Morphometric Effects of the Recruitment Maneuver on Saline-lavaged Canine Lungs

A Computed Tomographic Analysis

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Background: In the face of widespread use of lung-protective, low-volume ventilation in patients with acute lung injury, interest in the recruitment maneuver (RM) is growing. Little is known about lung morphometric effects of the RM as compared with positive end-expiratory pressure (PEEP) titration (PT) without the RM.

Methods: RM was defined as a stepwise change in PEEP from baseline to 10, 20, 30, and 20 cm H2O every 30 s, after which PEEP was reset at the lower inflection point + 2 cm H2O. For PT, PEEP was simply increased from baseline to the lower inflection point + 2 cm H2O. Both maneuvers were performed in 10 lung-lavaged dogs. Computed tomography of the lung was performed before and 30 s and 30 min after the maneuver.

Results: Thirty seconds after the maneuver, the decrease in the amount of nonaerated plus poorly aerated lung was greater in Hounsfield units in the caudal and dorsal lung regions were greater with the RM than with the PT. The hyperaerated lung volume after the RM tended to be greater than that after the PT. At 30 s and 30 min after the maneuver, gas plus tissue volume, gas-only volume, and gas–tissue ratio of the lung were greater with the RM than with the PT. At both time points after the maneuver, the coefficient of variation of regional Hounsfield units, an index of regional heterogeneity of aeration, was lower with the RM than with the PT.

Conclusions: Compared with PT, the RM resulted in a greater lung volume, better aeration of the most dependent lung, and less regional heterogeneity of aeration. However, the RM tended to induce a greater increase in hyperaerated lung volume than did the PT.

ALVEOLAR recruitment is an important goal in the treatment of acute respiratory distress syndrome (ARDS) or acute lung injury (ALI). Alveolar recruitment is used not only to reverse hypoxia but also to circumvent ventilator-associated lung injury associated with repetitive shearing of bronchioloalveolar units.1–3 To achieve alveolar recruitment in the ARDS or ALI lung, titrating positive end-expiratory pressure (PEEP) to a value near the lower inflection point (LIP) of the inflation pressure-volume (P–V) curve has long been in vogue.4–7 Accumulating evidence, however, indicates that alveolar recruitment continues well above the LIP,8–11 and thus titrating PEEP to the LIP on the inflational P–V curve is not adequate for maximal recruitment of an ARDS lung.12,13 Opening of collapsed alveoli in ARDS is known to require a distending pressure higher than the inspiratory pressure usually achieved during conventional ventilation, due to the heightened collapsing forces.8,9,11,14 Furthermore, reopening collapsed alveoli is time-dependent, requiring 20–60 s (which is presumably inversely related to the level of applied pressure).15–17 The concept of augmented (pressure \times time) for alveolar opening is now incorporated into a variety of maneuvers referred to as “recruitment maneuvers” (RMs).1,9,14,18,19

A few clinical and laboratory studies have investigated the physiologic effects of the RM with regard to gas exchange and respiratory mechanics.9,18–25 To our knowledge, however, little is known on how lung morphometry is affected by the RM in both quantitative and qualitative terms of recruitment. In addition, the RM could induce generalized and/or regional overdistension of the lung as was shown with the use of PEEP.7,24,25 Because the RM generally exploits higher airway pressures than a simple PEEP titration (PT),1,9,14,18,19 such untoward effects may occur to a greater degree with the RM than with the PT. In this study, we investigated the volumetric and topographic changes in the lung induced by the RM in surfactant-depleted canine lungs and compared them with those induced by a traditional method of recruitment, i.e., PT without the RM.

Materials and Methods

Preparation of Animals

Ten male mongrel dogs (mean weight ± SD, 21.0 ± 2.8 kg) were used for this study. Care and handling of the animals complied with the guidelines of the United States National Institutes of Health. Our institution’s animal care committee approved the experimental protocol. Ketamine (5 mg/kg) and atropine sulfate (0.1 mg/kg) were administered intramuscularly to prepare for general

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anesthesia, which was induced by an intravenous bolus injection of sodium pentobarbital (25 mg/kg) in two divided doses via a peripheral vein. Anesthesia was maintained by a continuous intravenous infusion of sodium pentobarbital (3 mg·kg⁻¹·h⁻¹), and muscle paralysis was maintained with a continuous intravenous infusion of pancuronium (0.1 mg·kg⁻¹·h⁻¹).

