The effects of one-lung ventilation mode on lung function in elderly patients undergoing esophageal cancer surgery

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Abstract
The objective of the present study was to explore the effects of different one-lung ventilation (OLV) modes on lung function in elderly patients undergoing esophageal cancer surgery. A total of 180 consecutive elderly patients (ASA Grades I–II, with OLV indications) undergoing elective surgery were recruited in the study. Patients were randomly divided into 4 groups (n=45). In Group A, patients received low tidal volume (VT < 8 mL/kg) + pressure controlled ventilation (PCV), low tidal volume (VT < 8 mL/kg) + volume-controlled ventilation (VCV) in Group B, high tidal volume (VT ≥ 8 mL/kg) + PCV in Group C and high tidal volume (VT ≥ 8 mL/kg) + VCV in Group D. Two-lung ventilation involved routine tidal volume (8–10 mL/kg) at a frequency of 12 to 18 times/min, and VCV mode. Clinical efficacy among 4 groups was compared. The partial pressure of end-tidal carbon dioxide (PetCO₂) did not significantly differ among 4 groups (all P > .05), and the oxygenation index and SO₂ in Group A were significantly higher than in the other groups (P < .05). The PetCO₂, peak airway pressure (Pₚₑᵃᵏ), platform airway pressure (Pₚₗᵃᵗ), and mean airway pressure (Pₘₑᵃⁿ) in Group A were significantly lower than those in the other groups (all P < .05). However, airway resistance (Rₐₘₑᵃⁿ) in Group B did not significantly differ (all P > .05). The incidence of pulmonary infection, anastomotic fistula, ventilator-induced lung injury, lung dysfunction, difficulty weaning from mechanical ventilation, and multiple organ dysfunction in Groups A and B were lower than that in Groups C and D (all P < .05). The expression levels of IL-6, tumor necrosis factor-α, and C-reactive protein in lavage fluid in Group A were significantly lower than those in the other groups (all P < .05). OLV with low tidal volume (VT < 8 mL/kg) + PCV (5 cmH₂O PEEP) improved lung function and mitigated inflammatory responses in elderly patients undergoing esophageal cancer surgery.

Abbreviations: ALI = acute lung injury, CRP = C-reactive protein, OLV = one-lung ventilation, PCV = pressure controlled ventilation, PetCO₂ = pressure of end-tidal carbon dioxide, P㎜ₑᵃᵐ = peak airway pressure, Pₚₗᵃᵗ = platform airway pressure, Rₐₘₑᵃⁿ = airway resistance, VCV = volume-controlled ventilation, VILI = ventilator-induced lung injury.

Keywords: esophageal cancer in the elderly, inflammatory reactions, low tidal volume, one-lung ventilation, pressure controlled ventilation, volume controlled ventilation

1. Introduction
One-lung ventilation (OLV) is extensively applied in chest surgery for esophageal cancer, lung cancer, lung abscess, and bronchiectasis.[1,2] It can enlarge the surgical field, separate healthy lung, reduce lung injury, and preserve lung function.[3] OLV is different from two-lung ventilation. Inappropriate tidal volume and ventilation mode may cause poor lung expansion, CO₂ retention, or lung hyperinflation, leading to ventilator-induced lung injury (VILI).[4] The expression levels of multiple inflammatory mediators, such as interleukin (IL)-6, tumor necrosis factor (TNF)-α, and C-reactive protein (CRP) in bronchoalveolar lavage fluid play an important role in the occurrence of acute lung injury (ALI) and perioperative complications.[5,6] Lung protective ventilation strategies (low tidal volume + positive end-expiratory pressure (PEEP) in ALI/acute respiratory distress syndrome are important for clinical prognosis.[7] Whether lung protective ventilation strategies in OLV can achieve good clinical effects is controversial. It was reported that low tidal volume could improve the efficacy of OLV, whereas other studies suggested that improvement of OLV by low tidal volume was limited.[8,9] The aim of this study was to further evaluate the effects of different tidal volumes combined with pressure-controlled ventilation (PCV) and volume-controlled ventilation (VCV) in OLV, and provide a reference for the appropriate selection of ventilation mode.

2. Patients and methods

2.1. Patients
A total of 180 elderly patients who were diagnosed with esophageal cancer in our hospital from January 2013 to January 2016 were consecutively selected in this study. Inclusion criteria: (1) aged from 60 to 75 years; (2) clinical TNM staging from I to III, with surgical indications and an estimated survival of at least 3 months; (3) American Society of Anesthesiologists (ASA) grades I–II, with OLV indications; (4) complete medical history
and follow-up with informed consents. Exclusion criteria: (1) primary pulmonary diseases, such as chronic obstructive pulmonary disease and respiratory failure; (2) other comorbidities, such as hypertension, diabetes, cardiovascular, and cerebrovascular diseases and liver or kidney dysfunction.

Patients were randomly divided into 4 groups (n=45): low tidal volume (VT < 8 mL/kg) + PCV (Group A), low tidal volume (VT < 8 mL/kg) + VCV (Group B), high tidal volume (VT ≥ 8 mL/kg) + PCV (Group C), and high tidal volume (VT ≥ 8 mL/kg) + VCV (Group D). Baseline characteristics among 4 groups were comparable, as illustrated in Table 1.

