Effect of Positive End-Expiratory Pressure (PEEP) Titration in Elderly Patients Undergoing Lobectomy

Authors' Contribution:
AE 1 Wenyu Yao
B 2 Bo Yang
B 3 Wenlong Wang
D 1 Qian Han
D 4 Fenghai Liu
G 1 Shiqiang Shan
E 1 Chao Wang
F 1 Mengliang Zheng

Background: Currently, one-lung ventilation in thoracoscopic lobectomy adopts mostly a protective ventilation mode, which includes low tidal volume (a tidal volume of 6 mL/kg predicted body weight), positive end-expiratory pressure (PEEP), and intermittent lung inflation. However, there is no clear conclusion regarding the value of PEEP in elderly patients undergoing lobectomy.

Material/Methods: Fifty patients who underwent video-assisted thoracoscopic unilateral lobectomy, aged 65 to 78 years, with a body mass index of 18 to 29 kg/m² and ASA grades I to III, were randomly divided into 2 groups (n=25 each): optimal oxygenation titration group (group O) and optimal compliance titration group (group C). Mean arterial pressure (MAP), heart rate (HR), and central venous pressure (CVP) were recorded in both groups at different time points. The radial artery blood samples were collected at 3 time points for blood gas analysis, and the void volume/tidal volume ratio was calculated. The peak airway pressure and PEEP values were recorded at 4 min after the completion of one-lung ventilation titration (T2), and the driving pressure was calculated.

Results: The best PEEP value of titration in the best compliance group was lower than that of the best oxygenation method, the peak was lower, and the dynamic lung compliance was higher; however, this had no effect on MAP and HR. The CVP was lower than optimal oxygenation at T2.

Conclusions: Dynamic lung compliance-guided PEEP titration improved lung function in elderly patients undergoing lobectomy.

Keywords: Thoracic Surgery, Video-Assisted • Aged • Respiration, Artificial • Respiratory Function Tests

Corresponding Author: Wenyu Yao, e-mail: ywy600@126.com
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Background

There is no consensus on how to choose the appropriate positive end-expiratory pressure (PEEP) value during one-lung ventilation (OLV) in current research reports. Improper PEEP levels have an impact on patient physiology. If the setting level is too low to achieve the desired purpose, it cannot produce the effect of applying PEEP. If the setting level is too high, the pulmonary vascular resistance increases, venous return blood volume decreases, intrapulmonary shunt increases, and arterial oxygen partial pressure level is reduced [1]. When the PEEP is too high, the alveoli can produce excessive expansion at the end of exhalation, resulting in mechanical or biological damage to the lung tissue [2]. Therefore, determining how to individualize the optimal PEEP level according to the respiratory condition of elderly patients has gradually attracted the attention of clinicians. The methods to determine the best PEEP levels include computed tomography scanning, electrical impedance tomography, ultrasound, P-V curve method, best oxygenation titration method, and best lung compliance titration method. Each method has its advantages and disadvantages [3-5]. There are few studies on the selection of PEEP values during OLV in elderly patients and the protective effect of PEEP values titrated by different titration methods on the lungs of elderly patients. Therefore, the effect of PEEP titrated by different methods during OLV on lung protection needs to be further confirmed.

Material and Methods

Study Design and Objectives

This single-center randomized controlled study was approved by the Cangzhou Central Hospital, China (ethics approval no. 2018-024-01, Clinical Trial Registration Identifier: ChiCTR1800017835). Informed consent was obtained from the patients or their relatives. Fifty patients with video-assisted thoracoscopic unilateral lobectomy who were aged 65 to 78 years and had a body mass index of 18 to 29 kg/m² and ASA grade I to III were enrolled. The inclusion criteria were as follows: (1) without circulatory system diseases, (2) without acute or chronic pulmonary inflammation, (3) without a history of chest surgery and trauma, (4) without a history of psychosis or nervous system diseases, and (5) without serious liver or kidney dysfunction. The random number table method was used to divide the patients into 2 groups (n=20 each): the best oxygen titration group (group O) and best compliance titration group (group C).