After orotracheal intubation with an 8.0-mm (internal diameter) endotracheal tube, the dogs were mechanically ventilated using the intermittent positive pressure ventilation mode with an Evita 4 ventilator (Dräger, Lubeck, Germany) at a pressure limit of 40 cm H₂O, tidal volume of 10 ml/kg, rate of 26/min, inspiratory-to-expiratory ratio of 1:1, inspiratory flow rate of 40 l/min, fractional concentration of inspired oxygen of 1.0, and PEEP of 0 cm H₂O. An 18-gauge cannula was introduced into the femoral artery. Three electrodes for electrocardiography were placed in appropriate positions on the dog’s trunk. The arterial catheter and the electrodes were connected to an Escort II pressure monitor (Medical Data Electronics, Arleta, CA) to monitor blood pressure and heart rate. The left external jugular vein was cut down for the insertion of a 7.0-French Swan-Ganz catheter (Baxter Healthcare Corporation, Irvine, CA), which was advanced to the pulmonary artery under the guidance of the pressure profile. The pulmonary artery catheter was connected to a COM-1 cardiac output computer (Baxter Healthcare Corporation).

**Saline Lavage, ALI, and Determination of the LIP**

After measurements of normal state had been made, lung lavage was performed three to four times using warmed (37° ± 1°C) normal saline at a dose of 40 ml/kg, which was administered via the endotracheal tube and removed by gravity. ALI was deemed established if PaO₂ taken 90 min after the last lavage was 300 mmHg or less. At the establishment of ALI, the LIP of the inflational P-V curve was determined by the interruption method, as described previously. The pressure corresponding to the intersection of the starting compliance and the inflational compliance was defined as the LIP. The mean LIP ± SD in seven experimental animals was 10.7 ± 1.4 cm H₂O. In the other three dogs in which the LIP was not easily discernible, 11 cm H₂O was arbitrarily chosen for the LIP.

**RM and PT**

Our method of performing the RM was designed to gradually apply and withdraw a high distending pressure over a prolonged period (Fig. 1: from the baseline level of 3 cm H₂O, PEEP was changed in stepwise manner to 10, 20, 30, and 20 cm H₂O, each step being 30 s (2 min in total duration). Because ventilation by the intermittent positive pressure ventilation mode was pressure limited at 40 cm H₂O, the tidal volume at the phase of the highest PEEP (30 cm H₂O) was accordingly reduced. After the RM, PEEP was reset at the determined LIP + 2 cm H₂O. The PT was performed by simply increasing the level of PEEP from 3 cm H₂O to the LIP + 2 cm H₂O. The two maneuvers were performed sequentially in random order with a baseline measurement in between. Five animals were treated with the RM first, whereas the others were treated with the PT first. Thirty minutes after the first maneuver, the dogs were disconnected from the ventilator circuit for 5 s so that the recruited lung resulting from the first maneuver could undergo passive collapse. The baseline ventilation with PEEP at 3 cm H₂O was resumed, and baseline data were collected in a second round 10 min later.
LUNG-MORPHOMETRIC EFFECTS OF RECRUITMENT MANEUVER

4. mean lung volume, \( (EELV - VPEP) \)
5. volume of tissue, \( (total \ volume \ of \ lung - volume \ of \ gas) \)
6. volume of tissue, \( (total \ volume \ of \ lung - volume \ of \ gas) \)
7. \( V_{NA} \), volume of voxels exhibiting +100 to −100 HU
8. poorly aerated lung volume (\( V_{HP} \)), volume of voxels exhibiting −100 to −500 HU
9. normal aerated lung volume, volume of voxels exhibiting −500 to −900 HU
10. hyperaerated lung volume (\( V_{HP} \)), volume of voxels exhibiting −900 to −1,000 HU
11. lung recruitment, decrease in the amount of collapse-prone lung with maneuver, as calculated by \( (V_{NA} + V_{PEP} \) of baseline at end expiration) − \( (V_{NA} + V_{PEP} \) after maneuver at end expiration)
12. change in regional aeration, (regional HU of before maneuver) − (regional HU of after maneuver)
13. heterogeneity of lung aeration, degree of variation of regional aeration, assessed by coefficient of variation (CV) of the HUs of 18 topographic lung regions
14. percent lung volume undergoing tidal recruitment, decrease in the amount of collapse-prone lung with tidal inspiration as calculated by \( ([V_{NA} + V_{PEP}] \) at end expiration) − \( ([V_{NA} + V_{PEP}] \) at end inspiration)/mean lung volume
15. percent lung volume undergoing tidal hyperinflation, increase in the amount of \( V_{H} \) with tidal inspiration, as calculated by \( ([V_{H}] \) at end inspiration) − \( ([V_{H}] \) at end expiration)/mean lung volume

Data Collection
CT scans, hemodynamics, and respiratory data for the dogs were obtained immediately before each maneuver (before), every 30 s during the RM or the first 2 min of the PT, and 30 s after each maneuver (after). Another set of data was obtained 30 min after each maneuver (delayed) to evaluate the effect of time on the lung morphology.

