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Article

Effects of Dexmedetomidine Combined with Remifentanil Anesthesia and Propofol Combined with Remifentanil Anesthesia on Perioperative Inflammatory Response and Pulmonary Function in Patients with Lung Cancer

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Abstract: To explore the effects of dexmedetomidine combined with remifentanil anesthesia and propofol combined with remifentanil anesthesia on perioperative inflammatory response and pulmonary function in patients with lung cancer. Totally 128 patients admitted to our hospital for lung cancer surgery were taken as the research object of this experiment. Among them, 67 cases were sedated with dexmedetomidine combined with remifentanil (Group A), and 61 cases were sedated with propofol combined with remifentanil (Group B). The changes of vital signs, respiratory interval (RR), blood oxygen saturation (SpO2) and blood sugar before and after sedation were recorded. The changes of inflammatory factors TNF-α, IL-6, IL-10, pulmonary function indexes FEV1, FVC, FEV1/FVC in the two groups at 24 hours after sedation were observed. Hemodynamic heart rate (HR), mean arterial pressure (MAP) and other indexes before and after sedation were observed. VAS pain score and MMSE score before and after sedation were compared between the two groups. The incidence of adverse reactions after sedation was observed in the two groups. The decrease of RR and SpO2 in Group B was more remarkable than that in Group A ($p < 0.05$). The elevation of blood sugar in Group A was lower than that in Group B ($p < 0.05$). Group A had lower levels of TNF-α and IL-6 and higher level of IL-10 ($p < 0.05$), and higher expression of FEV1, FVC and FEV1/FVC when compared with Group B ($p < 0.05$). The decrease of HR and MAP in Group B was greater than that in Group A ($p < 0.05$). VAS score was lower in Group A than Group B ($p < 0.05$), and MMSE score was higher in Group A than Group B ($p < 0.05$). The incidence of adverse reactions in Group A was lower than that in Group B, $p < 0.05$. Compared with propofol, dexmedetomidine combined with remifentanil anesthesia is more effective in improving postoperative inflammatory factors and pulmonary function of lung cancer patients, which is worthier of recommendation.

Keywords: Dexmedetomidine; propofol; remifentanil; lung cancer; inflammatory response; pulmonary function

1 Introduction

Lung cancer originates from the trachea, bronchial glands or mucosa of the lung and can spread and transfer through blood and lymphatic channels. It is a common primary malignant tumor of the lung [1]. The incidence and mortality rate of lung cancer are among the highest among all malignancies, posing a serious threat to the health and life of the population [2]. In recent years, most countries have successively

reported a remarkable increase in the incidence and mortality of lung cancer, and its incidence rate in men is higher than that in women [3]. At present, the cause of lung cancer is not fully understood [4]. Numerous data suggest that long-term smoking is bound up with the occurrence of lung cancer. Occupational and environmental contact, ionizing radiation, chronic lung infection, genetic and other factors, and air pollution will also increase the incidence rate [5]. Currently, the first clinical treatment for lung cancer is surgical resection, but most patients generally suffer from different degrees of wound pain after surgery, which leads to difficulty in expectoration and cough, and causes serious impact on the lungs [6]. Painful irritation, however, will gives rise to a large number of inflammatory factors released by the body, causing postoperative infection and other adverse reaction symptoms, affecting the surgical efficacy and perioperative recovery of patients [7]. Therefore, the postoperative administration of certain sedative and analgesic drugs can effectively reduce the incidence of adverse reactions and accelerate the perioperative recovery of patients.

Dexmedetomidine is a highly selective α2 adrenergic receptor agonist, which has the effects of sedation, analgesia, maintenance of hemodynamic stability and reduction of body stress response [8]. Propofol is a commonly used intravenous anesthetic in clinic and is widely used in intestinal surgery. It is often used in combination with other anaesthetic drugs [9]. clinically, remifentanil is mainly used for induction of general anesthesia and maintenance of analgesia during general anesthesia. As an opioid receptor agonist, remifentanil has clinical advantages such as rapid onset of action, rapid drug clearance and stable drug effect [10]. Previous studies have shown that dexmedetomidine combined with remifentanil has great sedative and analgesic effects [11]. Some studies also suggest that propofol combined with remifentanil anesthesia has high safety for patients undergoing laparoscopic radical resection of rectal cancer, and can improve the complications of patients [12]. However, there is still little research on the postoperative recovery of lung cancer patients after dexmedetomidine combined with remifentanil and propofol combined with remifentanil anesthesia. Therefore, this study aims to study the influence of dexmedetomidine combined with remifentanil anesthesia, and propofol combined with remifentanil anesthesia on perioperative inflammatory response and lung function of lung cancer patients, so as to provide reliable reference opinions for clinical selection of analgesic and sedative drugs for lung cancer patients in the future.

