BRITISH JOURNAL OF HOSPITAL MEDICINE

ARTICLE

Impact of Combining Esketamine With Erector Spinae Plane Block on Opioid Consumption, Inflammatory Stress, and Cognitive Function After Thoracoscopic Surgery

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Abstract

Aims/Background Esketamine exhibits strong sedative and analgesic effects. Similarly, erector spinae plane block (ESPB) blocks somatic and visceral nerves and is commonly used for pain relief in thoracic surgery. Therefore, this study aims to investigate the impacts of combining esketamine with ESPB on opioid consumption, inflammatory stress, and cognitive function after thoracoscopic surgery.

Methods This retrospective study collected clinical data from 114 patients who underwent thoracoscopic surgery at Jinhua Municipal Central Hospital, between January 2022 and January 2024. Based on anesthesia approaches, patients were divided into the ESPB (n = 62) and esketamine + ESPB groups (n = 52). Several variables, such as perioperative indicators, postoperative recovery, inflammatory stress, and cognitive function were compared between the two groups.

Results In both groups, the Numeric Rating Scale (NRS) score increased at 6 h postoperatively compared to at 1h, and gradually decreased at 12 h, 24 h, and 48 h ($p < 0.05$). Compared to the ESPB group, the NRS score was significantly decreased in the esketamine + ESPB group at 6 h, 12 h, 24 h, and 48 h after surgery ($p < 0.001$). The oxycodone consumption was significantly lower in the esketamine + ESPB group at 24 h and 48 h post-surgery than in the ESPB group ($p < 0.001$). Furthermore, the incidence of adverse reactions was 30.6% (19/62) in the ESPB group and 34.6% (18/52) in the esketamine + ESPB group, with the difference being statistically insignificant ($p = 0.652$). Compared to the ESPB group, the white blood cell (WBC) count, C-reactive protein (CRP), procalcitonin (PCT), interleukin (IL)-6, and tumor necrosis factor (TNF)-α levels were significantly decreased in the Esketamine + ESPB group at day 3 after surgery ($p < 0.001$). Compared to the ESPB group, the Montreal Cognitive Assessment Scale (MoCA) score was substantially elevated in the esketamine + ESPB group at days 1 and 3 after surgery ($p < 0.001$, $p = 0.001$).

Conclusion The combination of esketamine and ESPB effectively alleviated postoperative pain and reduced opioid consumption after thoracoscopic surgery. Furthermore, the combined approach significantly improved postoperative inflammatory stress and cognitive impairment compared to the use of ESPB alone without increasing adverse reactions.

Key words: esketamine; nerve block; sacrospinalis; thoracoscopic; opioid; cognition; inflammation

Submitted: 1 January 2025 Revised: 13 March 2025 Accepted: 28 March 2025

How to cite this article:
Zhu J, Chen Y, Shu L, Xu D, Lv H, Hu C, Zhao D. Impact of Combining Esketamine With Erector Spinae Plane Block on Opioid Consumption, Inflammatory Stress, and Cognitive Function After Thoracoscopic Surgery. Br J Hosp Med. 2025. https://doi.org/10.12968/hmed.2025.0002

Introduction

Thoracoscopic surgery is a clinical intervention that offers the advantages of minimal trauma and rapid postoperative recovery. Compared to traditional open-chest surgery, thoracoscopic surgery significantly reduces postoperative pain and

improves patients' quality of life (Wang et al, 2022). However, despite these benefits, approximately 22%–63% of patients still experience severe or chronic pain after thoracoscopic surgery, which adversely affects their recovery (Yan et al, 2023). Effective pain management is crucial for promoting postoperative recovery. Opioids are commonly used postoperative analgesics. However, high doses of opioids can result in adverse effects, including respiratory depression, gastrointestinal symptoms, urinary retention, immunosuppression, and hyperalgesia (Jung et al, 2020). Therefore, minimizing opioid dosage in postoperative analgesia is crucial.

Furthermore, thoracoscopic surgery can cause cognitive dysfunction in patients (Huang et al, 2022). Surgical trauma can also trigger inflammatory stress, and excessive inflammatory response can exacerbate cognitive impairment, hinder pain relief, and delay postoperative recovery (Huang et al, 2022). Therefore, controlling inflammation and preventing cognitive impairment are essential for promoting postoperative recovery.

