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Effects of ciprofol on respiratory-related adverse incidence in patients with obesity during painless gastroscopy: a prospective, randomized clinical trial

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Abstract

Background Ciprofol is an intravenous anesthetic agent which in low doses produces sedation. It was developed via structural modification of propofol. Ciprofol is claimed to reduce respiratory depression. The object of the present study was to investigate whether or not ciprofol did actually reduce respiratory depression or not in patients with obesity undergoing gastroscopy.

Methods A total of 84 patients with obesity scheduled for gastroscopy were enrolled. The participants were randomly allocated to receive sedation with ciprofol (group C) or propofol (group P). The primary outcome was the incidence of respiratory-related adverse events (AEs), whereas the secondary outcomes were the incidence of further intraoperative and postoperative AEs; procedure and anesthesia success rates; Narcotrend index (NI); induction dosage; procedure time; recovery time; discharge time; and satisfaction ratings from the patients, anesthesiologists, and endoscopists.

Results The incidence of respiratory-related AEs was significantly lower in group C than in group P (17.5% vs. 57.5%; $P<0.001$). The occurrence of hypotension and movement during procedural events in group C was markedly reduced compared with that in group P ($P=0.024$ and 0.007, respectively). No notable differences were observed in the occurrence of additional AEs or in the success rates of the procedure and anesthesia between the two groups ($P>0.05$). The three-point satisfaction levels were comparable between the groups ($P>0.05$).

Conclusions 0.4 mg/kg of ciprofol provides anesthesia comparable with 2.0 mg/kg of propofol. However, it is related to reduced respiratory-related AEs and hypotension during gastroscopy in patients with obesity; thus, ciprofol is preferred to propofol for anesthesia in obese patients.

Trial registration This study was registered in the Chinese Clinical Trial Registry (KYLS20230625; first registration date: 29/06/2023).

Keywords Ciprofol, Obesity, Gastroscopy, Respiratory-related adverse incidence

Background

Gastroscopy is an invasive procedure that is used to inspect the upper gastrointestinal tract. Moderate or deep sedation and general anesthesia are typically employed to alleviate pain during gastroscopy (Sasaki and Tanabe et al., 2013; Shin and Lee et al.,

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2014). Propofol, characterized by its rapid effect onset and short half-life, has been advocated for outpatient surgical sedation or anesthesia in various studies and worldwide endoscopic guidelines (Barends and Absalom et al., 2018; Early and Lightdale et al., 2018; Dossa and Dube et al., 2020). Despite these positive features, propofol may induce specific adverse effects, including cardiorespiratory suppression (Cote and Hovis et al., 2010) and pain upon injection (Tan and Onsiong 1998).

Adverse respiratory incidents occur frequently during endoscopy. The prevalence of hypoxemia during an upper gastrointestinal endoscopy is approximately 15% (Cote and Hovis et al., 2010). One-eighth of the global population is obese, with the numbers continuing to rise, especially in emerging nations (Robinson L and Roccaldo R et al., 2024). Respiratory depression and airway blockage may arise during sedation owing to the unique pathophysiological conditions of patients with obesity, including tongue ptosis and airway morphology. Consequently, individuals with obesity are at a heightened risk of developing hypoxemia during sedation or anesthesia compared with the general population (McVay and Fang et al., 2017; Laffin and Kendale et al., 2020).

Studies have demonstrated that ciprofol, a novel intravenous anesthetic with a molecular structure similar to propofol, has superior sedative qualities (Qin and Ren et al., 2017; Teng and Ou et al., 2021; Luo and Tu et al., 2022) and results in less respiratory depression and injection discomfort than propofol (Li and Wang et al., 2022). However, the safety and efficacy of sedatives in individuals with obesity have not been well assessed. The objective of this study was to ascertain whether ciprofol is more efficacious and has lesser side effects than propofol in patients with obesity. This single-center, randomized, controlled study evaluated individuals at risk of hypoxemia to investigate the effect of ciprofol on the occurrence of respiratory-related side effects in patients with obesity undergoing anesthesia for gastroscopy.

Methods

Design and patients

This was a prospective, randomized, parallel-group clinical trial registered at www.chictrorg.cn (ChiCTR2300073428; July 11, 2023). All participants provided informed consent before inclusion in the study, and the protocol was approved by the Ethics Committee of Shunde Hospital of Southern Medical University (No. KYLS20230625) on June 29, 2023 and conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

Participants

Patients scheduled for gastroscopy at Shunde Hospital of Southern Medical University in Foshan, China, from September 2023 to October 2023 were evaluated. Patients aged 18–65 years with a body mass index (BMI) of 28–39.9 kg/m^2 and an American Society of Anesthesiologists Physical Status (ASA PS) of I–II were considered eligible for the study. Patients with the following conditions or medical history were excluded: (1) contraindications for sedation or anesthesia or a history of (AEs related to sedation/anesthesia; (2) a history of an allergy to opioids, propofol, or ciprofol-containing ingredients (i.e., soybean oil, glycerol, triglycerides, yolk lecithin, sodium oleate, and sodium hydroxide); (3) participation in any pharmacological clinical trials within the preceding 3 months; (4) lactating or pregnant individuals; (5) known or predicted difficult airways (modified Mallampati score degree IV); and (6) severe hypertension (persistent hypertension above grade III after medication administration).