2 Patients and Methods

2.1 Data of Patients

Totally 128 patients admitted to our hospital (Zaozhuang Hospital of Traditional Chinese Medicine, Zaozhuang, Shandong, China) for lung cancer surgery from May 2016 to May 2018 were taken as the research object of this experiment. Among them, 67 cases were sedated with dexmedetomidine combined with remifentanil (Group A), and 61 cases were sedated with propofol combined with remifentanil (Group B). To compare the two groups. the gender is 52(77.61) male *vs.* 15(22.39) female in Group A, average aged 57.4 ± 5.3 years old, and 45(73.77) male *vs.* 16(26.23) female in Group B, with an average age of 58.1 ± 6.6. This study was conducted with the approval of the medical ethics committee, and all patients have been informed and signed informed consent.

2.2 Inclusion Criteria

All the patients were diagnosed with lung cancer by imaging and pathology, and could receive resection of lung cancer, patients had complete clinical data, patients cooperated with the follow-up, patients knew the objective of the study and signed the informed consent.

2.3 Exclusion Criteria

Patients were complicated with severe liver and kidney dysfunction, allergic to the drugs used, other malignant tumors and cardiac dysfunction, severe inflammation and immune deficiency, mental disorders or consciousness disorders.

2.4 Dosage and Method of Drug Use

Patients in Group A were sedated with dexmedetomidine (Pfizer, NY, USA), mixed with 0.9% sodium chloride (50 mL) and dexmedetomidine (200 μg), and administered by slow infusion, with an initial loading of 1 μg/kg/h and a subsequent pumping speed of 0.5 μg/kg/h. Patients in Group B were given propofol for sedation. The initial pumping speed was 0.2 mg/kg/h, and then the speed was adjusted to 0.4 mg/kg/h. Then both groups were maintained with remifentanil at a speed of 0.1–0.2 μg/kg/min.

2.5 Research Indicators

The changes of vital signs, respiratory interval (RR), blood oxygen saturation (SpO2) and blood sugar before and after sedation were recorded. The changes of inflammatory factors TNF-α, IL-6, IL-10 were observed and determined by ELISA (enzyme linked immunosorbent assay). Pulmonary function indexes FEV1 (Forced expiratory volume in one second), FVC (forced vital capacity), FEV1/FVC in the two groups at 24 hours after sedation were observed and determined using lung function detector. Hemodynamic heart rate (HR), mean arterial pressure (MAP) and other indexes before and after sedation were observed. VAS (visual analogue scale) pain score [13] and MMSE (Mini-mental State Examination) score [14] before and after sedation were compared between the two groups. The incidence of adverse reactions after sedation was observed in the two groups.

2.6 Statistical Methods

SPSS22.0 statistical software was applied to process the data results, and Graphpad7 was applied to graph the data results. Enumeration data were expressed with rate, and chi-square test was utilized for inter-group comparison. Measurement data were expressed in the form of (mean ± standard deviation). $p < 0.050$ indicated statistically significant.

3 Results

3.1 Comparison of General Data of Patients

There were no differences in age, gender, BMI, drinking, exercise habits, dietary habits, working environment, place of residence, nationality, or family medical history between the two groups ($p > 0.05$), as shown in Tab. 1.

Table 1: Comparison of general data between the two groups [n(%)]

	A(n = 67)	B(n = 61)	t/χ^2	p
Age (years)			0.664	0.508
	57.4 ± 5.3	58.1 ± 6.6		
Gender			0.257	0.612
Male	52(77.61)	45(73.77)		
Female	15(22.39)	16(26.23)		
BMI(KG/cm^2)			0.291	0.772
	25.62 ± 2.84	25.78 ± 3.38		
Drinking			0.049	0.825
Yes	43(64.18)	38(62.30)		
No	24(35.82)	23(37.70)		
Exercise habits			0.102	0.749
With	26(38.81)	22(36.07)		
Without	41(61.19)	39(63.93)		
Dietary habit			0.012	0.912
Regular	40(59.70)	37(60.66)		

