中国临床研究 Chin J Clin Res, December 2025, Vol.38, No.12

Cite as: Hao CH, Luan HF, Yang C, Gu XJ. Effect of opioid-free anesthesia on postoperative recovery quality in patients undergoing laparoscopic cholecystectomy [J]. Chin J Clin Res, 2025, 38(12):1822-1826.

DOI: 10.13429/j.cnki.cjcr.2025.12.007

Effect of opioid-free anesthesia on postoperative recovery quality in patients undergoing laparoscopic cholecystectomy

HAO Conghui*, LUAN Hengfei, YANG Chun, GU Xiaojiao

** Department of Anesthesiology, The Affiliated Lianyungang Hospital of Xuzhou Medical University, The First People's Hospital of Lianyungang, Lianyungang, Jiangsu 222000, China*

Corresponding author: GU Xiaojiao, E-mail: 675906152@qq.com

Abstract: Objective To explore the application effect of opioid-free general anesthesia in laparoscopic cholecystectomy and its impact on postoperative recovery quality in patients. **Methods** This was a prospective parallel randomized controlled trial. A total of 74 patients undergoing elective laparoscopic cholecystectomy at the First People's Hospital of Lianyungang from October 2022 to August 2023 were enrolled. They were divided into two groups using a random number table: the opioid group (OA group, n=37) and the opioid-free group (OFA group, n=37) . The primary outcome was the 15-item Quality of Recovery Score (QoR-15) on postoperative day 1 and day 2. Secondary outcomes included opioid-related adverse reactions on postoperative day 1, mean arterial pressure (MAP) , and bispectral index (BIS) values at six time points: upon entering the operating room (T0) , at the start of induction in OA group (T1) or 10 min after dexmedetomidine induction in OFA group (T1) , after tracheal intubation (T2) , before surgery (T3) , after skin incision (T4) , and after extubation (T5) . **Results** The QoR-15 scores of the OFA group were significantly higher than those of the OA group on postoperative day 1[110.0 (105.5, 112.0) *vs* 79.0 (76.5, 80.5)]and day 2[128.0 (127.0, 131.0) *vs* 94.0 (91.0, 97.0)] (P<0.05) . Compared with OA group, OFA group had lower incidence rate of adverse reactions such as headache[18.92% (7/37) *vs* 0, χ^2 =5.680, P=0.017], fatigue[21.62% (8/37) *vs* 2.7% (1/37) , χ^2 =4.554, P=0.033], and xerostomia[16.22% (6/37) *vs* 0, χ^2 =4.534, P=0.033]. There were statistically significant differences in MAP between the two groups at T1 and T3 (P<0.01) . **Conclusion** The application of opioid-free general anesthesia in laparoscopic cholecystectomy can significantly improve patient's postoperative recovery quality, reduce the incidence of postoperative adverse reaction such as headache, fatigue and xerostomia headache, and maintain more stable perioperative MAP.

Keywords: Opioid-free anesthesia; Postoperative recovery quality; Esketamine; Dexmedetomidine; Laparoscopic cholecystectomy

Fund program: Outstanding Youth Fund of Jiangsu Provincial Natural Science Foundation (BK 20240054)

Laparoscopic surgery, with advantages such as minimal invasiveness and fast recovery, has become the first-choice treatment for gallbladder diseases. However, despite continuous advances in surgical techniques, postoperative complications including varying degrees of abdominal incision pain, nausea and vomiting, and incision infection remain important factors affecting the quality of patient recovery [1]. In traditional anesthesia approaches, opioid anesthesia (OA) is widely used due to its potent analgesic effect, but its adverse reactions—such as nausea, vomiting, and respiratory depression—cannot be ignored. These may prolong hospital stays and compromise postoperative recovery quality [2]. Opioid-free anesthesia (OFA), which avoids opioid use during the perioperative period and adopts a multimodal analgesia strategy, has demonstrated multiple advantages in clinical practice. First, OFA significantly reduces opioid-related adverse reactions including respiratory depression, postoperative nausea and vomiting (PONV), and gastrointestinal function suppression, thereby enhancing patient safety and comfort. Second, by combining regional blocks (e.g., nerve block or epidural anesthesia), nonsteroidal anti-inflammatory drugs (NSAIDs), dexmedetomidine, and other adjuvant agents, OFA effectively controls surgical stress responses and pain while avoiding immunosuppression and addiction risks associated with opioids. It is particularly suitable for high-risk patients with obesity, obstructive sleep apnea, or a history of substance abuse [3]. Additionally, OFA promotes accelerated postoperative recovery by enabling early eating and ambulation, shortening hospital stays. Overall, as an innovative anesthesia strategy, OFA holds significant value in optimizing perioperative management and reducing opioid dependence [4]. It has also been well applied in obstetrics and gynecology, gastrointestinal laparoscopic surgery, and thyroid and breast surgery [5-6]. This study uses the 15-item Quality of Recovery (QoR-15) scale to evaluate the impact of OFA on postoperative recovery quality in patients undergoing laparoscopic cholecystectomy, as this scale comprehensively reflects patients' postoperative recovery status [7]. The aim of this study is to explore the effect of OFA on postoperative recovery quality in laparoscopic cholecystectomy patients, providing new insights and evidence for clinical anesthesia practice.

1 Materials and Methods

1.1 Study Design and Participants

This prospective, randomized, single-blind clinical study was conducted at the First People's Hospital of Lianyungang, from October 2022 to August 2023, with all patients signing informed consent forms. A total of 74 patients undergoing elective laparoscopic cholecystectomy were recruited, who were aged between 20 and 60 years and classified as American Society of Anesthesiologists (ASA) physical status class I or II. Exclusion criteria included (1) preoperative severe cardiac or pulmonary diseases; (2) history of allergy or contraindications to esketamine or NSAIDs such as severe risk of elevated blood pressure and intracranial pressure, poorly controlled or untreated hypertension, untreated or undertreated hyperthyroidism, and gastrointestinal bleeding; (3) mental illness or other chronic pain conditions; (4) being pregnant, lactating, or menstruating women. According to a computer-generated random number table, the patients were randomly divided into two groups with 37 cases each. The opioid-free anesthesia (OFA) group consisting of 20 males and 17 females, and the opioid anesthesia (OA) group including 18 males and 19 females. There were no statistically significant differences in general data like gender, age, body mass index (BMI), and ASA class between the two groups (P>0.05; see **Table 1**). Allocation results were sealed in numbered opaque envelopes, which were opened by anesthetic nurses only after patients signed the informed consent forms to carry out grouping, and both the implementers and subjects were blinded to the grouping information. This study was approved by the Medical Ethics Committee of the First People's Hospital of Lianyungang (Ethics approval number KY-20220711001-01).

