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Lung protection effect of EIT-based individualized protective ventilation strategy in patients with partial pulmonary resection

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Abstract. – OBJECTIVE: This study aimed to evaluate the lung protection effect of an individualized protective ventilation strategy based on lung impedance tomography (EIT) technology in patients with partial pulmonary resection.

PATIENTS AND METHODS: Eighty patients of any gender, American Society of Anesthesiologists (ASA) classification I-II, age 30-64 years and body mass index (BMI) 18-28 kg/m^2 who underwent elective thoracoscopic partial lung resection were selected and divided into 2 groups (n=40) using the random number table method: [positive end-expiratory pressure (PEEP) by electrical impedance tomography (EIT)] $PEEP_{EIT}$ group (experimental group) and control group. The $PEEP_{EIT}$ group used volume-controlled ventilation after one-lung ventilation, setting a tidal volume of 6 ml/kg and titrating the optimal PEEP value by EIT. Group C used volume-controlled ventilation after one-lung ventilation, setting a tidal volume of 6 ml/kg and a PEEP of 5 cm H_2O. Clinical data were collected and recorded at 5 min after double lung ventilation (T0), single lung ventilation, 30 min after PEEP setting (T1), 60 min after PEEP setting (T2), the end of surgery, 10 min after resumption of double lung ventilation (T3) and 10 min after removal of the tracheal tube (T4), and serum surface active substance-associated protein-A (SP-A) concentrations were measured at T0, T3 and 1 d after surgery (T5).

RESULTS: PEEP values were higher in the $PEEP_{EIT}$ group than in the control group at T1 and T2 (p-value <0.05); oxygenation index (OI) was higher in the $PEEP_{EIT}$ group compared to the control group at T2 and T3 (p-value <0.05); pulmonary dynamic compliance (Cdyn) was higher in the $PEEP_{EIT}$ group compared to the control group at T1 and T2 (p-value <0.05); intrapulmonary shunt rate (Qs/Qt) was lower in the $PEEP_{EIT}$ group compared to the control group at T1, T2 and at T3, the intrapulmonary shunt rate (Qs/Qt) was reduced in the $PEEP_{EIT}$ group compared to group C (p-value <0.05); at T5, the SP-A protein was reduced in the $PEEP_{EIT}$ group compared to group C. There was no statistically significant difference in the incidence of postoperative pulmonary complications between the two groups (p-value >0.05).

CONCLUSIONS: The EIT-guided individualized protective ventilation strategy has a lung-protective effect in patients undergoing thoracoscopic partial lung resection.

Key Words:
Lung resection, Single-lung ventilation, Lung impedance tomography, Individualization, Protective ventilation, Lung protection.

Introduction

With the development of thoracic surgery and the popularity of thoracoscopic techniques, the use of one-lung ventilation in anesthesia has become increasingly widespread and even indispensable[1,2]. Patients undergoing thoracic surgery, especially those requiring one-lung ventilation among them, have a high incidence of postoperative lung injury and pulmonary complications, which seriously affect their prognosis[3,4]. And intraoperative ventilation management may be a key factor affecting postoperative lung injury and pulmonary complications[5,6]. Therefore, the selection of an appropriate intraoperative protective ventilation strategy is of great significance for patients undergoing partial lung resection with single-lung ventilation.

Positive end-expiratory pressure (PEEP) is effective in avoiding VILI and has some lung-protective effects in thoracoscopic surgery[7,8]. However, setting a standardized fixed PEEP value is not suitable for every patient due to the existence of individual differences[9]. On the one hand, too

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high PEEP can overinflate the alveoli and cause lung injury while increasing the resistance of the pulmonary circulation, so that more blood flows to the non-ventilated side, further aggravating intrapulmonary shunts and reducing oxygenation[101]. It has now been established that small tidal volumes combined with high PEEP ventilation can lead to increased pneumonia and ventilator-related lung injury[11]. On the other hand, low PEEP prevents adequate alveolar opening and oxygenation, increasing the chance of complications such as postoperative pulmonary atelectasis[13].

Lung electrical impedance tomography (EIT) technology is non-invasive, radiation-free and presents dynamic images in real-time to monitor ventilation in the lung area and provide a visual reference for individualized ventilation[14]. Recent studies[6,7] have shown that titration of optimal PEEP values by EIT reduces the incidence of postoperative pulmonary complications in patients undergoing abdominal surgery. However, it remains to be explored whether an individualized protective ventilation strategy based on setting PEEP values by EIT can reduce lung injury and postoperative pulmonary complications in patients undergoing partial lung resection.

