Lower inflection point and recruitment with PEEP in ventilated patients with acute respiratory failure

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The lower inflection point (LIP) on the total respiratory system pressure-volume (P-V) curve is widely used to set positive end-expiratory pressure (PEEP) in patients with acute respiratory failure (ARF) on the assumption that LIP represents alveolar recruitment. The aims of this work were to study the relationship between LIP and recruited volume (RV) and to propose a simple method to quantify the RV. In 23 patients with ARF, respiratory system P-V curves were obtained by means of both constant-flow and rapid occlusion technique at four different levels of PEEP and were superimposed on the same P-V plot. The RV was measured as the volume difference at a pressure of 20 cmH2O. A third measurement of the RV was done by comparing the exhaled volumes after the same distending pressure of 20 cmH2O was applied (equal pressure method). RV increased with PEEP (P < 0.0001); the equal pressure method compares favorably with the other methods (P = 0.0001 by correlation), although individual data cannot be superimposed. No significant difference was found when RV was compared with PEEP in the group of patients with a LIP ≤5 cmH2O and the group with a LIP >5 cmH2O (76.9 ± 94.3 vs. 61.2 ± 51.3, 267.7 ± 109.9 vs. 209.6 ± 73.9, and 428.2 ± 216.3 vs. 375.8 ± 145.3 ml with PEEP of 5, 10, and 15 cmH2O, respectively). A RV was found even when a LIP was not present. We conclude that the recruitment phenomenon is not closely related to the presence of a LIP and that a simple method can be used to measure RV.

Acute respiratory failure; mechanical ventilation; pressure-volume curve; positive end-expiratory pressure

Recent studies on the clinical outcome of acute respiratory distress syndrome (ARDS) (3) have showed that a ventilatory strategy based on some measurement of respiratory mechanics, namely the pressure-volume (P-V) curve of the respiratory system (P-Vrs curve), can improve the survival of these patients (1). The mechanism invoked to explain this striking finding results from the combination of two strategies: 1) the so-called “open lung” approach (17, 25) aimed at preventing tidal alveolar collapse and reopening by setting the level of positive end-expiratory pressure (PEEP) just above the lower inflection point (LIP) (13); and 2) the so-called “lung protective” approach aimed at preventing over-distension by limiting the tidal volume below the upper inflection point (1). In this perspective, the P-Vrs curve may represent a fundamental tool to select the appropriate ventilatory parameters. However, there is the assumption that the LIP on the P-Vrs curve is the mechanical counterpart of the alveolar recruitment and that, after LIP, any kind of significant recruitment does not occur. Nonetheless, theoretical (12) and pathophysiological studies (14) challenge that assumption, whereas only a few studies have been performed to elucidate the relationships between alveolar recruitment and LIP (10, 37). Furthermore, measurement of the alveolar recruitment has not become part of common clinical practice, at least in part because of the complexity of the procedures.

METHODS

This investigation was undertaken with two purposes: first, to study the relationship between LIP and recruitment, and second, to propose a simple method to quantify alveolar recruitment in clinical settings.

Patients

Twenty-three patients (6 women, 17 men) admitted to the Intensive Care Unit of the Ospedale Maggiore of Parma (Italy) were enrolled in this study because they fulfilled the following admission criteria: 1) presence of an acute lung injury (ALI) defined by acute onset, arterial PO2 (PaO2)-to-fraction of inspired O2 (FIO2) ratio <300 Torr, and diffuse bilateral infiltrates on frontal chest radiograph (3); 2) mechanical ventilation through an endotracheal or tracheostomy tube; and 3) absence of an exclusion criteria. Exclusion criteria were a previous history of chronic airway disease (i.e., chronic obstructive pulmonary disease and asthma), heart failure, shock (suggested by mean arterial pressure of <60 mmHg), evident chest wall deformities, pneumothorax, and intracranial hypertension. The patient’s characteristics at the time of the inclusion into the study are shown in Table 1. All patients were mechanically ventilated with Drager.
Evita II (Dragerwerk, Lubeck, Germany), and they had been ventilated for 6.7 ± 5.5 days at the time of the study. The ventilator patterns as instituted by the attending physician and the arterial blood gases at the time of the enrollment are shown in Table 2.