Cardiac output was the average of three thermodilution measurements, determined with 10 ml normal saline at a temperature of 23°−25°C (computation constant, 0.595). Respiratory parameters (peak pressure, inspiratory pause pressure, and mean airway pressure) were taken directly from the digital display of the ventilator. Dynamic and static compliance of the respiratory system was calculated by tidal volume/(peak pressure − PEEP), and tidal volume/(inspiratory pause pressure − PEEP), respectively. In calculating compliances, the set PEEP was chosen instead of total PEEP because intrinsic PEEP was not observed in our model of ALI. Blood gas analysis was performed for simultaneous pairs of arterial blood and mixed venous blood. Shunt was calculated by (capillary oxygen content − arterial oxygen content)/(capillary oxygen content − mixed vein oxygen content) × 100.
Statistical Analysis

All data are expressed as mean ± SD. Friedman analysis was performed to test the difference between different conditions, followed by the Wilcoxon signed rank test if significant differences were detected. The CV was calculated as SD/mean. The correlation between two variables was tested by linear regression analysis. Normality of distribution of a continuous variable was examined by the Kolmogorov–Smirnov test. \( P < 0.05 \) was considered statistically significant.

Results

P-V Curve and Position of Tidal Ventilation Loop

Figure 2, above—constructed with the sequential points of EELV or gas-only volume and corresponding PEEP before, during the maneuver at 30-s intervals, and after the maneuver—shows both inflation and deflation curves with the RM, whereas only a smaller inflation curve is shown with the PT. The tidal ventilation loop, plotted with EELV, end-inspiratory lung volume, PEEP, and inspiratory pause pressure, was relocated higher after the RM than after the PT (fig. 2, below). The tidal excursion of airway pressure was smaller after the RM than after the PT for the same tidal volume.

Figure 3 shows representative scans of a dog’s lung with the RM and with the PT, respectively. Increased densities in the most dependent lung regions were noted after the PT. In contrast, such lesions were much less after the RM. Furthermore, the lung and thorax assumed a bigger and more rounded shape after the RM than after the PT.

Lung Recruitment, Tidal Recruitment–Hyperinflation, Total and Compartment Lung Volumes, and Gas-to-tissue Ratios of the Lung

\( V_{NA}, V_p \), normal aerated lung volume, and \( V_{H} \) in absolute amount and percent of total lung volume at baseline were similar between the maneuvers (table 1). Lung recruitment was greater with the RM than with the PT (190.3 ± 70.1 vs. 139.8 ± 72.7 ml, respectively; \( P = 0.035 \)). The increase in the normal aerated lung volume was greater with the RM than with the PT (783.3 ± 191.3 vs. 549.7 ± 115.7 ml, respectively; \( P = 0.028 \)). \( V_{H} \) increased with both maneuvers (both, \( P = 0.018 \)), and the increase tended to be greater with the RM than with the PT (138.8 ± 134.5 vs. 110.3 ± 104.6 ml, respectively; \( P = 0.075 \)). As assessed by percent of total lung volume, percent \( V_p \) after the RM was smaller than that after the PT, whereas other compartments were similar between the two maneuvers.

Percent lung volume undergoing tidal recruitment decreased after the RM (6.8 ± 5.3% at baseline and 1.5 ± 2.1% after maneuver; \( P = 0.036 \)), whereas percent lung volume undergoing tidal recruitment did not change after the PT (4.3 ± 5.2% and 2.6 ± 1.9%, respectively; \( P = 0.575 \)). Percent lung volume undergoing tidal hyperinflation did not change with both maneuvers: RM, 2.9 ± 2.2% at baseline and 2.9 ± 1.3% after maneuver (\( P = 0.612 \)); PT, 3.4 ± 2.0% at baseline and 3.0 ± 1.8% after maneuver (\( P = 0.128 \)).

