Effects of Positive End-expiratory Pressure and Different Tidal Volumes on Alveolar Recruitment and Hyperinflation

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Background: The morphologic effect of positive end-expiratory pressure (PEEP) and of different tidal volumes was studied by computed tomography to determine whether setting the tidal volume (VT) at the upper inflection point (UIP) of the pressure-volume (P-V) curve of the respiratory system or 10 ml/kg have different effects on hyperinflation and alveolar recruitment.

Methods: Alveolar recruitment and hyperinflation were quantified by computed tomography in nine patients with the acute respiratory distress syndrome (ARDS). First, end expiration was compared without PEEP and with PEEP set at the lower inflection point of the P-V curve; second, at end inspiration above PEEP, a reduced VT set at the UIP (rVT) and a standard 10 ml/kg VT (VT) ending above the UIP were compared. Three lung zones were defined from computed tomographic densities: hyperdense, normal, and hyperinflated zones.

Results: Positive end-expiratory pressure induced a significant decrease in hyperdensities (from 46.8 ± 15.1% to 38 ± 15.1% of zero end-expiratory pressure (ZEEP) area; P < 0.02) with a concomitant increase in normal zones (from 47.3 ± 20.9% to 56.5 ± 13.2% of the ZEEP area; P < 0.05), and a significant increase in hyperinflation (from 8.1 ± 5.9% to 17.8 ± 12.7% of ZEEP area; P < 0.01). At end inspiration, a significant increase in hyperinflated areas was observed with VT compared with rVT (53.1 ± 17.8% vs. 26.8 ± 17.3% of ZEEP area: P < 0.05), whereas no significant difference was observed for both normal and hyperdense zones.

Conclusions: Positive end-expiratory pressure promotes alveolar recruitment; increasing VT above the UIP seems to predominantly increase hyperinflation. (Key words: Lung(s); acute respiratory distress syndrome; barotrauma; hyperinflation; computed tomography. Ventilation: mechanical; positive end-expiratory pressure.)

THE standard for mechanical ventilation in the acute respiratory distress syndrome (ARDS) is a subject of debate. Barotrauma appears to occur more frequently with ARDS compared with other causes of ventilatory failure.1-3 The degree of lung inflation reached at end inspiration is considered one of the main determinants of mechanical ventilation-induced pulmonary lesions. Barotrauma has been especially attributed to the presence of high distending pressures,2-4 leading to the hypothesis that excessive hyperinflation must be reduced.

Acute respiratory distress syndrome is characterized by low pulmonary compliance and reduced aerated lung volumes.5-7 Regions of atelectatic lung or those with alveolar flooding are heterogeneous distributed with more normal regions, as shown by Gattinoni et al.5 Respiratory system compliance is low because the tidal volumes delivered go predominantly to the more normal regions, generating high inflation pressures.5,8 The goal of mechanical ventilation in ARDS appears, then, to be a compromise between the need for alveolar recruitment and the risk for excessive alveolar overdistension.9 A deliberate reduction of ventilation has already been proposed by Hickling et al.10,11 to limit peak airway pressure and barotrauma.

The pressure volume (P-V) curve of the respiratory system provides an assessment of the mechanical properties of the lungs.5,7,12 In patients with ARDS, the P-V curve traced above the relaxation volume of the respiratory system often shows a sigmoidal shape in which the lower inflection point has been used frequently to set the appropriate PEEP level.5,7,13,14 The upper inflec-
tion point (UITP) of the curve can indicate that a zone of decreased compliance is reached, suggesting alveolar overdistension in the aerated zones of the lungs. In a previous study, we used the UITP to set the delivered tidal volume (VT) in patients with ARDS, and we hypothesized that a pressure beyond this point could potentially induce excessive hyperinflation. When the plateau pressure corresponding to a 10-ml/kg VT was greater that the UITP, VT was reduced (rVT) in an attempt to set the plateau pressure less than the UITP. However, the morphologic effects of these ventilatory settings were not assessed. In nine sedated and paralyzed patients with ARDS, we used computed tomography (CT) to quantify the morphologic response of the lungs to PEEP and of two VTs. The aim of this study was to determine whether the UITP could represent a minimal pressure or a volume for which most of the recruitment would be obtained while hyperinflation was limited. For this purpose, we compared the effects of CT densities of a reduced volume set at the UITP (rVT) and a standard 10 ml/kg (VT) ending above this point.

