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# One-Lung Ventilation with Additional Ipsilateral Ventilation of Low Tidal Volume and High Frequency in Lung Lobectomy

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Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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**Background:** To investigate the protective effects of additional ipsilateral ventilation of low tidal volume and high frequency on lung functions in the patients receiving lobectomy.

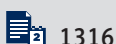
**Material/Methods:** Sixty patients receiving lung lobectomy were randomized into the conventional one-lung ventilation (CV) group (n=30) and the ipsilateral low tidal volume high frequency ventilation (LV) group (n=30). In the CV group, patients received only contralateral OLV. In the LV group, patients received contralateral ventilation and additional ipsilateral ventilation of low tidal volume of 1–2 ml/kg and high frequency of 40 times/min. Normal lung tissues were biopsied for the analysis of lung injury. Lung injury was scored by evaluating interstitial edema, alveolar edema, neutrophil infiltration, and alveolar congestion.

**Results:** At 30 min and 60 min after the initiation of one-lung ventilation and after surgery, patients in the LV group showed significantly higher ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen than those in the CV group (P<0.001). Lung injury was significantly less severe (2.7±0.7) in the LV group than in the CV group (3.1±0.7) (P=0.006).

**Conclusions:** Additional ipsilateral ventilation of low tidal volume and high frequency can decrease the risk of hypoxemia and alleviate lung injury in patients receiving lobectomy.

**MeSH Keywords:** **Anterior Temporal Lobectomy • High-Frequency Ventilation • Lung**

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## Background

One-lung ventilation (OLV) is commonly used in thoracic surgeries. By ventilating the contralateral lung and collapsing the ipsilateral lung, OLV avoids pollution of the contralateral lung by the excretions and blood from the ipsilateral lung, and provides a clear surgical field vision. However, intraoperative hypoxemia is a common complication of OLV [1–5]. OLV is also an important reason for postoperative acute lung injuries in patients receiving thoracic surgeries [6–10]. Acute lung injury is one of the major causes of death after thoracic surgery [11]. Ventilator-induced lung injury during OLV is further supported by the association between tidal volume exceeding 7–8 ml/kg predicted body weight and the release of systemic and pulmonary inflammatory mediators [12]. Various lung-protective strategies have been tried, such as lower tidal volume combined with positive end-expiratory pressure (PEEP) [13], preconditioning [14], dexmedetomidine [15], therapeutic hypercapnia [16], and protective ventilation modes [17,18].

In this study, we investigated the lung protective effect of additional ipsilateral ventilation of low tidal volume and high frequency in patients receiving lung lobectomy.

## Material and Methods

### Patients

A consecutive 60 patients receiving lung lobectomy from October 2012 to May 2014 at our hospital were included in this study. There were 48 males and 12 females with a mean age of 52.9 years (range, 39–50 years). The American Society of Anesthesiologists grade was I to II. Patients were excluded from the study if they had smoking history, intraoperative transfusion, OLV <1 hour, operation time >4 hour, or conversion to total lung resection. This study was approved by the Ethics Committee of our hospital. Informed consent was obtained from the patients or their legal surrogates.

### Ventilation protocol

Patients were randomly assigned into the conventional OLV (CV) group (n=30) and the ipsilateral ventilation of low tidal volume and high frequency (LV) group (n=30). At 30 min before anesthesia, all patients received intramuscular injection of 3 mg midazolam and 0.5 mg penehyclidine hydrochloride. General anesthesia was induced with intravenous injection of midazolam (0.05–0.1 mg/kg), sufentanil (0.3 µg/kg), and vecuronium bromide (0.1 mg/kg). The patient was intubated with a double-lumen tube (Sheridan, Mexico) connected to a ventilator (Aestiva/5 7900, GE Healthcare, USA). The fraction of inspired oxygen (FiO<sub>2</sub>) was 100% with a flow rate of 1.5 L/min.

The end-tidal carbon dioxide partial pressure (P<sub>ET</sub>CO<sub>2</sub>) was maintained at 35–45 mmHg.

Tow-lung ventilation was performed using the following parameters, tidal volume 10 ml/kg, ventilation frequency 12 times/min, and inspiratory-to-expiratory time (I/E) ratio 1:1.5. For OLV in the CV group, the following parameters were used, tidal volume 8 ml/kg, ventilation frequency 14 times/min, I/E ratio 1:1.5, and PEEP 5 cm of water. For OLV in the LV group, the contralateral lung ventilation was performed with tidal volume 6 ml/kg, ventilation frequency 12 times/min, and I/E ratio 1:1.5. Meanwhile, the ipsilateral lung was ventilated using the same type of ventilator with tidal volume 1–2 ml/kg, ventilation frequency 40 times/min, and I/E ratio 1:1.5.

