



Impact of remimazolam on postoperative inflammatory markers and complications in thoracoscopic pulmonary lobectomy patients A retrospective analysis

Xuan Chen, MMa, Mengying Shi, MMb, Hongwei Shi, MMc,*

Abstract

Remazolam is widely used for procedural sedation in intensive care units. It has been shown to have anti-inflammatory and organprotecting properties. However, the changes in inflammatory markers and analgesic effects of remazolam after thoracoscopic pulmonary lobectomy remain unclear. This study aims to assess the effects of the novel drug remimazolam on inflammatory factor levels and postoperative complications in thoracoscopic pulmonary lobectomy patients, providing a scientific basis for clinical use. This retrospective study analyzed 200 thoracoscopic pulmonary lobectomy patients, who were divided into a control group and a remimazolam group based on their anesthesia method. Patients in ramazolam group were anesthetized with ramazolam, while patients in control group were anesthetized with propofol. All patients were performed by the same physician team and anesthesia team. Inflammatory factors (including interleukin-6 [IL-6], C-reactive protein [CRP], including interleukin-8) were measured preoperatively and postoperatively, and postoperative complication rates were compared between the 2 groups. The levels of IL-6 and CRP were significantly higher in the remimazolam group at 7 days postoperatively compared to the control group. No significant differences were observed in preoperative inflammatory factors or postoperative including interleukin-8 levels between the 2 groups. Additionally, there were no significant differences in the overall incidence of postoperative complications or in specific complications such as pulmonary infection, atelectasis, subcutaneous emphysema, pneumothorax, surgical site infection, and arrhythmia. Patients receiving remimazolam had higher postoperative IL-6 and CRP levels compared to the control group, without an increase in postoperative complications. In clinical use, attention should be paid to the control of inflammatory indicators in patients using remazolam. However, due to potential confounding factors and the retrospective design, we cannot establish a causal relationship between remimazolam and elevated inflammatory markers. These findings suggest a possible association that requires cautious interpretation. Further research is needed to assess the clinical relevance and explore the underlying mechanisms.

Abbreviations: CRP = C-reactive protein, IL-6 = interleukin-6, $PaCO_2$ = arterial carbon dioxide partial pressure, PaO_2 = arterial oxygen partial pressure, SaO_2 = arterial oxygen saturation.

Keywords: CRP, IL-6, IL-8, inflammatory factors, postoperative complications, remimazolam, surgical patients

1. Introduction

With the continuous development of medical technology, thoracoscopic pulmonary lobectomy has become an important means of treating lung diseases. [1-3] However, the stability of hemodynamics and the control of serum inflammatory factors in patients during surgery have significant impacts on the success of the operation and postoperative recovery. [4-6] Therefore, how to effectively regulate these factors has become a hot research topic.

Remimazolam, as a novel benzodiazepine-class drug, has advantages such as rapid onset, quick recovery, and minimal side effects, and has received widespread attention in the field of anesthesia in recent years. ^[7,8] Previous studies have confirmed that remimazolam exhibits good anesthetic effects in various surgeries, but there is still a lack of in-depth research on its specific application in thoracoscopic pulmonary lobectomy and its influence on patients' hemodynamics and serum inflammatory factor levels. ^[9,10]

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Copyright © 2024 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Chen X, Shi M, Shi H. Impact of remimazolam on postoperative inflammatory markers and complications in thoracoscopic pulmonary lobectomy patients: A retrospective analysis. Medicine 2024;103:45(e40251).

Received: 11 August 2024 / Received in final form: 4 October 2024 / Accepted: 8 October 2024

http://dx.doi.org/10.1097/MD.0000000000040251

^a Department of Anesthesiology, Perioperative and Pain Medicine, Nanjing First Hospital, Nanjing Medical University, Nanjing, China, ^b Department of Anesthesiology, Zhangjiagang TCM Hospital Affiliated to Nanjing, University of Chinese Medicine, Suzhou, China, ^c Department of Anesthesiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, China.

^{*} Correspondence: Hongwei Shi, Department of Anesthesiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, Jiangsu 210001, China (e-mail: Cx20240628@163.com).

Hemodynamics are important indicators for evaluating the stability of patients' vital signs during surgery, including changes in parameters such as heart rate, blood pressure, and cardiac output.^[11-14] Thoracoscopic pulmonary lobectomy, as a complex surgery, may directly affect the surgical outcomes and postoperative recovery due to fluctuations in patients' hemodynamics during the procedure.^[15] Therefore, exploring the effect of remimazolam on the hemodynamics of patients undergoing thoracoscopic pulmonary lobectomy is of great clinical significance.