The aim of this study is to investigate whether setting individualized PEEP values based on EIT improves postoperative lung injury and pulmonary complications in patients undergoing partial lung resection compared to setting fixed PEEP values and to provide a clinical reference.

Patients and Methods

General Information

Eighty patients were selected for thoracoscopic partial lobectomy of the lung, of either sex, aged 30-64 years, with a body mass index of 18-28 kg/m^2 and an American Society of Anesthesiologists (ASA) classification of grade I-II. The random number table method was used to divide into 2 groups (n=40): the PEEP$_{EIT}$ group (experimental group) and the control group. The study was approved by the Ethics Committee of Xiangcheng People's Hospital, Suzhou, China, ethics number: (2020), and informed consent was signed by the patients and their families.

Exclusion Criteria

(1) Preoperative pulmonary infection, pulmonary alveoli, pulmonary atelectasis, pneumothorax, chronic obstructive pulmonary disease, and other severe respiratory diseases, pacemaker fitted.

(2) Implantable pumps such as automatic implantable defibrillators and severe cardiovascular diseases unable and tolerant to PEEP titration.

Methods

In both groups, patients were fasted for 8-12 h. Invasive arterial pressure (ABP) was monitored by right internal deep jugular vein cannulation and radial artery puncture during preparation for anesthesia. Dräger PulmoVista® 500 (Drägerwerk AG & Co., Lübeck, Germany) pulmonary impedance tomograph was tied to the 5th intercostal level. Midazolam 0.02-0.04 mg/kg, etomidate 0.15-0.3 mg/kg, sufentanil 0.5-1.0 ug/kg and rocuronium 0.6 mg/kg were administered for induction of general anesthesia.

Double-lumen tracheal tube selection: 35F for females, 37F for males; select the double-lumen tube on the opposite side of the operation. After the double-lumen tube is placed, it is positioned *via* fibreoptic bronchoscopy, and the positioning is checked again after lateral recumbency to ensure accurate positioning of the double-lumen tube before connecting to the anesthetic machine for volume-controlled ventilation, starting with double-lung ventilation, respiratory parameters set to VT 8 ml/kg, PEEP value set to 5FiO$_2$ 60%, fresh oxygen flow 2L/min, respiratory rate 12-16 breaths/min, inspiration to expiration ratio 1:2, maintain PETCO 230-40 mmHg (1 mmHg=0.133 KPa). For single lung ventilation, VT was adjusted to 6 ml/kg, PEEP$_{EIT}$ group was titrated by EIT and PEEP value was set individually, PEEP value was set to 6 cm H_2O in group C. The rest of the parameters remained unchanged. The protocol for studying the individual PEEP is shown in Figure 1.

Propofol (Batch No. 5C201102, Guangdong Jia Bo Pharmaceutical Co., Ltd. China), remifentanil (Approved No. 00A12011, Yichang Renfu Pharmaceutical Liquid Co., Ltd. China) and sevoflurane (Approved No. 20112731, Shanghai Hengrui Pharmaceutical Co., Ltd. China) were administered to maintain general anesthesia and cis-atracurium (Approved No. A11201209, ShangPharma Dongying Pharmaceutical Liquid Co., Ltd. China) was given as needed.

The bispectral index (BIS) value of 40-60 was maintained intraoperatively, the mean arterial pressure (MAP) fluctuation was kept within 20% of the basal value, and vasoactive drugs such as methotrexate or ephedrine were administered as required. When the chest was closed after the chest drain was placed, lung ventilation was performed with manual control (24-30 cm H_2O), followed by