Randomization and blinding

All recruited participants were randomly assigned to either group C or P by using computer-generated random numbers and opaque envelopes. An investigator performed the randomization and sealed the results in an opaque envelope. Before the trial's commencement, an anesthesiologist responsible for procedural sedation would unseal the allocated envelopes and administer the medication accordingly. This anesthesiologist cannot be blinded and is instructed not to disclose information about group allocation to any study personnel, except for in the case of unforeseen serious AEs during the procedure. Another anesthesia staff, blinded to the subsequent assessments, was responsible for assessing the research endpoints and collecting the data. The endoscopist, data collectors and patients were blinded.

Intervention and sedation/anesthesia protocol

An anesthesiologist evaluated the enrolled patients before surgery. Electrocardiogram data, physical status, medical history, and ASA PS classification were collected before surgery. They carefully evaluated patients' airway safety and screened individuals for obstructive sleep apnea utilizing the STOP-BANG questionnaire (Chung and Yegneswaran et al., 2008). Six hours of food fasting and two hours of clear fluid fasting were carried out prior to surgery. On the day of surgery, once the patients entered the preparation room, a peripheral venous infusion was placed in the right upper extremity for medication delivery. The patients were positioned in the left lateral decubitus position and received 5 L/min of oxygen via a nasal catheter until they regained full alertness

post-procedure. The heart rate (HR), blood pressure (BP), respiratory rate (RR), and pulse oxygen saturation (SpO_2) were continuously monitored and recorded in the left lateral position at six time points: (T_0, before anesthesia; T_1, at the disappearance of the eyelash reflex; T_2, after placement of the gastroscope; T_3, at the end of the operation; T_4, during full patient awakening; and T_5, at discharge from the hospital). The pulse oximeter was placed on the upper extremity opposite to the one with the blood pressure cuff to prevent inaccurate decreases in saturation during cuff inflation.

Sedation protocols involved either ciprofol or propofol in combination with dezocine. Dezocine has become one of the most widely used analgesics in China but is not marketed in other countries. Anesthesia induction was initiated with dezocine (1 mg/mL) administered at a dose of 0.05 mg/kg. Three minutes later, participates in the C group received 0.4 mg/kg ciprofol (2.5 mg/mL) while those in the P group received 2.0 mg/kg propofol (10 mg/mL). Ciprofol and propofol were administered for exceeded 30 s, with dosing adjusted according to lean body weight. The depth of sedation/anesthesia was evaluated 2 min after the administration of the initial dose using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score and the NI value.

The MOAA/S scores provides a detailed description of sedation/anesthesia levels, with scores ranging from 5 to 0 (Shin and Park et al., 2017). The NI value was continuously monitored using Narcotrend-Compact M (MT Monitor Technik, Germany) to objectively assess depth of consciousness (Kreuer and Wilhelm 2006). The procedure commenced after the patient achieved the MOAA/S score of ≤ 1. The NI value at this point became the reference NI for the patient to achieve the target depth of sedation/anesthesia.

Furthermore, half of the initial dose of ciprofol or propofol was provided as the supplemental dose in the corresponding group. Rescue dosing protocols were activated under either of the following conditions: (1) failure to achieve target sedation (the MOAA/S score of ≤ 1) within 2 min of initial administration; (2) emergence of motor or verbal reactions that may have an impact on the endoscopist's work. A maximum of three consecutive supplemental doses may be administered. If more than three supplemental doses were required within 5 min, the sedation protocol should be deemed ineffective, necessitating immediate implementation of an alternative anesthetic strategy. If sedation protocol failure occured in the ciprofol group, a rescue dose of propofol would be administered at approximately 0.2–0.5 mg/kg to achieve the target sedation/anesthesia depth.

Upon completion of the procedure, the patients were transferred to the post-anesthesia care unit (PACU) for monitoring and observation until fully awake. The modified Aldrete scale was used to evaluate recovery quality across five parameters: RR, BP, SpO_2, activity, and consciousness (Aldrete 1995). Patients could exit the PACU when their Aldrete score reached ≥ 9 or matched their respective pre-procedure levels. Before discharge, each patient completed a satisfaction questionnaire. Additionally, the satisfaction scores for both the endoscopists and anesthesiologists were measured using a numerical rating scale ranging from 0 to 5 (Supplementary Table S1).