The EELV, which did not differ at baseline (\( P = 0.1 \)), was greater after the RM than after the PT (\( P = 0.018 \)) (fig. 2, above). Gas-only volume of the lung, which did not differ at baseline (\( P = 0.483 \)), was greater after the RM than after the PT (\( P = 0.012 \)). Tissue volumes of the lung at baseline (524.3 ± 96.2 ml for RM and 516.0 ± 87.0 ml for PT; \( P = 0.499 \)) and after the maneuver (574.8 ± 119.1 and 550.7 ± 108.2 ml, respectively; \( P = 0.136 \)) did not differ between the RM and the PT. Tissue volume of the lung was not significantly changed by either the RM (\( P = 0.084 \)) or the PT (\( P = 0.311 \)). The gas-to-tissue ratio of the lung, which did not differ at baseline (0.77 ± 0.31 for RM and 0.76 ± 0.29 for PT; \( P = 0.865 \)), was higher after the RM than after the PT (2.02 ± 0.36 and 1.64 ± 0.27, respectively; \( P = 0.011 \)).

Regional Aeration of the Lung

Whereas the increase in regional aeration was similar at the apical and hilar levels with the two maneuvers, the increase in regional aeration at the caudal level was greater with the RM than with the PT (\( P = 0.026 \)) (fig. 4, above). Similarly, whereas the increase in regional aeration was similar in the ventral and middle planes with the two maneuvers, the increase in regional aeration in the dorsal plane was greater with the RM than with the PT (\( P = 0.006 \)) (fig. 4, below).

Heterogeneity of Overall Lung Aeration

The CV of the HU at end expiration was smaller after the RM than after the PT (0.13 ± 0.06 vs. 0.27 ± 0.11, respectively; \( P = 0.026 \)). The CV of the HU at end inspiration was also smaller after the RM than after the PT (0.19 ± 0.19 vs. 0.29 ± 0.18, respectively; \( P = 0.028 \)).

Physiologic Outcomes and Correlation between Lung Morphometry and Hemodynamics

Dynamic compliance (\( P = 0.021 \)) and static compliance of the respiratory system (\( P = 0.011 \)) were higher after the RM than after the PT (table 2). Shunt was lower after the RM than after the PT (\( P = 0.047 \)). \( P_{aCO_2} \) was increased with the RM, whereas not so with the PT. Cardiac output was lower (\( P = 0.017 \)) and pulmonary artery occlusion pressure was higher (\( P = 0.038 \)) after the RM than after the PT.

An increase in the EELV (fig. 5, above) and an increase in aerated EELV (fig. 5, below) induced by the RM or the PT both correlated with the maximum decrease in mean blood pressure recorded during both maneuvers.
**Time Effects on Lung Morphometry and Physiology with Both Maneuvers**

With the RM, the delayed EELV did not differ from the EELV after the maneuver ($P = 0.128$) (fig. 2, above). In contrast, with the PT, the delayed EELV was greater than the EELV after the maneuver ($P = 0.018$). With both maneuvers, the delayed values for the gas-only volume of the lung were greater than the values after the maneuver.

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**Fig. 2. (Above) Pressure–volume (P–V) curves of a dog’s lung obtained by tracing the sequential points of end-expiratory lung volume (EELV) or gas-only volume and corresponding positive end-expiratory pressure (PEEP) with the recruitment maneuver (solid lines) and the PEEP titration (dotted lines). The lowest open symbols represent the P–V points of baseline, the other open symbols in line represent the sequential P–V points during the maneuvers, the dotted symbols represent the P–V points 30 s after the maneuvers (after), and the closed symbols represent the P–V points 30 min after the maneuvers (delayed). $P < 0.05$, recruitment maneuver versus PEEP titration; $P < 0.05$, delayed versus after. (Below) The tidal ventilation loop within the P–V envelope before (lower loops) and after (upper loops) the recruitment maneuver (solid loops) or the PT (dashed loops) plotted with EELV, end-inspiratory lung volume (EILV), PEEP, and inspiratory pause pressure ($P_{\text{PAUSE}}$). Closed circles are end-expiratory P–Vs, and open circles are end-inspiratory P–Vs.**
With the RM, the delayed CVs of the HU at end expiration ($P < 0.05$) or at end inspiration ($P = 0.715$) did not differ from the values after the maneuver. In contrast, with the PT, the delayed CVs of the HU both at end expiration ($0.22 \pm 0.10$) and at end inspiration ($0.22 \pm 0.16$) improved relative to the values after maneuver ($P = 0.027$ and $P = 0.028$, respectively).

