Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Comparison of Anesthetic Effects between Esketamine Combined with Propofol and Remifentanil Combined with Propofol in Pediatric Painless Gastrointestinal Endoscopy

qian guo

gq112233@126.com

Shanghai Jiao Tong University School of Medicine

jing wu

Shanghai Jiao Tong University School of Medicine

yan luo

Shanghai Jiao Tong University School of Medicine

qiang li

Shanghai Jiao Tong University School of Medicine

ling gong

Shanghai Jiao Tong University School of Medicine

Research Article

Keywords: esketamine, propofol, remifentanil, pediatric endoscopy, hypoxemia

Posted Date: November 9th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11324360/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Comparison of Anesthetic Effects between Esketamine Combined with Propofol and Remifentanil Combined with Propofol in Pediatric Painless Gastrointestinal Endoscopy

Qian Guo 1, Jing Wu 1, Yan Luo 1, Qiang Li 1,* and Ling Gong 1,*

1 Department of Anesthesiology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China

*** Correspondence:** gongling112233@126.com

Abstract

Background: Pediatric gastrointestinal endoscopy often requires deep sedation while maintaining spontaneous ventilation and hemodynamic stability. Propofol is widely used but lacks analgesic properties and may cause dose-dependent respiratory and cardiovascular depression. This randomized controlled study compared esketamine–propofol with remifentanil–propofol for sedation in children undergoing painless gastrointestinal endoscopy. **Methods:** In this single-center randomized controlled study, 83 children undergoing elective painless gastrointestinal endoscopy were allocated to an esketamine–propofol group (PE group, n = 43) or a remifentanil–propofol group (PR group, n = 40). The primary outcome was the incidence of hypoxemia, defined as any peripheral oxygen saturation (SpO_2) <95% during the peri-procedural period. Secondary outcomes included peri-procedural heart rate, mean arterial pressure, SpO_2, awakening time, propofol consumption, physician satisfaction, and adverse events. **Results:** Hypoxemia occurred less frequently in the PE group than in the PR group (4/43, 9.3% vs. 13/40, 32.5%; P = 0.019). The PE group also had a shorter awakening time (9.95 ± 3.19 vs. 14.22 ± 4.70 min; P < 0.001) and lower total propofol consumption (190.47 ± 54.38 vs. 242.75 ± 72.64 mg; P < 0.001). SpO_2 was higher in the PE group at T1 (97.58 ± 1.80% vs. 96.05 ± 3.01%; P = 0.007), heart rate was higher at T2 (87.44 ± 14.37 vs. 74.65 ± 14.18 beats/min; P < 0.001), and mean arterial pressure was higher at T3 (68.46 ± 7.95 vs. 64.49 ± 6.44 mmHg; P = 0.014). Hypotension requiring ephedrine was less frequent in the PE group (2.3% vs. 30.0%; P = 0.002), and anesthesiologist satisfaction was higher (8.40 ± 0.69 vs. 7.93 ± 0.66; P = 0.002). No significant between-group differences were observed in endoscopist satisfaction, bradycardia requiring atropine, body movement, nausea or vomiting, or the requirement for supplementary propofol. **Conclusions:** In children undergoing painless gastrointestinal endoscopy, esketamine–propofol was associated with a lower incidence of hypoxemia, reduced propofol consumption, less frequent hypotension requiring ephedrine, and shorter awakening time than remifentanil–propofol, without increasing procedural movement or nausea and vomiting. These findings

suggest that esketamine–propofol may be a useful alternative sedation regimen for pediatric gastrointestinal endoscopy, although larger multicenter studies are warranted. **Trial registration:** Chinese Clinical Trial Registry, ChiCTR2600133316. Date of registration: 24 September 2026. Retrospectively registered.

Keywords: esketamine; propofol; remifentanil; pediatric endoscopy; hypoxemia

1. Introduction

Gastrointestinal endoscopy is an important diagnostic and therapeutic procedure in pediatric clinical practice and is widely used for the evaluation of gastrointestinal bleeding, suspected inflammatory bowel disease, polyps, persistent abdominal symptoms, and other gastrointestinal disorders [1,2]. Unlike most adults, children often have limited tolerance of endoscopic procedures because of anxiety, fear, discomfort, pharyngeal stimulation, and difficulty remaining still during examination. Consequently, deep sedation or general anesthesia is frequently required to provide adequate procedural conditions, minimize psychological distress, prevent movement-related complications, and improve the overall quality of endoscopic examination [1–3]. Pediatric endoscopy therefore places substantial demands on both procedural sedation and airway management.

However, sedation for pediatric gastrointestinal endoscopy presents particular challenges. Children have physiologic characteristics that can increase vulnerability to respiratory adverse events during deep sedation, and airway obstruction, apnea, and oxygen desaturation may develop rapidly during non-intubated procedures. Hemodynamic instability, including hypotension and bradycardia, may also occur and may require airway or pharmacological rescue interventions. Accordingly, contemporary procedural-sedation guidance emphasizes continuous physiologic monitoring, appropriate patient selection, and immediate availability of personnel and equipment capable of managing cardiorespiratory complications [4]. An optimal sedation regimen for pediatric gastrointestinal endoscopy should therefore provide sufficient hypnosis and analgesia while preserving spontaneous ventilation, maintaining cardiovascular stability, allowing rapid recovery, and minimizing drug-related adverse events.

Propofol is one of the most commonly used intravenous anesthetic agents for gastrointestinal endoscopy because of its rapid onset of action, predictable hypnotic effect, and relatively short recovery profile. It is also widely used in pediatric procedural sedation [5]. Nevertheless, propofol has no intrinsic analgesic effect, and dose escalation to suppress procedural stimulation may increase the risks of respiratory depression, airway obstruction, hypotension, and delayed recovery [5]. A large national survey of gastrointestinal endoscopy practice in China also showed that propofol is the most commonly used sedative agent and that propofol–opioid combinations are frequently employed in clinical practice [6]. For this reason, combining propofol with an analgesic agent is a common strategy to reduce propofol requirements while improving procedural tolerance.

