Cite as: Luo L, Sun H. The effects of esketamine before skin incision and during abdominal closure on postoperative gastrointestinal function, pain levels and serum indexes in gastric cancer patients [J]. Chin J Clin Res, 2025, 38(10): 1500-1504.

DOI: 10.13429/j.cnki.cjcr.2025.10.008

The effects of esketamine before skin incision and during abdominal closure on postoperative gastrointestinal function, pain levels and serum indexes in gastric cancer patients

LUO Li, SUN Hu

Department of Anesthesiology, Second Affiliated Hospital of Hainan Medical University, Haikou, Hainan 570311, China

Corresponding author: SUN Hu, E-mail: sunhu09@163.com

Abstract: **Objective** To explore the effects of different administration timings of esketamine before skin incision and during abdominal closure on postoperative gastrointestinal function, pain levels and serum indexes in gastric cancer patients. **Methods** This prospective study included 94 gastric cancer patients who underwent laparoscopic surgery at the Second Affiliated Hospital of Hainan Medical University from January 10, 2022 to March 30, 2023. They were randomly divided into control group, group A, and group B based on computer codes. After excluding 2 cases in both groups A and B, each group had 30 cases, respectively. The patients in the control group were infused with equal volume of physiological saline before and during abdominal closure. Group A received intravenous infusion of esketamine before incision and physiological saline during abdominal closure. Group B was infused with physiological saline before skin incision, and esketamine at abdominal closure. The dosage of administration for both group A and group B was 0.4 mg/kg. Surgical and anesthesia indicators, postoperative gastrointestinal function indicators, pain levels [the degree of pain was assessed using the Visual Analogue Scale (VAS)at 4 hours postoperatively (T1), 8 hours postoperatively (T2), 24 hours postoperatively (T3), and 48 hours postoperatively (T4)], and serum indicators among three groups were compared. **Results** There was a statistically significant difference in the anesthesia recovery time among group A, group B, and the control group [(10.56±1.51)min, (13.05±1.02)min, (9.86±1.15)min, F=54.489, P<0.01]. The anesthesia recovery time of group A and the control group was shorter than that of group B (P<0.05), while there was no statistically significant difference in surgical time and intraoperative bleeding among the three groups (P> 0.05). There was no statistically significant difference (P>0.05) between group A and group B in the time of first postoperative exhaust, defecation, eating, and recovery of bowel sounds, but both groups were significantly shorter than the control group (P<0.05). Compared to T1, the VAS scores at T2-T4 were higher in all three groups (P<0.05). The VAS scores of group A at T2 and T3 were higher than those of group B, with statistical significance (P<0.05). The VAS scores of group A and group B at T2 - T4 points were both higher than those of the control group (P<0.05). levels of interleukin (IL)-6, IL-10, and C-reactive protein (CRP) in group A were significantly lower than those in group B and control group 24 h postoperatively, while levels of IL-6, IL-10, and CRP in group B were significantly lower than those in the control group (P<0.05). **Conclusion** There was no significant difference in the effect of using esketamine before and after abdominal closure on postoperative gastrointestinal function in patients undergoing gastric cancer surgery. However, compared to administration of anesthesia during abdominal closure, administration of anesthesia before skin incision can reduce the levels of inflammatory factors in patients and shorten the time of anesthesia recovery.

Keywords: Esketamine; Timing of administration; Gastric cancer; Gastrointestinal function; Serum indicators

Fund program: Hainan Province Science and Technology Project Contract (BK20190632)

Gastric cancer is a common digestive tract tumor, with approximately 1.089 million new cases reported worldwide each year. It ranks third in both incidence and mortality among various malignant tumors in China [1-3]. Clinically, surgery is the main treatment approach, and laparoscopic surgery for gastric cancer is widely applied. However, inadequate postoperative analgesia may lead to stress responses in patients, a lowered pain threshold, hinder wound healing, affect intestinal function recovery, and prolong hospital stays [4]. High-quality analgesia is a crucial element for promoting rapid recovery after surgery and plays a positive role in improving the quality of postoperative recovery. Esketamine, the enantiomer of ketamine, is a non-specific N-methyl-D-aspartate (NMDA) receptor antagonist with good analgesic effects and a high safety profile. However, the impact of administering esketamine before skin incision versus during abdominal closure on postoperative gastrointestinal function and serum markers in patients remains unclear [5-6]. This study aims to explore the effects of the timing of esketamine administration on postoperative gastrointestinal function and serum markers in gastric cancer patients. The results are reported as follows.

1 Materials and methods

1.1 General information

This study was a prospective investigation, involving 94 gastric cancer patients who underwent laparoscopic surgery under general anesthesia with endotracheal intubation at the Second Affiliated Hospital of Hainan Medical University between January 10, 2022, and March 30, 2023. Inclusion criteria: (1) histopathological diagnosis of gastric cancer, clinical stage I–II; (2) indications for laparoscopic radical gastric cancer surgery; (3) informed consent obtained. Exclusion criteria: (1) allergies to dexmedetomidine, propofol, cisatracurium besilate, sufentanil, or esketamine; (2) coagulation disorders; (3) use of analgesics or sedatives within 3 months prior to admission. Exclusion criteria: (1) conversion to open surgery; (2) need for secondary surgery; (3) transfer to another hospital or withdrawal from the study; (4) postoperative infection; (5) postoperative blood loss >500 mL. Patients were randomly assigned into Group A (patients 1-32), Group B (patients 33-64), and the control group (patients 65-94) using computer-generated random numbers. After excluding patients according to the exclusion criteria, Group A included 30 patients, Group B included 30 patients, and the control group included 30 patients. In Group A, 17 males and 13 females, with a body mass index (BMI) ranging from 19.6 to 27.3 (24.26 ± 2.21) kg/m², and ages between 32 and 73 years (54.87 ± 5.78), American Society of Anesthesiologists (ASA) classification: 5 patients with ASA I, 25 patients with ASA II. In Group B, 17 males and 13 females, with a BMI ranging from 19.2 to 27.8 (23.93 ± 2.39) kg/m², and ages between 31 and 75 years (55.17 ± 5.74), ASA classification: 4 patients with ASA I, 26 patients with ASA II. In the control group, 15 males and 15 females, with a BMI ranging from 19.1 to 28.5 (23.84 ± 2.45) kg/m², and ages between 30 and 76 years (53.63 ± 8.08), ASA classification: 5 patients with ASA I, 25 patients with ASA II. There were no statistically significant differences in gender, BMI, age, or ASA classification among the three groups ($P > 0.05$). This study was approved by the Ethics Committee of the Second Affiliated Hospital of Hainan Medical University (Approval No. LW2021019).