**Table 1. Various Lung Volumes in Absolute Amount and Percent of Total Lung Volume at Baseline (Before), 30 s (After), and 30 min (Delayed) after the RM and the PT**

<table>
<thead>
<tr>
<th></th>
<th>RM</th>
<th></th>
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<th>PT</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Delayed</td>
<td>Before</td>
<td>After</td>
<td>Delayed</td>
</tr>
<tr>
<td>$V_{NA}$, ml (%)</td>
<td>182.1 ± 33.3</td>
<td>92.8 ± 29.3$^*$</td>
<td>94.5 ± 40.3$^*$</td>
<td>191.1 ± 56.0</td>
<td>99.0 ± 46.0$^*$</td>
<td>82.50 ± 38.7$^+$</td>
</tr>
<tr>
<td></td>
<td>(20.2 ± 4.5)</td>
<td>(5.6 ± 3.3)$^*$</td>
<td>(5.4 ± 1.2)$^*$</td>
<td>(21.4 ± 7.4)</td>
<td>(6.9 ± 2.3)$^*$</td>
<td>(5.1 ± 1.1)$^*$</td>
</tr>
<tr>
<td>$V_{PA}$, ml (%)</td>
<td>309.9 ± 41.5</td>
<td>209.0 ± 74.6$^*$</td>
<td>198.9 ± 72.5$^*$</td>
<td>287.9 ± 53.3</td>
<td>240.3 ± 50.5</td>
<td>217.4 ± 70.3</td>
</tr>
<tr>
<td></td>
<td>(35.2 ± 9.6)</td>
<td>(12.8 ± 3.5)$^*$</td>
<td>(11.3 ± 2.9)$^+$</td>
<td>(32.8 ± 8.8)</td>
<td>(17.4 ± 4.1)$^*$</td>
<td>(14.1 ± 3.7)$^*$</td>
</tr>
<tr>
<td>$V_{NA}$, ml (%)</td>
<td>416.7 ± 250.5</td>
<td>1,200.0 ± 240.2$^+$</td>
<td>1,242.8 ± 204.2$^+$</td>
<td>406.3 ± 226.2</td>
<td>856.0 ± 221.9$^*$</td>
<td>1,119.6 ± 178.2$^+$</td>
</tr>
<tr>
<td></td>
<td>(40.0 ± 8.7)</td>
<td>(66.2 ± 19.4)$^*$</td>
<td>(71.2 ± 10.2)$^*$</td>
<td>(40.8 ± 7.5)</td>
<td>(61.6 ± 16.7)$^*$</td>
<td>(72.3 ± 9.3)$^*$</td>
</tr>
<tr>
<td>$V_{PA}$, ml (%)</td>
<td>75.4 ± 82.1</td>
<td>214.1 ± 222.8$^+$</td>
<td>203.4 ± 220.0$^+$</td>
<td>68.8 ± 82.1</td>
<td>180.0 ± 181.9$^*$</td>
<td>178.3 ± 180.4$^*$</td>
</tr>
<tr>
<td></td>
<td>(6.9 ± 5.9)</td>
<td>(11.7 ± 9.6)$^*$</td>
<td>(12.3 ± 9.4)$^*$</td>
<td>(6.5 ± 5.5)</td>
<td>(11.8 ± 10.0)$^*$</td>
<td>(12.5 ± 9.3)$^*$</td>
</tr>
</tbody>
</table>

* $P < 0.05$ vs. before. † $P < 0.05$ vs. PT. ‡ $P < 0.05$ vs. after.

PT = positive end-expiratory pressure titration; RM = recruitment maneuver; $V_{NA}$ = atelectasis volume; $V_{PA}$ = poorly aerated volume; $V_{NA}$ = normal aerated volume; $V_{PA}$ = hyperaerated volume.
Nevertheless, the delayed values for the EELV (P = 0.018) and gas-only volume with the RM (P = 0.012) were greater than those with the PT (fig. 2, above). The delayed CVs of the HU with the RM at end expiration (0.13 ± 0.06) and at end inspiration (0.17 ± 0.16) were both less than those with the PT (P = 0.042 and P = 0.027, respectively). The delayed values for dynamic compliance (P = 0.013) and static compliance of the respiratory system (P = 0.011) with the RM were greater than those with the PT (table 2). The delayed value for shunt with the RM was lower than that with the PT (P = 0.037).

