# Effects of propofol or sevoflurane anesthesia on the perioperative inflammatory response, pulmonary function and cognitive function in patients receiving lung cancer resection

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**Abstract.** – OBJECTIVE: To investigate the effects of propofol and sevoflurane anesthesia on the inflammatory response, pulmonary function and cognitive function of patients undergoing lung cancer resection and their differences.

PATIENTS AND METHODS: 62 patients with lung cancer who underwent pulmonary lobectomy from January 2014 to January 2016 in Jining First People's Hospital were selected and randomly divided into two groups: the propofol group (n=31) and the sevoflurane group (n=31). Patients in the propofol group were treated with intravenous injection of propofol for anesthesia maintenance, whereas those in the sevoflurane group inhaled sevoflurane for anesthesia maintenance. All patients underwent surgical resection of the lobes by the same operator. Changes in the inflammatory response and pulmonary function of patients in the perioperative period were recorded before the induced anesthesia (t1), before one-lung ventilation (t2), after sternal closure by operation (t3) and at 24 h after operation (t4), respectively; the extubation time, eye opening time and response time of two groups of patients were recorded; mini-mental state examination (MMSE) was used to evaluate the changes in cognitive function in patients and detect the concentration of S100 calcium-binding protein β (S100β) in serum of patients before the induced anesthesia and at 24 h after operation, respectively.

RESULTS: The difference of partial pressure of alveolar-arterial oxygen (A-aDO$_2$), respiratory index (RI) and intra-pulmonary shunt fraction (Qs/Qt) of two groups of patients at t2 and t3 were significantly higher than those at t1 ($p<0.01$); during t2-t3, A-aDO2, RI and Qs/Qt of patients in the propofol group were significantly lower than those of patients in the sevoflurane group ($p<0.05$); the levels of interleukin-6 (IL-6) and matrix metalloproteinase-9 (MMP-9) in serum of patients after the induced anesthesia in the propofol group were significantly higher than those at t1, while the level of interleukin-10 (IL-10) was lower than that at t1 ($p<0.01$); during t2-t4, the levels of IL-6 and MMP-9 in serum of patients in the propofol group were significantly lower than those in patients in the sevoflurane group, while the level of IL-10 was significantly higher than that in patients in the sevoflurane group ($p<0.05$). The postoperative extubation time, eye opening time and response time of patients in the propofol group were significantly shorter than those of patients in the sevoflurane group ($p<0.05$). From intraoperative period to 24 h after operation, the prevalence rate of adverse reactions in patients in the propofol group was significantly lower than that in patients in the sevoflurane group ($p<0.05$); MMSE scores of two groups of patients at t4 were significantly lower than those at t1, while the concentration of S100β was significantly higher than that at t1 ($p<0.01$); at t4, the MMSE score of patients in the propofol group was significantly higher than that in the sevoflurane group, while the concentration of S100β was lower than that of patients in the sevoflurane group ($p<0.05$).

CONCLUSIONS: Compared with sevoflurane anesthesia, propofol anesthesia can significantly reduce the perioperative inflammatory response in patients receiving lung cancer resection, shorten the recovery time after operation, protect the pulmonary function of patients, improve postoperative cognitive function, and reduce the prevalence rate of intraoperative adverse reactions.

*Key Words*
    Propofol, Sevoflurane, Lung cancer, Perioperative period.

## Introduction

Lung cancer is one of the most common clinical malignant tumors, and the continuously aggravating air pollution increases the prevalence