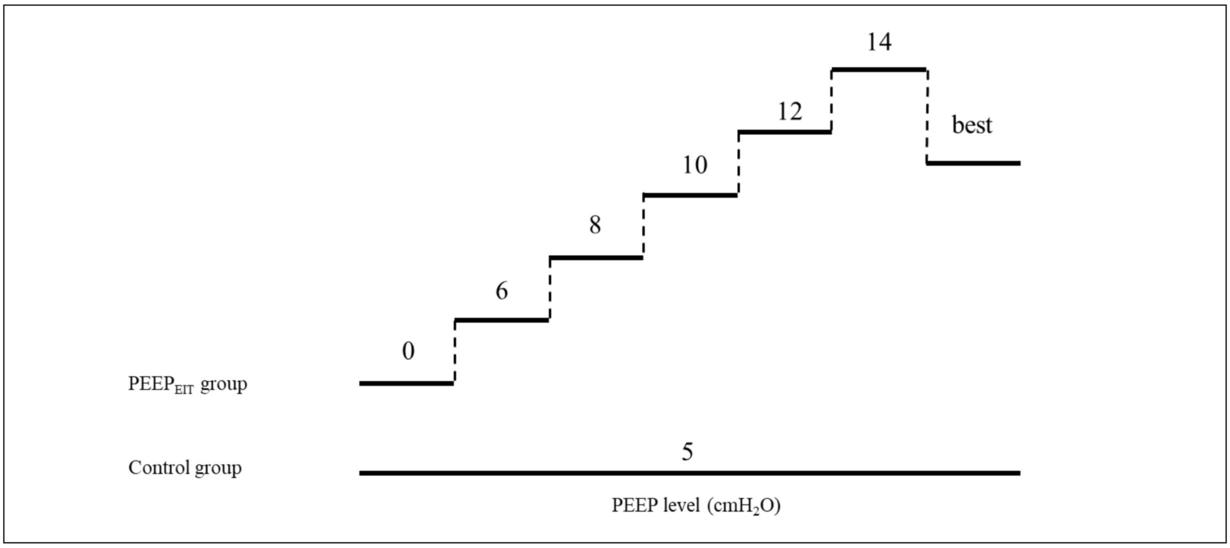

Figure 1. Protocol of study the individual PEEP.

volume-controlled ventilation with the same parameters as preoperative double-lung ventilation.

At the end of the procedure, they were taken to the awakening room. All patients were not changed and were ventilated with a double-lumen tracheal tube back to the depth of normal tracheal tube insertion followed by double-lung volume control ventilation. Neostigmine 1 mg in combination with atropine 0.5 mg was given to antagonize inotropy after the patient was awake.

Observation Indicators

(1) Steward score >4 is extubated, and after extubation, oxygen is administered by face mask at a flow rate of 5 L/min and the patient is admitted to the ward after respiratory circulation is stabilized.

(2) EIT titration PEEP method: For the EIT group, the appropriate EIT electrode belt is selected according to the patient's bust circumference, placed between the fifth intercostal, and a reference electrode is placed on the patient's

