. 3). The oxygenation index increased at injury but was not significantly altered from injury during any Paw. However, oxygenation index tended to be lower than injury at PCL + 6.

Optimal Mean Airway Pressure and Pulmonary Mechanics

The Paw that resulted in the maximum oxygenation without hemodynamic compromise (PCL + 6, 26.0 ± 1 cm H₂O) was approximately equal to the PMC on the expiratory limb of the P-V curve (26.0 ± 1 cm H₂O; r = 0.77, P < 0.05; table 1).

Table 1. Lung Mechanics and Optimal Mean Airway Pressure in Each Animal Studied

<table>
<thead>
<tr>
<th>Animal</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCL (cm H₂O)</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>21</td>
<td>19</td>
<td>19</td>
<td>20</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>PCL (cm H₂O)</td>
<td>36</td>
<td>36</td>
<td>38</td>
<td>38</td>
<td>40</td>
<td>41</td>
<td>42</td>
<td>39</td>
<td>2</td>
</tr>
<tr>
<td>PMC (cm H₂O)</td>
<td>25</td>
<td>26</td>
<td>27</td>
<td>27</td>
<td>25</td>
<td>25</td>
<td>26</td>
<td>26</td>
<td>1</td>
</tr>
<tr>
<td>PawOPT (cm H₂O)</td>
<td>26</td>
<td>26</td>
<td>26</td>
<td>27</td>
<td>25</td>
<td>25</td>
<td>26</td>
<td>26</td>
<td>1</td>
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<td>V @ PCL (ml)</td>
<td>200</td>
<td>200</td>
<td>300</td>
<td>400</td>
<td>500</td>
<td>280</td>
<td>360</td>
<td>320</td>
<td>109</td>
</tr>
<tr>
<td>V @ PCL (ml)</td>
<td>550</td>
<td>680</td>
<td>1,000</td>
<td>940</td>
<td>1,400</td>
<td>800</td>
<td>1,100</td>
<td>924</td>
<td>282</td>
</tr>
<tr>
<td>V @ PMC (ml)</td>
<td>570</td>
<td>680</td>
<td>1,100</td>
<td>920</td>
<td>1,350</td>
<td>760</td>
<td>1,000</td>
<td>911</td>
<td>267</td>
</tr>
</tbody>
</table>

All volumes measured at body temperature pressure saturated.

Animal = individual animal studied; PCL = lower corner pressure; PCU = upper corner pressure on the inflation limb of the P-V curve; PMC = point of maximal compliance change on the deflation limb of the P-V curve; PawOPT = optimal mean airway pressure for oxygenation during high-frequency oscillatory ventilation; V @ PCL = lung volume above functional residual capacity at PCL; V @ PCU = lung volume above functional residual capacity at P CU; V @ PMC = lung volume above functional residual capacity at PMC.

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Lung Volume above Functional Residual Capacity

The lung volume above functional residual capacity (FRC) at \( P_{CL} \) was 320 ± 109 ml at \( P_{CL} \), it was 924 ± 282 ml, and at PMC it was 911 ± 267 ml. There was a significant correlation between the lung volume above FRC at \( P_{CL} \) and at PMC (\( r = 0.98, P < 0.05 \); table 1).

Discussion

The major findings of this study can be summarized as follows: (1) a \( P_{aw} \) equal to the \( P_{CL} + 6 \) optimized oxygenation without adversely affecting hemodynamics; (2) a \( P_{aw} \) of \( P_{CL} + 2 \) yielded suboptimal oxygenation; (3) \( P_{aw} \) higher than \( P_{CL} + 6 \) did not further improve oxygenation but significantly impaired hemodynamics; and (4) the \( P_{CL} + 6 \) was essentially equal to the PMC of the deflation limb of the P-V curve with this degree of lung injury.

Mean Airway Pressure

During HFO, \( P_{aw} \) is the primary variable affecting oxygenation and is set independent of other variables on the oscillator. Because distal airway pressure changes during HFO are minimal, the \( P_{aw} \) during HFO can be viewed in a manner similar to the PEEP level in conventional ventilation. The pressure amplitude of the oscillations (\( \Delta P \)) are attenuated by the endotracheal tube and the conducting airways.\(^8\) According to Fort et al.,\(^8\) the SensorMedics 3100B high-frequency oscillator generates a pressure amplitude across a 8.0-mm endotracheal tube at a frequency of 5 Hz that is approximately 15% of the pressure amplitude measured proximal to the tube. As frequency increases, a greater percentage of the pressure amplitude is dissipated across the endotracheal tube. As a result, tidal recruitment as seen in conventional ventilation becomes negligible in HFO.\(^9\) Therefore, the \( P_{aw} \) during HFO that results in optimal oxygenation should be predictable from the P-V curve in a manner similar to that observed with PEEP in conventional ventilation.

