Intrinsic positive end-expiratory pressure during one-lung ventilation of patients with pulmonary hyperinflation. Influence of low respiratory rate with unchanged minute volume

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Background. We measured lung mechanics and gas exchange during one-lung ventilation (OLV) of patients with chronic obstructive pulmonary disease, using three respiratory rates (RR) and unchanged minute volume.

Methods. We studied 15 patients about to undergo lung surgery, during anaesthesia, and placed in the lateral position. Ventilation was with constant minute volume, inspiratory flow and FIO2. For periods of 15 min, RR of 5, 10, and 15 bpm were applied in a random sequence and recordings were made of lung mechanics and an arterial blood gas sample was taken. Data were analysed with the repeated measures ANOVA and paired t-test with Bonferroni correction.

Results. PaO2 changes were not significant. At the lowest RR, PaCO2 decreased (from 42 (SD 4) mm Hg at RR 15 to 41 (4) mm Hg at RR 10 and 39 (4) mm Hg at RR 5, P<0.01), and end-tidal carbon dioxide increased (from 33 (5) mm Hg at RR 15 to 35 (5) mm Hg at RR 10 and 36 (6) mm Hg at RR 5, P<0.01). Intrinsic positive end-expiratory pressure (PEEPi) was reduced even with larger tidal volumes (from 6 (4) cm H2O at RR 15 to 5 (4) cm H2O at RR 10, and 3 (3) cm H2O at RR 5, P<0.01), most probably caused by increased expiratory time at the lowest RR.

Conclusion. A reduction in RR reduces PEEPi and hypercapnia during OLV in anaesthetized patients with chronic obstructive lung disease.

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To facilitate thoracic surgery, one-lung ventilation (OLV) is a valuable technique. One lung is mechanically ventilated while the other is either occluded, or left open to the atmosphere. Generally a dependent lung tidal volume (VT) similar to that used in two-lung ventilation is recommended. 1 Respiratory frequencies around 15 bpm are commonly used during OLV. 2 Other authors recommend that the dependent lung should be ventilated with a tidal volume of 10–12 ml kg⁻¹ and the respiratory rates (RR) to maintain the arterial partial pressure of carbon dioxide (PACO2) at normal values. 2 These suggestions do not consider that many patients having lung surgery have chronic obstructive pulmonary disease (COPD) with airflow limitation and pulmonary hyperinflation. During the OLV of these patients, intrinsic positive end-expiratory pressure (PEEPi) is often present, and can be increased by an unfavourable ventilatory pattern. 3 Moreover, COPD patients have increased physiological dead space and can develop hypercapnia.

During the mechanical ventilation of these patients’ lungs, conditions that impede expiratory flow (increased airway resistance, and the resistance of the double-lumen
tube (DLT)) or poor settings of the ventilator may cause dynamic pulmonary hyperinflation (DPH) and PEEPi. In addition, alveolar overdilatation by severe DPH in the ventilated lung may divert pulmonary blood flow to the non-ventilated lung, and impair arterial oxygenation.

Increases in RR, \( V_t \), or a reduction of expiratory time (\( T_e \)) would encourage the development of PEEPi and DPH. Severe DPH causes circulatory depression and pulmonary barotrauma.

The settings for mechanical ventilation in patients with COPD during OLV to avoid excessive DPH and hypercapnia have not been clearly identified. Studies performed during OLV have mainly assessed the effect of \( V_t \) changes or the isolated effect of altered RR with unchanged \( V_t \). However, with constant RR, a greater \( V_t \) would promote PEEPi, while a smaller \( V_t \) would not be adequate because of dependent lung atelectasis and hypercapnia. If a constant \( V_t \) is chosen, with changes in RR, then an increase of RR would cause PEEPi and a decrease of RR would increase hypercapnia because of reduced minute ventilation. We tested if a ventilatory pattern, which combined a reduction in RR with a constant \( V_t \) increase, could control both hypercapnia and PEEPi during OLV of patients with chronic obstructive pulmonary disease.

### Materials and methods

The Institutional Review Board approved the investigation and informed consent was obtained from 15 patients undergoing elective thoracotomy for tumour resection and requiring OLV. Before surgery, pulmonary function was tested in the sitting position, including spirometry and static lung volumes determined by plethysmography (MasterScreen Body, Jaeger and Toennies, Erich Jaeger GmbH, Hoechberg, Germany). Only patients whose preoperative functional residual capacity (FRC) exceeded 120% of the predicted value were included in the study. Patient details and pulmonary function values are shown in Table 1.

