A Decremental PEEP Trial Identifies the PEEP Level That Maintains Oxygenation After Lung Recruitment

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OBJECTIVE: To assess the ability of a decremental trial of positive end-expiratory pressure (PEEP) to identify an optimal PEEP level that maintains oxygenation after a lung-recruitment maneuver. DESIGN: Prospective clinical trial. SETTING: Surgical intensive care unit of a university hospital. PATIENTS: Twenty sedated patients with acute lung injury and/or acute respiratory distress syndrome, ventilated for 1.2 ± 0.4 d. INTERVENTION: Each patient received up to 3 lung-recruitment maneuvers with continuous positive airway pressure of 40 cm H2O sustained for 40 s to increase the ratio of PaO2 to FiO2 by > 20%. Following the lung-recruitment maneuver, PEEP was set at 20 cm H2O and then the FiO2 was decreased until the oxygen saturation (measured via pulse oximetry [SpO2]) was 90–94%. PEEP was then decreased in 2-cm H2O steps until the SpO2 dropped below 90%. The step preceding the drop to below 90% was considered the optimal PEEP. The lung was then re-recruited and PEEP and FiO2 were set at the identified levels. The patients were followed for 4 h after the PEEP trial and the setting of PEEP and FiO2. RESULTS: After the lung-recruitment maneuver, all the patients' PaO2/FiO2 increased > 50%. The mean ± SD PaO2/FiO2 on the optimal decremental trial PEEP was 211 ± 79 mm Hg, versus 135 ± 37 mm Hg at baseline (p < 0.001), and was sustained at that level for the 4-h study period (227 ± 81 mm Hg at 4 h). FiO2 at baseline was 0.54 ± 0.12 versus 0.38 ± 0.12 (p < 0.001) at 4 h. PEEP was 11.9 ± 3.0 cm H2O at baseline and 9.1 ± 4.7 cm H2O (p = 0.011) at 4 h. CONCLUSION: A decremental PEEP trial identifies a PEEP setting that sustains for 4 h the oxygenation benefit of a 40-cm H2O, 40-s lung-recruitment maneuver. Key words: lung recruitment, acute respiratory distress syndrome, ARDS, acute lung injury, positive end-expiratory pressure, PEEP, mechanical ventilation. [Respir Care 2006; 51(10):1132–1139. © 2006 Daedalus Enterprises]
than required. The optimal PEEP is the minimum PEEP level that sustains the oxygenation benefit of the recruitment maneuver. This places the lung on the deflation limb of the P-V curve, which establishes a much greater lung volume than the same PEEP level without lung recruitment on the inspiratory limb of the P-V curve.4

We hypothesized that the oxygenation benefit of a lung-recruitment maneuver would be sustained for a 4-h period if post-recruitment PEEP was set with a decremental PEEP trial. We also hypothesized that lung recruitment performed early following the initial diagnosis of acute lung injury (ALI) or ARDS (by the American-European consensus conference definition)7 would result in a > 20% increase in the ratio of $P_{aO_2}$ to fraction of inspired oxygen ($F_{IO_2}$).

Methods

This study was approved by the ethics committee of Cairo University and the New Kasr El-Aini teaching hospital, where the research was performed. Informed consent was obtained from the family of every patient prior to enrollment in the study.

Patients

Patients considered for enrollment were all located in the surgical intensive care unit (ICU) of the New Kasr El-Aini Teaching Hospital of Cairo University. To be eligible for this study, a patient had to meet the American-European consensus conference definition of ALI or ARDS7 and require PEEP of ≥ 8 cm H2O to maintain arterial oxygen saturation (measured via pulse oximetry [$S_{pO_2}$]) > 90%. Patients were excluded if they were < 18 y old or > 75 y old; had a history of cardiac disease; had chest trauma (including lung contusion, hemothorax, or pneumothorax); had a history of severe chronic obstructive pulmonary disease; had bullae or blebs visible on chest radiograph; had a subclavian central venous line; or were hemodynamically unstable. Patients entering the ICU were screened daily, and patients who met the criteria were enrolled within 24 hours of meeting the criteria. All the patients enrolled had an arterial cannula for continuous blood-pressure monitoring and for obtaining arterial blood samples. Throughout the study, all the patients received continuous electrocardiography, pulse oximetry, and invasive blood-pressure measurement.