Materials and Methods

The study was approved by the institutional review board of our university, and informed consent was obtained from patients’ next of kin.

Patient Population

All patients admitted to the Henri Mondor Hospital medical intensive care unit from June 1992 to December 1995 who required mechanical ventilation with PEEP ≥ 5 cmH2O and an inspired oxygen fraction (FiO2) equal or greater than 50% for more than 24 h were studied prospectively to monitor the onset of ARDS. The lung injury score, as described by Murray et al., was computed daily for all patients. Patients having a lung injury score greater than 2.5, a chest roentgenogram showing diffuse bilateral parenchymal infiltrates, and a compatible cause were categorized as having ARDS. Twenty-five patients who met the criteria for ARDS could be studied using repeated P-V curves of the respiratory system. Among them, we selected nine patients for the study who were in the early phase of ARDS and hemodynamically stable and had a plateau pressure with a standard VT greater than the UITP, which justified a reduction of VT based on respiratory mechanics (as defined below). They had no exclusion criteria for measurement of respiratory mechanics (presence of chest tube with air leaks, chronic obstructive pulmonary disease, open or flail chest) or contraindications for the use of permissive hypercapnia (intracranial hypertension, major metabolic acidosis), and we could obtain informed consent from the next of kin. Table 1 shows their main characteristics.

Pressure-Volume Curve Monitoring

While patients were sedated with midazolam (0.1 mg/kg) and paralyzed with pancuronium bromide (0.1 mg/kg), the respiratory P-V curve was performed every 2 days according to the method described by Levy et al. and that was used by other investigators. The measurements needed to draw the P-V curves were obtained using a Servo 900C ventilator (Siemens, Elema, Sweden) equipped with an airway occlusion device and with flow and pressure transducers. This method was described previously. Before measurements the transducers were carefully calibrated by comparison with a Fleisch number 2 pneumotachograph connected to a pressure transducer (Validyne MP-45, ± 70 cmH2O, Northridge, CA). To simplify the method, the ventilator was equipped with an external device permitting change of the inspiratory duration for one breath without altering the inspiratory flow rate. Consequently, we could intermittently perform a single inflation of a preselected volume during normal ventilation without altering the inspiratory flow rate and without regard for previous lung history. The smallest volumes we used were 25–50 ml, and we used no volume greater than 1,600 ml or corresponding to a pressure greater than 60 cmH2O. At the end of each new tidal volume, an end-inspiratory pause longer than 3 s was held to measure the corresponding elastic recoil pressure of the respiratory system. These measured pressures and tidal volumes were plotted to construct the P-V curve. A mean of 16 measurements was used to construct each P-V curve (fig. 1). With this technique we could also measure the P-V curve during ventilation with PEEP. Between each flow interruption, baseline ventilation was resumed and no measurement was made until the end-expiratory alveolar pressure (total PEEP, including auto-PEEP, i.e., the gradient between the set external PEEP and the total PEEP) returned to the baseline value. The total PEEP (including auto-PEEP) was measured during an occlusion made at end-expiration using the expiratory hold button of the ventilator and recording the value at the end of a 2-s pause. The lower inflection point was defined as the lower point where the curve first deviated from its linear portion (fig. 1). The pres-
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Table 1. General Characteristics of Nine ARDS Patients Submitted to CT Scan Study

