



A randomized controlled trial of positive end-expiratory pressure on pulmonary oxygenation and biventricular function in esophageal cancer patients receiving one-lung ventilation under a lower FiO_2

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Background: Arterial oxygenation is often impaired during one-lung ventilation (OLV), due to both pulmonary shunt and atelectasis. Lower fraction of inspiration O_2 (FiO_2) may reduce inflammation and complications, but may increase the risk of hypoxemia. The aim of this randomized controlled parallel trial was to analyze whether higher positive end-expiratory pressure (PEEP) could improve oxygenation and maintain lower levels of inflammation during OLV under a lower FiO_2 .

Methods: One hundred and twenty patients with selective thoracotomy for esophageal cancer (EC) were classified randomly into four groups on a ratio of 1:1:1:1 using a computer-generated list, including Group A ($\text{FiO}_2 = 0.6$, PEEP = 0), Group B ($\text{FiO}_2 = 0.6$, PEEP = 5 cmH_2O), Group C ($\text{FiO}_2 = 1.0$, PEEP = 8 cmH_2O), and Group D ($\text{FiO}_2 = 1.0$, PEEP = 10 cmH_2O). The oxygenation and pulmonary shunt were primary outcomes. Haemodynamics, respiratory mechanics, serum IL-6 and IL-10 levels, and complications were taken as secondary outcomes. Follow-up was terminated until discharge.

Results: Two patients in Group A and two in Group D were excluded due to hypoxemia and hypotension, respectively. Then the data of 116 patients (Group A = 28, Group B = 30, Group C = 30, and Group D = 28) were assessed for final analysis. Compared with Group B, the partial pressure of oxygen (PaO_2) and dynamic compliance during OLV in Group D were significantly increased from 15 minutes to 60 minutes, while pulmonary shunt was significantly decreased ($P > 0.05$). Patients in Group D had higher levels of central venous pressure (CVP) and airway pressure (Paw) during OLV and higher levels of IL-6 and IL-10 after OLV compared with Group B ($P > 0.05$). No statistical differences were found in oxygen saturation (SaO_2), PvO_2 (partial pressure of oxygen in venous blood), partial pressure of end-tidal carbon dioxide (ETCO_2), partial pressure of carbon dioxide in artery (PaCO_2), heart rate (HR), mean arterial pressure (MAP), and complications among the four groups ($P > 0.05$).

Conclusions: Higher PEEP increased the oxygenation under 60% O_2 during OLV. However, the haemodynamics and respiratory mechanics changed, and the levels of inflammation increased. A higher PEEP under 60% O_2 during OLV is not recommended.

Trial Registration: Chinese Clinical Trial Registry ChiCTR1900024726.

Keywords: Positive end-expiratory pressure (PEEP); one-lung ventilation; low FiO_2

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Introduction

One lung ventilation (OLV) offers an operable and mobile minimally surgical field during thoracic surgery. However, lung atelectasis during OLV leads to a mismatched ventilation/perfusion ratio (V/Q) and threatens hypoxemia (1-4). Although high fraction of inspiration O₂ (FiO₂) (1.0) improved oxygenation (5), the following higher levels of inflammation remarkably raised acute respiratory distress syndrome (ARDS) risk, leading to increased postoperative mortality (6,7). Several reports have shown the independent risk factors for ARDS are high FiO₂ and airway pressure, as well as prolonged OLV (6-8), and maximizing the use of minimum FiO₂ under adequate oxygenation is the current recommended strategy for protective ventilation (3).

Our previous animal study has shown low FiO₂ (0.6) could produce less inflammation, oxidative stress, and lung injury than FiO₂ (1.0) after OLV [positive end-expiratory pressure (PEEP) = 0 cmH₂O, VT = 10 mL/kg] (8). However, 30% (3/10) of animals developed hypoxemia and required elevated FiO₂. We further studied the effect of low FiO₂ (0.6) in humans under a protective strategy (PEEP = 5 cmH₂O, V_T = 6 mL/kg) and all patients had lower oxidative stress and complications after OLV and only 6.7% (2/30) developed hypoxemia (9). Recently, Ferrando *et al.* showed an “individualized” PEEP level measurement of approximately 10 cmH₂O during OLV improved pulmonary oxygenation (10). However, whether the increased PEEP could improve pulmonary oxygenation and decrease hypoxemia under low FiO₂ (0.6) remains unknown. This research aimed to explore whether increased PEEP could improve pulmonary oxygenation and decrease hypoxemia under low FiO₂ (0.6) during OLV. The secondary objective was to study whether increased PEEP could induce lower inflammatory and lung injury under low FiO₂ (0.6).