Remifentanil is an ultra-short-acting μ-opioid receptor agonist characterized by rapid onset, potent analgesic activity, and rapid offset. Its pharmacodynamic interaction with propofol has been investigated specifically in children undergoing esophagogastroduodenoscopy, with remifentanil shown to reduce the propofol concentration required to suppress responses to endoscopic stimulation [7]. Propofol–remifentanil sedation has also been used successfully in spontaneously breathing children undergoing gastrointestinal endoscopy [8]. However, the respiratory effects of remifentanil remain clinically relevant. In a randomized pediatric study comparing propofol combined with remifentanil or fentanyl, remifentanil shortened awakening time and reduced propofol requirements but was associated with more frequent prolonged apnea and oxygen desaturation [9]. These findings highlight the balance between rapid recovery and respiratory safety when remifentanil is used during pediatric endoscopy.

Esketamine, the S-enantiomer of ketamine, is an N-methyl-D-aspartate receptor antagonist with both sedative and analgesic properties. Its pharmacological profile is attractive for procedural sedation because it can provide analgesia while generally exerting less respiratory depression than conventional opioid-based regimens. In addition, its sympathomimetic effects may partially counteract propofol-associated reductions in blood pressure. A multicenter randomized trial in children undergoing upper gastrointestinal endoscopy found that esketamine–propofol provided favorable procedural conditions and attenuated propofol-related hemodynamic changes compared with nalbuphine–propofol [10].

Several pediatric studies have further explored the use of esketamine in combination with propofol. A prospective randomized study in school-aged children undergoing gastroduodenoscopy showed that S-ketamine combined with propofol provided effective sedation, with dose-dependent effects on sedation quality and adverse events [11]. A dose-finding study subsequently demonstrated that increasing doses of esketamine substantially reduced the propofol dose required for successful upper gastrointestinal endoscopy in children, although higher esketamine doses were accompanied by a greater incidence of drug-related adverse effects [12]. These findings suggest that esketamine can produce a clinically meaningful propofol-sparing effect, but that dose selection remains important.

Evidence from adults also supports the potential respiratory and hemodynamic advantages of adding low-dose esketamine to propofol. In a multicenter randomized clinical trial involving 660 adults undergoing same-visit bidirectional endoscopy, low-dose esketamine significantly reduced the composite incidence of desaturation and hypotension and reduced total propofol requirements compared with placebo [13]. These findings are consistent with the hypothesis that esketamine may improve the balance between adequate sedation and cardiorespiratory stability during gastrointestinal endoscopy.

More recently, a meta-analysis focused specifically on pediatric gastrointestinal endoscopy found that adjunctive esketamine reduced recovery time and propofol consumption and was associated with higher mean heart rate and mean arterial pressure, while the overall effects on respiratory depression were less definitive [14]. Thus, although the available evidence supports esketamine as an effective adjunct to propofol, uncertainty remains regarding its comparative performance against commonly used opioid-based regimens in children.

In particular, direct randomized evidence comparing esketamine–propofol with remifentanil–propofol in pediatric gastrointestinal endoscopy remains limited. Previous pediatric trials have compared propofol–remifentanil with other anesthetic combinations. For example, a randomized study comparing propofol–ketamine with propofol–remifentanil in children undergoing gastroscopy demonstrated that both regimens were feasible but differed in induction conditions, awakening characteristics, and procedural performance [15]. However, ketamine and esketamine are pharmacologically related but not interchangeable, and the comparative respiratory and recovery profiles of esketamine–propofol and remifentanil–propofol therefore remain insufficiently characterized.

Hypoxemia is one of the most clinically important adverse events during pediatric procedural sedation. Even transient oxygen desaturation may reflect excessive respiratory depression or upper-airway obstruction and may prompt airway maneuvers, increased supplemental oxygen, or assisted ventilation. In addition to respiratory events, recovery time, propofol consumption, vasoactive rescue medication, procedural movement, and physician satisfaction are clinically relevant indicators of sedation quality and feasibility. A regimen that reduces hypoxemic events while maintaining adequate procedural conditions and allowing rapid recovery may therefore provide meaningful advantages in pediatric endoscopy practice.

Accordingly, the present single-center randomized controlled study compared esketamine–propofol with remifentanil–propofol in children undergoing elective painless gastrointestinal endoscopy. The primary outcome was the incidence of hypoxemia during the peri-procedural period. Secondary outcomes included peri-procedural hemodynamic and oxygenation variables, awakening time, propofol consumption, physician satisfaction, and adverse events. We aimed to determine whether esketamine–propofol could provide a clinically useful alternative to remifentanil–propofol for pediatric gastrointestinal endoscopic sedation.

2. Materials and Methods

2.1. Study Design and Ethical Considerations

This single-center, parallel-group randomized controlled study was conducted at the Endoscopy Center of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, between June 2024 and November 2025. The study compared esketamine–propofol with remifentanil–propofol for sedation in children undergoing elective painless gastrointestinal endoscopy.

The study protocol was approved by the Ethics Committee of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine (approval No. AF0406; approval date: 25 April 2024). Written informed consent was obtained from the legal guardians of all participants before enrollment, and assent was obtained from children when appropriate according to age and institutional requirements. The study was conducted in accordance with the Declaration of Helsinki and applicable institutional standards for clinical research involving pediatric participants.

This randomized controlled trial is reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The completed CONSORT checklist is provided as Additional file 1.

2.2. Participants

Children younger than 16 years who were scheduled to undergo elective painless gastrointestinal endoscopy were screened for eligibility.

The inclusion criteria were: (1) age <16 years; (2) scheduled for elective painless gastrointestinal endoscopy; (3) American Society of Anesthesiologists (ASA) physical status I–II; (4) normal or clinically acceptable routine blood test results and hepatic and renal function before the procedure; (5) no symptoms of an acute upper respiratory tract infection; and (6) written informed consent provided by a legal guardian.

The exclusion criteria were: (1) anticipated difficult airway or clinically significant cardiac, hepatic, renal, or pulmonary disease; (2) long-term use of analgesic, psychotropic, or anticoagulant medications; (3) a history of abnormal recovery from anesthesia or known allergy to any study medication; (4) body mass index >30 kg/m²; and (5) participation in another drug trial within the preceding 3 months.

Participants were excluded from the final analysis if the scheduled procedure was cancelled, a major protocol deviation occurred, or primary-outcome data were unavailable. The eligibility criteria were intended to identify children suitable for non-intubated procedural sedation without major underlying cardiopulmonary or systemic disease.

2.3. Randomization and Blinding

Eligible participants were randomly allocated in a 1:1 ratio to either the esketamine–propofol group (PE group) or the remifentanil–propofol group (PR group).