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex (M/F)</th>
<th>Age (yr)</th>
<th>rVT (mL/kg)</th>
<th>Crs (mL/cmH2O)</th>
<th>PEEP (cmH2O)</th>
<th>Pplat (cmH2O)</th>
<th>Pplat/VT ratio (cmH2O)</th>
<th>PaO2/FIO2 (mmHg)</th>
<th>LIS</th>
<th>Outcome (S/D)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>57</td>
<td>8.1</td>
<td>48</td>
<td>8</td>
<td>22</td>
<td>28</td>
<td>57</td>
<td>2.75</td>
<td>D</td>
<td>Vascular surgery, mesenteric infarction</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>16</td>
<td>8.6</td>
<td>31</td>
<td>14</td>
<td>25</td>
<td>32</td>
<td>187</td>
<td>3</td>
<td>S</td>
<td>Lyell’s syndrome, sepsis</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>59</td>
<td>6.6</td>
<td>47</td>
<td>12</td>
<td>23</td>
<td>31</td>
<td>88</td>
<td>3</td>
<td>D</td>
<td>Coma, nosocomial pneumonia</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>30</td>
<td>6</td>
<td>44</td>
<td>10</td>
<td>20</td>
<td>34</td>
<td>81</td>
<td>3.25</td>
<td>D</td>
<td>Bone marrow transplant</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>58</td>
<td>7</td>
<td>36</td>
<td>10</td>
<td>20</td>
<td>34</td>
<td>80</td>
<td>3.25</td>
<td>D</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>55</td>
<td>8</td>
<td>40</td>
<td>8</td>
<td>25</td>
<td>30</td>
<td>87</td>
<td>2.75</td>
<td>S</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>69</td>
<td>7.4</td>
<td>30</td>
<td>6</td>
<td>21</td>
<td>28</td>
<td>76</td>
<td>3</td>
<td>D</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>41</td>
<td>7.3</td>
<td>48</td>
<td>11</td>
<td>20</td>
<td>24</td>
<td>82</td>
<td>3</td>
<td>S</td>
<td>Leukemia, alveolar hemorrhage</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>72</td>
<td>8.5</td>
<td>30</td>
<td>12</td>
<td>28</td>
<td>34</td>
<td>78</td>
<td>3</td>
<td>S</td>
<td>Pneumonia</td>
</tr>
</tbody>
</table>

Mean | 51  | 7.5  | 39  | 10.1 | 23  | 30  | 91  | 3.0  | 37  | 0.2 |

LIS = Lung Injury Score; rVT = reduced tidal volume; Crs = respiratory system compliance calculated on the linear part of the PV curve; Pplat = plateau pressure at reduced VT; Pplat/VT = plateau pressure at 10 mL/kg VT; PaO2/FIO2 ratio = measured on ZEEP; S = survival; D = death.

sure level at the lower inflection point was used as a reference to set total PEEP. Because small levels of auto-PEEP were often present in these patients, external PEEP was adjusted to a total PEEP equal to the lower inflection point.

The UIP was determined from the curve performed above PEEP as follows: A straight line was traced on the linear part, as the best fit by eye, and the UIP was defined as the first point where the curve started to deviate consistently from the straight line. This is illustrated in figure 1. Using this definition, we found that intraobserver variability was ± 3 cmH2O for the pressure corresponding to the UIP and ± 50 mL for the corresponding volume. In addition, previously we had found that results obtained with this method were similar to those using a step-by-step regression analysis after computerization of the recorded data.

When UIP was found on the PV curve with PEEP,
the corresponding value of pressure was recorded and compared with the end-inspiratory plateau pressure during conventional mechanical ventilation with a 10-
ml/kg Vt above PEEP. When the plateau pressure was greater than the UIP level (which was the case in the nine patients studied), tidal volume was lowered such that plateau pressure was less than the UIP (rVT). Other respiratory parameters were kept unchanged. The PaO2/FiO2 ratio and PaCO2 were measured before and 12 h after VT reduction.

Computed Tomographic Protocol
The CT study was performed within the first 2 days after hyperventilation was achieved. A new PV curve was performed a few hours before the CT scan and was used for the settings during this procedure. We used a 8100 ST ventilator (Bird, Palm Springs, CA) with battery and oxygen cylinder, and we kept the ventilatory settings constant during patient transport within the hospital and during the procedure. At least two physicians cared for each patient during the procedure. The patient’s lungs were ventilated with FiO2 1 during the entire procedure. Each patient was sedated (0.1 mg/kg midazolam), paralyzed (0.1 mg/kg pancuronium bromide), and ventilated as described previously.

