Journal of Pain Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Comparative Efficacy of Esketamine vs Sufentanil with Propofol for Sedation in EUS: A Randomized, Controlled Study

Cuicui Liu[1,*], Yanting Wang[1,*], Yanwei Yin[2], Pei Wang[1], Xiangyu Ji[1], Jian Sun[1], Shuo Zhao[1], Yanfang Jia[1], Shanling Liu[1], Zangong Zhou[1]

[1]Daytime Anesthesiology Department, the Affiliated Hospital of Qingdao University, Qingdao, Shandong Province, People's Republic of China; [2]Pain Department, the Affiliated Hospital of Qingdao University, Qingdao, Shandong Province, People's Republic of China

*These authors contributed equally to this work

Correspondence: Zangong Zhou, Daytime Anesthesiology Department, the Affiliated Hospital of Qingdao University, 16 Jiangsu Road, Shinan District, Qingdao, Shandong Province, 266000, People's Republic of China, Tel +86 532-82912511, Email zhouzangong@qdu.edu.cn

Purpose: This randomized, controlled trial aimed to assess the sedative effects of esketamine and sufentanil combined with propofol during EUS.

Patients and Methods: Three hundred and forty patients undergone EUS were randomly divided into two groups to receive esketamine 0.25 mg/kg combined with propofol (esketamine group) or sufentanil 0.1 μg/kg combined with propofol (sufentanil group). The primary outcome measure was respiratory depression incidence. The secondary outcomes included the incidence of body movements, propofol dosage, lowest SPO_2 during the operation, and management of airway obstruction. In addition, other procedures and anesthesia-related outcomes, and postoperative complications were recorded.

Results: A total of 340 patients underwent randomization. Of these, 172 were assigned to the esketamine group and 168 were assigned to the sufentanil group. 1 patient in the esketamine group was lost in the follow-up. During the EUS, 9 patients (5.3%) in the esketamine group and 26 (15.5%) in the sufentanil group developed respiratory depression; this difference was statistically significant ($P = 0.002$). Regarding secondary outcomes, the incidence of body movements, induction dosage, supplemental times, and total dosage of propofol were much higher in the sufentanil group than in the esketamine group ($P < 0.05$). In addition, the lowest SPO_2 during the operation, occurrence rate of airway intervention, and management of airway obstruction were significantly different ($P < 0.05$). Compared to the sufentanil group, the induction time of sedation in the esketamine group was shorter, and the hemodynamics were more stable ($P < 0.05$). In addition, there were significant differences in the PACU incidence rates of nausea or vomiting between the two groups ($P < 0.05$), whereas the following day's complications showed no statistical difference.

Conclusion: Esketamine combined with propofol for sedation during EUS can decrease respiratory depression, reduce the dosage of propofol and PONV, and provide a more stable hemodynamic state. Consequently, esketamine could be considered as a potential alternative to sufentanil for sedation during EUS.

Keywords: esketamine, sedation, endoscopic ultrasound, respiratory depression

Introduction

Endoscopic ultrasound (EUS) has been a major breakthrough in the field of endoscopy. In EUS, endoscopy visualization and high-frequency ultrasound are combined in a minimally invasive procedure.[1] Nowadays, EUS has been widely used in the diagnosis and treatment of gastrointestinal disease, which has a good therapeutic effect on malignant and benign gastrointestinal, pancreatic and biliary diseases.[2,3] Owing to the addition of an ultrasound probe at the front end, EUS is much thicker than a conventional endoscope. In addition, because of the different examination methods, EUS usually requires a longer operative time than ordinary endoscopy. All these make EUS cause greater throat irritation in patients. Therefore, more stringent requirements have been proposed for anesthesia technology. Typically, opioids combined with

Received: 6 October 2024
Accepted: 1 January 2025
Published: 15 January 2025

propofol are the preferred sedative method for EUS. However, opioid-induced respiratory depression remains a major concern and carries a high risk in clinical applications.[4,5] Postoperative nausea and vomiting (PONV) is another common side effect of opioids that may lead to prolonged hospital stay.[6]

Esketamine, a right-handed split of ketamine, is an N-methyl-D-aspartic acid (NMDA) antagonist that has twice the anesthetic effect of ketamine. According to Jonkman's study, adequate doses of esketamine can reduce respiratory depression and improve hemodynamic, and the mechanism by which it alleviates respiratory depression may be attributed to an increase in opioids-induced ventilator CO_2 chemosensitivity.[7] Compared with sufentanil, esketamine can improve hemodynamics, reduce surgical stress and inflammatory responses, shorten anesthesia time, and promote the recovery of postoperative cognitive function.[8] In addition, due to its shorter time to elimination and recovery, fewer adverse reactions are associated with adverse reactions, such as psychiatric symptoms and respiratory secretions.[9] Previous studies have shown that esketamine combined with propofol can be safely used as sedative anesthesia for gastroscopy.[10,11] And it was reported that during colonoscopy, using esketamine along with propofol could reduce hypotension and enhanced respiration.[12] Another study found that the combination of esketamine with propofol can reduce tussis occurrence with good tolerability and relax the bronchus and also provides high clearance rates and low possibility of adverse reactions than the combination of propofol with sufentanil.[13] However, studies on the application of esketamine compared with opioids in EUS have not been reported.

This randomized, controlled study aimed to compare the sedative effects of esketamine and sufentanil combined with propofol in EUS.

Materials and Methods

This study was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University (Ethics Number: QYFYEC2023 −145) and was conducted in accordance with the ethical standards of the Declaration of Helsinki. The study was registered with the Chinese Clinical Trial Registry (ChiCTR2400090306) and informed consent were obtained from all the patients. From 12/20/2023 to 9/20/2024, patients scheduled for EUS fulfilled the inclusion criteria and received sedative anesthesia with esketamine-propofol or sufentanil-propofol.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: patients undergoing EUS under sedation, American Society of Anesthesiologists (ASA) grades I–III, age 18–75 years, and Mallampati grades I–III. The exclusion criteria were as follows: patients who may need to pump water into the esophagus and stomach during the examination process, sleep apnea history, evident difficult airway, BMI > 30, severe liver and kidney dysfunction, and refusal to participate.