Given the PEEP decrement trial results of Ferrando *et al.*, PEEP (8 cmH₂O) and PEEP (10 cmH₂O) were used as higher levels of PEEP in this research. The baseline level of pulmonary oxygenation was defined by the patients with protective strategy (FiO₂ = 0.6, PEEP = 5 cmH₂O). Previous studies have shown that IL-6 and IL-10 were associated with lung complications after OLV (11,12), and their serum

levels were also assessed. This study aimed to explore the safety and lung protective effect of this ventilation mode in patients with OLV, so as to seek an optimal and suitable lung protective ventilation mode for patients, and to open up a new design idea for lung protective ventilation strategies during OLV, which has important scientific theoretical value and broad clinical application prospects. We present the following article in accordance with the CONSORT reporting checklist (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-22-522/rc>).

Methods

Patients

This study enrolled patients with esophageal cancer (EC) who were scheduled to undergo elective open radical surgery in The Affiliated Cancer Hospital of Nanjing Medical University. EC was diagnosed under clinical data, laboratory index, gastroscopy and pathology. Patients were excluded if they met the following criteria: (I) pulse oxygen saturation (SpO₂) < 90% during this trial; (II) 20% reduction in blood pressure; (III) severe intraoperative arrhythmia and hemodynamic instability; (IV) operation time more than 6 hours or less than 1 hour; (V) patients with immune, endocrine, neurological, or blood vessel disease; (VI) patients with liver and kidney dysfunction, glaucoma, or mental illness. Patients were randomly divided into four parallel groups on a ratio of 1:1:1:1 using a computer-generated list: Group A (FiO₂ = 0.6, PEEP = 0 cm, n = 30), Group B (FiO₂ = 0.6, PEEP = 5 cm, n = 30), Group C (FiO₂ = 0.6, PEEP = 8 cm, n = 30), and Group D (FiO₂ = 0.6, PEEP = 10 cm, n = 30). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Nanjing Medical University (No. 2017_550). All patients were enrolled after obtaining written informed consent.

Anesthesia and intervention

All patients received left-sided double-lumen intratracheal intubation under total intravenous anesthesia, with

intramuscular injection of phenobarbital 0.1 g and atropine 0.5 mg 30 minutes before admission. After entering the operating room, a central venous catheter was placed in the right internal jugular vein and midazolam 0.05 mg·kg⁻¹, fentanyl 3–4 µg·kg⁻¹, propofol 1 mg·kg⁻¹, and cis-atracurium 0.2 mg·kg⁻¹ were induced with sequential intravenous injections. The left-sided double-lumen intratracheal tube was placed and confirmed by fiberoptic bronchoscope. Ventilation parameters in this trial were tidal volume (VT) =6–8 mL/ideal body weight, respiratory rate (RR) =12–14 beats/min, inspiratory to expiratory ratio =1:2, ETCO₂ =35–45 mmHg. These parameters remained constant, and the non-ventilated lung was directly connected to indoor air during OLV. FiO₂ was 0.6 in the four groups. Remifentanyl, propofol, and cis-atracurium were continuously pumped intravenously to maintain anesthesia, and the depth was monitored to maintain BIS between 40 and 60 intraoperatively.

VT was 6 mL/IBW, RR was 12–14 beats/min, and respiratory parameters were adjusted to maintain SpO₂ >90% and end-expiratory carbon dioxide partial pressure (PCO₂) at 35–45 mmHg. At the beginning of chest closure, 2 µg/kg fentanyl was intravenously injected, and two-lung ventilation (TLV) was restored by manual lung swelling (airway pressure was limited to less than 30 cmH₂O, lung swelling duration was 30–40 s). At the end of the operation, all patients were admitted to the ICU for synchronized intermittent mandatory ventilation. When the patients were awake, the double-lumen bronchial catheter was extubated. Postoperative analgesia was controlled intravenous analgesia.

