Original contribution

Effects of a 1:1 inspiratory to expiratory ratio on respiratory mechanics and oxygenation during one-lung ventilation in patients with low diffusion capacity of lung for carbon monoxide: a crossover study☆

Kyuho Lee MD ( Resident), Young Jun Oh MD, PhD (Professor), Yong Seon Choi MD, PhD (Assistant Professor), Shin Hyung Kim MD (Assistant Professor)*

Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Republic of Korea

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Abstract

Study Objective: To investigate the effects of a 1:1 inspiratory-to-expiratory (I:E) ventilation ratio on oxygenation and respiratory mechanics during one-lung ventilation (OLV) in patients with low diffusion capacity of lung for carbon monoxide (DLCO).

Design: Prospective, randomized, crossover study.

Setting: Operating room, university hospital.

Patients: Twenty-six patients with a preoperative DLCO less than 80% who were scheduled for lung lobectomy requiring OLV under general anesthesia.

Interventions: In the first group (n = 13), OLV was begun with a 1:1 I:E ratio, which was switched to a 1:2 I:E ratio after 30 minutes. In the second group (n = 13), the modes of ventilation were performed in the opposite order. Pressure-controlled ventilation with 5 cm H2O of positive end-expiratory pressure and a tidal volume of 5 to 8 mL/kg was applied during OLV.

Measurements: Arterial and central venous blood gas analyses were recorded and used to calculate intrapulmonary shunt fraction and physiologic dead space. These measurements were taken at 4 time points: 10 minutes after two-lung ventilation in the lateral decubitus position, 30 minutes after initiation of OLV, 30 minutes after switching the I:E ratio, and 10 minutes after two-lung ventilation was resumed.

Main Results: There was no difference in arterial oxygen tension during OLV between the 2 groups (P = .429). Arterial carbon dioxide tension and peak airway pressure were lower in the 1:1 group than in the 1:2 group (P = .003; P = .008). Physiologic dead space was also decreased in the 1:1 I:E ratio group (P = .003). Mean airway pressure and dynamic compliance were higher in the 1:1 group (P = .003; P = .007).

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* Correspondence: Shin Hyung Kim, MD, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea. Tel.: +82 2 2227 3556; fax: +82 2 364 2951.
E-mail address: tessar@yuhs.ac (S.H. Kim).

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1. Introduction

One-lung ventilation (OLV) is required for a variety of thoracic surgeries involving the lungs, esophagus, aorta, and mediastinum. Studies have suggested, however, that hypoxemia can occur in up to 5% to 10% of patients undergoing OLV, which may present a serious challenge to patient safety [1].

Use of a prolonged inspiratory-to-expiratory (I:E) ratio method was originally developed to improve oxygenation in patients with reduced lung function, as in cases of acute lung injury or acute respiratory distress syndrome (ARDS) [2]. A single previous study suggests that applying a 1:1 I:E ratio increases arterial oxygenation [3]. The basis of this practice is that longer inspiratory times increase the gas flow to the alveoli of slow time constants, thereby improving oxygenation [4]. However, our previous study, which applied volume-controlled ventilation (VCV) with a 1:1 I:E ratio during OLV, showed no improvement in oxygenation when compared with the conventional 1:2 I:E ventilation ratio [5].

One possible explanation of this result is that because enrolled patients had otherwise normal lung function, one healthy lung could provide sufficient oxygenation during OLV without resulting in hypoxemia. Thus, we hypothesized that the application of a 1:1 I:E ratio during OLV in patients with compromised lung function would have a positive impact on oxygenation when compared with the conventional 1:2 I:E ratio.

Generally, decreased diffusion capacity of lung for carbon monoxide (DLCO) is useful for detecting patients with restrictive lung disease, especially intrinsic type. DLCO reflects the gas exchange function of the lungs by determining whether gas can move from the alveoli, across the interstitium, and into the blood. It is performed by having the patient breathe in carbon monoxide (CO), which binds to hemoglobin. To reach the hemoglobin, the CO must diffuse across the alveolar-blood barrier. If there is thickening of the alveoli or interstitium, diffusion will be impaired, resulting in a decreased DLCO. Studies show that even in subjects with otherwise normal pulmonary function, diffusion capacity has a role in predicting postoperative morbidity [6,7]. Thus, we concluded that DLCO is an appropriate indicator for identifying patients with reduced lung function.