Esketamine, the S-enantiomer of ketamine, has a strong affinity for N-Methyl-D-aspartic acid (NMDA) receptors (NMDAR) and exhibits potent sedative and analgesic effects (Kan et al, 2024). Previous studies have reported that esketamine can alleviate postoperative depression, anxiety, and pain, inhibit inflammatory reactions, and reduce opioid-associated adverse impacts after thoracoscopic surgery (Gan et al, 2023; Lei et al, 2021). Moreover, erector spinae plane block (ESPB) is a nerve block approach that blocks somatic and visceral nerves, making it a commonly used method for pain relief in thoracic surgery (Helander et al, 2019). It achieved the effect of nerve block by injecting local anesthetic drugs into the plane of the erector spinae (also recognized as sacrospinalis). Additionally, the combination of esketamine and ESPB promotes postoperative recovery following thoracoscopic lung resection (Hu et al, 2025).

However, no study has evaluated the combined effects of esketamine and ESPB on opioid consumption, inflammatory stress, and cognitive function after thoracoscopic surgery. Hence, this study aims to investigate the effects of esketamine in combination with ESPB on these parameters. The findings may provide valuable clinical insights to promote postoperative recovery in patients undergoing thoracoscopic surgery.

Methods

Recruitment of Patients

This retrospective study collected the clinical data of patients who underwent thoracoscopic surgery at Jinhua Municipal Central Hospital, between January 2022 and January 2024. The inclusion criteria for patient selection were as follows: (1) patients who underwent thoracoscopic surgery; (2) patients aged >18 years; (3) those with American Society of Anesthesiologists (ASA) grade I, II, or III (American Society of Anesthesiologists, Committee on Economics, 2020); and (4) those with complete clinical data available. The exclusion criteria included: (1) patients with history of analgesic medication use before surgery; (2) patients with allergies to esketamine or use of alternative anesthesia regimen; (3) patients with conver-

sion to open surgery during the operation; (4) patients with severe liver and kidney dysfunction; and (5) patients with diagnosis of a mental illness.

Consequently, 114 patients who met the predetermined inclusion-exclusion criteria were included in the final analysis. The patient selection process is summarized in Fig. 1. Based on the differences in anesthesia methods, the patients were divided into the ESPB (n = 62) and esketamine + ESPB (n = 52) groups. Preoperative baseline characteristics of the patients were recorded, including sex, age, body mass index (BMI), ASA grade, smoking and drinking status, comorbidities, and years of education. The study was approved by the Jinhua Municipal Central Hospital Ethics Committee (Approval No: 20246501) and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from each study participant.