Remifentanil 0.2–0.4 µg/kg/min was continuously pumped to maintain anesthesia. Midazolam and vecuronium bromide were intermittently added. The bispectral index was maintained within 40 to 50. If the ipsilateral ventilation affected the surgical procedure, ventilation was temporarily paused. Ephedrine 10 mg was administered if the systolic blood pressure dropped below 20% of the baseline value. Atropine 0.2–0.5 mg was administered if the heart rate was less than 50 beats/min.

### Evaluation

Arterial blood samples were collected from the femoral artery before OLV (T<sub>0</sub>), at 30 min (T<sub>1</sub>) and 60 min (T<sub>2</sub>) after the initiation of OLV, and after the surgery (T<sub>3</sub>). Blood gas analyses were performed (ABL700, Radiometer, Denmark). Partial pressure of arterial carbon dioxide (PaCO<sub>2</sub>), partial pressure of arterial oxygen (PaO<sub>2</sub>), and FiO<sub>2</sub> were measured.

Normal lung tissues were harvested 5 cm away from the lesions at a mean time of 102.4 min (range, 73–123 min). A tissue sample of 1.0×1.0×1.0 cm was fixed in 10% formaldehyde for 24 hours. The tissue was embedded in paraffin and cut into 4-µm sections. The sections were stained with hematoxylin and eosin and observed under a light microscope. Interstitial edema, alveolar edema, neutrophil infiltration, and alveolar congestion were evaluated. Lung injury was assessed using a previously reported score system [19]: 0 point, no pathological changes; 1 point, mild pathological changes; 2 points, intermediate pathological changes; 3 points, severe pathological changes; 4 points, extremely severe pathological changes.

### Statistical analysis

Continuous data were presented as mean ± standard deviation and categorical data as frequencies. Comparison was made using Student's *t*-test or chi-square test when appropriate. All statistical analyses were performed using SPSS 17.0 (SPSS, Chicago, IL, USA). P<0.05 was considered statistically significant.

**Table 1.** General information and surgical data of the CV and LV groups.

	CV group (n=30)	LV group (n=30)	P-value
Sex – male/female	20/10	15/15	0.194
Age – yr	54.03±3.38	52.63±4.11	0.096
Body mass index – kg/m <sup>2</sup>	24.04±1.032	24.53±0.80	0.058
Surgical side – left/right	15/15	15/15	1
OLV time – min	118.17±13.05	123.53±11.13	0.051
Operation time – min	150.73±13.14	149.57±14.99	0.609
Fluid infusion – ml	1836.83±78.76	1869.87±65.91	0.059
Urine volume – ml	404.03±13.26	407.8±17.63	0.298

OLV – one-lung ventilation.

**Table 2.** Comparison of the PaO<sub>2</sub>/FiO<sub>2</sub> between the CV and LV groups.

Time point	CV group (n=30)	LV group (n=30)	P-value
T <sub>0</sub>	478.37±48.61	480.67±47.44	0.860
T <sub>1</sub>	242.57±33.22	292.33±42.20	<0.001
T <sub>2</sub>	230.97±26.84	311.77±33.39	<0.001
T <sub>3</sub>	364.53±72.82	391.30±44.82	0.012

## Results

The CV and LV groups were similar in general information, surgical side, OLV time, operation time, intraoperative fluid infusion, and urine volume (Table 1). At time point T<sub>0</sub>, the two groups showed no significant difference in ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO<sub>2</sub>/FiO<sub>2</sub>) (P=0.860, Table 2). However, at time points T<sub>1</sub> through T<sub>3</sub>, patients in the LV group showed significantly higher PaO<sub>2</sub>/FiO<sub>2</sub> than those in the CV group (P<sub>T<sub>1</sub></sub><0.001, P<sub>T<sub>2</sub></sub><0.001, P<sub>T<sub>3</sub></sub>=0.012). The normal lung tissue of the CV group showed significantly more severe pathological changes of interstitial edema, alveolar edema, neutrophil infiltration, and alveolar congestion than the LV group (Figure 1). In addition, the lung injury score was 2.7±0.7 in the LV group, which was significantly lower than 3.1±0.7 in the CV group (P=0.006). It was suggested that patients in the LV group had significantly less severe lung injury than those in the CV group.

