

Opioid-Free General Anesthesia for Short-Duration Orthopedic Procedures: A Randomized Controlled Trial

Shuyu Ma, Fangsheng Xu, Jianfeng Pu*

Department of Anesthesiology, Affiliated Changshu Hospital of Nantong University || Changshu No. 2 People's Hospital, Changshu, 215500, China

*Correspondence Author, pjh61255397@163.com

Abstract: **Objective:** To evaluate the clinical efficacy and perioperative safety of a multimodal opioid-free anesthesia (OFA) regimen in patients undergoing short-duration orthopedic procedures. **Methods:** Sixty patients scheduled for elective orthopedic procedures between January 2024 and June 2026, with American Society of Anesthesiologists (ASA) physical status I or II and an expected surgical duration of <2 h, were randomized 1:1 to an OFA group or an opioid-based anesthesia (OBA) group (n=30 each). The OFA regimen was based on dexmedetomidine, esketamine, and intravenous lidocaine, whereas the OBA regimen used sufentanil for induction and remifentanyl for maintenance. Heart rate (HR) and mean arterial pressure (MAP) were recorded before induction (T0), immediately after induction (T1), after laryngeal mask airway (LMA) insertion (T2), 10 min after induction (T3), before LMA removal (T4), and after LMA removal (T5). Time to LMA removal, post-anesthesia care unit (PACU) length of stay, Steward recovery score at PACU discharge, resting numerical rating scale (NRS) pain scores in the PACU and at 24 h, Richards-Campbell Sleep Questionnaire (RCSQ) score on postoperative day 1, rescue analgesia, postoperative nausea and vomiting (PONV), hypoxemia, bradycardia, hypotension, and other adverse events were recorded. **Results:** Compared with the OBA group, the OFA group had higher HR and MAP at T1, T3, and T4 (all $P<0.05$), whereas values at T0, T2, and T5 were comparable between groups. The 24-h resting NRS score was lower in the OFA group than in the OBA group (2.2 ± 1.2 vs. 3.2 ± 1.1 ; $P=0.002$), while the PACU NRS score did not differ significantly. The postoperative day 1 RCSQ score was higher with OFA (70.1 ± 8.0 vs. 57.3 ± 10.7 ; $P<0.001$). Time to LMA removal (12.7 ± 2.0 vs. 10.2 ± 2.0 min; $P<0.001$) and PACU stay (40.9 ± 4.8 vs. 36.4 ± 4.9 min; $P<0.001$) were longer in the OFA group. PONV occurred less frequently in the OFA group (6.7% vs. 30.0%; $P=0.020$). The incidences of rescue analgesia, hypoxemia, bradycardia, and hypotension were not significantly different between groups. **Conclusion:** A multimodal OFA regimen based on dexmedetomidine, esketamine, and lidocaine was feasible for short-duration orthopedic procedures and was associated with lower 24-h pain scores, better first-night subjective sleep quality, and less PONV. These potential benefits were accompanied by modestly prolonged emergence and PACU recovery, indicating that recovery efficiency and hemodynamic safety should be considered when implementing OFA.

Keywords: Opioid-free anesthesia, Esketamine, Dexmedetomidine, Lidocaine, Orthopedic surgery, Postoperative pain.

1. Introduction

Opioids provide reliable analgesia and suppression of nociceptive responses and remain an important component of general anesthesia. However, perioperative opioid exposure is associated with postoperative nausea and vomiting (PONV), respiratory depression, pruritus, urinary retention, gastrointestinal dysfunction, opioid tolerance, opioid-induced hyperalgesia, and a potential risk of persistent postoperative opioid use [1–3].