3. Methods

The study procedures were approved by the Ethics Committee of Jining No. 1 People’s Hospital Medical (No. 2015012). Patients were subject to 24-hours fasting for diet and water fasting for 4 hours before surgery. At preoperative 30 minutes, patients were administrated 0.5 mg atropine and 0.1 mg/kg (IM) midazolam. A central venous catheter was inserted in the internal jugular vein. Induction of anesthesia was performed by 0.1mg/kg midazolam, 0.5mg atropine and 0.1 mg/kg (IM) midazolam. A double-lumen endotracheal tube was inserted for continuous ventilation. Two-lung ventilation involved routine tidal volume – 8 mL/kg PEEP was used in PCV mode, and the set-up in VCV mode. OLV was performed according to the different groups, 5 cm H2O PEEP was used in PCV mode, and the set-up in VCV mode was the same as for two-lung ventilation.

3.1. Surgical procedures

First, we spared the latissimus dorsi and serratus anterior muscles subsequent to a postaxillar vertical skin incision, 4th intercostal thoracotomy without costectomy, the alimentary tract was reconstructed via posterior mediastinal route, placement of anastomosis was chosen between the residual esophagus and the gastric tube in the thoracic cavity and the gastric tube with sufficient blood supply was prepared by preservation of the arterial arcade of the omentum. The site of the anastomosis was chosen between the branches of the gastroepiploic arteries at the greater curvature of the gastric tube. Two-lung ventilation involved routine tidal volume (8–10 mL/kg), frequency of 12–18 times/min, and VCV mode. OLV was performed according to the different groups, 5 cm H2O PEEP was used in PCV mode, and the set-up in VCV mode was the same as for two-lung ventilation.

3.2. Observational indexes

The partial pressure of end-tidal carbon dioxide (PetCO2), oxygenation index, and SO2 were observed. Peak airway pressure (Ppeak), plateau airway pressure (Pplat), mean airway pressure (Pmean), and airway resistance (Rair) were continuously monitored with an AOU anesthesia machine. Patients were monitored for complications including pulmonary infection, anastomotic fistula, VILI, lung dysfunction, difficulty weaning from mechanical ventilation, and multiple organ dysfunctions. The expression of the inflammatory mediators, IL-6, TNF-α, and CRP was measured by ELISA. Bilateral lower lobe lavage was collected at 42 hours after segmental allergen provocation. The tip of the fiberoptic bronchoscope was inserted in the subsegmental and segmental bronchial opening, 30 mL normal saline was infused, and the lavage fluid was collected in a sputum collector by negative pressure (suction). Ideally, the collected volume was > 25% of the lavage fluid. The collected fluid was left to stand for 30 minutes, centrifuged at 2500g for 20 minutes, and the supernatant was stored at ~20°C. The ELISA kit was from Jiangsu Biyuntian Technology Co., Ltd, China, and was used according to the manufacturer’s instructions.

3.3. Statistical analysis

SPSS 20.0 software was used for statistical analysis. Numerical data are presented as mean ±SD. Intergroup comparisons were by one-way ANOVA, pair-wise comparisons were performed by LSD-t test, and intragroup comparisons were by paired t-test. Categorical data are presented as number (n) or percentage (%). Intergroup comparisons were by chi-square test and P < .05 was considered statistically significant.

4. Results

4.1. PetCO2, Oxygenation index and SO2

As shown in Table 2, as an indicator reflecting the state of pulmonary circulation, the PetCO2 did not significantly differ among different groups (all P > .05). The oxygenation index and SO2 in Group A were significantly higher than those in the other groups (all P < .05).

Table 1

| Group Parameter | A (n = 45) | B (n = 45) | C (n = 45) | D (n = 45) | F/χ² | P |
|-----------------|-----------|-----------|-----------|-----------|------|---|
| Male/Female     | 20/16     | 30/15     | 29/17     | 27/18     | 0.478 | .924 |
| Age, y          | 66.5±5.9  | 65.7±5.6  | 67.2±6.2  | 67.4±6.6  | 0.165 | .958 |
| BMI, kg/m²      | 23.4±2.6  | 22.6±2.8  | 23.2±2.7  | 22.8±2.5  | 0.086 | .984 |
| Oxygenation index (PaO2/FiO2, mm Hg) | 425.6±36.5 | 432.7±35.2 | 428.9±34.8 | 437.5±36.7 | 0.342 | .765 |
| PaCO2, mm Hg    | 36.8±3.5  | 37.2±3.9  | 38.5±3.4  | 35.9±3.2  | 0.242 | .859 |
| SO2 (%)         | 98.2±0.6  | 98.3±0.7  | 98.4±0.5  | 98.5±0.4  | 0.064 | .958 |
| FEV1 (l)        | 2.4±0.6   | 2.3±0.4   | 2.3±0.5   | 2.4±0.5   | 0.102 | .963 |
| FEV1%           | 90.2±8.3  | 91.3±8.6  | 89.7±9.2  | 92.2±9.3  | 0.268 | .824 |
| FVC (l)         | 3.2±0.7   | 3.0±0.8   | 3.1±0.6   | 3.2±0.8   | 0.196 | .837 |
| FVC%            | 92.5±13.4 | 93.3±14.2 | 94.2±13.8 | 93.6±15.3 | 0.203 | .768 |
| Maximum tumor diameter, cm | 3.6±0.8   | 3.5±0.9   | 3.7±1.2   | 3.8±1.3   | 0.365 | .764 |
| Upper esophageal cancer [n (%)] | 13       | 11       | 10       | 12       | 0.584 | .900 |
| Lower esophageal cancer [n (%)] | 32       | 34       | 35       | 33       | 0.452 | .929 |
| Phase I [n (%)] | 20       | 21       | 18       | 19       | 0.322 | .659 |
| Phase II [n (%)] | 25       | 24       | 27       | 26       | .056 | .496 |
| Operative time, min | 192.6±35.9 | 213.2±42.5 | 224.5±45.6 | 206.7±46.7 | 0.526 | .496 |
| One-lung ventilation time, min | 72.8±12.3 | 75.6±13.5 | 83.2±14.3 | 77.4±16.7 | 0.322 | .659 |

