Recruitment Maneuvers after a Positive End-expiratory Pressure Trial Do Not Induce Sustained Effects in Early Adult Respiratory Distress Syndrome

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Background: Recruitment maneuvers performed in early adult respiratory distress syndrome remain a matter of dispute in patients ventilated with low tidal volumes and high levels of positive end-expiratory pressure (PEEP). In this prospective, randomized controlled study the authors evaluated the impact of recruitment maneuvers after a PEEP trial on oxygenation and venous admixture (Qs/Qt) in patients with early extrapulmonary adult respiratory distress syndrome.

Methods: After a PEEP trial 30 consecutive patients ventilated with low tidal volumes and high levels of PEEP were randomly assigned to either undergo a recruitment maneuver or not. Data were recorded at baseline, 3 min after the recruitment maneuver, and 30 min after baseline. Recruitment maneuvers were performed with a sustained inflation of 50 cm H₂O maintained for 30 s.

Results: Compared with baseline the ratio of the arterial oxygen partial pressure to the fraction of inspired oxygen (PaO₂/FIO₂) and Qs/Qt improved significantly at 3 min after the recruitment maneuver (PaO₂/FIO₂, 139 ± 46 mm Hg versus 246 ± 111 mm Hg, P < 0.001; Qs/Qt, 30.8 ± 5.8% versus 21.5 ± 9.7%, P < 0.005), but baseline values were reached again within 30 min. No significant differences in PaO₂/FIO₂ and Qs/Qt were detected between the recruitment maneuver group and the control group at baseline and after 30 min. Recruitment maneuver group [n = 15]: PaO₂/FIO₂, 139 ± 46 mm Hg versus 138 ± 39 mm Hg; Qs/Qt, 30.8 ± 5.8% versus 29.2 ± 7.4%; control group [n = 15]: PaO₂/FIO₂, 145 ± 33 mm Hg versus 155 ± 52 mm Hg; Qs/Qt, 30.2 ± 8.5% versus 28.1 ± 5.4%.

Conclusion: In patients with early extrapulmonary adult respiratory distress syndrome who underwent a PEEP trial, recruitment maneuvers failed to induce a sustained improvement of oxygenation and venous admixture.

Despite recent advances in treatment strategies introduced during the last decade, adult respiratory distress syndrome (ARDS) remains one of the major challenges faced in the intensive care unit. The ARDS lung is characterized by a combination of atelectasis, surfactant dysfunction, and alveolar flooding caused by protein-rich pulmonary edema and interstitial inflammation predominantly occurring in dependent lung zones. Positive end-expiratory pressure (PEEP) has become an established ventilatory strategy for ARDS patients, leading to an increase in lung volume and consequently to improved gas exchange. Computed tomography guided studies demonstrated that alveolar recruitment increased significantly by increasing the level of PEEP. The effects of PEEP are markedly influenced by lung morphology assessed by computer tomography showing a prevalence of recruitment of collapsed areas in patients with more diffuse distribution of the densities.

Thus, lung protective ventilation strategies are based on two major concepts: 1) sufficiently high levels of PEEP to prevent cyclic opening and closing of alveoli and thus to maintain alveolar recruitment and 2) low tidal volumes to avoid high alveolar end-inspiratory distending pressures and alveolar overdistension. Two recent randomized controlled clinical trials have shown that a lung protective ventilation approach provides marked improvement in clinical outcome. On the other hand, it has been reported that low tidal ventilation leads to progressive atelectasis even when PEEP is set 2 cm H₂O above the lower inflection point of the static pressure volume curve. To recruit and to prevent atelectasis different techniques of recruitment maneuvers have been proposed as an adjunct to mechanical ventilation in recent years. Recruitment maneuvers performed by sustained inflations have received the most attention. The responsiveness to recruitment maneuvers depends on several factors such as the level of PEEP set before and after the recruitment maneuvers, the time point of the recruitment maneuvers, and the etiology of the ARDS. Grasso et al. reported that recruitment maneuvers improved oxygenation only in patients with early ARDS without impairment of chest wall mechanics. Furthermore, the responsiveness to recruitment maneuvers might be more pronounced in patients with indirect lung injury (extrapulmonary ARDS), as these lungs are those with the most likely "recruitable" atelectasis. However, this assumption is not proven by controlled randomized trials.
Early ARDS was defined as need for mechanical ventilation, worsened hemodynamics (systolic blood pressure >100 mm Hg with or without vasopressor support) who met the ARDS criteria of the American/European Consensus Conference on ARDS. Early ARDS was defined as need for mechanical ventilation for less than 72 h after diagnosis of ARDS. The underlying etiologies of extrapulmonary ARDS are shown in table 1.