In all patients, anaesthesia was induced and maintained with a variable rate continuous infusion of propofol (loading dose 2 mg kg\(^{-1}\)) followed by continuous infusion of 3–5 mg kg\(^{-1}\) h\(^{-1}\) and inhalation of isoflurane (<0.5 MAC). Epidural analgesia at the mid-thoracic level (Th5–Th8) (test dose of 3 ml 2% lidocaine with epinephrine 1/200 000 followed by a continuous infusion of bupivacaine 0.5% 2–5 ml h\(^{-1}\)) was started before induction of general anaesthesia and maintained continuously during surgery. Pancuronium (loading dose of 80 \( \mu \)g kg\(^{-1}\) and top up doses of 20 \( \mu \)g kg\(^{-1}\)) was used to allow tracheal intubation and to maintain neuromuscular block throughout surgery. The neuromuscular block was assessed by regular measurements of post-tetanic count during the procedure. A three-lead electrocardiogram, invasive radial arterial pressure and arterial oxygen saturation were monitored continuously. The Datex Ultima (SV capnometer (Datex Instrumentarium, Helsinki, Finland) was used to measure expired end-tidal carbon dioxide tension (\( E_{\text{CO}_2} \)), flow-volume and pressure–volume loops. In all patients, the bronchus of the dependent lung was intubated with an appropriate size (based on sex and height of the patients) DLT (Broncho-cath, Mallinckrodt Laboratories, Athlone, Ireland). This was correctly positioned using fiberoptic bronchoscopy, first in the supine position and then in the lateral position. The patients’ lungs were ventilated with 50% oxygen in air, with a constant inspiratory flow ventilator (Siemens Servo 900 C; Siemens Elema; Solna, Sweden). Initial settings were \( V_t \) 10 ml kg\(^{-1}\) and a rate of 10 bpm. External positive end-expiratory pressure (PEEP) was set to zero. Inspiratory time (\( T_i \)) was 33% of total cycle time (\( T_{tot} \)) and end-expiratory pause was 10% (of \( T_{tot} \)). The ventilator and the breathing system were inspected carefully and checked for potential leaks. After turning the patient in the lateral position and checking of the correct position of the DLT by bronchoscopy, the tracheal limb of the DLT was clamped and opened to the atmosphere to allow lung collapse. Three ventilatory rates of 5, 10 and 15 bpm (RR 5, RR 10, RR 15) were applied in a random sequence and maintained for 15 min. After each 15-min period, end-inspiratory and end-expiratory occlusions were performed to measure elastance and intrinsic positive pressure, and arterial blood gas samples were drawn. The occlusions were maintained until the airway pressure was stable. The airway pressure was recorded with an ink recorder (Gould Brush 2600, Gould Inc., Instrument Systems Division, Cleveland, OH, USA) with a paper speed of 25 mm s\(^{-1}\). Blood gas samples were analysed immediately after they were drawn, then corrected according to the patient’s temperature, with the Synthesis 350 (Instrumentation Laboratory, Milan, Italy) blood gas analyser.

From the recorded data, the elastic recoil pressure (\( P_{el,rs} \)) of the dependent lung-thorax was determined by subtracting the recorded PEEPi from the static end-inspiratory pressure. Static compliance of the respiratory system (\( C_{st,rs} \)) was obtained by dividing the expiratory tidal volume by \( P_{el,rs} \). The exhaled volume was corrected for the compliance of the respiratory circuit (7 ml cm H\(_2\)O\(^{-1}\)) to eliminate errors from the volume compressed in the tubing.

#### Table 1 Patient details and preoperative pulmonary function tests. FEV1, forced expiratory volume in 1 s

<table>
<thead>
<tr>
<th>Mean (n=15)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>63 (54-72)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>68</td>
</tr>
<tr>
<td>FRC (%)</td>
<td>162</td>
</tr>
<tr>
<td>RV (%)</td>
<td>183</td>
</tr>
<tr>
<td>( P_{aO_2} (\text{mm Hg}) ) room air, supine</td>
<td>38</td>
</tr>
<tr>
<td>( P_{aCO_2} (\text{mm Hg}) ) room air, supine</td>
<td>77</td>
</tr>
</tbody>
</table>

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The study was performed in the lateral position, before the surgical procedure started.

Statistical analysis

We used the Kolmogorov–Smirnov one-sample test to check that the samples were normally distributed. Repeated measures ANOVA was used to test for differences between RRs. Pairwise comparisons between groups were made, using Student’s paired t-test with the Bonferroni adjustment for multiple comparisons, using the GB-Stat 6.0 for IBM and compatibles (Dynamic Microsystems, Inc., 1996). P-values <0.05 were considered significant. Data are presented as mean (SD).

Results

All the patients had mild pulmonary hyperinflation. The pulmonary function tests and blood gas values are shown in Table 1. The perioperative measured and calculated variables at the different RRs are shown in Table 2.