Irregular	27(40.30)	24(39.34)		
Place of residence			0.015	0.901
City	51(76.12)	47(77.05)		
Countryside	16(23.88)	14(22.95)		
Nationality			0.029	0.864
Han	61(91.04)	55(90.16)		
Minority	6(8.96)	6(9.84)		
Family medical history			0.147	0.702
With	23(34.33)	19(31.15)		
Without	44(65.67)	42(68.85)		

3.2 Changes of Vital Signs before and after Sedation in the Two Groups

The changes of RR, SpO2 and blood sugar in the two groups before and after sedation drugs were observed, the results showed that RR, SpO2 decreased while blood sugar increased in both groups ($p < 0.05$). The decrease of RR and SpO2 in Group B was more remarkable than that in Group A ($p < 0.05$), and the increase of blood sugar in Group A was lower than that in Group B ($p < 0.05$). As shown in Fig. 1.

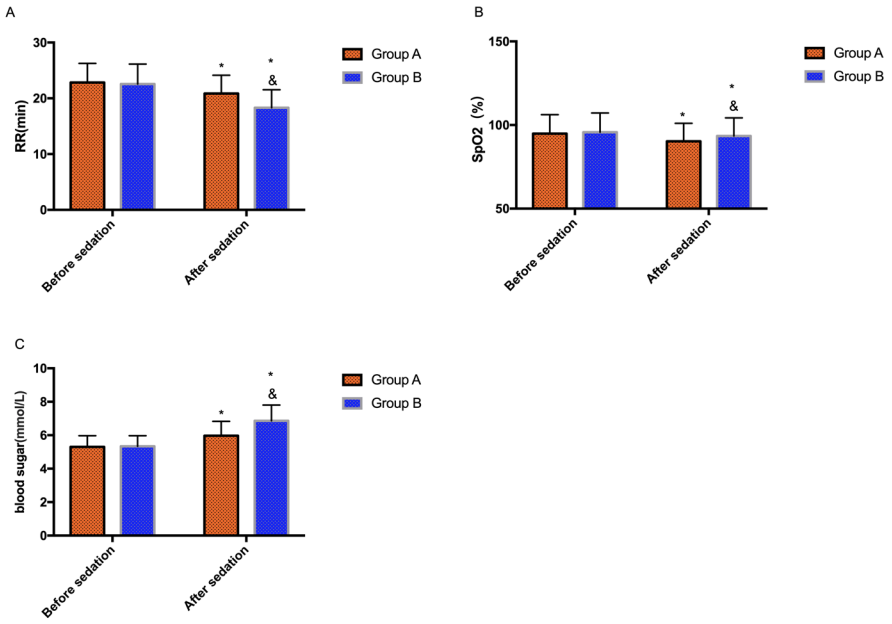

Figure 1: Changes of vital signs before and after sedation in the two groups. A, Changes of RR before and after sedation in the two groups. B, Changes of SpO2 before and after sedation in the two groups. C, Changes of blood sugar before and after sedation in the two groups. Note: * represents comparison with Group A before sedation, & represents comparison with Group A

3.3 Changes of Inflammatory Factors 24 Hours after Sedation in the Two Groups

The changes of inflammatory factors TNF-α, IL-6 and IL-10 at 24 hours after sedation were observed. Compared with Group B, Group A had lower levels of TNF-α and IL-6, ($p < 0.05$), but higher level of IL-10 ($p < 0.05$). As shown in Fig. 2.