Randomization and Blinding

The patients were divided into two groups using a computer-generated random number table at a ratio of 1:1. They then randomly received either esketamine-propofol or sufentanil-propofol as sedative anesthesia. The group assignments were confidential to the participants and operators as well as the postoperative care staff and data collectors. The anesthesiologist was aware of the grouping but was not involved in data collection and statistical analysis. All data collection and postoperative follow-up were performed by nurse anesthetists who were unaware of the group status.

Study Interventions

All patients were sedated according to a predefined sedation protocol. The patients fasted for at least 8 hours before surgery. After entering the operating room, patients were orally administered 10 mL Lidocaine Hydrochloride Gel for local anesthesia and then placed in the left lateral position and received oxygen at 5 L/min via a nasal catheter. Blood pressure (BP), electrocardiography (ECG), heart rate (HR), and oxygen saturation (SPO_2) were routinely monitored. Respiratory rate (RR) was obtained from multilead ECGs. After peripheral venous access was opened, 500 mL of normal saline was administered at a rate of 250 mL/h. As the induction of anesthesia, 0.25 mg/kg esketamine (Jiangsu Hengrui Pharmaceutical CO., Ltd) or 0.1 μg/kg sufentanil (Yichang Renfu Pharmaceutical CO., Ltd) were diluted to 10 mL with saline and injected slowly within 2 minutes, followed by 1.5–2 mg/kg propofol. After the eyelash reflex had disappeared, the endoscope was inserted. An

additional dose of 30 mg propofol was administered intravenously if the patient experienced body movements (body movements were divided into four levels: 1. No body movement; 2. Mild movements did not interfere with the operation; 3. Moderate body movements affected the operation; 4. Severe body movements that were different to control. Here, we classified classes 3 and 4 as positive body movements). If the systolic blood pressure was < 90 mmHg, 6 mg ephedrine was administered to raise the blood pressure. If the HR was < 50 times/min, 0.2 mg atropine was injected intravenously. During the operation, if the patients had reduced oxygenation due to respiratory obstruction, measures such as lifting the jaw, pressing the thorax, or inserting a nasopharyngeal airway were implemented. If the hypoxic state continued without improvement, the operating physician was required to withdraw the endoscope, and pressurized ventilation through a bag mask was implemented or intubation if necessary. After surgery, the patients were sent to the postanesthesia care unit (PACU) for further monitoring and could not return to the ward until the steward score reached 5.

Outcomes

Primary Outcome

The incidence of respiratory depression, defined as $SPO_2 \leq 90\%$ lasts for more than 10s, or respiratory rate ≤8 times/min, or respiratory arrest time ≥15s.

Secondary Outcomes

The secondary outcomes included the incidence of body movements, propofol induction dosage, supplemental time, and total dosage. The lowest SPO_2 during the operation, the need for airway intervention, and the management of airway obstruction were also recorded.

In addition, we recorded the total infusion volume, operation time, operator qualification, induction time of sedation, anesthesia time, procedure time, rate of immediate postoperative arousal, orientation recovery time, and PACU stay time in both the groups. Meanwhile, the BP, HR, SPO_2 and modified observer's assessment of alertness/sedation scale (MOAA/S) sedation scores at different time points as well as the number of cases requiring ephedrine and atropine were noted.

Postoperative complications, including immediate postoperative complications in the PACU, such as dizziness, nausea or vomiting, abdominal pain, or abdominal distension, and complications on the following day, including delirium, fever, dizziness, nausea or vomiting were recorded.

Finally, we investigated the satisfaction of patients and surgeons after operation. The score of endoscopists' satisfaction with sedation was determined using a 5 point scale (very dissatisfied = 1 to very satisfied = 5) after the procedure. Patients' satisfaction was measured using a visual analogue scale (VAS) correspond to a number of 0–5 after their full recovery.

Statistical Analyses

The sample size was calculated on the basis of the incidence of respiratory depression. According to previous studies,[14–16] the incidence of respiratory depression in patients receiving sufentanil in combination with propofol for sedation was 13.3–17.6%, with an average incidence of 15%. We expected the incidence to reduce to 5% in the esketamine group. With a power of 80% ($\alpha = 0.05$, $\beta = 0.2$), a sample size of 160 participants per group was required. We assumed that 5% of the patients would be lost to follow-up; therefore, at least 336 patients were required.

Data were analyzed using the SPSS software (version 25.0). Quantitative data are expressed as the mean and standard deviation (SD) or median (p25, p75), and qualitative data are presented as frequency and proportion. Data obtained at different time points were compared using a one-way repeated-measures ANOVA. For quantitative data, comparisons between two groups were made using *t*-tests or Mann–Whitney *U*-test. For qualitative data, chi-square or Fisher's test was used. Statistical significance was set at $P < 0.05$.

Results

Patient Inclusion and Characteristics

During 12/20/2023 to 9/20/2024, we screened 721 patients who underwent EUS under sedation. A total of 340 patients fulfilled the inclusion criteria and were randomly assigned to 2 groups (172 patients in the esketamine group and 168

patients in the sufentanil group). One patient in the esketamine group dropped out during the follow-up period. Finally, 339 participants completed the follow-up period and were included in statistical analysis (Figure 1).

The demographic data and baseline values of the patients are presented in Table 1. Statistical analysis revealed no differences between the two groups in terms of demographic characteristics and medical history ($P > 0.05$).