1.2 Methods

Both groups of patients were instructed to fast for 8 hours and abstain from fluids for 2 hours preoperatively. All patients undergoing elective cholecystectomy were screened following routine procedures based on the inclusion and exclusion criteria. Upon entering the operating room, all patients received routine preoperative preparations, including electrocardiography (ECG), non-invasive blood pressure measurement, bispectral index (BIS) monitoring, and peripheral oxygen saturation (SpO_2) detection. Intravenous access was established for medication administration and fluid therapy. Preoperatively, 10 mg of azasetron and 10 mg of dexamethasone were intravenously injected to prevent nausea and vomiting.

Anesthesia induction phase: for OA group, anesthesiologists slowly administered propofol (2-4 mg/kg) intravenously until loss of consciousness, followed by cisatracurium (0.2 mg/kg) and sufentanil (0.3 μg/kg). Anesthesia induction was initiated 5 minutes before tracheal intubation. For OFA group, 10 minutes before induction, dexmedetomidine hydrochloride (0.6 μg/kg) was infused intravenously at a constant rate. Subsequently, propofol (2-4 mg/kg) and cisatracurium (0.2 mg/kg) were injected intravenously in sequence, and esketamine (0.2 mg/kg) was given 2 minutes before tracheal intubation for induction.

Both groups received the inhaled anesthetic sevoflurane (1.5%-4.0%). The concentration of sevoflurane in the oxygen/air mixture was titrated [fraction of inspired oxygen (FiO_2) = 0.6, total gas flow = 2 L/min] to maintain a BIS value of 40-60. The ventilation mode was set to volume-controlled ventilation (VCV) with parameters: FiO_2 = 60%, oxygen flow = 2 L/min, tidal volume (VT) = 6-8 mL/kg, respiratory rate = 12 times/min, and inspiratory-expiratory ratio = 1:2. The end-tidal carbon dioxide partial pressure ($PETCO_2$) was maintained at 35-45 mmHg. During anesthesia, vital signs of patients in both groups were closely monitored, and all parameters were recorded every 5 minutes until transfer to the post-anesthesia care unit (PACU). Mechanical ventilation parameters were adjusted to maintain normal $P_{ET}CO_2$(35-40 mmHg). For analgesia, ropivacaine was used for local infiltration anesthesia, and 200 mg of acetaminophen was intravenously infused 30 minutes before the end of surgery. Postoperative rescue analgesia: when the Visual Analogue Scale (VAS) score ≥4, 40 mg of parecoxib sodium was intravenously administered with an interval ≥6 hours, and the maximum dose within 24 hours was 80 mg.

1.3 Observation Indicators

(1) Primary indicator: the recovery quality of all patients on the postoperative day 1 and 2 was evaluated using the QoR-15 scale. The QoR-15 scale includes 5 dimensions: physical comfort (5 items), emotional state (4 items), physical independence (2 items), psychological support (2 items), and pain (2 items). A higher score indicates better postoperative recovery quality.

(2) Secondary indicators: Opioid-related adverse reactions (nausea, vomiting, headache, fatigue, drowsiness, xerostomia, and postoperative respiratory depression). Respiratory depression was defined as SpO_2 <90% lasting ≥30 seconds within 24 hours postoperatively, or abnormal respiratory rate/ventilation requiring intervention.

Mean arterial pressure (MAP) and BIS values at the following time points: T0 (upon entering the operating room), T1 (start of induction in OA group / 10 minutes after dexmedetomidine induction in OFA group), T2 (after tracheal intubation), T3 (before surgery), T4 (after skin incision), and T5 (after extubation). Operative time, anesthesia start time, extubation time, and PACU stay .

1.4 Statistical Methods

Data were processed using SPSS 25.0 software. Measurement data were expressed as $\bar{x} \pm s$ and compared using independent sample t test. Continuous variables not following a normal distribution were

expressed as M (P_{25}, P_{75}) and compared using non-parametric tests. Count data were expressed as case (%) and compared using chi-square test or its correction method. The Holm correction method was used to adjust the original P values for postoperative adverse reactions. A P value <0.05 was considered statistically significant.

2 Results

2.1 Comparison of surgery-related indicators

There were no statistically significant differences in operative time, extubation time, or PACU stay time between the two groups (P>0.05). See **Table 1**.

2.2 Comparison of postoperative recovery quality

On the postoperative day 1, the scores of pain, physical comfort, physical independence, emotional state, and total QoR-15 score in the OA group were significantly lower than those in the OFA group (P<0.01). On the postoperative day 2, the total QoR-15 score and scores of all 5 dimensions in the OA group were significantly lower than those in the OFA group (P<0.01). See **Table 2**.

2.3 Comparison of adverse reactions

The incidence rates of headache, fatigue, and xerostomia in the OFA group were significantly lower than those in the OA group, with statistically significant differences (P<0.05). There were no statistically significant differences in the incidence rates of other adverse reactions such as nausea, vomiting, drowsiness, and respiratory depression between the two groups (P>0.05). See **Table 3**.

2.4 Comparison of MAP and BIS values at different intraoperative time points

There were statistically significant differences in MAP between the two groups at T1 and T3 time points (P<0.05), and the fluctuation amplitude of MAP in the OFA group was smaller. There were no statistically significant differences in BIS values between the two groups at T0-T5 time points (P>0.05). See **Figure 1**.

Tab.1 Comparison of general data and surgical-related indicators between two groups (n=37)

Group	Male/female (cases)	Age (years, $\bar{x}\pm s$)	BMI (kg/m^2, $\bar{x}\pm s$)	ASA classification (I/II, cases)	Operation time (min, $\bar{x}\pm s$)	Extubation time (min, $\bar{x}\pm s$)	PACU stay time (min, $\bar{x}\pm s$)
OA	18/19	45.6±10.8	23.6±2.3	19/18	48±14.7	14.5±2.3	34.4±3.8
OFA	20/17	44.2±9.9	23.5±2.0	22/15	43±11.9	13.7±2.2	35.4±3.1
***t*/χ^2 value**	0.216	0.617	0.202	0.491	1.637	1.505	1.150
***P* value**	0.642	0.454	0.546	0.320	0.148	0.783	0.368