During conventional ventilation, a PEEP equal to the \( P_{CL} + 6 \) has been shown to be effective in minimizing lung injury\(^10\) and pulmonary\(^11\) and systemic mediator activation\(^11\) and has been attributed to improving morality.\(^12\) We have shown that a higher \( P_{aw} \) was needed in HFO to optimize oxygenation. The reason for this difference may be the presence of tidal recruitment during conventional ventilation\(^16\) and the lack of tidal recruitment during HFO.\(^9\) The small tidal volumes during HFO may be unable to replenish the lung volume lost to reabsorption atelectasis because of V/Q mismatch or alveolar instability that conventional ventilation can, and thus the need for a higher \( P_{aw} \) compared with PEEP to optimize oxygenation.

The Pressure-Volume Curve

As noted in figure 1, a distinct change in the slope of the P-V curve (\( P_{CL} \)) occurs during the initial inspiratory phase. This had previously been thought to represent the area of the curve when lung recruitment occurred. However, as illustrated by Hickling,\(^16\) the \( P_{CL} \) may simply represent the airway pressure where recruitment of collapsed lung units begins, with recruitment continuing

Table 2. Gas Exchange Data

<table>
<thead>
<tr>
<th></th>
<th>BL 1</th>
<th>Injury</th>
<th>( P_{CL} + 2 )</th>
<th>( P_{CL} + 6 )</th>
<th>( P_{CL} + 10 )</th>
<th>( P_{CL} + 14 )</th>
<th>BL 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH(_a)</td>
<td>7.38 ± 0.04</td>
<td>7.35 ± 0.04</td>
<td>7.32 ± 0.04</td>
<td>7.32 ± 0.06</td>
<td>7.31 ± 0.07</td>
<td>7.31 ± 0.06</td>
<td>7.30 ± 0.04</td>
</tr>
<tr>
<td>PaCO(_2) (tor)</td>
<td>41 ± 5</td>
<td>40 ± 2</td>
<td>44 ± 4</td>
<td>44 ± 5</td>
<td>45 ± 6</td>
<td>46 ± 7</td>
<td>47 ± 5</td>
</tr>
<tr>
<td>BE(_a) (mM)</td>
<td>-0.3 ± 0.9</td>
<td>-3.3 ± 2.8</td>
<td>-2.4 ± 2.5</td>
<td>-2.3 ± 2.4</td>
<td>-2.7 ± 2.4</td>
<td>-2.9 ± 2.7</td>
<td>-3.4 ± 2.5</td>
</tr>
<tr>
<td>SvO(_2) (%)</td>
<td>88.2 ± 4.6</td>
<td>70.9 ± 13.5</td>
<td>72.8 ± 7.3</td>
<td>80.9 ± 6.5</td>
<td>75.4 ± 10.0</td>
<td>67.0 ± 17.5</td>
<td>60.0 ± 8.8*</td>
</tr>
<tr>
<td>OI</td>
<td>1.8 ± 0.2</td>
<td>14.3 ± 6.0</td>
<td>20.0 ± 12.5</td>
<td>11.8 ± 10.2</td>
<td>17.0 ± 15.4</td>
<td>27.3 ± 26.3</td>
<td>23.1 ± 4.5</td>
</tr>
</tbody>
</table>

All values are mean ± SD. Scheffe post hoc test: * \( P < 0.05 \) versus \( P_{CL} + 6 \).

BL = baseline; \( P_{CL} \) = lower corner pressure; HR = heart rate; MAP = mean arterial pressure; PAP = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; CVP = central venous pressure; SV = stroke volume; SVR = systemic vascular resistance; \( V O_2 \) = oxygen consumption.