AEs (hypotension, bradycardia, tachycardia, apnea, and respiratory depression) were assessed intraoperatively. An $SpO_2 < 93\%$ for 15 s was considered hypoxic. Under such a condition, the anesthesiologist performed the jaw trust maneuver during the procedure. If hypoxia did not improve, the gastroscope was removed and the patient lungs were ventilated with pure oxygen via the mask with the aid of a breathing balloon. Atropine (0.5 mg) was administered intravenously in the presence of bradycardia (heart rate < 50 beats/min; duration > 30 s). A mean arterial or systolic BP (SBP) 20% lower or higher than the baseline BP was considered hypotensive or hypertensive, respectively. In cases of severe hypotension (drop in SBP > 30% of baseline), rapid intravenous fluid resuscitation was initiated immediately. If hypotension persisted despite fluid challenge, intravenous dopamine 1–2 mg was administered as a bolus. A second dopamine bolus could be repeated after 5 min if needed.

Measurements and data collection

The primary safety endpoint of this study was the incidence of respiratory-related AEs, including the occurrence of any of the following during sedation/anesthesia: (1) respiratory depression: cardiac monitoring showing a respiratory rate of less than 8 breaths/min for 30 s or longer; (2) apnea: loss of respiratory movement in the chest for ≥ 15 s; and (3) hypoxemia: cardiac monitoring showing an SpO_2 of less than 93% for ≥ 15 s.

Secondary safety outcomes included the incidence of AEs (e.g.; bradycardia, hypotension, injection pain, choking, body movement, nausea, and vomiting). The efficacy outcomes included (1) the success rate of gastroscopy (The successful anesthesia to the gastroscopy must meet the following three requirements: successful completion of the procedure, no need for alternative sedation, and no more than three instances of rescue sedation within 5 min); (2) the success rate of anesthesia (MOAA/S ≤ 1 achieved by initial dose induction of anesthetic drugs); (3) the NI; (4) the total dose (the amount of medication given during the procedure); (5) procedure time (gastroscopy from entry to exit); (6) recovery time (time from the last dose to the patient fully awake); (7) discharge time (time from the last dose to discharge criteria); (8)

supplementary anesthesia during the procedure; and (9) three-point satisfaction scores (0–5 points each) evaluated from the anesthesiologist, endoscopist, and patient on an evaluation form scale, with 0 indicating dissatisfaction and 5 indicating very satisfaction.

Sample size estimation and statistical analysis

PASS (version 15.0) was used to compute the sample size. According to two Chinese multicenter randomized controlled trials, pre-testing indicated a 12% incidence of respiratory depression in patients with obesity receiving ciprofol compared with a 40% incidence in the propofol control group. The recommended total of 84 participants was calculated to achieve a statistical power of 0.8 and a significance level (alpha) of 0.05, accounting for an expected attrition rate of 20% throughout the study.

The statistical program SPSS (version 26.0) was used for data processing and analysis. The mean and standard deviation are expressed as normally distributed continuous variables, whereas non-normally distributed continuous variables are expressed as medians and quartiles. Independent *t*-tests or Wilcoxon rank-sum tests were used for the between-group comparisons of continuous variables. Repeated measures of variance or Friedman's tests were used to compare the baseline and point-in-time values within a group. When the assumption of homogeneity of variance was unmet, pairwise comparisons between groups were conducted using Welch's analysis of variance. Bonferroni post-hoc tests were used for multiple comparisons. Categorical variables are expressed as frequencies (percentages) and analyzed between groups using Pearson's chi-square test or Fisher's exact test. The tests were deemed statistically significant at P value < 0.05.

Results

Characteristics of the enrolled patients

A total of 84 individuals were initially screened in this study, with four exclusions: one patient withdrew consent prior to drug administration, one patient had delayed surgery due to a respiratory infection, one patient had a procedure lasting more than 30 min, and one patient did not abstain from clear liquids preoperatively. All 80 remaining patients were recruited for the trial (Fig. 1). The demographic and surgical characteristics of the patients are presented in Table 1. There were no statistically significant differences in the general condition of the patients in terms of age, sex ratio, weight, height, BMI, ASA status, STOP-Bang score, HBP history, or duration of operation between the two groups (all $P > 0.05$).

Primary endpoint

Compared with that in group P, the overall incidence of respiratory-related AEs was lower in group C ($P < 0.001$). Specifically, the incidence of respiratory depression and hypoxemia was lower in group C than in the group P ($P = 0.001$ and 0.034, respectively). The difference in the incidence of apnea between the two groups was not statistically significant (Table 2).

Secondary endpoints

Patients in group P exhibited a higher incidence of hypotension and movement during procedural events than those in group C ($P = 0.024$ and 0.007, respectively). No significant difference was found in the incidence of additional AEs during anesthesia, including hypertension, bradycardia, injection pain, cough, dizziness, nausea, and vomiting, between the two groups ($P > 0.05$; Table 2).