Randomization was performed using a computer-generated allocation sequence with block randomization. Group assignments were placed in sequentially numbered, opaque, sealed envelopes. Before each procedure, a designated anesthesia nurse opened the corresponding envelope and prepared the allocated study medication. Allocation concealment was maintained until participant enrollment had been completed and the study medication was prepared.

Because the anesthesiologist responsible for drug administration had to administer the assigned regimen, blinding of the administering anesthesiologist was not feasible. Endoscopists, post-anesthesia care unit staff, postoperative outcome assessors, and investigators responsible for statistical analysis were unaware of treatment allocation whenever feasible.

2.4. Sedation Protocol

All participants fasted before the procedure according to institutional pediatric fasting guidelines. After arrival in the endoscopy unit, intravenous access was established and routine physiological monitoring was initiated, including heart rate (HR), non-invasive blood pressure, mean arterial pressure (MAP), and peripheral oxygen saturation (SpO_2). Supplemental oxygen was administered via a nasal cannula or face mask according to routine institutional practice. Airway rescue equipment, assisted ventilation devices, and emergency medications were available throughout the procedure.

Participants in the PE group received intravenous esketamine at 0.25 mg/kg, followed by propofol 2.0–2.5 mg/kg for induction. Propofol was subsequently administered at 4–6 $mg \cdot kg^{-1} \cdot h^{-1}$ for maintenance of sedation.

Participants in the PR group received intravenous remifentanil at 0.5 μg/kg, followed by propofol 2.0–2.5 mg/kg for induction. Propofol was similarly maintained at 4–6 $mg \cdot kg^{-1} \cdot h^{-1}$.

Additional propofol was administered when sedation was considered inadequate, as indicated by body movement, coughing, swallowing, or other responses to endoscopic stimulation. The number of supplementary propofol administrations and whether each participant required supplementary propofol were recorded.

Airway interventions, including adjustment of oxygen flow, jaw thrust, or assisted ventilation, were performed when clinically indicated in response to oxygen desaturation or airway obstruction. Ephedrine was administered when systolic blood pressure decreased by >30% from baseline or when clinically significant hypotension occurred. Atropine was administered for clinically significant bradycardia

according to institutional practice. All rescue interventions, additional sedative administration, and peri-procedural adverse events were recorded prospectively on the anesthesia record.

2.5. Outcomes and Definitions

The primary outcome was the incidence of peri-procedural hypoxemia. Hypoxemia was defined a priori as any recorded SpO_2 value <95% during the observation period. Hypoxemia was determined from recorded SpO_2 measurements rather than solely from manually entered adverse-event markers. For the primary outcome, the proportion of participants experiencing at least one hypoxemic episode was compared between the PE and PR groups. The treatment effect was additionally expressed as a relative risk (RR) with a corresponding 95% confidence interval (CI).

HR, MAP, and SpO_2 were recorded at six predefined peri-procedural time points: T0, before induction; T1, after induction and endoscope insertion; T2–T4, predefined intra-procedural observation points according to the anesthesia record; and T5, at awakening or recovery. MAP was calculated using the following formula: [MAP=(SBP+2 × DBP)/3].

where SBP represents systolic blood pressure and DBP represents diastolic blood pressure. Between-group comparisons of HR, MAP, and SpO_2 were performed at each predefined observation time point.

Anesthesia-related outcomes included anesthesia onset time, awakening time, initial propofol dose, total propofol consumption, the number of supplementary propofol administrations, and the proportion of participants requiring supplementary propofol. Awakening time was defined as the interval from discontinuation of anesthetic administration to recovery of adequate consciousness for routine post-anesthesia assessment. Because the two study groups received different adjunctive agents with different pharmacological properties and units of measurement, the absolute doses of esketamine and remifentanil were not directly compared as an efficacy outcome.

At the completion of the procedure, satisfaction was assessed separately by the endoscopist and anesthesiologist using a 10-point numerical rating scale, with higher scores indicating greater satisfaction with the procedural or anesthetic conditions.

Prespecified adverse events included hypoxemia, hypotension requiring ephedrine, bradycardia requiring atropine, body movement, and nausea or vomiting. All outcomes were assessed during the peri-procedural observation period until recovery from anesthesia.

Hypotension requiring ephedrine and bradycardia requiring atropine were analyzed as clinically relevant rescue-treatment events rather than as isolated changes in individual blood pressure or heart rate measurements.

2.6. Analysis Population and Sample Size

A total of 83 randomized participants were included in the final analysis, including 43 participants in the PE group and 40 participants in the PR group. All randomized participants had available primary-outcome data, and no participant was excluded after allocation because of missing primary-outcome data or major protocol deviations. The primary analysis was therefore based on participants according to their randomized treatment assignment. The available study records used for preparation of the present manuscript did not contain a reproducible formal a priori sample-size calculation based on the expected incidence of hypoxemia. Therefore, no retrospective reconstruction of the original sample-size calculation was performed, and all eligible randomized participants with available primary-outcome data during the study period were included in the analysis.

2.7. Statistical Analysis

Continuous variables were assessed for distributional characteristics and are presented as mean ± standard deviation (SD) when approximately normally distributed. Categorical variables are presented as numbers and percentages. Between-group comparisons of continuous variables, including baseline characteristics, anesthesia-related outcomes, physician satisfaction scores, and HR, MAP, and SpO_2 values at individual predefined time points, were performed using independent-samples Student's *t*-tests when the assumption of approximate normality was considered acceptable. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. For 2 × 2 contingency tables, continuity-corrected chi-square tests were used where applicable, and Fisher's exact *P* values were additionally calculated when clinically relevant event counts were small. The primary outcome, incidence of hypoxemia, was compared between the PE and PR groups using categorical-data methods. The effect size for hypoxemia was expressed as the relative risk (RR) with a corresponding 95% confidence interval. Categorical secondary outcomes included the proportion of participants requiring supplementary propofol and the incidences of hypotension requiring ephedrine, bradycardia requiring atropine, body movement, and nausea or vomiting. No imputation was performed for missing data. Analyses were based on available observations for each outcome. All statistical tests were two-sided, and a *P* value <0.05 was considered statistically significant. Statistical analyses were performed using Python 3 with the pandas and SciPy packages. Tables and figures were generated from the original study dataset using reproducible scripts.

2.8. Trial Registration

The trial was registered with the Chinese Clinical Trial Registry (ChiCTR; registration number: ChiCTR2600133316; date of registration: 24 September 2026). As registration took place after the first participant was enrolled, the trial was retrospectively registered.

