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Esketamine attenuates hemodynamic oscillations during anesthesia induction in elderly gastrointestinal surgical patients: a randomized trial

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Abstract

Background Patients undergoing gastrointestinal tumor surgery face heightened susceptibility to hemodynamic instability during anesthesia induction, a risk further exacerbated by preoperative fasting. Oscillatory blood pressure fluctuations increase perioperative risks. Esketamine's sympathomimetic properties may counteract propofol-induced hypotension. This study aimed to evaluate the impact of adjunctive esketamine on hemodynamic instability incidence during induction.

Methods This prospective, double-blind RCT (ChiCTR2200060641, registered on June 6, 2022) enrolled ASA I-III patients (18–75 years) scheduled for gastrointestinal tumor surgery at Foshan First People's Hospital (Jun 2022-May 2023). Patients were randomized 1:1 to receive IV esketamine (0.2 mg/kg) or saline placebo during induction. Anesthesia was induced with propofol (1.5–2.0 mg/kg), sufentanil (0.2 μg/kg), and cisatracurium (0.3 mg/kg). The primary outcome was the incidence of hemodynamic instability (defined as hypertension [MAP > 20% baseline], hypotension [MAP < 65 mmHg or > 20% decrease], tachycardia [HR > 100 bpm], bradycardia [HR < 50 bpm], or vasopressor use) from induction to 5 min post-intubation. The secondary outcomes included intraoperative ephedrine consumption, postoperative recovery time, extubation time, duration of post-anaesthesia care unit (PACU) stay, emergence agitation, cough during intubation, and other adverse effects.

Results The incidence of hemodynamic instability was significantly lower in the esketamine group than in the control group during induction (29.3% vs. 55.9%; OR = 0.33, 95% CI: 0.18–0.60; $P < 0.001$). Specifically, esketamine reduced hypotension (27.2% vs. 44.1%; $P = 0.016$) and hypertension (3.3% vs. 12.9%; $P = 0.016$). Ephedrine use was lower (12.0% vs. 24.7%; $P = 0.025$). CO was preserved in the esketamine group but declined significantly in the control group post-induction ($P < 0.05$). Cough incidence was reduced with esketamine (8.7% vs. 32.3%; $P < 0.001$). No differences existed in recovery times, emergence agitation, or PONV.

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Conclusions Adjunctive low-dose esketamine (0.2 mg/kg) during propofol-based induction significantly attenuates hemodynamic instability and preserves cardiac output in gastrointestinal surgery patients, without delaying recovery. This approach enhances cardiovascular safety during high-risk induction.

Trial registration This study was registered with the Chinese Clinical Trial Registry (ChiCTR2200060641) on June 6, 2022.

Introduction

Gastrointestinal tumors rank among the most prevalent malignancies worldwide, accounting for approximately 15% of all cancer cases and contributing significantly to morbidity and mortality [1]. The incidence and mortality of these diseases are particularly elevated in developed nations, imposing substantial demands on healthcare systems [2, 3]. Surgical resection remains the cornerstone of curative treatment for early-stage, localized disease, with general anesthesia essential for optimizing surgical conditions and patient comfort. However, compared with other surgical methods, preoperative preparation for gastrointestinal surgery, including prolonged fasting, bowel preparation, and liquid diets, frequently predisposes patients to greater hemodynamic instability during anesthesia induction [4, 5].

Unlike isolated hypotensive or hypertensive events, oscillating blood pressure—characterized by rapid fluctuations between hypotension and hypertension—is associated with significantly worse clinical outcomes. Enhanced visit-to-visit blood pressure variability independently predicts adverse cardiovascular events, including myocardial infarction, stroke, and mortality, across diverse populations [6]. In the perioperative context, such hemodynamic oscillations subject the vasculature to abrupt shear stress changes, increasing the risk of endothelial dysfunction, myocardial ischemia, acute kidney injury, and cerebral hypoperfusion [7–10]. Propofol and opioids remain the mainstays of anesthetic induction but exhibit synergistic vasodilatory and negative inotropic effects, frequently precipitating hypotension [11, 12]. Clinically, profound hypotension may necessitate urgent tracheal intubation under inadequate anesthetic depth, triggering a reflex sympathetic surge and, consequently, severe hypertension [13]. Although strategies such as fluid resuscitation, vasoactive agents, and careful anesthetic titration aim to stabilize blood pressure, excessive fluid administration risks exacerbating tissue edema, and inappropriate vasopressor dosing can paradoxically amplify hemodynamic lability [14]. Consequently, current approaches often inadequately mitigate the dual risks posed by alternating hypotensive and hypertensive episodes during induction.