**Measurements**

Flow was measured with a heated pneumotachograph (no. 2, Fleish, Lausanne, Switzerland) connected to a differential pressure transducer (MP-45, ±2 cmH2O; Validyne, North-...
ridge, CA), which was inserted through the cones between the Y piece of the circuit and the proximal tip of the endotracheal or tracheostomy tube. The pneumotachograph was calibrated by means of a supersyringe with the gas mixture in use and was linear over the experimental range of flow. The instrumental dead space was 120 ml. Changes in volume were obtained by numerical integration of the flow signal. Pressure at the airway opening (Pao) was sampled through a side port on the piece between the pneumotachograph and the artificial airway and connected through an air-filled noncompliant catheter to a differential pressure transducer (MP-80, Validyne). To reduce the effects of the compliance and resistance of the ventilator circuit, a single length of standard, noncompliant tubing (2-cm internal diameter and 60 cm long) was used, and the humidifier was omitted from the inspiratory line of the ventilator throughout the procedure. Before each set of measurements, the cuff of the tracheal tube or tracheal cannula was inflated with an extra volume of 3 ml of air, and airways were suctioned free of centrally retained secretions; special care was taken to avoid air leaks in the equipment’s connections and around the cuff of the endotracheal tube.

All signals were recorded on a personal computer (Macintosh II CI; Apple Computer, Cupertino, CA) via an analog-to-digital converter (MacLab Analog Digital Instrument, Castle Hill, NSW, Australia) at a sample rate of 100 Hz and stored in diskettes for subsequent computer analysis.

All patients had an indwelling radial catheter inserted as standard clinical procedure for blood-gas collection and pressure monitoring. Blood gases were measured by mean of an automated blood-gas analyzer (IL BG3; Instrumentation Laboratory, Lexington, MA). Heart rate, pulse oximetry, and systemic arterial pressure were monitored throughout the study (Sirecust 1281, Siemens Medical Electronics, Danvers, MA), and during the measurements a physician not involved in the study was always present for patient care.

Procedure

At the time of the study, the patients were in a stable, hemodynamic condition. The investigation was performed with the patient in the supine position, sedated with a continuous infusion of fentanyl (0.02–0.03 μg·kg⁻¹·min⁻¹) and diazepam (0.6 μg·kg⁻¹·min⁻¹), and paralyzed with vecuronium (0.1 mg/kg, followed by 0.05 mg/kg if necessary). The ventilator setting established by the attending physician (Table 2) was maintained stable throughout the study, except for the level of PEEP. Indeed, four levels of PEEP, corresponding to 0, 5, 10, and 15 cmH₂O, were applied in a random order and maintained for 20–30 min before each set of measurements.

Alveolar Recruitment

The amount of alveolar recruitment was measured according to the principle that, if an alveolar recruitment occurs, this causes an increase in the lung volume for the same distending pressure (15, 28, 35). Three methods were applied to this purpose. Two were based on the P-Vrs curves obtained by means of the supersyringe (19) and by the occlusion technique (28) at the different levels of PEEP. The third method was based on the measurement of the lung volume at the same distending pressure.

Constant-flow method. This method was described in a previous study (24). Briefly, a supersyringe (volume: 2 liters) was connected to the circuit through an Y piece to maintain the selected PEEP at the start of the P-V curve. The supersyringe was moved at a low, constant rate (50 ml/s) by an electric engine. The inflation volume was set at 10–12 ml/kg. At the final inflation volume, the engine automatically reversed the syringe to the starting pressure. Before initiating the inflation, the syringe and the circuit were put in communication to allow pressure equilibration, and the expiratory time was prolonged (minimum time, 5 s) to eliminate the intrinsic PEEP (PEEPi), if present. Then the ventilator limb of the Y connection was clamped, and syringe flow was started. In some instances, the set volume at zero end-expiratory pressure (ZEEP) was higher than the corresponding volume at other PEEP levels because of the need to have all of the curves superimposed. To construct the curves, the Pao was plotted against the corresponding change in lung volume. Values of Pao were referred to the atmospheric pressure. Changes in lung volume were referred to the static equilibrium volume (i.e., relaxation volume) of the total respiratory system (VR) by adding to the inspiratory volume the change of the lung volume due to the PEEP. The latter was measured as the volume exhaled after PEEP was removed at the end of a complete expiration (i.e., the change in the functional residual capacity (ΔFRC) due to the PEEP) (9). The P-Vrs curves were plotted on the same x-y-axis by adding the ΔFRC to the inflation volume of the syringe. The magnitude of alveolar recruitment at each level of PEEP was then estimated as the volume difference from the P-Vrs curve corresponding to a single level of PEEP and the P-Vrs curve at ZEEP along a vertical line drawn at the preselected pressure value of 20 cmH₂O (Fig. 1).