Primary endpoints

An arterial catheter was introduced into the radial artery, and a central vein line (two lumens 20 cm long) was placed through the right internal jugular vein into the right atrium and its location confirmed by chest X-ray. Before OLV (T1), OLV 10 minutes (T2), OLV 15 minutes (T3), OLV 30 minutes (T4), OLV 60 minutes (T5), and OLV 120 minutes (T6) for blood gas analyses, artery and venous blood samples were collected. At the same time, peak airway pressure (P_{peak}), mean arterial pressure (MAP), heart rate (HR), and airway pressure (Paw) were documented.

The calculation formulas of the shunt fraction were as follows:

$$Qs/Qt = (CcO_2 - CaO_2)/(CcO_2 - CvO_2) \quad (11,12);$$

$$CaO_2 = (1.36 \times \text{hemoglobin} \times SaO_2) + (0.0031 \times PaO_2);$$

$$CvO_2 = (1.36 \times \text{hemoglobin} \times SvO_2) + (0.0031 \times PvO_2);$$

$$CcO_2 = ((FiO_2 \times (P_B - P_{H_2O}) - PaCO_2 / \text{Respiratory quotient}) \times 0.0031) + 1.36 \times \text{hemoglobin};$$

P_B, 760 mmHg; P_{H₂O}, 47 mmHg; respiratory quotient, 0.8.

Dynamic compliance was calculated as V_T/(P_{peak} - PEEP).

Venous blood samples were collected at T1, T5, TLV 30 minutes (T7), and 24 h postoperatively (T8). The serum samples of all patients were centrifugated at 3,000 rpm for 20 min, then stored at -80 °C for biochemical evaluation. IL-6 and IL-10 concentrations were measured using human IL-6 and IL-10 ELISA kits, respectively, as described in the instructions.

Secondary endpoints

The hospital stays, clinical pulmonary infection score (CPIS) and complications of patients as the secondary endpoints were assessed in this trial.

Statistical analysis

Data analysis was performed by SPSS 20.0 software (IBM Corporation, Armonk, NY, USA). Continuous data with normal distribution were performed using ANOVA and Kolmogorov-Smirnov analyses with mean ± standard deviation (mean ± SD). Continuous data with skewed distribution were analyzed by Kruskal-Wallis and Fisher's precision probability tests, and presented as median and quartile [M (Q1, Q3)]. Categorical data were expressed by the numbers and proportions [n (%)], and the chi-square test was utilized to compare differences between groups. Two-sided P<0.05 was considered statistically significant.

Results

A total of 120 EC patients were enrolled between June 1, 2015 and June 30, 2018. All patients were followed up until discharge. The participant flow showed in *Figure 1*. In Group A, hypoxemia occurred in two patients, requiring FiO₂ enhancement during OLV. The two patients were excluded. In Group D, hypotension occurred in two patients (blood pressure dropped from 152/80 to 98/64 mmHg, and from 130/80 to 85/50 mmHg) requiring reduction of PEEP. The two patients were excluded. Then the data of 116 patients (Group A =28, Group B =30 Group C =30, and Group D =28) were assessed for final analysis.