The primary aim of this study was to investigate the effects of a minimally prolonged 1:1 I:E ventilation ratio on oxygenation compared with the conventional 1:2 I:E ventilation ratio used during OLV in patients with reduced preoperative DLCO undergoing thoracoscopic lung lobectomy. In addition, we evaluated respiratory mechanics and hemodynamic changes to compare the effects of this different I:E ratio during OLV.

2. Methods

This study was approved by the Institutional Review Board of Severance Hospital, Yonsei University Health System (ref: 1-2011-0058). After written informed consent was obtained from all participants, 26 patients aged 24 to 77 years with the American Society of Anesthesiologists physical status of II to IV who were scheduled for thoracoscopic lung lobectomy requiring OLV under general anesthesia were enrolled in this study. All patients underwent preoperative pulmonary function tests before surgery, and those with a DLCO more than 80% of the predicted value were excluded. Patients with a history of coronary artery occlusive disease, cerebrovascular disease, renal insufficiency, tobacco abuse, and obesity (body mass index > 30 kg/m²) were also excluded. The patients were randomly assigned into 2 groups. In the first group (n = 13), OLV was begun with a 1:1 I:E ratio and then switched to a 1:2 I:E ratio after 30 minutes. In the second group (n = 13), the mode of ventilation was performed in the opposite order. This randomized controlled trial took place at the surgery center of Severance Hospital in Seoul, Korea, between February and December 2012.

All patients received midazolam 0.04 mg/kg via intramuscular route (maximum dose, 2.5 mg) for premedication. Standard monitoring devices were applied after arrival in the operating room. Anesthesia was induced with 1.5 mg/kg propofol and 1.0 μg/kg remifentanil. Tracheal intubation with a left-sided double-lumen tube (Broncho-Cath; Mallinkrodt Medical, Inc, Athlone, Ireland) was facilitated with 0.9 mg/kg rocuronium, and the position of the double-lumen tube was confirmed with a fiberoptic bronchoscope. The lungs were initially ventilated in pressure-controlled ventilation (PCV) mode (Zeus ventilator, Dräger Medical, Lübeck, Germany) with a tidal volume of 5 to 8 mL/kg, an I:E ratio of 1:2, a respiratory rate of 8 to 12 breaths per minute of 100% oxygen, and a positive end-expiratory pressure (PEEP) of 5 cm H₂O. The tidal volume and the respiratory rate were controlled to adjust the end-tidal carbon dioxide in the range of 38 ± 2 mm Hg, and after the appropriate tidal volume and respiratory rate were found, the settings were fixed during the measurement periods. After induction of anesthesia, a 20-gauge radial artery catheter was placed, and a 7F central venous catheter (Arrow International,
Reading, PA) was inserted into the right internal jugular vein. The central venous catheter length was calculated using a height-based formula for optimal placement near the right atrium. Anesthesia was maintained with 1.0% to 2.0 sevoflurane, remifentanil 0.1 to 0.3 μg/kg/min, and rocuronium 5.0 to 10.0 μg/kg/min. After changing the patient’s position from supine to lateral decubitus, the location of the double-lumen tube was reconfirmed with the fiberoptic bronchoscope.

All hemodynamic and respiratory variables were measured in the lateral decubitus position. Arterial and central venous blood gas analyses were recorded and used to calculate intrapulmonary shunt fraction and physiologic dead space (Vd/Vt). These measurements were taken at 4 time points: 10 minutes after 2-lung ventilation (TLV) in the lateral decubitus position (TLVbaseline), 30 minutes after initiation of OLV, 30 minutes after switching the I:E ratio (from 1:1 to 1:2 for the first group and from 1:2 to 1:1 for the second group), and 10 minutes after TLV was resumed (TLVend).