Protocol

On enrollment, patients were sedated with a bolus of propofol (0.25–0.75 mg/kg), until there was no evidence of spontaneous breathing effort. Sedation was maintained with a continuous infusion of propofol (10–100 μg/kg/min) during both the recruitment procedure and the subsequent decremental PEEP trial. None of the patients required paralyzing agents for performance of the protocol. Before any recruitment procedure, the patient’s airways were suctioned with an in-line suction catheter. Care was exercised during the study not to disconnect the ventilator. In-line suctioning was performed as needed. Prior to performing the recruitment maneuver, baseline gas-exchange and hemodynamic data were obtained. Throughout the study period, the patients were maintained in the supine position.

Patients were then stabilized on an $F_{IO_2}$ of 1.0 for 20 min, after which another set of blood-gas and hemodynamic data were obtained. The recruitment maneuver was performed on an $F_{IO_2}$ of 1.0, using CPAP of 40 cm H2O applied for up to 40 s. The recruitment maneuver was discontinued if one of the following conditions was observed: $S_{pO_2}$ decreased to < 88%; heart rate increased to > 140 beats/min or decreased to < 60 beats/min; mean arterial pressure decreased to < 60 mm Hg or decreased by > 20 mm Hg from baseline; or cardiac arrhythmia appeared. Immediately following the recruitment maneuver, mechanical ventilation was resumed with pressure-assist/control at a peak pressure of 35 cm H2O (pressure-control setting 15 cm H2O) and PEEP set at 20 cm H2O, with $F_{IO_2}$ of 1.0. After 5 min, hemodynamics and gas exchange were evaluated. If the $P_{aO_2}$ at an $F_{IO_2}$ of 1.0 had less than a 20% increase, the maneuver was repeated, provided the first recruitment maneuver had not been aborted because of one of the above-stated conditions. A total of up to 3 recruitment maneuvers could be performed. A > 20% $P_{aO_2}/F_{IO_2}$ increase was targeted because we considered this a clinically important increase.

If, following the recruitment maneuver, the $P_{aO_2}$ increased > 20%, the $F_{IO_2}$ was gradually decreased (by 0.05–0.2 every 15–20 min), until $S_{pO_2}$ stabilized between 90% and 94%. PEEP was then lowered by 2 cm H2O every 15–20 min until the $S_{pO_2}$ fell below 90%. The PEEP level immediately preceding the $S_{pO_2}$ drop to below 90% was considered the optimal PEEP to maintain the oxygenation benefit of the recruitment maneuver. Once the optimal PEEP was identified, $F_{IO_2}$ was increased to 1.0 and a final recruitment maneuver was performed (CPAP of 40 cm H2O for 40 s). Following the maneuver the PEEP and $F_{IO_2}$ were set at the levels identified during the decremental PEEP trial. Fifteen to 20 min after stabilization another set of gas-exchange and hemodynamic data were obtained (initial PEEP settings). The patients were then maintained on the exact same ventilator settings, with minimal disturbance over the next 4 h. Following the setting of PEEP, the propofol infusion was decreased or stopped, and assist/control or pressure support ventilation resumed. Control of sedation at this time was determined by the staff managing the patient. Data were gathered at 1 h and 4 h after setting.
the PEEP and FIO2 determined in the decremental PEEP trial.

All the patients before and during the protocol were maintained on pressure-assist/control ventilation, with a short inspiratory time (≤ 1.0 s) or pressure-support with a target tidal volume of 6–7 mL/kg actual body weight. The rate was patient-determined or set to achieve a PaCO2 of 35–45 mm Hg. PEEP and FIO2 at baseline were set by physicians who were not involved in the study, to maintain PaO2 > 60 mm Hg. Throughout the study period, medical management was not altered. Specifically, fluid management and diuresis were unaltered. Prior to and throughout the study, patients were maintained in the supine position. All patients were ventilated (model 7200, Puritan-Bennett, Carlsbad, California) and SpO2 was monitored (model 90491, Space Labs Medical, Issaquah, Washington).