3. Results

3.1. Participant Flow and Baseline Characteristics

A total of 83 children were enrolled and randomized, with 43 assigned to the esketamine–propofol group (PE group) and 40 assigned to the remifentanil–propofol group (PR group). All randomized participants completed the study and were included in the final analysis. No participant was lost to follow-up or excluded after randomization because of missing primary outcome data or major protocol deviations (Figure 1).

Baseline characteristics were comparable between the two groups (Table 1). There were no statistically significant between-group differences in age, sex distribution, height, weight, body mass index, or procedure duration. Mean age was 9.12 ± 3.86 years in the PE group and 9.85 ± 4.45 years in the PR group (P = 0.426). Procedure duration was also similar between groups (26.47 ± 8.74 vs. 29.45 ± 10.08 min, P = 0.155). These findings indicated that the two groups were generally comparable before assessment of the study outcomes.

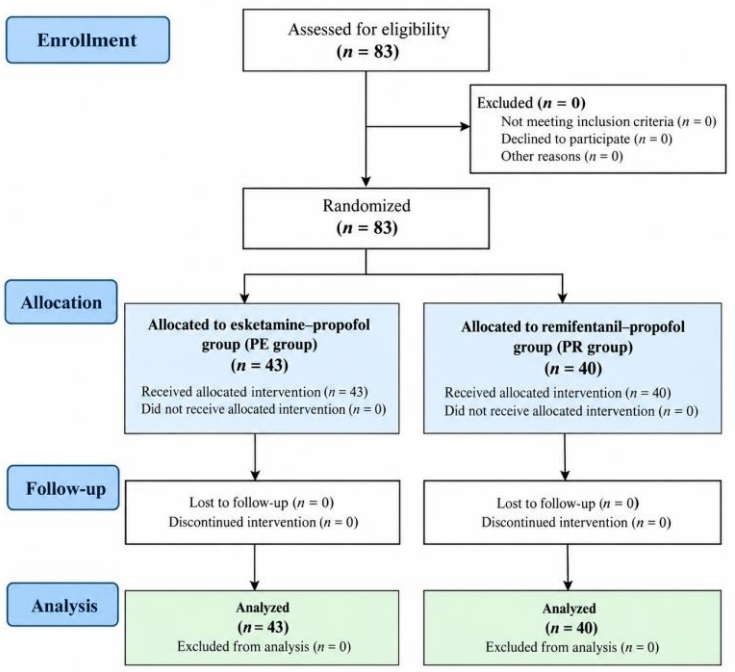


Figure 1. CONSORT-style participant flow diagram.

Table 1. Baseline characteristics of children in the PE and PR groups.

Item	PE group (n = 43)	PR group (n = 40)	P value
Age (years)	9.12 ± 3.86	9.85 ± 4.45	0.426
Sex (male/female)	25/18	24/16	0.863
Height (cm)	138.81 ± 25.78	141.47 ± 29.26	0.662
Weight (kg)	35.75 ± 17.64	39.29 ± 21.08	0.411
BMI (kg/m²)	17.30 ± 3.30	17.98 ± 3.72	0.382
Procedure duration (min)	26.47 ± 8.74	29.45 ± 10.08	0.155

Values are presented as mean ± standard deviation or male/female. PE, esketamine–propofol; PR, remifentanil–propofol.

3.2. Hemodynamic and Oxygenation Variables

Peri-procedural changes in HR, MAP, and SpO_2 at the six predefined observation time points are presented in Table 2 and Figure 2. Baseline HR, MAP, and SpO_2 at T0 did not differ significantly between the two groups.

At T1, SpO_2 was significantly higher in the PE group than in the PR group (97.58 ± 1.80% vs. 96.05 ± 3.01%, $P = 0.007$), whereas HR and MAP were not significantly different between groups at this time point. At T2, HR was significantly higher in the PE group than in the PR group (87.44 ± 14.37 vs. 74.65 ± 14.18 beats/min, $P < 0.001$), while the between-group differences in MAP and SpO_2 did not reach statistical significance. At T3, MAP was significantly higher in the PE group than in the PR group (68.46 ± 7.95 vs. 64.49 ± 6.44 mmHg, $P = 0.014$). No statistically significant between-group differences in HR, MAP, or SpO_2 were observed at T4 or T5.

These findings showed that the principal between-group differences in peri-procedural physiological variables were observed in SpO_2 shortly after induction and endoscope insertion, HR at T2, and MAP at T3.

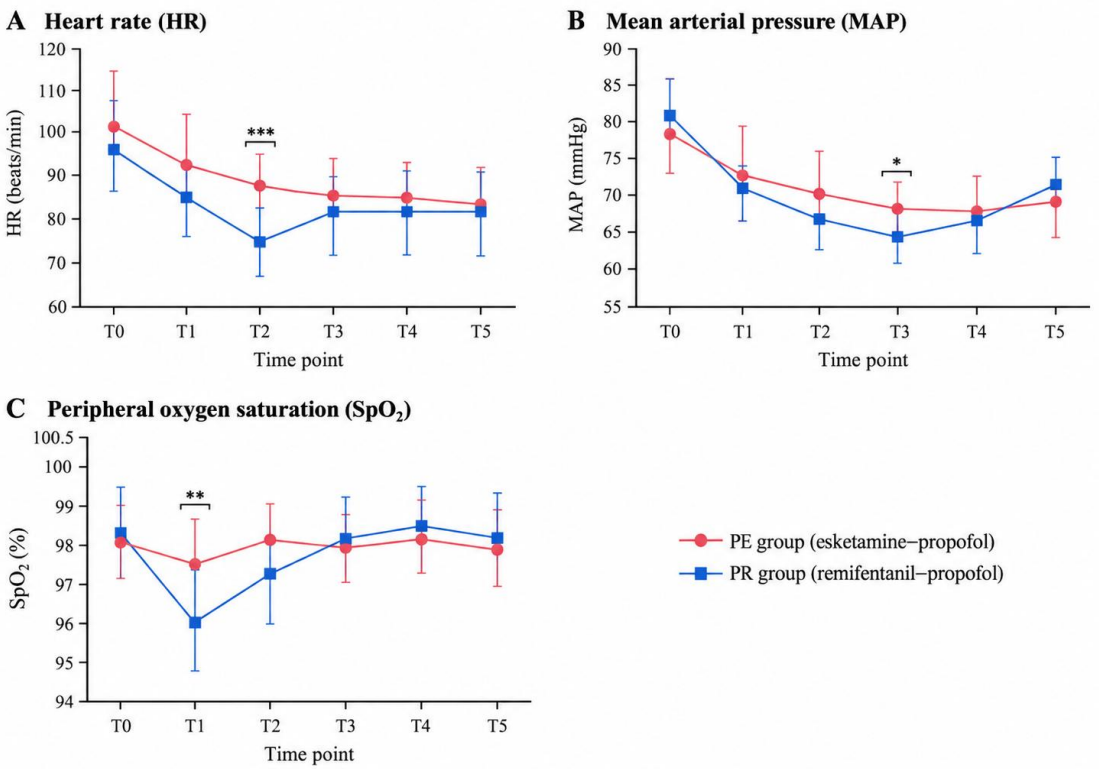


Figure 2. Hemodynamic and oxygenation variables at different peri-procedural time points in the PE and PR groups.