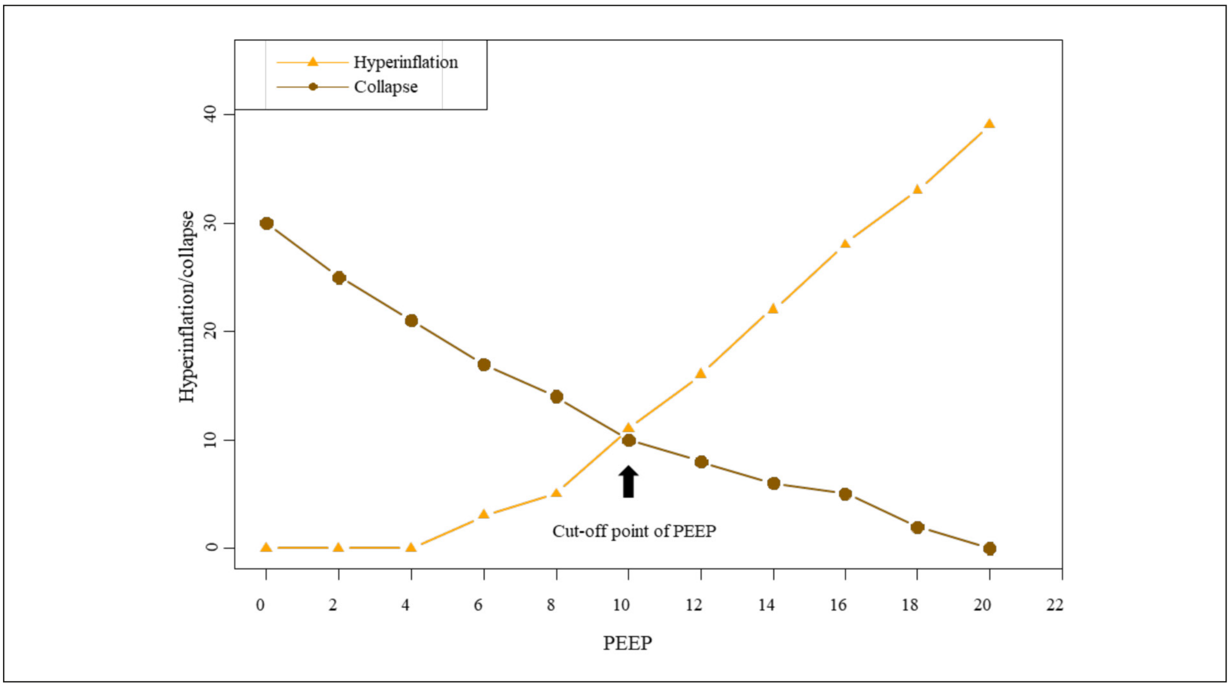

Figure 2. Setting optimal PEEP based on EIT.

abdomen. The electrode strip was then connected to the EIT screen for visualization. After dividing the range of lung ventilation from ventral to dorsal to 4 parts, EIT quantifiably shows the percentage of total tidal volume from the 4 regions of interest (ROI) of the lungs. After recruitment maneuvers using PEEP increments, PEEP was upregulated from 0 cmH_2O-3 cmH_2O -5 cmH_2O -8 cmH_2O -10 cmH_2O -12 cmH_2O -14 cmH_2O -16 cmH_2O at 30-minute intervals between each adjustment, recording the percentage of total ventilation of each part at different PEEPs and the driving pressure and tidal volume (VT). The compliance of the dorsal and ventral regions is calculated separately, and the compliance calculation formula is shown in Equation (1). Depict the two parts of the compliance curve, and the intersection point is the best PEEP.

Crs ROI (ml/cmH_2O) = (VT ROI(%) × VT(ml))/(Driving pressure(cmH_2O))………… Equation (1)

After storage as an EIT file the PEEP titration was analyzed by means of its data analysis software PV500 PC software (Dräger, Germany) for the optimal PEEP values at the equilibrium point of lung collapse and lung hyperinflation. The cut-off point of optimal PEEP guided by EIT is shown in Figure 2.

(3) Baseline demographics were recorded: gender, age, BMI, ASA classification, history of hypertension, history of diabetes, history of smoking, lung function, duration of surgery, volume of fluids administered, mode of surgery (wedge/lobotomy) and number of vasoactive drugs used.

(4) Clinical data were collected and recorded at 5 min after double-lung ventilation (T0), at 30 min after single-lung ventilation with PEEP set (T1), at 30 min after PEEP set (T2), at the end of the procedure and 10 min after the resumption of double-lung ventilation (T3), and at 10 min after removal of the tracheal tube (T4). These include (i) dynamic lung compliance (Cdyn), peak airway pressure (P_{peak}), PEEP values at T0, T1, T2, and T3; (ii) MAP and oxygenation index (OI) and intrapulmonary shunt rate (Qs/Qt) at T0, T1, T2, T3 and T4.

(5) Serum lung surface active substance-associated protein-A (SP-A) concentrations were measured by enzyme-linked immunoassay at T0, T3, and 1d postoperatively, and the occurrence of pulmonary complications such as respiratory failure, pulmonary atelectasis, and pulmonary infections were recorded during the postoperative hospital stay.

Statistical Analysis

SPSS 25.0 software (IBM Corp., Armonk, NY, USA) was used for analysis. Normally distributed measures were expressed as mean±standard deviation ($\bar{x}$±s), *t*-test for two independent samples was used for comparison between 2 groups, and χ^2 test was used for comparison of count data. The *p*-value <0.05 was considered a statistically significant difference.

Results

General Information

The differences in gender, age, BMI, ASA classification, history of hypertension, history of diabetes mellitus, smoking history, lung function, duration of surgery, volume of infusion, surgical approach (wedge/lobotomy) and number of vasoactive drugs used between the two groups were not statistically significant (*p*-value >0.05), as shown in Table I.