Rapid inspiratory occlusion method. This method has been described in detail elsewhere (28). Briefly, during the tidal ventilation, a rapid end-inspiratory occlusion maneuver was performed by manually clamping the circuit between the Y piece and the pneumotachograph at the end of the inspiration at different tidal volumes ranging between 0.1 and 1.2 liters. A minimum of 10 steps was considered necessary to construct a P-Vrs curve. The changes in volume were ob-

Fig. 1. Measurement of the alveolar recruitment with positive end-expiratory pressure (PEEP) on the pressure-volume curves of the respiratory system (P-Vrs curves) drawn with the constant-flow method in a representative patient. Recruitment is computed as the difference in volume along the vertical line representing a pressure of 20 cmH₂O. Segments a, b, and c represent the recruited volume (RV) at PEEP of 5, 10, and 15 cmH₂O, respectively. Pao, airway opening pressure.
tained by rotating the volume knob of the ventilator while maintaining unchanged the other ventilatory parameters. If necessary, inspiratory-to-expiratory ratio was prolonged to allow completion of the inspiration when high-volume steps were selected. The occlusion was maintained for 3–5 s, and pressure at the end of the plateau was recorded. The P-V points were then plotted to construct the P-Vrs curve. Similar to the P-Vrs curve obtained with the supersyringe, the Pao was referred to the atmospheric pressure, and changes in lung volume were referred to Vr, by adding to the test volume the change in the end-expiratory volume due to the combined effect of PEEP and PEEPi, if present. The latter was obtained by subtracting the exhaled tidal volume with PEEP from the total exhaled volume after PEEP was removed. The P-Vrs curves at each level of PEEP were superimposed on the same P-V plot as illustrated in Fig. 2. The recruited volume was estimated as the difference between the P-Vrs curve corresponding to a single level of PEEP and the P-Vrs curve at ZEEP along a vertical line drawn at the preselected pressure value of 20 cmH2O (Fig. 2).

Equal pressure method. The third method is conceptually identical to the two methods previously described, but it is independent from the construction of the P-Vrs curves. It consists of measuring the volume exhaled to the atmosphere after inflating the lung at the same distending pressure of 20 cmH2O during the course of the mechanical ventilation at different levels of PEEP. The targeted distending pressure of 20 cmH2O was obtained by switching the ventilator from the standard mode to the BIBAP (biphasic intermittent positive airway pressure) mode of the Drager Evita. In this mode of ventilation, the ventilator generates two different pressures and maintains those pressures for two corresponding different times. For the aim of the study, the first pressure was set at 20 cmH2O for a time of 6 s, and this setting was maintained unchanged throughout the study. The second pressure was set at a value equal to the selected PEEP during standard ventilation for a time of 4 s. At the end of the inflation time, the patient was disconnected from the ventilator, and the exhaled volume was recorded until Vr was reached, as evidenced by zero value on the expiratory flow trace. The exhaled volume obtained with this maneuver (V20) at each level of PEEP was compared with the corresponding exhaled volume at ZEEP, with the difference being the volume recruited at that level of PEEP with respect to ZEEP (Fig. 3).