Opioid-free anesthesia (OFA) does not simply replace one opioid with a single alternative drug. Instead, it uses a multimodal combination of agents with complementary mechanisms, including α_2 -adrenoceptor agonists, N-methyl-D-aspartate (NMDA) receptor antagonists, intravenous local anesthetics, and nonsteroidal anti-inflammatory drugs, to provide hypnosis, analgesia, and antinociception without routine intraoperative opioid administration. Randomized trials and meta-analyses suggest that OFA may reduce PONV and some opioid-related adverse effects; however, its effects on postoperative pain and recovery remain inconsistent and appear to depend on the surgical setting and the specific drug combination used [3–7].

Short-duration orthopedic procedures are generally limited in operative time but encompass patients with heterogeneous ages and surgical stimuli. These characteristics place

simultaneous demands on intraoperative hemodynamic stability, rapid emergence, postoperative comfort, and early recovery. We therefore compared a multimodal OFA regimen based on dexmedetomidine, esketamine, and intravenous lidocaine with conventional opioid-based anesthesia (OBA) in patients undergoing short-duration orthopedic procedures. We focused on postoperative pain, first-night sleep quality, PONV, recovery characteristics, and perioperative safety.

2. Materials and Methods

2.1 Study Design and Participants

This prospective, single-center, randomized controlled trial was approved by the Ethics Committee of Changshu Second People's Hospital (approval No. 2023-KY-CK09). Written informed consent was obtained from all participants. Patients undergoing elective orthopedic surgery under general anesthesia with a laryngeal mask airway between January 2024 and June 2026 were screened. Eligible patients were of either sex, had ASA physical status I or II, and had an expected surgical duration of < 2 h. Surgical procedures included knee arthroscopy, proximal femoral nail antirotation (PFNA), patellar internal-fixation removal, and percutaneous vertebroplasty.

Exclusion criteria were severe cardiac, hepatic, renal, or pulmonary disease; severe arrhythmia; gastrointestinal ulcer

disease; glaucoma; long-term use of analgesic or sedative drugs; anticoagulant therapy; alcohol abuse; allergy to any study medication; participation in another drug trial within the previous 3 months; contraindication to LMA use; high risk of pulmonary aspiration; or any other condition judged by the investigators to preclude enrollment. Patients were allocated in a 1:1 ratio to the OFA or OBA group using a random-number table, with 30 patients in each group.

2.2 Anesthesia Protocols

Preoperative fasting and fluid intake followed enhanced-recovery principles. After arrival in the operating room, an intravenous line was established and electrocardiography, noninvasive blood pressure, pulse oximetry (SpO₂), end-tidal carbon dioxide (PETCO₂), and bispectral index (BIS) were monitored. Baseline HR and MAP were recorded after 5 min of quiet rest.

Before anesthetic induction, all patients received intravenous penicillin hydrochloride 0.5 mg to reduce glandular secretions and parecoxib sodium 40 mg for preemptive analgesia. Dexamethasone 5 mg and ondansetron 5 mg were administered prophylactically to prevent postoperative nausea and vomiting.

In the OFA group, dexmedetomidine 0.3 µg/kg was infused over 10 min, followed by a continuous infusion at 0.3 µg·kg⁻¹·h⁻¹. Anesthesia was induced with esketamine 0.3 mg/kg, lidocaine 1.5 mg/kg, propofol 1.5–2.0 mg/kg, and cisatracurium 0.15–0.20 mg/kg. Esketamine and lidocaine were subsequently infused at 0.15 mg·kg⁻¹·h⁻¹ and 1.5 mg·kg⁻¹·h⁻¹, respectively. Dexmedetomidine was discontinued approximately 20 min before the anticipated end of surgery, whereas esketamine and lidocaine were discontinued at the end of surgery.

In the OBA group, anesthesia was induced with sufentanil 0.2–0.3 µg/kg, propofol 1.5–2.0 mg/kg, and cisatracurium 0.15–0.20 mg/kg. Remifentanyl was infused at 0.05–0.15 µg·kg⁻¹·min⁻¹ during surgery and titrated according to hemodynamic responses and surgical stimulation; the infusion was stopped at the end of surgery.