Table 3. Systemic and Pulmonary Hemodynamics

<table>
<thead>
<tr>
<th></th>
<th>BL 1</th>
<th>Injury</th>
<th>( P_{CL} + 2 )</th>
<th>( P_{CL} + 6 )</th>
<th>( P_{CL} + 10 )</th>
<th>( P_{CL} + 14 )</th>
<th>BL 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (min(^{-1}))</td>
<td>128 ± 16</td>
<td>143 ± 14</td>
<td>149 ± 29</td>
<td>152 ± 19</td>
<td>144 ± 15</td>
<td>137 ± 10</td>
<td>156 ± 21</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>111 ± 4</td>
<td>111 ± 10</td>
<td>102 ± 8</td>
<td>103 ± 13</td>
<td>97 ± 15</td>
<td>96 ± 16</td>
<td>101 ± 13</td>
</tr>
<tr>
<td>PAP (mmHg)</td>
<td>16 ± 3</td>
<td>16 ± 2</td>
<td>21 ± 3*</td>
<td>23 ± 5*</td>
<td>24 ± 5*</td>
<td>25 ± 4*</td>
<td>20 ± 4</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>9 ± 3</td>
<td>6 ± 2</td>
<td>10 ± 3*</td>
<td>11 ± 3*</td>
<td>12 ± 3*</td>
<td>13 ± 3*</td>
<td>9 ± 4</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>6 ± 2</td>
<td>6 ± 2</td>
<td>8 ± 2</td>
<td>10 ± 3*</td>
<td>10 ± 3*</td>
<td>11 ± 2*</td>
<td>7 ± 2</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>28 ± 3</td>
<td>25 ± 2</td>
<td>24 ± 3</td>
<td>24 ± 6</td>
<td>16 ± 1.2†</td>
<td>17 ± 1.2†</td>
<td>27 ± 6</td>
</tr>
<tr>
<td>SVR (dyn · s · cm(^{-5}))</td>
<td>2,410 ± 108</td>
<td>2,409 ± 184</td>
<td>2,152 ± 171</td>
<td>2,171 ± 235</td>
<td>2,742 ± 249</td>
<td>3,040 ± 212††</td>
<td>1,926 ± 201††</td>
</tr>
<tr>
<td>( V O_2 ) (ml/min)</td>
<td>89 ± 20</td>
<td>94 ± 30</td>
<td>111 ± 37</td>
<td>101 ± 28</td>
<td>82 ± 27</td>
<td>85 ± 27</td>
<td>91 ± 25</td>
</tr>
</tbody>
</table>

All values are mean ± SD. Scheffe post hoc test: * \( P < 0.05 \) versus Injury, † \( P < 0.05 \) versus \( P_{CL} + 2 \), † † \( P < 0.05 \) versus \( P_{CL} + 6 \).

BL = baseline; \( P_{CL} \) = lower corner pressure; HR = heart rate; MAP = mean arterial pressure; PAP = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; CVP = central venous pressure; SV = stroke volume; SVR = systemic vascular resistance; \( V O_2 \) = oxygen consumption.

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throughout inflation until the $P_{CU}$ is established. The change in slope at the $P_{CU}$ may represent the airway pressure causing overdistension\(^1^7\) or, as proposed by Hickling, may simply represent the airway pressure where recruitment during inflation decreases or stops.\(^1^6\) On the deflation limb of the P-V curve, the PMC identifies the airway pressure below which lung volume rapidly decreases. As shown in our example, the lung volume at PMC is approximately 85–90% of the total volume delivered during the P-V curve measurement and approximates the lung volume at $P_{CU}$.

**Optimal Oxygenation**

If Hickling\(^1^6\) is correct regarding the significance of the P-V curve during HFO, oxygenation should improve at $P_{aw}$ above $P_{CU}$. This is exactly what we found. It is also reasonable to expect that optimal oxygenation during HFO would occur at a $P_{aw}$ equivalent to the PMC. As lung volume at PMC is approximately equal to the lung volume at $P_{CU}$ (fig. 1 and table 1) or a volume reflective of maximal lung recruitment,\(^1^6\) $P_{aw}$ above PMC would not be expected to further improve oxygenation, since additional lung volume is not recruited beyond $P_{CL}$ and the maintenance of $P_{aw}$ or lung volume above this level may simply reflect an overdistending $P_{aw}$ or lung volume. The extent of the lung injury did not improve over time. As noted in table 2 and figures 2 and 3, there were no difference among the data obtained at injury and second baseline. However, we would caution direct extrapolation of our data to patients because ARDS in patients is not a surfactant deficiency problem. Multiple causes account for the development of ARDS, and we have not shown that a similar response would occur in patients.