Statistical Analysis

Data are expressed as mean ± standard deviation and percentages. We used the Kolmogorov-Smirnov and Lilliefors tests for normality. All data were normally distributed, except for PEEP level. Comparison of physiologic variables that were normally distributed over time were performed via analysis of variance for repeated measures. When significant differences were identified, post-hoc analysis was performed with the Newman-Keul test. Non-normally distributed data (PEEP) were compared using the nonparametric Friedman’s analysis of variance (also repeated measured analysis). When significant differences were identified, post-hoc analysis was performed with the Wilcoxon matched-pairs test. A p value < 0.05 was considered significant. All statistical calculations were performed using spreadsheet software (Excel, Microsoft, Redmond, Washington) and statistics software (SPSS, Chicago, Illinois).

Results

We studied a total of 20 patients, who had not received previous recruitment maneuvers and were not requiring vasoactive drugs (Table 1). Their age range was 20–65 y (mean 41.5 ± 14 y). Their body-weight range was 53–97 kg (mean 75.7 ± 13.7 kg). Fourteen (70%) patients were
With 6 patients there were protocol violations; the FIO$_2$ unaltered prior to recruitment. Before RM this step should have been decreased until S pO$_2$ to baseline, in all but 2 patients. Before RM = On FIO$_2$ of 1.0, just prior to the recruitment maneuver. After RM = On FIO$_2$ of 1.0 and PEEP of 20 cm H$_2$O, 5 min after the recruitment maneuver. After Trial = Fifteen to 20 min after stabilization on the PEEP and FIO$_2$ selected in the PEEP/FIO$_2$ trial. 1 h = 1 h after PEEP/FIO$_2$ trial. 4 h = 4 h after PEEP/FIO$_2$ trial. * p < 0.05 versus baseline. # p < 0.01 versus baseline.

All the patients had chest radiography within 24 h of the study, and arterial blood pressure was continuously monitored in all patients. P$_{aCO_2}$, pH, heart rate, and arterial blood pressure remained stable throughout the study period (see Table 2), whereas respiratory rate decreased (p = 0.010). No recruitment maneuver was aborted because of an adverse event, nor was any barotrauma identified.

**Discussion**

The most important findings of this study are:

1. A decremental PEEP trial following a lung-recruitment maneuver identified the optimal PEEP level that sustained, for a 4-h period, the oxygenation level obtained by the recruitment maneuver.

2. All the patients responded to the lung-recruitment maneuvers, based on prespecified oxygenation criteria.

3. Some of the patients required 2 recruitment maneuvers to achieve an oxygenation response.

4. All the patients tolerated the recruitment maneuvers (40 cm H$_2$O for 40 s) without any adverse events.
5. Regardless of PEEP level or the performance of a recruitment maneuver, many ARDS patients responded with a marked increase in $P_aO_2/FIO_2$ when the $FIO_2$ was increased to 1.0.

Ever since Ashbaugh et al. first used PEEP to manage ARDS, there has been controversy over the approach to setting PEEP. Most clinicians set PEEP based on a stated or unstated algorithm that relates PEEP to $FIO_2$. Others have proposed the use of the inspiratory limb of the P-V curve. And still others have adjusted PEEP to achieve an oxygenation target without hemodynamic compromise. If the goal is to establish the minimum PEEP that maintains the improved oxygenation from a lung-resection maneuver, instead of a decremental trial after recruitment, without a PEEP trial. Our data are consistent with that of Tugrul et al., who performed a similar decremental PEEP trial after lung-recruitment in 24 ARDS patients. However, they did not perform a second set of recruitment maneuvers after identifying the optimal PEEP, nor did they do multiple recruitment maneuvers, and their recruitment maneuver was with CPAP of 45 cm H2O for 30 s. They found sustained benefit for 6 h after their recruitment maneuver. As in our study, they found no adverse effects, and the recruitment maneuvers were well tolerated.