Protocol

After the enrollment, the four levels of PEEP were applied in random order. For each level of PEEP, we performed, in sequence, the following maneuvers: P-Vrs curve with the supersyringe for the construction of P-Vrs curve with the constant-flow method, the series of volume steps for the construction of the P-Vrs curve with the rapid inspiratory occlusion method, the end-expiratory occlusion for the PEEP measurement, V20 measurement, change in the end-expiratory volume, and ΔFRC measurements. After the patients were disconnected from the ventilator, the standard ventilation was resumed until tidal volume; flow, peak, and plateau pressures; and arterial saturation returned to their baseline values.

Data Analysis

The P-Vrs curves at each level of PEEP were drawn from pressure and volume values using the graphic option of the Excel 4 software (Microsoft, Redmond, WA). From the P-Vrs curves obtained with the supersyringe, the following parameters were derived (10, 24): 1) LIP and 2) static inflation compliance.

To objectively determine the LIP, the pressure and volume data obtained with the constant-flow method were fitted to a sigmoidal equation of the form

\[ V = a + \frac{b}{1 + e^{-(P - c)/d}} \]

where V is volume, P is pressure, a (in units of volume) is the lower asymptote, b (in terms of volume) is distance from the lower to the upper asymptote, c (in units of pressure) is the mathematical inflection point of the curve (i.e., the point at which the curvature changes direction), and d (in terms of pressure) is the distance from c within which most of the volume change occurs (11, 36). The sigmoidal equation had an excellent fit, yielding R² values ranging from 0.996 to 0.999 (mean ± SD: 0.998 ± 0.001). The LIP was considered as the point of maximum increase in compliance (Pmci), where the rate of change of upward slope is maximal and was calculated as Pmci = c + 1.37d (11).

Static inflation compliance was computed as the ratio of the change in volume to the corresponding change in the airway pressure over the linear portion of the P-V curve.

Recruited volume. The amount of lung volume recruited with PEEP was estimated in triplicate. 1) From the P-V curves drawn with the constant-flow method and superimposed on the same P-V diagram, the recruited volume at a single level of PEEP was measured as the difference in volume from the P-V curve at that level of PEEP and the P-V curve at ZEEP for the same pressure of 20 cmH2O (Fig. 1). 2) An identical measurement was taken on the P-V curve done with the rapid inspiratory occlusion method (Fig. 2). 3) From the V20 recording, the recruited volume at a single level of PEEP was computed as the difference between the V20 measured at that level of PEEP and V20 measured at ZEEP (Fig. 3, bottom).
Statistical Analysis

All values are expressed as means ± 1 SD. The values of recruited volume obtained with different methods and for different levels of PEEP were compared with ANOVA for repeated measures, and a Student-Newman-Keuls post hoc analysis was performed if the global F test indicated statistical significance. The agreement between recruited volume measured with the three different methods was analyzed with the Bland-Altman method (4). Regression analysis was performed using the least squares method. Statistical significance was determined at P < 0.05.

RESULTS

As illustrated in Fig. 4, the amount of the recruited volume increased with increasing levels of PEEP. There was no significant difference among the methods used to estimate the alveolar recruitment at any level of PEEP. A significant correlation was found between recruited volume obtained with the three different methods, whereas the Bland and Altman test of the agreement showed some degree of variability among individual data (Fig. 5).

As shown in Table 2, a LIP was present on the P-Vrs curve in 19 of the 23 patients, averaging 6.5 ± 4.4 cmH2O. In four patients, no LIP was evident on the P-Vrs curve; in eight other patients the LIP was <5 cmH2O, averaging 2.9 ± 1.4 cmH2O; whereas in the remaining 11 patients the LIP was >5 cmH2O, averaging 8.3 ± 1.7 cmH2O.

To investigate the relationship between LIP and alveolar recruitment, we first separated the patients into three groups: those with no LIP, with LIP ≤5 cmH2O, and with LIP >5 cmH2O. Because only four patients showed no LIP on the P-Vrs curve, we decided to group these patients with those with a LIP ≤5 cmH2O. Last we performed the analysis in two groups: group A, the 12 patients without LIP or with LIP ≤5 cmH2O; and group B the 11 patients with LIP >5 cmH2O. Figure 6 shows that the amount of the alveolar recruitment increased with increasing level of PEEP in both groups. By comparing the amount of recruitment at each level of PEEP, we did not find any significant difference between the two groups with low (group A) and high (group B) LIP for the three different methods (Table 3).