Compared with racemic ketamine, the S(+)-enantiomer of ketamine possesses potent sedative and analgesic properties with a faster clearance rate and a lower incidence of psychotomimetic side effects [15–17]. Crucially, esketamine causes minimal respiratory depression and exerts sympathomimetic effects by inhibiting neuronal norepinephrine reuptake, leading to increased catecholamine levels and peripheral vasoconstriction [18, 19]. This sympathomimetic activity counteracts the circulatory depression commonly induced by propofol, suggesting the potential for enhanced hemodynamic stability when the two agents are combined [20].

On the basis of these pharmacological properties, we hypothesized that adjunctive low-dose esketamine during propofol-based anesthetic induction would better maintain hemodynamic stability in elderly patients undergoing gastrointestinal tumor resection.

This randomized, controlled trial therefore evaluated the impact of low-dose esketamine combined with propofol on the incidence and severity of oscillatory hemodynamic instability during anesthesia induction. By quantifying both the frequency of alternating hypotensive–hypertensive episodes, we aimed to assess the efficacy of this regimen in promoting peri-induction cardiovascular stability, with the ultimate goal of improving patient outcomes. We hypothesize that, compared with propofol alone, the addition of low-dose esketamine will reduce the incidence oscillatory hemodynamic instability and thereby improve cardiovascular stability during anesthesia induction.

Materials and methods

Study design

This prospective, double-blind, randomized controlled trial was conducted at The First People's Hospital of Foshan in accordance with the CONSORT guidelines from June 30, 2022, to May 30, 2023. The study protocol received approval from the Ethics Committee of The First People's Hospital of Foshan (Approval No. 2022-21) and was registered with the Chinese Clinical Trial Registry (ChiCTR2200060641, registered on June 6, 2022). Written informed consent was obtained from all participants prior to enrollment.

Inclusion and exclusion criteria

Patients who met the criteria for American Society of Anesthesiologists (ASA) physical status I to III, were aged between 18 and 75 years, and were scheduled for gastrointestinal tumor surgery under general anesthesia were included in this study.

The following exclusion criteria were applied: history of mental or brain diseases; contraindications or allergies to the test drug; evident difficult airway; history of substance abuse; grade III hypertension; symptomatic cardiovascular or pulmonary diseases; severe hepatic or renal dysfunction; increased intracranial or intraocular pressure; history of hyperthyroidism; and refusal to participate in the study.

Randomization and masking

The participants were randomized at a 1:1 ratio to receive either esketamine or saline. Randomized sequences were generated by an independent statistician via computer software and sealed in opaque envelopes. The envelopes were opened before anesthesia by an anesthesia nurse not involved in the subsequent study procedures. Patients in the esketamine group received an intravenous injection of 0.2 mg/kg esketamine (230112BL, Jiangsu Heng Rui Pharmaceutical Co. Ltd.), whereas patients in the control group received an intravenous injection of 0.1 ml/kg saline during the induction of general anesthesia. Esketamine was diluted to a concentration of 2 mg/ml in an isotonic saline solution. This dilution process was carried out by an independent staff member who was not involved in the subsequent phases of the research. Additionally, measures were taken to ensure that the shape, volume, and color of the syringes used in both the esketamine and control groups were identical. The allocation of study drugs was concealed from the anesthesiologist, outcome evaluator, and patients, ensuring the blinding of the study.

Anesthesia protocol and procedure

Prior to induction, all patients fasted for at least 6 h and abstained from fluids for 2 h. In the operating room, standard monitors, including an ECG, heart rate (HR), noninvasive blood pressure (NBP), pulse oximetry (SpO_2), and the bispectral index (BIS), were used. Intravenous access was established in the patient's upper limb, followed by the infusion of sodium lactated Ringer's solution at a rate of 5 $ml{\cdot}kg^{-1}{\cdot}h^{-1}$.

