Although the risk of intraoperative hypoxia appears to be less than in previous decades, it still remains a dangerous potential complication during OLV. The appropriate tidal volume (TV) during one-lung ventilation (OLV) is still a matter of debate. Based on the work of Katz, who compared 7 and 14 mL/kg TV, textbooks and papers recommend using high TV to avoid intraoperative hypoxia and atelectasis. Numerous authors have reported that high TV dur-

Effects of different tidal volumes for one-lung ventilation on oxygenation with open chest condition and surgical manipulation: a randomised cross-over trial

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ABSTRACT

Background. The ideal tidal volume (TV) during one-lung ventilation (OLV) remains controversial. High TVs may increase the incidence of postoperative lung injury after thoracic surgery. There is nonetheless little evidence that the use of low TV during OLV will fail to provide adequate arterial oxygenation. We evaluated the influence of low (5 mL/kg) and high (10 mL/kg) TV on arterial oxygenation during one-lung ventilation in clinical conditions.

Methods. A hundred patients scheduled for lung surgery were studied. Patients were randomly assigned to either 30 minutes of one-lung ventilation with a TV of 10 mL/kg at a rate of 10 breaths/minute (Group 10, N.=50) or a TV of 5 mL/kg with 5 cmH2O PEEP at a rate of 20 breaths/minute (Group 5, N.=50). According to the rules of crossover design during the subsequent 30 minutes, each patient received the alternative management. Arterial blood partial pressures, hemodynamic responses, and ventilatory parameters were recorded. Results are presented as means ± SDs; P<0.05 was considered statistically significant.

Results. PaO2 was unaffected by TV (10 mL/kg: 218±106 versus 5 mL/kg: 211±119 mmHg, P=0.29). Calculated intrapulmonary shunt fraction was also similar with each TV during OLV (5 mL/kg: 25±9% versus 10 mL/kg: 24±8%, P=0.14). In contrast, low TV significantly increased PaCO2 (10 mL/kg: 39±6 versus 5 mL/kg: 44±8 mmHg, P<0.001). There were significant differences both in peak (10 mL/kg: 27±6 versus 5 mL/kg: 21±5 cmH2O, P<0.001) and plateau airway pressure values (10 mL/kg: 22±6 versus 5 mL/kg: 18±5 cmH2O, P<0.001) during OLV.

Conclusion. Low TV (5 mL/kg) accompanied by 5 cmH2O PEEP provides comparable arterial oxygenation and intrapulmonary shunt fraction during one-lung ventilation as higher TV (10 mL/kg) without PEEP.

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Key words: Tidal volume - One lung ventilation - Oxygenation - Anesthesia.
ing OLV might increase the incidence of acute lung injury, due to the large peak inspiratory pressures, end-inspiratory volumes, and shearing forces due to cyclic opening-closing of the alveoli.\textsuperscript{7-11} Low TV during OLV has both advantages (lower risk of postoperative acute lung injury and respiratory distress syndrome, and lower concentrations of circulating inflammatory factors) and disadvantages (worse intraoperative atelectasis, more intrapulmonary shunt, hypoxia, and hypercapnia).\textsuperscript{12, 13} There is nonetheless little evidence that the use of low TV during OLV will fail to provide adequate arterial oxygenation or worsen intra-pulmonary shunt.\textsuperscript{14-16} The lower limit for TV is unclear because the extent to which TV influences oxygenation and shunt fraction during OLV remains unknown. Application of external positive end-expiratory pressure can decrease the incidence of atelectasis due to prevention of lung collapse, and minimizes alveolar injury by preventing cyclic opening-closing during OLV. However, the optimal level of PEEP remains unknown.\textsuperscript{17} Previous studies reported that the use of high TV with PEEP or the use of low TV without PEEP worsens the oxygenation and is injurious for the lung.\textsuperscript{7, 8, 18-20} It is widely accepted the use of low TV should be accompanied by PEEP whereas high TV can be used safely without PEEP;\textsuperscript{2} we thus considered 5 mL/kg\textsuperscript{-1} TV with 5 cmH\textsubscript{2}O PEEP and 10 mL/kg\textsuperscript{-1} TV without applied PEEP to be an appropriate comparison.