In the whole patient group, the PaO2/FiO2 increased significantly with PEEP (176.4 ± 78, 189.9 ± 95.9, 213.9 ± 105.2, and 237.5 ± 127.6 Torr at PEEP of 0, 5, 10, and 15 cmH2O, respectively; P < 0.0001), and a significant positive correlation (r = 0.43, P < .001) was found between changes in the PaO2/FiO2 and the recruited volume. However, when the regression analysis was performed separately in groups A (low LIP) and B (high LIP), a significant correlation was found in the latter and not in the former (Fig. 7).
Inflation respiratory system compliance did not change significantly by changing PEEP from 0 to 15 cmH2O in the whole patient group and in groups A and B (Table 4). Moreover inflation compliance of the respiratory system was not significantly different between groups A and B at each level of PEEP (P = 0.37, 0.34, 0.55, and 0.93 for PEEP of 0, 5, 10, and 15 cmH2O, respectively).

DISCUSSION

The results of this study show that, in ventilated patients with ALI or ARDS, there is a poor relationship between the level of LIP and the amount of the alveolar recruitment determined by application of PEEP. In addition, we present a simplified method suitable for bedside measurement of alveolar recruitment.

LIP and Alveolar Recruitment

The conventional concept is that the LIP on the P-V curve reflects the average critical pressure needed to reopen those regions of the lung that close during expiration (22). This assumption underlies the development of a ventilatory strategy including the level of PEEP at a pressure slightly above the LIP (1, 2, 7). However, only a few studies have specifically addressed the relationship between the LIP and the amount of alveolar recruitment (14, 37). They showed a quite loose relationship, suggesting that recruitment was occurring also when PEEP was raised above the LIP. Our results are in line with these findings. We observed not only a consistent amount of recruitment with PEEP above the LIP in patients with a LIP on the P-V curve, but also the occurrence of an increasing amount of recruitment with PEEP in patients without a LIP.

The poor relationship between LIP and recruitment can be explained in different ways. First, the LIP on the P-Vrs curve can be due to the chest wall rather than to the lung mechanics (24). Second, mechanisms other than alveolar recruitment can be taken into account to explain the LIP on the P-V curve. They include reflex bronchoconstriction, pneumoconstriction due to a release of inflammatory mediators, and a peribronchial edema (21). Also, extreme expiratory flow limitation in the smallest airways has been invoked as a mechanism underlying LIP (16).
shown by theoretical and experimental studies (12, 20), the LIP could signal the beginning rather than the achievement of a complete alveolar recruitment. Fourth, a recent experimental work (18) suggests that LIP can be better attributed to an opening of closed distal airways rather than a true alveolar recruitment that occurs as a separate phenomenon at higher pressure (31, 33). In fact in four patients, we could measure a consistent recruitment in the absence of a LIP on the P-V curve. Last, it has been shown that the lung damage in acute respiratory failure is not distributed homogeneously (8), and, after application of PEEP, recruitment of previously collapsed lung zones can coexist with hyperdistention of normally inflated zones. In this case, the alveolar recruitment may not induce significant changes in the slope of the P-V curve.

Our results can have some clinical implications. In fact, as long as the reopening of all recruitable alveoli is considered among the end points of the ventilatory strategy in ALI and ARDS, the LIP in the P-Vrs curve cannot be further considered as the method of choice to measure lung recruitment during application of PEEP with the 3 different methods of measurement. Significant difference vs. +5- and †10-cmH2O PEEP within the same group and with the same method of measurement, \( P < 0.001 \).