Hemodynamic measurements included heart rate, systolic arterial pressure, diastolic arterial pressure, and central venous pressure. Respiratory variables included peak airway pressure (Ppeak), mean airway pressure (Pmean), and dynamic compliance (Cdyn). End-tidal carbon dioxide was measured using a capnography instrument installed within the ventilator. The oxygen content (CxO2) in the arterial and central venous blood was calculated using the following equation: CxO2 = 1.36 × Hb × SxO2 + 0.0031 × PxO2, in which Hb is hemoglobin concentration (grams per deciliter) and SxO2 is oxygen saturation. Because the ventilation was provided with 100% oxygen, intrapulmonary shunt fraction (Qs/Qt) was determined using the following standard formula: Qs/Qt = (CcO2 − CaO2)/(CcO2 − CvO2), where CcO2 is calculated capillary O2 content, assuming that the pulmonary capillary O2 partial pressure is equal to arterial O2 partial pressure (PaO2) and the central venous O2 saturation (ScvO2) is equal to the mixed venous O2 saturation (SvO2) [8,9]. Vd/Vt was calculated according to the Hardman and Aitkenhead equation: Vd/Vt = 1.14 × (PaCO2 − PE′CO2)/PaCO2 − 0.005. Arterial and central venous blood samples were analyzed using an automated blood gas analyzer (Stat Profile CCX; Nova Biomedical, Waltham, MA). The study was planned to terminate if mean arterial pressure decreased by more than 20% relative to the postinduction value requiring administration of a vasoactive drug, if SpO2 measured by pulse oximetry declined to less than 90%, or if PaO2 decreased to less than 60.0 mm Hg during OLV.

The sample size calculation was performed based on our previous study [5]. Achievement of 80% power to detect approximately 25% improvement in PaO2 using a 1:1 I:E ratio with an α level of .05 using independent t tests required inclusion of 26 patients. Because this study was designed as a crossover study, 13 patients were required for each group. All data are expressed as mean ± SDs or the number of patients. Comparison of demographic data between the groups was performed using the χ2 test, Fisher exact test, or an independent t test, as appropriate. Data comparisons between the 2 groups at each time point were made using a paired t test. Changes between time points within a group were compared using univariate analysis of variance with post hoc comparisons using Dunnett’s test. Statistical analyses were performed with the Statistical Package for the Social Sciences version 20.0 (SPSS, Inc, Chicago, IL). P <.05 was considered to be statistically significant.

3. Results

A total of 26 patients were enrolled in this study. Patient characteristics are shown in Table 1. None of the patients developed dangerous hypoxemia (SpO2 <90% or PaO2 <60.0 mm Hg) or hypotension requiring vasoactive drugs during OLV, and therefore, the study was successfully completed by all patients.

Respiratory variables measured at each time point are shown in Table 2. Arterial carbon dioxide tension (PaCO2), Vd/Vt, and Ppeak of group 1:1 were significantly lower than that of group 1:2 (P = .003; P = .003; P = .008). Pmean and Cdyn on the other hand, were higher in group 1:1 than in group 1:2 (P = .003; P = .007). There were no significant differences in pH, PaO2, Qs/Qt, venous oxygen tension, or venous carbon dioxide tension during OLV between the 2 groups (P = .429).

Compared with baseline values, initiation of OLV was associated with a significant increase in Ppeak (P <.001), Pmean (P <.001), Vd/Vt (P <.001), and Qs/Qt (P <.001), whereas Cdyn (P <.001) and PaO2 (P <.001) were decreased.

Hemodynamic variables measured at each time point are shown in Table 3. There were no significant hemodynamic changes throughout the study period between the OLV 1:1 and 1:2 group. None of the patients developed postoperative

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient characteristics, results of preoperative pulmonary function studies, and surgical data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>16/10</td>
</tr>
<tr>
<td>Age (y)</td>
<td>60.8 (13.4)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167.0 (8.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>65.1 (9.1)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.1 (2.8)</td>
</tr>
<tr>
<td>FVC (%)</td>
<td>80.3 (16.7)</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>82.9 (15.1)</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>74.8 (10.7)</td>
</tr>
<tr>
<td>DLCO (%)</td>
<td>70.7 (7.6)</td>
</tr>
<tr>
<td>OLV time (min)</td>
<td>148.9 (61.1)</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>11.9 (1.6)</td>
</tr>
</tbody>
</table>

BMI = body mass index; FVC = forced vital capacity; FEV1 = forced expiratory volume in 1 second; Hb = hemoglobin. Values are expressed as means (SDs).
pneumonia or required reintubation for respiratory compromise during the postoperative course.