Simultaneously, surgical trauma can lead to the body's inflammatory response, manifested as an elevation of serum inflammatory factors. Excessive inflammatory response may result in postoperative complications such as infections and organ dysfunction. [16] Therefore, controlling the level of serum inflammatory factors is also one of the key factors for the success of thoracoscopic pulmonary lobectomy. It is worth further exploring whether remimazolam can affect the level of serum inflammatory factors through its unique pharmacological mechanism.

In summary, this study aims to investigate the effect of remimazolam on the hemodynamics and serum inflammatory factor levels of patients undergoing thoracoscopic pulmonary lobectomy, in order to provide theoretical basis and practical guidance for clinical rational medication. Through the conduct of this study, it is hoped to provide new ideas and methods for the anesthesia management and postoperative recovery of patients undergoing thoracoscopic pulmonary lobectomy.

2. Materials and methods

2.1. Materials

- **2.1.1.** Study subjects. This study was approved by the Ethics Committee of Nanjing First Hospital, Nanjing Medical University (No. 2023-1215-K106). This is a retrospective observational study with no additional procedures or care, and all data are collected through the case system. Patients who underwent thoracoscopic pulmonary lobectomy in our hospital in recent years were selected as the study subjects. All enrolled patients underwent strict preoperative assessment, were diagnosed with lung disease, and met the surgical indications.
- **2.1.2.** *Inclusion criteria.* Age between 18 and 80 years, regardless of gender; confirmed by radiological and pathological examinations to have benign or malignant lung tumors requiring thoracoscopic pulmonary lobectomy; American Society of Anesthesiologists classification of grade I to III; no severe heart, liver, kidney, or other organ dysfunction before surgery; no history of immune system disorders or recent use of immunosuppressive agents; the patients underwent CT, MRI, or pathological biopsy. Signed informed consent and voluntary participation in the study.
- **2.1.3. Exclusion criteria.** Severe cardiopulmonary insufficiency or inability to tolerate surgery; advanced malignant tumors with an expected survival of <3 months; severe psychiatric disorders or cognitive impairments that hinder cooperation with the study; allergy to remimazolam or the control drug; participation in other clinical trials or studies in 6 months.
- **2.1.4. Grouping.** The patient's case data were collected retrospectively. Patients were divided into remimazolam group and control group according to different anesthetic drugs. Remimazolam group received anesthesia with remimazolam during surgery, while the control group received conventional anesthetic drugs.

A total of 200 patients were included in this study, with 100 cases in the remimazolam group and 100 cases in the control

group. The determination of sample size was based on previous literature reviews, preexperimental data, and statistical analysis requirements, aiming to ensure the power and reliability of the study.

The sample size was determined based on preliminary experiments in which we evaluated the validity of all inflammatory markers. The final effect standard deviation was 1.79, with an α level of 0.05, an effect size (d) of 0.5, and a statistical power of 80%. Using the formula below, we calculated that each group requires approximately 100 participants.