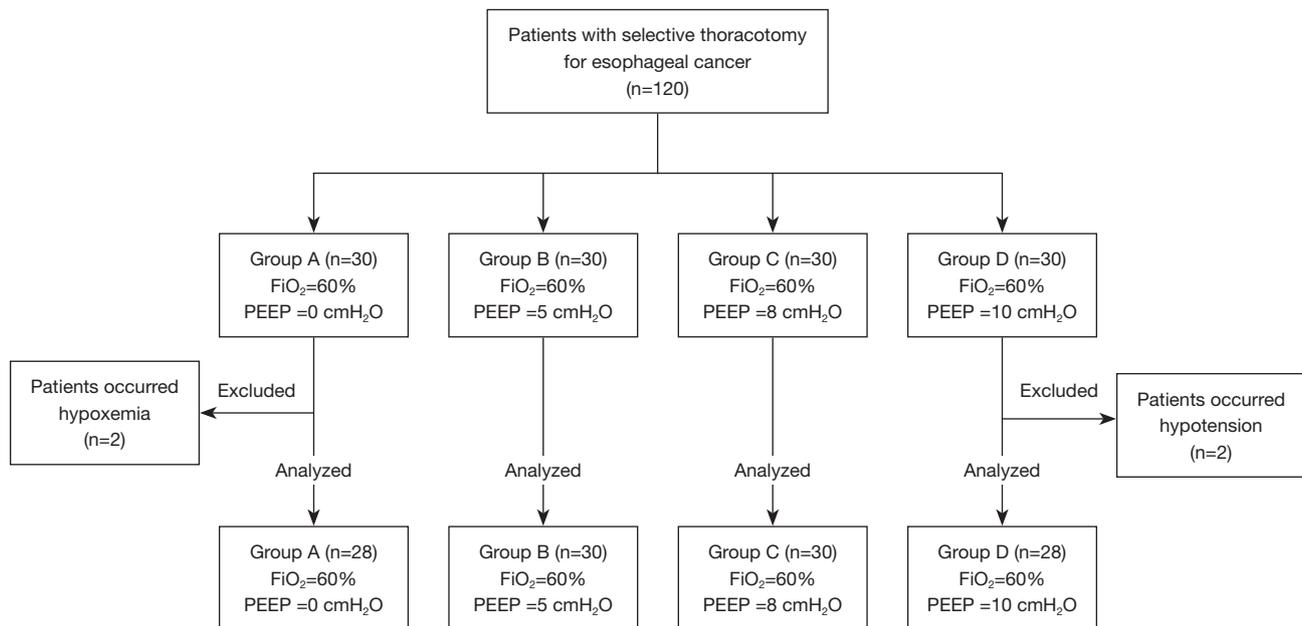


Figure 1 Flowchart for the randomized controlled trial. FiO₂, fraction of inspiration O₂; PEEP, positive end-expiratory pressure.

Clinical characteristics of 118 patients in the four groups are shown in *Table 1*. While the bleeding volumes of patients in Group D were significantly higher than others, no significant differences were observed in age, gender, BMI, drinking, smoking, HB, infusion volume, urination volume, ASA grade, TNM grade, lung function, OLV, and operation time.

Within the first 30 minutes after OLV initiation, PaO₂ decreased (*Figure 2A*), while Qs/Qt increased (*Figure 2B*), with PaO₂ and Qs/Qt reaching their nadir. Group D had significantly higher PaO₂ and lower Qs/Qt than Group B from OLV 15 minutes to OLV 60 minutes. Similarly, the dynamic compliance in Group D were significantly higher than Group B between 15 and 60 minutes during OLV (*Figure 3A*). During the whole OLV, there were no differences in PaO₂ and Qs/Qt between Groups B and C. PaO₂ were significantly higher and Qs/Qt in group B were lower than those in Group A at OLV 30 minutes. No significant difference was found in SaO₂, PvO₂, ETCO₂, and PaCO₂ among the four groups at each point (*Table 2*).

In the first 10 minutes, CVP and Paw increased after OLV initiation then remained stable during OLV (*Figure 3B, 3C*). Compared with Group A and B during OLV, the levels of CVP in Groups C and D were higher, while the Paw level

in Group D was significantly higher than in the other three groups.

During OLV, the levels of IL-6 and IL-10 slowly increased and there were no differences between the four groups at 60 minutes (*Figure 4*). After restarting TLV, the levels of IL-6 and IL-10 rapidly increased, and 30 minutes after restart and 24 h postoperatively, the levels of IL-6 and IL-10 in Group A and B were higher and lower, respectively, compared with those in Groups C and D (*Figure 4*). After surgery, there were more patients with CPIS over 6 in Group A ($P < 0.001$). While there were no significant differences in the hospital stay and complications among these four groups ($P > 0.05$), complications in Groups A and D were more serious (*Table 3*).

Discussion

Although a study previously published showed a higher PEEP could reduce pulmonary shunt and increase PaO₂ during OLV (10), it remains unclear whether higher PEEP can increase oxygenation at low FiO₂ during OLV. Our study showed a higher PEEP (10 cmH₂O) could increase the levels of PaO₂ and decrease those of Qs/Qt during the first 60 minutes of OLV. In Group D, two patients were