In both groups, total intravenous anesthesia was maintained with propofol at an initial infusion rate of 4–8 mg·kg⁻¹·h⁻¹ and titrated according to BIS and clinical signs to maintain a BIS value of 40–60. After insertion of a second-generation LMA, volume-controlled ventilation was used with a tidal volume of 6–8 mL/kg predicted body weight. Respiratory rate was adjusted to maintain PETCO₂ at 35–45 mmHg, with an inspired oxygen fraction of approximately 0.5–0.6.

Hypotension was defined as MAP <65 mmHg or a >30% decrease from baseline lasting ≥1 min and was treated with ephedrine or phenylephrine as clinically indicated. Bradycardia was defined as HR <50 beats/min and was treated with atropine when necessary. Hypoxemia was defined as SpO₂ <90% for ≥10 s or the need for airway interventions such as jaw thrust or positive-pressure mask ventilation.

If, in the OFA group, MAP or HR increased by >20% from baseline for >2 min despite a BIS of 40–60 and after inadequate hypnotic depth had been excluded, esketamine 0.1 mg/kg was given as non-opioid rescue. If the response remained uncontrolled, remifentanyl rescue was permitted for patient safety and was recorded as intraoperative opioid rescue.

After surgery, patients were transferred to the PACU. Resting pain was assessed using an 11-point NRS ranging from 0 (no pain) to 10 (worst imaginable pain). If NRS was ≥4 or the patient requested analgesia, flurbiprofen axetil 50 mg was administered intravenously. If NRS remained ≥4 after 10 min, sufentanil 5 µg was given intravenously. Rescue analgesia within 24 h was recorded. Moderate-to-severe nausea or vomiting was treated with intravenous ondansetron 4 mg.

2.3 Outcomes

HR and MAP were recorded at six predefined time points: before induction (T0), immediately after induction (T1), after LMA insertion (T2), 10 min after induction (T3), before LMA removal (T4), and after LMA removal (T5). Time to LMA removal, PACU length of stay, and Steward recovery score at PACU discharge were recorded. Resting NRS pain scores were assessed in the PACU and at 24 h after surgery. Subjective sleep quality during the first postoperative night was evaluated on postoperative day 1 using the Richards-Campbell Sleep Questionnaire (RCSQ), which ranges from 0 to 100, with higher scores indicating better sleep quality. Rescue analgesia, PONV, hypoxemia, bradycardia, hypotension, and other adverse events were recorded.

2.4 Sample Size Calculation

The primary outcome was the resting NRS pain score at 24 h after surgery. In a pilot study, the 24-h resting NRS scores were 2.1±1.2 in the OFA group and 3.1±1.2 in the OBA group. For a two-sample comparison of means with a two-sided α of 0.05 and 80% power, at least 23 patients were required per group. Allowing for a 20% dropout rate, the planned sample size was 30 patients per group, for a total of 60 patients.

2.5 Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality. Normally distributed data are presented as mean±standard deviation and were compared between groups using independent-samples t tests. Repeated HR and MAP measurements were analyzed using repeated-measures analysis of variance; the Greenhouse-Geisser correction was applied when the sphericity assumption was violated, and Bonferroni-adjusted post hoc comparisons were performed as appropriate. Non-normally distributed continuous variables are presented as median and interquartile range [M (IQR)] and were compared using the Mann-Whitney U test. Categorical variables are presented as number (%) and were compared using the χ² test when expected cell counts were adequate; otherwise, Fisher's exact test was used. All tests were two-sided, and P<0.05 was considered statistically

significant.

3. Results

3.1 Baseline Characteristics

All 60 randomized patients completed the study and were included in the analysis, with 30 patients in each group. There were no statistically significant between-group differences in age, sex, body mass index (BMI), ASA physical status, type of surgery, surgical duration, or anesthesia duration (all $P>0.05$; Table 1).