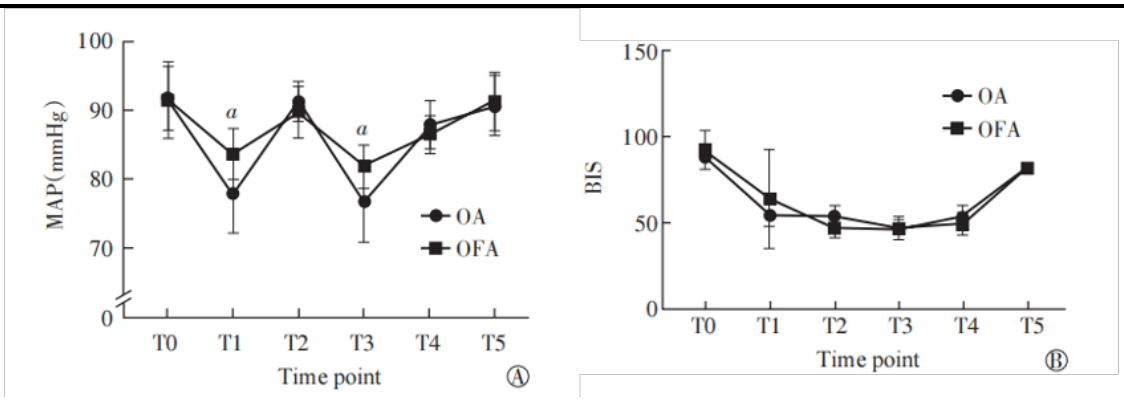
Tab.2 Comparison of QoR-15 postoperative recovery quality scores between two groups [n = 37, $M(P_{25}, P_{75})$]

Group	Time	Pain	Physical comfort	Physical independence	Psychological support	Emotional state	Total score
OA	**Postoperative day 1**	11.0(10.0,11.5)	16.0(15.0,16.5)	14.0(13.0,14.0)	15.0(15.0,16.0)	23.0(21.5,24.0)	79.0(76.5,80.5)
	Postoperative day 2	13.0(12.0,13.0)	20.0(18.0,21.0)	16.0(15.5,17.0)	18.0(16.0,19.0)	27.0(25.0,30.0)	94.0(91.0,97.0)
OFA	**Postoperative day 1**	15.0(14.0,16.0)	29.0(28.0,32.0)	16.0(15.0,17.0)	15,0(15.0,16.5)	32.0(30.5,35.0)	110.0(105.5,112.0)
	Postoperative day 2	20.0(18.0,20.0)	36.0(35.0,37.0)	17.0(16.5,18.0)	19.0(17.0,20.0)	37.0(36.0,39.0)	128.0(127.0,131.0)
***Z*/*P* $_{\text{postoperative day 1}}$ value**		7.266/<0.001	7.452/<0.001	7.119/<0.001	0.479/0.632	7.435/<0.001	7.414/<0.001
***Z*/*P* $_{\text{postoperative day 2}}$ value**		7.552/<0.001	7.442/<0.001	3.422/<0.001	2.337/<0.001	7.427/<0.001	7.419/<0.001

Note: $Z/P_{\text{postoperative day 1}}$ value refer to the Z value and P value from the comparison between the two groups on postoperative day 1; $Z/P_{\text{postoperative day 2}}$ value refer to the Z value and P value from the comparison between the two groups on postoperative day 2.

Tab. 3 Comparison of the incidence of adverse reactions between two groups (n = 37, case)

Group	Nausea	Vomiting	Headache	Fatigue	Drowsiness	Xerostomia	Postoperative respiratory depression
OA	7	5	7	8	6	6	7
OFA	1	1	0	1	2	0	1
χ^2 value	3.504	1.632	5.680	4.544	1.261	4.534	3.504
***P* value**	0.061	0.201	0.017	0.033	0.261	0.033	0.061



Note: A, MAP; B, BIS ; ^aP<0.05 when compared with Group OA.

Fig.1 Comparison of intraoperative MAP and BIS values between two groups

3 Discussion

The results of this study indicate that in patients undergoing elective laparoscopic cholecystectomy, compared with the OA group, the OFA group showed significantly improved postoperative recovery quality, particularly in dimensions of the QoR-15 questionnaire such as emotional state, physical comfort, physical independence, and pain scores [8]. Additionally, this study found that the incidence of postoperative headache, fatigue, and xerostomia was lower in the OFA group than in the OA group. In recent years, the combination of esketamine, dexmedetomidine, and inhalational anesthesia has emerged as a novel anesthetic approach. This study revealed that OFA significantly improved the quality of postoperative recovery and reduced the occurrence of opioid-related adverse events compared to traditional anaesthesia. These results are consistent with those of multiple other studies. For example, Choi *et al.* [9] reported that in patients undergoing gynecologic laparoscopic surgery, the recovery quality score of the OFA group on the first postoperative day was significantly higher than that of the remifentanil anesthesia group. Furthermore, Fiore *et al.* [10] confirmed via systematic review and meta-analysis that the OFA group effectively reduced the occurrence of adverse reactions such as constipation, vomiting, and headache. In this study, the OFA group significantly improved postoperative pain, physical comfort, self-care ability, psychological support, and emotional state through the combined use of esketamine, dexmedetomidine, and NSAIDs. Specifically, esketamine in the OFA group blocks the binding of glutamate to N-methyl-D-aspartate (NMDA) receptors, inhibits central sensitization, thereby improving postoperative pain scores and increasing recovery quality scores [11]. Moreover, the antidepressant effect of esketamine may be related to the association between NMDA receptor overactivation and depression, as esketamine can improve emotional state by blocking NMDA receptors [6,12-13]. Additionally, dexmedetomidine, as a highly selective α2 adrenoceptor agonist, inhibits sympathetic activity, reduces nervous system excitability, exerts anxiolytic and sedative effects, thereby alleviating postoperative tension in patients and improving their postoperative sleep quality [14].

The lower incidence of adverse reactions in the OFA group compared to the OA group is presumably related to the synergistic effect of esketamine and dexmedetomidine in multimodal analgesia and physiological stability. First, the core of the OFA strategy lies in providing sufficient analgesia and stress inhibition through non-opioid pathways [15]. Dexmedetomidine, via its highly selective α2 adrenergic receptor agonist effect, provides stable sedation and analgesia, and effectively inhibits sympathetic stress responses induced by surgery [16]. Meanwhile, low-dose esketamine not only supplements analgesia as a potent NMDA receptor antagonist and prevents hyperalgesia but also maintains circulatory stability by exciting the sympathetic nervous system, offsetting the risk of bradycardia and hypotension that may be caused by dexmedetomidine [17]. This pharmacological complementarity allows the OFA regimen to avoid opioid-related adverse reactions (e.g., postoperative nausea and vomiting, respiratory depression) associated with high-dose opioids while also preventing hemodynamic fluctuations that may result from single-drug use [18].