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rate of lung cancer year by year[1,2]. Limitations of examination methods of lung cancer lead to patients being diagnosed with lung cancer in the advanced phase. Surgical resection, radiotherapy, chemotherapy, molecular targeted therapeutic drugs, etc., are main treatments for lung cancer patients, and unilateral pulmonary lobectomy is the preferred treatment with best curative effects for lung cancer patients, which is expected to eradicate lung cancer, thus significantly increasing the survival rate of patients[3]. Inflammatory responses and trauma caused during operation damage the physiological function, which often affect surgical effects and the postoperative quality of life of patients, seriously influence the prognosis of patients with lung cancer[4]. Masato et al[5] studied and found that some narcotic drugs can effectively reduce inflammatory responses caused during operation, reduce damages of operation to patients and increase the success rate of operation. Therefore, it is of great significance to select appropriate narcotic drugs during lung cancer operation. Propofol, as a powerful general anesthetic, is characterized by fast onset, rapid recovery time and less adverse reactions. It is widely used in clinical patients for preoperative sedative anesthesia[6]. Cao et al[7] found that propofol anesthesia can significantly reduce the impact of operation on the cognitive function of patients. Sevoflurane, as a new type of anesthetic, can play an anesthetic role by inhibiting N-methyl-D-aspartate (NMDA) receptors, and it provides effective anesthetic effects for elders and children[8]. However, the difference between propofol and sevoflurane anesthesia has not been studied. In this investigation, the effects of propofol and sevoflurane on the anesthesia of patients with lung cancer were evaluated by analyzing the effects of propofol and sevoflurane on the perioperative inflammatory response, pulmonary function and cognitive function.

## Patients and Methods

### Patients

A total of 62 patients with lung cancer who underwent pulmonary lobectomy from January 2014 to January 2016 in Jining First People's Hospital were selected. All the enrolled patients were diagnosed with lung cancer after the unilateral pulmonary lobectomy, and it was confirmed that there was no local and distant metastasis after operation. Besides, all of them were American Society of Anesthesiologists (ASA) I-II patients, and met the conditions of pulmonary lobectomy. Patients meeting the above conditions were randomly divided into two groups: the propofol group (n=31) and the sevoflurane group (n=31). In the propofol group, there were 20 males and 11 females at the age of (68.3±13.5) years old; in the sevoflurane group, there were 18 males and 13 females at the age of (65.5±16.2) years old. The cardiopulmonary function of the included patients was basically normal, and they had no other wasting diseases, chronic inflammation or cognitive impairment. Patients whose mini-mental state examination (MMSE) score <24 points were excluded. The above patients were treated with the same chemotherapeutics and care programs before operation, and differences in age, gender and the course of disease between two groups of patients were not statistically significant. This study was approved by the Ethics Committee of Jining First People's Hospital. All the patients signed the informed consent, and all the clinical and pathological data of them during hospitalization were retained.

### Anesthesia Process

All the patients were intramuscularly injected with midazolam at 30 min before anesthesia (Jiangsu Nhwa Pharmaceutical Co., Ltd. Xuzhou, China). After the injected volume reached 0.1 mg/kg, 3 μg/kg fentanyl was injected intravenously, and a multifunctional monitor [General Electric (GE), Boston, MA, USA] was connected for monitoring various physiological indicators of patients. Patients in the propofol group underwent the induced anesthesia with 1 mg/kg propofol (Xi'an Libang Pharmaceutical Co, Ltd. Xi'an, China), and the anesthesia was maintained at 6 mg/kg/h. Patients in the sevoflurane group received the induced anesthesia with 8% sevoflurane (Abbott, Abbott Park, IL, USA), and 2% sevoflurane was used to maintain anesthesia. After the ventilation for 3 min, the intubation was conducted in the trachea, and the anesthesia machine was connected for mechanical ventilation for patients. The infusion rate was regulated during the operation so that the patients' central venous pressure reached 5-10 cm Hg. The surgeons' heart rate and blood pressure fluctuations were controlled so that they did not exceed 20% of the base value. At 30 min before the end of the operation, the injection of muscle relaxants was stopped, and the use of anesthetics was discontinued during the suturing process. When patients could clearly

hear the instructions of the physician and responded to them and the independent respiratory rate reached 16-22 times/min, the extubation could be conducted. When the condition of patients met the departure standard of the recovery room, they could be sent back to the ward. At the end of the operation, the extubation time, eye opening time and response time of two groups of patients were recorded in detail. Extubation time: the time from stopping the use of anesthetics to opening patients' mouths for pulling out the endotracheal tube; eye opening time: the time from stopping the use of anesthetics to patients responding to the external stimuli and orders and opening their eyes; response time: the time from stopping the use of anesthetics to patients relatively clearly answering the doctor's questions.