Procedure and Anesthesia-Related Outcomes

The dosage of esketamine and sufentanil in two groups were respectively 16.69 ± 2.44 mg and 6.6 ± 0.94 μg. Statistical analysis showed that the sedation induction time in the esketamine group was significantly lower than that in the sufentanil group ($P < 0.05$). The application of vasoactive agents (ephedrine and atropine) was much lower in the esketamine group than in the sufentanil group ($P < 0.05$). However, there were no differences in the other procedures or anesthesia-related outcomes ($P > 0.05$) (Table 2). Figure 2 shows vital signs and sedation scores at each time point. As

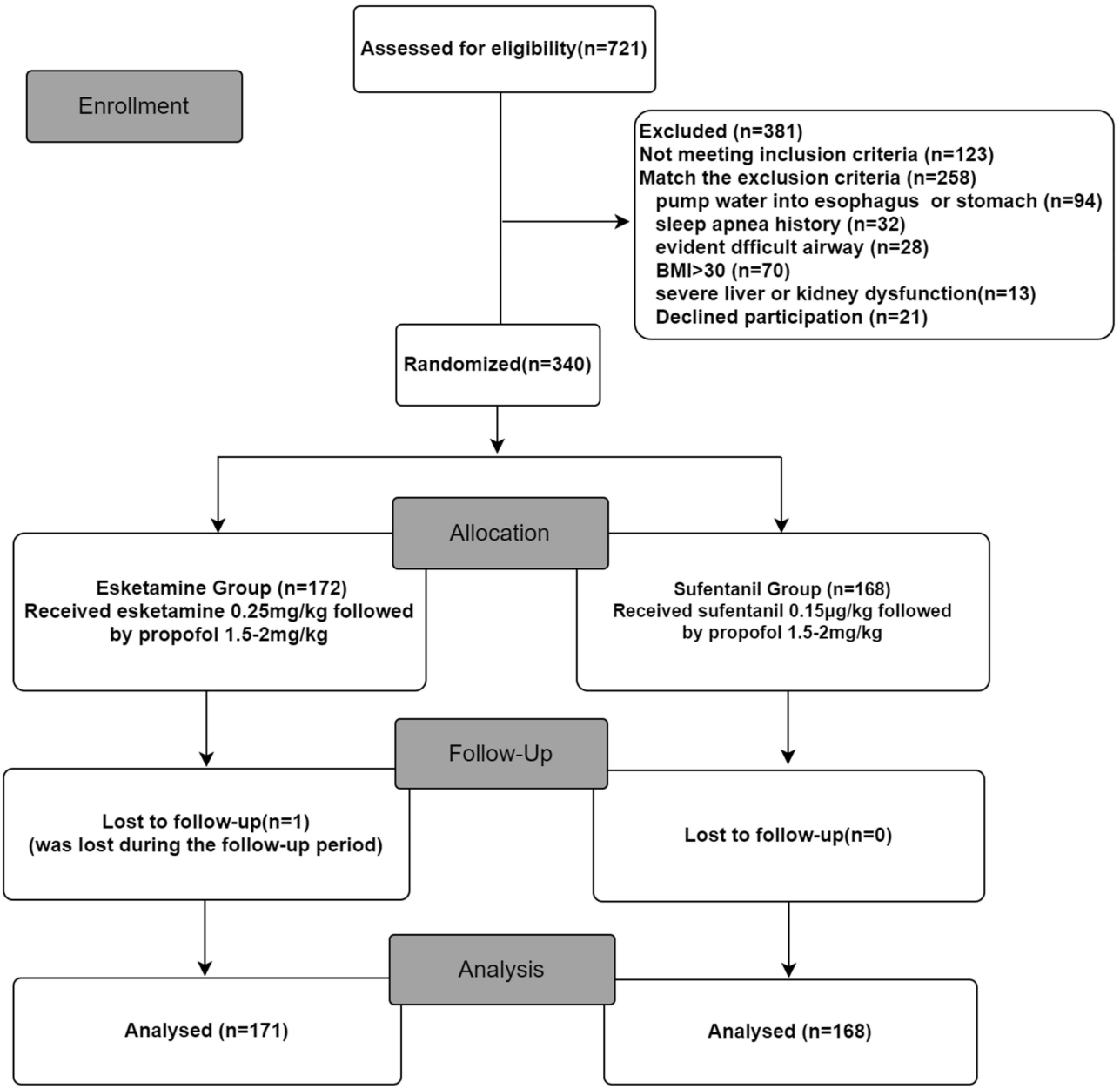

Figure 1 Flow diagram of patient progress through the phases of the randomized trial.

Table 1 Patient Demographic Characteristics

Variable	Esketamine Group (n = 171)	Sufentanil Group (n = 168)	*P* value
Age (years)	59.51 (52, 67)	58.7 (51, 68)	0.563
Gender (Males/Females)	98/73	90/78	0.489
Height (cm)	167.24 ± 6.98	166.12 ± 7.41	0.154
Weight (kg)	66.75 ± 9.74	65.99 ± 9.38	0.463
BMI (kg/m^2)	23.83 ± 2.94	23.90 ± 2.93	0.837
ASA grade			0.393
I, n (%)	53 (31.6)	63 (37.5)	
II, n (%)	110 (64.3)	96 (57.1)	
III, n (%)	7 (4.1)	9 (5.4)	
Lesion type, n (%)			0.846
Pancreatic disease, n (%)	87 (50.9)	81 (48.2)	
Hepatocholangiolithiasis, n (%)	34 (19.9)	33 (19.6)	
Duodenal neoplasms, n (%)	14 (8.2)	20 (11.9)	
Cholangiocarcinoma, n (%)	31 (18.1)	30 (17.9)	
Other disease, n (%)	5 (2.9)	4 (2.4)	
Mallampati score (I/II)	117/54	121/47	0.468
Snore, n (%)	35 (20.5)	30 (17.9)	0.582
Alcohol intake, n (%)	56 (32.7)	65 (38.7)	0.254
Smoking history, n (%)	46 (26.9)	49 (29.2)	0.642
Motion sickness, n (%)	36 (21.1)	32 (19)	0.645
Complication			
Hypertension, n (%)	58 (33.9)	53 (31.5)	0.642
Diabetes, n (%)	15 (8.8)	17 (10.1)	0.671
Coronary heart disease, n (%)	16 (9.4)	12 (7.2)	0.469
Allergic history, n (%)	37 (21.6)	33 (19.6)	0.689
Operation history, n (%)	48 (28.1)	57 (33.9)	0.243

Notes: Data are presented as mean ± SD or median (p25, p75) for continuous variables, and count (percentage) for categorical variables.
Abbreviations: BMI, Body Mass Index, ASA, American Society of Anesthesiologists.