Comparison of MAP, PEEP, OI, Cdyn, P_{peak} and Qs/Qt between the C and $PEEP_{EIT}$ Groups at Different Time Points

At T0, T1, T2, T3, and T4, there was no statistically significant difference in MAP between the two groups (*p*-value >0.05); at T1 and T2, the $PEEP_{EIT}$ group set a significantly higher PEEP value than the control group (*p*-value <0.05); increased oxygenation index (OI) in the $PEEP_{EIT}$ group compared to group C at T1, T2, and T3 (*p*-value <0.05); increased pulmonary dynamic compliance (Cdyn) in the $PEEP_{EIT}$ group compared to the control group at T1 and T2 (*p*-value <0.05); increased peak airway pressure (P_{peak}) in the $PEEP_{EIT}$ group compared to group C at T1 and T2 (*p*-value <0.05); At T1, T2 and T3, the intrapulmonary shunt rate (Qs/Qt) was reduced in the $PEEP_{EIT}$ group compared to the control group (*p*-value <0.05), as shown in Table II.

Comparison of Serum Surfactant Protein A Levels Between the C and $PEEP_{EIT}$ Groups at Different Time Points

At T5, SP-A protein was reduced in the $PEEP_{EIT}$ group compared to group C (*p*-value <0.05); at T0 and T3, there was no statistically significant difference between the two groups (*p*-value >0.05), see Table III.

Table I. Comparison of baseline demographics and general conditions during operation between the C and $PEEP_{EIT}$ groups.

Characteristic	Control group (n=40)	$PEEP_{EIT}$ group (n=40)	*p*-value
Sex (Male/Female)	23/17	19/21	0.370
Age (years)	49.4±9.5	50.3±9.0	0.682
BMI ($kg{\cdot}m^{-2}$)	23.1±3.2	24.3±3.5	0.119
ASA grade (I/II)	26/14	21/19	0.256
Hypertension (cases, %)	10 (25%)	14 (35%)	0.329
Diabetes (cases, %)	13 (32.5%)	8 (20%)	0.204
Smoking (cases, %)	14 (35%)	11 (27.5%)	0.469
FEV1/FVC	88.0±4.4	87.3±4.1	0.433
Operation time (min)	79.9±20.6	72.9±23.3	0.158
Transfusion volume (cases, %)	3 (7.5%)	5 (12.5%)	0.709
Procedure (Wedge/lobectomy)	32/8	29/11	0.431
Vasoactive drugs used (cases, %)	6 (15%)	12 (30%)	0.108

BMI: Body mass index; ASA: American Society of Anesthesiologists; FEV1/FVC: Forced expiratory volume 1/ forced vital capacity; $PEEP_{EIT}$: positive end-expiratory pressure (PEEP) by electrical impedance tomography (EIT).

Table II. Comparison of MAP, PEEP, OI, Cdyn, P_{peak} and Qs/Qt between the C and $PEEP_{EIT}$ groups at different time points.

Parameters	Group	T0	T1	T2	T3	T4
MAP (mmHg)	Control group	73.6±8.1	80.6±9.4	74.9±8.9	72.1±7.4	77.0±10.5
	$PEEP_{EIT}$ group	75.4±8.8	78.9±10.8	76.9±10.2	71.4±8.5	78.3±11.0
PEEP (cmH_2O)	Control group	-	5	5	-	-
	$PEEP_{EIT}$ group	-	10.6±1.9	10.6±1.9	-	-
OI mmHg	Control group	458.2±72.7	240.1±55.0	276.9±64.2	411.7±69.6	394.6±71.0
	$PEEP_{EIT}$ group	464.3±63.6	285.2±67.9	331.6±73.9	448.2±80.1	438.0±78.4
Cdyn (cmH_2O)	Control group	25.6±5.2	15.4±4.6	16.1±5.3	26.0±5.5	-
	$PEEP_{EIT}$ group	24.3±4.7	18.9±4.8	19.6±5.0	25.2±5.0	-
P_{peak} (cmH_2O)	Control group	19.6±3.6	25.2±4.0	25.4±3.7	19.6±3.3	-
	$PEEP_{EIT}$ group	18.9±3.4	27.2±2.9	27.3±2.9	18.8±2.9	-
Qs/Qt	Control group	10.4±3.3	23.0±5.2	22.2±4.0	9.7±3.2	9.4±3.0
	$PEEP_{EIT}$ group	9.3±3.4	19.4±3.8	19.1±3.4	10.9±3.6	8.8±3.5

MAP: mean arterial pressure; PEEP: positive end-expiratory pressure; $PEEP_{EIT}$: positive end-expiratory pressure (PEEP) by electrical impedance tomography (EIT); Cdyn: pulmonary dynamic compliance; Qs/Qt: intrapulmonary shunt rate.