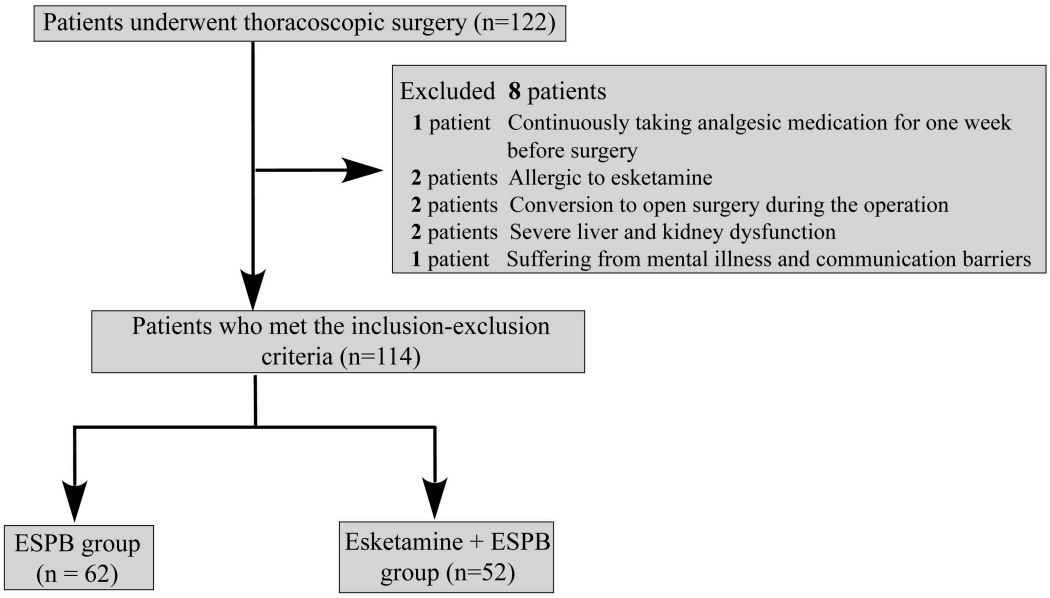

Fig. 1. A flow chart of patient recruitment. ESPB, erector spinae plane block.

Anesthesia Procedure

Patients were kept in fasting for 8 hours before surgery and were not allowed to drink fluids for 4 hours. Key indicators, including electrocardiogram (ECG), blood pressure, oxygen saturation and bispectral index (BIS) were continuously monitored throughout the process. Initially, a peripheral venous channel was established, and ESPB was conducted before anesthesia induction. The ESPB procedure involved utilizing an ultrasound probe to scan approximately 2.0–2.5 cm along the spinous processes at T4 and T5 in the midsagittal plane. Under ultrasound guidance, the needle was advanced through the trapezius, rhomboid, and erector spinae muscles from superficial to deep and 30 mL of 0.5% ropivacaine (H20052716, Qilu Pharmaceutical, Jinan, China) was injected between the erector spinae muscle and the transverse processes of T4 and T5.

After 15 minutes, an alcohol swab was used to test the temperature perception. Successful ESPB was determined by the loss of temperature sensation at T4–T6

spinous processes, extending from the posterior median line to the axillary line (Wang et al, 2023). After ESPB, anesthesia induction was initiated through intravenous administration of midazolam (0.05 mg/kg, H20143222, Jiangsu Enhua Pharmaceutical Co., Ltd., Xuzhou, China), sulfentanil (0.6 μg/kg, H20054171, Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China), propofol (2 mg/kg, Fresenius Kabi Austria GmbH, Graz, Austria), and cisatracurium besilate (0.9 mg/kg, H20213778, H20213438, Hangzhou Hongyou Pharmaceutical Technology Co., Ltd., Hangzhou, China). Mechanical ventilation was conducted through the transoral placement of a bronchial catheter. Furthermore, for maintaining anesthesia, sevoflurane was administered using a medical anesthesia machine (Carestation 620, GE Healthcare, Chicago, IL, USA), along with an intravenous infusion of propofol (4–8 mg/kg/h) and remifentanil (0.1–0.4 μg/kg/min, H20030197, Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China), maintaining a BIS level of 40–60.

Additionally, patients in the esketamine + ESPB group received an intravenous injection of esketamine (0.5 mg/kg, H20193336, Jiangsu Hengrui Medicine Co., Ltd., Lianyungang, China) before thoracoscopic surgery. Moreover, continuous intravenous injection of esketamine (0.25 mg/kg/h) was maintained until 30 minutes before the end of the procedure. Meanwhile, Ondansetron (8 mg, H10960148, Ningbo Tianheng Pharmaceutical Co., Ltd., Ningbo, China) was intravenously infused before the completion of surgery. After surgery, propofol and remifentanil injections were discontinued, and patients were transferred to the postanesthesia care unit for further monitoring.

Postoperative Awakening and Pain Management

The patients were considered fully awake when they regained consciousness and could respond to verbal stimuli or simple inquiries. The bronchial catheter was removed once the swallowing reflex was completely restored. Postoperative pain management was performed using a patient-controlled analgesia (PCA) pump.

In the ESPB + esketamine group, the analgesic drug included esketamine (1 mg/kg), sufentanil (1.5 μg/kg), and dexmedetomidine (200 μg, H20130027, Chenxin Pharmaceutical Co., Ltd., Jining, China), all diluted in saline to a total volume of 100 mL. In the ESPB group, the analgesic solution included sufentanil (1.5 μg/kg), and dexmedetomidine (200 μg), diluted in saline to 100 mL. The parameters of the analgesic pump were set as follows: a continuous infusion rate of 2 mL/h, a locking interval of 15 min, and a single additional bolus dose of 2 mL.