Table 2 Procedure and Anesthesia-Related Outcomes

Variable	Esketamine Group (n = 171)	Sufentanil Group (n = 168)	*P* value
Esketamine dosage (mg)	16.69 ± 2.44		
Sufentanil dosage (μg)		6.60 ± 0.94	
Infusion quantity (mL)	175 (150, 225)	175 (150, 200)	0.622
Operation time (morning/afternoon)	145/26	147/21	0.287
Operative qualification			0.717
< 3 years, n (%)	20 (11.7)	22 (13.1)	
3–10 years, n (%)	91 (53.2)	82 (48.8)	
> 10 years, n (%)	60 (35.1)	64 (38.1)	
Induction time of sedation (seconds)	35 (30, 35)	35 (35, 40)	<0.001
Anesthesia time (min)	22 (19, 225)	22 (18, 27)	0.764
Procedure time (min)	20 (17, 23)	20 (16.25, 24)	0.765
Immediate postoperative arousal, n (%)	134 (78.4)	138 (82.1)	0.382
Orientation recovery time (min)	8 (7, 9)	8 (6, 9)	0.642
Ephedrine application, n (%)	13 (7.6)	26 (15.5)	0.023
Atropine application, n (%)	11 (6.4)	22 (13.1)	0.039
Intraoperative cough, n (%)	7 (4.1)	9 (5.4)	0.583
Intraoperative hiccup, n (%)	6 (3.5)	4 (2.4)	0.539

(*Continued*)

https://doi.org/10.2147/JPR.S498499

Table 2 (Continued).

Variable	Esketamine Group (n = 171)	Sufentanil Group (n = 168)	*P* value
PACU stay time (min)	15.18 ± 3.91	14.67 ± 3.98	0.236
Satisfaction for anesthesia			
Patient	5 (5, 5)	5 (5, 5)	0.494
Surgeon	5 (5, 5)	5 (5, 5)	0.204

Notes: Data are presented as mean ± SD or median (p25, p75) for continuous variables, and count (percentage) for categorical variables.
Abbreviation: PACU, postanesthesia care unit.

can be seen from the curve, MAP, HR, and RR in the esketamine group were significantly higher than those in the sufentanil group after anesthesia induction and during the procedure (Figure 2A, B and D). However, there was no significant difference in sedation scores (MOAA/S) between the two groups, except at T4 (Figure 2C).

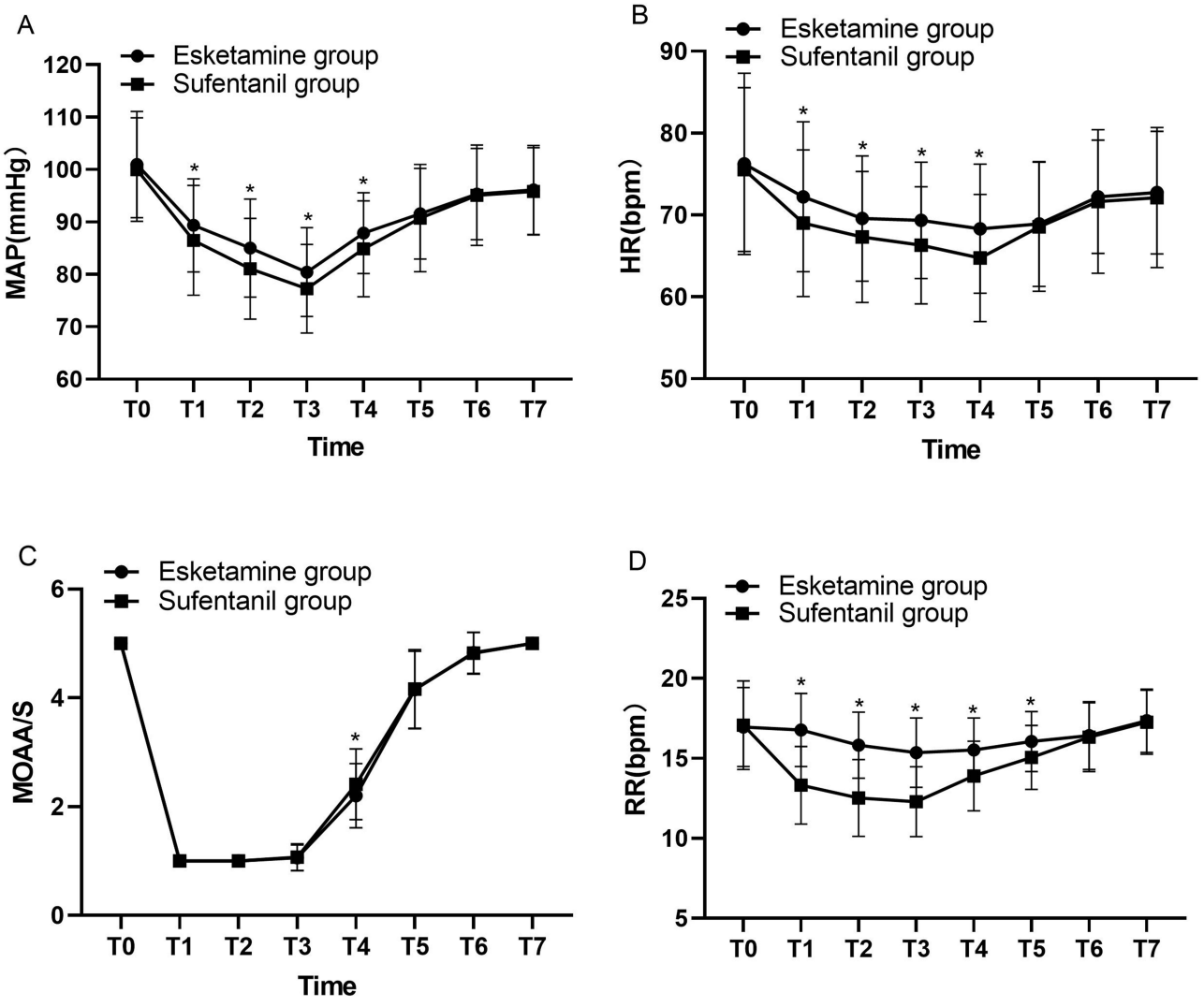

Figure 2 Vital signs and sedation scores at each time point. (**A-D**) The MAP, HR, MOAA/S and RR of the two groups at each time point. MAP: Mean Arterial Pressure; HR: Heart Rate; MOAA/S: Modified observer's assessment of alertness/sedation scale. RR: Respiratory Rate. T0, before anesthesia; T1, immediately after anesthesia induction; T2, endoscope passed through the throat; T3, endoscope reached the target position; T4, 10 minutes after the start of procedure; T5, end of the procedure; T6, patient entered the PACU; T7, patient leaved the PACU. (*P<0.05).