With a reduced RR and unchanged minute volume, $V_t$ (and $T_{tot}$ and expiratory time ($T_e$)) increased. These changes were proportional to the changes in the RR (i.e. $\times 2$ or $\times 1.5$). Peak inspiratory airway pressure ($P_{peak}$) and $P_{plateau}$ were significantly greater when the RR was decreased ($P<0.01$, repeated measures ANOVA).

$P_{el,rs}$ increased at lower RR ($P<0.01$, repeated measures ANOVA), but $C_{st,rs}$ did not change significantly (Table 2). During dependent-lung ventilation, PEEPi values greater than 10 cm H$_2$O were found in only two patients (at RR 10 and RR 15). Zero PEEPi values were recorded in four patients at RR 5 and another one at RR 10. Despite the larger $V_t$ at lower RR, PEEPi was less ($P<0.01$, repeated measures ANOVA). This value was significantly less at RR 5 compared with RR 10 and RR 15 ($P<0.01$, Bonferroni t-test), but without statistical significance when comparing RR 15 and RR 10 (Table 2 and Fig. 1).

Arterial partial pressure of oxygen was not affected (Table 2). $P_{aCO_2}$ was less ($P<0.01$, Bonferroni t-test) at RR 5 in comparison with RR 15 or RR 10. $P_{E-CO_2}$ increased ($P<0.01$, repeated measures ANOVA) when the RR was reduced (Table 2). Consequently, the arterial to end-tidal carbon dioxide partial pressure difference ($P_{aCO_2}-P_{E-CO_2}$) was significantly less when the RR was small (Table 2).

Discussion

Our main findings were a decrease of PEEPi when RR was reduced, along with a decrease in $P_{aCO_2}$ and $P_{E-CO_2}$, and with an increased $P_{peak}$, $P_{plateau}$, and $P_{el,rs}$ ($P<0.01$, repeated measures ANOVA) (Table 2 and Fig. 1).

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Table 2 Respiratory mechanics and blood gas values during the three RRs. Values are mean (SD). Student’s t-test with Bonferroni adjustment for multiple comparisons. *P<0.01 comparing RR 10 with RR 15. †P<0.01 comparing RR 5 with RR 10. ‡P<0.01 comparing RR 5 with RR 15. Pel, elastic recoil pressure

<table>
<thead>
<tr>
<th>RR 5</th>
<th>RR 10</th>
<th>RR 15</th>
<th>P-values repeated measures ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_t$ (ml)</td>
<td>1234 (197)*</td>
<td>623 (97)†</td>
<td>433 (81)*</td>
</tr>
<tr>
<td>$P_{peak}$ (cm H$_2$O)</td>
<td>33 (5)*</td>
<td>26 (6)†</td>
<td>24 (5)*</td>
</tr>
<tr>
<td>$P_{plateau}$ (cm H$_2$O)</td>
<td>21 (5)*</td>
<td>17 (6)†</td>
<td>14 (5)*</td>
</tr>
<tr>
<td>PEEPi (cm H$_2$O)</td>
<td>3 (3)*</td>
<td>5 (4)†</td>
<td>6 (4)</td>
</tr>
<tr>
<td>Pel (cm H$_2$O)</td>
<td>18 (6)*</td>
<td>11 (6)†</td>
<td>7 (5)*</td>
</tr>
<tr>
<td>Crs,rt (ml cm H$_2$O$^{-1}$)</td>
<td>82 (41)</td>
<td>75 (38)</td>
<td>97 (83)</td>
</tr>
<tr>
<td>$P_{CO_2}$ (cm H$_2$O)</td>
<td>36 (6)*</td>
<td>35 (5)†</td>
<td>33 (5)*</td>
</tr>
<tr>
<td>$P_{PEEPi}$ (cm H$_2$O)</td>
<td>39 (4)*</td>
<td>41 (4)†</td>
<td>42 (4)</td>
</tr>
<tr>
<td>$P_{aO_2}$ (mm Hg)</td>
<td>200 (58)</td>
<td>193 (65)</td>
<td>191 (69)</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mm Hg)</td>
<td>2 (3)*</td>
<td>7 (5)†</td>
<td>8 (5)*</td>
</tr>
</tbody>
</table>

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Fig 1 Flow-volume loop measured with the Datex Ultima SV Capnometer (Datex Instrumentarium, Helsinki, Finland) of one patient when changing the respiratory rate.
Co-existing lung disease is the rule rather than exception in patients undergoing lung surgery. The volume, frequency and timing of gas delivered to the dependent lung can have important, disease-specific effects on the cardiovascular and respiratory systems.14

Until now, a low RR has not been studied during OLV in patients with pulmonary hyperinflation in a randomized fashion. Robinson and co-workers15 describe two ventilator-dependent patients with cystic fibrosis who could not be managed with conventional ventilation during sequential double-lung transplantation. Lung implantation was facilitated by OLV at a slow rate (6 bpm) with a long T1 (5 s) and a long Tc (5 s), implantation of donor lung, by decreasing hypercapnia and reducing pulmonary arterial pressure.