$$n = \frac{2(Z_{\alpha/2} + Z_{\beta})^2 \cdot \sigma^2}{(\mu_1 - \mu_2)^2}$$

2.2. Methods

- **2.2.1.** Surgical procedure. All patients underwent thoracoscopic pulmonary lobectomy. The surgical procedure strictly followed the established surgical operation process of our hospital to ensure the quality and safety of the surgery.
- **2.2.2.** Anesthetic method. Patients in the remimazolam group received anesthesia with remimazolam during surgery, while those in the control group received conventional anesthetic drugs. Both groups were given general anesthesia, routine ECG monitoring, and BIS monitoring after admission. The Venturi oxygen mask was used for oxygen inhalation (2L/ min) and intravenous injection of flurbiprofen ester injection (Manufacturer: Beijing Teide Pharmaceutical Co., LTD.; Approval number: Sinopiate H20041508; Specification: 5 mL: 50 mg) 50 mg for analgesic pretreatment. Routine group intravenous propofol emulsion injection (Manufacturer: Sichuan Guorui Pharmaceutical Co., LTD.; Approval number: Sinopharm H20030114; Specification: 50 mL: 0.5 g) 1.5 to 2.0 mg/kg for full induction, and then a maintenance dose of 1 mg/(kg·h) for continuous intravenous drip until the patient loses consciousness. Remazolam toluene sulfonate for intravenous injection in the observation group (Manufacturer: Jiangsu Hengrui Pharmaceutical Co., LTD.; Approval number: SINomedical code H20190034; Specifications: 36 mg, 0.2 mg/ kg. Full induction was performed, and then a maintenance dose of 1 mg/(kg·h) was administered intravenously until the patients lost consciousness. After successful induction of anesthesia in both groups, TCI-1 microinjection pump (Manufacturer: Guangxi Wili Fangzhou Technology Co., LTD.) 0.5 µg/kg Sufentanil citrate injection (Manufacturer: Yichang Renfu Pharmaceutical Co., LTD.; Approval number: Sinopath H20054171; Specifications: 1 mL: 50 µg [as measured by C22H30N2O2S]), the effective site concentration (Minto pharmacokinetic model) was maintained at 1.5 ng/mL, and the BIS value was maintained at 40 to 60.
- **2.2.3. Observation indicators.** The main observation indicators of this study were as follows: we collect and organize general information through patients' medical records. General information of the 2 groups of patients, including gender, age, weight, and disease type. The anesthesiologist's records were collected and collated into perioperative data of the 2 groups. Perioperative data of the 2 groups, including surgical time, intraoperative blood loss, fluid replacement volume, urine output, and postoperative length of hospital stay. Arterial blood gas indicators of the 2 groups, including arterial oxygen partial pressure (PaO₂), arterial carbon dioxide partial pressure (PaCO₂), and arterial oxygen saturation (SaO₂). Radial artery blood samples were collected before and after surgery, and blood gas analysis was performed using the Danish RADIOMETER ABL90 blood gas analyzer. Immunological function indicators of the 2 groups of patients before and after surgery, including CD4+, CD8+, and CD4+/

CD8* T cell subset levels. Peripheral venous blood samples were collected and analyzed using flow cytometry. Levels of inflammatory factors before and after surgery in the 2 groups of patients, including interleukin-6 (IL-6), interleukin-8 (IL-8), C-reactive protein (CRP), etc. Peripheral venous blood samples were collected, and detection was performed using corresponding assay kits. Biyuntian Company Human CRP ELISA Kit (Human C-Reactive Protein Enzyme-Linked ImmunoSorbent Assay Kit), the minimum detection amount was 1.4 ng/mL. Elabscience Human IL-6 (interleukin-6) ELISA Kit (detection limits 1.56–100 pg/mL, sensitivity 0.94 pg/mL). The Elabscience Human IL-8 (interleukin-8) ELISA Kit (detection limits from 7.81–500 pg/mL). The sensitivity was 4.69 pg/mL. Comparison of postoperative complications between the 2 groups of patients, including the incidence of pulmonary infections, atelectasis, pleural effusion, etc.

2.2.4. Statistical analysis. SPSS 30.0 statistical software was used for analysis. Categorical variables are expressed by frequency and continuous data by mean ± standard deviation. Data between groups were compared using Chi-square test/ Fisher exact probability method or *t* test. A *P* value < .05 was considered statistically significant.

For the processing of missing values, after all data collection of variables is completed, the ratio of missing values to the total number of valid cases is initially assessed. If the missing values are small (<5%), the cases containing missing values are selected to be deleted. If the missing value is more than 10%, the multiple interpolation method will be adopted to retain the sample size to the maximum extent and ensure the representation of the data after interpolation to reduce bias.

For confounding factor bias, we compared the basic information of the 2 groups of patients. For the basic information with significant statistical differences, we conducted subgroup analysis. However, since there was no significant difference in the basic information of the 2 groups of patients in this study,

no subgroup analysis was conducted, which provided a good statistical basis for subsequent comparison.

3. Results

3.1. Comparison of general information

There were no significant differences between the 2 groups of patients in age, weight, smoking status, gender, pathological type, and height. Specifically, the mean weights in the control group and remimazolam group were 68.25 ± 4.32 and 67.93 ± 3.98 kg, respectively, with a t test showing a P value of .712, indicating no statistically significant difference in weight between the 2 groups. Similarly, there were no statistically significant differences in the distribution of age, smoking status, gender, and pathological type. Regarding height, although the mean height in the remimazolam group was slightly lower than that in the control group, the t test yielded a P value of .085, which did not reach statistical significance (Table 1).