Following group allocation, anaesthesia was induced in a strictly sequential manner: sufentanil 0.2 μg kg^{-1} was administered first; immediately thereafter, patients received either 0.2 mg kg^{-1} esketamine or an equal volume of saline; propofol 1.5–2.0 mg kg^{-1} was then titrated to loss of consciousness (BIS ≤ 60), followed by cis-atracurium 0.3 mg kg^{-1}. Tracheal intubation was performed exactly 5 min after the start of the initial sufentanil bolus, without neuromuscular monitoring. Mechanical ventilation was set in volume-controlled mode (12–14 breaths/min) to maintain end-tidal carbon dioxide ($PETCO_2$) at 35–45 mmHg with an FiO_2 of 0.5 (oxygen flow 2 L/min). After induction of general anesthesia and prior to the start of surgery, all patients received ultrasound-guided transversus abdominis plane (TAP) blocks with 0.33% ropivacaine (30 ml per side) to reduce intraoperative analgesic requirements and enhance perioperative analgesia. Anaesthesia was maintained with a balanced intravenous–inhalational technique, identical for every patient. Sevoflurane was inhaled at 0.5 MAC throughout the procedure and discontinued approximately 30 min before the end of surgery. Propofol infusion (2–4 mg kg^{-1} h^{-1}) was titrated to maintain BIS 45–55 untill the end of the surgery. Continuous remifentanil (0.1–0.2 μg kg^{-1} min^{-1}) provided analgesia. All doses were adjusted in real time according to surgical stimulus and BIS to maintain haemodynamic stability within ± 20% of baseline. Cisatracurium (0.02–0.03 mg/kg) was added every 30 min. The temperature was maintained at > 36 °C with active warming.

Postoperative analgesia was provided by a combination of the intraoperatively administered TAP block and patient-controlled intravenous analgesia (PCIA). The PCIA regimen consisted of sufentanil at a dose of 2 μg/kg, diluted to a total volume of 100 ml. The pump was set to deliver a continuous background infusion of 2 ml/h, with a bolus dose of 1 ml, a lock-out interval of 15 min, and a maximum limit of 4 ml/h.

Hemodynamics were recorded every minute during induction and every three minutes thereafter. Hypotension (MAP < 65 mmHg or > 20% decrease from baseline) was treated with fluid boluses or vasoactive drugs. Hypertension (MAP > 20% above baseline) was managed by deepening anesthesia or administering urapidil (0.5 mg/kg). Bradycardia (HR < 50 bpm) was treated with 0.25–0.5 mg of atropine, and tachycardia (HR > 100 bpm) was treated with esmolol. Postoperative nausea and vomiting were treated with 4 mg of ondansetron. Following surgery, patients were transferred to the postanesthesia care unit (PACU) for recovery, where a wake-extubation technique was implemented.

Outcome assessments

The primary outcome of the study was the incidence of hemodynamic instability from induction initiation to 5 min postintubation. Hemodynamic instability was defined as the occurrence of any of the following events: hypertension, hypotension, tachycardia, bradycardia, and the administration of vasoactive drugs to maintain hemodynamic stability during the anesthesia induction period. The secondary outcomes were as follows:

1) Hemodynamic indicators, including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR), were measured at the following time points: prior to anesthesia (T1), immediately before

tracheal intubation (T2), immediately after tracheal intubation (T3), 3 min after tracheal intubation (T4), and 5 min after tracheal intubation (T5).
2) Cardiac output (CO) at T1–T5, measured via transthoracic echocardiography, uses Doppler techniques to measure blood flow velocity at the left ventricular outflow tract (LVOT) for the determination of stroke volume (SV) at various intervals.
3) Frequency and total dose of ephedrine administered during induction.
4) Extubation time: interval from anesthetic discontinuation to tracheal extubation.
5) Recovery time: interval from anesthetic discontinuation to eye opening or response to verbal commands.
6) PACU stay duration: time from surgery end to PACU discharge.
7) Delirium: Delirium was assessed in the PACU via the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) [21].
8) Postoperative pain: VAS score upon PACU discharge [22].
9) Adverse events: incidence of cough during induction, visual disturbances or psychiatric symptoms in PACU, respiratory depression (SpO_2 < 90%), PONV, and vertigo within 48 hours postoperatively.

Statistical analysis

The sample size was calculated via PASS 15.0 software on the basis of the primary outcome incidence of hemodynamic instability. Preliminary data indicated a 50% incidence in gastrointestinal surgery patients. To detect a 40% relative reduction with esketamine, with a power (1–β) of 0.8 and a two-sided α of 0.05, 91 patients per group were needed. To achieve a 10% dropout rate, 100 patients were enrolled in each arm.

Analyses were performed on the full analysis set (modified intention-to-treat) via SPSS version 26.0. The overall incidence of hemodynamic instability was compared via the chi-square test. Normally distributed continuous variables are presented as the means ± SDs and were analyzed by repeated-measures ANOVA for time-point comparisons, with between-group differences assessed by independent t tests. Nonparametric data are expressed as medians (IQRs) and were compared via the Mann–Whitney U test. Categorical variables are presented as counts (%) and were compared via the χ^2 test. A two-sided P < 0.05 was considered statistically significant.