### Monitoring of the Perioperative Pulmonary Function

The following time points were set for monitoring the pulmonary function of patients: before the induced anesthesia (t1), before one-lung ventilation (t2), after sternal closure by operation (t3) and at 24 h after operation (t4). Arterial blood was collected, and blood gas analysis was conducted using a blood gas analyzer. The difference of partial pressure of alveolar-arterial oxygen (A-aDO$_2$), respiratory index (RI) and intra-pulmonary shunt fraction (Qs/Qt) of two groups of patients were calculated so as to evaluate the pulmonary function of two groups of patients.

### Monitoring of Inflammatory Responses

During the operation, 2 mL arterial blood of each group was collected with an anticoagulant tube. The supernatant was collected at 4°C after the centrifugation for 10 min at 4000 rpm and reserved at -80°C for standby application. Interleukin-6 (IL-6), interleukin-10 (IL-10) and matrix metalloproteinase-9 (MMP-9) enzyme-linked immunosorbent assay (ELISA) kits were used, respectively, to detect the levels of the corresponding inflammatory factors in serum of patients in each group, and the operation was carried out in strict accordance with the instructions of the ELISA kit.

### Evaluation of the Cognitive Function

MMSE scale was used to evaluate the cognitive function of patients before anesthesia and at 24 h after operation, respectively. Scores of the patients were recorded in detail. The concentration of S100 calcium-binding protein β (S100β) in serum of patients in each group was measured by the ELISA kit, thus reflecting the cognitive function of each group.

### Evaluation of Adverse Reactions

The occurrence of adverse reactions during the operation in patients of each group was recorded in detail. Adverse reactions mainly included low blood pressure, bradycardia, nausea and vomiting and analgesia. The pain index of patients was evaluated by the visual analogue scale (VAS), and the analgesic condition of them was analyzed.

### Statistical Analysis

The data were expressed as mean ± standard deviation, and data process was analyzed by Statistical Product and Service Solutions 19.0 software (SPSS Inc., Armonk, NY, USA). The *t*-test was used for intergroup comparisons, and $x^2$-test was used for count data. The analysis of variance followed by Post Hoc Test (Least Significant Difference) was used for comparisons among multiple groups. *p*<0.05 represented that the difference was statistically significant.

## Results

### General Data

A total of 62 lung cancer patients were randomly divided into the propofol group and the sevoflurane group. The examinations for them were completed within 24 h after admission. Gender, age, body mass index (BMI), ejection fraction (EF) and American Society of Anesthesiologists (ASA) grade of patients in each group were recorded in detail. General data of two groups of patients are shown in Table I. Differences in gender, age, BMI, EF and ASA grade between two groups of patients were not statistically significant (*p*>0.05).

### Comparison of the Pulmonary Function Between Two Groups of Patients

A-aDO$_2$, RI and Qs/Qt of two groups of patients at t1, t2, t3 and t4 were measured, respectively. The results are shown in Figure 1: A-aDO$_2$, RI and Qs/Qt of two groups of patients at t2 and t3 were significantly higher than those at t1 (*p*<0.01), which were equivalent to those at t4; A-aDO$_2$, RI and Qs/Qt of patients in the sevoflurane group at t2 and t3 were significantly higher than those of patients in the propofol group at the corresponding time points (*p*<0.01).

**Table I.** General data of two groups of patients ($\overline{x}\pm s$).

| Group | Gender (male/female) | Age (years old) | BMI (kg/m²) | EF | ASA grade (I/II) |
|---|---|---|---|---|---|
| Propofol group | (20/11) | 68.3±13.5 | 25.2±1.9 | 0.59±0.04 | (17/14) |
| Sevoflurane group | (18/13) | 65.5±16.2 | 25.6±2.3 | 0.61±0.02 | (15/16) |
| $p$ | >0.05 | >0.05 | >0.05 | >0.05 | >0.05 |
| $t$ | 0.832 | 0.653 | 0.721 | 0.855 | 0.639 |