Computed tomography was performed using a Siemens Somatom DRH2 machine. Exposures were taken at 125 kV, 350 mAs, and 960 projections. Slice thickness was 1 mm. After obtaining the frontal scout view, three levels of exposure were obtained: the first close to the level of the aortic arch (upper view), the second close to the carina (middle view), and the third 5 cm under the second (lower view). From one ventilatory setting to the other, the position of the patient inside the machine was kept unchanged for each level of cut; thus we did not ensure that the internal anatomic landmarks were the same (e.g., due to lung inflation, the position of the carina could be altered for the same level of cut). For each lung, the region of interest, corresponding to the whole lung parenchyma, was manually determined for each slice (inside the ribs or the pleural effusion and at the edge of the mediastinum). The areas of the contoured lungs were computed using the EVA VAO program (Siemens, Erlangen, Sweden). Using a VAX computer, the frequency distribution of the CT numbers were computed using 36 equally spaced intervals from -1,000 to +100 Hounsfield Units (HU), by steps of 30 HU. Analysis of the structure-function relation consisted of defining three compartments corresponding to hyperinflated zones (-1,000 to -800 HU), normally (or only poorly) aerated areas (-800 to -150 HU), and the nonaerated or hyperdense areas (-150 to +100 HU). The area of each lung was measured for all the levels and respiratory modalities. For each ventilatory setting, three curves were generated for each lung, corresponding to the three levels of exposure. Thus six curves (for the two lungs) of frequency distribution for the CT numbers were obtained for each patient.

The three exposures were repeated for four situations as follows: (1) at end expiration with the PEEP level selected from the PV curve and a rVT (PEEP); (2) at end inspiration with PEEP and a rVT, selected at the UIP (rVT); (3) at end inspiration with PEEP and a standard nonreduced tidal volume (Vt = 10 ml/kg) (Vt); (4) finally, at end expiration with atmospheric (zero) level of end-expiratory pressure (ZEEP). For each section, the endotracheal tube was briefly clamped for 6 s. Because PEEP-induced alveolar recruitment may occur much more gradually that the decrease in lung volume observed after PEEP release, the patients were always studied without PEEP as the last procedure.

Analysis of the Computed Tomographic Images
Because the mean cross-sectional area of the thorax enclosed in each slice increased from ZEEP to the other investigated situations, this surface could be expressed in all situations as a percentage of the surface area at ZEEP for the same anatomic level of cut (upper, middle, or lower views). For each situation, the relative distribution of the three ranges of densities (hyperdense, normal, and hyperinflated) was calculated. The percentage taken by each range of densities at any given lung volume was then multiplied by the coefficient of change in total surface area relative to ZEEP for the corresponding cut, to compare the changes of each range of densities at PEEP, rVT, and Vt always referring to ZEEP. The numbers obtained reflected the increase in the number of voxels occupied by each range of densities compared with ZEEP area. For instance, if one range of densities occupied 50% of the total area at ZEEP and still 50% at PEEP while the total surface area had increased by 20% (×1.2), then the number of voxels occupied by this range of densities had increased from 50% to 60% (50% ×1.2) of ZEEP area. To compare the different situations, results are expressed in percentages of ZEEP area. The relative distribution (i.e., not referred to ZEEP) is also given in table 3, but no comparison of the different end-inspiratory or end-expiratory levels is reported.

The percentage of densities of the two lungs were averaged for the upper (near the aortic arch), middle

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Table 2. Arterial Blood Gases before and 12 h after Vt Reduction While Patients’ Lungs Were Ventilated with PEEP

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>PaO2/FiO2 (mmHg) Before</th>
<th>PaO2/FiO2 (mmHg) After</th>
<th>PaO2 (mmHg) Before</th>
<th>PaO2 (mmHg) After</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>111</td>
<td>151</td>
<td>47</td>
<td>54</td>
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<tr>
<td>2</td>
<td>213</td>
<td>180</td>
<td>42</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>157</td>
<td>121</td>
<td>49</td>
<td>72</td>
</tr>
<tr>
<td>4</td>
<td>166</td>
<td>100</td>
<td>48</td>
<td>65</td>
</tr>
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<td>5</td>
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<td>80</td>
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<td>67</td>
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<td>6</td>
<td>93</td>
<td>123</td>
<td>36</td>
<td>54</td>
</tr>
<tr>
<td>7</td>
<td>153</td>
<td>155</td>
<td>39</td>
<td>52</td>
</tr>
<tr>
<td>8</td>
<td>153</td>
<td>224</td>
<td>48</td>
<td>63</td>
</tr>
<tr>
<td>9</td>
<td>129</td>
<td>98</td>
<td>46</td>
<td>58</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>141 ± 137</td>
<td>44 ± 62*</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

*P < 0.001 versus values before and after Vt reduction (Student’s t test).

(near the carina), and lower (basal part) parts of the lungs.

Statistical Analysis

All data are reported as mean ± SD. Two comparisons were performed using the percentage of densities, expressed in percentage of ZEEP area: (1) end expiration, comparing ZEEP and PEEP and (2) end inspiration, comparing rVt and Vt. A paired t test was used for these comparisons.