Results

Demographic data

A total of 210 patients were screened for eligibility in this study. Ten patients were excluded because they either did not meet the inclusion criteria or refused to participate. Ultimately, 200 patients were enrolled. During the study, eight patients in the esketamine group and seven patients in the control group were excluded because of incorrect medication administration. Consequently, 92 patients in the esketamine group and 93 patients in the control group were included in the statistical analysis (Fig. 1). There were no significant differences between the two groups in terms of age, sex, weight, height, BMI, or ASA status ($P > 0.05$) (Table 1).

Primary endpoints

The incidence of hemodynamic instability during induction (from anesthetic administration to 5 minutes postintubation) was significantly lower in the esketamine group than in the control group (29.3% vs. 55.9%, OR (95% CI): 0.33 (0.18–0.60), P=0.000). Specifically, hypotension occurred less frequently in the esketamine group (27.2% vs. 44.1%; P = 0.016), as did hypertension (3.3% vs. 12.9%; P = 0.016). The need for ephedrine was reduced in the esketamine group (12.0% vs. 24.7%; P = 0.025). There were no significant between-group differences in the rates of tachycardia or bradycardia (both P >0.05) (Table 2).

Secondary endpoints

A repeated-measures ANOVA revealed significant overall fluctuations in SBP, MAP, and HR from T1–T5 (P < 0.05) (Figure 2A-D). Pairwise comparisons indicated that at T2, the control group showed a significant decrease in SBP and MAP compared with baseline, followed by an increase at T3, whereas the esketamine group maintained relatively stable levels. Heart rate analysis demonstrated a significant decrease in HR in the control group at T2 compared with baseline, followed by a significant increase at T3 (P< 0.05); no statistically significant changes in HR were observed in the esketamine group at these time points (Figure 2A-D).

In terms of cardiac output (CO), the control group showed a statistically significant decrease from T2 through T4 compared with baseline (P < 0.05) (Figure 2E). Conversely, the esketamine group consistently preserved CO across all time points (T2–T4).

There were no significant between-group differences in recovery time, extubation time, PACU length of stay, emergence agitation incidence, RASS scores, anesthesia recovery delirium scores, or VAS pain scores (all $P > 0.05$) (Table 3).

The perioperative adverse events are summarized in Table 4. No cases of respiratory depression or vision disturbances occurred in either group. However, the incidence of cough during induction was markedly lower in the esketamine group than in the control group (8.7% vs. 32.3%; $P < 0.001$). There were no significant differences