Additionally, postoperative pain was evaluated using the Numeric Rating Scale (NRS). NRS score, a commonly used tool for postoperative pain management, contains 0–10 scale, where 0 indicates no pain and 10 indicates the most severe pain (Farrar et al, 2001; Gerbershagen et al, 2011). Patients were asked to rate their pain by selecting a number from 0 to 10 based on their pain perception. Professional anesthesiologists documented NRS scores at 1, 6, 12, 24, and 48 h after the procedure. If the NRS score exceeded 4, intravenous oxycodone (H20203622, Northeast Pharmaceutical Group Shenyang First Pharmaceutical Co., Ltd., Shenyang, China) was infused as a rescue analgesic.

Perioperative Indicators

Intraoperative indicators of patients were recorded, including operation duration, total dosage of propofol and remifentanil, and intraoperative blood loss. Postoperative evaluations included awakening time, NRS scores at 1, 6, 12, 24, and 48 h after surgery, and oxycodone consumption at 24 and 48 h post-surgery. Furthermore, adverse reactions occurring within 48 hours post-surgery were also recorded, including nausea, vomiting, hallucinations, urinary retention, infection, and hematoma.

Inflammatory Markers

Fasting venous blood samples were collected from patients one day before the operation and on postoperative days 1 and 3. White blood cell (WBC) count was analyzed using a blood cell analyzer (BC5390, Myriad, ShenZhen, China). C-reactive protein (CRP) levels were assessed using the immune scattering turbidity method with an automatic biochemical analyzer (WonTech™OTA-400, Shenyang Wantai Medical Equipment Co., Ltd., Shenyang, China). Enzyme-linked immunosorbent assay (ELISA) was used to determine interleukin (IL)-6 (EHC007), tumor necrosis factor (TNF)-α (EHC103a), and procalcitonin (PCT) (EHC069; Beijing Xinbosheng Biotechnology, Beijing, China) levels.

Evaluation of Cognitive Function

The Montreal Cognitive Assessment Scale (MoCA) was used to assess the cognitive function one day before the operation and on the postoperative days 1 and 3. The MoCA score provides a clear and quantitative measure in evaluating cognitive function and is widely applied for assessing postoperative cognitive dysfunction (Luo and Li, 2021; Nasreddine et al, 2005). Patients completed the assessment scale queries, and a professional psychologist calculated the total score.

The MoCA has a total score of 30 points, with higher scores indicating better cognitive function. Additionally, for patients with $\leq$12 years of education, one point was added to their MOCA score, though the total score could not exceed 30 points (Chen et al, 2016).

Statistical Analysis

Statistical analysis was conducted using SPSS 21.0 software (IBM, Armonk, NY, USA). The Shapiro-Wilk test was applied to determine the normality of the data. Normally distributed measurement data were expressed as mean $\pm$ standard deviation and comparison between groups was performed using an independent sample *t*-test, while intra-group comparison was conducted using a paired sample *t*-test. The data with skew distribution was expressed as median and quartiles, and analyzed using the Mann-Whitney U test. Moreover, categorical variables were expressed as counts and percentages (n, %), and analyzed using the chi-square test with Yates' correction, or Fisher's exact test, as appropriate. The criterion for significant differences was set as $p < 0.05$.

Table 1. Comparison of general information between the two groups.

General information	ESPB group (n = 62)	Esketamine + ESPB group (n = 52)	t/χ^2	p-value
Sex (n, %)			0.010	0.921
Male	34 (54.84%)	29 (55.77%)		
Female	28 (45.16%)	23 (44.23%)		
Age (years)	42.32 ± 8.29	45.33 ± 9.35	1.821	0.071
BMI (Kg/m^2)	24.02 ± 3.37	24.68 ± 3.44	1.032	0.304
ASA grade (n, %)			0.074	0.964
I	11 (17.74%)	9 (17.31%)		
II	48 (77.42%)	41 (78.84%)		
III	3 (4.84%)	2 (3.85%)		
Smoking (n, %)			0.057	0.812
No	30 (48.39%)	24 (46.15%)		
Yes	32 (51.61%)	28 (53.85%)		
Drinking (n, %)			0.005	0.942
No	27 (43.55%)	23 (44.23%)		
Yes	35 (56.45%)	29 (55.77%)		
Comorbidities (n, %)			0.487	0.922
Hypertension	13 (20.97%)	10 (19.23%)		
Coronary heart disease	3 (4.84%)	2 (3.85%)		
Diabetes	8 (12.90%)	9 (17.31%)		
No comorbidities	38 (61.29%)	31 (59.62%)		
Years of education (n, %)			0.566	0.452
>12 years	33 (53.23%)	24 (46.15%)		
≤12 years	29 (46.77%)	28 (53.85%)		