FEV = forced expiratory volume, FVC = forced vital capacity.
The opening of lung tissues acts as an important cause of VILI.[11] The shear force caused by excessive stretching or repeated stretch should be adjusted when two-lung ventilation is changed to OLV. The parameters, including tidal volume and ventilation mode, were significantly lower in Group A than in the other groups, indicating that OLV with low tidal volume (VT < 8mL/kg)+PCV (5cmH2O PEEP) could provide sufficient oxygen and expel CO2. The levels of Ppeak, Pplat, and Pmean, were significantly lower in Group A than in the other groups, while the levels of Ram, between different groups were not significantly different, indicating that the ventilation mode in Group A could improve airway pressure and reduce ALI caused by high airway pressure in lung tissues or lung collapse caused by low airway pressure. High Ppeak with high VT may cause ALI.[13] Licker et al.[14] reported that protective OLV with low tidal volume could decrease the incidence of ALI in lobectomy patients and shorten the time of hospitalization. The incidences of complications in both Group A and Group B were lower than in Group C and Group D, indicating that low tidal volume was more important than high tidal volume for reducing perioperative complications.

Pathological analysis identified necrosis and detachment of alveolar epithelial cells, increased capillary permeability, pulmonary interstitial edema, and alveolar atrophy and atelectasis. These pathological changes further activated the inflammatory response, resulting in the production of large amounts of inflammatory mediators and adhesion molecules, and the accumulation and activation of inflammatory cells, ultimately resulting in cascade inflammatory responses. These inflammatory mediators were released in the blood through the pulmonary circulation, and caused multiple organ dysfunction or failure.[12]

In the present study, PetCO2 between the groups was not different, whereas the oxygenation index and SO2 in group A were significantly higher than in the other groups, indicating that OLV with low tidal volume (VT < 8mL/kg)+PCV (5cmH2O PEEP) could provide sufficient oxygen and expel CO2. The levels of Ppeak, Pplat, and Pmean, were significantly lower in Group A than in the other groups, while the levels of Ram, between different groups were not significantly different, indicating that the ventilation mode in Group A could improve airway pressure and reduce ALI caused by high airway pressure in lung tissues or lung collapse caused by low airway pressure. High Ppeak with high VT may cause ALI.[13] Licker et al.[14] reported that protective OLV with low tidal volume could decrease the incidence of ALI in lobectomy patients and shorten the time of hospitalization. The incidences of complications in both Group A and Group B were lower than in Group C and Group D, indicating that low tidal volume was more important than high tidal volume for reducing perioperative complications.

The expression of IL-6, TNF-α, and CRP in the lavage fluid from patients in Group A were significantly down-regulated compared with those in the other groups, while the levels of IL-6, TNF-α, and CRP in the lavage fluid from patients in Group A were significantly lower compared with those in the other groups, indicating that OLV significantly activates the inflammatory response, resulting in the production of large amounts of inflammatory mediators and adhesion molecules, and the accumulation and activation of inflammatory cells, ultimately resulting in cascade inflammatory responses. These inflammatory mediators were released in the blood through the pulmonary circulation, and caused multiple organ dysfunction or failure.[12]

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The expression levels of IL-6, TNF-α, and CRP among 4 groups.

| Group parameter | A (n=45) | B (n=45) | C (n=45) | D (n=45) | F    | P   |
|-----------------|----------|----------|----------|----------|------|-----|
| IL-6, µmol/L    | 156.3±32.4 | 192.4±36.5 | 232.5±42.4 | 256.4±45.7 | 6.532 | .000 |
| TNF-α, µmol/L   | 56.4±13.2  | 77.2±21.4  | 89.3±16.5 | 93.2±18.9 | 5.854 | .000 |
| CRP, mg/L       | 12.3±3.5   | 16.4±4.2   | 18.7±4.5  | 18.5±4.7  | 5.326 | .000 |

CRP = C-reactive protein.

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