Primary and Secondary Outcomes

Nine patients (5.3%) in the esketamine group and 26 (15.5%) in the sufentanil group developed respiratory depression; this difference was statistically significant ($P = 0.002$).

With regard to secondary outcomes, the incidence of body movements, induction dosage, supplemental times, and total dosage of propofol were much higher in the sufentanil group than in the esketamine group ($P < 0.05$). In addition, the lowest SPO_2 during the operation, occurrence rate of airway intervention, and management of airway obstruction were significantly different ($P < 0.05$). The most common airway intervention was lift jaw, and none of the patients required intubation. (Table 3).

Postoperative Complications

Postoperative complications, including immediate complications in the PACU and complications on the following day are shown in Table 4. There were significant differences in the PACU incidence rates of dizziness, and nausea or vomiting between the two groups ($P < 0.05$). However, the following day's complications showed no statistically significant differences ($P > 0.05$). One patient in the esketamine group developed fever after the examination and chest computed tomography (CT) is shown in Figure 3.

Table 3 Primary and Secondary Outcomes

Variable	Esketamine Group (n = 171)	Sufentanil Group (n = 168)	*P* value
Primary outcome			
Respiratory depression, n (%)	9 (5.3)	26 (15.5)	0.002
Secondary outcomes			
Body movements, n (%)	58 (33.9)	81 (48.2)	0.007
Propofol usage			
Induction dosage (mg)	100 (100, 110)	110 (100, 110)	0.026
Supplemental times	0 (0, 1)	0 (0, 1)	0.008
Total dosage (mg)	110 (100, 130)	120 (100, 140)	0.003
Lowest SPO_2 during operation (%)	96 (95, 97)	95 (93, 96)	<0.001
Need for airway intervention, n (%)	47 (27.5)	65 (38.7)	0.028
Management of airway obstruction, n (%)			
Lift jaw	42 (24.6)	62 (36.9)	0.014
Pressing the thorax	2 (1.2)	9 (5.4)	0.029
Mask pressure ventilation	4 (2.3)	6 (3.6)	0.540
Insert nasopharyngeal airway	2 (1.2)	6 (3.6)	0.171
Intubation	0(0)	0(0)	

Notes: Data are presented as medians (p25, p75) for continuous variables and as counts (percentages) for categorical variables.

Table 4 Postoperative Complications

Variable	Esketamine Group (n = 171)	Sufentanil Group (n = 168)	*P* value
Immediate complications	20 (11.7)	27 (16.1)	0.244
Dizziness	10 (5.8)	19 (11.3)	0.072
Nausea or vomiting	6 (3.5)	16 (9.5)	0.025
Abdominal pain or abdominal distension	8 (4.7)	5 (3.0)	0.415
Complications on the following day	6 (3.5)	10 (6.0)	0.289
Delirium	0 (0)	0 (0)	1
Fever	1 (0.6)	0 (0)	1
Dizziness	4 (2.3)	4 (2.4)	1
Nausea or vomiting	2 (1.2)	6 (3.6)	0.171

Note: Data were presented as count (percentage).

https://doi.org/10.2147/JPR.S498499

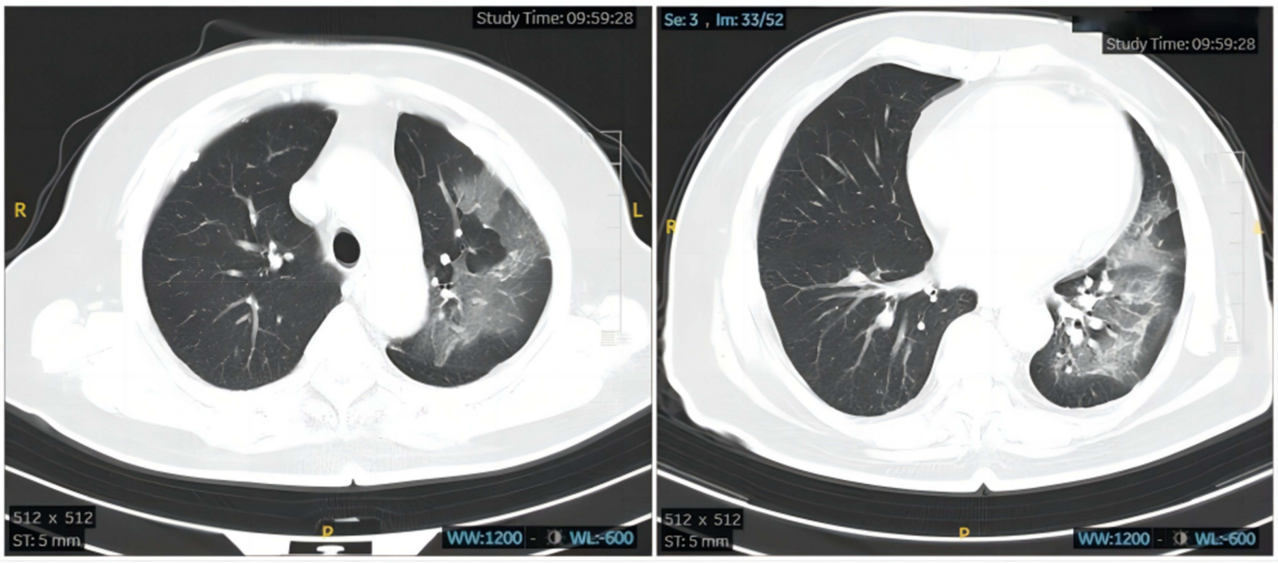

Figure 3 Chest computed tomography (CT) of the feverish patient.