Contrary to our study and the study by Tugrul et al., others have not found a sustained benefit from lung-recruitment maneuvers, and their recruitment maneuver was with CPAP of 45 cm H2O for 30 s. They found sustained benefit for 6 h after their recruitment maneuver. As in our study, they found no adverse effects, and the recruitment maneuvers were well tolerated.

### Table 2: Gas Exchange, Ventilatory, and Hemodynamic Variables at All Stages of the Study (mean ± SD)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Before RM</th>
<th>After RM</th>
<th>After Trial</th>
<th>1 Hour</th>
<th>4 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>$FIO_2$ (L/min)</td>
<td>0.54 ± 0.12</td>
<td>1.00 ± 0.0*</td>
<td>1.00 ± 0.0*</td>
<td>0.38 ± 0.12*</td>
<td>0.38 ± 0.12*</td>
<td>0.38 ± 0.12*</td>
</tr>
<tr>
<td>PEEP (cm H2O)</td>
<td>11.9 ± 3.0</td>
<td>11.9 ± 3.0</td>
<td>20 ± 0.0*</td>
<td>9.1 ± 4.7†</td>
<td>9.1 ± 4.7†</td>
<td>9.1 ± 4.7†</td>
</tr>
<tr>
<td>$P_aCO_2$ (mm Hg)</td>
<td>34.8 ± 7.7</td>
<td>36.2 ± 7.7</td>
<td>36.2 ± 7.4</td>
<td>35.5 ± 7.8</td>
<td>35.2 ± 7</td>
<td>35.9 ± 7.6</td>
</tr>
<tr>
<td>pH</td>
<td>7.42 ± 0.1</td>
<td>7.40 ± 0.1</td>
<td>7.41 ± 0.1</td>
<td>7.42 ± 0.1</td>
<td>7.43 ± 0.1</td>
<td>7.43 ± 0.1</td>
</tr>
<tr>
<td>$S_pO_2$ (%)</td>
<td>92.7 ± 5.2</td>
<td>98.6 ± 1.3*</td>
<td>99.0 ± 0.0*</td>
<td>93.5 ± 3.4</td>
<td>94.2 ± 3.1</td>
<td>94.5 ± 3.3</td>
</tr>
<tr>
<td>$V_L$ (mL)</td>
<td>479 ± 102.7</td>
<td>475 ± 108.1</td>
<td>503 ± 141.2</td>
<td>497 ± 139.3</td>
<td>504 ± 133.1</td>
<td>499 ± 132.9</td>
</tr>
<tr>
<td>$f$ (breaths/min)</td>
<td>25.1 ± 6.3</td>
<td>23.3 ± 6.†</td>
<td>21.0 ± 3.7*</td>
<td>21.4 ± 4.5*</td>
<td>21.6 ± 4.2*</td>
<td>22.1 ± 4.5†</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>114.4 ± 17.4</td>
<td>113.3 ± 17.5†</td>
<td>110.0 ± 16.7†</td>
<td>111.2 ± 20.4</td>
<td>110.5 ± 19.9</td>
<td>110.2 ± 19.0</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>12.0 ± 3.7</td>
<td>11.0 ± 3.4†</td>
<td>10.5 ± 3.2*</td>
<td>10.5 ± 3.2†</td>
<td>10.9 ± 3.6</td>
<td>11 ± 3.6</td>
</tr>
<tr>
<td>PIP (mm Hg)</td>
<td>86.9 ± 12.3</td>
<td>84.0 ± 12.2</td>
<td>84.1 ± 13.0</td>
<td>83.1 ± 10.1</td>
<td>81.9 ± 12.6</td>
<td>83.9 ± 12.1</td>
</tr>
</tbody>
</table>