Anesthesia Method

After the patient entered the operating room, a patient monitor (model 866066, Philips, Germany) was used to monitor the electrocardiogram, heart rate (HR), mean arterial pressure (MAP), SpO₂ bilateral bispectral index, and muscle relaxation. The venous channel was opened, and a catheter was placed through the radial artery under local anesthesia to monitor the invasive arterial blood pressure. The patient inhaled pure oxygen through the mask, and anesthesia induction was started. Midazolam 0.05 mg/kg, sufentanil 0.4 to 0.6 µg/kg, propofol 1 to 2 mg/kg, and cisatracurium 0.2 mg/kg were used to induce general anesthesia. When the train-of-four count was 0 and the post-tetanic count was ≥1, the trachea was intubated with a double lumen tube (Willy Rusch GmbH, Germany). The location of the double lumen tube was confirmed by fiberoptic bronchoscopy before and after the patient’s lateral positioning. During OLV, the non-ventilated side was opened, and the Drager anesthesia machine (Perseus A500) was connected for intermittent positive pressure ventilation. Respiratory parameters during bilateral lung ventilation were as follows: inhaled oxygen concentration of 100%, tidal volume of 8 mL/kg, predicted body weight, ventilation frequency of 12 times/min, and inspiratory respiratory ratio of 1: 1.5. The end-expiratory carbon dioxide partial pressure (ETCO₂) was adjusted between 35 and 40 mmHg (1 mmHg=0.133 kPa). To maintain the anesthesia, 1% to 2% sevoflurane was inhaled and an intravenous pump of dexmedetomidine 0.01 µg·kg⁻¹·min⁻¹, remifentanil 0.1 to 0.3 µg·kg⁻¹·min⁻¹, and cisatracurium 5 mg/h was administered. The bispectral index value was maintained between 40 and 60. The fluctuation of the intraoperative MAP should not exceed 20% of the baseline value, and the train-of-four count should be ≤2. A double-lumen central venous catheter was inserted into the right internal jugular vein to monitor the central venous pressure (CVP) and infusion. During the operation, target-guided fluid therapy, mainly crystalloid fluid, was used. When the reduction in MAP exceeded 20% before induction, ephedrine 6 mg or methoxyamine 2 mg was injected intravenously, as appropriate. Based on the patient’s response to the drug and volume status, continuous infusion of vasoactive drugs or the use of glue body fluid volume expansion was determined. HR, MAP, arterial oxygen saturation, and ETCO₂ were continuously monitored (Datexengstrom, Finland).

During OLV, the best oxygenation method titration group (group O) had a tidal volume of 6 mL/kg, respiratory rate of 14 to 16 breaths/min, PEEP increase from 3 cmH₂O, and increase of 1 cmH₂O every 4 min until the arterial partial pressure of oxygen (PaO₂) was the highest. The best method of lung compliance (group C) was a tidal volume of 6 mL/kg, respiratory rate of 14 to 16 breaths/min, PEEP of 3 cmH₂O, and 1 cmH₂O every 4 min until the best lung compliance was achieved.

Data Collection and Measurement

MAP, HR, and CVP were recorded in both groups at the time of bilateral ventilation (T1), 4 min after the completion of OLV
Table 1. Comparison of general conditions and intraoperative conditions of patients (n=25).

| Group             | Group O                  | Group C                  | P       |
|-------------------|--------------------------|--------------------------|---------|
| Age (years)       | 68.80±3.71               | 68.72±3.66               | 0.661   |
| Sex (male/female) | 16/9                     | 14/11                    |         |
| Weight (kg)       | 70.58±7.95               | 68.89±4.87               | 0.282   |
| PreoperativePaO₂ (mmHg) | 70.66±13.51           | 75.45±15.33              | 0.544   |
| PreoperativePaCO₂ (mmHg) | 40.36±3.58            | 45.23±8.51               | 0.367   |
| Preoperative FEV1 (% of predicted value) | 80.91±13.63        | 78.91±10.54              | 0.763   |
| Preoperative FVC (% of predicted value) | 90.61±18.15       | 90.61±18.15              | 0.672   |
| Operation duration (min) | 254.0±38.2           | 253.5±45.3               | 0.684   |
| One lung ventilation time (min) | 200.3±33.5          | 210.2±27.6               | 0.561   |
| Intraoperative blood loss (mL) | 132.0±51.4         | 146.3±69.3               | 0.472   |
| Intraoperative fluid volume (mL) | 1615.4±134.4       | 1659.4±132.7             | 0.403   |

There was no significant difference between the 2 groups in the relevant indicators of the preoperative general and intraoperative conditions (P>0.05).

Results

There was no significant difference between the 2 groups in the relevant indicators of the preoperative general and intraoperative conditions (P>0.05; Table 1).