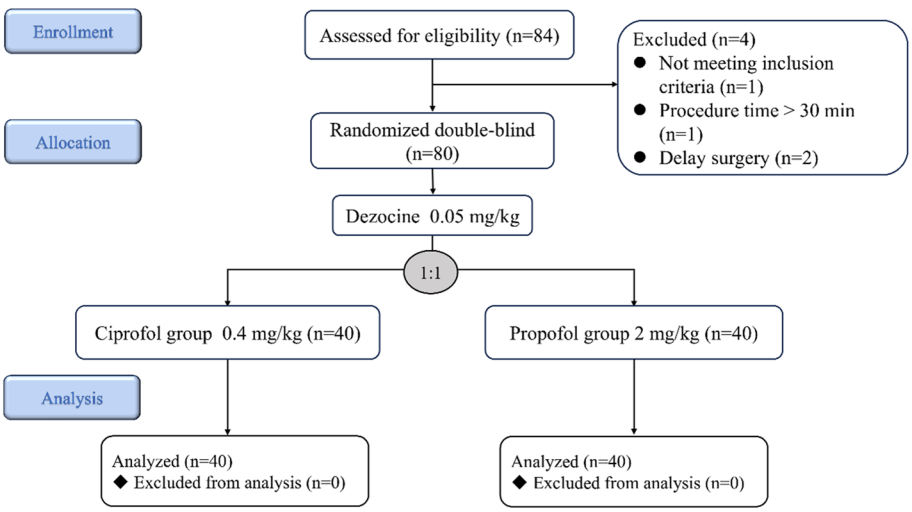

Fig. 1 Flow diagram of patient enrollment, allocation, and analysis

Table 1 Demographics and clinical parameters of the study patients

	Group C ($n=40$)	Group P ($n=40$)	*P*-value
Age (years)	44.5 ± 8.0	48.0 ± 9.8	0.087
Sex, *n* (%)			/
Female	14 (35.0)	14 (35.0)	
Male	26 (65.0)	26 (65.0)	
Weight (kg)	82.3 ± 8.4	84.4 ± 8.3	0.265
Height (m)	1.7 ± 0.1	1.7 ± 0.1	0.549
BMI (kg/m^2)	29.8 ± 1.6	30.2 ± 1.5	0.298
ASA PS, *n* (%)			0.366
I	19 (47.5)	15 (37.5)	
II	21 (52.5)	25 (62.5)	
STOP-Bang score	2.6 ± 1.1	2.9 ± 1.4	0.208
HBP history, *n* (%)	6 (15.0)	7 (17.5)	0.762
Duration of operation (min)	6.3 ± 1.9	6.1 ± 2.5	0.611

Data are provided as the mean ± standard deviation, or number (%)

BMI body mass index, *ASA* American Society of Anesthesiologists Physical Status, *HBP* high blood pressure

Table 2 Summary of the adverse events

	Group C ($n=40$)	Group P ($n=40$)	*P*-value
Respiratory-related AEs, *n* (%)	7 (17.5)	23 (57.5)	< 0.001*
Respiratory depression, *n* (%)	5 (12.5)	18 (45.0)	0.001*
Apnea, *n* (%)	2 (5.0)	5 (12.5)	0.235
Hypoxemia, *n* (%)	3 (7.5)	10 (25.0)	0.034*
Hemodynamic-related AEs, *n* (%)			
Hypotension, *n* (%)	12 (30.0)	22 (55.0)	0.024*
Hypertension, *n* (%)	1 (2.5)	0 (0.0)	0.314
Bradycardia, *n* (%)	0 (0.0)	2 (5.0)	0.152
Injection pain, *n* (%)	0 (0.0)	1 (2.5)	0.314
Cough, *n* (%)	7 (17.5)	5 (12.5)	0.531
Movement during procedure, *n* (%)	12 (30.0)	24 (60.0)	0.007*
Dizziness, *n* (%)	3 (7.5)	2 (5.0)	0.644
Nausea/vomiting, *n* (%)	0 (0.0)	1 (2.5)	0.314

Data are provided as the number (%)

AE = adverse event

* $P < 0.05$, group C vs. group P

The gastroscopy success rate in both groups was 100%. None of the patients in group C required a rescue dose of propofol. The percentage of goal anesthesia levels attained at the initial dose was 30% in both the ciprofol and propofol groups. The NI was similar between groups C and P ($P = 0.392$). No significant differences were observed in the proportion of supplementary anesthesia (70% vs. 75%, $P = 0.617$) and frequency of supplementary anesthesia (1.1 ± 0.5 vs. 1.2 ± 0.7, $P = 0.576$) between the ciprofol and propofol groups (Table 3).

The total dosages of ciprofol and propofol were 35.6 ± 6.2 and of 181.8 ± 42.0 mg, respectively. The dosages of ciprofol used in the procedure were four to five times lower than those of propofol ($P < 0.001$). No significant differences were noted in the dosage of dezocine between the two groups ($P > 0.05$). The time from discontinuation of anesthetic medication to complete awareness and other recovery-related durations were the same for both ciprofol and propofol ($P > 0.05$; Table 3).

Patients, anesthesiologists, and endoscopists reported similar satisfaction levels in the ciprofol group compared with those in the propofol group ($P > 0.05$; Table 4).