Comparison of Lung Complications and Days of Hospital Stay Between the C and $PEEP_{EIT}$ Groups

There was no statistically significant difference in the incidence of postoperative pulmonary complications between the two groups (*p*-value >0.05) and no statistically significant difference in the number of days in hospital between the two groups (*p*-value >0.05), see Table IV.

Discussion

Studies[8,15] have shown that pulmonary protective ventilation (small tidal volume + appropriate PEEP + alveolar resuscitation) can increase lung compliance, improve oxygen partial pressure and reduce postoperative lung injury and pulmonary complications in patients undergoing thoracic surgery. However, due to the existence of individual differences, the pathophysiology of the lung changes and responds differently in different patients during one-lung ventilation, and setting a standardized fixed PEEP value is difficult to adapt to each patient. Therefore, in this study, the use of EIT-titrated individualized PEEP was compared with a protective ventilation strategy using fixed PEEP (5 cm H_2O) during single-lung ventilation in patients undergoing thoracoscopic surgery. The results of this study showed that a protective ventilation strategy using EIT-titrated individualized PEEP during one-lung ventilation helped to improve their oxygenation index and dynamic lung compliance, reduced intrapulmonary shunts but increased PEEP values and peak airway pressures; reduced postoperative lung injury but failed to reduce postoperative pulmonary complications and hospital days.

Table III. Comparison of serum surfactant protein A levels between the C and $PEEP_{EIT}$ groups at different time points [ng/L, ($\bar{x}$±s)].

Group	T0	T3	T5
Control group	33.1±3.5	38.6±5.2	54.8±5.2
$PEEP_{EIT}$ group	31.8±3.9	37.1±4.6	48.6±6.8[a]
p-value	0.107	0.177	0.000

Compared with control group, $p^a < 0.05$.

Table IV. Comparison of lung complications and days of hospital stay between the C and $PEEP_{EIT}$ groups.

Group	Lung complications (cases, %)	Hospital stays (days)
Control group	8	7.5±1.5
$PEEP_{EIT}$ group	3	7.2±1.2
p-value	0.105	0.370

Michelet et al[16] showed that the intraoperative oxygenation index was increased with a lower PEEP setting (4-5 cm H_2O) and decreased with a higher PEEP setting (8-10 cm H_2O) compared with a lower PEEP setting (4-5 cm H_2O) in patients on single-lung ventilation. The results of this study showed that the PEEP value was significantly higher in patients with EIT-guided individualized PEEP compared to those with fixed PEEP (5 cm H_2O) (9.1±2.3 *vs.* 5 cm H_2O, $p<0.05$), and the oxygenation index was significantly higher, showing the opposite effect of ventilation compared to the previous study. The possible reasons for this are that in the previous study[17], PEEP values were increased but individualized PEEP was not used, which, due to the existence of individual differences, allowed some patients with single-lung ventilation set at higher PEEP values to overinflate the alveoli, causing lung injury, and at the same time increased the resistance to the pulmonary circulation, so that more blood flow was directed to the non-ventilated side, further aggravating intrapulmonary shunts and reducing oxygenation. In contrast, in the present study, EIT-titrated individualized PEEP, as a balance between lung collapse and hyperinflation, is more conducive to ensuring alveolar ventilation with good ventilation, while avoiding excessive PEEP causing lung injury and exacerbation of intrapulmonary shunts[17]. The results of a study by Pereira et al[6] in patients undergoing laparoscopic surgery showed that the optimal PEEP obtained by applying EIT can improve intraoperative oxygenation, which is consistent with our findings.