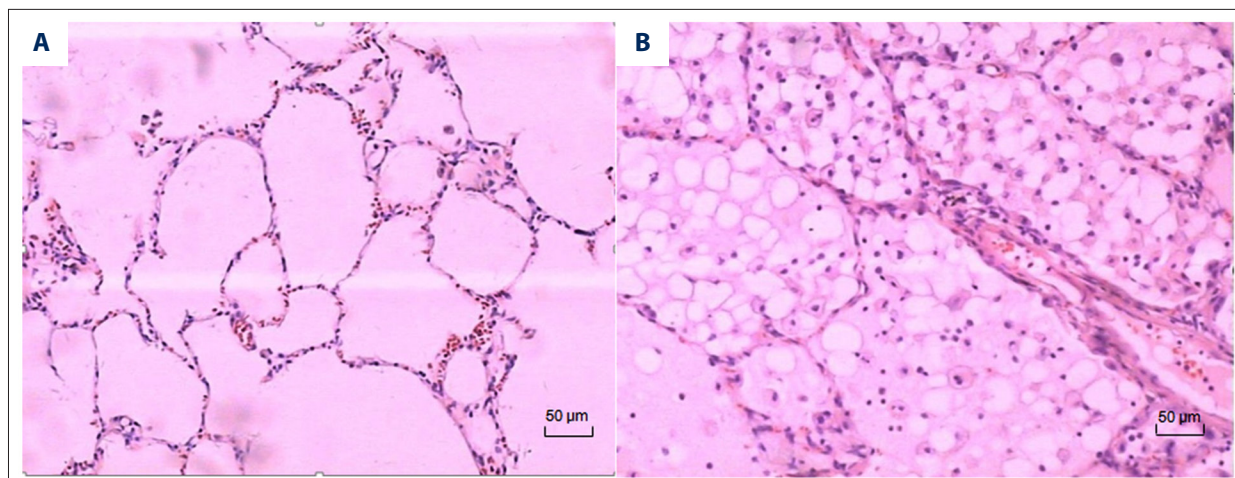
## Discussion

In this randomized study, we compared the lung protective effects of two ventilation modes in patients receiving lobectomy. In the CV group, patients received only contralateral OLV. In the LV group, patients received contralateral ventilation and ipsilateral ventilation of low tidal volume and high

frequency. We found that patients in the LV group had significantly higher PaO<sub>2</sub>/FiO<sub>2</sub> and significantly less severe lung injury than those in the CV group.

In our study, the ipsilateral ventilation was started with a tidal volume of 1 ml/kg and gradually increased to 2 ml/kg, with a ventilation frequency of 40 times/min. This technique can minimize the effects on surgical procedures, and in the meanwhile, moderately inflate the collapsed lung and improve ventilation and oxygenation. After the initiation of OLV, the PaO<sub>2</sub> at time points T<sub>1</sub> and T<sub>2</sub> was lower than that at T<sub>0</sub> in both groups. However, the LV group showed significantly lower reduction in PaO<sub>2</sub> than the CV group (P<0.001). PaO<sub>2</sub>/FiO<sub>2</sub> reflects damages of the lung vessels and alveoli. Lower PaO<sub>2</sub>/FiO<sub>2</sub> indicates more severe lung injury and is a commonly used diagnostic criterion for acute lung injury. We found that at time points T<sub>1</sub> through T<sub>3</sub>, patients in the LV group showed significantly higher PaO<sub>2</sub>/FiO<sub>2</sub> than those in the CV group (P<sub>T<sub>1</sub></sub><0.001, P<sub>T<sub>2</sub></sub><0.001, P<sub>T<sub>3</sub></sub>=0.012). These results suggest that the ipsilateral ventilation of low tidal volume increased oxygenation.

Patients in our study all had lung diseases. To exclude any possible disturbing factors, we chose patients without smoking history, and no inhalation anesthetics were used for maintaining anesthesia. The pathological changes of interstitial edema, alveolar edema, neutrophil infiltration, and alveolar congestion were significantly less severe in the LV group than in



**Figure 1.** The pathological changes of normal lung tissues (hematoxylin and eosin staining). Interstitial edema, alveolar edema, neutrophil infiltration, and alveolar congestion were significantly less severe in the LV group (A) than in the CV group (B).

the CV group. We speculate that the ipsilateral ventilation of low tidal volume might avoid excessive collapse of the alveoli and decrease the surface tension. This may result in reduced sucking effect of the surface tension in the alveoli and less fluid effusion from the capillaries, leading to alleviated lung injury. In addition, the ipsilateral ventilation might help to alleviate lung injury by reducing the release of oxygen radical and attenuating the neutrophil infiltration during restoration of two-lung ventilation [12,20–22].

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## Conclusions

The use of ipsilateral low tidal volume ventilation and contralateral conventional ventilation can successfully isolate the bilateral lungs in lobectomy. The use of additional ipsilateral ventilation also decreases the risk of hypoxemia and alleviates postoperative lung injury.