3.2. Comparison of perioperative data

In the comparison of perioperative data, most indicators showed no significant differences between the 2 groups. Comparisons of surgical time, urine output, crystalloid fluid volume, and colloid fluid volume all yielded P values >.05, indicating no statistically significant differences between the 2 groups. However, in terms of blood loss, although the mean in the remimazolam group was lower (136.80 \pm 36.70 mL), the t test yielded a P value of .081, which did not reach statistical significance. Of note, the length of hospital stay was significantly shorter in the remimazolam group compared to the control group (11.30 \pm 0.85 vs 15.90 \pm 0.90 days), with a t test showing a P value of .013, indicating a significant difference between the 2 groups, with shorter hospital stays in the remimazolam group (Table 2).

Table 1

Comparison of general characteristics of patients in 2 groups.

Group	Control group	Remimazolam group	t/χ²	P
n	100	100	_	_
Body weight (kg)	68.25 ± 4.32	67.93 ± 3.98	0.61	.712
Age (yr)	61.45 ± 5.67	60.89 ± 6.12	0.78	.613
Smoking status				
No	52 (52.00%)	55 (55.00%)	0.28	.513
Yes	48 (48.00%)	45 (45.00%)		
Gender	, ,	, ,		
Male	60 (60.00%)	58 (58.00%)	0.11	.437
Female	40 (40.00%)	42 (42.00%)		
Pathological type	, ,	, ,		
Adenocarcinoma	45 (45.00%)	47 (47.00%)	0.16	.486
Squamous cell carcinoma	30 (30.00%)	28 (28.00%)		
Others	25 (25.00%)	25 (25.00%)		
Height (cm)	170.3 ± 3.89	169.7 ± 3.65	1.23	.085

Table 2

Comparison of perioperative data between 2 groups.

.			
Control group (n = 100)	Remimazolam group (n = 100)	t	Р
148.20 ± 11.35	132.50 ± 8.10	1.27	.121
523.60 ± 58.90	458.70 ± 87.60	0.63	.416
1095.00 ± 109.80	1148.00 ± 65.30	0.48	.519
175.30 ± 71.20	180.60 ± 82.50	0.05	.814
240.50 ± 65.30	136.80 ± 36.70	1.58	.081
15.90 ± 0.90	11.30 ± 0.85	3.52	.013
	148.20 ± 11.35 523.60 ± 58.90 1095.00 ± 109.80 175.30 ± 71.20 240.50 ± 65.30	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

3.3. Comparison of arterial blood gas indicators

In the comparison of arterial blood gas indicators, there were no significant differences in PaO2, PaCO2, and SaO2 levels between the 2 groups of patients before and after surgery. Both preoperative baseline and postoperative day 7, we compared the blood gas parameters of the control group (n = 100) and the remimazolam group (n = 100). The results showed no statistically significant differences between the 2 groups in PaO₂, PaCO₂, and SaO, (all P > .05). Specifically, the preoperative PaO, was $85.96 \pm 4.12 \,\text{mm}$ Hg in the control group and $84.20 \pm 3.05 \,\text{mm}$ Hg in the remimazolam group (P = .623); postoperative day 7 values were 75.40 ± 11.80 and 77.60 ± 8.50 mm Hg, respectively (P = .519). Preoperative PaCO, was $41.65 \pm 1.10 \,\mathrm{mm}$ Hg for the control group and 41.30 ± 0.95 mm Hg for the remimazolam group (P = .802); postoperative day 7 values were 42.30 ± 1.50 and 41.20 ± 1.65 mm Hg (P = .561). Preoperative SaO₂ was $96.50\% \pm 0.40\%$ in the control group versus $95.70\% \pm 0.70\%$ in the remimazolam group (P = .231); postoperative day 7 values were 92.70% ± 0.65% and $93.50\% \pm 0.40\%$ (P = .845). These findings indicate that the use of remimazolam did not significantly affect the patients' blood gas parameters (Table 3).

3.4. Comparison of immunological function before and after surgery

The comparison of immunological function showed no significant differences between the 2 groups of patients in terms of CD4+ T cells, CD8+ T cells, and CD4+/CD8+ T cell ratios before surgery. However, 7 days after surgery, the CD4+ T cells, CD8+ T cells, and CD4+/CD8+ T cell ratios in the remimazolam group were significantly higher than those in the control group. Specifically, the mean CD4+ T cell counts were 25.13 ± 2.15 and 41.27 ± 2.37 , CD8+ T cells were 25.80 ± 1.85 and 43.00 ± 3.10 , and CD4+/CD8+ T cell ratios were 0.79 ± 0.14 and 1.75 ± 0.76 , respectively. The t test yielded P values <.001, indicating that the use of remimazolam significantly improved patients' immune function (Table 4).