Patients with direct lung injury (pulmonary ARDS) caused by pneumonia or aspiration as well as with a documented hypotension (defined as systolic blood pressure <100 mm Hg despite of catecholamine support), significant arrhythmias, cardiogenic lung edema, and barotrauma of any form (detected by chest radiography) were excluded from the study.

Routine monitoring included continuous monitoring of heart rate by electrocardiogram and arterial oxygen saturation by pulse oxymetry. An arterial catheter was placed in the radial artery for continuous invasive blood pressure monitoring and for intermittent arterial blood sampling. A 7.0-French fiberoptic pulmonary artery flotation catheter (CCOMbo™; Edwards Lifesciences, Critical Care Division, Irvine, CA) was inserted into the proximal pulmonary artery for continuous measurement of mixed venous oxygen saturation, pulmonary arterial blood pressure, and cardiac index. In all patients chest radiography was routinely performed to detect extra-alveolar air within 24 h after recruitment maneuvers.

The time line of the study protocol is presented in a schematic diagram in figure 1. All patients were sedated with sufentanil/midazolam and paralyzed with rocuronium during the study period. Mechanical ventilation was performed with a pressure controlled mode with a decelerating ramp flow waveform (Dräger Evita™ Ventilator; Lübeck, Germany). The inspiratory plateau pressure was initially adjusted to the value that produced a tidal volume of approximately 6 ml/kg predicted body weight but did not exceed 30 cm H2O, as used in the Acute Respiratory Distress Syndrome Network Trial. Initial PEEP and inspiratory oxygen fraction (FiO2) were set to obtain an arterial oxygen partial pressure (PaO2) between 70 and 80 mm Hg. The initial ventilator rate was set to maintain arterial carbon dioxide partial pressure (PaCO2) between 40 and 50 mm Hg.

For further improvement of oxygenation a PEEP trial was performed. Based on best oxygenation PEEP was increased by using increments of 2 cm H2O tested in a range between 8 cm H2O (lowest initial PEEP) and 20 cm H2O. The set PEEP was maintained for a 30-min equilibration period, after which blood gas concentrations were determined. Plateau pressure was increased in the same degree to maintain constant ventilation but not to exceed 35 cm H2O. In case of a plateau pressure of 35 cm H2O, higher PaCO2 concentrations between 50 and 70 mm Hg were accepted as long as pH was maintained at ≥7.2 (permissive hypercapnia). “Best” PEEP was defined as the PEEP level at which the greatest PaO2 improvement was observed without worsening hemodynamics, defined as a 20% drop in cardiac output or blood pressure. If no “best” PEEP could be identified during the...
PEEP trial, PEEP was set at a high level of 15 cm H₂O, referring to previous clinical studies.  

According to our intensive care unit protocol intrinsic PEEP was measured for each PEEP step of the PEEP trial by an end-expiratory occlusion maneuver (Dräger Evita). The ventilator rate was increased as long as no intrinsic PEEP occurred. Respiratory system compliance (Crs) was obtained by dividing expiratory tidal volume (VT) by the difference between inspiratory plateau pressure (Pplat) and total PEEP (Crs = VT/Pplat – PEEPtot).

After the PEEP trial the patients were randomly assigned either to undergo a recruitment maneuver (RM group, n = 15) or to be ventilated by the same ventilatory strategy but without a recruitment maneuver (control group, n = 15). Randomization was performed using a computer-generated list (MS Excel 2000; Microsoft Inc, Redmond, WA). After a time period of 2 h for PEEP induced alveolar recruitment baseline data were recorded in both groups. Arterial blood gas analysis and hemodynamic measurements were recorded at baseline (immediately before the recruitment maneuver), 3 min after the recruitment maneuver, and 30 min after baseline. In the control group values were documented 30 min after baseline.