Table 1: Baseline characteristics of the study population

Variable	OFA group (n=30)	OBA group (n=30)	P value
Age (years)	54.9±15.3	59.3±13.1	0.236
BMI (kg/m ²)	23.3±2.8	24.2±2.1	0.153
Male/female, n	12/18	16/14	0.438
ASA I/II, n	14/16	13/17	1.000
Type of surgery, n			1.000
Knee arthroscopy	10	10	
PFNA	7	7	
Patellar fixation removal	7	7	
Percutaneous vertebroplasty	6	6	
Surgical duration (min)	50.0±12.7	53.6±13.5	0.289
Anesthesia duration (min)	76.8±12.9	80.7±14.5	0.277

Data are presented as mean±SD or number of patients. ASA, American Society of Anesthesiologists; PFNA, proximal femoral nail antirotation.

3.2 Perioperative Heart Rate and Mean Arterial Pressure

HR and MAP at T0, T2, and T5 were comparable between groups (all $P>0.05$). Post hoc comparisons showed that HR and MAP were higher in the OFA group at T1, T3, and T4 than in the OBA group (all $P<0.05$; Table 2).

Table 2: Heart rate and mean arterial pressure at predefined perioperative time points

Variable/time point	OFA group (n=30)	OBA group (n=30)	P value
HR (beats/min)			
T0	74.6±6.1	72.8±6.3	0.266
T1	70.4±7.9	63.9±7.1	0.001
T2	72.2±7.3	69.6±7.1	0.167
T3	71.7±7.1	64.7±6.5	<0.001
T4	73.0±8.2	66.7±6.4	0.001
T5	74.4±7.4	73.8±7.1	0.736
MAP (mmHg)			
T0	90.2±7.0	86.7±8.2	0.079
T1	83.7±8.5	76.0±6.0	<0.001
T2	87.9±8.2	85.7±5.8	0.237
T3	88.1±8.7	78.9±7.0	<0.001
T4	87.7±7.6	80.2±6.3	<0.001
T5	91.9±8.4	89.6±6.2	0.228

Data are mean±SD. HR, heart rate; MAP, mean arterial pressure. T0, before induction; T1, immediately after induction; T2, after LMA insertion; T3, 10 min after induction; T4, before LMA removal; T5, after LMA removal.

3.3 Recovery, Pain, and Sleep Outcomes

Time to LMA removal and PACU length of stay were longer in the OFA group than in the OBA group (both $P<0.001$), while the Steward recovery score at PACU discharge was similar between groups. PACU resting NRS scores did not differ significantly. By contrast, the 24-h resting NRS score was lower in the OFA group (2.2±1.2 vs. 3.2±1.1; $P=0.002$), and the postoperative day 1 RCSQ score was higher in the

OFA group (70.1±8.0 vs. 57.3±10.7; $P<0.001$; Table 3).

Table 3: Recovery, pain, and sleep outcomes

Outcome	OFA group (n=30)	OBA group (n=30)	P value
Time to LMA removal (min)	12.7±2.0	10.2±2.0	<0.001
PACU length of stay (min)	40.9±4.8	36.4±4.9	<0.001
Steward score [M (IQR)]	6 (6, 6)	6 (6, 6)	0.654
PACU resting NRS	2.5±0.8	2.9±1.2	0.138
24-h resting NRS	2.2±1.2	3.2±1.1	0.002
Postoperative day 1 RCSQ	70.1±8.0	57.3±10.7	<0.001

Data are mean±SD unless otherwise indicated. LMA, laryngeal mask airway; PACU, post-anesthesia care unit; NRS, numerical rating scale; RCSQ, Richards-Campbell Sleep Questionnaire.

3.4 Rescue Analgesia and Adverse Events

The proportion of patients requiring rescue analgesia within 24 h was numerically lower in the OFA group than in the OBA group, but the difference was not statistically significant (13.3% vs. 33.3%; $P=0.067$). PONV occurred less frequently in the OFA group (6.7% vs. 30.0%; $P=0.020$). The incidences of hypoxemia, bradycardia, hypotension, and dreams or hallucinations did not differ significantly between groups. No serious drug-related adverse events occurred (Table 4).