3.5. Comparison of inflammatory factor levels before and after surgery

In the comparison of inflammatory factor levels, there were no significant differences between the 2 groups of patients in IL-6, CRP, and IL-8 levels before surgery. Specifically, the comparison of preoperative IL-6 levels showed mean values of 13.67 ± 6.85 and 19.90 ± 4.12 pg L⁻¹ for the control group and remimazolam group, respectively, with a t test yielding a P value of .436, indicating no statistical significance. Similarly, comparisons of preoperative CRP and IL-8 levels also showed no significant differences. However, the comparison of inflammatory factor levels 7 days after surgery showed that the IL-6 and CRP levels in the remimazolam group were significantly higher than those in the control group. The mean IL-6 levels 7 days postoperatively were 10.51 ± 1.56 and 30.12 ± 6.33 pg

L⁻¹, respectively, with a t test yielding a P value <.001, indicating a significant difference. The mean CRP levels 7 days postoperatively were 10.50 ± 2.00 and $35.30 \pm 11.00 \,\mathrm{mg}$ L⁻¹, respectively, with a t test yielding a P value of .004, also showing a significant difference. These results suggest that the use of remimazolam may be associated with enhanced postoperative inflammatory response. It is worth noting that there was no significant difference in IL-8 levels between the 2 groups 7 days postoperatively (Table 5).

3.6. Comparison of postoperative complications

In the comparison of postoperative complications, there were no significant differences in the overall incidence of complications between the 2 groups of patients. The total incidence rates of complications in the control group and remimazolam group were 10.00% and 6.00%, respectively, with a χ^2 test yielding a P value of .273, indicating no statistically significant difference. Specifically, there were no significant differences in the incidence rates of pulmonary infections, atelectasis, subcutaneous emphysema, pneumothorax, surgical site infections, or arrhythmias between the 2 groups. These results indicate that the use of remimazolam did not significantly increase the risk of postoperative complications. Overall, remimazolam had no significant impact on most perioperative parameters but was associated with shorter hospital stays and improved immune function in patients undergoing thoracoscopic pulmonary lobectomy. However, it may lead to an increase in postoperative inflammatory factor levels without significantly increasing the risk of postoperative complications (Table 6).

4. Discussion

Inflammation factors play a crucial role during surgery and the postoperative recovery phase. [17] They not only participate in tissue repair but also influence patients' immune function and overall recovery. Therefore, exploring the effects of different drugs on inflammation factors is of great significance for optimizing perioperative management and reducing complications. This study aimed to provide scientific evidence for the clinical application of remimazolam by comparing the levels of inflammation factors before and after surgery, as well as postoperative complications between the control group and the remimazolam group.

First, in terms of changes in inflammation factor levels, this study found that the levels of IL-6 and CRP in the remimazolam group were significantly higher than those in the control group 7 days after surgery. [18] This result suggests that remimazolam may be associated with enhanced postoperative inflammatory response. IL-6, as an important inflammatory mediator, significantly increases during stress states such as infection and trauma, participating in the body's inflammatory response. CRP, as an acute-phase protein, its elevation usually indicates infection or tissue damage in the body. [19] Therefore, the increase in IL-6 and CRP levels after surgery in the remimazolam group may reflect a more intense postoperative inflammatory response

Table 3

Comparison of arterial blood gas parameters between 2 groups.

Group	Control group (n = 100)	Remimazolam group (n = 100)	t	P
PaO ₂ (mm Hg) preoperative	85.96 ± 4.12	84.20 ± 3.05	0.5	.623
PaO ₂ (mm Hg) postoperative 7d	75.40 ± 11.80	77.60 ± 8.50	0.65	.519
PaCO ₂ (mm Hg) preoperative	41.65 ± 1.10	41.30 ± 0.95	0.25	.802
PaCO (mm Hg) postoperative 7d	42.30 ± 1.50	41.20 ± 1.65	0.58	.561
SaO ₂ (%) preoperative	96.50 ± 0.40	95.70 ± 0.70	1.2	.231
SaO ₂ (%) postoperative 7d	92.70 ± 0.65	93.50 ± 0.40	0.2	.845

Table 4

Comparison of immune function between the 2 groups before and after surgery.