In the comparison of circulation indices, CVP in group O was significantly higher than that in group C at T2 (9.36±1.66 cmH₂O vs 5.64±1.19 cmH₂O, P<0.05). Compared with T1, the CVP in the 2 groups increased significantly at T2 (P<0.05). The MAP decreased significantly at T2 compared with at T1 in group O (71.96±3.19 mmHg vs 86.00±2.66 mmHg, P<0.05) and group C (69.88±3.89 mmHg vs 84.68±3.51 mmHg, P<0.05; Table 2). The results of respiratory mechanics showed that at T2, the driving pressure value of group O (12.88±2.47 cmH₂O) was higher than that of group C (10.80±1.73 cmH₂O) (P<0.01), and the PIP and PEEP values of group O were higher than that of group C (24.12±2.76 cmH₂O vs 18.48±1.05 cmH₂O and 11.24±1.71 cmH₂O vs 7.68±1.28 cmH₂O, respectively). The dynamic lung compliance value in group C was higher than that in group O (79.67±11.86 mL/cmH₂O vs 52.48±5.68 mL/cmH₂O; Table 3). Regarding the gas exchange indices, at T2, PaO₂ in group O was significantly higher than that in group C (202.28±59.66 mmHg vs 112.23±87.4 mmHg). Compared with T1, the PaO₂ at T2 and T3 decreased significantly in both groups. The value of VD/VT in group C was significantly higher than that in group O at T2 and T3 (0.09±0.03 vs 0.07±0.02 and 0.13±0.04 vs 0.11±0.04, respectively). The VD/VT of the 2 groups were significantly higher at T3 than at T1 (Table 4).

Discussion

We studied the PEEP levels of the 2 titration methods in elderly patients undergoing thoracotomy and compared the effects of the methods on respiration and circulation. The PEEP value of optimal oxygenation titration (11.24±1.71 cmH₂O) was...
Table 2. Comparison of 2 groups of circulation indexes (n=25).

| Index        | Group       | T1        | T2        | T3        |
|--------------|-------------|-----------|-----------|-----------|
| MAP (mmHg)   | Group O     | 86.00±2.66| 71.96±3.19| 82.08±5.28|
|              | Group C     | 84.68±3.51| 69.88±3.89| 82.44±3.64|
| HR (times/min)| Group O    | 75.28±4.47| 73.12±5.24| 76.48±4.54|
|              | Group C     | 77.16±4.57| 72.80±5.52| 78.40±3.12|
| CVP (cmH₂O)  | Group O     | 4.68±1.41 | 9.36±1.66 | 4.88±0.73 |
|              | Group C     | 4.28±1.02 | 5.64±1.19 | 4.60±0.76 |

Compared with group O, * P<0.05. Compared with T1, * P<0.05. In the comparison of circulation indices, central venous pressure (CVP) in group O was significantly higher than that in group C at 4 min after the completion of OLV titration (T2) (9.36±1.66 cmH₂O vs 5.64±1.19 cmH₂O, P<0.05). Compared with time of bilateral ventilation (T1), the CVP in the 2 groups increased significantly at T2 (P<0.05). The mean arterial pressure (MAP) decreased significantly at T2 compared with that at T1 in group O (71.96±3.19 mmHg vs 86.00±2.66 mmHg, P<0.05) and group C (69.88±3.89 mmHg vs 84.68±3.51 mmHg, P<0.05).

Table 3. Comparison of respiratory mechanics indexes at 4 min after the completion of the one-lung ventilation titration (T2) time point.

| Group        | DP (cmH₂O) | PIP (cmH₂O) | PEEP (cmH₂O) | Cdyn (mL/cmH₂O) |
|--------------|------------|-------------|--------------|----------------|
| Group O      | 12.88±2.47 | 24.12±2.76  | 11.24±1.71   | 52.48±5.68     |
| Group C      | 10.80±1.73 | 18.48±1.05  | 7.68±1.28    | 79.67±11.86    |
| P value      | 0.01       | 0.01        | 0.01         | 0.01           |

The results of respiratory mechanics showed that at T2, the driving pressure (DP) value of group O (12.88±2.47 cmH₂O) was higher than that of group C (10.80±1.73 cmH₂O) (P=0.01), and the peak airway pressure (PIP) and positive end-expiratory pressure (PEEP) values of group O were higher than that of group C (24.12±2.76 cmH₂O vs 18.48±1.05 cmH₂O and 11.24±1.71 cmH₂O vs 7.68±1.28 cmH₂O, respectively). The dynamic lung compliance (Cdyn) value in group C was higher than that in group O (79.67±11.86 mL/cmH₂O vs 52.48±5.68 mL/cmH₂O).