1.2 Methods

All gastric cancer patients were instructed to fast for 8 hours and avoid drinking for 4 hours before surgery. Upon entering the operating room, an intravenous access was established, and Ringer's lactate (Manufacturer: Zhejiang Shapais Pharmaceuticals Co., Ltd.; Drug approval No. H20063251; Specification: 500 mL) was infused. The patients' basic vital signs were closely monitored, including heart rate, diastolic blood pressure, systolic blood pressure, blood oxygen saturation, respiratory rate, and bispectral index (BIS). Before anesthesia induction, oxygen was inhaled through a mask for 5 minutes. Then, 1 μg/kg of dexmedetomidine hydrochloride injection (Manufacturer: Hunan Kelun Pharmaceutical Co., Ltd.; National Drug Approval Number: H20183150; Specification: 1 mL: 100 μg) was intravenously pumped, followed by continuous pumping of dexmedetomidine hydrochloride injection at 0.2 μg/(kg·h) until 40 minutes before the end of surgery.

Anesthesia induction: Intravenous infusion of propofol (Manufacturer: Xi'an Libang Pharmaceutical Co., Ltd.; National Drug Approval Number: H19990282; Specification: 20 mL: 0.2 g) at 1.5-2 mg/kg, cisatracurium besilate (Manufacturer: Beijing Tide Pharmaceutical Co., Ltd.; National Drug Approval Number: H20203696; Specification: 5 mL: 10 mg) at 25 mg/kg, and Sufentanil Citrate Injection (Manufacturer: Yichang Humanwell Pharmaceutical Co., Ltd.; National Drug Approval Number: H20054172; Specification: 2 mL: 100 μg) at 0.3-0.5 μg/kg. Mechanical ventilation was initiated after satisfactory muscle relaxation, with parameters set as follows: tidal volume 6-8 mL/kg, respiratory rate 10-12 breaths/min, and end-tidal carbon dioxide 35-40 mmHg. During the operation, intravenous anesthesia was maintained with BIS at 40-60. The maintenance drug doses were: sufentanil 10-20 μg/(kg·h), propofol 5-10 mg/(kg·h), and cisatracurium besilate 0.15 mg/(kg·h). Anesthesiologists adjusted the drug doses in real time according to the patients' intraoperative vital signs and surgical progress.

Both Group A and Group B received intravenous pumping of Esketamine Hydrochloride Injection (Manufacturer: Jiangsu Hengrui Medicine Co., Ltd.; National Drug Approval Number: H20193336; Specification: 2 mL: 50 mg) at 0.4 mg/kg. Administration timing: Group A received the drug before skin incision and 20 mL of normal saline during abdominal closure; Group B received the drug during abdominal closure and 20 mL of normal saline before skin incision. Control group: The control group received equal volume of normal saline before skin incision and during abdominal closure.

1.3 Observation indicators

(1) Surgical and anesthesia-related parameters, including operation time, intraoperative blood loss, and anesthesia recovery time. (2) Postoperative gastrointestinal function indicators, including time to first flatus, first bowel movement, resumption of eating, and return of bowel sounds. (3) Pain levels assessed using the visual analog scale (VAS) at 4 hours (T1), 8 hours (T2), 24 hours (T3), and 48 hours (T4) postoperatively [7]. (4) Serum markers, 4 mL of fasting elbow venous blood was collected from patients in the morning when they entered the operating room and 24 hours after surgery. The blood was centrifuged for 10 minutes using a centrifuge (Manufacturer: Fresenius Kabi AG; National Medical Device Registration Number: Import 20183100418; Model: AmiCORE). After serum separation, the levels of interleukin (IL)-6, IL-10, and C-reactive protein (CRP) were detected using an automatic chemiluminescence immunoassay analyzer (Manufacturer: Beckman Coulter, Inc., USA; National Medical Device Registration Number: Import 20242220249; Model: DxI 9000).

1.4 Statistical methods

Data were analyzed using SPSS 26.0 software. Kolmogorov-Smirnov test confirmed normal distribution of continuous variables, which were expressed as $\bar{x}\pm s$.

Comparisons between groups were conducted using one-way analysis of variance (ANOVA) and repeated-measures analysis of variance for time-dependent data. Pairwise comparisons were performed using LSD-*t* test. Categorical data were expressed as case (%), and chi-square tests were used. $P < 0.05$ was considered statistically significant.

2 Results

2.1 Comparison of surgery and anesthesia-related indicators among the three groups

The anesthesia recovery time in Group A and the control group was shorter than that in Group B ($P < 0.05$), while there were no statistically significant differences in operation time or intraoperative blood loss among the three groups ($P > 0.05$). See **Table 1.**

2.2 Comparison of postoperative gastrointestinal function-related indicators among the three groups

There were no statistically significant differences in the time to first postoperative exhaust, defecation, eating, or recovery of bowel sounds between Group A and Group B ($P > 0.05$), but these times in Group A and Group B were significantly shorter than those in the control group ($P < 0.05$). See **Table 2.**

2.3 Comparison of pain condition among the three groups

Compared with T1, the VAS scores of the three groups at T2-T4 were higher ($P < 0.05$). The VAS score of Group A at T2-T3 was higher than that of Group B, with a statistically significant difference ($P < 0.05$). The VAS scores of Group A and Group B at T1-T4 were lower than those of the control group ($P < 0.05$). In the repeated measures ANOVA, the time effect, inter-group effect, and time-group interaction effect of the three groups were statistically significant ($P < 0.05$). See **Table 3.**

2.4 Comparison of serum indicators among the three groups

When entering the operating room, there were no statistically significant differences in the levels of IL-6, IL-10, or CRP among the three groups ($P > 0.05$). At 24 hours after surgery, the serum indicators of each group were significantly higher than those when entering the operating room ($P < 0.05$). At 24 hours after surgery, the levels of IL-6, IL-10, and CRP in Group A were significantly lower than those in Group B and the control group, and the levels in Group B were significantly lower than those in the control group ($P < 0.05$). See **Table 4.**

Tab.1 Comparison of surgery and anesthesia-related indicators among the three groups (n=30, $\bar{x}\pm s$)

Group	Operation time（min）	Intraoperative blood loss（mL）	Anesthesia recovery time（min）
Group A	212.37±27.44	156.90±59.25	10.56±1.51[a]
Group B	215.27±24.84	158.67±63.34	13.05±1.02
Control group	216.35±26.17	165.25±58.74	9.86±1.15[a]
***F* value**	0.186	0.159	54.489
***P* value**	0.831	0.853	＜0.001

Note: Compared with Group B, [a]$P < 0.05$.