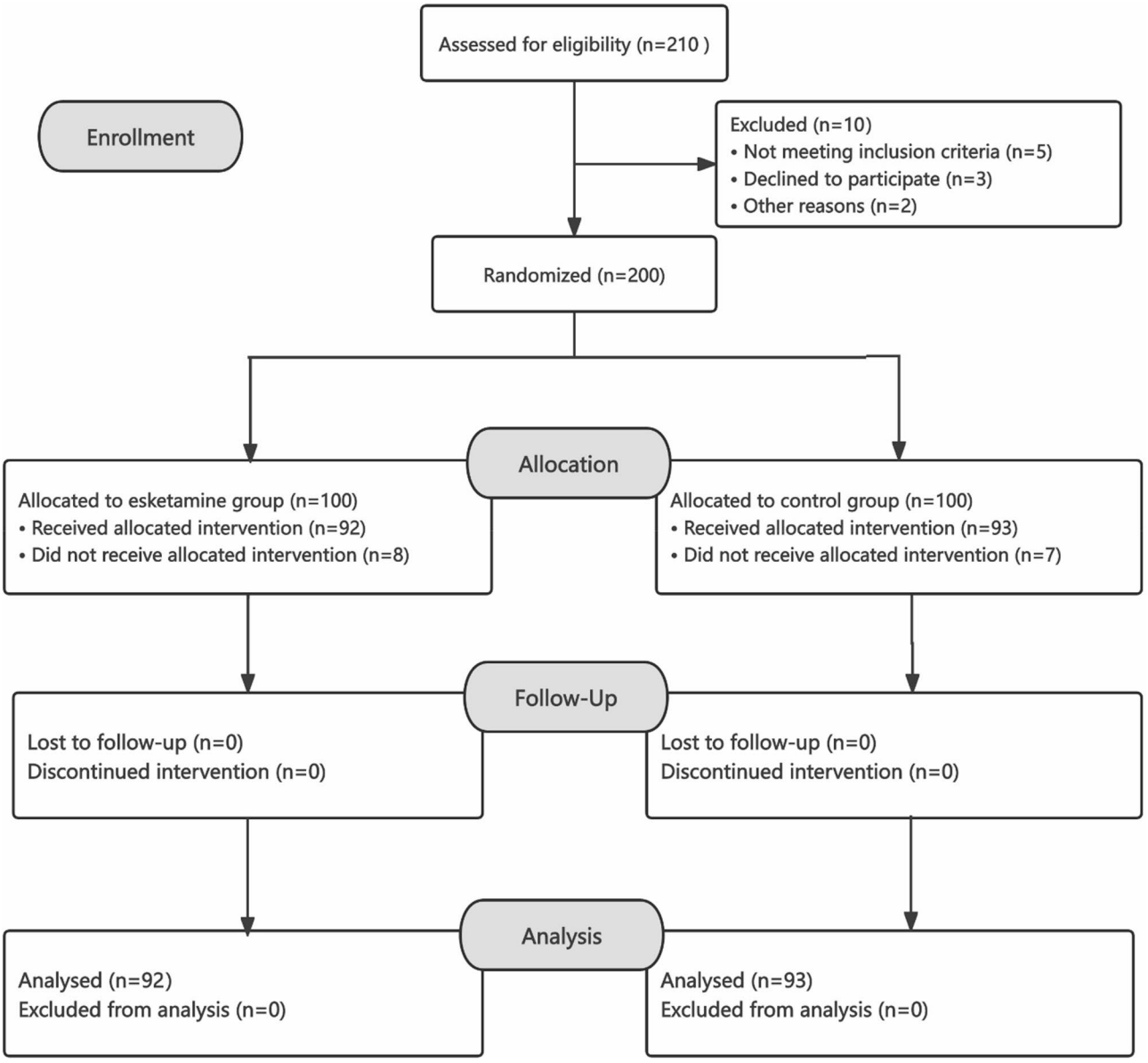


Fig. 1 CONSORT study flow diagram

between the groups in emergence agitation during wake-up, postoperative nausea and vomiting, or vertigo (all $P > 0.05$) (Table 4). In the esketamine group, two patients experienced brief auditory hallucinations immediately after extubation. These episodes lasted approximately 10–15 minutes, resolved spontaneously without intervention, and did not recur during the 7-day follow-up.

Discussion

In this randomized, double-blind trial, we demonstrated that adjunctive low-dose esketamine (0.2 mg/kg) with standard propofol-opioid induction significantly reduced the incidence of hemodynamic instability during anesthesia induction in elderly patients undergoing gastrointestinal surgery. The esketamine group maintained more stable SBP, MAP, and HR, preserved cardiac output, and required less ephedrine than the control group, highlighting improved cardiovascular stability without increasing adverse recovery events. Esketamine also reduced the incidence of intubation-related coughing, contributing to a smoother induction process.

Previous studies have reported that hypotension during anesthesia induction is common, particularly in elderly patients, and is associated with adverse outcomes such as myocardial ischemia, acute kidney injury, and increased postoperative morbidity and mortality. [23–29]. In our study, hemodynamic instability occurred in 55.9% of control patients, compared with 29.3% in the esketamine

Table 1 Comparison of different characteristics between the two groups

Characteristics	Esketamine group ($n=92$)	Control group ($n=93$)	SMDs
Age (years)	57.51 ± 11.35	56.67 ± 11.11	0.075
Gender (male/female)	53/39	53/40	0.012
Weight (kg)	60.29 ± 10.20	58.81 ± 9.28	0.152
Height (cm)	161.99 ± 8.34	161.62 ± 7.69	0.046
BMI (kg/m^2)	22.89 ± 2.84	22.47 ± 2.93	0.146
ASA status (I/II)	5/87	10/83	0.198
Blood pressure (I/II)			0.160
Normal, n (%)	45(48.9)	53(57.0)	
Grade I hypertension, n (%)	32(34.8)	28(30.1)	
Grade II hypertension, n (%)	15(16.3)	12(12.9)	

Note: Data are presented as the means ± standard deviations or numbers

Abbreviations: *SMDs* Standardized mean differences, *BMI* Body mass index, *ASA* American Society of Anesthesiologists

Table 2 Comparison of the incidence of hemodynamic events during anesthesia induction between the two groups