Discussion

In this study, we compared the sedative effects of esketamine and sufentanil combined with propofol in EUS and found fewer patients occurred respiratory depression in the esketamine group than in the sufentanil group.

EUS is typically performed in patients under sedation anesthesia. During the procedure, the endoscope occupies the oral cavity, making it more difficult for anesthesiologists to manage the airway. Therefore, it is necessary to explore a method of anesthesia with minimal impact on breathing. Propofol is the predominant drug used for sedation owing to its rapid onset of action and short recovery time. Since EUS usually takes a longer time, an increased dose of propofol is often required to complete the anesthesia. However, high doses of propofol can also cause respiratory and circulatory suppression. A previous study showed that 12.8% of patients experienced hypoxemia with propofol for endoscopic sedation.[17] Therefore, in daily clinical applications, anesthesiologists usually use propofol in combination with small-dose opioids, which can increase the analgesic effect while reducing the applied dose of propofol. However, this combination may increase the risk of respiratory depression leading to hypoxemia. Opioids may cause a decrease in respiratory rate, which further leads to a decrease in oxygenation. This phenomenon was also observed (Figure 2D). Goyal R et al reported that even administered by experienced anesthesiologists, the combination of propofol and fentanyl would still cause a decrease in oxygenation in 48.2% of patients.[18] A recent study also reported that during sedation in ERCP, 15.7% of patients in propofol-alfentanil group showed hypoxia.[19] In previous studies, the amount of sufentanil used for endoscopy varied. However, we could get ranges of sufentanil dosing in endoscopy. It was reported that 0.05 μg/kg sufentanil was the most suitable program for painless gastroscopy.[20] For children undergoing painless gastroscopy under general anesthesia, 0.03–0.05 μg/kg sufentanil combined with propofol can deliver better anesthetic effect than propofol combined with fentanyl.[21] Another study reported that 0.1 μg/kg sufentanil combined with propofol be a suitable alternative sedative agent for elderly patients undergoing gastroscopy due to its safety profile.[22] According to our daily clinical application and reference to previous literatures, we set the doses of sufentanil to 0.1 μg/kg. In the current research, 26 of 168 patients developed respiratory depression in sufentanil-propofol group with a percentage of 15.5% and this finding match those previous studies. The application of esketamine significantly improved this index by reducing the incidence of respiratory depression to 5.3%. Simultaneously, the patients' body movements during the operation were also significantly reduced.

As esketamine has both sedative and analgesic effects, when combined with propofol, it can significantly reduce the dosage of propofol. Eberl et al reported that esketamine can reduce the dosage of propofol by approximately 20% in operation.[23] Other studies have also observed that esketamine can decrease propofol consumption in patients undergoing

gastroscopy.[10,24] In the present study, we also observed that the induction dosage, supplemental times, and total dosage of propofol were all reduced in the esketamine group. Circulatory suppression is another complication associated with propofol combined with sufentanil. In this study, we found that MAP and HR were much more stable in the esketamine group and the application of vasoactive agents was much less than that in the sufentanil group. These findings are in accordance with those of a recent study[25] and indicate that the combination of esketamine and propofol provides more stable hemodynamics. In addition, we compared anesthesia-related data between the two groups and observed that the esketamine group required a shorter induction time for sedation. However, other outcomes, such as immediate post-operative arousal, orientation recovery time, and PACU stay time, did not differ. These results indicate that esketamine can accelerate induction and has no effect on postoperative recovery. Study has even found that the awakening time of esketamine combined with propofol is shorter than propofol alone.[10] Author speculated that this may be related to the reduced amount of propofol.

As we know, nausea and vomiting are common side effects of opioids, the incidence of opioids-induced nausea and vomiting is estimated to be 10%–40%.[26] We concerned the postoperative complications and found that esketamine significantly reduce the incidence of nausea or vomiting in the PACU. Previous studies have reported that ketamine produces psychotomimetic symptoms, perceptual aberrations, and cognitive impairments.[27] As a right-handed split of ketamine, the use of S-ketamine did not result in increased psychotomimetic side effects.[28] Consistent with these researches, our second day's follow-up showed no patient developed delirium, indicating that esketamine combined with propofol did not increase any comorbidities and can be safely used in EUS.

Before the initiation of the trial, most patients in our center were sedation with sufentanil combined with propofol. The study demonstrated that the combination of esketamine and propofol resulted in a decrease in respiratory depression, a reduction in propofol dosage and PONV, and a more stable hemodynamic state, which might not only save drugs costs but also make it easier for anesthesiologists to manage patients' breathing and vital signs. We suggest the current study may help anesthesiologists to choose a more appropriate sedation regimen in EUS. In addition, future studies should be conducted to investigate the advantages of esketamine in other endoscopic procedures such as gastroscopy, colonoscopy, bronchoscope and endoscopic retrograde cholangiopancreatography (ERCP). At present, researches on esketamine mainly focuses on its association with depression. Multiple studies have found that esketamine can effectively alleviate symptoms in patients with depression or reduce the occurrence of postpartum depression.[29,30] However, there is relatively limited literatures on the potential psychiatric effects of esketamine when used as an anesthetic agent. Meanwhile, the potential cost and availability may limit its application in routine anesthesia either. So, despite the potential advantages of esketamine in certain aspects, its clinical application still needs to be evaluated with caution and consideration of the specific circumstances and potential risks of the patients.