Tab.2 Comparison of postoperative gastrointestinal function-related indicators among the three groups (n=30, d, $\bar{x}\pm s$)

Group	Time to return of bowel sounds bowel sounds (d)	Time to first flatus (d)	Time to resumption of eating (d)	Time to first defecation (d)
Group A	0.82±0.51[a]	1.79±0.58[a]	2.18±0.43[a]	2.69±0.53[a]
Group B	0.78±0.45[a]	1.73±0.53[a]	2.04±0.39[a]	2.75±0.62[a]
Control group	1.36±0.74	2.35±0.82	2.88±0.45	3.55±0.65
***F* value**	9.349	8.160	33.787	19.073
***P* value**	＜0.001	＜0.001	＜0.001	＜0.001

Note: Compared with the control group, [a]$P < 0.05$.

Tab.3 Comparison of VAS scores among the three groups (n=30, points, $\bar{x}\pm s$)

Group	T1	T2	T3	T4
Group A	1.09±0.60[a]	1.85±0.58[a]	2.17±0.62[a]	1.52±0.55[a]
Group B	0.99±0.41[a]	1.43±0.61[ab]	1.57±0.43[ab]	1.34±0.40[a]
Control group	1.57±0.33	2.23±0.65	2.58±0.52	1.90±0.61
$F_{time}/F_{group}/F_{interaction}$		60.579/61.873/3.792		
$P_{time}/P_{group}/P_{interaction}$		0.001/0.001/0.013		

Tab.4 Comparison of serum indicators among the three groups （$\bar{x}\pm s$）

Group	IL-6（pg/mL）		IL-10（pg/mL）		CRP（mg/L）	
	At admission to the operating room	24 h after surgery	At admission to the operating room	24 h after surgery	At admission to the operating room	24 h after surgery
Group A	1.52±0.58	36.38±2.85[ab]	1.86±0.42	22.36±3.42[ab]	2.33±0.52	82.33±5.17[ab]
Group B	1.54±0.60	41.36±2.97[abc]	1.88±0.50	28.30±3.18[abc]	2.38±0.56	90.36±5.28[abc]
Control group	1.49±0.45	45.22±2.74[a]	1.87±0.48	32.45±3.65[a]	2.35±0.51[a]	95.45±5.88[a]
***F* value**	0.063	72.295	0.014	65.887	0.068	44.155
***P* value**	0.939	＜0.001	0.986	＜0.001	0.935	＜0.001

3 Discussion

Laparoscopic gastric cancer surgery is invasive, which can cause abnormal hemodynamics, affect the nervous and immune systems, and result in moderate to severe postoperative pain [8-10]. Poor pain control can affect the recovery of body function. Esketamine has antidepressant, anti-inflammatory, sedative, and analgesic effects. It can achieve sedative and analgesic effects by non-competitively antagonizing NMDA receptors, acting on opioid receptors, gamma-aminobutyric acid (GABA) receptors, cholinergic receptors to activate dopamine receptors and L-type voltage-gated calcium channels, thereby blocking sodium ion channels and activating potassium ion channels [11-12]. Studies have shown that esketamine has significantly better sedative and analgesic effects than ketamine, and has less impact on patients' mental state, circulatory system stability, and respiratory depression, with faster postoperative recovery [13-15].

There were no statistically significant differences in operation time or intraoperative blood loss between group A and group B. However, from a neurobiological

perspective, the anesthesia recovery time in group A and the control group was shorter than that in group B. This may be because esketamine administration before skin incision (group A) allowed the drug to take effect in the early stage of surgery, regulated the excitability of the central nervous system, and reduced the continuous stimulation of surgical trauma on the nervous system, thereby helping patients recover from anesthesia earlier. In contrast, esketamine administration during abdominal closure (group B) may only affect the nervous system in the late stage of surgery. At this time, surgical trauma has caused a certain degree of cumulative damage to the nervous system, leading to a relatively prolonged recovery time. Consistent with previous studies, Zhang *et al.* [16] also found that intravenous injection of esketamine during skin suture prolonged patients' recovery time. However, the prolonged recovery time in this study did not meet the criteria for delayed recovery, indicating that although the timing of esketamine administration affects recovery time, it remains safe within a reasonable range. Future studies can further explore the optimal timing of esketamine administration before the end of surgery (e.g., administering the drug in a specific stage shortly before the end of surgery) to minimize recovery time without affecting its sedative and analgesic effects.

Previous literature suggests that esketamine can increase gastrointestinal motility indicators such as gastric antral contraction frequency, gastric antral contraction amplitude, and gastric antral motility index in intensive care unit patients, and accelerate gastrointestinal peristalsis [17]. In this study, the time to first postoperative exhaust, defecation, eating, and recovery of bowel sounds in group A and group B was significantly shorter than that in the control group, which fully confirms the positive role of esketamine in promoting the recovery of gastrointestinal function. In addition, relevant Meta-analyses also suggest that ketamine analgesia can significantly improve gastrointestinal motility in patients with traumatic brain injury [18]. However, there are few studies on the effect of different administration timings on the recovery of gastrointestinal function. In this study, there were no statistically significant differences in postoperative gastrointestinal function indicators between gastric cancer patients who received esketamine pumping before skin incision and those who received it before abdominal closure. The reason may be that the promoting effect of esketamine on gastrointestinal function is persistent throughout the entire process of surgical trauma and anesthesia, and is not affected by the difference in administration timing between the early and late stages of surgery [19].

The analgesic mechanism of esketamine is mainly related to its antagonism of NMDA receptors. By blocking NMDA receptors, esketamine can inhibit the transmission and amplification of pain signals in the central nervous system, thereby reducing the degree of pain in patients. This study compared the VAS scores of the three groups at different time points. The results showed that esketamine application significantly reduced the degree of early postoperative pain, and patients who received the drug before abdominal closure had lower pain degrees at 8 and 24 hours after surgery. This suggests that esketamine administration during abdominal closure may provide more effective analgesia in specific postoperative time periods, which may be related to the body's sensitivity to pain and the pharmacokinetics (distribution and metabolism) of the drug in the body.

The quality of anesthesia and postoperative recovery is a key indicator for evaluating patients' early postoperative recovery and anesthesia effect. Surgical trauma and acute pain stimulation can activate the body's inflammatory response system, leading to increased levels of inflammatory factors such as IL-6, IL-10, and CRP. This study showed that administering a certain dose of esketamine to patients before surgical trauma and acute pain stimulation can significantly reduce systemic inflammation in the early postoperative period, which is consistent with the research results of Lin *et al.* [20]. The reason may be that esketamine reduces the inflammatory response by inhibiting the activation of inflammatory cells and the synthesis of inflammatory factors. Early administration can intervene in the early stage of inflammatory response initiation, inhibit the transmission and amplification of inflammatory signals, and thus reduce the degree of inflammatory response.