(A) Heart rate (HR). (B) Mean arterial pressure (MAP). (C) Peripheral oxygen saturation (SpO_2). Values are presented as mean ± SD. Between-group comparisons were performed at each predefined time point. $P < 0.05$, $P < 0.01$, $P < 0.001$. PE, esketamine–propofol; PR, remifentanil–propofol.

Table 2. Hemodynamic and oxygenation variables at different time points.

Time	Group	HR (beats/min)	MAP (mmHg)	SpO_2 (%)
T0	PE (n = 43)	101.40 ± 16.77	78.54 ± 9.99	98.09 ± 1.21
	PR (n = 40)	96.17 ± 20.03	80.43 ± 10.54	98.33 ± 1.33
	P value	0.204	0.405	0.409
T1	PE (n = 43)	92.19 ± 15.66	72.25 ± 9.43	97.58 ± 1.80
	PR (n = 40)	84.80 ± 18.82	70.87 ± 8.05	96.05 ± 3.01
	P value	0.057	0.478	0.007
T2	PE (n = 43)	87.44 ± 14.37	70.40 ± 9.68	98.12 ± 1.40
	PR (n = 40)	74.65 ± 14.18	67.05 ± 6.91	97.28 ± 2.73
	P value	<0.001	0.072	0.086
T3	PE (n = 43)	84.88 ± 14.11	68.46 ± 7.95	97.98 ± 1.12
	PR (n = 40)	81.12 ± 17.24	64.49 ± 6.44	98.20 ± 1.36

	P value	0.283	0.014	0.42
T4	PE (n = 43)	84.30 ± 15.18	68.04 ± 7.91	98.14 ± 1.17
	PR (n = 40)	80.97 ± 18.66	66.62 ± 8.06	98.45 ± 1.08
	P value	0.378	0.42	0.213
T5	PE (n = 43)	82.88 ± 12.52	69.00 ± 8.05	97.95 ± 1.29
	PR (n = 40)	81.72 ± 20.12	71.49 ± 7.79	98.20 ± 1.24
	P value	0.756	0.156	0.378

Values are presented as mean ± standard deviation. HR, heart rate; MAP, mean arterial pressure; SpO_2, peripheral oxygen saturation.

3.3. Anesthesia-Related Outcomes

Anesthesia-related outcomes are summarized in Table 3. Anesthesia onset time was similar between the PE and PR groups (14.21 ± 6.27 vs. 14.90 ± 9.68 s, P = 0.703).

Awakening time was significantly shorter in the PE group than in the PR group (9.95 ± 3.19 vs. 14.22 ± 4.70 min, P < 0.001). Total propofol consumption was also significantly lower in the PE group (190.47 ± 54.38 vs. 242.75 ± 72.64 mg, P < 0.001). In contrast, the initial propofol dose did not differ significantly between groups (78.26 ± 31.66 vs. 89.12 ± 35.84 mg, P = 0.148).

The number of supplementary propofol administrations was comparable between groups (0.53 ± 0.67 vs. 0.47 ± 0.68, P = 0.687). Similarly, the proportion of participants requiring supplementary propofol did not differ significantly, occurring in 19 of 43 participants (44.2%) in the PE group and 15 of 40 participants (37.5%) in the PR group (P = 0.692). Thus, although total propofol consumption was lower and recovery was faster in the PE group, the need for supplementary propofol during the procedure was similar between groups.

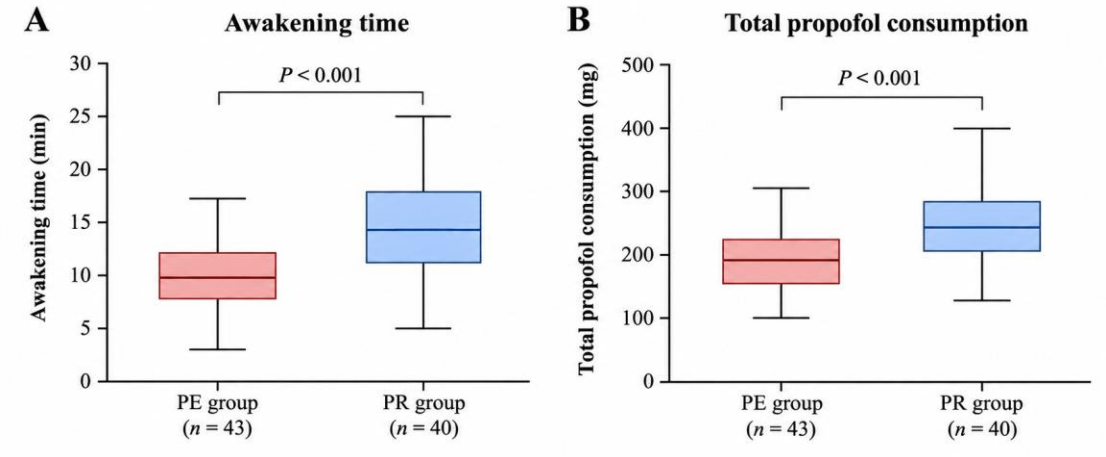


Figure 3. Awakening time and total propofol consumption in the PE and PR groups.

(A) Awakening time. (B) Total propofol consumption. P < 0.001 for comparisons between the PE and PR groups. PE, esketamine–propofol; PR, remifentanil–propofol.

Table 3. Comparison of anesthesia-related outcomes.