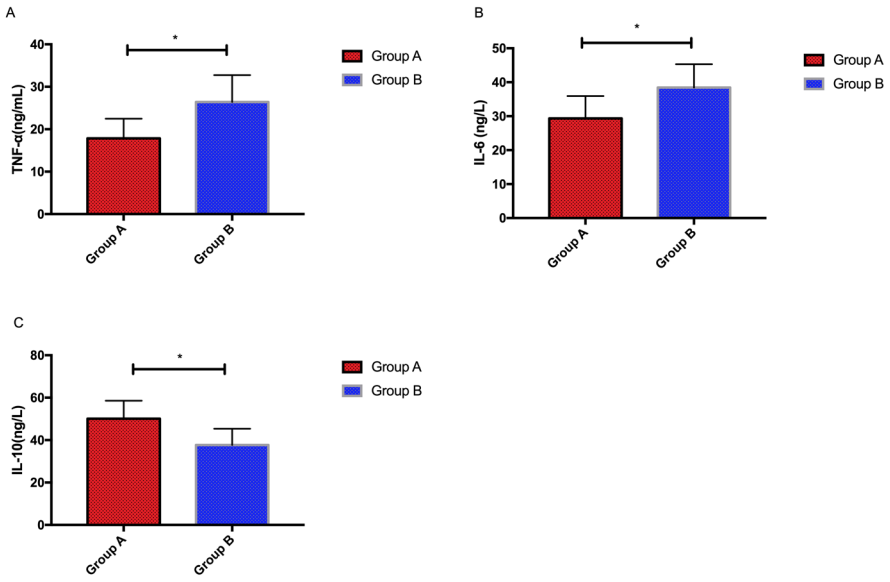

Figure 2: Changes of inflammatory factors TNF-α, IL-6 and IL-10 at 24 hours after sedation. A, Changes of TNF-α at 24 hours after sedation in the two groups. B, Changes of IL-6 at 24 hours after sedation in the two groups. C, Changes of IL-10 at 24 hours after sedation in the two groups. * denotes $p < 0.05$

3.4 Changes of Pulmonary Function 24 Hours after Sedation in the Two Groups

The changes of pulmonary function indexes of FEV1, FVC, FEV1/FVC in both groups were observed 24 hours after sedation. The results showed that the expression of FEV1, FVC, FEV1/FVC in Group B were lower than those in Group A ($p < 0.05$). As shown in Fig. 3.

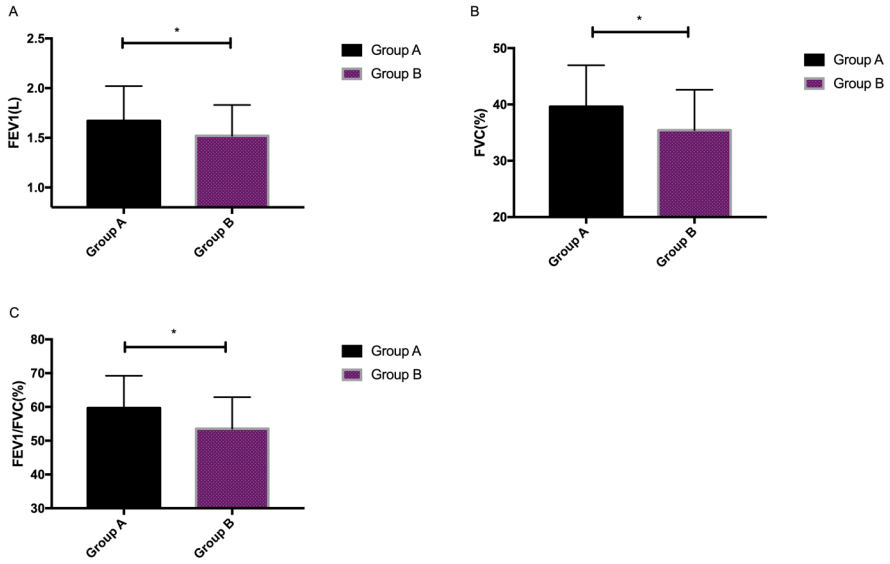

Figure 3: Changes of pulmonary function at 24 hours after sedation in the two groups. A, Changes of FEV1 at 24 hours after sedation in the two groups. B, Changes of FVC at 24 hours after sedation in the two groups. C, Changes of FEV1/FVC at 24 hours after sedation in the two groups. * denotes $p < 0.05$

3.5 Changes of Hemodynamics before and after Sedation in the Two Groups

The changes of hemodynamics HR and MAP before and after sedation in both groups were recorded. The results revealed that there were no remarkable changes of hemodynamics in the two groups before sedation ($p > 0.05$). After sedation, HR and MAP decreased in both groups, and the decrease in Group B was larger than that in Group A ($p < 0.05$). As shown in Fig. 4.