4. Discussion

This prospective, randomized, controlled crossover study was designed to clarify the effects of a 1:1 I:E ratio during OLV in patients with reduced lung function. Overall, this method had significant effects on respiratory mechanics such as reduced Ppeak and Vd/Vt, increased Pmean, and improved Cdyn. However, no changes in oxygenation were observed, and there was no effect on decreasing Qs/Qt when compared with the conventional 1:2 I:E ventilation ratio. Hemodynamic variables were similar during OLV in the lateral decubitus position regardless of the ventilatory mode used.

Previous studies have demonstrated that a prolonged I:E ratio such as 1.5:1 or even 1:1 results in increased oxygenation [3,10], and we referred to these findings when designing our study. We considered applying inverse ratio ventilation such as 2:1 or 3:1, but because an excessively prolonged I:E ratio has potential risks of inducing barotrauma, hypotension, and activation of cytokines, which are known to be associated with lung injury, we hypothesized that a 1:1 I:E ratio would be appropriate for both improving oxygenation and minimizing the risk of complications [11].

In addition, because our previous study was unable to clarify any change in oxygenation between 1:1 and 1:2 I:E ratios in patients with normal lung function [5], we enrolled patients with reduced lung function based on DLCO, as this ventilatory strategy had shown improvement in oxygenation in patients with compromised lungs due to acute lung injury or ARDS [2]. Furthermore, we applied PCV in this study instead of VCV. Although controversial due to its high initial flow rate and decelerating inspiratory flow pattern, PCV is associated with improved lung mechanics and oxygenation compared with VCV in patients who require OLV [12,13]. For this reason, we concluded that this ventilatory mode was more suitable for our study.

Despite our expectation, no significant changes in oxygenation were observed in this study. There are several possible explanations for these results. The major difference between our study and reference studies [3,10] was the requirement of OLV. Unlike TLV, oxygenation during OLV depends mainly on Qs/Qt through the nonventilated lung and V/Q mismatch in the ventilated lung as well as other factors such as cardiac output, venous saturation, and hemoglobin level [1]. Although we did not directly measure cardiac output in this study, an increase in Pmean could be the main cause of decreased cardiac output with a prolonged I:E ratio [12-15]. Decreased cardiac output may lead to a decrease in both intrapulmonary shunt and venous oxygen saturation.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Respiratory variables measured at each time point</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>TLVbaseline</td>
</tr>
<tr>
<td>pH</td>
<td>7.40 (0.04)</td>
</tr>
<tr>
<td>PacO₂ (mm Hg)</td>
<td>37.4 (4.6)</td>
</tr>
<tr>
<td>PacO₂ (mm Hg)</td>
<td>420.1 (68.5)</td>
</tr>
<tr>
<td>Qs/Qt (%)</td>
<td>21.2 (1.5)</td>
</tr>
<tr>
<td>Pvo₂ (mm Hg)</td>
<td>60.1 (17.1)</td>
</tr>
<tr>
<td>Pvo₂ (mm Hg)</td>
<td>47.7 (4.9)</td>
</tr>
<tr>
<td>Vd/Vt (%)</td>
<td>11.0 (1.5)</td>
</tr>
<tr>
<td>Ppeak (cm H₂O)</td>
<td>13.5 (2.5)</td>
</tr>
<tr>
<td>Pmean (cm H₂O)</td>
<td>6.0 (1.7)</td>
</tr>
<tr>
<td>Cdyn (mL/cm H₂O)</td>
<td>38.9 (7.9)</td>
</tr>
</tbody>
</table>

Pvo₂ = venous oxygen tension; Pvo₂ = venous carbon dioxide tension.
Values are expressed as means (SDs).
* P < .05 vs group 1:2.
** P < .05 vs TLVbaseline in each group.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Hemodynamic variables measured at each time point</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>TLVbaseline</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>72.1 (13.5)</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>119.1 (20.2)</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>66.0 (11.5)</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>8.8 (3.1)</td>
</tr>
</tbody>
</table>

HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; CVP = central venous pressure.
* P < .05 vs TLVbaseline in each group.
One-lung ventilation and I:E ratio

with a decrease in PaO2 during OLV [16,17]. Despite that, there was no difference in initial (TLVbaseline) and final (TLVend) hemoglobin levels (P = .062), and decreased cardiac output due to increased Pmean and inadequate tissue oxygenation may have induced the lack of significant difference in PaO2 between the 2 groups.