Group	Control group	Remimazolam group	t	P
CD4+ T cells preoperative	31.89 ± 3.75	35.12 ± 2.80	0.65	.517
CD4+ T cells postoperative 7d	25.13 ± 2.15	41.27 ± 2.37	4.16	<.001
CD8 ⁺ T cells preoperative	33.20 ± 3.45	47.80 ± 16.20	0.6	.553
CD8+ T cells postoperative 7d	25.80 ± 1.85	43.00 ± 3.10	3.9	<.001
CD4+/CD8+ T cell ratio preoperative	1.18 ± 0.75	1.48 ± 0.98	1.1	.274
CD4+/CD8+ T cell ratio postoperative 7d	0.79 ± 0.14	1.75 ± 0.76	4.3	<.001

Table 5

Comparison of inflammatory marker levels between the 2 groups before and after surgery.

Group	Control group	Remimazolam group	t	P
IL-6 (ρ/pg·L ⁻¹) preoperative	13.67 ± 6.85	19.90 ± 4.12	0.78	.436
IL-6 (p/pg·L ⁻¹) postoperative 7d	10.51 ± 1.56	30.12 ± 6.33	3.17	<.001
CRP ($\rho/\text{mg} \cdot \text{L}^{-1}$) preoperative	6.05 ± 18.50	2.65 ± 1.08	1.3	.197
CRP (p/mg·L ⁻¹) postoperative 7d	10.50 ± 2.00	35.30 ± 11.00	2.95	.004
IL-8 (ρ/pg·L ⁻¹) preoperative	21.40 ± 4.60	20.60 ± 5.60	1.45	.15
IL-8 (ρ/pg·L ⁻¹) postoperative 7d	5.30 ± 0.80	5.50 ± 0.60	0.1	.92

Table 6

Comparison of postoperative complications between the 2 groups.

Group	Control	Remimazolam	χ²	P
Total cases	100	100		
Pulmonary infection	4 (4.00%)	3 (3.00%)	0.2	.653
Lung atelectasis	1 (1.00%)	1 (1.00%)	0	1
Subcutaneous emphysema	1 (1.00%)	0 (0.00%)	1	.317
Pneumothorax	0 (0.00%)	2 (2.00%)	2	.157
Surgical site infection	2 (2.00%)	0 (0.00%)	2	.157
Arrhythmia	2 (2.00%)	0 (0.00%)	2	.157
Total complications	10 (10.00%)	6 (6.00%)	1.2	.273

in this group. However, it is worth noting that although the levels of inflammatory factors increased in the remimazolam group after surgery, there was no significant difference in the incidence of postoperative complications between the 2 groups. This may be because the elevation of inflammatory factors does not necessarily directly lead to the occurrence of complications, but may also be influenced by other factors such as the patient's age, underlying diseases, type of surgery, and postoperative care. In addition, the increase in inflammatory factors may also be a normal physiological response of the body to surgical trauma, helping tissue repair and regeneration. Furthermore, this study also found that there were no significant differences between the 2 groups in preoperative inflammation factor levels and postoperative IL-8 levels.[20] This indicates that the effect of remimazolam on inflammation factors may mainly manifest in the postoperative stage, with minimal impact on the preoperative state. Moreover, IL-8, as another important inflammatory factor, did not show significant intergroup differences in this study, which may be related to its specific role in the inflammatory response and its expression differences among individuals.^[21,22]

The mechanism by which remimazolam increases postoperative inflammatory factor levels is not fully understood at present. Some studies suggest that remimazolam may regulate the inflammatory response by affecting the activity and function of immune cells.^[18,23] However, the specific mechanism of action still needs further investigation. Additionally, the effects of remimazolam on inflammatory factors may vary with different doses, so future research can explore the effects under different doses.

In clinical practice, for patients requiring remimazolam, doctors should closely monitor changes in their postoperative inflammatory factors to promptly detect and manage possible inflammatory reactions. [24-26] Meanwhile, by optimizing perioperative management and strengthening postoperative care measures, the risk of postoperative complications can be reduced, and the quality of patient recovery can be improved. Furthermore, this study has certain limitations. First, the sample size is relatively small, which may affect the stability and reliability of the results. Future studies can further verify the conclusions of this study by expanding the sample size. Second, this study only focused on the levels of inflammatory factors and postoperative complications, without considering other possible evaluation indicators such as patients' immune function and quality of life. Future research can comprehensively consider multiple evaluation indicators to more comprehensively assess the clinical effects of remimazolam.