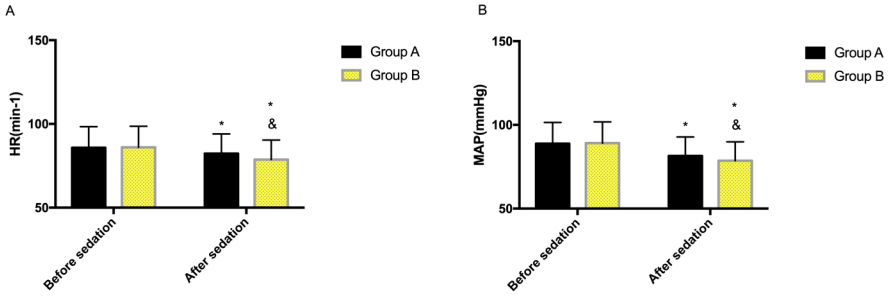

Figure 4 Changes of hemodynamic before and after sedation in the two groups. A, Changes of HR before and after sedation in the two groups. B, Changes of MAP before and after sedation in the two groups. Note: * represents comparison with Group A before sedation, & represents comparison with Group A

3.6 Comparison of VAS Pain Score and MMSE Score before and after Sedation between the Two Groups

There was no considerable difference in VAS score before sedation between the two groups ($p > 0.05$). After sedation, VAS score in Group A was evidently lower than that in Group B ($p < 0.05$). There was no remarkable difference in MMSE score between the two groups before sedation ($p > 0.05$). After sedation, MMSE score increased notably in both groups, and Group A had higher MMSE scores than Group B, $p < 0.05$. As shown in Fig. 5.

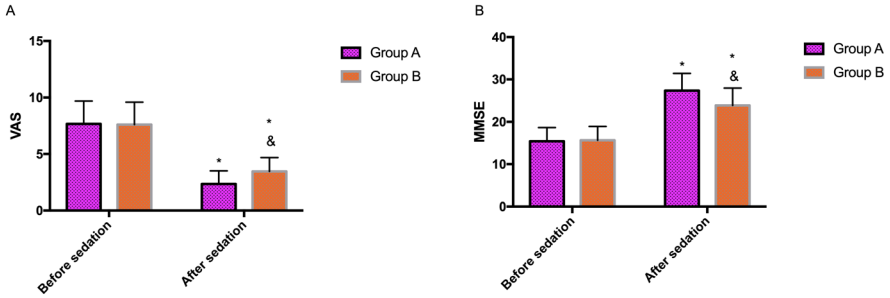

Figure 5: Comparison of VAS pain score and MMSE score before and after sedation between the two groups. A, Changes of VAS pain score before and after sedation in the two groups. B, Changes of MMSE score before and after sedation in the two groups. Note: * represents comparison with Group A before sedation, & represents comparison with Group A

3.7 Incidence of Adverse Reactions after Sedation Between the Two Groups

The incidence of nausea and vomiting, dizziness, respiratory depression, incision infection, pulmonary infection, drowsiness and other adverse reactions after sedation were observed in the two groups. The total incidence of adverse reactions in Group A was 4.48%, which was notably lower than that in Group B (14.75%), $p < 0.05$. As shown in Tab. 2.

Table 2: Incidence of adverse reactions after sedation between the two groups

	Group A (n = 67)	Group B (n = 61)	X2	*p*
Nausea and vomiting	1(1.49)	2(3.28)		
Dizziness	1(1.49)	2(3.28)		
Respiratory depression	0(0.00)	2(3.28)		
Incision infection	0(0.00)	0(0.00)		
Pulmonary infection	0(0.00)	1(1.64)		
Drowsiness	1(1.49)	2(3.28)		
Total incidence rate (%)	4.48	14.75	3.969	0.046

4 Discussion

Lung cancer is a disease with extremely high morbidity and mortality [15]. With the degradation of the environment and the change of people's life styles, its prevalence is getting younger and younger, and the incidence rate is increasing year by year, which has become one of the major diseases endangering human life and health [16]. Currently, lung cancer is mainly treated by surgery, with local resection, extended resection, thoracotomy and assisted endoscopic surgery [17]. The selection of effective and safe anesthesia among various surgical methods is of great significance to relieve the pain of patients and help patients recover after surgery [18]. According to previous studies, dexmedetomidine combined with remifentanil anesthesia and propofol combined with remifentanil anesthesia have a high utilization rate in surgical operations [19,20], but there is still little research on postoperative recovery of lung cancer. Therefore, this study will focus on the influence of perioperative inflammatory response and lung function of lung cancer patients to study whether it has better auxiliary effect on postoperative recovery of lung cancer patients.