ASA I, Normal healthy patient; ASA II, Patient with mild systemic disease; ASA III, Patient with severe systemic disease; ESPB, erector spinae plane block; BMI, body mass index; ASA, American Society of Anesthesiologists.

Results

Comparison of General Characteristics Between the Two Groups

The ESPB group included 34 males and 28 females, with a mean age of 42.32 ± 8.29 years. The esketamine + ESPB group consisted of 29 males and 23 females, with a mean age of 45.33 ± 9.35 years. There were no significant differences in general information between the two groups ($p > 0.05$, Table 1).

Comparison of Perioperative Indicators Between the Two Groups

As shown in Table 2, no significant differences were found between the ESPB and esketamine + ESPB groups regarding operation duration, amount of blood loss, and awakening time ($p > 0.05$). However, the dosage of propofol and remifentanil was significantly lower in the esketamine + ESPB group than in the ESPB group ($p = 0.046$, 0.013). In both groups, NRS scores increased at 6 h postoperatively compared to 1 h ($p < 0.05$) but gradually decreased at 12 h, 24 h, and 48 h postoperatively. Compared to the ESPB group, the NRS score was substantially reduced

Table 2. Comparison of perioperative indicators between the two groups.

Perioperative-related indicators	ESPB group (n = 62)	Esketamine + ESPB group (n = 52)	*t*/Z	*p*-value
Operation duration (min)	152.63 ± 24.77	147.00 ± 26.43	1.172	0.244
Dosage of propofol (mg)	812.92 ± 164.07	750.42 ± 166.13	2.014	0.046
Dosage of remifentanil (μg)	1205.73 ± 300.16	1080.31 ± 215.50	2.517	0.013
Amount of blood loss (mL)	70.71 ± 24.84	67.73 ± 19.10	0.707	0.481
Awakening time (min)	11.02 ± 2.41	11.17 ± 2.06	0.353	0.724
NRS scores after surgery (point)				
1 h	3 (3, 4)	3 (3, 4)	1.102	0.270
6 h	5 (4, 5)^{a}	4 (3, 4)^{a}	7.985	<0.001
12 h	4 (3, 4)^{b}	3 (2, 3)^{ab}	7.548	<0.001
24 h	3 (3, 3)^{b}	2 (2, 2)^{abc}	9.253	<0.001
48 h	2 (2, 2)^{abcd}	2 (1, 2)^{abc}	5.755	<0.001
Oxycodone consumption after surgery (mg)				
24 h	4.42 ± 1.01	3.73 ± 0.97	3.699	<0.001
48 h	6.59 ± 1.27^{d}	5.01 ± 0.88^{d}	7.573	<0.001

$^{a}p < 0.05$ vs. 1 h; $^{b}p < 0.05$ vs. 6 h; $^{c}p < 0.05$ vs. 12 h; $^{d}p < 0.05$ vs. 24 h. ESPB, erector spinae plane block; NRS, Numeric Rating Scale.

in the esketamine + ESPB group at 6 h, 12 h, 24 h, and 48 h postoperatively ($p < 0.001$). Additionally, oxycodone consumption at 24 h and 48 h postoperatively was lower in the esketamine + ESPB group than in the ESPB group ($p < 0.001$).

Furthermore, patients in both groups experienced adverse reactions within 48 h postoperatively, including nausea, vomiting, hallucinations, and urinary retention. These symptoms gradually alleviated or disappeared with the extension of time. The overall incidence of adverse reactions was 30.6% (19/62) in the ESPB group and 34.6% (18/52) in the esketamine + ESPB group, with no statistically significant difference ($p = 0.652$, Table 3).