The vital sign data at each time point during gastroscopy are shown in Figs. 2, 3, 4, and 5. The HR of both groups varied around the baseline after medication delivery. In group P, the mean HR decreased at T_3. The mean SBP in the two groups exhibited a declining trend following medication delivery. The average RR exhibited a minor change after administration in both the groups. At T_2, T_3, and T_4 following anesthesia initiation, the mean RR in the propofol group was lower than that in the ciprofol group. In both patient groups, the SpO_2 levels decreased at T_3 ($P < 0.05$; Table 5).

Discussion

This study shows that ciprofol results in less respiratory and circulatory depression than propofol, and reduces anesthetic use and the incidence of respiratory depression and hypotension in obese patients undergoing painless gastroscopy. Our data indicate that 0.04 mg/kg of ciprofol may provide a more effective anesthetic option than 2.0 mg/kg of propofol for individuals with obesity. Few studies have assessed the effect of ciprofol on individuals with obesity; therefore, this study focused on the efficacy of ciprofol in patients with obesity undergoing painless gastroscopy, which holds great clinical significance.

BMI is globally used for classifying body weight, with individuals with a BMI ≥ 28 kg/m^2 classified as those with obesity in Asia owing to regional population differences. Ciprofol, a new 2,6-disubstituted phenol derivative, is a highly selective agonist of the gamma-aminobutyric acid type A receptor, exhibiting about four to five times the activity of propofol (Qin and Ren et al., 2017; Hu and Ou et al., 2021). Previous studies have shown that in painless gastrointestinal endoscopy, ciprofol provides effective sedation/anesthesia and reduces the incidence of AEs such as hypotension and respiratory depression (Li and Wang et al., 2022). Based on preliminary data (Zeng and Wang et al., 2022) and the results of pharmacokinetic

Table 3 Intra- and post-intervention characteristics due to sedation induced by ciprofol and propofol

	Group C ($n=40$)	Group P ($n=40$)	*P*-value
Success rate of gastroscopy, *n (%)*	40 (100)	40 (100)	/
Success rate of anesthesia, *n* (%)	12 (30.0)	12 (30.0)	/
Narcotrend values (induction by the initial dose)	60.4 ± 10.8	58.5 ± 8.9	0.392
Supplementary anesthesia, *n* (%)			0.617
Yes	28 (70.0)	30 (75.0)	
No	12 (30.0)	10 (25.0)	
Frequency of supplementary anesthesia (times)	1.1 ± 0.5	1.2 ± 0.7	0.576
Total amount of ciprofol/propofol (mg)	35.6 ± 6.2	181.8 ± 42.0	< 0.001*
Dose of dezocine (mg)	4.0 ± 0.4	4.1 ± 0.5	0.486
Recovery time (min)	9.6 ± 2.8	8.2 ± 3.5	0.067
Discharge time (min)	23.5 ± 2.4	23.4 ± 3.4	0.909

Data are presented as mean ± standard deviation or number (%)

The Narcotrend values were recorded after ciprofol/propofol induction using the initial dose

NI Narcotrend Index

* $P < 0.05$, group C vs. group P

Table 4 Summary of the satisfaction ratings

	Group C ($n=40$)	Group P ($n=40$)	*P*-value
Patients' satisfaction	4.9 ± 0.3	4.9 ± 0.4	0.734
Anesthesiologists' satisfaction	4.6 ± 0.6	4.3 ± 0.8	0.081
Endoscopists' satisfaction	4.7 ± 0.5	4.6 ± 0.5	0.368

Data are presented as mean ± standard deviation

* $P < 0.05$, group C vs. group P

and pharmacodynamic studies (Wei and Qiu et al., 2017), ciprofol (0.4 mg/kg) was selected for comparison with propofol (2.0 mg/kg) to assess the efficacy and safety of anesthesia in patients with obesity undergoing painless gastroscopy in the present study.

Respiratory complications including respiratory depression, apnea, and hypoxemia are the predominant intraoperative AEs associated with painless gastroscopy. Hypoxia may be attributed to central or obstructive apnea or hypopnea. The severity of hypoxia depends on the capacity of oxygen reserves and the extent of respiratory center depression during sedation/anesthesia. Patients with obesity are at high risk of respiratory depression and airway obstruction during sedation (Kang and Lu et al., 2021) due to tongue drop, abnormal airway anatomy (Shobatake and Itaya-Hironaka et al., 2019), reduced gas reserve, and lower functional residual gas volume (Qadeer and Rocio Lopez et al., 2009). In critical cases, intraoperative oxygen desaturation may threaten patient safety (Meidert and Chouker et al., 2020). In this