### Table 3. Recruited volume at increasing level of PEEP with the 3 different methods of measurement of the alveolar recruitment

<table>
<thead>
<tr>
<th>Recruited Volume, ml</th>
<th>Whole group</th>
<th>Group A</th>
<th>Group B</th>
<th>( P ) (A vs. B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{Constant-flow method} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEEP 5</td>
<td>81 ± 99.7</td>
<td>112.6 ± 121.9</td>
<td>46.5 ± 54.7</td>
<td>0.11</td>
</tr>
<tr>
<td>PEEP 10</td>
<td>225.9 ± 127.6</td>
<td>246.2 ± 151.7</td>
<td>203.8 ± 97.4</td>
<td>0.44</td>
</tr>
<tr>
<td>PEEP 15</td>
<td>378.7 ± 214.8</td>
<td>419.2 ± 268.4</td>
<td>334.6 ± 134.7</td>
<td>0.36</td>
</tr>
<tr>
<td>( P ) (ANOVA)</td>
<td>(&lt; 0.000001)</td>
<td>(&lt; 0.00001)</td>
<td>(&lt; 0.000001)</td>
<td></td>
</tr>
<tr>
<td>( \text{Rapid inspiratory occlusion method} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEEP 5</td>
<td>90.9 ± 93.3</td>
<td>114.5 ± 107.2</td>
<td>65.1 ± 71.3</td>
<td>0.21</td>
</tr>
<tr>
<td>PEEP 10</td>
<td>240.4 ± 112.2</td>
<td>264.4 ± 129.6</td>
<td>214.2 ± 88.0</td>
<td>0.29</td>
</tr>
<tr>
<td>PEEP 15</td>
<td>418.6 ± 215.3</td>
<td>446.8 ± 271.8</td>
<td>387.9 ± 136.8</td>
<td>0.52</td>
</tr>
<tr>
<td>( P ) (ANOVA)</td>
<td>(&lt; 0.000001)</td>
<td>(&lt; 0.00001)</td>
<td>(&lt; 0.000001)</td>
<td></td>
</tr>
<tr>
<td>( \text{Equal pressure method} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEEP 5</td>
<td>69.4 ± 75.6</td>
<td>76.9 ± 94.3</td>
<td>61.2 ± 51.3</td>
<td>0.63</td>
</tr>
<tr>
<td>PEEP 10</td>
<td>239.9 ± 97.9</td>
<td>267.7 ± 109.9</td>
<td>209.6 ± 73.9</td>
<td>0.16</td>
</tr>
<tr>
<td>PEEP 15</td>
<td>403.1 ± 183.6</td>
<td>428.2 ± 216.3</td>
<td>375.8 ± 145.3</td>
<td>0.51</td>
</tr>
<tr>
<td>( P ) (ANOVA)</td>
<td>(&lt; 0.000001)</td>
<td>(&lt; 0.00001)</td>
<td>(&lt; 0.000001)</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD. Group A, 12 patients without LIP or with LIP ≤ 5 cmH2O; group B, 11 patients with LIP > 5 cmH2O; PEEP 5, 10, and 15: positive end-expiratory pressure of 5, 10, and 15 cmH2O.
Another limitation of our (as well as other) studies consists of the assumption that the respiratory system returns to the same resting volume when the airway is open to the atmosphere after the lungs have been ventilated at different levels of PEEP. Although this assumption has never been validated, some studies provide some data that could be considered not to be in contrast with it. For example, Ranieri and associates (29) reported that lung volume measured with the respiratory inductive plethysmography returned the same value, as evidenced by the respiratory inductive plethysmography signal, after eight patients were ventilated with different levels of PEEP, then disconnected from the ventilator, and allowed to breath out to resting volume. Recently, Cakar and associates (5) found in dogs with oleic acid-induced respiratory failure that the FRC measured with the helium dilution technique after PEEP was dropped to 0 from 8 or 15 cmH2O did not change significantly before and after a recruitment maneuver consisting of a single 30-s sustained inflation at 60-cmH2O airway pressure.

Last, the method of measurement of the recruited volume assumes that the chest wall compliance does not change significantly during the study period; this is an acceptable condition.

The previous method of measurement of the recruitment using lung mechanics compared the lung volume on the P-Vrs curve traces at different levels of PEEP and superimposed on the same diagram. This is a complex and time-consuming task that has been used only for experimental purposes. By contrast, our method is simpler because it does not need the P-Vrs curves and directly compares the volume expired at the same distending pressure for different levels of PEEP. This simple method may allow frequent measurements of the recruitment in the clinical setting; for example, to set the ventilatory strategy in patients with acute respiratory failure.