The purpose of the present study was to compare the effects of low (5 mL/kg\textsuperscript{-1}) and high (10 mL/kg\textsuperscript{-1}) TV, without analyzing the independent effect of PEEP, on arterial oxygenation, shunt fraction and ventilatory mechanics during OLV, in patients with open chest, in the lateral position and during surgical manipulation.

Materials and methods

Study population

After approval from the local Ethics Committee (DEOEC RKEB/IKEB 2976-2009; this study was registered at http://www.clinicaltrials.gov; identifier: NCT01513018), written informed consent was obtained from 100 ASA I-III patients scheduled for lung resection surgery. Preoperatively lung-function tests with whole-body plethysmography, arterial blood gas analysis while breathing room air, ECG, preoperative echocardiography, computerized tomographic lung scan, and bronchoscopy were done. Exclusion criteria were severe cardiovascular disease and severe alteration of the preoperative pulmonary function, with FEV\textsubscript{1} <70% and FEV\textsubscript{1}/FVC ≥70% of the predicted value.

Anesthesia

Patients were premedicated with 5 mg midazolam and 0.5 mg atropine intramuscularly 30 minutes before arrival to the operating room. An epidural catheter was inserted at the mid-thoracic level (T5-8); after a successful test dose, an infusion of 0.125% bupivacaine was started at a rate of 0.1 mg/kg\textsuperscript{-1}/hour\textsuperscript{-1} and subsequently maintained throughout surgery. Anaesthesia was induced with a combination of 2 mg/kg\textsuperscript{-1} propofol, 2 µg/kg\textsuperscript{-1} fentanyl. Intubation was facilitated by administration of 0.2 mg/kg\textsuperscript{-1} cis-atracurium. Anaesthesia was maintained with sevoflurane in 100% oxygen. The concentration of sevoflurane was titrated to a target Bispectral Index (BIS) between 40 and 60 (Covidien, Dublin, Ireland) and it was ranged between 0.8-1.2 Vol%. Neuromuscular block was monitored with acceleromyography (TOF Watch SX, NV Organon, Oss, the Netherlands).

The patients’ tracheas were intubated with double-lumen endotracheal tubes (DLT) (Broncho-Cath, Mallinckrodt Medical Ltd, Athlone, Ireland). The correct position of the DLT was confirmed by fiber-optic bronchoscopy in both supine and lateral positions. Standard monitoring included five-leads ECG, continuous arterial pressure monitoring via a catheter inserted into the radial artery, central venous catheter, NIBP, core temperature at the tympanic membrane, and pulse oximetry. Normothermia was maintained with forced-air (Bair Hugger 750, 3M, Eden Prairie, MN, USA). During two-lung ventilation (TLV) a volume-controlled square-wave flow pattern ventilation with 10 mL/kg\textsuperscript{-1} TV with a respiratory rate of 10 was used and I:E ratio was kept at 1:2 (Draeger Primus, Draeger Lü...
beck, Germany). For adjusting the TV the actual body weight was used. After induction of general anesthesia and intubation, both lungs were ventilated as described above, in supine position for 10 minutes. Thereafter, arterial blood was again sampled for gas analysis and hemodynamic and ventilatory parameters were simultaneously recorded. The patients were then turned into the lateral position and proper insertion of the DLT was confirmed by fiber-optic visualization. TLV was continued with the same pattern for 10 minutes and all measurements were repeated.

**Study protocol**

After a recruitment maneuver, following the guidelines described in the literature, holding a constant airway pressure of 40 cmH2O was applied to the whole lung for 10 s) OLV was started in the lateral position, from the time the thoracic cavity was opened. Considering the fact that a recruitment maneuver under an FiO2 1.0 can last up to 30 minutes, and the fact that hypoxic pulmonary vasoconstriction becomes maximal after approximately 10-15 minutes, measurements were made every 30 minutes to reach a steady state for PaO2. Patients were randomly assigned to 30 minutes of ventilation with either a TV of 10 mL/kg-1 TV without external PEEP and respiratory rate of 10 breaths/minute-1 (Group 10, N.=50) or to a TV of 5 mL/kg-1 with 5 cmH2O PEEP and a respiratory rate of 20 breaths/minute-1 (Group 5, N.=50). According to the rules of crossover design during the subsequent 30 minutes, each patient received the alternative management (Figure 1). Randomization was based on computer-generated codes that were maintained in sequentially numbered sealed opaque envelopes until after induction of anesthesia. During the subsequent 30 minutes of OLV, the alternative ventilatory management was used. Before ventilatory settings were changed, the recruitment maneuver was repeated. The I:E ratio, and the FiO2 were kept constant throughout the study. From the time of closure of thoracic cavity, TLV was started with the pattern described above and FiO2 of 0.4 oxygen in air was used to avoid absorption atelectasis in the postoperative period.