In conclusion, for gastric cancer patients undergoing laparoscopic surgery, there is no statistically significant difference in the effect of 0.4 mg/kg esketamine administration before skin incision and before abdominal closure on the recovery of postoperative gastrointestinal function. However, intravenous pumping of esketamine before skin incision has better effects in reducing postoperative inflammatory factor levels and promoting early recovery. This study has the following limitations: First, it is a single-center study with a small sample size, resulting in poor representativeness. Second, it did not analyze the antidepressant effect of different doses of esketamine, nor its effect on the quality of postoperative recovery. Therefore, it is still necessary to design multicenter prospective studies with larger sample sizes, set more influencing factors, increase observation indicators and follow-up time, to finally determine the optimal administration timing, dose, and safety of esketamine.

Conflict of interest None

Reference

[1] Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. CA Cancer J Clin, 2021, 71(3): 209-249.

[2] Cao W, Chen HD, Yu YW, et al. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020[J]. Chin Med J (Engl), 2021, 134(7): 783-791**[In Chinese]**

[3] Chinese Society of Gastric Cancer, China AntiCancer Association. China Anti-Cancer Association guidelines for holistic integrative management of gastric cancer(Lite Version)[J]. Chin J Clin Oncol, 2022, 49(14): 703-710. **[In Chinese]**

[4] He J, Chen WQ, Li ZS, et al. Guidelines for screening, early diagnosis and early treatment of gastric cancer in China (2022, Beijing)[J]. Chin J Dig Surg, 2022, 21(7): 827-851. **[In Chinese]**

[5] Lin GW, Hu QL, Yang ZL. Effect of esketamine combined with butorphanol for postoperative analgesia of women after cesarean women and its influence on the postpartum status of the women[J]. Chin J Fam Plan, 2022, 30(5): 1050-1054. **[In Chinese]**

[6] Zhu Y, Wang H, Wu QL. Effects of sub-anesthetic esketamine on regional cerebral oxygen saturation and awakening quality in elderly patients undergoing laparoscopic radical gastrectomy for gastric cancer[J]. Jiangsu Med J, 2023, 49(11): 1157-1160. **[In Chinese]**

[7] Shafshak TS, Elnemr R. The visual analogue scale versus numerical rating scale in measuring pain severity and predicting disability in low back pain[J]. J Clin Rheumatol, 2021, 27(7): 282-285.

[8] Zhang YH, Li JF, Tang J, et al. Study on stress, immune changes and complications of laparoscopic radical gastrectomy for advanced gastric cancer[J]. Chin J Clin Res, 2018, 31(2): 150-153. **[In Chinese]**

[9] Bai RH, Jia ZY, Zhang XT, et al. Anesthetic effect of dexmedetomidine in laparoscopic D2 radical gastrectomy and its influence on hemodynamics, visual analogue scale and Ramsay sedation score after operation[J]. Cancer Res Clin, 2019, 31(10): 666-669. **[In Chinese]**

[10] Wang Y, Zuo F, Han FM, et al. Inflammatory response and pain factors after laparoscopic resection of advanced gastric cancer[J]. China J Endosc, 2022, 28(4): 19-24. **[In Chinese]**

[11] Nowak W, Grendas LN, Sanmarco LM, et al. Pro-inflammatory monocyte profile in patients with major depressive disorder and suicide behaviour and how ketamine induces anti-inflammatory M2 macrophages by NMDAR and mTOR[J]. EBioMedicine, 2019, 50: 290-305.

[12] Surjan J, Grossi JD, Del Porto JA, et al. Efficacy and safety of subcutaneous esketamine in the treatment of suicidality in major depressive disorder and bipolar depression[J]. Clin Drug Investig, 2022, 42(10): 865-873.

[13] Zhou Y, Wang YY, Deng HH. Progress in clinical application of esketamine combined with other anesthetic drugs[J]. Chin J Clin Res, 2024, 37(8): 1160-1163, 1171. **[In Chinese]**

[14] Li LY, Xin Y, Peng XY, et al. Effect of different administration methods of esketamine on postoperative pain after thoracoscopic lung surgery[J]. Chin J Clin Res, 2024, 37(8): 1192-1196. **[In Chinese]**

[15] Singh JB, Fedgchin M, Daly E, et al. Intravenous esketamine in adult treatment-resistant depression: a double-blind, double-randomization, placebo-controlled study[J]. Biol Psychiatry, 2016, 80(6): 424-431.

[16] Zhang C, He JQ, Shi QY, et al. Subanaesthetic dose of esketamine during induction delays anaesthesia recovery a randomized, double-blind clinical trial[J]. BMC Anesthesiol, 2022, 22(1): 138.

[17] Chan K, Burry LD, Tse C, et al. Impact of ketamine on analgosedative consumption in critically ill patients: a systematic review and meta-analysis[J]. Ann Pharmacother, 2022, 56(10): 1139-1158.

[18] Patanwala AE, Martin JR, Erstad BL. Ketamine for analgosedation in the intensive care unit: a systematic review[J]. J Intensive Care Med, 2017, 32(6): 387-395.

[19] Jiang LL, Du XX. Research progress on the clinical application of esketamine[J]. Chin J Clin Res, 2024, 37(12): 1830-1833. **[In Chinese]**

[20] Lin YM, Fu MJ, Chen JS. Study on the molecular mechanism of esketamine inhibiting LPS-induced astrocyte apoptosis and inflammatory response by up-regulating the expression of miR-138-5p[J]. Int J Lab Med, 2023, 44(8): 908-913. **[In Chinese]**