Table 1 Clinical characteristics

Variables	Group A (n=28)	Group B (n=30)	Group C (n=30)	Group D (n=28)	P
Age (years), mean \pm SD	63.10 \pm 5.985	63.90 \pm 5.720	63.33 \pm 6.493	64.37 \pm 4.694	0.829
Male, n (%)	11 (39.2)	12 (40.0)	17 (56.7)	13 (43.3)	0.502
BMI (kg/m ²), mean \pm SD	23.83 \pm 6.223	23.69 \pm 3.513	23.67 \pm 3.409	23.33 \pm 2.315	0.927
Smoking index, M (Q1, Q3)	600 (500, 1,100)	600 (375, 600)	600 (375, 850)	460 (400, 600)	0.362
Smoking cessation, n (%)	14 (50.0)	16 (53.3)	12 (40.0)	18 (64.2)	0.342
Drinking, n (%)	14 (50.0)	15 (50.0)	13 (43.3)	19 (63.3)	0.429
OLV duration (min), mean \pm SD	172.5 \pm 44.3	170.8 \pm 58.0	162.8 \pm 42.5	178.7 \pm 47.8	0.212
Surgery duration (min), mean \pm SD	205.6 \pm 52.8	194.2 \pm 51.6	193 \pm 45.2	213.3 \pm 43.1	0.230
FEV1 >80%, n (%)	28 (100.0)	29 (96.7)	29 (96.57)	26 (92.9)	0.602
Infusion volume (mL), mean \pm SD	1,982 \pm 356	2,224 \pm 709	1,946 \pm 208	1,922 \pm 417	0.465
Bleeding volume (mL), mean \pm SD	183.3 \pm 58	162.1 \pm 40.0	169.6 \pm 73.7	236.2 \pm 153.4	0.011
Urine output (mL), mean \pm SD	230.7 \pm 83.7	248.6 \pm 132.6	232.1 \pm 178.6	226.6 \pm 88	0.818
Hb (g/L), mean \pm SD	12.2 \pm 1.5	12.0 \pm 1.4	11.6 \pm 1.6	12.5 \pm 1.4	0.245
ASA, n					0.950
II	27	29	28	26	
III	1	1	2	2	
TNM stage, n					0.957
T1N0M0/T2N0M0/T1N1M0	2/14/10	1/15/11	0/16/12	1/14/12	
T2N1M0/T2N2M0/T3N0M0	2/0/0	3/0/0	2/0/0	1/0/0	

BMI, body mass index; OLV, one-lung ventilation; FEV1, forced expiratory volume in first second; Hb, hemoglobin; ASA, American Standards Association; TNM, tumor, node, metastasis.

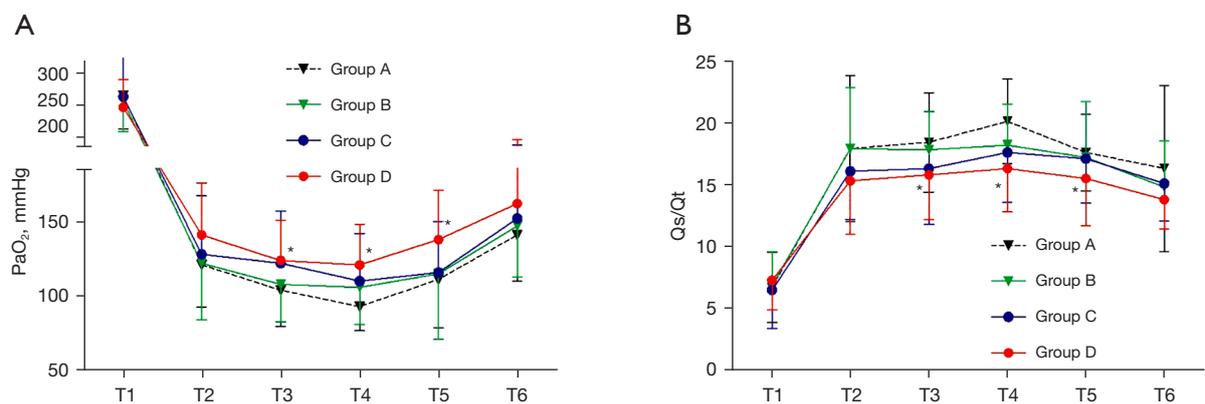


Figure 2 Dynamic changes of PaO₂ and Qs/Qt among EC patients during OLV in four groups. Comparison of the level of PaO₂ (A) and Qs/Qt (B) in Group A, Group B, Group C, and Group D at pre-OLV (T1), OLV 10 minutes (T2), OLV 15 minutes (T3), OLV 30 minutes (T4), OLV 60 minutes (T5), and OLV 120 minutes (T6). *, P<0.05 (compared with Group B). PaO₂, partial pressure of oxygen; Qs/Qt, pulmonary shunt; EC, esophageal cancer. OLV, one-lung ventilation.