Table 4. Comparison of gas exchange indexes.

| Index       | Group      | T1        | T2        | T3        |
|-------------|------------|-----------|-----------|-----------|
| PaO₂ (mmHg) | Group O    | 270.56±32.03| 202.28±59.66| 238.18±36.57|
|             | Group C    | 261.91±35.54| 112.23±8.74| 225.42±41.31|
| PaCO₂ (mmHg)| Group O    | 40.85±2.08 | 42.2±1.59 | 42.58±1.56 |
|             | Group C    | 40.72±2.41 | 42.26±1.71| 42.79±1.40 |
| VD/VT       | Group O    | 0.07±0.03  | 0.07±0.02 | 0.11±0.04  |
|             | Group C    | 0.08±0.04  | 0.08±0.03 | 0.12±0.04  |

Compared with group O, * P<0.05. Compared with T1, * P<0.05. Regarding the gas exchange indices, at the completion of one-lung ventilation titration (T2), PaO₂ in group O was significantly higher than that in group C (202.28±59.66 mmHg vs 112.23±8.74 mmHg). Compared with time of bilateral ventilation (T1), T2, and 10 min after the resumption of bilateral ventilation after intubation (T3) decreased significantly in both groups. The value of void volume/tidal volume ratio (VD/VT) in group C was significantly higher than that in group O at T2 and T3 (0.09±0.03 vs 0.07±0.02 and 0.13±0.04 vs 0.11±0.04, respectively). Compared with at T1, the VD/VT of the 2 groups were significantly higher at T3.
significantly higher than that of optimal lung compliance titration (7.68±1.28 cmH$_2$O; P<0.05), which is consistent with results reported by Chen et al [6]. Our study differs from Chen's in that the CVP increased rather than decreased when titrated with the best oxygenation method, which may be related to the fact that our research participants were elderly patients, who are more likely to experience fluctuations in circulation.

Some studies [7] used dynamic lung compliance titration to measure the PEEP value, starting from 20 cmH$_2$O and gradually reducing the titration. However, considering that 20 cmH$_2$O in elderly patients with OLV can cause hemodynamic changes, an excessively high PEEP can lead to decreased blood pressure [8]. Therefore, in the present study, we adopted the method of gradually increasing the PEEP value after pulmonary dilation, starting from 3 cmH$_2$O. However, due to the limitations of the experimental conditions and the lack of postoperative follow-up, no differences in postoperative pulmonary complications related to patients’ surgical conditions were observed.

Peak airway pressure and driving pressure are respiratory mechanics indices related to ventilation in elderly patients during anesthesia in surgery [9]. Peak airway pressure is the maximum airway pressure reached by ventilation during inhalation, and the value can indicate the degree of alveolar dilation [10]. Driving pressure is the result of tidal volume corrected by dynamic lung compliance, which may indicate alveolar injury caused by the change in respiratory phase during ventilation. An increase in the driving pressure can increase the risk of postoperative respiratory complications [11]. The results of this study showed that compared with group O, the driving pressure decreased, PIP decreased, and dynamic lung compliance increased in group C 10 min after the completion of OLV titration, indicating that PEEP titration guided by dynamic lung compliance can have a positive effect on the respiratory mechanics of elderly patients during anesthesia in surgery.

Owing to anatomical and mechanical lung changes that occur with age, maintaining normal PaCO$_2$ levels depends on the increase in the total minutes of ventilation, that is, the sum of alveolar ventilation and dead space ventilation (VD) [12]. The VD/VT index can show alveolar closure and ventilation and it can reflect the ratio of non-oxygenated gas in the lung to total ventilation [13]. During OLV, we should avoid the increase of VD/VT, try to increase arterial oxygen partial pressure, improve oxygenation, and reduce cardiovascular complications. An increase in VD/VT often indicates poor prognosis [14]. However, the abnormal increase of VD/VT indicates the imbalance of pulmonary ventilation and blood flow, which becomes the main mechanism of respiratory failure [15]. Therefore, VD/VT is helpful to judge the prognosis of acute respiratory distress. In addition, the level of VD/VT is closely related to the formation of pulmonary and microvascular thrombosis. Spece et al [16] also believe that the increase of VD/VT level is an independent high risk factor of pulmonary embolism, increasing the risk of death.

The results of the present study showed that there was no difference between the 2 groups in terms of the change in VD/VT. However, VD/VT increased significantly after OLV.

Conclusions

In summary, the PEEP value titrated by the best compliance method was lower than that titrated by the best oxygenation method. The peak was lower and the dynamic lung compliance was higher but had no effect on MAP and HR, and the CVP was also lower than that titrated by the best oxygenation method. Therefore, dynamic lung compliance-guided PEEP titration can improve lung function in elderly patients undergoing lobectomies.

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