This study has several limitations. First, the sample size was calculated based on the total QoR-15 score as the primary outcome indicator; thus, the comparison of the incidence of secondary adverse events such as headache is an exploratory analysis with limited statistical power. Second, although adverse events were recorded, fixed postoperative assessment time points may not fully capture all transient or atypical adverse reactions, leading to a risk of underestimation. Additionally, this study did not conduct detailed statistics and comparison of the doses of propofol or sevoflurane used for maintenance anesthesia, so the potential impact of these drugs on differences in recovery quality cannot be completely ruled out. Nevertheless, the strengths of this study include strictly following the principles of randomized controlled trials and, for the first time, systematically evaluating the improvement effect of this specific OFA regimen on patient-reported outcomes (QoR-15) in the laparoscopic cholecystectomy population, providing strong preliminary evidence for future confirmatory studies with larger sample sizes. Future research should focus on clarifying the specific neurophysiological mechanisms and use more continuous and precise monitoring methods to comprehensively assess the postoperative recovery process.

In conclusion, in laparoscopic cholecystectomy, the QoR-15 score of the OFA group was significantly higher than that of the OA group, with a lower incidence of postoperative headache and more stable perioperative hemodynamics. Therefore, opioid-free multimodal general anesthesia is safe and feasible.

Conflict of Interest None

References

[1] Toleska M, Dimitrovski A. Is opioid-free general anesthesia more superior for postoperative pain versus opioid general anesthesia in laparoscopic cholecystectomy?[J]. Pril (Makedon Akad Nauk Umet Odd Med Nauki), 2019, 40(2): 81-87.

[2] Hublet S, Galland M, Navez J, et al. Opioid-free versus opioid-based anesthesia in pancreatic surgery[J]. BMC Anesthesiol, 2022, 22(1): 9.

[3] Léger M, Perrault T, Pessiot-Royer S, et al. Opioid-free anesthesia protocol on the early quality of recovery after major surgery (SOFA trial): a randomized clinical trial[J]. Anesthesiology, 2024, 140(4): 679-689.

[4] Wu MC, Yang FF, Cai N, et al. Affects for stress reaction and hemodynamics by multimodal opioid free anesthesia on patients with video-assisted thoracoscopic surgery[J]. Chin J Clin Res, 2024, 37(12): 1839-1844. **[In Chinese]**

[5] Massoth C, Schwellenbach J, Saadat-Gilani K, et al. Impact of opioid-free anaesthesia on postoperative nausea, vomiting and pain after gynaecological laparoscopy - A randomised controlled trial[J]. J Clin Anesth, 2021, 75: 110437.

[6] Wang D, Long YQ, Sun Y, et al. Opioid-free total intravenous anesthesia for thyroid and parathyroid surgery: Protocol for a randomized, double-blind, controlled trial[J]. Front Med (Lausanne), 2022, 9: 939098.

[7] Choi JY, Lee HS, Kim JY, et al. Comparison of remimazolam-based and propofol-based total intravenous anesthesia on postoperative quality of recovery: a randomized non-inferiority trial[J]. J Clin Anesth, 2022, 82: 110955.

[8] Myles PS, Shulman MA, Reilly J, et al. Measurement of quality of recovery after surgery using the 15-item quality of recovery scale: a systematic review and meta-analysis[J]. Br J Anaesth, 2022, 128(6): 1029-1039.

[9] Bagshaw O, McCormack J, Brooks P, et al. The safety profile and effectiveness of propofol-remifentanil mixtures for total intravenous anesthesia in children[J]. Paediatr Anaesth, 2020, 30(12): 1331-1339.

[10] Fiore JF, El-Kefraoui C, Chay MA, et al. Opioid versus opioid-free analgesia after surgical discharge: a systematic review and meta-analysis of randomised trials[J]. Lancet, 2022, 399(10343): 2280-2293.

[11] Shoib S, Kotra M, Javed S, et al. Esketamine-a quick-acting novel antidepressant without the disadvantages of ketamine[J]. Horm Mol Biol Clin Investig, 2022, 43(4): 505-511.

[12] Gao SL, Zhang PF, Wang EQ, et al. Research progress of esketamine and postoperative delirium[J]. Chin J Clin Res, 2024, 37(8): 1164-1167. **[In Chinese]**

[13] Zanos P, Moaddel R, Morris PJ, et al. NMDAR inhibition-independent antidepressant actions of ketamine metabolites[J]. Nature, 2016, 533(7604): 481-486.

[14] Guo YL, Chen LN, Gao ZQ, et al. Is esketamine-based opioid-free anesthesia more superior for postoperative analgesia in obstructive sleep apnea patients undergoing bariatric surgery? A study protocol[J]. Front Med, 2022, 9: 1039042.

[15] Tochie JN, Bengono Bengono RS, Metogo JM, et al. The efficacy and safety of an adapted opioid-free anesthesia regimen versus conventional general anesthesia in gynecological surgery for low-resource settings: a randomized pilot study[J]. BMC Anesthesiol, 2022, 22(1): 325.

[16] Modir H, Moshiri E, Yazdi B, et al. Efficacy of dexmedetomidine-ketamine vs. fentanylketamine on saturated oxygen, hemodynamic responses and sedation in cystoscopy: a doubleblinded randomized controlled clinical trial[J]. Med Gas Res, 2020, 10(3): 91-95.

[17] Zhou N, Liang XS, Gong JP, et al. S-ketamine used during anesthesia induction increases the perfusion index and mean arterial pressure after induction: a randomized, double-blind, placebo-controlled trial[J]. Eur J Pharm Sci, 2022, 179: 106312.

[18] Gong WY, Zhang SG, Li XL, et al. Dexmedetomidine is superior to midazolam for sedation and cerebral protection in postoperative hypertensive intracerebral hemorrhage patients: a retrospective study[J]. J Int Med Res, 2020, 48(9): 300060520957554.