**Discussion**

In this study, we demonstrated a difference between the RM and the PT (without the RM) on the radiologic morphometry of the lung in an animal model of ALI. In quantitative terms, the RM brought about a greater recruitment of the lung. In addition, lung volume (both EELV and gas-only volume) after the RM was greater than that after the PT, and this difference persisted for 30 min. However, our results also demonstrated the risk of lung overinflation with the RM, although the proportion of hyperaerated lung after the maneuver was similar between the two methods of recruitment.

A few important qualitative differences between the two methods of recruitment were also noted. The complex curve plotted for the RM demonstrated that the end-expiratory P-V of the lung was transferred onto a deflation curve within the short time frame of the ma-

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**Table 2. Physiologic Parameters at Baseline (Before), 30 s (After), and 30 min (Delayed) after the RM and the PT**

<table>
<thead>
<tr>
<th>Respiratory mechanics</th>
<th>RM Before</th>
<th>RM After</th>
<th>RM Delayed</th>
<th>PT Before</th>
<th>PT After</th>
<th>PT Delayed</th>
</tr>
</thead>
<tbody>
<tr>
<td>P_{aw} (cm H₂O)</td>
<td>17.1 ± 2.8</td>
<td>22.9 ± 4.9†</td>
<td>23.3 ± 3.0‡</td>
<td>17.4 ± 1.8</td>
<td>24.8 ± 2.9*</td>
<td>24.8 ± 3.2*</td>
</tr>
<tr>
<td>P_{raw} (cm H₂O)</td>
<td>13.0 ± 2.2</td>
<td>19.3 ± 2.9†</td>
<td>20.0 ± 3.1‡‡</td>
<td>13.4 ± 1.9</td>
<td>21.6 ± 2.8*</td>
<td>21.4 ± 2.9*</td>
</tr>
<tr>
<td>P_{aw} (cm H₂O)</td>
<td>8.6 ± 1.2</td>
<td>15.7 ± 2.5†</td>
<td>16.1 ± 2.1‡‡</td>
<td>8.7 ± 1.2</td>
<td>16.9 ± 2.1*</td>
<td>16.9 ± 2.1*</td>
</tr>
<tr>
<td>PEEP (cm H₂O)</td>
<td>3.1 ± 0.4</td>
<td>12.2 ± 2.5*</td>
<td>12.4 ± 2.3*</td>
<td>3.1 ± 0.3</td>
<td>12.3 ± 2.2*</td>
<td>12.2 ± 2.4*</td>
</tr>
<tr>
<td>C_{dyn,rs} (ml/cm H₂O)</td>
<td>15.3 ± 5.0</td>
<td>20.8 ± 5.9†</td>
<td>19.9 ± 5.4†</td>
<td>14.6 ± 3.3</td>
<td>17.3 ± 3.8*</td>
<td>18.0 ± 4.7*</td>
</tr>
<tr>
<td>C_{stat,rs} (ml/cm H₂O)</td>
<td>22.0 ± 7.6</td>
<td>33.7 ± 12.7†</td>
<td>30.5 ± 12.1†</td>
<td>20.6 ± 5.9</td>
<td>23.6 ± 5.9*</td>
<td>24.4 ± 7.1*</td>
</tr>
<tr>
<td>Blood gases and shunt</td>
<td></td>
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<tr>
<td>pH</td>
<td>7.26 ± 0.06</td>
<td>7.24 ± 0.06*</td>
<td>7.24 ± 0.07</td>
<td>7.26 ± 0.06</td>
<td>7.23 ± 0.07*</td>
<td>7.25 ± 0.06</td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>41 ± 7</td>
<td>46 ± 8*</td>
<td>44 ± 7</td>
<td>43 ± 10</td>
<td>47 ± 3</td>
<td>43 ± 9</td>
</tr>
<tr>
<td>PaO₂ (mmHg)</td>
<td>228 ± 119</td>
<td>464 ± 152†</td>
<td>490 ± 103†</td>
<td>206 ± 135</td>
<td>399 ± 147*</td>
<td>414 ± 75*</td>
</tr>
<tr>
<td>HCO₃⁻ (mEq/l)</td>
<td>18 ± 1</td>
<td>19 ± 2</td>
<td>19 ± 1</td>
<td>19 ± 2</td>
<td>18 ± 3</td>
<td>18 ± 2</td>
</tr>
<tr>
<td>Shunt (%)</td>
<td>38 ± 24</td>
<td>17 ± 20†</td>
<td>16 ± 21†</td>
<td>42 ± 16</td>
<td>23 ± 21*</td>
<td>21 ± 19*</td>
</tr>
</tbody>
</table>

* P < 0.05 vs. before. † P < 0.05 vs. PT. ‡ P < 0.05 vs. after.