### Comparison of the Inflammatory Response Between Two Groups of Patients

Arterial blood of patients in each group was extracted at t1, t2, t3 and t4, respectively. The levels of IL-6, IL-10 and MMP-9 in the body of two groups of patients were measured using the ELISA kit. The results are shown in Figure 2: the levels of IL-6 and MMP-9 in two groups of patients at each time point (t2, t3 and t4) after the induced anesthesia were significantly higher than those at t1, while the level of IL-10 was lower than that at t1 ($p<0.01$). During t2-t4, compared with those in 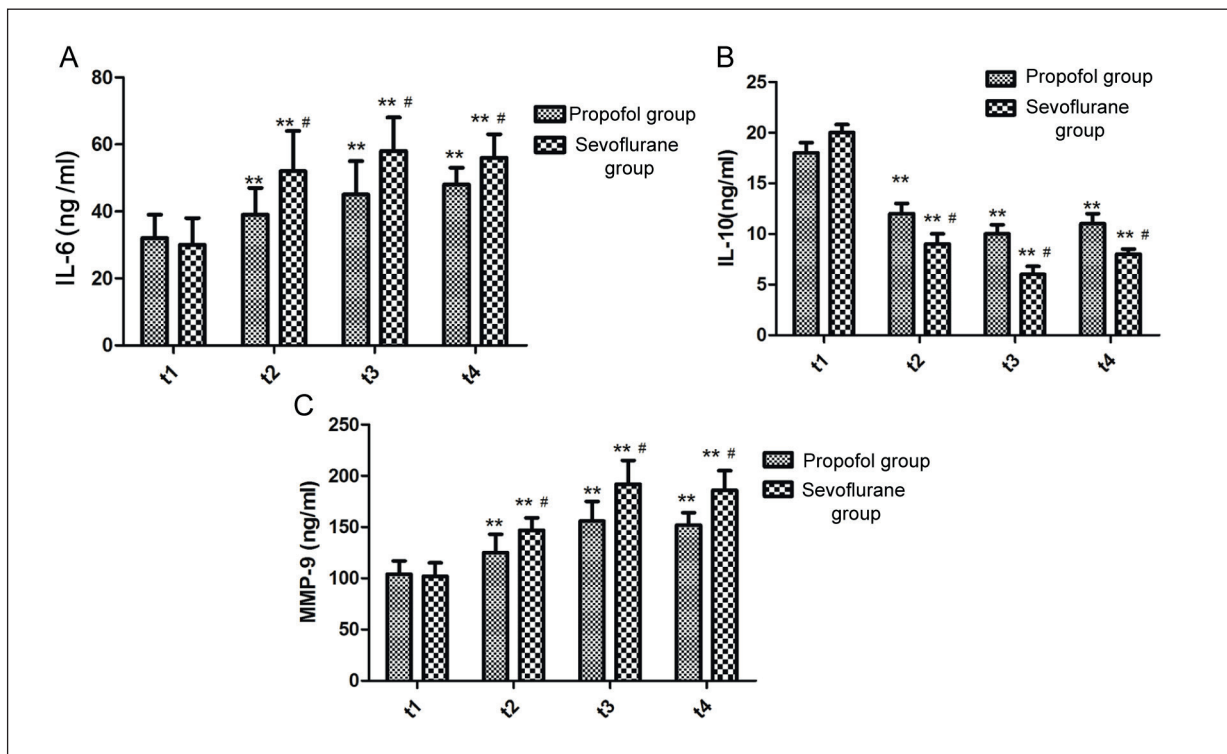patients in the propofol group, the levels of IL-6 and MMP-9 in patients in the sevoflurane group were significantly increased, while the level of IL-10 was significantly decreased ($p<0.05$).