Table 4: Rescue analgesia and adverse events

Outcome	OFA group (n=30)	OBA group (n=30)	P value
Rescue analgesia	4 (13.3)	10 (33.3)	0.067
PONV	2 (6.7)	9 (30.0)	0.020
Hypoxemia	1 (3.3)	4 (13.3)	0.353
Bradycardia	5 (16.7)	2 (6.7)	0.424
Hypotension	4 (13.3)	3 (10.0)	1.000
Dreams or hallucinations	2 (6.7)	0 (0.0)	0.492

Data are n (%). Fisher's exact test was used when expected cell counts were insufficient. PONV, postoperative nausea and vomiting.

4. Discussion

In this randomized trial, a multimodal OFA regimen based on dexmedetomidine, esketamine, and intravenous lidocaine was compared with conventional OBA using sufentanil and remifentanyl in patients undergoing short-duration orthopedic procedures. The main findings were that OFA was associated with a lower resting pain score at 24 h, better subjective sleep quality during the first postoperative night, and a lower incidence of PONV. In contrast, early PACU pain was similar between groups, while time to LMA removal and PACU stay were modestly prolonged with OFA. These findings suggest that the potential value of OFA in this setting may lie in reducing postoperative opioid-related morbidity and improving selected recovery outcomes rather than accelerating immediate recovery.

The lower 24-h resting NRS score observed with OFA is biologically plausible because the regimen combined agents acting at complementary targets. Dexmedetomidine provides α_2 -adrenoceptor-mediated sedation, sympatholysis, and analgesic-sparing effects; esketamine antagonizes NMDA receptors and may reduce central sensitization and hyperalgesia; and intravenous lidocaine has antinociceptive, anti-inflammatory, and antihyperalgesic properties. Previous systematic evidence has shown that complete avoidance of intraoperative opioids does not consistently produce superior

postoperative analgesia, although it can reduce opioid exposure without substantially worsening pain [3]. A 2024 randomized trial in shoulder arthroscopy found that esketamine-dexmedetomidine OFA provided acceptable analgesia and reduced PONV [6], while another randomized study using lidocaine plus esketamine reported broadly comparable postoperative pain relative to a sufentanil-based regimen [7]. In our study, the approximately 1-point difference in 24-h NRS favored OFA; however, this difference should be interpreted together with rescue analgesic use and overall recovery rather than on statistical significance alone.

Perioperative hemodynamics differed between the two strategies. HR and MAP were higher in the OFA group at T1, T3, and T4, whereas there were no significant differences at T0, T2, or T5. This pattern suggests less pronounced hemodynamic depression after induction and during selected intraoperative periods in the OFA group. Esketamine may preserve sympathetic tone and partially offset the cardiovascular depressant effects of propofol and dexmedetomidine, while sufentanil and remifentanyl in the OBA group exert stronger suppression of sympathetic responses. A study in older patients undergoing hip surgery similarly reported fewer anesthesia-related hemodynamic complications with dexmedetomidine-esketamine OFA [8]. Nevertheless, dexmedetomidine itself can cause bradycardia and hypotension. Importantly, the POFA trial was stopped early because of an excess of serious adverse events in the opioid-free arm, including clinically relevant bradycardia and hypoxemia [4]. In the present study, bradycardia was numerically more frequent with OFA (16.7% vs. 6.7%), although the difference was not statistically significant. Given the small sample size, these findings should not be interpreted as evidence that the regimen is free from cardiovascular risk.