Submission Received: 2025-02-04/ **Revised:**2025-03-17

·论　著·

切皮前与关腹时艾司氯胺酮给药对胃癌患者术后胃肠功能、疼痛程度及血清指标的影响

罗丽，　孙虎
海南医科大学第二附属医院麻醉科，海南 海口 570311

摘要：目的　探讨艾司氯胺酮在切皮前与关腹时不同给药时机对胃癌患者术后胃肠功能恢复、疼痛程度及血清炎症因子水平的影响。**方法**　本研究为前瞻性分析，纳入2022年1月10日至2023年3月30日经海南医科大学第二附属医院接受腹腔镜手术治疗的94例胃癌患者，依据计算机编号随机分为对照组、A组和B组，A组和B组各剔除2例后，最终每组均为30例。对照组患者切皮前和关腹时均泵注等容量生理盐水，A组于切皮前静脉泵注艾司氯胺酮，关腹时泵注生理盐水；B组切皮前泵注生理盐水，于关腹时泵注艾司氯胺酮，A组和B组给药剂量均为0.4 mg/kg。比较3组患者的手术与麻醉相关指标、术后胃肠功能相关指标、疼痛情况[术后4 h(T1)、术后8 h(T2)、术后24 h(T3)、术后48 h(T4)采用视觉模拟评分(VAS)评估疼痛程度]、血清指标。**结果**　A组、B组和对照组麻醉苏醒时间比较差异有统计学意义[(10.56±1.51)min，(13.05±1.02)min，(9.86±1.15)min，F=54.489，P<0.01]。A组和对照组麻醉苏醒时间短于B组(P<0.05)，而3组手术时间、术中出血量比较差异无统计学意义(P>0.05)。A组和B组术后首次排气、排便、进食、肠鸣音恢复的时间对比差异无统计学意义(P>0.05)，但两组相较于对照组均有明显缩短(P<0.05)。相较于T1，T2~T4时间点3组的VAS评分均更高(P<0.05)。T2、T3时的A组VAS评分高于B组(P<0.05)，A组与B组T1~T4时间点的VAS评分均高于对照组(P<0.05)。术后24 h，A组白细胞介素(IL)-6、IL-10、C反应蛋白(CRP)水平显著低于B组和对照组，B组IL-6、IL-10、CRP水平显著低于对照组(P<0.05)。**结论**　胃部恶性肿瘤手术患者在切皮前和关腹前应用艾司氯胺酮对术后胃肠功能的影响无差异，但相较于关腹前用药，切皮前用药可降低患者炎症因子水平，缩短麻醉苏醒时间。

关键词：艾司氯胺酮；给药时机；胃癌；胃肠功能；血清指标
中图分类号：R735.2　**文献标识码：**A　**文章编号：**1674-8182(2025)10-1500-05

The effects of esketamine before skin incision and during abdominal closure on postoperative gastrointestinal function, pain levels and serum indexes in gastric cancer patients

LUO Li, SUN Hu
Department of Anesthesiology, Second Affiliated Hospital of Hainan Medical University, Haikou, Hainan 570311, China
Corresponding author: SUN Hu, E-mail: sunhu09@163.com

Abstract: Objective　To explore the effects of different administration timings of esketamine before skin incision and during abdominal closure on postoperative gastrointestinal function, pain levels and serum indexes in gastric cancer patients. **Methods**　This prospective study included 94 gastric cancer patients who underwent laparoscopic surgery at the Second Affiliated Hospital of Hainan Medical University from January 10, 2022 to March 30, 2023. They were randomly divided into control group, group A, and group B based on computer codes. After excluding 2 cases in both groups A and B, each group had 30 cases, respectively. The patients in the control group were infused with equal volume of physiological saline before and during abdominal closure. Group A received intravenous infusion of esketamine before incision and physiological saline during abdominal closure. Group B was infused with physiological

DOI：10.13429/j.cnki.cjcr.2025.10.008
基金项目：海南省科技项目合同书(BK20190632)
通信作者：孙虎，E-mail：sunhu09@163.com
出版日期：2025-10-20

QR code for English version

saline before skin incision, and esketamine at abdominal closure. The dosage of administration for both group A and group B was 0.4 mg/kg. Surgical and anesthesia indicators, postoperative gastrointestinal function indicators, pain levels [the degree of pain was assessed using the Visual Analogue Scale (VAS) at 4 hours postoperatively (T1), 8 hours postoperatively (T2), 24 hours postoperatively (T3), and 48 hours postoperatively (T4)], and serum indexes among three groups were compared. **Results** There was a statistically significant difference in the anesthesia recovery time among group A, group B, and the control group [(10.56±1.51) min, (13.05±1.02) min, (9.86±1.15) min, F=54.489, P<0.01]. The anesthesia recovery time of group A and the control group was shorter than that of group B (P<0.05), while there was no statistically significant difference in surgical time and intraoperative bleeding among the three groups (P>0.05). There was no statistically significant difference (P>0.05) between group A and group B in the time of first postoperative exhaust, defecation, eating, and recovery of bowel sounds, but both groups were significantly shorter than the control group (P<0.05). Compared to T1, the VAS scores at T2-T4 were higher in all three groups (P<0.05). The VAS scores of group A at T2 and T3 were higher than those of group B, with statistical significance (P<0.05). The VAS scores of group A and group B at T2-T4 points were both higher than those of the control group (P<0.05). Levels of interleukin(IL)-6, IL-10, and C-reactive protein (CRP) in group A were significantly lower than those in group B and control group 24 h postoperatively, while levels of IL-6, IL-10, and CRP in group B were significantly lower than those in the control group (P<0.05). **Conclusion** There was no significant difference in the effect of using esketamine before and after abdominal closure on postoperative gastrointestinal function in patients undergoing gastric cancer surgery. However, compared to administration of anesthesia during abdominal closure, administration of anesthesia before skin incision can reduce the levels of inflammatory factors in patients and shorten the time of anesthesia recovery.

Keywords: Esketamine; Timing of administration; Gastric cancer; Gastrointestinal function; Serum indicators

Fund program: Hainan Province Science and Technology Project Contract (BK20190632)

胃癌是一种常见的消化道肿瘤，全球范围内胃癌每年新增108.9万例，在国内各类恶性肿瘤中发病率和死亡率均居第三位[1-3]。临床多以手术切除为主要治疗手段，腹腔镜胃癌手术在临床上广泛应用，但术后镇痛不足会导致患者术后出现应激反应，疼痛阈值降低，不利于伤口愈合，影响肠道功能恢复，延长住院时间[4]。优质的镇痛是促进患者术后快速康复的重要环节，对改善术后恢复质量具有积极意义。艾司氯胺酮是氯胺酮的对映异构体，属于非特异性N-甲基-D-天冬氨酸(NMDA)受体拮抗剂，其镇痛效果较好且安全可靠。然而，在切皮前给药和关腹时给药对患者术后胃肠功能及血清指标影响的差异并不明确[5-6]。本研究将深入探讨艾司氯胺酮给药时机对胃癌患者术后胃肠功能及血清指标的影响，现报道如下。