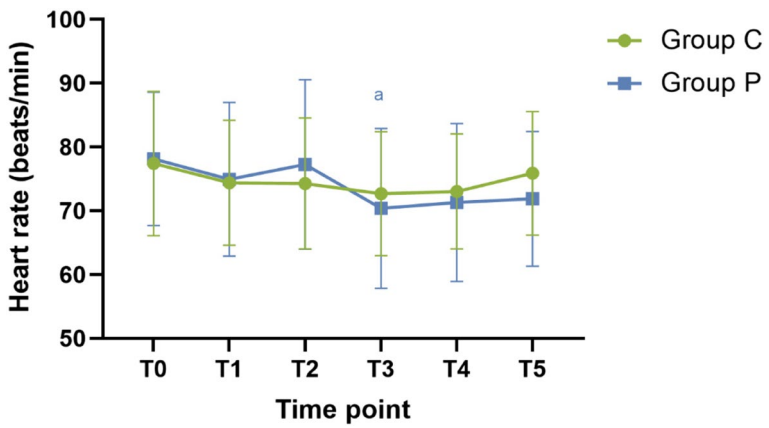

Fig. 2 Comparison of heart rate between the two groups. Note: T_0 : before anesthesia, T_1: at the disappearance of the eyelash reflex, T_2 : after placement of the gastroscope, T_3 : at the end of the operation, T_4 : during full patient awakening, T_5 : at discharge from the hospital, *: group C vs. group P, a: vs. T_0, b: vs. T_1, c: vs. T_5

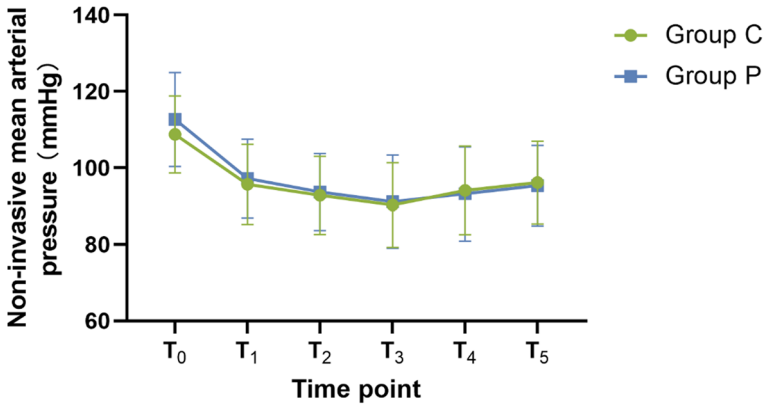

Fig. 3 Comparison of non-invasive mean arterial pressure between the two groups. Note: T_0: before anesthesia, T_1 : at the disappearance of the eyelash reflex, T_2 : after placement of the gastroscope, T_3 : at the end of the operation, T_4 : during full patient awakening, T_5 : at discharge from the hospital, *: group C vs. group P, a: vs. T_0, b: vs. T_1, c: vs. T_5

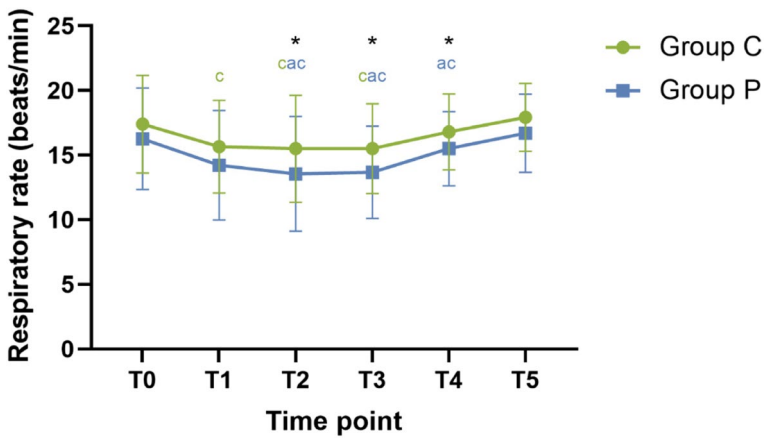

Fig. 4 Comparison of respiratory rate between the two groups. Note: T_0 : before anesthesia, T_1 : at the disappearance of the eyelash reflex, T_2 : after placement of the gastroscope, T_3 : at the end of the operation, T_4 : during full patient awakening, T_5 : at discharge from the hospital, *: group C vs. group P, a: vs. T_0, b: vs. T_1, c: vs T_5

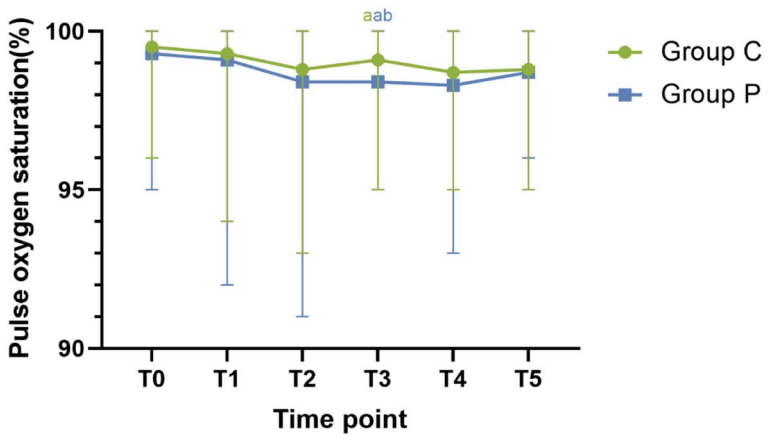

Fig. 5 Comparison of pulse oxygen saturation between the two groups. Note: T_0 : before anesthesia, T_1 : at the disappearance of the eyelash reflex, T_2 : after placement of the gastroscope, T_3 : at the end of the operation, T_4 : during full patient awakening, T_5 : at discharge from the hospital, *: group C vs. group p, a: vs. T_0, b: vs. T_1, c: vs.T_5