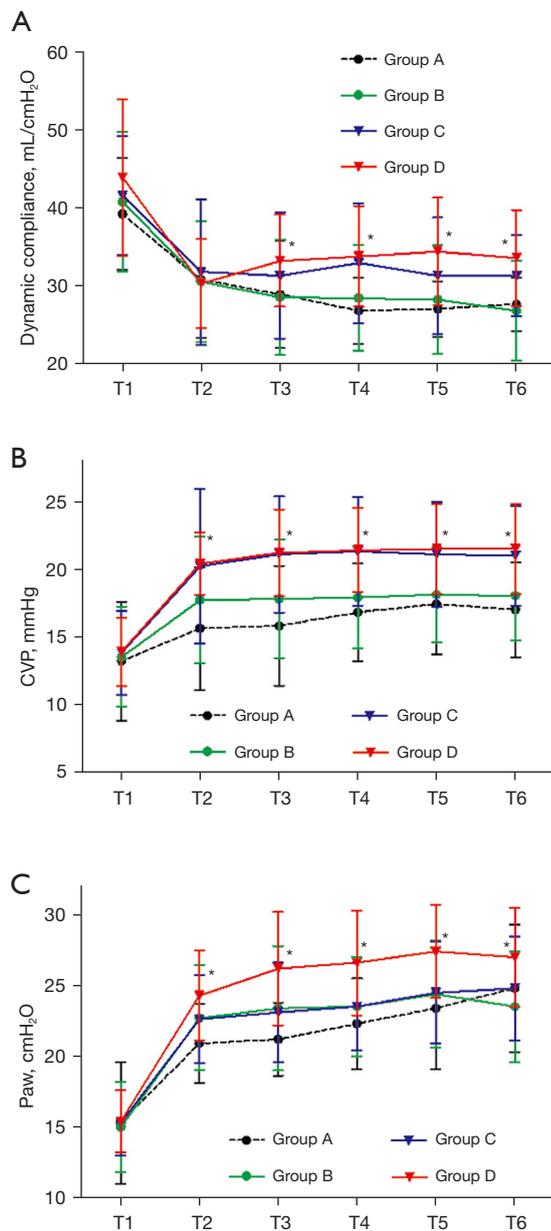


Figure 3 Dynamic changes of dynamic compliance, CVP, and Paw among EC patients during OLV in four groups. Comparison of the levels of dynamic compliance (A) CVP (B) and Paw (C) in Group A, Group B, Group C, and Group D at pre-OLV (T1), OLV 10 minutes (T2), OLV 15 minutes (T3), OLV 30 minutes (T4), OLV 60 minutes (T5), and OLV 120 minutes (T6). *, $P < 0.05$ (compared with Group B). CVP, central venous pressure; Paw, airway pressure; EC, esophageal cancer; OLV, one-lung ventilation.

excluded due to hypotension, and the levels of CVP and Paw also increased in the higher PEEP group during OLV. More importantly, the levels of IL-6 and IL-10 increased in higher PEEP patients, and although there were no significant differences in complications, those in patients with 10 cmH₂O PEEP were more serious.

Hypoxic pulmonary vasoconstriction (HPV) refers to the reflex contraction of vascular smooth muscle due to low regional partial pressure of oxygen (PO₂) in the pulmonary circulation (13). It has two distinct phases (14-19), with phase 1 beginning in a matter of seconds and reaching its lowest point at 15 minutes. When moderate hypoxia (PO₂ 30 to 50 mmHg) lasts for over 30 to 60 minutes, HPV begins to enter phase 2 and PVR is increased further, reaching its peak at 2 hours. Therefore, PaO₂ reaches its lowest level 20 to 30 minutes after the onset of OLV, then gradually increases during the following 1 to 2 hours. In our study, a higher PEEP (10 cmH₂O) increased levels of PaO₂ and decreased levels of Qs/Qt between 15 minutes and 60 minutes during OLV. As shown in *Figure 3A*, the higher degree of dynamic compliance partially overcame the mismatched V/Q ratio, leading to the increase in PaO₂. Therefore, patients can benefit from a higher PEEP (10 cmH₂O) to pass the hypoxic period within the first 30 minutes of OLV.

A higher PEEP led to haemodynamics and respiratory mechanics changes. First, two patients in Group D who were excluded developed hypotension and their blood pressures returned after reducing PEEP to 5 cmH₂O. Second, the remaining patients had higher CVP and Paw during OLV. Kim *et al.* showed that the more the biventricular diastolic function decreased, the more PEEP increased (20), suggesting this may be the main reason for haemodynamics changes. Third, the bleeding volume in Group D was higher than other groups, and haemodynamics changes may be the reason for higher bleeding during surgery.