Item	PE group (n = 43)	PR group (n = 40)	P value
Anesthesia onset time (s)	14.21 ± 6.27	14.90 ± 9.68	0.703
Awakening time (min)	9.95 ± 3.19	14.22 ± 4.70	<0.001
Initial propofol dose (mg)	78.26 ± 31.66	89.12 ± 35.84	0.148
Total propofol consumption (mg)	190.47 ± 54.38	242.75 ± 72.64	<0.001
Supplementary propofol administrations, n	0.53 ± 0.67	0.47 ± 0.68	0.687
Participants requiring supplementary propofol, n (%)	19 (44.2)	15 (37.5)	0.692

Values are presented as mean ± standard deviation or n (%).

3.4. Physician Satisfaction

Physician satisfaction scores are shown in Table 4. Endoscopist satisfaction did not differ significantly between the PE and PR groups (8.50 ± 0.60 vs. 8.40 ± 0.70, P = 0.488).

In contrast, anesthesiologist satisfaction was significantly higher in the PE group than in the PR group (8.40 ± 0.69 vs. 7.93 ± 0.66, P = 0.002).

Table 4. Comparison of physician satisfaction scores.

Item	PE group (n = 43)	PR group (n = 40)	P value
Endoscopist satisfaction	8.50 ± 0.60	8.40 ± 0.70	0.488
Anesthesiologist satisfaction	8.40 ± 0.69	7.93 ± 0.66	0.002

Scores ranged from 1 to 10, with higher scores indicating greater satisfaction.

3.5. Adverse Events

The incidence of peri-procedural adverse events is summarized in Table 5 and Figure 4. Hypoxemia, defined as any recorded SpO_2 value <95%, occurred in 4 of 43 participants (9.3%) in the PE group and 13 of 40 participants (32.5%) in the PR group. The incidence of hypoxemia was therefore significantly lower in the PE group (P = 0.019 by chi-square test; Fisher's exact P = 0.013).

Based on these event rates, the relative risk of hypoxemia in the PE group compared with the PR group was approximately 0.29 (95% CI, 0.10–0.81), corresponding to a markedly lower observed risk of hypoxemia in participants receiving esketamine–propofol.

Hypotension requiring ephedrine occurred in 1 participant (2.3%) in the PE group compared with 12 participants (30.0%) in the PR group and was significantly less frequent in the PE group (P = 0.002; Fisher's exact P < 0.001).

There were no statistically significant between-group differences in bradycardia requiring atropine, which occurred in 5 participants (11.6%) in the PE group and 6 participants (15.0%) in the PR group (P = 0.898). Body movement was observed in 17 participants (39.5%) in the PE group and 15 participants (37.5%) in the PR group (P = 1.000). Nausea or vomiting occurred in 3 participants in each group (7.0% vs. 7.5%, P = 1.000).

Overall, the PE regimen was associated with lower incidences of hypoxemia and hypotension requiring ephedrine, without significant increases in bradycardia, procedural movement, or nausea and vomiting.

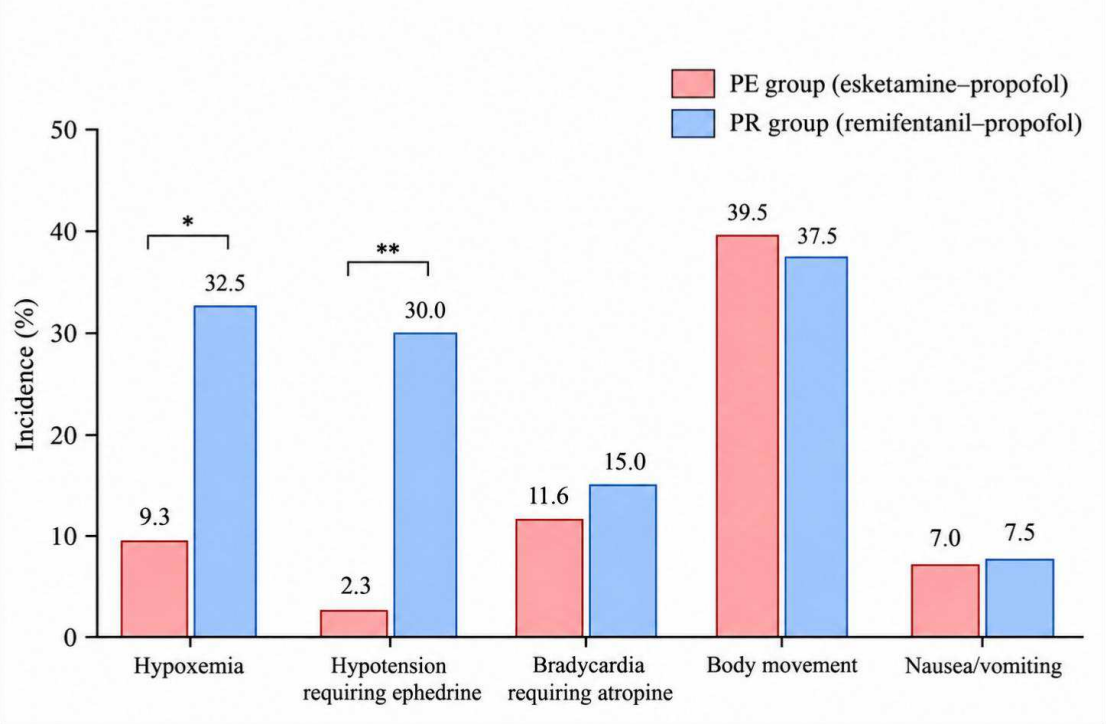


Figure 4. Incidence of adverse events in the PE and PR groups. Hypoxemia was defined as any SpO_2 value <95%.

Table 5. Comparison of adverse events.

Adverse event	PE group (n = 43)	PR group (n = 40)	χ^2	P value	Fisher's exact P
Hypoxemia (any SpO_2 <95%)	4 (9.3)	13 (32.5)	5.497	0.019	0.013
Hypotension requiring ephedrine	1 (2.3)	12 (30.0)	10.011	0.002	<0.001
Bradycardia requiring atropine	5 (11.6)	6 (15.0)	0.017	0.898	0.751
Body movement	17 (39.5)	15 (37.5)	0	1	1
Nausea/vomiting	3 (7.0)	3 (7.5)	0	1	1

Categorical variables are presented as n (%).

4. Discussion

The principal finding of this randomized controlled study was that esketamine–propofol was associated with a lower incidence of peri-procedural hypoxemia than remifentanil–propofol in children undergoing painless gastrointestinal endoscopy. Hypoxemia occurred in 9.3% of children in the PE group compared with 32.5% in the PR group. The PE group also showed lower total propofol consumption, shorter awakening time, and less frequent hypotension requiring ephedrine, without significant increases in body movement, supplementary propofol use, bradycardia requiring atropine, or nausea and vomiting. These findings suggest that esketamine may provide a favorable balance between adequate procedural sedation and preservation of respiratory and hemodynamic stability.