1 资料与方法

1.1 一般资料 本研究为前瞻性研究，研究对象为2022年1月10日至2023年3月30日于海南医科大学第二附属医院接受气管插管全身麻醉下腹腔镜手术治疗胃癌患者，共94例。纳入标准：(1) 手术病理组织检查为胃癌，且临床分期为Ⅰ~Ⅱ期；(2) 符合腹腔镜下胃癌根治术适应证者；(3) 知情同意且签署同意书。排除标准：(1) 对右美托咪定、丙泊酚、苯磺顺阿曲库铵、舒芬太尼、艾司氯胺酮药物过敏者；(2) 凝血功能障碍者；(3) 入院前3个月服用过镇痛、镇静药物者。剔除标准：(1) 转为开腹手术者；(2) 需二次手术者；(3) 中途转院或退出研究者；(4) 术后感染者；(5) 术后失血量>500 mL者。用计算机编号随机分组法分为A组(1~32号)、B组(33~64号)和对照组(65~94号)。根据剔除标准，A组剔除1例失血量>500 mL患者和1例术后感染患者，B组剔除1例转为开腹手术患者和1例需行二次手术患者，最终A组30例，B组30例，对照组30例。A组男性17例，女性13例，身体质量指数(BMI) 19.6~27.3 (24.26±2.21) kg/m^2，年龄32~73 (54.87±5.78)岁，美国麻醉医师协会(ASA)分级为Ⅰ级5例，Ⅱ级25例。B组男性17例，女性13例，BMI 19.2~27.8(23.93±2.39)kg/m^2，年龄31~75(55.17±5.74)岁，ASA分级为Ⅰ级4例，Ⅱ级26例。对照组男性15例，女性15例，BMI 19.1~28.5(23.84±2.45)kg/m^2，年龄30~76(53.63±8.08)岁，ASA分级为Ⅰ级5例，Ⅱ级25例。3组性别、BMI、年龄、ASA分级比较差异无统计学意义(P>0.05)。本研究经海南医科大学第二附属医院伦理委员会批准(审批号LW2021019)。

1.2 方法 所有胃癌患者手术前均禁饮4 h，禁食8 h，入手术室后建立静脉通道，输注乳酸钠林格(生产厂家：浙江莎普爱思药业股份有限公司；国药准字

H20063251；规格：500 mL），密切监测患者的各项基础生命体征，包括心率、舒张压、收缩压、血氧饱和度、呼吸频率、脑电双频指数（bispectral index，BIS）。麻醉诱导前面罩吸氧 5 min，静脉泵注盐酸右美托咪定注射液（生产厂家：湖南科伦制药有限公司；国药准字 H20183150；规格：1 mL∶100 μg）1 μg/kg，之后持续泵注盐酸右美托咪定注射液 0.2 μg/（kg·h），直至术毕前 40 min。麻醉诱导：静脉输注丙泊酚（生产厂家：西安力邦制药有限公司；国药准字 H19990282；规格：20 mL∶0.2 g）1.5～2 mg/kg、苯磺顺阿曲库铵（生产厂家：北京泰德制药股份有限公司；国药准字 H20203696；规格：5 mL∶10 mg）25 mg/kg、枸橼酸舒芬太尼注射液（生产厂家：宜昌人福药业有限责任公司；国药准字 H20054172；规格：2 mL∶100 μg）0.3～0.5 μg/kg，肌松满意后予以机械通气，参数设置：潮气量 6～8 mL/kg，呼吸频率 10～12 次/min，呼气末二氧化碳 35～40 mmHg。手术过程中静脉麻醉维持 BIS 40～60。维持药物剂量：舒芬太尼 10～20 μg/（kg·h），丙泊酚 5～10 mg/（kg·h），苯磺顺阿曲库铵 0.15 mg/（kg·h），麻醉医师根据患者术中生命体征参数以及手术进程予以实时调整药物剂量。A 组与 B 组均予以盐酸艾司氯胺酮注射液（生产厂家：江苏恒瑞医药股份有限公司；国药准字 H20193336；规格：2 mL∶50 mg）静脉泵注 0.4 mg/kg。给药时机：A 组于切皮前给药，关腹时泵注生理盐水 20 mL；B 组于关腹时给药，切皮前则泵注生理盐水 20 mL。对照组患者切皮前和关腹时均泵注等容量生理盐水。

1.3　观察指标　（1）手术与麻醉相关指标，包括手术时间、术中出血量、麻醉苏醒时间。（2）术后胃肠功能相关指标，包括术后首次排气、排便、进食、肠鸣音恢复的时间。（3）疼痛情况，分别于术后 4 h（T1）、术后 8 h（T2）、术后 24 h（T3）、术后 48 h（T4）采用视觉模拟评分（VAS）[7]评价患者疼痛程度。（4）血清指标，分别于入室时、术后 24 h 取患者清晨空腹肘静脉血液 4 mL，用离心机（生产厂家：费森尤斯卡比股份有限公司；国械注进 20183100418；型号规格：AmiCORE）离心处理 10 min，分离血清后，用全自动化学发光免疫分析仪［生产厂家：贝克曼库尔特（美国）股份有限公司；国械注进 20242220249；型号规格：DxI 9000］检测白细胞介素（interleukin，IL）-6、IL-10、C 反应蛋白（C-reactive protein，CRP）水平。

1.4　统计学方法　选用 SPSS 26.0 软件分析数据。经 Kolmogorov-Smirnov 检验验证计量资料符合正态分布，用 $\bar{x}\pm s$ 表示，多组间比较采用单因素方差分析及重复测量资料的方差分析，两两比较采用 LSD-t 检验；计数资料用例（%）表示，进行 χ^2 检验。$P<0.05$ 为差异有统计学意义。

2　结　果

2.1　3 组手术与麻醉相关指标比较　A 组和对照组麻醉苏醒时间短于 B 组（$P<0.05$），而 3 组手术时间、术中出血量比较差异无统计学意义（$P>0.05$）。见表 1。

2.2　3 组术后胃肠功能相关指标比较　A 组和 B 组术后首次排气、排便、进食、肠鸣音恢复的时间比较差异无统计学意义（$P>0.05$），但 A 组和 B 组相较于对照组均明显缩短（$P<0.05$）。见表 2。

2.3　3 组疼痛情况比较　相较于 T1，T2～T4 时间点 3 组 VAS 评分均更高（$P<0.05$）。T2～T3 时间点的 A 组 VAS 评分高于 B 组，差异有统计学意义（$P<0.05$），A 组与 B 组 T1～T4 时间点的 VAS 评分均低于对照组（$P<0.05$）。重复方差测量中，3 组的时间效应、组间效应、时间和组间交互效应有统计学意义（$P<0.05$）。见表 3。

表 1　3 组手术与麻醉相关指标对比　（n=30，$\bar{x}\pm s$）

Tab.1　Comparison of surgery and anesthesia indexes among the three groups　（n=30，$\bar{x}\pm s$）