As previously shown (21), we did not find significant differences in the levels of inflammation during OLV. However, after OLV, inflammation levels were higher in Group D than Group B. Previous studies showed hyperoxia during OLV increased the levels of inflammation and oxidative stress, leading to a higher risk of complications after surgery (21,22). Our previous research studied the benefits of lower FiO₂ in lowering inflammation, oxidative

Table 2 Clinical parameters in different lung ventilation treatments among the four groups

Variables	Group	T1	T2	T3	T4	T5	T6
SaO ₂ * (mmHg), mean ± SD	A	99.9±0.3	98.1±2.0	97.5±2.0	96.3±2.1	97.7±1.7	98.7±1.2
	B	99.9±0.2	97.5±2.2	97.6±1.9	96.9±2.1	96.9±2.5	98.6±1.4
	C	99.9±0.2	98.2±1.8	97.8±2.1	97.0±2.1	97.2±2.2	98.8±1.4
	D	99.8±0.3	98.1±1.8	97.6±1.7	96.9±2.1	97.8±1.8	99.0±1.0
PvO ₂ (mmHg), mean ± SD	A	43.0±2.9	37.4±3.5	36.3±3.8	35.3±3.0	35.4±4.3	35.0±2.7
	B	43.5±3.7	37.0±2.5	35.8±3.2	34.9±3.9	35.8±5.0	35.2±2.0
	C	43.7±2.5	36.3±4.1	34.6±2.9	34.1±3.2	34.6±2.9	36.1±3.2
	D	43.3±2.1	34.8±3.8	35.0±4.2	33.9±2.6	36.0±3.9	38.3±3.7
PaCO ₂ (mmHg), mean ± SD	A	42.5±4.3	41.3±6.1	39.5±3.7	41.3±5.8	40.6±6.3	39.8±7.1
	B	43.4±4.8	43.3±5.4	41.4±5.9	41.7±6.8	43.0±4.4	42.4±6.6
	C	43.6±6.1	42.3±11.4	39.7±3.6	39.3±4.2	42.5±4.3	39.7±3.8
	D	44.7±5.6	40.3±6.1	41.2±6.0	40.5±6.2	42.5±4.0	40.4±7.6
ETCO ₂ (mmHg), mean ± SD	A	35.6±5.3	36.6±4.2	36.0±4.1	36.0±3.8	35.2±3.3	35.3±3.3
	B	35.0±3.5	38.4±3.8	37.7±4.1	37.5±4.5	37.0±4.9	37.0±4.5
	C	35.4±3.9	38.3±5.8	37.9±5.8	37.0±6.9	37.0±4.7	36.9±4.7
	D	34.1±4.0	36.3±2.9	36.4±3.1	35.4±3.4	35.6±3.7	36.4±4.1
HR (beats/min), mean ± SD	A	74.2±12.5	75.0±12.1	77.3±9.6	76.8±10.8	73.6±12.8	72.5±18.8
	B	76.7±11.8	77.8±11.3	78.2±11.6	78.3±12.9	74.3±11.0	69.2±10.6
	C	74.7±9.9	76.3±9.1	78.3±9.3	77.2±11.7	73.0±10.8	67.6±9.7
	D	74.3±13.0	75.5±13.6	77.1±15.5	73.9±11.9	70.1±11.4	68.3±10.1
MAP (mmHg), mean ± SD [#]	A	97.8±11.8	98.3±13.1	13.2±2.4	98.3±11.0	101.6±94.3	98.8±12.4
	B	99.8±13.9	102.2±12.7	12.3±2.3	101.5±14.3	97.7±12.5	96.1±12.4
	C	97.3±14.9	104.5±10.2	98.9±11.9	103.5±12.6	98.9±13.2	93.7±10.8
	D	95.8±14.2	105.4±14.9	100.6±13.7	99.4±14.0	101.0±13.0	97.8±11.6

T1, preoperative; T2, OLV 10 min; T3, OLV 15 min; T4, OLV 30 min; T5, OLV 60 min; T6, OLV 120 min; *, the SaO₂ in patients with hypoxemia was significantly lower than patients in other groups; #, the MAP in patients with hypotension in Group D was significantly lower than patients in other groups. SaO₂, oxygen saturation; SD, standard deviation; PvO₂, partial pressure of oxygen in venous blood; PaCO₂, partial pressure of carbon dioxide in artery; ETCO₂, partial pressure of end-tidal carbon dioxide; HR, heart rate; MAP, mean arterial pressure; OLV, one-lung ventilation.

stress, and lung injury (8,9). Although higher PEEP increased oxygenation, the levels of inflammation also increased. Given the higher levels of inflammation and more serious complications in Group D, we believe the small sample size led to the similar rates of complications in the four groups.