Table 5 Comparison of NiMAP, HR, RR, and SpO_2 at each time point among the two groups

		T_0	T_1	T_2	T_3	T_4	T_5
HR (bpm)	Group C ($n=40$)	77.4 ± 11.3	74.4 ± 9.8	74.3 ± 10.3	72.7 ± 9.7	73.0 ± 9.0	75.9 ± 9.7
	Group P ($n=40$)	78.1 ± 10.5	75.0 ± 12.0	77.3 ± 13.3	70.4 ± 12.5[a]	71.3 ± 12.4	71.9 ± 10.6
	P-value	0.767	0.823	0.262	0.356	0.478	0.082
NiMAP (mmHg)	Group C ($n=40$)	108.8 ± 10.1	95.7 ± 10.5[a]	92.8 ± 10.2[a]	90.3 ± 11.1[a]	94.1 ± 11.6[a]	96.2 ± 10.8[a]
	Group P ($n=40$)	112.7 ± 12.3	97.2 ± 10.3[a]	93.7 ± 10.1[a]	91.2 ± 12.2[a]	93.2 ± 12.3[a]	95.4 ± 10.5[a]
	P-value	0.125	0.520	0.698	0.732	0.737	0.738
RR (bpm)	Group C ($n=40$)	17.4 ± 3.8	15.7 ± 3.6[c]	15.5 ± 4.1[c]	15.5 ± 3.5[c]	16.8 ± 2.9	17.9 ± 2.6
	Group P ($n=40$)	16.3 ± 3.9	14.2 ± 4.2	13.6 ± 4.4[ac]	13.7 ± 3.6[ac]	15.5 ± 2.9	16.7 ± 3.0
	P-value	0.195	0.108	0.045[*]	0.023[*]	0.049[*]	0.057
SpO_2 (%)	Group C ($n=40$)	100.0 [99.0–100.0]	100.0 [99.0–100.0]	99.0 [98.0–100.0]	99.0 [98.3–100.0][a]	99.0 [98.0–100.0]	99.0 [98.0–100.0]
	Group P ($n=40$)	100.0 [99.0–100.0]	100.0 [99.0–100.0]	99.0 [98.0–100.0]	99.0 [97.0–100.0][ab]	99.0 [97.3–100.0]	99.0 [98.0–100.0]
	P-value	0.651	0.891	0.807	0.131	0.223	0.336

Data are presented as mean ± standard deviation or median [interquartile range]

HR heart rate, *NiMAP* non-invasive mean arterial pressure, *RR* respiratory rate, *SPO_2* pulse oxygen saturation

[*] $P < 0.05$, group C vs. group P

[a] $P < 0.05$, vs. T_0

[b] $P < 0.05$, vs. T_1

[c] $P < 0.05$, vs. T_5

study, no significant differences were noted in BMI and STOP-Bang scores between the two groups, indicating a comparable risk of respiratory depression in both groups. Our data showed that the incidence of respiratory complications was lower in the ciprofol than in the propofol group, particularly in patients with respiratory depression and hypoxemia. Li et al. reported similar results and speculated that ciprofol may induce reduced respiratory depression in the central nervous system or airway collapse (Li and Wang et al., 2022). Besides, ciprofol was reported to reduce the risk of hypoxic events and decreases the frequency of respiratory emergencies requiring management.

Hypotension is also a common anesthetic complication during gastroscopy. In this study, on comparing the baseline BP levels, it was found that both groups of patients who received propofol or ciprofol showed a reduction in their BP levels. The HR fluctuated around baseline in all groups after drug administration. Hypotension occurred in both groups; however, we found that the patients receiving ciprofol had more stable hemodynamics than those receiving propofol. Teng et al. also showed that ciprofol might reduce anesthesia-related hemodynamic depression compared to propofol during colonoscopy (Teng and Ou et al., 2021). Propofol may cause hypotension by inhibiting myocardial contraction (Kanaya and Gable et al., 2005) or vascular tone (Nagakawa and Yamazaki et al., 2003), which may also contribute to the hypotension caused by ciprofol. However, further studies are required to explore the specific mechanisms of action. Moreover, because of the higher potency of ciprofol than propofol, the amount of drug needed to achieve anesthesia is reduced, resulting in fewer cardiovascular depressant side effects (Jiang and Jiao et al., 2021). This logic partly explains why the incidence of hypotension was lower in group C than in group P. Ciprofol was also found to have less effect on HR than on BP in a phase II clinical trial (Teng and Ou et al., 2021).