The results of this study showed that patients on EIT-guided setting of individualized protective ventilation had significantly higher PEEP, significantly higher peak airway pressure (P_{peak}) and significantly higher dynamic lung compliance compared to controls. This result is consistent with the findings of a study involving altered respiratory mechanics in elderly patients on one-lung ventilation reported by Liu et al[18]. A prior study[19] has shown that improved oxygenation with PEEP is closely related to maintaining alveolar expansion and reducing intrapulmonary shunts. However, too low a PEEP setting is ineffective in maintaining alveolar expansion, and too high a PEEP setting increases pulmonary circulatory resistance and increases intrapulmonary shunts[11]. The use of EIT-titrated individualized PEEP maintains alveolar expansion while reducing intrapulmonary shunts. The results of this study show that individualized PEEP obtained with EIT reduces the intrapulmonary shunt rate (Qs/Qt); with one-lung ventilation, Qs/Qt correlates with the trend in oxygenation index: as intrapulmonary shunt rate increases, oxygenation index decreases and vice versa, a trend that is consistent with a previous report[20] in the literature. Excessive PEEP settings can reduce the amount of blood returned to the heart and bring about dramatic fluctuations in the circulatory system[20]. In contrast, in the results of this study, there was no significant difference in MAP at each time point and no significant difference in the use of vasoactive drugs between the two groups of patients. Possible reasons for this were analyzed: firstly, although the EIT-guided individualized PEEP was higher than the set fixed PEEP value (5 cm H_2O), it did not reach the high limit for affecting the circulatory system, and it has been reported in the literature that the continuous administration of PEEP up to 20 cm H_2O has a significant inhibition of the circulatory system[21]. Secondly, no patients of advanced age were included in this study and the circulatory system was relatively stable.

In single-lung ventilation, both hypoxia and intrapulmonary shunts can cause lung injury[22,23]. The results of a study by Goto et al[24] showed that serum SP-A levels are a reliable and sensitive specific indicator of the extent of lung tissue injury. The results of this study showed that patients with individualized PEEP under EIT guidance had a higher oxygenation index at all time points and less intrapulmonary shunts compared to those with fixed PEEP (5 cm H_2O) during one-lung ventilation, and that SP-A protein was significantly lower at T5. Such results suggest that the EIT-guided setting of individualized PEEP reduces postoperative lung injury in patients on single-lung ventilation. However, there was no significant difference in the comparison of postoperative complications and hospital days between the two groups of patients. Analysis of possible reasons for this: firstly, the main aim of this study was to study lung injury, using the more sensitive serum SP-A level as the main indicator for sample size calculation. Secondly, elderly patients were not included in this study and relatively few postoperative complications occurred. Thirdly, both groups of patients in this study used lung-protective ventilation (small tidal volume + appropriate PEEP + alveolar resuscitation) strategy, which reduced the possibility of postoperative pulmonary complications. The sample size will be expanded at a later stage and include elderly patients for further in-depth studies based on EIT.

Limitations

This study has some limitations. Firstly, residual anesthetic drugs may affect respiration and cause postoperative pulmonary atelectasis[25]. We did not perform postoperative anesthetic drug residue monitoring and cannot exclude the possible effects of anesthetic drug residue on OI and postoperative pulmonary atelectasis. However, certain precautions were made in our study to avoid, as far as possible, the effect of residual anesthetic drugs on the outcome of the study. Secondly, as no elderly cases were included in this study, no serious hemodynamic alterations occurred during individualized titration of PEEP values, but the risk of hemodynamic instability during titration still needs to be guarded against. Thirdly, due to the strict inclusion and exclusion criteria used, the population of this study was relatively narrow. Respiratory diseases such as pulmonary infections, pulmonary alveoli, pulmonary atelectasis, pneumothorax, and chronic obstructive pulmonary disease were excluded from this study to prevent their interference with the test results. The group will later expand the sample size and include elderly patients for a more in-depth study of the lung-protective effects of EIT.

Conclusions

In summary, the EIT-guided individualized protective ventilation strategy has a lung-protective effect in patients undergoing thoracoscopic partial lung resection.

Ethics Approval

The study was approved by the Ethics Committee of Suzhou Xiangcheng People's Hospital, Suzhou, China, ethics number: (2020) Lun Research Approval No. (007).

Informed Consent

The informed consent was signed by the patients and their families.

Availability of Data and Materials

All data are available upon request to the corresponding author.

Conflict of Interest

The authors declare no conflict of interest.

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Authors' Contributions

J. Zha and Y.-J. Yu performed the majority of experiments; G.-R. Li and S.-C. Wang analyzed the data; S.-G. Qiao and C. Wang drew charts; H.-L. Bo designed and coordinated the research; J. Zha and Y.-J. Yu wrote the paper. All authors reviewed the manuscript. All authors have read and approved the manuscript.

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