**Recruitment Maneuver**

Ventilation at a lung volume equal to that at PMC (on the deflation limb of the P-V curve) was insured by using a recruitment maneuver before the random setting of each $P_{aw}$. As noted in figure 1, the lung volume maintained above FRC at any specific $P_{aw}$ is dependent on whether the $P_{aw}$ is set by going up the inflation limb of the P-V curve or down the deflation limb. In figure 1, a $P_{aw}$ of 26 cm H$_2$O established on the inflation limb resulted in a lung volume of 400 ml above FRC, whereas when the same $P_{aw}$ is established on the deflation limb, lung volume above FRC is 680 ml.

The use of a recruitment maneuver for the purpose of opening the lung and insuring ventilation on the defla-
tion limb of the P-V curve during HFO was first proposed by Kolton et al.\textsuperscript{18} They and other investigators\textsuperscript{14,19,20} set the P\textsubscript{aw} at 25–30 cm H\textsubscript{2}O for 10–15 s. We used a P\textsubscript{aw} of 50 cm H\textsubscript{2}O for 60 s as a recruitment maneuver. This pressure exceeded P\textsubscript{CL} in all animals and insured that a pressure sufficient to open recruitable lung was applied. Because we were using a large animal model (30-kg sheep) compared with the small animals (premature monkeys\textsuperscript{20} or 2.5–4.0-kg rabbits\textsuperscript{14,18,19}) used by other investigators, and because in our pilot data we could not recruit the lung with lower pressures, higher pressures were used. However, in this study and others\textsuperscript{21} using this particular lung injury model, recruitment maneuvers at similar pressures could be applied without the development of barotrauma. The use of high-pressure recruitment maneuvers during ARDS has been proposed by numerous groups.\textsuperscript{12,21–24} Peak alveolar pressures of 40 cm H\textsubscript{2}O held for 15 s were required by Rothen et al.\textsuperscript{25} to recruit healthy lungs after 20 min of general anesthesia. Sjöstrand et al.\textsuperscript{25} required peak airway pressure of 55 cm H\textsubscript{2}O maintained for 5–10 min to recruit lung in a porcine model of ARDS. Fujino et al.\textsuperscript{21} found that maximal recruitment required 60 cm H\textsubscript{2}O peak airway pressure applied for 2 min in a sheep saline lavage ARDS model. In patients with ARDS, Gattinoni et al.\textsuperscript{24} reported the need for 46 cm H\textsubscript{2}O peak airway pressure to recruit collapsed lung, while Amato et al.\textsuperscript{12} applied 35–40 cm H\textsubscript{2}O continuous positive airway pressure for 30–40 s, and Lapinsky et al.\textsuperscript{25} applied 40 cm H\textsubscript{2}O for 20 s to recruit collapsed lung in ARDS patients. None of these studies reported barotrauma or a sustained hemodynamic compromise resulting from the recruitment maneuver.

**Limitations**

The major limitation of this study is that it was performed on a saline lavage injury animal model of ARDS and not in patients. ARDS in patients is rarely, if ever, solely a result of surfactant deficiency. Multiple causes are responsible for primary pulmonary and extrapulmonary ARDS. As a result, the response of the ARDS lung may be very different from that of the saline lavage injured lung. In addition, the P-V curve findings in our model were very consistent across animals; as a result, we cannot conclude that these findings would have been observed if the level of lung injury resulted in markedly different P-V curve results. The steps in P\textsubscript{aw} evaluated (P\textsubscript{CL} + 2, + 6, + 10 and + 14) were large (4 cm H\textsubscript{2}O), and as a result it is impossible to know if a P\textsubscript{aw} equal to P\textsubscript{CL} + 4 or + 8 would have resulted in better gas exchange than P\textsubscript{CL} + 6. This potential clearly affects the strength of the implications of the correlation between P\textsubscript{CL} + 6 and PMC. Finally, this was a short-term random application of different P\textsubscript{aw} values, which prevented us from evaluating the effects of this approach on ventilator-induced lung injury. Consequently, care must be exercised in the extrapolation of these data to humans or other animal models. In addition, the short time frames for which each P\textsubscript{aw} was applied and the use of each animal as its own control prevented identification of any long-term effects of each P\textsubscript{aw}.

In conclusion, in this saline lavage injury model of ARDS, the optimal P\textsubscript{aw} during HFO is equal to P\textsubscript{CL} + 6, which in this model correlated with the PMC on the deflation limb of the P-V curve. Increases in P\textsubscript{aw} above P\textsubscript{CL} + 6 did not further improve oxygenation but did result in hemodynamic compromise.

**References**