### Comparison of Awakening Time After Operation Between Two Groups of Patients

The extubation time, eye opening time and response time of two groups of patients after operation were recorded in detail. As shown in Figure 3, the extubation time, eye opening time and response time of patients in the propofol group were significantly shorter than those of patients in the sevoflurane group, and the differences were statistically significant ($p<0.05$).
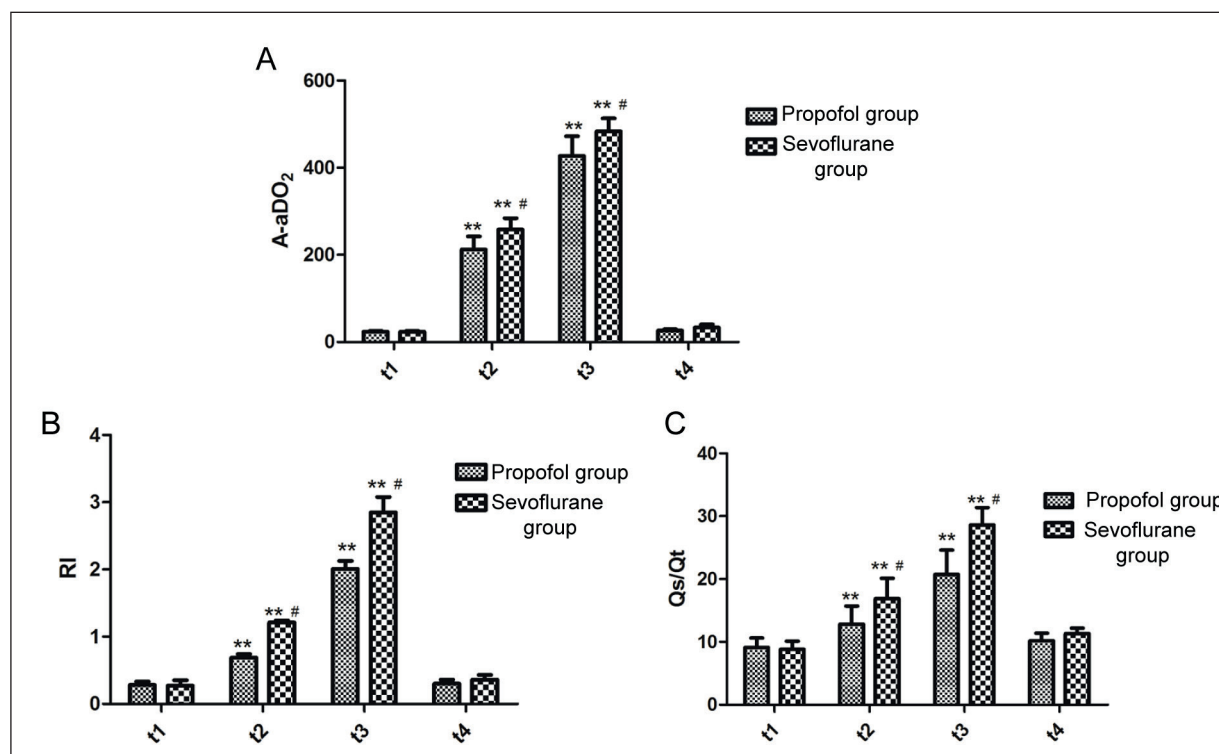


**Figure 1.** Evaluation of the pulmonary function. **A**, A-aDO$_2$; **B**, RI; **C**, Qs/Qt; A-aDO$_2$, RI and Qs/Qt of two groups of patients at t2 and t3 are significantly higher than those at t1 ($p<0.01$); A-aDO$_2$, RI and Qs/Qt of patients in the sevoflurane group at t2 and t3 are significantly higher than those of patients in the propofol group, **$p<0.01$ vs. t1, #$p<0.05$ vs. propofol group.
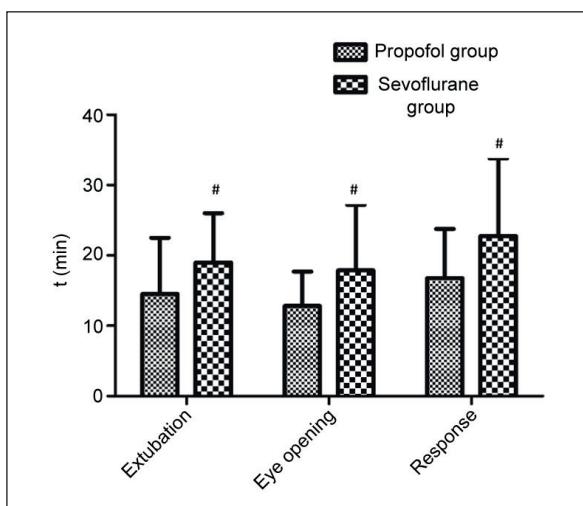
**Figure 2.** Evaluation for the inflammatory response. **A**, concentration of IL-6 in serum; **B**, concentration of IL-10 in serum; **C**, concentration of MMP-9 in serum. The levels of IL-6 and MMP-9 in two groups of patients at t2, t3 and t4 are significantly higher than those at t1, while the level of IL-10 is lower than that at t1 ($p<0.01$). The levels of IL-6 and MMP-9 in patients in the sevoflurane group are significantly lower than those in patients in the propofol group, **$p<0.01$ vs. t1, #$p<0.05$ vs. propofol group.