As recruitment maneuver we chose a sustained inflation as reported in several studies.  

The sustained inflation was performed by increasing the plateau pressure to an inflation pressure of 50 cm H₂O, which was maintained for 30 s. Ventilatory settings and hemodynamic management remained unchanged throughout the study period.

Criteria for premature termination of the recruitment maneuver and return to basal ventilation were a more than 30% decrease in mean arterial pressure or a decrease of the arterial oxygen saturation to less than 85%.

Statistical Analysis

All data showed normal distribution as determined by Kolmogorov-Smirnov analysis, and are reported as mean ± SD. Statistical analysis was performed by paired Student t test (parametric data) or one-way analysis of variance with Bonferroni post hoc test for multiple comparisons.  

Statistical analysis was performed by paired Student t test (parametric data) or one-way analysis of variance with Bonferroni post hoc test for multiple comparisons. SPSS version 11.0 for Windows (SPSS Inc, Chicago, IL) was used for statistical analysis. P values < 0.05 were considered as statistically significant.

Results

There were no significant differences between the patients of the RM group and the control group with respect to age, weight, or the severity of ARDS as expressed by the PaO₂/FIO₂ ratio (table 1). After the PEEP trial PEEP was increased from 10.2 ± 2.1 to 15.1 ± 1.2 cm H₂O in the RM group and from 10.2 ± 1.4 to 14.5 ± 1.5 cm H₂O in the control group. According to the criteria of our study protocol no intrinsic PEEP was present in our patients. Thus, the applied PEEP values were equivalent to the total PEEP values. Ventilatory settings of the two groups were comparable and are shown in table 2.

The PEEP trial led to a significant improvement in PaO₂/FIO₂ in the RM group (117 ± 31 mm Hg to 139 ± 46; P < 0.05) and in the control group (116 ± 22 mm Hg to 145 ± 35 mm Hg; P < 0.05). No significant differences in PaO₂/FIO₂ were detected between the RM group and the control group.

Compared to baseline PaO₂/FIO₂ increased and Qs/Qt decreased significantly at 3 min after the recruitment maneuver (table 3). PaO₂/FIO₂ and Qs/Qt returned to baseline values within 30 min after the recruitment maneuver (P = 1.0). No significant differences in gas exchange, Qs/Qt, or Crs could be detected between the two groups at baseline and 30 min after baseline measurements (table 3).

Table 2. Ventilatory Pattern of the RM and Control Groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>RM group</th>
<th>Control group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pplat (cm H₂O)</td>
<td>29 ± 3.5</td>
<td>28.7 ± 3.0</td>
<td>0.722</td>
</tr>
<tr>
<td>PEEP (cm H₂O)</td>
<td>15.1 ± 1.2</td>
<td>14.5 ± 1.3</td>
<td>0.474</td>
</tr>
<tr>
<td>VT (ml)</td>
<td>452 ± 93</td>
<td>501 ± 92</td>
<td>0.275</td>
</tr>
<tr>
<td>RR (min⁻¹)</td>
<td>20.6 ± 7.9</td>
<td>18.9 ± 4.5</td>
<td>0.216</td>
</tr>
<tr>
<td>FIO₂</td>
<td>0.68 ± 0.1</td>
<td>0.63 ± 0.1</td>
<td>0.449</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

Table 3. Gas Exchange and Respiratory Mechanics of the RM and Control Groups at Specified Time Points