In our study, the recruited volume with the equal-pressure method was compared with recruited volume

**Table 4. Values of Crs_{inf} for the 4 different levels of PEEP**

<table>
<thead>
<tr>
<th>Crs_{inf}, ml/cmH2O</th>
<th>PEEP 0</th>
<th>PEEP 5</th>
<th>PEEP 10</th>
<th>PEEP 15</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole group</td>
<td>52.9 ± 13.8</td>
<td>52.6 ± 14.4</td>
<td>53.4 ± 17.9</td>
<td>50.8 ± 20.5</td>
<td>0.56</td>
</tr>
<tr>
<td>Group A</td>
<td>55.4 ± 14.4</td>
<td>55.4 ± 17.2</td>
<td>55.6 ± 21.6</td>
<td>51.1 ± 26.3</td>
<td>0.45</td>
</tr>
<tr>
<td>Group B</td>
<td>50.2 ± 13.1</td>
<td>49.6 ± 10.5</td>
<td>51.0 ± 13.3</td>
<td>50.4 ± 12.8</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Crs_{inf}, compliance of the respiratory system measured on the linear portion of the pressure-volume curve of the respiratory system obtained with the constant-flow method.
measured on the P-Vrs curves built up with the rapid occlusion method and the constant-flow method. The results of the regression analysis provided a significant correlation (see Fig. 5). However, in the Bland-Altman analysis, we found some disagreement not only between our method and P-V methods, but also between the two P-V methods. These findings could be explained by a different recruitment status of the lung at different times due to the maneuvers imposed by the study’s protocol or by an intraindividual variability of the alveolar recruitment. To our knowledge, this issue has not been sufficiently investigated yet.

**LIP, Recruitment, and Oxygenation**

In the whole patient group, the stepwise increase in the amount of the recruited volume with increasing levels of PEEP showed a direct, significant correlation with the changes in arterial oxygenation, in keeping with the notion that recruitment plays a role in improving pulmonary gas exchange (6). However, when we separated the patients into two groups, namely a group without a LIP or a LIP ≤ 5 cmH2O and a group with a LIP > 5 cmH2O, we found that the correlation between the amount of recruitment with PEEP and the amount of pulmonary oxygenation was still significant in the patients with LIP > 5 cmH2O, whereas it was not significant in patients with a LIP ≤ 5 cmH2O. There was no significant correlation even between the two subgroups of patients comprising group A, i.e., four patients with no LIP and eight patients with a LIP < 5 cmH2O. This latter finding is somewhat surprising but can be explained in several ways. The increase in lung volume, for example, could occur in conjunction with overexpansion of normally compliant alveolar units with resultant diversion of the blood flow to the less ventilated diseased units with no improvement and even worsening of the oxygenation (30). Moreover, as evidenced by Rothen and associates (32), in normal humans under general anesthesia, the recruited lung zones can have a low ventilation-perfusion ratio, and in this case the alveolar recruitment could result in a small improvement in arterial oxygenation, especially when, as in our patients, a FiO2 < 1 is applied. Last, as already discussed in the previous section, plastoelastic behavior of the lung tissue can explain part of the increase in recovered volume, and it cannot be excluded that a such phenomenon could prevail in the group A patients.

**Conclusions**

In the present study, we have shown that LIP is not related to the achievement of the maximal alveolar recruitment because the recruitment further increases when PEEP is set above the LIP. Moreover we found that the absence of a LIP on the P-Vrs curve does not preclude the possibility of recruitment with PEEP. These results suggest that, in the perspective of the achievement of an optimal alveolar recruitment, the use of P-Vrs curve must be reevaluated. In particular, if the achievement of an optimal alveolar recruitment is considered as an independent aim of the ventilatory strategy in patients with acute respiratory failure, a direct measurement of this parameter should be recommended.

Further studies in this field could help to improve the ventilatory management of ARDS patients, a factor that by itself can be related to their survival, as recently demonstrated by the results of the ARDS network’s study (34).

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**REFERENCES**


Recruitment with PEEP in ARF patients