**Measurements**

During OLV, the partial pressure of oxygen in arterial blood (PaO2), the partial pressure of carbon dioxide in arterial blood (PaCO2), peak
inspiratory airway pressure (Ppeak), plateau inspiratory airway pressure (Pplat), hemodynamic parameters were recorded 30 min after each change in the ventilatory setting. Airway pressures were measured by the anesthesia machine. Surgical manipulation on the operated lung was temporarily stopped to allow data collection. After the study period, OLV with the same ventilatory settings was continued to allow the completion of surgery.

Postoperative monitoring and care

All patients were admitted postoperatively to a postanaesthesia care unit for at least a 12-24 hours postoperative monitoring that included serial blood gas analysis measurements and a first-day postoperative chest X-ray. During this period oxygen therapy through nasal cannula was provided as was necessary for proper oxygenation and epidural analgesia was continued to provide appropriate pain control.

Statistical analysis

Intrapulmonary shunt fraction calculations were performed using the nomogram of Benatar et al.22 PaO₂ between 60 and 100 mmHg were considered to be abnormally low. PaO₂ <60 mmHg or SaO₂ <90% were considered severe hypoxemia.

Table I.—Demographic characteristics, preoperative pulmonary function, and arterial blood gases at room air in the two groups of patients. Data expressed as means ± SDs.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>50</td>
<td>50</td>
<td>0.9</td>
</tr>
<tr>
<td>Male/female (N.)</td>
<td>35/15</td>
<td>31/19</td>
<td>0.9</td>
</tr>
<tr>
<td>Side of thoracotomy (right/left) (N.)</td>
<td>28/22</td>
<td>30/20</td>
<td>0.86</td>
</tr>
<tr>
<td>Lobectomy (N.)</td>
<td>42</td>
<td>44</td>
<td>0.82</td>
</tr>
<tr>
<td>Pneumonectomy (N.)</td>
<td>8</td>
<td>6</td>
<td>0.8</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>63 ± 12</td>
<td>64 ± 12</td>
<td>0.6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69 ± 10</td>
<td>68 ± 11</td>
<td>0.48</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170 ± 7</td>
<td>171 ± 6</td>
<td>0.68</td>
</tr>
<tr>
<td>FEV₁ (% predicted) *</td>
<td>92 ± 15</td>
<td>91 ± 13</td>
<td>0.76</td>
</tr>
<tr>
<td>FVC (% predicted) †</td>
<td>98 ± 15</td>
<td>96 ± 16</td>
<td>0.76</td>
</tr>
<tr>
<td>FEV₁/FVC (% predicted) †</td>
<td>99 ± 9</td>
<td>98 ± 12</td>
<td>0.79</td>
</tr>
<tr>
<td>PaO₂ (mmHg) ‡</td>
<td>88 ± 20</td>
<td>86 ± 14</td>
<td>0.41</td>
</tr>
<tr>
<td>PaCO₂ (mmHg) §</td>
<td>38 ± 4</td>
<td>38 ± 4</td>
<td>0.83</td>
</tr>
</tbody>
</table>

* FEV₁: forced expiratory volume in 1 s, †FVC: forced vital capacity, ‡PaO₂: arterial oxygen partial pressure, §PaCO₂: arterial carbon-dioxide partial pressure.

One hundred patients provided an 80% power to detect a two-tailed difference of 50 mmHg in PaO₂ during OLV with an α error of 5% based on an expected standard deviation of 100 mmHg.23,24 Distribution normality was determined using the Shapiro-Wilk test. Student’s t tests were used for intergroup comparisons of preoperative values and analysis of data obtained during two-lung ventilation. Data obtained during one-lung ventilation were analyzed with two-way repeated-measures of ANOVA with “randomization order” and “TV” being considered independent variables. Results are presented as means ± SDs; P<0.05 is considered statistically significant. SAS for Windows 9.2. (SAS Institute Inc. Cary, NC USA) was used for statistical analysis.