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline</th>
<th>3 min post-RM</th>
<th>30 min post-Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO₂/FIO₂ (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RM group</td>
<td>139 ± 46</td>
<td>246 ± 111†</td>
<td>138 ± 39†</td>
</tr>
<tr>
<td>Control group</td>
<td>145 ± 33</td>
<td>–</td>
<td>155 ± 52</td>
</tr>
<tr>
<td>Paco₂ (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RM group</td>
<td>48.6 ± 12.1</td>
<td>47.6 ± 13</td>
<td>46.4 ± 12</td>
</tr>
<tr>
<td>Control group</td>
<td>48 ± 7.4</td>
<td>–</td>
<td>47.1 ± 6.7</td>
</tr>
<tr>
<td>Svo₂ (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RM group</td>
<td>70.4 ± 6.1</td>
<td>72.4 ± 5.6</td>
<td>70 ± 6.2</td>
</tr>
<tr>
<td>Control group</td>
<td>70.3 ± 6.5</td>
<td>–</td>
<td>70.3 ± 7.0</td>
</tr>
<tr>
<td>Qs/Qt (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RM group</td>
<td>30.8 ± 5.8</td>
<td>21.5 ± 9.7‡</td>
<td>29.2 ± 7.4‡</td>
</tr>
<tr>
<td>Control group</td>
<td>30.2 ± 8.5</td>
<td>–</td>
<td>28.1 ± 5.4</td>
</tr>
<tr>
<td>Qs/Qt (ml/cm H₂O)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RM group</td>
<td>34.1 ± 12.6</td>
<td>36.9 ± 15.1</td>
<td>35.7 ± 13.5</td>
</tr>
<tr>
<td>Control group</td>
<td>36.9 ± 11.5</td>
<td>–</td>
<td>37.4 ± 11.8</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

Crs = respiratory system compliance; FIO₂ = inspiratory fraction of oxygen; PaCO₂ = arterial CO₂ partial pressure; PaO₂ = arterial oxygen partial pressure; Qs/Qt = venous admixture; RM = recruitment maneuver; Svo₂ = mixed venous oxygen saturation.

† P < 0.001 3 min post-RM versus baseline; † P < 0.001 30 min after baseline versus 3 min post-RM; ‡ P < 0.005 3 min post-RM versus baseline; § P < 0.005 30 min after baseline versus 3 min post-RM.
The recruitment maneuver was well tolerated in all cases and no change in any hemodynamic variables could be found at 3 min after the recruitment maneuver compared to baseline values (table 4). In both groups no significant differences of the hemodynamic variables could be detected at 30 min compared to baseline measurements (table 4).

**Discussion**

The main finding of our prospective, randomized controlled study was that in patients with early extrapulmonary ARDS who underwent a PEEP trial, a recruitment maneuver resulted in only short-term improvement of oxygenation and decrease of venous admixture. Within 30 min after the recruitment maneuver oxygenation and venous admixture returned to baseline values. No significant differences of these variables were detectable between the RM group and the control group at baseline and 30 min after baseline measurements. As no changes of hemodynamic variables were found at any specified time points, we can state that the transient improvement of oxygenation as well as the inversely decrease in venous admixture was not influenced by hemodynamic factors.

Our results confirm previously published evidence from experimental data. In an animal model of acute lung injury Van der Kloot et al. found only modest improvement of oxygenation 15 min after recruitment maneuvers when dogs were ventilated with a PEEP level higher than the lower inflection point of the static pressure volume curve. Furthermore, the interaction of PEEP and the efficacy of recruitment maneuvers was investigated in several clinical studies. Although previous publications investigated the effects of recruitment maneuvers in nonrandomized, uncontrolled settings or without PEEP trial our study is the first randomized controlled trial to investigate the effects of a recruitment maneuver after a PEEP trial in early extrapulmonary ARDS, which resembles the clinical situation of a recruitment maneuver in the setting of lung protective ventilation. Grasso et al. showed that in early ARDS patients without impairment of chest wall mechanics a sustained inflation performed with 40 cm H₂O and maintained for 40 s increased PaO₂/FIO₂ by 175 ± 23%. Loss of beneficial effects of the recruitment maneuver could be observed within 30 min. In contrast to our study no PEEP trial was performed before the recruitment maneuver and the patients were ventilated with considerably lower mean levels of PEEP of approximately 9 cm H₂O. PEEP and FIO₂ were only set to obtain an arterial oxygen saturation of 90–95% or an arterial oxygen partial pressure of 60–80 mm Hg, or both. In another nonrandomized and uncontrolled study, Villagra et al. reported that a 2 min lasting recruitment maneuver performed at a peak pressure of 50 cm H₂O resulted only in a transient and statistically not significant improvement of oxygenation. In this study PEEP was set 3–4 cm H₂O above the lower inflection point of the static pressure volume curve. However, baseline values were reached again 15 min after the recruitment maneuver.