组别	手术时间（min）	术中出血量（mL）	麻醉苏醒时间（min）
A 组	212.37±27.44	156.90±59.25	10.56±1.51[a]
B 组	215.27±24.84	158.67±63.34	13.05±1.02
对照组	216.35±26.17	165.25±58.74	9.86±1.15[a]
F 值	0.186	0.159	54.489
P 值	0.831	0.853	<0.001

注：与 B 组比较，[a]P<0.05。

表 2　3 组术后胃肠功能相关指标对比　（d，$\bar{x}\pm s$）

Tab.2　Comparison of postoperative gastrointestinal function indexes among the three groups　（d，$\bar{x}\pm s$）

组别	例数	术后肠鸣音恢复时间	术后首次排气时间	术后首次进食时间	术后首次排便时间
A 组	30	0.82±0.51[a]	1.79±0.58[a]	2.18±0.43[a]	2.69±0.53[a]
B 组	30	0.78±0.45[a]	1.73±0.53[a]	2.04±0.39[a]	2.75±0.62[a]
对照组	30	1.36±0.74	2.35±0.82	2.88±0.45	3.55±0.65
F 值		9.349	8.160	33.787	19.073
P 值		<0.001	<0.001	<0.001	<0.001

注：与对照组比较，[a]P<0.05。

表 3　3 组 VAS 评分对比　（n=30，分，$\bar{x}\pm s$）

Tab.3　Comparison of VAS scores among the three groups　（n=30，point，$\bar{x}\pm s$）

组别	T1	T2	T3	T4
A 组	1.09±0.60[a]	1.85±0.58[ac]	2.17±0.62[ac]	1.52±0.55[ac]
B 组	0.99±0.41[a]	1.43±0.61[abc]	1.57±0.43[abc]	1.34±0.40[ac]
对照组	1.57±0.33	2.23±0.65[c]	2.58±0.52[c]	1.90±0.61[c]
$F_{时间}/F_{组间}/F_{交互}$ 值		60.579/61.873/3.792		
$P_{时间}/P_{组间}/P_{交互}$ 值		0.001/0.001/0.013		

注：与对照组比较，[a]P<0.05；与 A 组比较，[b]P<0.05；与本组 T1 时间点比较，[c]P<0.05。

2.4 3组血清指标比较 入室时，3组患者组间IL-6、IL-10、CRP水平比较差异无统计学意义（$P>0.05$）；术后24 h各组血清指标均显著高于入室时（$P<0.05$）。术后24 h，A组IL-6、IL-10、CRP显著低于B组和对照组，B组IL-6、IL-10、CRP显著低于对照组（$P<0.05$）。见表4。

表4 3组血清指标对比 （$\bar{x}\pm s$）

Tab.4 Comparison of serum indexes among the three groups （$\bar{x}\pm s$）

项目	例数	IL-6(pg/mL)		IL-10(pg/mL)		CRP(mg/L)	
		入室时	术后24 h	入室时	术后24 h	入室时	术后24 h
A组	30	1.52±0.58	36.38±2.85^{ab}	1.86±0.42	22.36±3.42^{ab}	2.33±0.52	82.33±5.17^{ab}
B组	30	1.54±0.60	41.36±2.97^{abc}	1.88±0.50	28.30±3.18^{abc}	2.38±0.56	90.36±5.28^{abc}
对照组	30	1.49±0.45	45.22±2.74^{a}	1.87±0.48	32.45±3.65^{a}	2.35±0.51	95.45±5.88^{a}
F值		0.063	72.295	0.014	65.887	0.068	44.155
P值		0.939	<0.001	0.986	<0.001	0.935	<0.001

注：与入室时比较，$^{a}P<0.05$；与对照组比较，$^{b}P<0.05$；与A组比较，$^{c}P<0.05$。

3 讨 论

腹腔镜胃癌手术具有创伤性，会导致患者血流动力学发生异常，影响神经系统、免疫系统，造成术后中重度疼痛[8-10]。若疼痛控制不佳，会影响机体功能恢复。艾司氯胺酮同时具备抗抑郁、抗炎和镇静镇痛作用，能够通过非竞争性拮抗NMDA受体以及作用于阿片类受体、γ-氨基丁酸受体、胆碱能受体激活多巴胺受体、L型电压门控钙通道，进而阻断钠离子通道和激活钾离子通道实现镇静镇痛作用[11-12]。有研究发现，艾司氯胺酮镇静镇痛作用显著优于氯胺酮，而且对患者精神、循环系统稳定性、呼吸抑制等方面的影响较小，术后苏醒更快[13-15]。

A组和B组患者手术时间、术中出血量差异无统计学意义，但从神经生物学角度分析，A组和对照组麻醉苏醒时间短于B组，这可能是因为切皮前给药（A组）使得艾司氯胺酮在手术早期就开始发挥作用，调节了中枢神经系统的兴奋性，减少了手术创伤对神经系统的持续刺激，从而有助于患者更早地从麻醉状态恢复。而关腹时给药（B组）可能在手术后期才开始对神经系统产生影响，此时手术创伤已经对神经系统造成了一定程度的累积性影响，导致苏醒时间相对延长。与以往研究对比，Zhang等[16]的研究也发现缝皮时静脉注射艾司氯胺酮会延长患者苏醒时间。然而，本研究中苏醒时间的延长并未达到苏醒延迟的标准，提示艾司氯胺酮的使用时机虽然影响苏醒时间，但在合理范围内仍具有安全性。未来研究可以进一步探索手术结束前使用艾司氯胺酮的最佳时机，例如在手术即将结束前的某个特定阶段提前给药，以最大程度缩短苏醒时间，同时不影响其镇静镇痛效果。

既往文献提示，艾司氯胺酮能够提高重症监护室患者胃窦收缩频率、胃窦收缩幅度、胃窦运动指数等胃肠运动指标，加快胃肠蠕动[17]。本研究中，A组与B组术后首次排气、排便、进食、肠鸣音恢复时间相较于对照组均有明显缩短，充分验证了艾司氯胺酮在促进胃肠功能恢复中具有积极作用。此外，相关meta分析报道也认为氯胺酮镇痛能够明显改善创伤性颅脑损伤患者胃肠运动功能[18]。但关于不同给药时机对患者胃肠功能恢复情况的影响研究较少，本研究结果中，切皮前泵注艾司氯胺酮和关腹前泵注艾司氯胺酮，胃癌患者术后的胃肠功能指标差异无统计学意义，分析其原因在于在手术创伤和麻醉的整个过程中，艾司氯胺酮对胃肠功能的促进作用具有一定的持续性，不受给药时机在手术前后阶段的差异影响[19]。