We also compared the gain or loss of percentage of ZEEP area, expressed as a difference between consecutive levels and analyzed for comparison of the two end-inspiratory values. This analysis was selected because it allows a graphic expression of our results and is presented in a figure. The results of both types of analysis are fully consistent. Probability values < 0.05 were considered significant.

Results

Patients

Table 1 indicates the mean characteristics of the nine patients studied and the relevant parameters concerning settings of mechanical ventilation. Table 2 lists the effects of Vt reduction on PaO2/FiO2 and PaO2 while patients’ lungs were ventilated with PEEP. In all patients, a lower inflection point and an UIP could be observed on the P-V curve.

The data given here are average values for the three levels of scanning performed and for both lungs (six cuts).

Effect of Lung Volume on Distribution of Densities

Table 3 shows the relative distribution of hyperinflated zones, normally aerated zones, and hyperdensities expressed as percentages of the different lung volumes (ZEEP, PEEP, rVt, Vt) for the mean values. At ZEEP, the lung surface was approximately equally divided into normal zones and hyperdense areas.

Comparison between Zero End-expiratory Pressure and Positive End-expiratory Pressure (End Expiration)

Positive end-expiratory pressure induced a significant increase in both normal (from 47.3 ± 20.9% to 56.5 ± 13.2% of ZEEP area; P < 0.05) and hyperinflated zones (from 8.1 ± 5.9% to 17.8 ± 12.7% of ZEEP area; P < 0.01), and a significant reduction in densities (from 46.8 ± 18% to 38 ± 15.1% of ZEEP area; P < 0.02). An example of this effect can be observed in figures 2 and 3.

Comparison of Reduced Tidal Volume and Tidal Volume (End Inspiration)

When comparing rVt to Vt, the amount of hyperinflated zones increased significantly (26.8 ± 17.3% vs. 33.4 ± 17.4% of ZEEP area; P < 0.05), whereas no significant reduction in densities occurred (34.3 ± 13.8% vs. 32 ± 11.5% of ZEEP area; P = 0.10). The normal areas did not differ between the two volumes (58.5 ± 12.5% vs. 58.6 ± 13.8% of ZEEP area; P = 0.96). Again, such effects can be observed in figures 2 and 3.

In addition, the gain or loss of the percentage of ZEEP area taken by each zone at PEEP, rVt, or Vt are presented in figure 4 to provide a visual display of the results; the increase in hyperinflated zones was significant from rVt to Vt (P < 0.02), but the decrease in hyperdense zones was not significant from rVt to Vt.

Discussion

We found in this study that a significant decrease in CT densities, suggestive of alveolar recruitment, was obtained at end expiration with PEEP in sedated and paralyzed patients with ARDS. Comparison of the end-inspiratory effects of a rVt set at the UIP with those of a standard Vt showed that the gain in volume thus obtained was essentially at the expense of hyperinflated...
Table 3. Relative Distribution of the Three Types of Lung Densities Expressed in Percentage of the Total Surface Area
Measured at Each Ventilatory Setting, and Increase in Total Surface Area Relative to ZEEP

<table>
<thead>
<tr>
<th></th>
<th>End-expiration</th>
<th>End-inspiration</th>
<th>ANOVA (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ZEEP</td>
<td>PEEP</td>
<td>rVT</td>
</tr>
<tr>
<td>Hyperinflation (%)</td>
<td>8.1 ± 5.9</td>
<td>15.6 ± 11.0</td>
<td>22.2 ± 13.9</td>
</tr>
<tr>
<td>Normal (%)</td>
<td>47.3 ± 20.9</td>
<td>50.3 ± 11.1</td>
<td>49.1 ± 10.9</td>
</tr>
<tr>
<td>Hyperdense (%)</td>
<td>46.8 ± 18.0</td>
<td>34.1 ± 14.3</td>
<td>28.7 ± 11.6</td>
</tr>
<tr>
<td>Increase in surface area relative to ZEEP (%)</td>
<td>—</td>
<td>12.2 ± 4.5</td>
<td>19.6 ± 5.4</td>
</tr>
</tbody>
</table>

zones. Indices of recruitment and hyperinflation were observed at most lung volumes above ZEEP, as other investigators have found. A rVT set from the P-V curve caused less hyperinflation than a larger VT. Although a mild recruitment continued to occur (i.e., a decrease in densities from rVT to VT), this was not significant.