Results

Patients characteristics, arterial partial pressures, pulmonary function tests, were similar in both groups of patients (Table I).

There were no significant differences in PaO₂, PaCO₂, calculated intrapulmonary shunt (Qs/Qt), ventilatory and hemodynamic values during TLV in the supine and lateral decubitus positions (Table II).

There was no significant effect of sequence of randomization on any outcome (PaO₂: P=0.7; PaCO₂: P=0.4; Qs/Qt: P=0.3; Ppeak: P=0.3; Pplat: P=0.2); all results are thus presented as a
surgery, where the effects of different TVs were investigated during OLV. Our primary result is that arterial oxygenation and shunt fraction are similar with TVs of 5 mL/kg⁻¹ and 10 mL/kg⁻¹ during OLV with open chest in the lateral position, during surgical manipulation in patients with normal lung function.

The TV to be used to maintain adequate oxygenation during OLV remains controversial. Based on the work of Katz, textbooks and reviews recommend using high TV because TV less than 8 mL/kg⁻¹ can lead to atelectasis that may increase the incidence of hypoxemia. However, traditionally OLV has been performed with high TV without added external PEEP because high TV with external PEEP (5-10 cm-H₂O) promotes alveolar hyperinflation which can lead to lung injury.

There is growing evidence that smaller TV during OLV than during two-lung ventilation...
helps preventing lung injury.7-9, 13, 28 As might be expected, low TVs reduced inspiratory airway pressures, which may reduce pressure-related lung injuries that sometimes accompany one-lung ventilation.8 The effect of low TV on oxygenation is controversial. The conclusions of the present study correspond to the findings of Kozian et al.27 who compared TVs of 5 and 10 mL/kg⁻¹ for OLV in piglets and evaluated lung density distribution. They found a TV of 5 mL/kg⁻¹ along with PEEP after an alveolar recruitment maneuver a safe alternative to larger TVs. However, in their study, respiratory rate was different using different TVs, thus minute volume was not identical, the constant level of PaCO₂ indicates constant alveolar ventilation. In contrast, in our study the minute ventilation was kept constant with doubling the respiratory rate at low TV. This double respiratory rate produced a reduction in alveolar ventilation and CO₂ retention. Licker et al.14 found that use of low TV with PEEP and recruitment maneuvers serves adequate oxygenation during OLV. In our study, we evaluated smaller TVs than commonly clinically used. However our results are different from the results of Roze et al.16 who found that at the same plateau pressure, an increased PEEP with low TV worsened oxygenation. In our study only 5 cmH₂O PEEP was used with low TV, whereas Roze’s used 9 cmH₂O PEEP which can lead to compression of alveolar capillaries due to overdistension and has the potential to worsen oxygenation (although clinically not significantly). It has to be noted, that compression of alveolar capillaries due to overdistension would produce an increase in dead space (and an increase in PaCO₂) but it would only slightly reduce PaO₂ due to the shunt effect (diversion of blood flow to less ventilated areas). This effect on PaO₂ would only be apparent at low FiO₂.

The amount of abnormally low arterial oxygen partial pressure was similar in each of our groups, and neither ventilation strategy produced serious hypoxemia (PaO₂<60 mmHg).

Use of PEEP during ventilation with low TV is also controversial. Application of external positive end-expiratory pressure can decrease the incidence of atelectasis due to prevention lung collapse and minimizes the alveolar injury preventing cyclic opening-closing during OLV. However, the optimal level of PEEP remains unknown.17, 29 Some studies reported beneficial effects on oxygenation 30-32 whereas others reported no benefit or worsening of oxygenation.4, 33, 34 Many now believe that ventilation with low TV without added external PEEP worsens oxygenation and promotes alveolar re-recruitment.35, 36 Kim et al.15 did not found difference in PaO₂/FiO₂ ratio using low TV with and without PEEP. This observation suggests that application of PEEP cannot compensate for hypoxia due to atelectasis caused by low TVs. We thus compared low TV with PEEP and high TV without PEEP as this is probably the safest clinical approach — and one that has been used in many previous studies.37, 38

The use of a TV of 5 mL/kg⁻¹ was associated with an increased PaCO₂, but this increase remained between the limits of normocapnia. Once low TV is used, the respiratory rate has to be doubled to maintain the constant minute ventilation. This leads to an increased dead-space ventilation and increased PaCO₂.