艾司氯胺酮的镇痛作用机制主要与其对NMDA受体的拮抗有关。通过阻断NMDA受体，艾司氯胺酮可以抑制疼痛信号在中枢神经系统的传递和放大，从而降低患者疼痛程度。本研究比较了3组患者在不同时间点下的VAS评分，结果显示，应用艾司氯胺酮能够显著降低患者术后早期疼痛程度，且关腹前用药后患者在术后8、24 h疼痛程度更低，提示关腹时用药可能在术后特定时间段内提供更有效的镇痛效果，可能与此时机体对疼痛的敏感性以及药物在体内的分布和代谢动力学有关。麻醉和手术后恢复质量是评价患者术后早期恢复以及麻醉效果的重要评价指标。手术创伤和急性疼痛刺激会激活机体的炎症反应系统，导致炎症因子如IL-6、IL-10、CRP等水平升高。本研究显示在手术创伤和急性疼痛刺激前提前予以患者一定剂量艾司氯胺酮能够在术后早期显著降低全身炎症，与林玉美等[20]研究结果一致。分析其原因在于艾司氯胺酮通过抑制炎症细胞活化和因子合成来降低炎症反应，早期给药可以在炎症反应启动的早期阶段进行干预，抑制炎症信号传导和放大，从而减轻炎症反应程度。

综上所述，行腹腔镜手术治疗的胃癌患者在切皮前和关腹前应用0.4 mg/kg艾司氯胺酮对术后胃肠功能恢复的影响差异无统计学意义，但切皮前静脉泵注艾司氯胺酮在降低术后炎症因子水平，提早苏醒的应用效果更好。本研究存在以下不足：第一，本次为单中心研究，纳入病例数较少，代表性欠佳；第二，未分析不同剂量艾司氯胺酮的抗抑郁和术后恢复质量、改善效果。因此仍需设计更大样本量的多中心前瞻性研究，设置更多的影响因素，增加观察指标和随访时间，以最终确定艾司氯胺酮的使用时机、剂量和安全性。

利益冲突 无

参考文献

[1] Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. CA Cancer J Clin, 2021, 71(3): 209-249.

[2] Cao W, Chen HD, Yu YW, et al. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020[J]. Chin Med J (Engl), 2021, 134(7): 783-791.

[3] 中国抗癌协会胃癌专业委员会. CACA胃癌整合诊治指南(精简版)[J]. 中国肿瘤临床, 2022, 49(14): 703-710.

[4] 赫捷, 陈万青, 李兆申, 等. 中国胃癌筛查与早诊早治指南(2022, 北京)[J]. 中华消化外科杂志, 2022, 21(7): 827-851.

[5] 林贵文, 胡青林, 杨志来. 艾司氯胺酮复合布托啡诺对剖宫产术后镇痛效果及产后状态的影响[J]. 中国计划生育学杂志, 2022, 30(5): 1050-1054.

[6] 朱越, 王昊, 吴巧玲. 亚麻醉剂量艾司氯胺酮对腹腔镜胃癌根治术老年患者局部脑氧饱和度及苏醒质量的影响[J]. 江苏医药, 2023, 49(11): 1157-1160.

[7] Shafshak TS, Elnemr R. The visual analogue scale versus numerical rating scale in measuring pain severity and predicting disability in low back pain[J]. J Clin Rheumatol, 2021, 27(7): 282-285.

[8] 张焱辉, 李靖锋, 唐俊, 等. 腹腔镜胃癌根治术对进展期胃癌的应激、免疫变化及并发症的影响[J]. 中国临床研究, 2018, 31(2): 150-153.

[9] 白日虹, 贾志勇, 张晓婷, 等. 腹腔镜胃癌D2根治术中右美托咪定麻醉效果及对术后血流动力学、疼痛视觉模拟评分及Ramsay镇静评分的影响[J]. 肿瘤研究与临床, 2019, 31(10): 666-669.

[10] 王颖, 左方, 韩凤梅, 等. 进展期胃癌腹腔镜切除术后炎性反应和疼痛因子研究[J]. 中国内镜杂志, 2022, 28(4): 19-24.

[11] Nowak W, Grendas LN, Sanmarco LM, et al. Pro-inflammatory monocyte profile in patients with major depressive disorder and suicide behaviour and how ketamine induces anti-inflammatory M2 macrophages by NMDAR and mTOR[J]. E Bio Medicine, 2019, 50: 290-305.

[12] Surjan J, Grossi JD, Del Porto JA, et al. Efficacy and safety of subcutaneous esketamine in the treatment of suicidality in major depressive disorder and bipolar depression[J]. Clin Drug Investig, 2022, 42(10): 865-873.

[13] 周颖, 王韵烨, 邓海洪. 艾司氯胺酮联合其他麻醉药物的临床应用进展[J]. 中国临床研究, 2024, 37(8): 1160-1163, 1171.

[14] 李靓宇, 辛艳, 彭霄艳, 等. 艾司氯胺酮不同给药方式对胸腔镜肺手术术后疼痛的影响[J]. 中国临床研究, 2024, 37(8): 1192-1196.

[15] Singh JB, Fedgchin M, Daly E, et al. Intravenous esketamine in adult treatment-resistant depression: a double-blind, double-randomization, placebo-controlled study[J]. Biol Psychiatry, 2016, 80(6): 424-431.

[16] Zhang C, He JQ, Shi QY, et al. Subanaesthetic dose of esketamine during induction delays anaesthesia recovery a randomized, double-blind clinical trial[J]. BMC Anesthesiol, 2022, 22(1): 138.

[17] Chan K, Burry LD, Tse C, et al. Impact of ketamine on analgosedative consumption in critically ill patients: a systematic review and meta-analysis[J]. Ann Pharmacother, 2022, 56(10): 1139-1158.

[18] Patanwala AE, Martin JR, Erstad BL. Ketamine for analgosedation in the intensive care unit: a systematic review[J]. J Intensive Care Med, 2017, 32(6): 387-395.

[19] 姜乐乐, 杜晓宣. 艾司氯胺酮临床应用的研究进展[J]. 中国临床研究, 2024, 37(12): 1830-1833.

[20] 林玉美, 符明君, 陈基胜. 艾司氯胺酮通过上调miR-138-5p表达抑制LPS诱导的星形胶质细胞凋亡和炎症反应的分子机制研究[J]. 国际检验医学杂志, 2023, 44(8): 908-913.

收稿日期：2025-02-04 **修回日期**：2025-03-17 **编辑**：王宇