Methodologic Limitations of Computed Tomographic Analysis

For the purpose of this study, we arbitrarily fixed three thresholds to separate three ranges of densities from CT analysis. This was defined with regard to the distribution of densities in normal lungs. The dense zones are easy to define because densities around zero HU are usually absent from normal lungs and clearly indicate atelectasis or lung parenchymal condensation. The definition of hyperinflated zones is more a matter of discussion. It has been showed that CT evidence of lung density gives a good reflection of the overall degree of hyperinflation. Low densities, especially in the range 800 HU or lower, have been associated with enlargement of distal airways and well correlated with pulmonary function tests that indicate airway obstruction and hyperinflation. It is not possible to discriminate emphysema from pulmonary hyperinflation. Even in normal lungs it is possible to find zones below 800 HU, which corresponded to our definition of hyperinflation, and other recent reports suggest that the limit for emphysema should be about 900 HU. At ZEEP, several patients had already a minor percentage

![Fig. 2. Thoracic computed tomographic images in patient 8. The three figures above represents the three level of cuts obtained at end expiration without PEEP (ZEEP); the three figures below are the middle level cut, at end inspiration with a reduced tidal volume (rVT) or a 10-ml/kg tidal volume (VT 10 ml), respectively. Note that recruitment is spectacular with PEEP and almost maximal with rVT.](image-url)

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Fig. 3. Thoracic computed tomographic scan at the middle level obtained in patient 9 at four different conditions of ventilation: (1) end expiration at zero level of end-expiratory pressure (ZEEP); (2) end expiration with PEEP (PEEP); (3) end inspiration with a reduced tidal volume (rVT) and PEEP (PEEP + Lim VT); and (4) end inspiration with a 10 ml/kg Vt and PEEP (PEEP + Vt 10).

Fig. 4. Absolute gain or loss of the percentage of zero end-expiratory pressure (ZEEP) area taken by the three types of lung densities (mean ± SEM) relative to ZEEP, in nine patients studied at four different conditions of ventilation (ZEEP, positive end-expiratory pressure [PEEP], reduced tidal volume [rVT], tidal volume [VT]). The three types of lung densities were hyperinflated areas, normally aerated areas, and hyperdense areas. The comparison shown is performed between rVT and Vt: *P < 0.05; ns, nonsignificant.

of lung units already in the “hyperinflated” zone. This could be due to the order in which the different conditions were studied (ZEEP after PEEP), resulting in a certain degree of persistent effect of applied PEEP. In addition, patients with chronic obstructive pulmonary disease have been excluded from the study, but we cannot exclude the presence of subpleural bullae or of minor emphysematous changes. Because our patients had been mechanically ventilated for several days at the time of the study, it is also possible that barotraumatic lesions, such as minor cysts or bullae, had already developed, explaining why hyperinflated zones were already present on ZEEP. The same threshold for hyperinflation thus may be difficult to apply to each individual. We believe, however, that fixing an arbitrary limit permits an analysis of the overall effect of a ventilatory setting. Because all barotraumatic lesions, such as bullae, cysts, and areas of local hyperdistention were included in this zone, it can be considered as a poorly specific but highly sensitive definition. The only difference between rVT and Vt was observed in this zone of densities, whereas normal zones were not modified. If this range of densities included a large part of normally inflated alveoli, the normal zones and this zone should have changed concomitantly. Therefore the finding of increased hyperinflation without a change in normal zones or in hyperdense areas observed with PEEP and a 10-ml/kg Vt suggests a risk of hyperinflation.

We studied only three slices, which represent a small percentage of the lungs. In addition, as the lung inflates it enlarges both in the ventral-dorsal and cephalad-caudal planes. Thus we could wonder whether the CT slices captured the same part of the lungs but under different conditions. Analyzing contiguous slices clearly would have been more accurate, allowing the lungs to be thoroughly examined. This time-consuming analysis was difficult in such critical patients. We assume that the results given by this analysis are representative of

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what happened in the whole lung. The similar behavior of the three levels of cuts with the different ventilatory settings also reinforces this assumption. Hypermaintenance and normal zones increased significantly from ZEEP to VT at the three levels of cuts, and hyperdensities significantly decreased at the three lung levels (hyperdensities decreased at the upper level, from 46.4 ± 20.6% to 25 ± 20% and at the lower level from 51.3 ± 10.7% to 42.6 ± 14%). This is consistent with previous data, suggesting that one basal CT section was representative of the whole lung.