PONV is one of the most clinically apparent adverse effects associated with perioperative opioid exposure. In our study, the 24-h incidence of PONV decreased from 30.0% with OBA to 6.7% with OFA. This direction is consistent with previous randomized trials. Massoth et al. reported improved PONV-related outcomes with multimodal OFA in gynecologic laparoscopy [5], Xue et al. observed less PONV with esketamine-dexmedetomidine OFA in shoulder arthroscopy [6], and a randomized trial in thoracoscopic lung resection likewise demonstrated a reduction in PONV with OFA [9]. The benefit may reflect both avoidance of intraoperative opioids and a lower subsequent requirement for rescue opioids. Because dexamethasone and other baseline perioperative measures were standardized between groups in our trial, the observed difference is more likely to be attributable to the anesthetic-analgesic strategy itself. However, PONV was a secondary outcome and the number of events was small; the magnitude of effect therefore requires confirmation in larger studies.

Another notable finding was the higher postoperative day 1 RCSQ score in the OFA group. Postoperative sleep is affected by pain, surgical stress, inflammation, environmental disruption, and perioperative medications. Dexmedetomidine decreases noradrenergic output through α_2 -adrenoceptor signaling in the locus coeruleus, producing a sedative state that shares some characteristics with non-rapid eye movement

sleep. Recent randomized evidence suggests that low-dose intraoperative dexmedetomidine may improve early postoperative RCSQ scores and may influence melatonin secretion [10]. A randomized trial in women undergoing breast cancer surgery also reported an improvement in postoperative sleep disturbances with dexmedetomidine [11]. In addition, pain and PONV can themselves fragment sleep; therefore, the lower 24-h pain score and reduced PONV observed in the OFA group may have contributed to the higher RCSQ score. Because we assessed only the first postoperative night using a subjective questionnaire and did not use polysomnography or actigraphy, our results do not establish an improvement in objective sleep architecture.

The prolonged time to LMA removal and PACU stay with OFA deserves particular attention in short-duration procedures, for which rapid turnover is often an important practical goal. Xue et al. observed a shorter PACU stay with esketamine-dexmedetomidine OFA in shoulder arthroscopy [6], highlighting that emergence profiles are highly dependent on drug selection, dose, and discontinuation timing. Dexmedetomidine has a relatively prolonged terminal elimination profile and may contribute to residual sedation when combined with esketamine, lidocaine, and propofol. Although dexmedetomidine was stopped approximately 20 min before the end of surgery in our protocol, time to LMA removal was prolonged by approximately 2.5 min and PACU stay by approximately 4.5 min. For high-throughput short procedures, these delays may be operationally relevant. Thus, OFA should be optimized to balance opioid avoidance with efficient emergence rather than treating complete opioid elimination as an end in itself.

This study has several limitations. First, it was a single-center trial with a small sample size, and the sample-size calculation was based on the 24-h NRS score rather than low-frequency safety outcomes such as PONV, hypoxemia, and bradycardia. Second, the study included several orthopedic procedures—including knee arthroscopy, PFNA, internal-fixation removal, and percutaneous vertebroplasty—with substantial heterogeneity in patient age, baseline pain, and surgical stimulus. Although procedure distribution was similar between groups after randomization, residual heterogeneity may have influenced pain and recovery outcomes. Future trials should use stratified randomization or restrict enrollment to more homogeneous procedures. Third, the anesthesiologist delivering the intervention could not be blinded to the OFA and OBA regimens, introducing potential performance bias. We also did not use an objective nociception monitor to guide titration of antinociceptive therapy. Finally, sleep was evaluated only during the first postoperative night using the RCSQ, and follow-up was limited to 24 h; consequently, the effects of OFA on longer-term sleep, persistent pain, and global quality of recovery remain uncertain.

5. Conclusion

A multimodal opioid-free anesthesia regimen based on dexmedetomidine, esketamine, and intravenous lidocaine was feasible for short-duration orthopedic procedures and was associated with lower 24-h resting pain scores, less PONV, and better subjective sleep quality during the first

postoperative night. However, OFA modestly prolonged LMA removal and PACU recovery, and potential dexmedetomidine-related bradycardia and hypotension remain clinically relevant considerations. Larger randomized trials in more homogeneous surgical populations are needed to confirm these findings and to define an OFA regimen that optimally balances analgesia, safety, and recovery efficiency.

