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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 ($PetCO_2$) did not significantly differ among 4 groups (all $P > .05$), and the oxygenation index and SO_2 in Group A were significantly higher than in the other groups ($P < .05$). The $PetCO_2$, peak airway pressure (P_{peak}), platform airway pressure (P_{plat}), and mean airway pressure (P_{mean}) in Group A were significantly lower than those in the other groups (all $P < .05$). However, airway resistance (R_{aw}) among 4 groups 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 cmH_2O 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, $PetCO_2$ = pressure of end-tidal carbon dioxide, P_{peak} = peak airway pressure, P_{plat} = platform airway pressure, R_{aw} = 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, CO_2 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 IIb, 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

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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 0.1 mg/kg midazolam, 2 μg/kg fentanyl, 0.1 mg/kg vecuronium, and 1.5 mg/kg propofol. A double-lumen endotracheal tube was inserted for continuous infusion of propofol, atracurium, and remifentanil for induction of anesthesia.

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 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 H_2O 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 ($PetCO_2$), oxygenation index, and SO_2 were observed. Peak airway pressure (P_{peak}), plateau airway pressure (P_{plat}), mean airway pressure (P_{mean}), and airway resistance (R_{aw}) 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 > 2/5 of the lavage fluid. The collected fluid was left to stand for 30 minutes, centrifuged at 2500*g* 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. $PetCO_2$, Oxygenation index and SO_2

As shown in Table 2, as an indicator reflecting the state of pulmonary circulation, the $PetCO_2$ did not significantly differ among different groups (all $P > .05$). The oxygenation index and SO_2 in Group A were significantly higher than those in the other groups (all $P < .05$).

Table 1

Baseline parameters of patients among 4 groups.

Group Parameter	A (n = 45)	B (n = 45)	C (n = 45)	D (n = 45)	F/χ^2	*P*
Male/Female	29/16	30/15	28/17	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/m^2	23.4 ± 2.6	22.6 ± 2.8	23.2 ± 2.7	22.8 ± 2.5	0.086	.984
Oxygenation index (PaO_2/FiO_2, mm Hg)	425.6 ± 36.5	432.7 ± 35.2	428.9 ± 34.8	437.5 ± 36.7	0.342	.765
$PaCO_2$, mm Hg	36.8 ± 3.5	37.2 ± 3.9	36.5 ± 3.4	35.9 ± 3.2	0.242	.859
SO_2 (%)	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	.863
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		
Phase I [n (%)]	20	21	18	19	0.452	.929
Phase II [n (%)]	25	24	27	26		
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.

Table 2

$PetCO_2$, oxygenation index and SO_2.

Group parameter	A (n = 45)	B (n = 45)	C (n = 45)	D (n = 45)	F	P
$PetCO_2$, mm Hg	45.3 ± 4.6	44.2 ± 4.3	42.6 ± 4.5	43.2 ± 4.6	0.263	.831
Oxygenation index, mm Hg	356.8 ± 42.5	332.4 ± 53.7	312.6 ± 50.8	321.7 ± 52.2	5.326	.000
SO_2, %	99.2 ± 0.8	98.3 ± 0.6	97.6 ± 0.5	96.5 ± 0.7	4.659	.012

4.2. The levels of P_{peak}, P_{plat}, P_{mean}, and R_{aw}

As shown in Table 3, the levels of P_{peak}, P_{plat}, and P_{mean} in Group A were significantly lower compared with those in the other groups (all $P < .05$). The levels of R_{aw} did not significantly differ among 4 groups (all $P > .05$).

4.3. The incidence of complications

As shown in Table 4, the incidence rates of complications in Groups A and B were significantly lower compared with those in Groups C and D (all $P < .05$).

4.4. The expression of IL-6, TNF-α, and CRP

As shown in Table 5, the expression levels 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 (all $P < .05$).

5. Discussion

Basal lung function and the tolerance to surgery and anesthesia are poor in older patients. Extended use of OLV is an independent risk factor for postoperative pulmonary dysfunction and perioperative complications.[10] Thus, appropriate mode of OLV is necessary for older patients who undergo chest surgery. The parameters, including tidal volume and ventilation mode, should be adjusted when two-lung ventilation is changed to OLV. The shear force caused by excessive stretching or repeated opening of lung tissues acts as an important cause of VILI.[11] Pathological analysis identified necrosis and detachment of alveolar epithelial cells, increased capillary permeability, pulmonary interstitial edema, and alveolar atrophy 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, $PetCO_2$ between the groups was not different, whereas the oxygenation index and SO_2 in group A were significantly higher than in the other groups, indicating that OLV with low tidal volume (VT < 8 mL/kg) + PCV (5 cmH_2O PEEP) could provide sufficient oxygen and expel CO_2. The levels of P_{peak}, P_{plat}, and P_{mean} were significantly lower in Group A than in the other groups, while the levels of R_{aw} 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 P_{peak} 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 lavage fluid was significantly lower in Group A compared with the other groups. We performed OLV in patients undergoing radical surgery for

Table 3

The levels of P_{peak}, P_{plat}, P_{mean} and R_{aw} (cmH_2O) among 4 groups.

Group parameter	A (n = 45)	B (n = 45)	C (n = 45)	D (n = 45)	F	P
P_{peak}	15.6 ± 4.7	18.2 ± 5.3	22.4 ± 5.6	23.3 ± 6.1	4.123	.016
P_{plat}	12.6 ± 3.8	15.4 ± 3.6	18.5 ± 4.2	19.2 ± 4.3	4.436	.010
P_{mean}	10.2 ± 3.6	13.6 ± 3.8	14.2 ± 4.0	14.5 ± 4.1	4.521	.007
R_{aw}	4.6 ± 0.9	4.3 ± 0.8	4.4 ± 0.6	4.5 ± 0.7	0.559	.421

Table 4

The incidence of complications [n (%)] among 4 groups.

Parameter Group	Pulmonary infection	Anastomotic fistula	VILI	Pulmonary dysfunction	Difficulty weaning from mechanical ventilation	Multiple organ dysfunction	Incidence of complications
A (n = 45)	1	1	1	1	0	0	8.9
B (n = 45)	2	1	2	1	0	0	13.3
C (n = 45)	3	2	3	2	1	1	26.7
D (n = 45)	4	3	3	2	1	0	28.9
χ^2							8.335
P							.040

VILI = ventilator-induced lung injury.

Table 5

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.

esophageal cancer and found that the inflammatory response was significantly lower with PCV (VT 5–6 mL/kg) than with VCV. Additionally, the PCV mode provided much more protection. TNF-α is mainly produced by activated macrophages, and alveolar macrophages play important roles in the regulation of the pro-inflammatory response in lung ischemia-reperfusion injury.[15] As a pro-inflammatory cytokine, TNF-α can promote the expression of several interleukins, IFN-γ, and adhesion molecules. IL-6 is an important inflammatory factor in the pathogenesis of re-expansion pulmonary edema, where it can promote the accumulation of neutrophils in the lung and further induce lung injury.[16] CRP is a sensitive marker of early lung injury. The expression levels of IL-6, TNF-α, and CRP are intimately associated with the incidence, severity, and prognosis of lung injury.[17]

In conclusion, OLV with low tidal volume + PCVF can improve the lung function and reduce the severity of inflammation in elderly patients undergoing esophageal cancer surgery. These combined techniques deserve to be applied in clinical practice.

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