Comparison of Inflammatory Marker Levels Between the Two Groups

There were no significant differences in WBC, CRP, PCT, IL-6, and TNF-α levels between the two groups one day before operation ($p > 0.05$). In both groups, these markers were significantly elevated one day after surgery compared to preoperative levels ($p < 0.05$) and subsequently declined by the third postoperative day ($p < 0.05$). Compared to the ESPB group, the Esketamine + ESPB group demonstrated substantially reduced PCT, IL-6, and TNF-α levels one day after operation ($p < 0.05$). Furthermore, WBC, CRP, PCT, IL-6, and TNF-α levels were significantly lower in the Esketamine + ESPB group by the third postoperative day ($p < 0.001$, Table 4).

Comparison of Cognitive Function Between the Two Groups

There was no significant difference in MoCA score between the two groups one day before the procedure. In both groups, the MoCA score decreased one day after surgery compared to preoperative levels ($p < 0.05$) and then increased at 3

Table 3. The adverse reactions occur within 48 h after the procedure.

Experimental group	Nausea	Vomiting	Hallucinations	Urinary retention	Infection	Hematoma	Overall incidence
ESPB group (n = 62)	7 (11.3%)	8 (12.9%)	3 (4.8%)	1 (1.6%)	0	0	19 (30.6%)
Esketamine + ESPB group (n = 52)	9 (17.3%)	7 (13.5%)	2 (3.8%)	0	0	0	18 (34.6%)
χ^2	0.849	0.008	0.041$^{\#}$	/	/	/	0.203
p-value	0.357	0.930	0.840$^{\#}$	>0.999$^{\$}$	/	/	0.652

$^{\#}$ chi test with Yates' correction; $^{\$}$ Fisher's exact test.

Table 4. Comparison of inflammatory indicator levels between the two groups.

Indicator		ESPB group (n = 62)	Esketamine + ESPB group (n = 52)	*t*	*p*-value
WBC (10^9/L)	1 day before operation	8.89 ± 1.11	9.13 ± 1.08	1.164	0.247
	1 day after operation	19.04 ± 1.87*	18.35 ± 2.15*	1.833	0.070
	3 days after operation	12.52 ± 2.19*&	10.75 ± 2.34*&	4.166	<0.001
CRP (mg/L)	1 day before operation	13.86 ± 3.54	12.85 ± 2.98	1.629	0.106
	1 day after operation	75.31 ± 17.14*	69.58 ± 16.42*	1.812	0.073
	3 days after operation	44.40 ± 14.81*&	32.24± 9.75*&	5.069	<0.001
PCT (ng/mL)	1 day before operation	1.12 ± 0.25	1.20 ± 0.19	1.894	0.061
	1 day after operation	5.95 ± 0.98*	5.62 ± 0.73*	2.005	0.047
	3 days after operation	2.19 ± 0.72*&	1.54 ± 0.54*&	5.365	<0.001
IL-6 (pg/mL)	1 day before operation	8.25 ± 1.17	8.31 ± 1.29	0.260	0.795
	1 day after operation	15.96 ± 3.51*	14.22 ± 2.75*	2.904	0.004
	3 days after operation	11.11 ± 2.60*&	9.11 ± 1.74&	4.728	<0.001
TNF-α (pg/mL)	1 day before operation	108.96 ± 17.25	112.25 ± 18.73	0.975	0.332
	1 day after operation	258.69 ± 21.22*	245.87 ± 23.78*	3.041	0.003
	3 days after operation	154.59 ± 19.56*&	130.24 ± 10.61*&	8.036	<0.001

*$p < 0.05$ vs. 1 day before operation; &$p < 0.05$ vs. 1 day after operation. WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α.

Table 5. Comparison of cognitive function between the two groups.