*p < 0.01 compared to baseline value
†p < 0.05 compared to baseline value

Before RM = 0h baseline ventilator settings with $FIO_2$ 1.0, before recruitment maneuver (RM)
After RM = $FIO_2$ 1.0 and PEEP 20 cm H2O
PEEP = positive end-expiratory pressure
After Trial = 15–20 min after setting the PEEP and $FIO_2$, based on the decremental PEEP/$FIO_2$ trial
1 hour = 1 hour after the PEEP/$FIO_2$ trial
4 hours = 4 hours after the PEEP/$FIO_2$ trial
$FIO_2$ = fraction of inspired oxygen
$S_pO_2$ = arterial oxygen saturation measured via pulse oximetry
$V_L$ = tidal volume
$V$ = respiratory rate
HR = heart rate
MAP = mean arterial pressure
PIP = peak inspiratory pressure.
Lapinsky et al.12 used the same PEEP following the initial recruitment maneuver; but when the recruitment benefit was lost, the lungs were again recruited and PEEP set at a higher level. They used as many as 3 recruitment maneuvers, with increasing PEEP after each maneuver. The key to sustaining the oxygenation benefit is to determine the post-recruitment PEEP required in each patient.

Effect of 100% Oxygen

We set the FIO2 at 1.0 prior to and during the recruitment maneuver to provide a margin of safety if the recruitment maneuver caused marked hemodynamic instability. Increasing the FIO2 above 0.5 in ARDS may markedly improve the Pao2/FIO2. This effect is based on the ventilation-perfusion relationship, cardiac output, and hemoglobin level. The baseline Pao2/FIO2 (at FIO2 0.54) increased on average 48% simply by increasing the FIO2 to 1.0. Of the 20 patients studied, only 3 did not have a Pao2/FIO2 increase > 20% when we increased FIO2 to 1.0. The mean FIO2 of these patients was 0.63 ± 0.15, and their Pao2 at baseline was 60.6 ± 6.1 mm Hg, versus 105.6 ± 33.0 mm Hg at FIO2 of 1.0. After lung recruitment, decreasing the FIO2 from 1.0 to 0.38, with the PEEP maintained at 20 cm H2O, resulted in an Sao2 of 95.2%. As emphasized by others, this effect of FIO2 on Pao2/FIO2 in ARDS may have profound effects on enrolling patients into clinical trials.

Lung Recruitment

At an FIO2 of 1.0, the recruitment maneuver with CPAP of 40 cm H2O increased the average Pao2/FIO2 by approximately 50%. This allowed a 31% decrease from the original FIO2 (from 0.54 ± 0.1 to 0.38 ± 0.1) and a 23% decrease from the original PEEP (from 11.9 ± 3.0 cm H2O to 9.1 ± 4.7 cm H2O). We expected to be able to decrease the FIO2 following the recruitment maneuver, but were surprised by the decrease in PEEP. On close examination (see Fig. 3), some patients may have been on excessive PEEP prior to the recruitment maneuver. In 6 patients, PEEP was decreased ≥ 5 cm H2O after the lung recruitment. This overall PEEP decrease was greater than the small PEEP increases in the other 14 patients. This clearly shows the benefit of placing lung volume on the deflation limb of the P-V curve following lung recruitment. On the deflation limb, PEEP levels similar to those on the inflation limb result in the maintenance of improved oxygenation. We presume that this oxygenation improvement was a result of lung-volume recruitment, since no change in hemodynamics was observed. Our data are consistent with those of the recruitment-responsive group in the study by Grasso et al. That is, our patients were recruited early in their ventilator course (1.2 ± 0.4 d) and shortly after their diagnosis of ARDS/ALI. In addition, the only difference we found between patients who required 2 recruitment maneuvers and those who required only one was that all 3 patients who required 2 maneuvers were in their 2nd day of ARDS/ALI.

Many approaches to lung-recruitment maneuvers have been published. We chose to be conservative in the recruitment pressure we applied, to avoid hemodynamic compromise and barotrauma. Not a single recruitment maneuver was aborted and no patient developed a pneumothorax. We may have been able to recruit a greater lung volume had we used higher recruitment pressure, but that could have caused hemodynamic compromise and barotrauma. Our use of multiple recruitment maneuvers may have offset in some patients the lack of higher recruitment pressure. Most likely, the combination of time and pressure determines the success of a recruitment maneuver; that is, the higher the recruiting pressure, the shorter the recruiting time necessary to achieve a similar level of alveolar recruitment. In addition, the patients studied were ideally suited to respond to a recruitment maneuver; they were mostly postoperative, in their first or second day of ventilatory support, hemodynamically stable, and were suctioned prior to the recruitment maneuver. Patients outside of those conditions may not respond in a similar manner.