It is worth mentioning that one patient developed symptoms such as high fever, chills, and cough approximately four hours after EUS, accompanied by increased leukocyte and C-reactive protein (CRP) levels. The chest CT performed the next day revealed multiple flaky ground-glass density shadows in the patient's left lung (Figure 3). The patient was then diagnosed with aspiration pneumonia, and she had a good prognosis after antimicrobial therapy. Aspiration pneumonia is a rare complication of painless endoscopies. Friedrich et al reported that 0.3% of patients who underwent outpatient endoscopy developed signs of respiratory symptoms suspicious for infection during a 24-hour phone follow-up, but none required hospitalization.[31] Another research demonstrated that the probability of aspiration after painless gastroscopy was 0.2%.[32] However, in patients with high-risk factors for reflux, the proportion was significantly higher. Lin et al reported that the proportion of aspiration pneumonia in patients with retained gastric food content reached 4.8%.[33] In the future, we will also increase the sample size to carry out research in this area.

This study has some limitations. First, to minimize the impact on breathing, we excluded patients with sleep apnea and those who may have difficult airways, as well as patients who were obese; therefore, the sedation regimen for these patients remains to be explored. Second, this was a single-center study, and further multicenter studies are required. Third, the study period was relatively short, and there may be limitations in observing the long-term impact of sedation effects. Finally, according to our daily clinical application and reference to previous literatures,[34,35] we set the doses of sufentanil and esketamine to 0.1 μg/kg and 0.25 mg/kg, therefore additional studies with other doses should be considered.

https://doi.org/10.2147/JPR.S498499

Conclusion

This randomized controlled trial aims to assess the sedative effects of esketamine and sufentanil combined with propofol during EUS. These findings demonstrate that the combination of esketamine and propofol resulted in a decrease in respiratory depression, a reduction in propofol dosage and PONV, and a more stable hemodynamic state. Consequently, esketamine could be considered as a potential alternative to sufentanil for sedation during EUS.

Data Sharing Statement

The original contributions presented in this study are included in the article, further inquiries can be directed to the corresponding author (email, zhouzangong@qdu.edu.cn).

Acknowledgments

This study has made every effort to avoid any conflicts of interest that may affect the impartiality of the research results during its design and implementation. Nevertheless, we acknowledge that any study may have certain potential biases. In order to enhance transparency, we hereby state that during the process of data collection, analysis, and interpretation, we have taken all necessary measures to minimize the impact of these potential biases. We commit that all research processes and results are based on principles of objectivity, fairness, and science.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Mann R, Goyal H, Perisetti A, Chandan S, Inamdar S, Tharian B. Endoscopic ultrasound-guided vascular interventions: current insights and emerging techniques. *World J Gastroenterol*. 2021;27(40):6874–6887. doi:10.3748/wjg.v27.i40.6874
2. Sooklal S, Chahal P. Endoscopic ultrasound. *Surg Clin North Am*. 2020;100(6):1133–1150. doi:10.1016/j.suc.2020.07.003
3. Fabian A, Bor R, Bosze Z, et al. Endoscopic ultrasound in the lower gastrointestinal tract. *Orv Hetil*. 2023;164(30):1176–1186. doi:10.1556/650.2023.32794
4. Frasco PE, Sprung J, Trentman TL. The impact of the joint commission for accreditation of healthcare organizations pain initiative on perioperative opiate consumption and recovery room length of stay. *Anesth Analg*. 2005;100(1):162–168. doi:10.1213/01.ANE.0000139354.26208.1C
5. Dahan A, van Lemmen M, Jansen S, Simons P, van der Schrier R. Buprenorphine: a treatment and cause of opioid-induced respiratory depression. *Br J Anaesth*. 2022;128(3):402–404. doi:10.1016/j.bja.2021.12.001
6. Liu SS, Strodtbeck WM, Richman JM, Wu CL. A comparison of regional versus general anesthesia for ambulatory anesthesia: a meta-analysis of randomized controlled trials. *Anesth Analg*. 2005;101(6):1634–1642. doi:10.1213/01.ANE.0000180829.70036.4F
7. Jonkman K, van Rijnsoever E, Olofsen E, et al. Esketamine counters opioid-induced respiratory depression. *Br J Anaesth*. 2018;120(5):1117–1127. doi:10.1016/j.bja.2018.02.021
8. Tu W, Yuan H, Zhang S, et al. Influence of anesthetic induction of propofol combined with esketamine on perioperative stress and inflammatory responses and postoperative cognition of elderly surgical patients. *Am J Transl Res*. 2021;13(3):1701–1709.
9. Zanos P, Moaddel R, Morris PJ, et al. Ketamine and ketamine metabolite pharmacology: insights into therapeutic mechanisms. *Pharmacol Rev*. 2018;70(3):621–660. doi:10.1124/pr.117.015198
10. Zheng L, Wang Y, Ma Q, et al. Efficacy and safety of a subanesthetic dose of esketamine combined with propofol in patients with obesity undergoing painless gastroscopy: a prospective, double-blind, randomized controlled trial. *Drug Des Devel Ther*. 2023;17:1347–1356. doi:10.2147/DDDT.S408076
11. Xu Y, Zheng Y, Tang T, Chen L, Zhang Y, Zhang Z. The effectiveness of esketamine and propofol versus dezocine and propofol sedation during gastroscopy: a randomized controlled study. *J Clin Pharm Ther*. 2022;47(9):1402–1408. doi:10.1111/jcpt.13678
12. Fu M, Sheng B, Liu R, et al. Impact of different doses of esketamine on the incidence of hypotension in propofol-based sedation for colonoscopy: a randomized controlled trial. *Ther Adv Drug Saf*. 2024;15:20420986241278499. doi:10.1177/20420986241278499
13. Hou HJ, Liu L, Tian M, Xue FS. Comparison of the effects of esketamine, sufentanil, or lidocaine combined with propofol on tussis reflection during upper gastrointestinal endoscopy: study protocol for a randomised, two centre, three-blind, controlled trial. *Trials*. 2024;25(1):24. doi:10.1186/s13063-023-07812-0
14. Zhang S, Wang J, Ran R, Peng Y, Xiao Y. Efficacy and safety of remimazolam tosylate in hysteroscopy: a randomized, single-blind, parallel controlled trial. *J Clin Pharm Ther*. 2022;47(1):55–60. doi:10.1111/jcpt.13525
15. Cao Y, Chi P, Zhou C, Lv W, Quan Z, Xue FS. Remimazolam tosilate sedation with adjuvant sufentanil in Chinese patients with liver cirrhosis undergoing gastroscopy: a randomized controlled study. *Med Sci Monit*. 2022;28:e936580. doi:10.12659/MSM.936580
16. Chen L, Wang M, Xiang H, Lin X, Cao D, Ye L. Prediction of effect-site concentration of sufentanil by dose-response target controlled infusion of sufentanil and propofol for analgesic and sedation maintenance in burn dressing changes. *Burns*. 2014;40(3):455–459. doi:10.1016/j.burns.2013.08.002
17. Cote GA, Hovis RM, Ansstas MA, et al. Incidence of sedation-related complications with propofol use during advanced endoscopic procedures. *Clin Gastroenterol Hepatol*. 2010;8(2):137–142. doi:10.1016/j.cgh.2009.07.008