Submission received:2025-02-10/ **Revised:** 2025-05-28

·论　著·

无阿片麻醉对腹腔镜胆囊切除术患者术后恢复质量的影响

郝聪会[1]，　栾恒飞[1]，　杨春[2]，　顾小姣[1]

1. 徐州医科大学附属连云港医院　连云港市第一人民医院麻醉科，江苏 连云港 222000；

2. 南京医科大学第一附属医院麻醉与围术期医学科，江苏 南京 210029

摘要：目的　探讨无阿片药物全身麻醉在腹腔镜胆囊切除术中的应用效果，及对患者术后恢复质量的影响。**方法**　本研究设计类型为前瞻性平行随机对照试验，纳入了2022年10月至2023年8月连云港第一人民医院择期行腹腔镜胆囊切除术的患者74例，采用随机数字表法分为两组：阿片组37例（OA 组）和无阿片组37例（OFA 组）。主要研究指标为患者术后 1 d 和 2 d 的 15 项术后恢复质量评分（QoR-15）；次要研究指标为术后 1 d 的阿片类药物相关不良反应及围手术期平均动脉压（MAP）和脑电双频谱指数（BIS）值[入手术室时（T0）、OA 组诱导开始时（T1）或 OFA 组右美托咪定诱导后 10 min 时（T1）、气管插管后（T2）、术前（T3）、切开皮肤后（T4）、拔管后（T5）6个时间点]。**结果**　OFA 组患者术后 1 d [110.0（105.5，112.0）分 *vs* 79.0（76.5，80.5）分，Z=7.414，P<0.01] 和 2 d [128.0（127.0，131.0）分 *vs* 94.0（91.0，97.0）分，Z=7.419，P<0.01] 的 QoR-15 评分显著高于 OA 组。OFA 组患者头痛[18.92%（7/37）*vs* 0，χ^2=5.680，P=0.017]、乏力[21.62%（8/37）*vs* 2.7%（1/37），χ^2=4.554，P=0.033]和口干[16.22%（6/37）*vs* 0，χ^2=4.534，P=0.033]等不良反应发生率显著低于 OA 组。两组患者在 T1 和 T3 时刻的 MAP 差异有统计学意义（P<0.01）。**结论**　腹腔镜胆囊切除术中应用无阿片药物全身麻醉可显著提高患者术后恢复质量，术后头痛、乏力、口干等不良反应发生率低，围手术期 MAP 更加稳定。

关键词： 无阿片麻醉；术后恢复质量；艾司氯胺酮；右美托咪定；腹腔镜胆囊切除术

中图分类号： R614.2　**文献标识码：** A　**文章编号：** 1674-8182（2025）12-1822-05

Effect of opioid-free anesthesia on postoperative recovery quality in patients undergoing laparoscopic cholecystectomy

HAO Conghui*, LUAN Hengfei, YANG Chun, GU Xiaojiao

*Department of Anesthesiology, The Affiliated Lianyungang Hospital of Xuzhou Medical University, The First People's Hospital of Lianyungang, Lianyungang, Jiangsu 222000, China

Corresponding author: GU Xiaojiao, E-mail: 675906152@qq.com

Abstract: Objective　To explore the application effect of opioid-free general anesthesia in laparoscopic cholecystectomy and its impact on postoperative recovery quality in patients. **Methods**　This was a prospective parallel randomized controlled trial. A total of 74 patients undergoing elective laparoscopic cholecystectomy at the First People's Hospital of Lianyungang from October 2022 to August 2023 were enrolled. They were divided into two groups using a random number table: the opioid group (OA group, n=37) and the opioid-free group (OFA group, n=37). The primary outcome was the 15-item Quality of Recovery Score (QoR-15) on postoperative day 1 and day 2. Secondary outcomes included opioid-related adverse reactions on postoperative day 1, mean arterial pressure (MAP), and bispectral index (BIS) values at six time points: upon entering the operating room (T0), at the start of induction in OA group (T1) or 10 min after dexmedetomidine induction in OFA group (T1), after tracheal intubation (T2), before surgery (T3), after skin incision (T4), and after extubation (T5). **Results**　The QoR-15 scores of the OFA group were significantly

DOI: 10.13429/j.cnki.cjcr.2025.12.007

基金项目： 江苏省自然科学基金杰出青年基金（BK20240054）

通信作者： 顾小姣，E-mail：675906152@qq.com

出版日期： 2025-12-20

QR code for English version

higher than those of the OA group on postoperative day 1 [110.0 (105.5, 112.0) *vs* 79.0 (76.5, 80.5), Z=7.414, P<0.01] and day 2 [128.0 (127.0, 131.0) *vs* 94.0 (91.0, 97.0), Z=7.419, P<0.01]. Compared with OA group, OFA group had lower incidence rate of adverse reactions such as headache [18.92% (7/37) *vs* 0, χ^2=5.680, P=0.017], fatigue [21.62% (8/37) *vs* 2.7% (1/37), χ^2=4.554, P=0.033], and dry mouth [16.22% (6/37) *vs* 0, χ^2=4.534, P=0.033]. There were statistically significant differences in MAP between the two groups at T1 and T3 (P<0.01). **Conclusion** The application of opioid-free general anesthesia in laparoscopic cholecystectomy can significantly improve patient's postoperative recovery quality, reduce the incidence of postoperative adverse reaction such as headache, fatigue and dry mouth, and maintain more stable perioperative MAP.

Keywords: Opioid-free anesthesia; Postoperative recovery quality; Esketamine; Dexmedetomidine; Laparoscopic cholecystectomy

Fund program: Outstanding Youth Fund of Jiangsu Provincial Natural Science Foundation (BK 20240054)

腹腔镜胆囊切除术作为一种微创手术，因其创伤小、恢复快等优点，已成为胆囊疾病治疗的首选方法。然而，术后不同程度腹部切口疼痛、恶心呕吐和切口感染等并发症仍然是影响患者恢复质量的重要因素[1]。传统的麻醉方法中，阿片类药物麻醉（opioid anesthesia，OA）因其强效的镇痛作用被广泛使用，但其不良反应也不容忽视，如恶心、呕吐、呼吸抑制等，这些都可能延长患者的住院时间，影响患者术后恢复质量[2]。无阿片类药物麻醉（opioid-free anesthesia，OFA）在围手术期避免使用阿片类药物，采用多模式镇痛策略，在临床应用中展现出多方面的优势。首先，OFA显著降低了阿片类药物相关不良反应，如呼吸抑制、术后恶心呕吐（postoperative nausea and vomiting，PONV）和胃肠功能抑制，从而提升患者的安全性及舒适度。其次，通过联合区域阻滞（如神经阻滞或硬膜外麻醉）、非甾体抗炎药（nonsteroidal anti-inflammatory drug，NSAID）、右美托咪定等辅助药物，OFA能有效控制手术应激反应和疼痛，同时避免阿片类药物导致的免疫抑制和成瘾风险，尤其适用于肥胖、阻塞性睡眠呼吸暂停或药物滥用史的高危患者[3]。此外，OFA有助于加速术后康复，促使患者早期进食和活动，缩短住院时间。总体而言，OFA作为一种创新的麻醉策略，在优化围手术期管理、减少阿片依赖方面具有重要价值[4]。OFA现已在妇产科、胃肠外科腹腔镜手术以及甲乳外科手术中也得到较好的应用[5-6]。本研究采用15项恢复质量评分量表（15-item Quality of Recovery，QoR-15）评估OFA对腹腔镜胆囊手术患者术后恢复质量的影响，能够全面反映患者的术后恢复情况[7]。本研究旨在探讨OFA对腹腔镜胆囊手术患者术后恢复质量的影响，为临床麻醉实践提供新的思路和依据。