BP = blood pressure; C_{dyn,rs} = dynamic compliance of the respiratory system; C_{stat,rs} = static compliance of the respiratory system; PA = pulmonary artery pressure; PAOP = pulmonary artery occlusion pressure; PEEP = positive end-expiratory pressure; P_{aw, peak}, P_{aw, max}, P_{aw, min} = peak, inspiratory pause, mean airway pressures, respectively; PT = PEEP titration; RM = recruitment maneuver.
The indiscriminate use of PEEP as equivalent to the prevention of derecruitment are two distinct phenomena. The growing recognition that recruitment and the prevention of derecruitment (i.e., the subsequent opening of collapsed lung units) are necessary for the conversion of the most dependent lung regions into functioning units.

The CVs for the regional HU in our study suggest that the lung aeration, at a static condition, was more homogeneous along the gravitational (sternovertebral) and nongravitational (cephalocaudal) axes after the RM than after the PT. Improved homogeneity of aeration in a lung with ALI should translate into at least two physiologic advantages. First, oxygenation may improve through a better ventilation–perfusion match. Second, evenly distributed aeration will alleviate the elastic interdependence force impinging on collapsed lung units. The latter aspect, not assessed in the present study, might be worth investigating to determine whether an RM can reduce ventilator-associated lung injury more than a PEEP adjustment without an RM.

After the RM, the proportion of the lung subjected to tidal recruitment decreased from the baseline, suggesting that repeated phasic alveolar collapse could be less after the RM. However, such a decrease in tidal recruitment was not observed with the PT. In view of the importance of shearing damage in the mechanism of ventilator-associated lung injury, this result supports the RM as a necessary component of lung-protective ventilation.

Interestingly, the delayed (30 min later) lung volume after the PT increased significantly relative to the lung volume immediately after the PT (30 s), which contrasts with the stability of lung volume after the RM over the same period. This phenomenon may be explained by the “avalanche effect,” i.e., the subsequent opening of collapsed lung units may have been facilitated by the elastic interdependence of adjacent recruited units. Nevertheless, both EELV and gas-only volume after the PT did not reach the values observed after the RM at least during our study period. Consistent with this, the delayed values of physiologic parameters, such as compliance and shunt, were still more favorable with the RM.

Considering the qualitative and quantitative superiority of the RM over the PT in our study, it might be insufficient to use the inflation limb of the P-V curve to optimize recruitment in the ARDS lung. The LIP is inaccurate in predicting optimal recruitability. First, once tidal ventilation is resumed after P-V plotting, the tidal P-V loop will no longer remain on the same previous inflation limb. Second, the phenomenon of recruitment may continue above the LIP. Third, the LIP may represent the opening pressure of the small airways, whereas true recruitment of the collapsed alveoli re-
quires a much higher pressure than required for opening small airways.5,8,10 In this study, the difference between the two maneuvers also obviously involved the inflation pressure imposed on the lung over the first 2 min of the maneuver: the inflation pressure of the RM was 40 cm H₂O, whereas that of the PT to the LIP peaked around 25 cm H₂O. In view of recent data, a recruiting pressure as high as 60–70 cm H₂O may be necessary for alveolar opening.9,22,23

Unlike the pressure factor, the time factor for the RM has not received much attention until recently. In a pioneering study reported 51 yr ago, Day et al.15 showed that a certain time as well as a minimum threshold pressure was necessary to reverse atelectasis of the lung. Interestingly, they found that the (pressure × time) function for satisfactory inflation was similar across a variety of animal species. The time adopted for the RM has varied from 10 s to 2 min depending on the investigator.1,9,15,18,19 Further studies are required to define the optimum duration for the application of high pressure in patients with ARDS to avoid jeopardizing hemodynamic or respiratory stability. The lack of change in lung volume over the 30 min after the RM suggests that the 2-min period used in our protocol may have been sufficient, at least for our dogs and our pressure strategy.

It is noteworthy that the increase in the EELV correlated with the maximal decrease in blood pressure seen during the 2-min period of intervention. This phenomenon might reflect the greater transmission of airway pressure to the pleura as the lung becomes more compliant.53 The stronger correlation of blood pressure with the “ aerated EELV” (lung volume exclusive of non-aerated volume) than with the total EELV in our study suggests that transmission of airway pressure to the pleura occurred through “functioning” lung units. In view of the lower cardiac output, the higher pulmonary artery pressure after the RM than after the PT is more likely to be a spurious result and lends support to the concept described above. Therefore, the larger the recruitment, the greater the decrease in blood pressure during the maneuver that should be anticipated. This could be a drawback of the RM at the bedside although transient in duration, because systemic oxygen delivery (arterial oxygen content × cardiac output) could be compromised despite improved oxygenation of the blood in the lung.