**Figure 3.** Evaluation of awakening time after operation. The extubation time, eye opening time and response time of patients in the propofol group are significantly shorter than those of patients in the sevoflurane group, #$p<0.05$ vs. propofol group.

## Comparison of the Prevalence Rate of Adverse Reactions Between Two Groups of Patients

Adverse reactions of two groups of patients within the period from being anesthetized to 24 h after operation were recorded in detail, whose types mainly include low blood pressure, bradycardia, nausea and vomiting and analgesia. As shown in Table II, the prevalence rate of adverse reactions in patients in the propofol group was significantly lower than that in patients in the sevoflurane group in the period from receiving operation to 24 h after operation ($p<0.01$).

## Comparisons of the Cognitive Function and the Concentration of Serum S100β After Operation Between Two Groups of Patients

MMSE scale was used to evaluate the cognitive function of two groups of patients before and at 24 h after operation, respectively, and the results are shown in Figure 4. The concentration of serum S100β in two groups of patients at t1, t2, t3 and t4 were detected using the ELISA kit, and the results are shown in Figure 5, indicating

**Table II.** Incidence rate of adverse reactions of two groups of patients.

| Group | Low blood pressure (n) | Bradycardia (n) | Nausea and vomiting (n) | Analgesia (n) | Incidence rate (%) |
|---|---|---|---|---|---|
| Propofol group | (1) | (1) | (0) | (2) | 12.9 |
| Sevoflurane group | (3) | (0) | (3) | (4) | 32.3 |
| $p$ | | | | | <0.01 |
| $t$ | | | | | 0.439 |

that the difference in the preoperative MMSE score between two groups of patients was not statistically significant ($p>0.05$), but MMSE scores of patients at 24 h after operation in the propofol group were significantly higher than those of patients in the sevoflurane group ($p<0.05$). The concentration of serum S100β in two groups of patients at t2, t3 and t4 was higher than that at t1 ($p<0.01$), and the concentration of S100β in patients in the sevoflurane group was higher than that in the propofol group during t2- t4 ($p<0.05$).

## Discussion

The prevalence rate and mortality rate of lung cancer are increasing year by year, and lung cancer has replaced liver cancer to become the most common cause of death for patients[9]. Surgical resection, radiotherapy and chemotherapy have become the most effective treatments for lung cancer, but acute lung injury (ALI) and other organ injuries caused by lung tissue resection,

seriously restrict the success of operation[10]. Chen et al[11] found that ALI/acute respiratory distress syndrome (ARDS) produced by unilateral pneumonectomy in lung cancer patients may be associated with injury produced during operation and one-lung ventilation. Hung et al[12] found that lung tissue resection often leads to tissue injury, seriously affecting the prognosis, but effective intravenous anesthetics can inhibit inflammatory responses and protect lung tissues and cells. According to Piegeler et al[13], inhibiting the aggregation of neutrophil and the release of inflammatory factors and increasing the expression level of antioxidant proteins can effectively reduce the lung injury caused by unilateral pulmonary lobectomy. It was found by Shi et al[14] that propofol anesthesia can effectively inhibit the production of inflammatory factors *in vivo* and reduce the inflammatory response caused by operation *in vivo*.

In this study, the comparisons of the effects of propofol and sevoflurane anesthesia on the perioperative inflammatory response, pulmonary function, and cognitive function in patients receiving lung cancer resection, showed that compared with sevoflurane, propofol played a more powerful
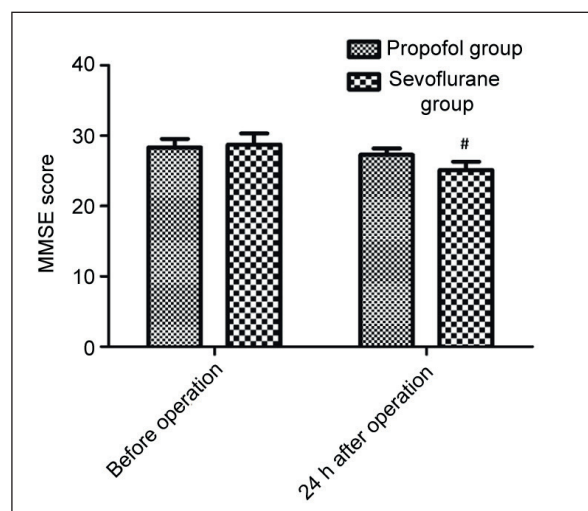