1 资料与方法

1.1 *资料与方法* 这项前瞻性、随机、单盲临床研究于2022年10月至2023年8月在连云港第一人民医院进行。所有患者均签署知情同意书。本研究招募了74例择期行腹腔镜胆囊切除术的患者，美国麻醉医师协会（American Society of Anesthesiologists，ASA）分级为Ⅰ级或Ⅱ级，年龄20~60岁。排除标准：（1）术前患有严重心脏或肺部疾病；（2）有艾司氯胺酮或NSAID过敏史或禁忌证（血压和颅内压升高的严重危险，高血压控制不良或未治疗，甲状腺功能亢进未治疗或治疗不足，胃肠道出血）；（3）存在精神疾病或其他慢性疼痛状况；（4）孕妇、哺乳期妇女或经期妇女。根据计算机生成的随机数字表，患者被随机分为两组，各37例。OFA组男20例，女17例；OA组男18例，女19例。两组患者性别、年龄、身体质量指数（body mass idex，BMI）、ASA分级等一般资料比较差异无统计学意义（P>0.05）。见表1。分配结果密封于编号不透光信封中，仅在患者签署知情同意书后由麻醉护士开启执行分组。实施者与受试者均对分组信息设盲。本研究经连云港市第一人民医院医学伦理会批准同意（伦理批号：KY-20220711001-01）。

1.2 *方法* 两组患者术前禁饮2 h、禁食8 h。所有行择期胆囊切除术的患者将根据纳入和排除标准的常规程序进行访问。入手术室后，所有患者均进行常规术前准备，包括心电图、无创血压测量、脑电双频谱指数（bispectral index，BIS）和外周血氧饱和度（saturation of peripheral oxygen，SpO_2）检测。建立静脉通路，用于药物管理和液体治疗。术前给予阿扎司琼10 mg和地塞米松10 mg静脉注射预防恶心呕吐的发生。

麻醉诱导期：OA组，麻醉医生依次缓慢静脉注射

丙泊酚 2~4 mg/kg 至患者意识消失、静脉推注顺阿曲库铵 0.2 mg/kg、舒芬太尼 0.3 μg/kg，于气管插管前 5 min 进行麻醉诱导；OFA 组，诱导前 10 min，以恒定速率静脉泵注盐酸右美托咪定 0.6 μg/kg，之后依次静脉推注丙泊酚 2~4 mg/kg、顺阿曲库铵 0.2 mg/kg、气管插管前 2 min 给予艾司氯胺酮 0.2 mg/kg 进行麻醉诱导。两组均给予吸入麻醉剂七氟醚 1.5%~4.0%。滴定氧气/空气混合物中的七氟醚浓度[吸入氧浓度(fraction of inspired oxygen，FiO_2)：60%，总气体流量 2 L/min]，以保持 BIS 值 40~60。呼吸模式设置为容积控制通气(volume control ventilation，VCV)，呼吸参数设置为吸入气中的 FiO_2 60%，氧流量 2 L/min，潮气量(tidal volume，VT) 6~8 mL/kg，呼吸频率 12 次/min，吸呼比为 1∶2，维持呼气末二氧化碳分压(end-tidal carbon dioxide partial pressure，$P_{ET}CO_2$) 35~45 mmHg。麻醉后严密监测两组患者术中的各项生命指标，所有监测参数每 5 min 记录一次，直到患者被转移到麻醉恢复室(postanesthesia care unit，PACU)。应用机械通气并调整参数以维持正常的 $P_{ET}CO_2$ (35~40 mmHg)。镇痛策略采用罗哌卡因局部浸润麻醉，手术结束前 30 min 对乙酰氨基酚 200 mg 静脉滴注。术后患者补救镇痛措施：统一在视觉模拟评分(Visual Analogue Scale，VAS)≥4 分时静脉给予帕瑞昔布钠 40 mg，间隔≥6 h，24 h 最大剂量 80 mg。

1.3　观察指标　(1) 主要指标：通过 QoR-15 量表评估所有患者术后第 1 天和术后第 2 天的恢复质量。QoR-15 量表包括身体舒适(5 项)、情绪状态(4 项)、身体独立(2 项)、心理支持(2 项)、疼痛(2 项)五个方面，分数越高代表术后恢复质量越好。(2) 次要指标：包括阿片类药物相关不良反应发生情况(恶心、呕吐、头痛 、乏力、嗜睡、口干和术后呼吸抑制)。其中呼吸抑制定义为术后 24 h 内 SpO_2<90%持续≥30 s，或需干预的呼吸频率/通气异常。除患者基本情况外，术中记录患者进入手术室时(T0)、OA 组诱导开始时(T1)或 OFA 组右美托咪定诱导后 10 min 时(T1)、气管插管后(T2)、术前(T3)、切开皮肤后(T4)、拔管后(T5)时间点的平均动脉压(mean arterial pressure，MAP)和 BIS 值。记录手术时间、麻醉开始时间、拔管时间、PACU 停留时间。

1.4　统计学方法　采用 SPSS 25.0 软件进行数据处理。计量资料以 $\bar{x}\pm s$ 表示，比较采用独立样本 t 检验。不符合正态分布的连续变量用 $M(P_{25},P_{75})$ 表示，组间比较应采用非参数检验。计数资料以例(%)表示，比较采用 χ^2 检验或其校正法。采用 Holm 校正方法对术后不良反应发生情况的原始 P 值进行了调整，P<0.05 为差异有统计学意义。

2　结　果

2.1　两组患者手术相关指标比较　两组患者手术时间、拔管时间和在 PACU 停留时间比较，差异无统计学意义(P>0.05)。见表 1。

2.2　两组患者术后恢复质量比较　两组患者术后第 1 天在疼痛、身体舒适度、身体独立、情绪状态及 QoR-15 总分比较，OA 组显著低于 OFA 组(P<0.01)。两组患者术后第 2 天 QoR-15 总分及五个维度得分比较，OA 组显著低于 OFA 组(P<0.01)。见表 2。

表 1　两组一般资料和手术相关指标　(n = 37)

Tab.1　Comparison of general data and surgical-related indicators between two groups　(n = 37)