Respiratory adverse events are a major concern during pediatric gastrointestinal endoscopy because deep sedation, airway instrumentation, and endoscope insertion may occur simultaneously. Previous studies have shown that transient oxygen desaturation and airway-related events are among the most common adverse events during pediatric endoscopic sedation [16–18]. The lower rate of hypoxemia observed in the PE group is therefore clinically relevant. A possible explanation is the different respiratory profiles of the two adjunctive agents. Remifentanil provides potent analgesia but, particularly when combined with propofol, may increase the risk of respiratory depression. By contrast, ketamine and esketamine provide both sedation and analgesia while generally preserving spontaneous ventilation to a greater extent. Earlier pediatric studies comparing ketamine-based regimens with opioid-containing combinations have reported similar advantages in respiratory stability, although the magnitude of benefit has varied according to drug dose and procedural setting [19,20].

The hemodynamic findings were also consistent with a potential advantage of the esketamine-containing regimen. HR was higher in the PE group at T2 and MAP was higher at T3, while hypotension requiring ephedrine occurred much less frequently in the PE group. These isolated time-point differences should not be interpreted as evidence of consistently higher HR or MAP throughout the procedure, because most measurements were comparable between groups. Nevertheless, together with the lower requirement for ephedrine, they suggest less pronounced cardiovascular depression with esketamine–propofol. This finding is pharmacologically plausible because the sympathomimetic effect of esketamine may partially counteract propofol-induced vasodilation and hypotension. Previous pediatric endoscopy studies have likewise suggested that ketamine- or esketamine-containing combinations can help maintain hemodynamic stability during procedural sedation [21,22].

Another important finding was the significant reduction in total propofol consumption in the PE group. Mean total propofol use was approximately 52 mg lower with esketamine–propofol, despite similar initial propofol doses and no significant difference in the proportion of children requiring supplementary propofol. This indicates a propofol-sparing effect without an obvious reduction in procedural adequacy. Dose-finding studies in children have shown that ketamine or esketamine can reduce the propofol dose required to suppress responses to gastroscope insertion [23,24]. Reducing cumulative propofol exposure may be clinically useful because higher propofol doses are associated with greater respiratory and cardiovascular depression.

The shorter awakening time in the PE group is also noteworthy. Awakening occurred approximately 4 min earlier than in the PR group. This difference may be related, at least in part, to the lower cumulative propofol exposure. Recovery time is an important practical consideration in pediatric day-case endoscopy because prolonged sedation may delay post-anesthesia observation and discharge. Previous pediatric trials have shown that recovery profiles vary considerably among sedation regimens, and that faster awakening must be interpreted together with respiratory and hemodynamic outcomes rather than as an isolated measure of efficacy [24,25].

Importantly, the apparent cardiorespiratory advantages of esketamine–propofol were not accompanied by poorer procedural conditions. Body movement, endoscopist satisfaction, and the requirement for supplementary propofol were similar between groups. Anesthesiologist satisfaction was higher in the PE group, which may reflect the combination of fewer hypoxemic events, less frequent need for vasoactive rescue, and faster recovery. However, satisfaction scores are subjective and should not be considered direct measures of workload or procedural safety.

Several limitations should be acknowledged. First, this was a single-center study with a relatively small sample size, and the available study records did not include a reproducible formal a priori sample-size

calculation based on the expected incidence of hypoxemia. Second, the study included a broad pediatric age range, and age-related differences in pharmacodynamic response were not explored. Third, hypoxemia was defined as any SpO_2 <95%, which is sensitive but may include brief episodes of uncertain clinical significance; duration, nadir SpO_2, and severity were not quantified. Fourth, airway interventions were recorded when clinically required but were not analyzed as separate outcomes. Finally, the present findings apply to the specific esketamine and remifentanil dosing regimens used and should not be generalized to other dose combinations without further study.

In conclusion, esketamine–propofol was associated with a lower incidence of hypoxemia, less frequent hypotension requiring ephedrine, reduced propofol consumption, and shorter awakening time than remifentanil–propofol in children undergoing painless gastrointestinal endoscopy. These benefits were achieved without significant differences in procedural movement or supplementary propofol requirements. Larger multicenter studies are needed to confirm these findings and to further define the optimal esketamine dose for pediatric endoscopic sedation.

5. Conclusions

Esketamine–propofol was associated with a lower incidence of hypoxemia, less frequent hypotension requiring ephedrine, reduced propofol consumption, and shorter awakening time than remifentanil–propofol in children undergoing painless gastrointestinal endoscopy, without compromising procedural conditions. These findings support esketamine–propofol as a potential alternative sedation regimen, although larger multicenter studies are needed for confirmation.

Author Contributions： Conceptualization, Q.G. and L.G.; methodology, Q.G., J.W., and Y.L.; investigation, Q.G., J.W., and Y.L.; data collection, Q.G., J.W., and Y.L.; formal analysis, Q.G. and Q.L.; data curation, Q.G. and J.W.; visualization, Q.G.; writing—original draft preparation, Q.G.; writing—review and editing, J.W., Y.L., Q.L., and L.G.; supervision, Q.L. and L.G.; project administration, L.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine (approval No. AF0406; approval date: 25 April 2024).

Consent for publication: Not Applicable.

Informed Consent Statement: Written informed consent was obtained from the legal guardians of all participants before enrollment. Assent was also obtained from children when appropriate according to age and institutional requirements.

Data Availability Statement: The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available because they contain information relating to pediatric participants and are subject to institutional and ethical restrictions.

Acknowledgments: The authors would like to thank the staff of the Endoscopy Center and the Department of Anesthesiology at Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, for their assistance with this study. The authors also thank all participating children and their families for their cooperation.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Mahoney, L.B.; Lightdale, J.R. The evolution of sedation for pediatric gastrointestinal endoscopy. Gastrointest. Endosc. Clin. N. Am. 2023, 33, 213–234.

2. Chung, H.K.; Lightdale, J.R. Sedation and monitoring in the pediatric patient during gastrointestinal endoscopy. Gastrointest. Endosc. Clin. N. Am. 2016, 26, 507–525.