Data Availability Statement

Research data supporting this study's conclusions can be obtained through a reasonable data-sharing agreement with the institutional review body at the Changshu No. 2 People's Hospital. Further inquiries about the datasets can be directed to the corresponding author on reasonable request.

Ethics Statement

The study was approved by the Ethics Committee of Changshu No. 2 People's Hospital (No. 2023-KY-CK09). Written informed consent was obtained from all participants.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the Changshu Municipal Health Commission Key Project [csws202011] and the Changshu Municipal Science and Technology Plan [CY202322]. The funding source was not involved in any aspect of the study, including its design; collection, analysis, or interpretation of data; or the writing and approval of the manuscript.

Declaration of Interests

The authors report no conflicts of interest in this work.

References

- [1] Kharasch ED, Clark JD. Opioid-free anesthesia: time to regain our balance[J]. *Anesthesiology*, 2021, 134(4): 509-514.
- [2] Forget P. Opioid-free anaesthesia. Why and how? A contextual analysis[J]. *Anaesth Crit Care Pain Med*, 2019, 38(2): 169-172.
- [3] Frauenknecht J, Kirkham KR, Jacot-Guillarmod A, et al. Analgesic impact of intra-operative opioids vs. opioid-free anaesthesia: a systematic review and meta-analysis[J]. *Anaesthesia*, 2019, 74(5): 651-662.
- [4] Beloeil H, Garot M, Lebuffe G, et al. Balanced opioid-free anesthesia with dexmedetomidine versus balanced anesthesia with remifentanyl for major or intermediate noncardiac surgery: the POFA randomized clinical trial[J]. *Anesthesiology*, 2021, 134(4): 541-551.
- [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] Xue Z, Yan C, Liu Y, et al. Opioid-free anesthesia with esketamine-dexmedetomidine versus opioid-based anesthesia with propofol-remifentanyl in shoulder arthroscopy: a randomized controlled trial[J]. *BMC Surg*, 2024, 24: 228.
- [7] Hu Y, Zhang QY, Qin GC, et al. Balanced opioid-free anesthesia with lidocaine and esketamine versus balanced anesthesia with sufentanil for gynecological endoscopic surgery: a randomized controlled trial[J]. *Sci Rep*, 2024, 14: 11759.
- [8] Ye Q, Hu Y, Xing Q, et al. The effects of opioid-free anesthesia with dexmedetomidine and esketamine on postoperative anesthetic-related complications for hip surgery in the elderly[J]. *Int J Gen Med*, 2024, 17: 6291-6302.
- [9] Feng CD, Xu Y, Chen S, et al. Opioid-free anaesthesia reduces postoperative nausea and vomiting after thoroscopic lung resection: a randomised controlled trial[J]. *Br J Anaesth*, 2024, 132(2): 267-276.
- [10] Mei B, Yang X, Yang Y, et al. Intraoperative dexmedetomidine infusion improved postoperative sleep quality and melatonin secretion in patients undergoing elective thoroscopic lung surgery: a prospective, randomized study[J]. *Nat Sci Sleep*, 2024, 16: 2009-2020.
- [11] Dong Y, Wang M, Li W, et al. Effect of dexmedetomidine infusion on postoperative sleep disturbances in women with breast cancer: a monocentric randomized-controlled double-blind trial[J]. *Anaesth Crit Care Pain Med*, 2024, 43(3): 101358.
- [12] Su X, Wang DX. Improve postoperative sleep: what can we do?[J]. *Curr Opin Anaesthesiol*, 2018, 31(1): 83-88.
- [13] Wang X, Lin C, Lan L, et al. Perioperative intravenous S-ketamine for acute postoperative pain in adults: a systematic review and meta-analysis[J]. *J Clin Anesth*, 2021, 68: 110071.
- [14] Weerink MAS, Struys MMRF, Hannivoort LN, et al. Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine[J]. *Clin Pharmacokinet*, 2017, 56(8): 893-913.