组别	男/女(例)	年龄(岁，$\bar{x}\pm s$)	BMI(kg/m^2，$\bar{x}\pm s$)	ASA 分级(Ⅰ/Ⅱ，例)	手术时间(min，$\bar{x}\pm s$)	拔管时间(min，$\bar{x}\pm s$)	PACU 停留时间(min，$\bar{x}\pm s$)
OA 组	18/19	45.6±10.8	23.6±2.3	19/18	48±14.7	14.5±2.3	34.4±3.8
OFA 组	20/17	44.2±9.9	23.5±2.0	22/15	43±11.9	13.7±2.2	35.4±3.1
χ^2/t 值	0.216	0.617	0.202	0.491	1.637	1.505	1.150
P 值	0.642	0.454	0.546	0.320	0.148	0.783	0.368

表 2　两组患者 QoR-15 术后恢复质量评分的比较　[n=37，分，$M(P_{25},P_{75})$]

Tab.2　Comparison of QoR-15 postoperative recovery quality scores between two groups　[n=37，point，$M(P_{25},P_{75})$]

组别	时间	疼痛	身体舒适度	身体独立	心理支持	情绪状态	总分
OA 组	术后第 1 天	11.0(10.0,11.5)	16.0(15.0,16.5)	14.0(13.0,14.0)	15.0(15.0,16.0)	23.0(21.5,24.0)	79.0(76.5,80.5)
	术后第 2 天	13.0(12.0,13.0)	20.0(18.0,21.0)	16.0(15.5,17.0)	18.0(16.0,19.0)	27.0(25.0,30.0)	94.0(91.0,97.0)
OFA 组	术后第 1 天	15.0(14.0,16.0)	29.0(28.0,32.0)	16.0(15.0,17.0)	15.0(15.0,16.5)	32.0(30.5,35.0)	110.0(105.5,112.0)
	术后第 2 天	20.0(18.0,20.0)	36.0(35.0,37.0)	17.0(16.5,18.0)	19.0(17.0,20.0)	37.0(36.0,39.0)	128.0(127.0,131.0)
$Z/P_{术后第1天}$ 值		7.266/<0.001	7.452/<0.001	7.119/<0.001	0.479/0.632	7.435/<0.001	7.414/<0.001
$Z/P_{术后第2天}$ 值		7.552/<0.001	7.442/<0.001	3.422/<0.001	2.337/<0.001	7.427/<0.001	7.419/<0.001

注：$Z/P_{术后第1天}$ 值为两组术后第 1 天比较的 Z 值和 P 值；$Z/P_{术后第2天}$ 值为两组术后第 2 天比较的 Z 值和 P 值。

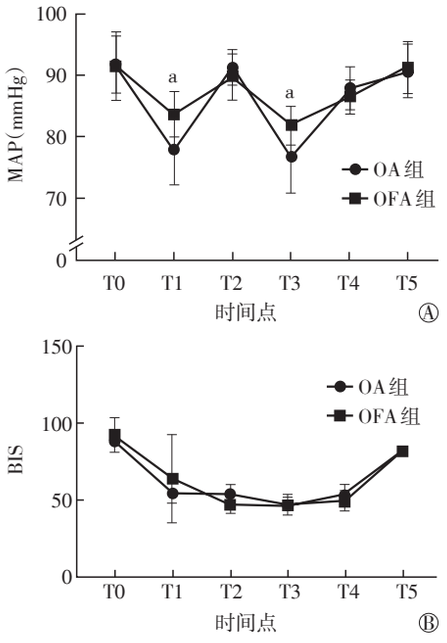
2.3　两组患者不良反应发生情况　OFA组头痛、乏力和口干发生率显著低于OA组，差异有统计学意义（P<0.05）；其他如恶心、呕吐、嗜睡及呼吸抑制的发生率两组差异无统计学意义（P<0.05）。见表3。

2.4　两组患者术中不同时间点MAP和BIS值的比较　两组患者MAP在T1和T3时刻比较差异有统计学意义（P<0.05），OFA组MAP的波动幅度更小。两组患者T0~T5时间点BIS值比较差异无统计学意义（P>0.05）。见图1。

表3　两组患者不良反应发生情况比较　（n=37，例）

Tab.3　Comparison of the incidence of adverse reactions between two groups　（n=37，case）

组别	恶心	呕吐	头痛	乏力	嗜睡	口干	术后呼吸抑制
OA组	7	5	7	8	6	6	7
OFA组	1	1	0	1	2	0	1
χ^2值	3.504	1.632	5.680	4.544	1.261	4.534	3.504
P值	0.061	0.201	0.017	0.033	0.261	0.033	0.061



注：A为两组MAP比较，B为两组BIS比较；与OA组比较，^aP<0.05。

图1　两组患者术中MAP及BIS值的比较

Fig.1　Comparison of intraoperative MAP and BIS values between two groups

3　讨　论

本研究结果显示，在择期行腹腔镜胆囊切除术的患者中，与OA组相比，OFA组术后恢复质量有显著的改善，特别是OFA组患者QoR-15问卷中的情绪状态、身体舒适度、身体独立性和疼痛评分等方面[8]。且本研究发现OFA组患者术后头痛、乏力和口干的发生率低于OA组。近年来，艾司氯胺酮和右美托咪啶联合吸入麻醉已成为一种新型麻醉方式。本研究发现，与传统麻醉相比，OFA显著提高了患者的术后恢复质量，减少了阿片类药物相关不良事件。这一发现与多项研究结果一致。例如，Choi等[9]报道，在接受妇科腹腔镜手术的患者中，OFA组的术后第1天的恢复质量评分显著高于瑞芬太尼麻醉组。此外，Fiore等[10]通过系统回顾和荟萃分析证实，OFA组有效减少了便秘、呕吐、头痛等不良反应的发生。在本研究中，OFA组通过联合使用艾司氯胺酮、右美托咪定和NSAID，显著改善了术后疼痛、身体舒适度、自理能力、心理支持和情绪状态。具体而言，OFA组通过使用艾司氯胺酮，阻断N-甲基-D-天冬氨酸（N-methyl-D-aspartate，NMDA）受体与谷氨酸的结合，抑制中枢敏化，从而改善术后疼痛评分和提高恢复质量评分[11]。并且，NMDA受体过度激活与抑郁症相关，而艾司氯胺酮可通过阻断NMDA受体改善情绪状态[6,12-13]。并且，右美托咪定作为一种高选择性的α_2-受体激动剂，通过抑制了交感神经活性，降低神经系统的兴奋性，发挥抗焦虑和镇静作用，从而缓解了患者术后紧张的情绪，提高患者术后睡眠质量[14]。