**Figure 4.** MMSE score. MMSE scores of patients at 24 h after operation in the propofol group are significantly higher than those of patients in the sevoflurane group, #$p<0.05$ vs. propofol group.
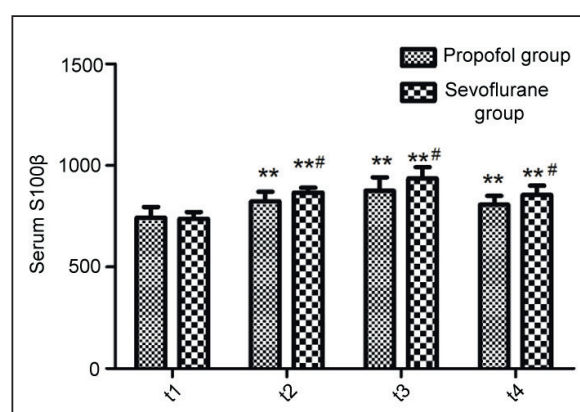


**Figure 5.** Concentration of serum S100β. The concentration of serum S100β in two groups of patients at t2, t3 and t4 is higher than that at t1, and the concentration of S100β in patients in the sevoflurane group is higher than that in the propofol group during t2- t4, #$p<0.05$ vs. propofol group.

role in inhibiting inflammatory responses, and it significantly reduced the expression level of pro-inflammatory cytokine IL-6 and increased the expression level of anti-inflammatory cytokine IL-10. Zhao et al[15] studied and found that the concentration of MMP-9 in serum of patients with pneumonia can be significantly increased. MMP-9 can damage lung tissues by increasing the activity of elastases, promoting the adhesion of neutrophils and vascular endothelium, and hydrolyzing adhesion proteins and connexins[16,17]. In this work, it was found that lung cancer resection could significantly increase the expression level of MMP-9 in serum of patients, that is, lung cancer resection could induce the occurrence of inflammatory responses in the body; the level of MMP-9 in serum of patients in the propofol group after operation was significantly decreased compared with that of patients in the sevoflurane group. The above results revealed that the inhibition effect of propofol anesthesia on inflammatory responses in the body of patients undergoing lung cancer resection was better than that of sevoflurane anesthesia. In this study, the effects of anesthetics on the pulmonary function of patients were evaluated by evaluating the effects of propofol and sevoflurane anesthesia on A-aDO$_2$, RI, and Qs/Qt of patients in the perioperative period and at 24 h after operation. The results indicated that propofol could protect the pulmonary function of patients in a more effective way than sevoflurane. Pulmonary lobectomy often leads to the phenomenon that patients can only breathe with the unilateral lung lobe, and at this time the hypoxic pulmonary vasoconstriction of non-ventilated lung is an important factor affecting arterial oxygen pressure, so A-aDO$_2$, RI and Qs/Qt can be used as indicators for evaluating the pulmonary function of patients[18]. MMSE scale is one of the important scales for evaluating the cognitive function, which has the advantages of simple operation, high effectiveness and high reliability[19]. We found that MMSE scores of patients after operation were significantly lower than those before operation. In particular, lung cancer resection damaged the cognitive function of patients to a certain degree; under the influence of surgical removal of lung tissues, lung cancer resection would decrease the ratio of patients' ventilatory capacity to blood flow to a certain degree, thus leading to the emergence of hypoxemia in patients and damaging the cognitive function of patients[20]. MMSE scores of patients in the propofol group were significantly higher than those of patients in the sevoflurane group, that is, propofol could

better protect the cognitive function than sevoflurane. Comparisons of intraoperative awakening time and the prevalence rate of adverse reactions showed that propofol was safer than sevoflurane, and was more worthy of being promoted.

## Conclusions

We showed that propofol anesthesia for lung cancer resection of patients can effectively reduce the perioperative inflammatory response, protect the pulmonary function of patients, shorten their postoperative awakening time and protect the cognitive function, These effects are significantly better than sevoflurane.

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### Conflict of Interest

The authors declared no conflict of interest.

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