		ESPB group (n = 62)	Esketamine + ESPB group (n = 52)	z	*p*-value
MoCA score	1 day before operation	28 (26, 29)	27 (26, 28)	1.385	0.166
	1 day after operation	22 (21, 24)*	24 (23, 25)*	3.991	<0.001
	3 days after operation	25 (24, 27)*&	27 (26, 28)&	3.450	0.001

*$p < 0.05$ vs. 1 day before operation; &$p < 0.05$ vs. 1 day after operation. MoCA, Montreal Cognitive Assessment Scale.

days after operation ($p < 0.05$). Compared to the ESPB group, the MoCA score was substantially higher in the esketamine + ESPB group on postoperative days 1 and 3 ($p < 0.001$, $p = 0.001$, Table 5).

Discussion

Thoracoscopic surgery is widely adopted in clinical practice. However, some patients still experience postoperative pain, which significantly affects the quality of recovery (Sun et al, 2020). Therefore, a comprehensive pain management approach is crucial for postoperative recovery. This study observed that the combination of esketamine and ESPB offers adequate analgesia for patients undergoing thoracoscopic surgery, with better outcomes than ESPB alone. Postoperative pain, as evidenced by an increase in NRS scores, elevated 6 hours after surgery. However, pain was progressively relieved with the prolonged effect of analgesic drugs, and the NRS score decreased. Furthermore, NRS scores were significantly lower in the esketamine + ESPB group than in the ESPB group at 6 h, 12 h, 24 h, and 48 h postoperatively. Additionally, the consumption of opioid oxycodone for rescue analgesia was significantly lower in the esketamine + ESPB group compared to the ESPB group. Similarly, previous studies also investigated the analgesic effects of esketamine and ESPB. Esketamine was found to reduce both acute and chronic pain after thoracoscopic lung surgery (Lei et al, 2021), while ESPB has been reported to be effective in managing pain during thoracic surgery (Koo et al, 2022; Pirsaharkhiz et al, 2020).

No studies have explored the role of combining esketamine and ESPB in alleviating postoperative pain. However, the combined application of these two approaches appears to have better analgesic effects in thoracoscopic surgery, possibly due to their synergistic effect. The erector spinae muscle, which consists of the spinalis, longissimus thoracis, and iliocostalis muscles, is located along the back. ESPB method involves injecting anesthetic agents into the erector spinae muscle, where the anesthesia spreads to the surrounding spinal nerves and intercostal space, providing pain relief (Kot et al, 2019). However, the analgesic effect of ESPB is limited in duration, often requiring postoperative opioid administration. Esketamine, an NMDAR antagonist, has a strong binding affinity for NMDAR, opioid μ receptors, and monoamine receptors. Its analgesic effect is superior to ketamine (Kawczak et al, 2024; Mion and Himmelseher, 2024). Both esketamine and ESPB

offer analgesic effects, but in combination, they further enhance pain relief and reduce the need for postoperative opioid consumption. Additionally, ESPB inhibits the efferent activation of the sympathetic nervous system (Viderman et al, 2022), while esketamine stimulates the sympathetic nervous system (Suleiman et al, 2025) counteracting the inhibitory effect of ESPB. This interaction may help maintain stable blood pressure and heart rate, resulting in overall hemodynamic stability.

In this study, the combination of ESPB and esketamine did not significantly impact intraoperative indicators. There were no significant differences between the two groups regarding operation duration, blood loss, or awakening time. Although the combination of esketamine and ESPB has a higher incidence of postoperative adverse than in ESPB alone, the difference was statistically insignificant. These results suggest that the combination of esketamine and ESPB is safe during thoracoscopic surgery without elevating adverse effects. A cross-sectional study in Germany reported that 21.55% of emergency patients experienced side effects using low-dose esketamine, with no side effects; 2% of patients reported mild nausea and 0.8% experienced vivid dreams (Häske et al, 2023).

In our study, the most common adverse reactions were nausea and vomiting, followed by hallucinations; only one case exhibited mild urinary retention. These findings align with the previous research outcomes. Additionally, while ESPB may cause adverse reactions such as hematoma and puncture site infection (White et al, 2021), no adverse effects were observed in our study. For the nausea, vomiting, and hallucinations, patients did not receive treatment but were closely monitored. However, in more severe conditions, patients received antiemetic or central inhibitory drugs for symptomatic relief. For urinary retention, a urinary catheter was inserted to relieve symptoms, and patient's symptoms improved after discontinuing anesthesia drugs.