OFA组患者不良反应发生率低于OA组，推测可能与艾司氯胺酮与右美托咪定在多模态镇痛与生理功能稳定方面的协同效应有关。首先，OFA策略的核心在于通过非阿片类药物途径提供充分的镇痛与应激抑制[15]。右美托咪定通过其高选择性α_2-肾上腺素受体激动作用，提供了稳定的镇静、镇痛效果，并能有效抑制手术引发的交感神经应激反应[16]。与此同时，低剂量的艾司氯胺酮不仅作为强效的NMDA受体拮抗剂补充镇痛、预防痛觉过敏，还能通过兴奋交感神经系统来维持循环稳定，抵消了右美托咪定可能引起的心动过缓与低血压风险[17]。这种药理学的互补性，使得OFA方案在避免大剂量阿片类药物相关不良反应（如PONV、呼吸抑制）的同时，也避免了单一用药可能带来的血流动力学波动[18]。

本研究存在一些局限性。首先，本研究的主要样本量是基于QoR-15总分这一主要结局指标进行计算的，因此对于头痛等次要不良事件发生率的比较属于探索性分析，其统计效能可能有限。其次，尽管记录了不良事件，但固定的术后评估时间点可能无法完全捕捉到所有短暂或非典型的不良反应，从而存在低估的风险。此外，本研究未对维持麻醉所用的丙泊酚或七氟烷等药物剂量进行详细统计与比较，无法完全排除这些药物对恢复质量差异的潜在影响。尽管如此，本研究的优势在于严格遵循了随机对照试验的原则，并首次在腹腔镜胆囊切除术人

群中系统性地评估了该特定OFA方案对患者报告结局(QoR-15)的改善效果,为未来更大样本量的确证性研究提供了有力的初步证据。未来的研究应侧重于阐明其具体神经生理机制,并采用更连续、精密的监测手段来全面评估术后恢复过程。

综上,在腹腔镜胆囊切除术中,OFA组QoR-15评分明显高于OA组,且OFA组患者术后头痛发生率较低,围手术期血流动力学更加稳定。因此,采用无阿片类药物的多模式全身麻醉是安全可行的。

利益冲突 无

参考文献

[1] Toleska M, Dimitrovski A. Is opioid-free general anesthesia more superior for postoperative pain versus opioid general anesthesia in laparoscopic cholecystectomy? [J]. Pril (Makedon Akad Nauk Umet Odd Med Nauki), 2019, 40(2): 81-87.

[2] Hublet S, Galland M, Navez J, et al. Opioid-free versus opioid-based anesthesia in pancreatic surgery [J]. BMC Anesthesiol, 2022, 22(1): 9.

[3] Léger M, Perrault T, Pessiot-Royer S, et al. Opioid-free anesthesia protocol on the early quality of recovery after major surgery (SOFA trial): a randomized clinical trial [J]. Anesthesiology, 2024, 140(4): 679-689.

[4] 吴美潮, 杨芳芳, 蔡宁, 等. 多模式无阿片药物麻醉对胸腔镜手术患者应激反应及血流动力学的影响[J]. 中国临床研究, 2024, 37(12): 1839-1844.

[5] Massoth C, Schwellenbach J, Saadat-Gilani K, et al. Impact of opioid-free anaesthesia on postoperative nausea, vomiting and pain after gynaecological laparoscopy-A randomised controlled trial [J]. J Clin Anesth, 2021, 75: 110437.

[6] Wang D, Long YQ, Sun Y, et al. Opioid-free total intravenous anesthesia for thyroid and parathyroid surgery: protocol for a randomized, double-blind, controlled trial [J]. Front Med (Lausanne), 2022, 9: 939098.

[7] Choi JY, Lee HS, Kim JY, et al. Comparison of remimazolam-based and propofol-based total intravenous anesthesia on postoperative quality of recovery: a randomized non-inferiority trial [J]. J Clin Anesth, 2022, 82: 110955.

[8] Myles PS, Shulman MA, Reilly J, et al. Measurement of quality of recovery after surgery using the 15-item quality of recovery scale: a systematic review and meta-analysis [J]. Br J Anaesth, 2022, 128(6): 1029-1039.

[9] Choi H, Song JY, Oh EJ, et al. The effect of opioid-free anesthesia on the quality of recovery after gynecological laparoscopy: a prospective randomized controlled trial [J]. J Pain Res, 2022, 15: 2197-2209.

[10] Fiore JF, El-Kefraoui C, Chay MA, et al. Opioid versus opioid-free analgesia after surgical discharge: a systematic review and meta-analysis of randomised trials [J]. Lancet, 2022, 399(10343): 2280-2293.

[11] Shoib S, Kotra M, Javed S, et al. Esketamine-A quick-acting novel antidepressant without the disadvantages of ketamine [J]. Horm Mol Biol Clin Investig, 2022, 43(4): 505-511.

[12] 高世龙, 张培福, 王恩强, 等. 艾司氯胺酮与术后谵妄的研究进展[J]. 中国临床研究, 2024, 37(8): 1164-1167.

[13] Zanos P, Moaddel R, Morris PJ, et al. NMDAR inhibition-independent antidepressant actions of ketamine metabolites [J]. Nature, 2016, 533(7604): 481-486.

[14] Guo YL, Chen LN, Gao ZQ, et al. Is esketamine-based opioid-free anesthesia more superior for postoperative analgesia in obstructive sleep apnea patients undergoing bariatric surgery? A study protocol [J]. Front Med, 2022, 9: 1039042.

[15] Tochie JN, Bengono Bengono RS, Metogo JM, et al. The efficacy and safety of an adapted opioid-free anesthesia regimen versus conventional general anesthesia in gynecological surgery for low-resource settings: a randomized pilot study [J]. BMC Anesthesiol, 2022, 22(1): 325.

[16] Modir H, Moshiri E, Yazdi B, et al. Efficacy of dexmedetomidine-ketamine vs. fentanylketamine on saturated oxygen, hemodynamic responses and sedation in cystoscopy: a double blinded randomized controlled clinical trial [J]. Med Gas Res, 2020, 10(3): 91-95.

[17] Zhou N, Liang XS, Gong JP, et al. *S*-ketamine used during anesthesia induction increases the perfusion index and mean arterial pressure after induction: a randomized, double-blind, placebo-controlled trial [J]. Eur J Pharm Sci, 2022, 179: 106312.

[18] Gong WY, Zhang SG, Li XL, et al. Dexmedetomidine is superior to midazolam for sedation and cerebral protection in postoperative hypertensive intracerebral hemorrhage patients: a retrospective study [J]. J Int Med Res, 2020, 48(9): 300060520957554.

收稿日期:2025-02-10 **修回日期**:2025-05-28 **编辑**:李方