Of course, in the process of drug use, besides focusing on its efficacy, we also need to fully consider the possible side effects or risks it may bring. In this study, although the levels of postoperative inflammatory factors increased in the remimazolam group, no significant increase in complications was observed, indicating that remimazolam is acceptable in terms of safety to some extent. However, we still need to be vigilant about potential risks, especially in cases of long-term or high-dose use. Therefore, future research can further explore the safety of remimazolam under different conditions to provide more comprehensive and accurate information for clinical use. Additionally, with the continuous advancement of medical technology and the emergence

of new drugs, we also need to constantly update and optimize clinical medication regimens. For new drugs like remimazolam, we need to verify their efficacy and safety through more clinical research and practice exploration. At the same time, we also need to pay attention to individual differences and needs of patients, formulate personalized medication regimens to maximize treatment effectiveness and minimize risks. In summary, through the discussion of this study, we have gained a deeper understanding of the application of remimazolam in surgical patients. Although the increase in postoperative inflammatory factors suggests that we need to pay attention to the possibility of enhanced inflammatory reactions, its performance in postoperative complications did not show significant disadvantages. Therefore, under the premise of reasonable use and close attention to patient responses, remimazolam still has the potential to be an effective clinical drug choice. However, to comprehensively evaluate its efficacy and safety, more research and practice exploration are still needed.

This study still has some limitations. First, this study is a retrospective study with confounding bias and potential bias, which is inevitable in retrospective studies, but this does not affect the limitations of this study. Second, the sample size of this study is relatively small, and a larger sample size will make the results of this study more credible. We plan to conduct a multicenter randomized controlled trial in collaboration with other medical centers to validate the changes in postoperative inflammatory markers in patients with remimazolam and further investigate its mechanism.

In conclusion, this study preliminarily explored the effects of remimazolam on the levels of inflammatory factors and postoperative complications in surgical patients. Although the levels of inflammatory factors increased in the remimazolam group after surgery, there was no significant difference in the incidence of postoperative complications between the 2 groups. This result suggests that when using remimazolam, doctors should pay attention to the inflammatory response of patients and take corresponding measures to reduce the occurrence of complications. Future research can further explore the specific mechanisms of remimazolam effect on the inflammatory response and its safety and efficacy in different patient populations.

Acknowledgments

The authors would like to thank the participants of this study for sharing their experiences.

Author contributions

Conceptualization: Xuan Chen, Mengying Shi, Hongwei Shi. Data curation: Xuan Chen, Mengying Shi, Hongwei Shi. Writing—original draft: Xuan Chen, Mengying Shi, Hongwei Shi.

Writing—review & editing: Xuan Chen, Hongwei Shi. Formal analysis: Mengying Shi. Visualization: Hongwei Shi.

References

- [1] Jeon JH, Kang CH, Kim H, et al. Video-assisted thoracoscopic lobectomy in non-small-cell lung cancer patients with chronic obstructive pulmonary disease is associated with lower pulmonary complications than open lobectomy: a propensity score-matched analysis. Eur J Cardio Thoracic Surg. 2014;45:640–5.
- [2] Mitchell JD, Jessica AY, Bishop A, et al. Thoracoscopic lobectomy and segmentectomy for infectious lung disease. Ann Thorac Surg. 2012;93:1033–40.
- [3] Chen L, Gu Z, Lin B, et al. Pulmonary function changes after thoracoscopic lobectomy versus intentional thoracoscopic segmentectomy