18. Goyal R, Hasnain S, Mittal S, Shreevastava S. A randomized, controlled trial to compare the efficacy and safety profile of a dexmedetomidine-ketamine combination with a propofol-fentanyl combination for ERCP. *Gastrointest Endosc*. 2016;83(5):928–933. doi:10.1016/j.gie.2015.08.077
19. Dong SA, Guo Y, Liu SS, et al. A randomized, controlled clinical trial comparing remimazolam to propofol when combined with alfentanil for sedation during ERCP procedures. *J Clin Anesth*. 2023;86:111077. doi:10.1016/j.jclinane.2023.111077
20. Zhang L, Bao Y, Shi D. Comparing the pain of propofol via different combinations of fentanyl, sufentanil or remifentanil in gastrointestinal endoscopy. *Acta Cir Bras*. 2014;29(10):675–680. doi:10.1590/S0102-86502014001600008
21. Wang Y, Yang H, Cai W, Ni H. Effects of propofol combined with sufentanil on painless gastroscopy and hemodynamics in children under general anesthesia. *Am J Transl Res*. 2023;15(7):4942–4950.
22. Hu B, Jiang K, Shi W, et al. Effect of remimazolam tosilate on respiratory depression in elderly patients undergoing gastroscopy: a multicentered, prospective, and randomized study. *Drug Des Devel Ther*. 2022;16:4151–4159. doi:10.2147/DDDT.S391147
23. Eberl S, Koers L, van Hooft J, et al. The effectiveness of a low-dose esketamine versus an alfentanil adjunct to propofol sedation during endoscopic retrograde cholangiopancreatography: a randomised controlled multicentre trial. *Eur J Anaesthesiol*. 2020;37(5):394–401. doi:10.1097/EJA.0000000000001134
24. Zhan Y, Liang S, Yang Z, et al. Efficacy and safety of subanesthetic doses of esketamine combined with propofol in painless gastrointestinal endoscopy: a prospective, double-blind, randomized controlled trial. *BMC Gastroenterol*. 2022;22(1):391. doi:10.1186/s12876-022-02467-8
25. Yang H, Zhao Q, Chen HY, et al. The median effective concentration of propofol with different doses of esketamine during gastrointestinal endoscopy in elderly patients: a randomized controlled trial. *Br J Clin Pharmacol*. 2022;88(3):1279–1287. doi:10.1111/bcp.15072
26. Cherny NI. Opioid analgesics: comparative features and prescribing guidelines. *Drugs*. 1996;51(5):713–737. doi:10.2165/00003495-199651050-00002
27. Ali F, Gerhard DM, Sweasy K, et al. Ketamine disinhibits dendrites and enhances calcium signals in prefrontal dendritic spines. *Nat Commun*. 2020;11(1):72. doi:10.1038/s41467-019-13809-8
28. Ithnin FB, Tan DJA, Xu XL, Tan CH, Sultana R, Sng BL. Low-dose S+ ketamine in target-controlled intravenous anaesthesia with remifentanil and propofol for open gynaecological surgery: a randomised controlled trial. *Indian J Anaesth*. 2019;63(2):126–133. doi:10.4103/ija.IJA_605_18
29. Reif A, Bitter I, Buyze J, et al. Esketamine nasal spray versus quetiapine for treatment-resistant depression. *N Engl J Med*. 2023;389(14):1298–1309. doi:10.1056/NEJMoa2304145
30. Chen Y, Guo Y, Wu H, et al. Perioperative adjunctive esketamine for postpartum depression among women undergoing elective cesarean delivery: a randomized clinical trial. *JAMA Network Open*. 2024;7(3):e240953. doi:10.1001/jamanetworkopen.2024.0953
31. Friedrich K, Scholl SG, Beck S, et al. Respiratory complications in outpatient endoscopy with endoscopist-directed sedation. *J Gastrointestin Liver Dis*. 2014;23(3):255–259. doi:10.15403/jgld.2014.1121.233.kf1
32. Agostoni M, Fanti L, Gemma M, Pasculli N, Beretta L, Testoni PA. Adverse events during monitored anesthesia care for GI endoscopy: an 8-year experience. *Gastrointest Endosc*. 2011;74(2):266–275. doi:10.1016/j.gie.2011.04.028
33. Lin E, Gao Y, Wright A, Kim JJ. Practice patterns and outcomes of patients with retained gastric food content encountered during endoscopy. *Clin Transl Gastroenterol*. 2023;14(3):e00559. doi:10.14309/ctg.0000000000000559
34. Lin Z, Li S, Zhou Y, et al. A comparative study of esketamine-dexmedetomidine and sufentanil-dexmedetomidine for sedation and analgesia in lung tumor percutaneous radiofrequency ablation (PRFA): a randomized double-blind clinical trial. *BMC Anesthesiol*. 2023;23(1):304. doi:10.1186/s12871-023-02266-y
35. Zhu X, Chen L, Zheng S, Pan L. Comparison of ED95 of butorphanol and sufentanil for gastrointestinal endoscopy sedation: a randomized controlled trial. *BMC Anesthesiol*. 2020;20(1):101. doi:10.1186/s12871-020-01027-5