	Esketamine group ($n=92$)	Control group ($n=93$)	OR (95%CI)	χ^2	*P* Value
Hypertension, n (%)	3(3.26)	12(12.9)	0.23(0.06–0.84)	5.771	0.016
Hypotension, n (%)	25(27.2)	41(44.1)	0.47(0.26–0.88)	5.764	0.016
Tachycardia, n (%)	3(3.3)	7(7.5)	0.41 (0.10–1.65)	1.646	0.199
Bradycardia, n (%)	5(5.4)	4(4.3)	1.28(0.33–4.92)	0.128	0.720
Frequency of ephedrine use, n (%)	11(12.0)	23(24.7)	0.41(0.19–0.91)	5.031	0.025
Total occurrences, n (%)	27 (29.3)	52(55.9)	0.33(0.18–0.60)	13.34	0.000

Note: Data are presented as the number (proportion; %), OR (95% CI)

Abbreviations: *OR* Odds ratio, *CI* Confidence interval

group, highlighting the stabilizing effect of adjunctive low-dose esketamine. This reduction may be attributed to esketamine's sympathomimetic properties, which increase circulating norepinephrine and support cardiovascular function, as reflected in the lower frequency and dosage of ephedrine required in the esketamine group [30, 31].

In the control group, we observed pre-intubation hypotension followed by post-intubation increases in SBP and MAP, accompanied by transient heart rate changes and higher ephedrine use. Transthoracic echocardiography revealed a concomitant decline in cardiac output in this group, despite similar MAPs, whereas CO remained stable in the esketamine group. These findings indicate that blood pressure alone may not reliably reflect perfusion and underscore the benefit of esketamine in preserving forward flow during induction, particularly in elderly patients with reduced cardiovascular reserve and potential fluid deficits [4].

Transthoracic echocardiography, a validated noninvasive method for assessing cardiac output (CO) in perioperative settings [32], revealed that although both groups experienced comparable reductions in SBP and MAP prior to intubation, only the control group showed a significant decline in CO. In contrast, CO in the esketamine group remained stable throughout induction. The control group also required nearly twice as much ephedrine as the esketamine group (24.7% vs. 12.0%) to manage hypotension. Notably, despite restoring arterial pressure, vasoactive agents did not fully normalize forward flow, as evidenced by persistently lower CO values in the control group at 3 and 5 minutes after intubation. These findings highlight that blood pressure alone may not reliably reflect perfusion, particularly in elderly patients at risk for end-organ hypoperfusion, and support the use of continuous or point-of-care CO monitoring during induction.

Esketamine's ability to preserve CO appears to result primarily from its sympathomimetic properties, including inhibition of norepinephrine reuptake, increased systemic vascular resistance, and enhanced cardiac contractility [16–18, 20]. These actions counteract the vasodilatory and myocardial depressant effects of propofol, maintaining forward flow and stabilizing hemodynamics. In our study, CO remained significantly higher in the esketamine group at T2–T4, despite comparable fluid management. Heart rate increases were modest and clinically acceptable, suggesting a favorable balance between sympathetic stimulation and autonomic control. In contrast, the control group exhibited transient post-intubation tachycardia, likely reflecting compensatory sympathetic activation. Prior studies have shown that esketamine can increase CO by up to 25% at plasma concentrations of approximately 1.7 μmol/L without provoking reflex tachycardia [33, 34], consistent with our findings.

Although ketamine derivatives have raised concerns about delayed emergence and postoperative delirium, emerging evidence supports the safety of low-dose esketamine. In our study, a single bolus of 0.2 mg/kg esketamine did not prolong extubation or emergence times, nor did it increase the incidence of emergence agitation or delirium. These findings align with previous reports in both pediatric and elderly populations. For instance, a randomized trial in children undergoing tonsillectomy reported a reduction in emergence agitation (5% vs. 27.5%) without prolonging extubation time following 0.25 mg/kg esketamine at the end of surgery [35]. In elderly patients undergoing hip or knee arthroplasty, perioperative low-dose esketamine (0.2 mg/kg loading, 0.125 mg/kg/h infusion) did not increase postoperative