Although there were no adverse reactions during the lung-recruitment maneuvers we conducted, clearly there is the potential for hemodynamic compromise and barotrauma. Recent animal data from Lim et al. clearly show
depressed cardiac output during lung recruitment. Similar concerns were raised by Nielsen et al.,26 for cardiac surgical patients, and by Grasso et al.,13 for patients who are ventilated for a lengthy period before the performance of a recruitment maneuver. However, if the patients are appropriately fluid managed, we and others have not observed a marked hemodynamic effect during lung recruitment.1,2,12,13,20,21,27,28

Limitations

The primary limitation to this study is that it is not a randomized controlled trial, so we are not able to make any conclusions regarding outcome. Another important limitation is that the post-recruitment-maneuver observation period was only 4 h, because of which we cannot comment on the ability of this PEEP-setting method to sustain the benefit of a lung-recruitment maneuver for a longer period. We also used 100% oxygen to stabilize patients before and during the recruitment maneuver, so we cannot be sure that this did not induce atelectasis. Also, varying the FIO2 during the protocol may have directly affected Pao2/FIO2. However, at optimal PEEP, Pao2/FIO2, FIO2, and PEEP were all significantly better than baseline values, which indicates that the post-recruitment response was not simply the reversal of induced atelectasis. In addition, we did not measure static lung compliance at each phase of the study.

The use of pulse-oximetry values (SpO2) instead of Pao2, measured from arterial blood may have caused us to select an inappropriate PEEP level in some patients. The accuracy of the pulse oximeter is ± 4–5% at 2 standard deviations,29 which may have prevented us from identifying the optimal PEEP in the 4 patients whose Pao2/FIO2 decreased over the 4-h evaluation period (see Fig. 1). In addition, we waited about 15 min between the decremental PEEP steps, which may have been too short a period to ensure stability of oxygenation at individual steps in some patients.

Additionally, we cannot state that it is better to first adjust FIO2, then PEEP, or PEEP first then FIO2. We decreased FIO2 to the lowest level that placed SpO2 in our target range, to ensure we could rapidly identify a change in SpO2 as PEEP was decreased. Also, setting PEEP at 20 cm H2O after recruitment and then slowly decreasing PEEP may have assisted in lung recruitment. During the application of 16–20 cm H2O PEEP, peak pressure was above 30 cm H2O, which might have furthered recruitment. Additional work needs to be performed on the exact approach to a decremental PEEP/FIO2 trial.

The patients studied were all from a surgical ICU, although some did have pneumonia and sepsis, so our data should be cautiously generalized to the overall population of patients in a medical ICU.

Finally, we cannot be sure that alveolar recruitment actually occurred, versus redistribution of airway/alveolar fluid,30 since lung volume was not measured. However, our ability to sustain this benefit for a 4-h period at a PEEP level ≤ prerecruitment PEEP argues for alveolar recruitment. In addition, oxygenation as a surrogate outcome measure has been questioned.9,31,32 Although improvements in arterial blood gases are often perceived as reflecting improvement in disease, there are multiple examples in the literature of strategies that yield oxygenation benefit without improvement in outcome.9,31,32

Future Directions

Additional study of lung-recruitment maneuvers is needed. The best approach to performing a lung-recruitment maneuver and a decremental PEEP trial, and the expected and potential complications of recruitment maneuvers need to be determined. Most importantly, appropriately designed randomized controlled trials need to be performed to assess the role of recruitment maneuvers on patient outcome.

Conclusion

In summary, a decremental PEEP/FIO2 trial following a lung-recruitment maneuver can identify the optimal PEEP/FIO2 that sustains the oxygenation benefit of a recruitment maneuver for 4 h. Lung recruitment, when used early in the course of ARDS/ALI, results in a large increase in Pao2/FIO2.

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REFERENCES