3. Patino, M.; Glynn, S.; Soberano, M.; Putnam, P.; Hossain, M.M.; Hoffmann, C.; Samuels, P.; Kibelbek, M.J.; Gunter, J. Comparison of different anesthesia techniques during esophagogastroduodenoscopy in children: A randomized trial. Paediatr. Anaesth. 2015, 25, 1013–1019.

4. American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, et al. Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018. Anesthesiology 2018, 128, 437–479.

5. Mekitarian Filho, E.; Riechelmann, M.B. Propofol use in newborns and children: Is it safe? A systematic review. J. Pediatr. (Rio J.) 2020, 96, 289–309.

6. Zhou, S.; Zhu, Z.; Dai, W.; Qi, S.; Tian, W.; Zhang, Y.; et al. National survey on sedation for gastrointestinal endoscopy in 2758 Chinese hospitals. Br. J. Anaesth. 2021, 127, 56–64.

7. Drover, D.R.; Litalien, C.; Wellis, V.; Shafer, S.L.; Hammer, G.B. Determination of the pharmacodynamic interaction of propofol and remifentanil during esophagogastroduodenoscopy in children. Anesthesiology 2004, 100, 1382–1386.

8. Abu-Shahwan, I.; Mack, D. Propofol and remifentanil for deep sedation in children undergoing gastrointestinal endoscopy. Paediatr. Anaesth. 2007, 17, 460–463.

9. Hirsh, I.; Lerner, A.; Shnaider, I.; Reuveni, A.; Pacht, A.; Segol, O.; Pizov, R. Remifentanil versus fentanyl for esophagogastroduodenoscopy in children. J. Pediatr. Gastroenterol. Nutr. 2010, 51, 618–621.

10. Zheng, X.; Huang, J.; Wei, S.; Tao, Y.; Shen, Y.; Wang, Y.; He, P.; Zhang, M.; Sun, Y. Efficacy and safety comparison of esketamine–propofol with nalbuphine–propofol for upper gastrointestinal endoscopy in children: A multicenter randomized controlled trial. Front. Pediatr. 2023, 11, 1126522.
11. Wang, J.; Hu, W.; Zhao, X.; et al. Sedative effect and safety of different doses of S-ketamine in combination with propofol during gastro-duodenoscopy in school-aged children: A prospective, randomized study. BMC Anesthesiol. 2022, 22, 346.
12. Zheng, X.S.; Shen, Y.; Yang, Y.Y.; He, P.; Wang, Y.T.; Tao, Y.Y.; Zheng, J.J.; Sun, Y. ED50 and ED95 of propofol combined with different doses of esketamine for children undergoing upper gastrointestinal endoscopy: A prospective dose-finding study using the up-and-down sequential allocation method. J. Clin. Pharm. Ther. 2022, 47, 1002–1009.
13. Song, N.; Yang, Y.; Zheng, Z.; Shi, W.C.; Tan, A.P.; Shan, X.S.; Liu, H.; Meng, L.; Peng, K.; Ji, F.H. Effect of esketamine added to propofol sedation on desaturation and hypotension in bidirectional endoscopy: A randomized clinical trial. JAMA Netw. Open 2023, 6, e2347886.
14. Yu, Y.; et al. Efficacy and safety of esketamine for pediatric gastrointestinal endoscopy: A meta-analysis and trial sequential analysis. Front. Pharmacol. 2024, 15, 1379101.
15. Damps, M.; Stołtny, L.; Siemek-Mitela, J.; Lekstan, A.; Krzych, Ł.; Kucewicz-Czech, E. Comparison of propofol-ketamine versus propofol-remifentanil in children anaesthetized for gastroscopy. Anaesthesiol. Intensive Ther. 2019, 51, 262–267.
16. Najafi N, Veyckemans F, Vanhonacker D, Legrand C, Van de Velde A, Vandenplas Y, et al. Incidence and risk factors for adverse events during monitored anaesthesia care for gastrointestinal endoscopy in children: a prospective observational study. Eur J Anaesthesiol. 2019;36(6):390–399.
17. Chiaretti A, Benini F, Pierri F, Vecchiato K, Ronfani L, Agosto C, et al. Safety and efficacy of propofol administered by paediatricians during procedural sedation in children. Acta Paediatr. 2014;103(2):182–187.
18. van Beek EJA, Leroy PLJM. Safe and effective procedural sedation for gastrointestinal endoscopy in children. J Pediatr Gastroenterol Nutr. 2012;54(2):171–185.
19. Tosun Z, Aksu R, Guler G, Esmaoglu A, Akin A, Aslan D, et al. Propofol-ketamine vs propofol-fentanyl for sedation during pediatric upper gastrointestinal endoscopy. Paediatr Anaesth. 2007;17(10):983–988.
20. Akbulut UE, Saylan S, Sengu B, Akcali GE, Erturk E, Cakir M. A comparison of sedation with midazolam-ketamine versus propofol-fentanyl during endoscopy in children: a randomized trial. Eur J Gastroenterol Hepatol. 2017;29(1):112–118.

21. Shetabi H, Shahhosseini S, Mohamadpour N, Shafa A. Comparison of the effect of adding low-dose ketamine to dexmedetomidine and propofol on the quality of sedation and hemodynamic response in children during upper gastrointestinal endoscopy: a double-blind randomized clinical trial. Anesth Pain Med. 2023;13(2):e134581.
22. Chu T, Zhou S, Wan Y, Liu Q, Xin Y, Tian Z, Yan T, Xu A. Comparison of remimazolam and propofol combined with low dose esketamine for pediatric same-day painless bidirectional endoscopy: a randomized, controlled clinical trial. Front Pharmacol. 2024;15:1298409.
23. Xia N, et al. Median effective dose (ED50) of esketamine combined with different doses of propofol for children to inhibit the response to gastroscope insertion: a prospective dose-response clinical study. BMC Anesthesiol. 2026;26:300.
24. Amer AM, Youssef AM, El-Ozairy HS, El-Hennawy AM. Propofol-ketamine versus dexmedetomidine-ketamine for sedation during upper gastrointestinal endoscopy in pediatric patients: a randomized clinical trial. Braz J Anesthesiol. 2020;70(6):620–626.
25. Karacaer F, Biricik E, Ilgınel M, Küçükbingöz Ç, Ağın M, Tümgör G, et al. Remifentanil-ketamine vs. propofol-ketamine for sedation in pediatric patients undergoing colonoscopy: a randomized clinical trial. Braz J Anesthesiol. 2018;68(6):597–604.