Lowering the RR, with unchanged minute volume implies an increase in Vt. In patients without significant pulmonary disease, OLV during general anaesthesia decreases arterial oxygenation because of atelectasis in the dependent lung.9 However, patients with COPD do not develop atelectasis and decrease in FRC during anaesthesia,16 presumably because of long standing hyperinflation.

In obstructive airway disease, lung injury with alveolar leaks may be caused by dynamic hyperinflation during mechanical ventilation. Some authors believe that increased inspiratory airway pressures are necessary to overcome airway resistance when high inspiratory flows are used, as a large part of the inspiratory pressure is not transmitted to the alveoli.17 18 Because alveolar distending volume is not readily measured clinically, Pplateau measured during an inspiratory pause is generally accepted as a reasonable estimate of peak alveolar pressure.19 20 During positive pressure ventilation, the Pplateau, below which lung injury is unlikely is approximately 35 cm H2O, commonly believed to correspond to an alveolar pressure of approximately 30 cm H2O. For safer OLV conditions, Slinger21 suggested limiting Pplateau to 25 cm H2O. Given this range of opinion, careful monitoring of patients managed with this approach is mandatory. In the present study, the Pplateau was generally less than this value (except a single value of 26 cm H2O at RR 5) despite the Vt increases from 433 (81) ml at RR 15 to 623 (97) ml at RR 10 and 1234 (197) ml at RR 5. The duration of OLV periods in this study was short and the patients were anaesthetized and paralysed, but concern could arise from long-term use of low-rate ventilation.

At large values of Vt, an increased PEEPi might be expected, because in addition to the degree of airflow obstruction, one of the major determinants in the development of PEEPi is the Vt to be exhaled in a fixed fraction of time.22 Nevertheless, besides Vt, the main determinant of dynamic hyperinflation and PEEPi in COPD patients is the absolute value of Tc and not the T1/Ttot ratio per se.4 Therefore, considering a given respiratory system with its specific compliance and its expiratory and inspiratory resistances, for a fixed T1 fraction, PEEPi will increase when RR is raised (reduction of Tc) and decrease when the RR is reduced (increase of Tc). Small changes in Tc did not affect PEEPi because the volume expelled per unit time near the end of exhalation is very small.23 In patients with COPD and acute respiratory failure, while PEEPi was increased by Tc shorter than 3 s, prolonging Tc more than 3 s had little effect on PEEPi.6 Both studies were of mechanically ventilated patients with an acute exacerbation of COPD, and the effect of prolonging Tc on gas exchange were not assessed. In the present study of stable COPD patients during OLV in the lateral position, with constant inspiratory time fraction (T1=33% of Ttot), a reduced RR and increased Vt, increased the Tc from 2.6 s at RR 15 to 4 s at RR 10 and 8 s at RR 5 bpm, respectively. In contrast to the findings of Rossi, because of the parallel increase of Vt in our study, a decrease of PEEPi was observed only at the very long Tc associated with the RR 5 bpm (Table 2 and Fig. 1).

An insignificant increase of PaCO2 when RR was decreased (and Vt increased) supports the results of previous studies.9 11 Increased inspiratory airway pressures causing increased vascular resistance in the dependent lung of some patients could explain the lack of consistently improved oxygenation during high Vt ventilation.9 24

In this study, the high RR (15 bpm) and small Vt ventilation caused hypercapnia with a mean PaCO2 of 43 mm Hg. When ventilation was performed at low RR (5 bpm) and high Vt, mean PaCO2 decreased significantly to 39 mm Hg. This value approached the preoperative values (38 (4) mm Hg). The reduced PaCO2-PEEP suggests altered intrapulmonary gas distribution at low RR, but differences in ECO2 may also simply reflect the fact that, with a significant positive slope of the capnogram, prolonging expiration itself will increase ECO2 without necessarily reflecting any change in gas exchange.

This ventilatory pattern—lowered RR (and increased Vt) with constant minute volume—may represent a simple way to reduce PEEPi and hypercapnia during OLV in patients with pulmonary hyperinflation, as changing RR or Vt alone increases either the PEEPi, or the PaCO2. Careful monitoring of these patients for the risk of barotrauma is mandatory. However, given the lack of significant effect on oxygenation (the hallmark of OLV), it is difficult to recommend the technique of high Vt, low RR OLV for routine practice. This ventilatory management should be reserved for patients with severe COPD in whom PEEPi and hypercapnia would possibly complicate OLV.

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