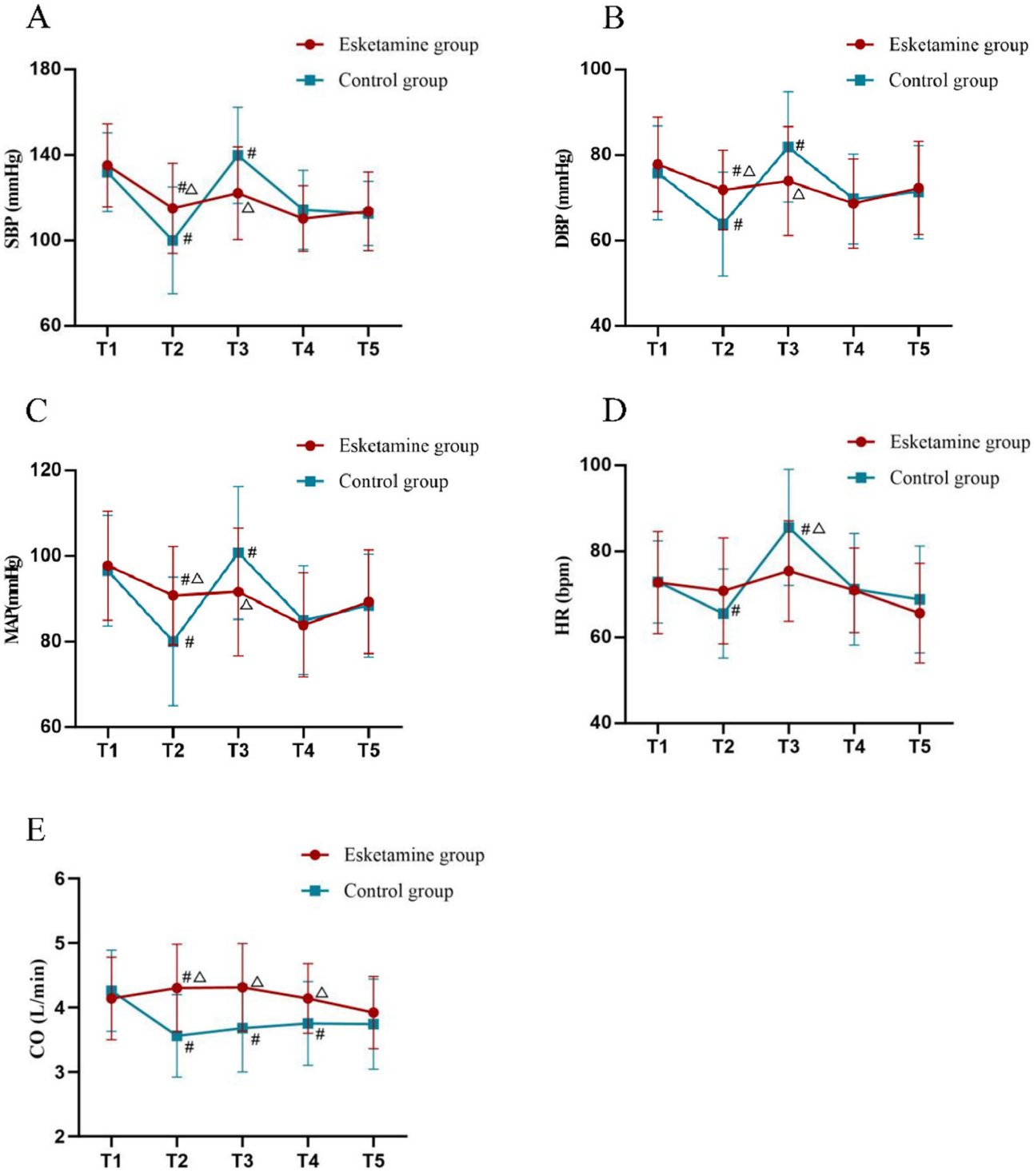


Fig. 2 Comparison of hemodynamic variables at different time points between the two groups. (**A**). SBP; (**B**). DBP; (**C**). MAP; (**D**). HR; (**E**). CO. Note: Data are presented as the mean ± standard deviation; Compared with the T1 timepoint in the two groups,$^{\#}P< 0.05$. Compared with the control group, the samples in the experimental group were treated at the same time points; $\triangle P < 0.05$. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; CO, cardiac output; T1, prior to anesthesia; T2, immediately before tracheal intubation; T3, immediately after tracheal intubation; T4, 3 min after tracheal intubation; T5, 5 min after tracheal intubation

Table 3 The operation time, recovery time, extubation time, duration of PACU stay, VAS score, RASS score, and recovery delirium score between the two groups

	Esketamine group (*n* = 92)	Control group (*n* = 93)	*P* Value
Operation time (min)	243.75 ± 77.31	252.60 ± 85.64	0.462
Recovery time (min)	31.87 ± 23.37	32.46 ± 16.26	0.842
Extubation time (min)	39.22 ± 24.56	39.15 ± 24.44	0.985
Duration of PACU stay (min)	88.00 ± 36.31	90.32 ± 32.16	0.645
VAS score	2(1,3)	2(2,3)	0.528
RASS score	4(4,5)	4(4,5)	0.989
Recovery delirium score	0(0,1)	0(0,1)	0.972