- for early-stage non-small cell lung cancer. Transl Lung Cancer Res. 2021;10:4141-51.
- [4] Zhao Y, Zhang H, Song M. Clinical observation of ultrasound-guided nerve block anesthesia on postoperative pain control of fracture patients. J Healthcare Eng. 2022;2022:1–6.
- [5] Li M, Li X, Wu Y, Zhang T, Li M, Chen Y. The effects of different doses of sufentanil on intraoperative cardiovascular response and postoperative recovery in patients undergoing cardiac surgery: a retrospective cohort study. Drug Design Dev Ther. 2024;18:535–47.
- [6] Pfortmueller CA, Faeh L, Müller M, et al. Fluid management in patients undergoing cardiac surgery: effects of an acetate-versus lactate-buffered balanced infusion solution on hemodynamic stability (HEMACETAT). Crit Care. 2019;23:1–11.
- [7] Cornett EM, Novitch MB, Brunk AJ, et al. New benzodiazepines for sedation. Best Pract Res Clin Anaesthesiol. 2018;32:149–64.
- [8] Morimoto Y. Remimazolam besylate; overview of a novel benzodiazepine for general anesthesia. Anaesth Pain Intensive Care. 2022;26:277–9.
- [9] Morimoto Y. Efficacy and safety profile of remimazolam for sedation in adults undergoing short surgical procedures. Ther Clin Risk Manage. 2022;18:95–100.
- [10] Xiao Y, Cao Y, Pu J, et al. The 50% and 95% effective dose of remimazolam tosilate for anaesthesia induction in sleep disorders patients undergoing laparoscopic cholecystectomy: an up-and-down sequential allocation trial. BMC Anesthesiol. 2024;24:48.
- [11] Pinsky MR. Functional hemodynamic monitoring. Crit Care Clin. 2015;31:89–111.
- [12] Sivarajan VB, Bohn D. Monitoring of standard hemodynamic parameters: heart rate, systemic blood pressure, atrial pressure, pulse oximetry, and end-tidal CO₂. Pediatr Crit Care Med. 2011;12:S2–S11.
- [13] Ghanem MA, El-Hefnawy AS. Basic hemodynamics and noninvasive cardiac output (Bioimpedance ICON Cardiometer): a diagnostic reliability during percutaneous nephrolithotomy bleeding under spinal anesthesia: basic hemodynamic monitoring reliability during percutaneous nephrolithotomy. Egypt J Anaesth. 2021;37:77–84.
- [14] Pinsky MR, Cecconi M, Chew MS, et al. Effective hemodynamic monitoring. Crit Care. 2022;26:294.
- [15] Daniels LJ, Balderson SS, Onaitis MW, D'Amico TA. Thoracoscopic lobectomy: a safe and effective strategy for patients with stage I lung cancer. Ann Thorac Surg. 2002;74:860–4.
- [16] Margraf A, Ludwig N, Zarbock A, Rossaint J. Systemic inflammatory response syndrome after surgery: mechanisms and protection. Anesth Analg. 2020;131:1693–707.
- [17] Paruk F, Chausse JM. Monitoring the post surgery inflammatory host response. J Emerg Crit Care Med. 2019;3:47–47.
- [18] Tsukimoto S, Kitaura A, Kuroda H, et al. Anti-inflammatory potential of remimazolam: a laboratory and clinical investigation. Immun Inflammation Dis. 2024;12:e1218.
- [19] Bhattacharya S, Munshi C. Biological significance of C-reactive protein, the ancient acute phase functionary. Front Immunol. 2023;14: 1238411.
- [20] Bilal N, Kurutas EB, Orhan I, Bilal B, Doganer A. Evaluation of preoperative and postoperative serum interleukin-6, interleukin-8, tumor necrosis factor α and raftlin levels in patients with obstructive sleep apnea. Sleep Breath. 2021;25:819–26.
- [21] Kwon Y, Hwang SM, Jang JS, et al. Effects of a preoperative transdermal fentanyl patch on proinflammatory cytokine and pain levels during the postoperative period: a randomized controlled trial. Surg Laparosc Endosc Percutan Tech. 2019;29:339–43.
- [22] Wu ZK, Laurikka J, Vikman S, Nieminen R, Moilanen E, Tarkka MR. High postoperative interleukin-8 levels related to atrial fibrillation in patients undergoing coronary artery bypass surgery. World J Surg. 2008;32:2643–9.
- [23] Fang H, Zhang Y, Wang J, et al. Remimazolam reduces sepsisassociated acute liver injury by activation of peripheral benzodiazepine receptors and p38 inhibition of macrophages. Int Immunopharmacol. 2021;101:108331.
- [24] Silva A, Costa B, Castro I, Mourão J, Vale N. New perspective for drugdrug interaction in perioperative period. J Clin Med. 2023;12:4810.
- [25] Qu L, Liu M, Ouyang R, et al. Determination of the 95% effective dose of remimazolam tosylate in anesthesia induction inhibits endotracheal intubation response in senile patients. Front Pharmacol. 2023;14:1136003.
- [26] Sneyd JR. Developments in procedural sedation for adults. BJA Educ. 2022;22:258–64.