Recently the ARDS Clinical Trials Network published a randomized crossover study reporting that greatest increments from baseline arterial oxygen saturation were larger within 10 min after a recruitment maneuver than after sham recruitment maneuvers (1.7 ± 0.2% versus 0.6 ± 0.3%), but the beneficial effects on gas exchange appeared to be of brief duration. In contrast to our study, the mean levels of PEEP were slightly lower (13.8 ± 3.0 cm H₂O) and the recruitment maneuver was performed by applying a continuous positive airway pressure of only 55-40 cm H₂O for 30 s. Moreover, the authors reported that recruitment maneuvers had similar effects on oxygenation in patients with ARDS from pulmonary and extrapulmonary causes. On the other hand, several studies have reported that the responsiveness to recruitment maneuvers is more pronounced in patients with indirect lung injury (extrapulmonary ARDS) with a predominance of alveolar collapse and interstitial edema than in patients with pulmonary ARDS, which is characterized by prevalent lung tissue consolidations because of inflammatory exsudate. Based on these studies, our protocol was designed only for patients with extrapulmonary ARDS ventilated with high levels of PEEP. Thus, we are able to state that in these patients recruitment maneuvers failed to induce a sustained improvement of oxygenation and venous admixture.
As our data showed only a significant short-term improvement of oxygenation and decrease of venous admixture after the recruitment maneuver, one might argue that in our study the PEEP applied after the recruitment maneuver was insufficient for sustained recruitment. Therefore the question remains whether the observed changes in our study could have been preserved by adaptation of the PEEP level after the recruitment maneuver, as suggested by some authors.17, 25, 27 Lapinsky et al. reported a sustained effect in improving arterial oxygen saturation in 10 of 14 patients after a recruitment maneuver. The four nonresponders to initial recruitment maneuvers achieved a maintained improvement in oxygenation only after an increase in the subsequent PEEP level and by repeating the sustained inflation demonstrating the importance of adequate PEEP after a recruitment maneuver.17 There is clinical and research evidence that PEEP induced alveolar recruitment is a time-dependent process.31, 32 It cannot be excluded that in the study of Lapinsky et al. the time period between the increase of PEEP after ineffective recruitment maneuvers and the repeated sustained inflation was probably too short to differentiate between the effects of recruitment maneuvers and PEEP.

**Study Limitations**

As our study was aimed at clarifying the course of changes in oxygenation induced by recruitment maneuvers over time at high levels of PEEP, we did not include any resetting of ventilatory parameters after the recruitment maneuvers into our protocol. We chose a PEEP trial based on best oxygenation being a widespread approach in routine practice and applied in clinical trials.4, 18 However, we want to point out that most of our patients revealed acceptable oxygenation after the PEEP trial.

A variety of different techniques for performing recruitment maneuvers were reported.15–19 No consensus exists concerning the “optimal” recruitment technique or the maximum for recruitment pressure or the duration and frequency of recruitment maneuvers. Therefore it may be possible that other strategies for setting PEEP or performing the recruitment maneuver may lead to results other than those of this investigation. However, our recruitment maneuver was certainly sufficient to cause an acute change in oxygenation of a magnitude similar to that noted by other authors.17, 18, 22

Computed tomography guided studies have shown that recruitability of the lung may be affected by lung morphology rather than by the etiology of ARDS.2, 5, 59 As to technical reasons, our protocol did not include chest computed tomography during the study period. Thus, we cannot answer to which extent the extrapulmonary etiology of early ARDS was actually associated with diffuse distribution of densities that should have the greatest potential for a beneficial recruiting response.9 Further studies have to investigate the interaction of the effects of recruitment maneuvers and the morphological aspects of extrapulmonary ARDS.

In conclusion, our data demonstrate that in patients with early extrapulmonary ARDS who underwent a PEEP trial recruitment maneuvers performed with 50 cm H2O of continuous positive airway pressure and maintained for 30 s failed to induce a sustained improvement of oxygenation and venous admixture.

**References**


23. Hickling KC: Best compliance during a decremental, but not incremental, positive end-expiratory pressure trial is related to open-lung positive end-expiratory pressure: A mathematical model of acute respiratory distress syndrome lungs. Am J Respir Crit Care Med 2001; 163:69–78