Note: Data are presented as the means ± standard deviations or medians (25th and 75th quartiles)

Abbreviations: *VAS* Visual analog scale, *RASS* Richmond Agitation-Sedation Scale, *PACU* Postanesthesia care unit

Table 4 Incidence of adverse events in the perioperative period between the two groups

	Esketamine group (*n* = 92)	Control group (*n* = 93)	χ2	*P* Value
Respiratory depression, n (%)	0(0)	0(0)	-	-
Cough during induction, n (%)	8(8.7)	30(32.3)	15.732	0.000
Emergence agitation, n (%)	4(4.3)	8(8.6)	1.380	0.240
Nausea, n (%)	25(27.2)	35(37.6)	2.309	0.129
Vomiting, n (%)	20(21.7)	25(26.9)	0.664	0.415
Vertigo, n (%)	2(2.2)	0(0)	2.044	0.153
Vision disturbances, n (%)	0(0)	0(0)	-	-
Psychiatric symptoms, n (%)	2(2.2)	0(0)	2.044	0.153

Note: Data are presented as the number (proportion; %)

delirium or recovery times, and adverse psychomimetic effects were rare [36]. Similarly, in elderly gastrointestinal surgery patients, low-dose esketamine improved postoperative analgesia and reduced inflammatory markers such as IL-6 without increasing nausea, vomiting, nightmares, or delirium [37]. Collectively, these data indicate that low-dose esketamine during induction provides hemodynamic and analgesic benefits without compromising recovery or cognitive outcomes, whereas higher doses or prolonged infusions may pose risks, highlighting the need for careful dose optimization in elderly surgical patients.

Individual responses to S-ketamine may vary, and certain patients may benefit more than others. In elderly patients undergoing gastrointestinal surgery, factors such as reduced cardiovascular reserve, impaired baroreflex sensitivity, baseline sympathetic tone, and preoperative fluid deficits—exacerbated by prolonged fasting and bowel preparation—predispose some patients to greater hemodynamic fluctuations. Patients with lower baseline catecholamine reserves or diminished autonomic compensation are more likely to experience hypotension and may therefore derive greater benefit from the sympathomimetic properties of S-ketamine, which increase circulating norepinephrine, enhance vascular tone, and support cardiac contractility. Age-related pharmacokinetic changes, such as reduced hepatic clearance, may further modify individual hemodynamic responses.

This study has several limitations. First, we did not assess markers of organ perfusion compromise (e.g., lactate, creatinine, or myocardial enzymes), which limits our ability to directly link improved hemodynamic stability to organ protection. Second, our analysis focused exclusively on the induction period, without evaluating the effects of esketamine during anesthesia maintenance, late emergence, or on long-term organ outcomes. Although low-dose esketamine reduced induction-related hemodynamic instability, we did not determine whether this translated into lower rates of postoperative cardiac, renal, or neurological complications. Prior studies have shown that even brief but severe hypotension during induction is associated with increased risks of myocardial injury, acute kidney injury, stroke, and mortality [28, 29, 38]. Finally, our single-dose design leaves open the question of whether continuous infusion or higher dosing could provide additional benefit or increase adverse effects. Future studies should investigate optimal dosing strategies and long-term outcomes, particularly in high-risk elderly patients.

Conclusions

Adjunctive low-dose esketamine significantly attenuates the roller-coaster blood pressure pattern of induction—reflected by a 40% reduction in the incidence of hemodynamic instability—and preserves cardiac output, all while reducing cough and vasopressor use. These findings highlight the potential of esketamine to increase the safety of anesthesia induction in high-risk elderly individuals.

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Authors' contributions

Chuang-qiang Zhang and Da-qing Liu participated in data collection, analysis, interpretation, and writing throughout the study process. Cong Geng, Yu-xuan Tan and Hui-ming Zeng assisted with data collection, whereas Bi-yun Chen and Zhuo Zhen collated the data. Jian He and Han-bing Wang played important roles in the conception of the study process, conceptualization, design, interpretation, and revision of the manuscript. All the authors read and approved the final manuscript. Chuang-qiang Zhang and Da-qing Liu are co-first authors.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The research protocol for this project has been meticulously designed, incorporating a detailed and comprehensive informed consent form that thoroughly safeguards the rights and well-being of the participants, adhering to the principles outlined in the Helsinki Declaration. After careful review by the Ethics Committee, this study was approved by the Ethics Committee of The First People's Hospital of Foshan; the ethical approval number assigned is 2022–21.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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