Furthermore, adverse effects, including injection pain, postoperative dizziness, nausea, and vomiting, were evaluated; however, none were observed. A possible reason for no observing any adverse events could be because the study participants were individuals under 65 years of age and the dosage provided was small, calculated based on lean body mass. In summary, ciprofol is safe and beneficial for patients with obesity who undergo painless gastroscopy.

A single intravenous dose of ciprofol (0.3–0.9 mg/kg, enhances the depth of sedation or anesthesia, as evidenced by a gradual decrease in the MOAA/S score (Teng and Ou et al., 2021). This was associated with an increase in the injected dose and plasma concentration of the drug. A score of ≤ 1 on the MOAA/S was reached at approximately 2 min, accompanied by loss of consciousness, loss of responsiveness, and a diminished response to painful stimuli. Sedation levels may be inconsistently assessed because they were determined using the subjective MOAA/S score. In this study, NI monitoring was used to determine the precise degree of anesthesia. Although studies have indicated a substantial

correlation between the bispectral index monitor values and MOAA/S score (Meidert and Chouker et al., 2020), NI monitoring during gastrointestinal sedation/anesthesia increases the patients' cost burden. Therefore, NI monitoring is only an additional objective tool in the field of research and may not be applicable to short-term outpatient surgical procedures.

According to the available studies on the dose of propofol administered to patients with obesity, Ingrande et al. (Ingrande and Brodsky et al., 2011) and van Kralingen et al. (van Kralingen and Diepstraten et al., 2010) reported that lean body weight was the optimal dose scale for propofol in the induction of anesthesia in patients with obesity during painless gastroscopy. Thus, our data showed a low anesthesia success rate and high NI in both groups. We found that although the average dose of ciprofol was four to five times lower than that of propofol, there were no differences in the incidence of successful gastroscopy and anesthesia, NI, recovery time, or discharge time between the two groups. Furthermore, the incidence of movement during the procedure was lower in the ciprofol than in the control group. Similar to the results of Luo et al. (Teng and Ou et al., 2021), ciprofol was not inferior to propofol in terms of anesthesia and recovery time in this study. The chemical structures and pharmacokinetics of the two drugs are analogous (Liao and Li et al. 2022), and the superior selective binding affinity of ciprofol to its receptors enables the generation of sedative and anesthetic effects comparable to those of propofol at lower dosages (Qin and Ren et al., 2017). Furthermore, to comprehensively validate the effects of anesthesia, we evaluated the satisfaction levels of patients, endoscopists, and anesthesiologists during the procedure. Tripartite satisfaction levels were comparable between the two groups.

Regrettably, ciprofol has not been on the market for a long time and there is still a lack of long-term experience and validation of data over a broad range of clinical situations. The absence of safety proofs in certain populations has significantly restricted the extensive application of ciprofol. Furthermore, anesthesiologists possess excellent expertise in propofol administration and are better adept at managing its adverse effects. Nonetheless, the safety advantages of ciprofol may provide a more stable anesthetic procedure in a clinical setting and effectively reduce intraoperative respiratory problems, especially in obese patients.

The study has a few limitations. First, due to the relatively small sample size of the study, there is a possibility of a statistical bias. Second, this study was conducted in patients with ASA I or II, and the applicability of the findings to patients with higher ASA classifications requires further examination. Due to ethical considerations, we did not investigate anesthesia in individuals with severe obesity. Finally, patients aged >65 years were excluded. We believe that older patients are also at high risk of respiratory depression and exhibit heightened sensitivity to medicine; hence, age must be considered when establishing the best sedation protocol for this demographic.

Conclusions

In conclusion, the incidence of respiratory and circulatory adverse effects of ciprofol in painless gastroscopy in patients with obesity was low. Furthermore, the anesthesia effect was found to be precise and the drug was not inferior to propofol in relieving patient discomfort and improving the tolerance and satisfaction of endoscopic procedures. Therefore, ciprofol use can better ensure the safety of endoscopic diagnosis and treatment during sedation and anesthesia.

Supplementary Information

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Supplementary Material 1: Table S1. Satisfaction evaluation forms.

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Not applicable.

Authors' contributions
YJ. Z. and D. X. conceived the study, obtained approval, reviewed the literature, performed chart reviews, and wrote and revised the manuscript. D. X., F. L., M. C., Y. Y., G. L. conceived data acquisition, statistical analysis, and data interpretation. Y. Z. assisted with study conception, creating the study design and revised the manuscript. All the authors approved the fnal version of the manuscript and agreed to be accountable for all aspects of the work.

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Data availability
Data is provided within the manuscript or supplementary information files.The datasets generated and/or analysed in the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval was obtained from the Medical Ethics Committee of Shunde Hospital of Southern Medical University (approval no. KYLS20230625). This study was conducted in accordance with the 1964 Declaration of Helsinki and its amendments. Written informed consent was obtained from all the participants or their families before initiating any study-related activities.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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