CT has contributed significantly to the advances of the concept and treatment of ALI or ARDS. Previous CT studies on ALI or ARDS, however, mostly involved a single (usually juxtadiaphragmatic) region or a few slices of the lung because of the technical difficulties associated with whole-lung scanning.7,8,28 The validity of lung-morphometric data determined on a single or even three CT sections has been seriously questioned, because such limited data have been shown to be biased and correlated poorly with data from the whole lung.54 The main reason for the discrepancy arises from the inhomogeneity of lung injury along the cephalocaudal axis of the lung. The present study exploited the CT data from the whole lung and analyzed both the cephalocaudal axis and the sternovertebral axis. In previous studies,10,27 in which the whole lung was scanned, the scanning necessitated an apnea of 15–20 s in the subjects, which may be too long to be acceptable in a clinical setting. The present study used an advanced CT technique, i.e., a multidetector row scanner, which allowed whole-lung scanning in less than one half of the respiration hold of the study by these investigators. Setting aside the concern of radiation hazard, this CT technique with a shorter period of apnea might be more useful in the clinical situation for ARDS than previous CT techniques. In our study, we considered lung recruitment as the conversion of collapse-prone lung (the composite volume of non-aerated lung and poorly aerated lung) into collapse-resistant lung (normal aerated lung and hyperaerated lung), not merely as the increase in gas volume into these regions as defined in previous studies.8,24 Because “tissue” in these lung regions becomes the “substance” for shearing damage in a collapse-prone lung,55–57 salvaging this composite volume inclusive of tissue may be a clinically relevant concept in ARDS or ALI.

Obviously, lung injury induced by saline lavage does not represent all the possible pathophysiologic diversity of human ARDS. Moreover, our results may not be reproducible in ARDS at a more advanced stage, in which compressive atelectasis is considered to be less extensive than in the early stage of the disease.58 Even in the present study with an acute form of lung injury, the volume of hyperaerated lung was significantly increased with both RM and PT. This finding is in line with the recent CT report on ARDS patients7–24,25 and indicates that alveolar recruitment employing a high proximal airway pressure may occur at the expense of hyperaeration in some regions of the lung. Therefore, the aforementioned effects of the RM as compared with the PT must be carefully weighed against this complication in clinical application. The optimal strategies for determining recruiting pressure and its duration are as yet unclear. It has been suggested that the end-expiratory pressure should be higher than the prerecruitment level to preserve the immediate result of recruitment.18,21,39 Ideally, a point at which the critical closing pressure is most concentrated needs to be determined for the application of holding pressure (PEEP) that best preserves recruitment.12,15 Our data on the relationship between lung volume and hemodynamics are incomplete in that blood pressure is influenced by factors other than left ventricular preload. A continuous measurement of stroke volume and systemic and pulmonary vascular resistance during the RM are necessary to better understand the interaction between the changes in lung volume and hemodynamics that occur with the maneuver. The increase in PaCO₂ after the RM could have been related to a compromised tidal volume during the RM associated with the ventilation mode (pres-
sure-limited mode) and increased wasted ventilation from the increased volume of hyperinflated lung and/or decreased cardiac output compared with the baseline. However, because mixed expired Pco₂ or ventilation-perfusion distribution was not determined in the animals, the mechanisms of this phenomenon cannot be ascertained for the present study. The lower cardiac output after the RM or PT, especially cardiac output at 30 s, compared with baseline could have contributed to the decrease of shunt.⁴⁰ In view of the stability of shunt over time with the RM and similarity of cardiac output between both maneuvers at 30 min, however, the decrease of shunt between maneuvers was more attributable to the quantitative or qualitative difference in morphologic change of the lung.

In conclusion, in a canine saline-lavaged lung, the lung-morphometric effects of a RM were different from those of a PT to the LIP, in both qualitative and quantitative terms. Compared with the PT, the RM resulted in a greater functioning lung volume, better aeration of the most dependent lung, and less regional heterogeneity of lung aeration. However, the RM tended to induce a greater increase in hyperinflated lung volume than did the PT.

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