The use of 100% Fio2 can produce atelectasis and thus may have influenced our results. The need for 100% oxygen during ZEEP application was made mandatory by the risk of life-threatening desaturation in our patients. First, Fio2 was not modified during the procedure and therefore probably did not noticeably influence the effects of the changes induced by ventilatory settings. Second, it has been shown that Fio2 has no influence on shunt in patients with severe pneumonia and shunt, a feature very similar to ARDS.

**Interpretation of the Pressure-Volume Curve of the Respiratory System**

The setting of PEEP and of rVT was performed from the analysis of the PV curve of the respiratory system. Specifically, a lower and an UIP were determined and used as indicative of the two levels of alveolar pressure within which tidal ventilation should occur. There is a large amount of literature concerning the setting of PEEP according to the lower inflection point. It corresponds to a change in respiratory system compliance suggesting the occurrence of alveolar recruitment. Our results confirm the benefit of applying this opening pressure but also show that recruitment is accompanied by hyperinflation. The assumption that local alveolar hyperdistention may create barotraumatic lesions, and may also reproduce what has been repeatedly referred to as volutrauma in animal studies, led us to consider that excessive hyperinflation should be avoided. To limit the hyperinflation in normally aerated areas, we used the information provided by the PV curve. The UIP corresponds to the point where the PV relation begins to flatten, leading to the hypothesis that some alveoli are starting to be excessively hyperinflated. We previously assessed the corresponding value of this point, in terms of VT above PEEP and end-inspiratory plateau pressure, in a group of 25 patients with ARDS. We found that in 85% of patients, the UIP corresponded to a lower VT than the usual 10-ml/kg VT, and this finding led us to reduce VT and end-inspiratory plateau pressure. When partitioning the chest wall and the lung components of the PV curve, we found that UIP was only dependent on the lung characteristics, provided that some exclusion criteria were used in patient selection.

Our data suggest that a reduction in VT from 10 ml/kg to a smaller volume, titrated on the PV curve, has noteworthy effects on hyperinflation in carefully selected patients. When keeping VT constant,Gattinoni et al. showed that incremental levels of PEEP allowed a more homogeneous distribution of gas, reducing the reopening-collapsing tissue. The data gathered by Gattinoni et al. also suggested that the recruitment was essentially obtained at end-inflation and that the lung was kept open by using PEEP to avoid the end-expiratory collapse of the alveoli. The total amount of recruitment measured at end inspiration remained similar for plateau pressures ranging from 21 to 46 cmH2O. It thus appeared of value to try to identify a minimal pressure or a volume for which most of the recruitment would be obtained while limiting hyperinflation. Increasing VT above the UIP predominantly lead to overdistension in our study. Indeed, between rVT and VT, hyperinflation was the only significant change compared with recruitment. In addition, despite an increase in lung volume, there was no significant modification of normal zones from rVT to VT; this again suggested that even if our limit for hyperinflation was arbitrary, the gain in volume was not obtained by a predominant increase of normally inflated zones. There are obvious limits to this analysis, however. The small number of patients in this study, the downward trend observed in the hyperdense distribution from rVT to VT, and the fact that we studied only two points of the PV curve makes it difficult to ensure that the maximal recruitment was achieved in all patients at the UIP. The clinical relevance of the use of the PV curve to titrate VT thus remains to be tested.

Intentional reduction of VT results in alveolar hypventilation, carbon dioxide retention, and acidemia. Although such a strategy of ventilation may appear substantiated by experimental studies, several effects would also be expected in patients. Two studies in patients, reported from Hickling et al. and based on retrospective data, suggested that such a strategy could be beneficial in patients with ARDS. It seems mandatory, however, to demonstrate the utility of such a technique before applying it systematically in the critical care environment.

In conclusion, we found that the use of PEEP, as pre-
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viously shown, is justified based on its effect on alveolar recruitment. Increasing Vt above UIP induced a mild, nonsignificant recruitment and essentially caused further hyperinflation. The clinical consequences of such a strategy in terms of the incidence of barotrauma, complications, and death in patients with ARDS are unknown and need to be studied.

References