In order to compare which drug between dexmedetomidine and propofol is more suitable for lung cancer surgery, we first compared the RR, SpO2 and blood sugar of patients in the two groups. The results showed that RR, SpO2 in Group B were lower than those in Group A after surgery, while blood sugar was higher, which confirmed that the vital signs in Group A were better than those in Group B, suggesting that dexmedetomidine might be more effective in maintaining the vital signs of lung cancer patients. Secondly, we compared the changes of inflammatory factors in the two groups after operation, and found that IL-6 and TNF-α in Group B were higher than those in Group A, while IL-10 was lower than that in Group A. As clinically recognized inflammatory factors, the value of IL-6 and TNF-α have been proved in many studies [21]. After the operation, the patient has inflammatory reaction and oxidative stress reaction due to invasive and traumatic operation, if effective intervention measures and treatment are not carried out at this time, the risk of incision infection, necrosis and other tissue infection may be caused [22]. IL-10, as an inflammatory inhibitor, can effectively improve the inflammatory response of the patient's body and has a notable effect on protecting the body's rehabilitation after surgery [23]. The detection results of inflammation-related factors between the two groups also indicated that dexmedetomidine has a more significant control effect on inflammatory response of lung cancer patients and may have higher application value in the future. According to previous studies, dexmedetomidine also has extremely high application value in radical colon cancer surgery [24], which can also support the results of our experiment. Our comparison of the pulmonary function of the two groups of patients after sedation showed that the pulmonary function of Group A was higher than that of Group B. The changes of hemodynamics in the two groups were observed, and we found that HR and MAP in Group A were higher than those in Group B after sedation. The above results showed that dexmedetomidine is superior to propofol in lung cancer surgery. We speculate that the difference between the two groups mainly relies on the different nature of the drugs. Dexmedetomidine, as a highly selective α2- adrenoceptor, can reduce the release of epinephrine in patients. Dexmedetomidine not only has sedative effect on patients, but also has sedative effect on various cellular and endocrine activities in the body [25]. It is especially suitable for the operation in which the cell tissue will produce intense secretion and active activity. Through sedation of cells and tissues, a series of oxidative stress and inflammatory reactions can be avoided. Propofol, as a strong fat-soluble drug, accelerates

chloride ion conduction and activates γ-aminobutyric acid receptor-human ossein cross-linked complex to play a sedative role [26]. However, in the process of anesthesia, propofol can affect the body's neuroendocrine response, leading to the enhancement of hypothalamus - prepituitary gland - hypothalamic-pituitary-adrenal axis activity, thus causing increased secretion of catecholamines and glucocorticoid, inhibiting the immune function of the body [27]. We also confirmed this through references on the effects of propofol. Therefore, we infer that the key to propofol's less effective application in lung cancer than dexmedetomidine is immunosuppression. Immune function, as a key part of wound repair and defense against foreign invasion, is of great importance after surgery. Propofol has a certain inhibitory effect on immune function, which leads to the reduction of patients' ability to resist oxidative stress reaction and inflammatory reaction, and also limits the repair ability of the internal environment of the body, thus causing the difference between the two groups. On the contrary, dexmedetomidine is found to be able to enhance the stability of T lymphocytes, and it has been found in previous studies to have a great protective effect on the integrity of T lymphocyte subsets [28], confirming that dexmedetomidine has little impacts on patients' immune function. This is also consistent with our above inference, indicating that dexmedetomidine has little effect on the immune function of patients. In addition, we also compared the VAS pain score, MMSE score and adverse reactions of the two groups of patients, and found that all the investigation results in group A were better than those in Group B, which further confirmed that dexmedetomidine was more suitable for lung cancer surgery.

The above conclusions are based on the results of this experiment and the analysis and conjecture of previous studies. We need further experiments to verify the exact mechanism of action of dexmedetomidine and propofol. In addition, since we did not test the immune function of the patients in this experiment, we cannot exclude the possibility of errors in our inference. Moreover, due to the short period of experimental, we cannot evaluate the long-term prognosis of the two groups of patients. All these deficiencies deserve further experiments to confirm them.

5 Conclusion

To sum up, compared with propofol, dexmedetomidine combined with remifentanil anesthesia has a more significant improvement effect on postoperative inflammatory factors and lung function of lung cancer patients, which is worthier of recommendation.

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Conflicts of Interest: The authors declare that they have no conflicts of interest to report regarding the present study.

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