Surgical injuries can trigger inflammatory reactions, with inflammatory cells such as monocytes and macrophages releasing cytokines that trigger an inflammatory cascade. An excessive inflammatory response may lead to infection and organ dysfunction, limiting postoperative recovery (Chen et al, 2024). It has been reported that the serum IL-6 and TNF-α levels increase after video-assisted thoracic surgery (Menna et al, 2019). CRP and PCT are the major markers of inflammation and infection, and during thoracic surgery, elevated levels of these indicators are closely associated with infection and surgical outcomes (Caviezel et al, 2017; Perrella et al, 2022). In our study, a significant increase in WBC, CRP, PCT, IL-6, and TNF-α level was found on the first day after the operation compared to preoperative levels, indicating postoperative inflammatory stress. These indicators were decreased on day 3 after surgery, suggesting a gradual decline in the inflammatory response. Furthermore, compared to the ESPB group, the levels of WBC, CRP, PCT, IL-6, and TNF-α were substantially reduced in the ketamine group. The combined approach helped alleviate postoperative inflammatory stress after thoracoscopic surgery. Similarly, previous studies reported the efficacy of esketamine and ESPB in alleviating postoperative inflammation (Albayrak et al, 2024; Tu et al, 2021), aligning with our results.

Research has shown that thoracoscopic surgery can lead to postoperative cognitive impairment in patients (Wang et al, 2024). The underlying mechanism is assumed to involve inflammatory factors that enter the central nervous system through the blood-brain barrier or vagus nerve, promoting neuroinflammation and interfering with neural activity, thereby leading to cognitive dysfunction (Safavynia and Goldstein, 2019). This study observed a significant reduction in MoCA scores one day after thoracoscopic surgery compared to preoperative levels, suggesting that the procedure impairs cognitive function, consistent with previous research. The MoCA scores gradually increased over time, indicating a recovery in cognitive function. Moreover, the combination of esketamine and ESPB significantly improved cognitive function after thoracoscopic surgery, with a more pronounced effect than ESPB alone.

Despite several promising findings, this study has some limitations. Firstly, it was a retrospective study with a small sample size, which may introduce bias and limit the generalizability of the findings. To further validate these results, a prospective study with a large sample is warranted. Additionally, we did not investigate the long-term effects on pain, inflammation, and cognitive function. Previous research reported the incidence rate of chronic pain in 35.3% of cases after thoracoscopic surgery, significantly impacts patients' quality of life (Chen et al, 2023). Furthermore, future studies should investigate the long-term benefits of esketamine and ESPB through extended follow-up.

Conclusion

The combination of esketamine and ESPB effectively alleviates postoperative pain and reduced opioid consumption after thoracoscopic surgery. Furthermore, this combination approach helps relieve inflammatory stress and improve cognitive function recovery after surgery. Additionally, the combination does not increase adverse effects. Overall, the combined strategy shows superior analgesic effects compared to ESPB alone and improves postoperative rehabilitation. This study provides valuable clinical evidence for postoperative analgesia and rehabilitation after thoracoscopic surgery.

Key Points

- Postoperative pain significantly affects the quality of postoperative recovery after thoracoscopic surgery. The combination of esketamine and ESPB significantly reduces postoperative pain and attenuates opioid consumption.
- The combination of esketamine and ESPB reduces postoperative inflammatory stress.
- The combined approach effectively improves cognitive function after thoracoscopic surgery.
- The combination of esketamine and ESPB does not significantly increase the incidence of adverse reactions compared to ESPB alone.

Availability of Data and Materials

All data generated or analyzed during this study are available from the corresponding author upon reasonable request.

Author Contributions

JQZ and DZ designed the research study. YLC, LPS and DJX performed the research. HYL and CHH analyzed the data. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The research was approved by the Jinhua Municipal Central Hospital Ethics Committee (Approval No: 20246501) and implemented in accordance with the Declaration of Helsinki. All patients signed the informed consent form.

Acknowledgement

Not applicable.

Funding

This study is supported by Jinhua Science and Technology Plan Project Social Development Key Project (2023-3-120).

Conflict of Interest

The authors declare no conflict of interest.

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