There are several limitations in this trial that require caution in interpreting our findings. Firstly, further subgroup analyses based on age or gender could not be performed owing to sample size limitations. Secondly, there is no significant deterioration of pulmonary function in the patients. Whether the PEEP titration strategy is valuable

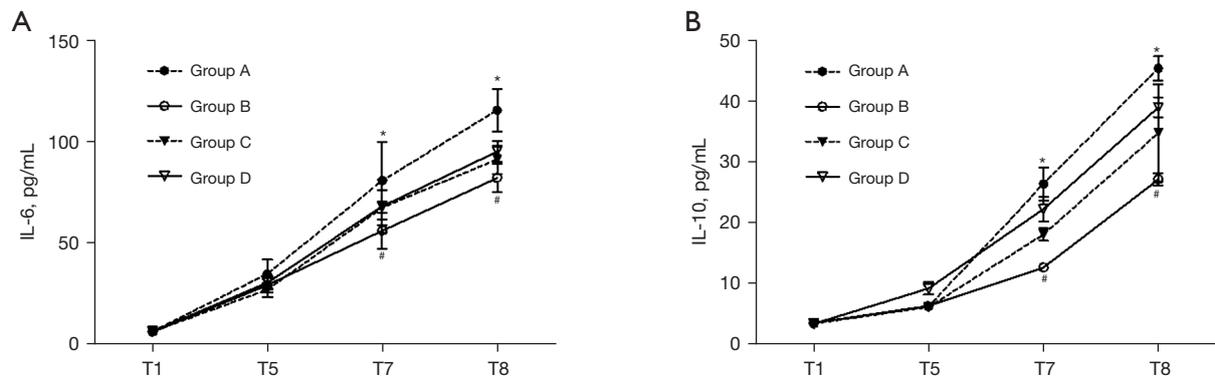


Figure 4 Serum IL-6 and IL-10 levels among EC patients in four groups. Comparison of serum IL-6 (A) and IL-10 levels (B) in Groups A, B, C, and D at T1 (pre-OLV), T5 (OLV 60 minutes), T7 (30 minutes after switching back to TLV), and T8 (24 hours post-operation). *, $P < 0.05$ (compared with Group C); #, $P < 0.05$ (compared with Group D). EC, esophageal cancer; OLV, one-lung ventilation; TLV, two-lung ventilation.

Table 3 Clinical outcomes among the four groups

Variables	Group A (n=28)	Group B (n=30)	Group C (n=30)	Group D (n=28)	P
Hospital stays (d), M (Q1, Q3)	14 (13, 17)	13 (13, 14)	14 (13, 14)	14 (13, 18)	0.135
CPIS*, n					<0.001
≥6	9	0	1	2	
0–6	17	30	29	26	
Complications, n	3	7	4	6 [#]	0.228
Empyema	1				
Incision infection	2	4	2	1	
Hydrothorax	1	2			
Pneumonia	1	1	2	1	
Delirium				1	
Hypoxemia	1			1 [¶]	

*, Group B, C, and D were combined when Fish test was performed; #, another two complications: urinary tract bleeding and chylothorax; ¶, the patient was transferred to a superior hospital due to refractory hypoxemia; M (Q1, Q3), median and quartile; n, number; CPIS, clinical pulmonary infection score.

for critically ill patients still needs further explore. Future studies with well-design, large sample size should confirm our findings.

Conclusions

The findings show a higher PEEP increased oxygenation under 60% O₂ during OLV. However, the haemodynamics and respiratory mechanics changed, and the levels of inflammation increased. Given the effect of higher FiO₂

under protective strategy, a higher PEEP under 60% O₂ during OLV is not recommended.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Nanjing Medical University (No. 2017_550). All participants were enrolled after written informed consent was obtained.

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