There were no significant differences in calculated intrapulmonary shunt values. We note, though, that intrapulmonary shunt fractions were calculated using the nomogram of Benatar et al.22 Better estimates would be available from a pulmonary artery catheter, but invasive monitoring is not routine in our department. A constant FiO₂ of 1.0 during the study was motivated by safety because of the lack of experience in the use of such low TVs in humans. However, the same FiO₂ was used in all patients. This high FiO₂ might accelerate atelectasis after the alveolar recruitment maneuver,39 but we did not find any differences in PaO₂. Moreover, it seems unlikely that at such a high FiO₂, that an alveolar recruitment maneuver applied 30 minutes before the measures could influence the obtained data. Additionally, administration of higher FiO₂ has also a methodological background: while using high FiO₂, small changes in the shunt fraction may lead to consequently larger changes in PaO₂ and therewith may enhance the comparison of the effects of different ventilatory strategies. After finishing OLV, TLV was continued with FiO₂ of 0.4 in air to avoid the absorption atelectasis in the postoperative period.
There were significantly higher values of static compliance (Crs) using high TV during OLV than using low TV. Higher plateau inspiratory pressures usually reduce compliance. Although, an increased Pplat is logically observed after increasing the TV; however, the increase in TV and the increase of the Pplat are not linearly correlated which may explain the higher compliance using high TV.

We have to mention several limitations to our study. First, only patients with no or minor alterations of the pre-operative pulmonary function were studied. Of course many patients having thoracic surgery present with various degrees of COPD and pulmonary hyperinflation. Some are chronically hypoxic, and others are hypercapnic. We excluded patients with serious cardiac co-morbidities and severely abnormal lung function tests, as mentioned in the methods section. The extent to which our results can be generalized to sicker patients remains to be determined.

A second limitation is that our cross-over design may have decreased the intersubject variation and it is widely used in clinical research in investigation of acute effects on oxygenation, because patients served as their own controls. A consequence of our cross-over design is that we were unable to evaluate any long-term effects of this TV management. It thus remains possible that low or high TV is preferable for reasons beyond their acute effects on arterial oxygenation and pulmonary shunt. We did not observe any acute lung injury, ARDS, pulmonary edema, or pneumonia within 72 postoperative hours.

Third, we have studied patients in the lateral position, with open chest and during surgical manipulation. In the lateral position, the eventually gravitational effect on the redistribution of pulmonary blood flow during OLV is already present, so it would have no more influence on the findings of the study. The open chest and surgical manipulation were preferred to reproduce as much as possible the clinical conditions during OLV. Unfortunately, we cannot quantify the amount of blood flow redistribution due to the surgical manipulation, which might influence the results of the present study. However, surgery was temporarily stopped to allow data collection.

Fourth, for setting TVs we have used actual body weight rather than ideal body weight because there is no consensus how to adjust for body weight. Furthermore, our patients were mostly of typical body mass so adjustment would little influence applied TVs.

Conclusions

A protective ventilator strategy for OLV in humans, during lung surgery, with such a reduced TV as (5 mL/kg⁻¹) accompanied by 5 cmH₂O PEEP provides a safe arterial oxygenation and reduced inspiratory airway pressures, as compared to higher TVs without PEEP in patients with normal lung function. There are several factors which have effects on oxygenation, therefore the explanation of our results is complex: although despite the minute ventilation was the same, the alveolar ventilation was different, presumably the alveolar volume and the volume of the atelectatic areas remained the same using different TV; although the airway pressures were different, the extent of alveolar overdistension was the same. Major limitation is that the difference between intervention in two independent parameters, therefore conclusions are difficult to draw, further studies are required to analyze independently the effect of PEEP and TV.

Key messages

— Low TV with moderate PEEP can be safely administered for patients undergoing OLV for thoracic surgical procedures.
— Using a crossover design, it was found that low TV with moderate PEEP does reduce oxygenation.
— The extent to which our results can be generalized to sicker patients remains to be determined.

References


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