This study showed that use of a 1:1 I:E ratio reduced Ppeak by 6.4% when compared with a conventional 1:2 I:E ratio, which could be beneficial in decreasing the risk of barotrauma [18]. In addition, Pmean was increased by 8.6% in the 1:1 I:E ratio group when compared with the 1:2 I:E ratio group. As low Pmean usually requires extrinsic PEEP for adequate alveolar distension during OLV with low tidal volume [19], a higher Pmean in the 1:1 I:E ratio lessens the need for applying PEEP, which is also helpful in reducing Ppeak.

In our study, the Vd/Vt was reduced by 34.2% in the 1:1 I:E ratio group compared with the 1:2 I:E ratio group. Because an increase in dead space requires a corresponding increase in tidal volume to achieve sufficient gas exchange, this considerable reduction of Vd/Vt clearly demonstrates a beneficial effect of the 1:1 I:E ventilation ratio in improving the efficiency of alveolar ventilation.

The compliance of the dependent lung is decreased by lung compression due to gravitational effects, reduction of chest wall compliance, surgical stimuli, and high airway pressure in the lateral decubitus position during OLV, and for these reasons, the dependent lung is more likely to develop atelectasis and alveolar collapse [1]. Our study showed that PCV with a 1:1 I:E ratio effectively improved dynamic lung compliance during OLV by 7.0% compared with an I:E ratio of 1:2, suggesting that atelectasis and alveolar collapse in the dependent lung can be reduced significantly by this simple change in ventilation mode.

Moreover, because none of our patients developed postoperative pneumonia or required reintubation for respiratory compromise during their postoperative course, further studies that apply an even more prolonged I:E ratio such as 1.5:1 or 2:1 could be performed to clarify the relationship between oxygenation and I:E ratio during OLV.

There are several limitations to this study. First, although decreased DLCO is a useful predictor in detecting restrictive lung disease, the selection of reference values for DLCO remains controversial because interlaboratory differences are reported considerable [20,21]. The evaluation of DLCO can be affected by several factors including hemoglobin concentration, age, body muscle mass, posture, back tension of CO2, alveolar oxygen tension, lung volume, and instrument error, which all can have substantial effects on the test value [20].

Second, the time course of changes in Qs/Qt and PaO2 during OLV is still not well established. Therefore, we had a set the time of measurement at 30 minutes after the onset of OLV in either ventilator mode according to previous studies, although the optimal time of assessment remains unclear [22,23].

Third, we could not provide a standardized tidal volume or respiratory rate to the patients. A fixed ventilator setting resulted in hypercapnea or hypocapnea in some cases, due to different physical characteristics of each individual. Adjustments of tidal volume and respiratory rate were inevitable to maintain the similar end-tidal carbon dioxide values across all patients. Once the appropriate tidal volume and respiratory rate were found, they remained unchanged during the measurement periods. Nonetheless, diversity of these settings might have negatively affected the statistical accuracy.

Fourth, although calculation of intrapulmonary shunt fraction required measurement of ScvO2, it was done based on ScvO2 because our patients had normal cardiac function and the operation did not require a pulmonary artery catheter. In addition, pulmonary capillary O2 partial pressure was assumed to be equal to PaO2 and was replaced by it when calculating the shunt fraction. This assumption may not be valid in our patients because they had impaired gas exchange abilities. However, there were no alternatives available to calculate the exact value of pulmonary capillary O2 partial pressure, and the use of PaO2 in the shunt fraction calculation was inevitable.

Lastly, another potential limitation of this study is that operations on the left lungs and the right lungs were compared altogether. It is possible that the left lateral decubitus position may not be comparable to the right lateral decubitus position with respect to oxygenation, as previous studies reported that distribution of ventilation and perfusion between the two patient positions are not similar [24,25].

In conclusion, it should be emphasized that PCV with an I:E ratio of 1:1 is a viable alternative ventilatory strategy for OLV with regard to reducing Ppeak, improving Cdyn, and increasing the efficiency of alveolar ventilation without significant hemodynamic changes during OLV in the lateral decubitus position, although this did not result in substantial improvement in oxygenation.

References


