

The Median Effective Dose of Ciprofol Combined with Sufentanil for Inhibiting Responses to Gastroscope Insertion in Obese Patients: A Prospective, Single-Center Study

Zhouya Xue^{1,2,*}, Xiang Liu^{1,2,*}, Weisheng Qian¹, Nan Yang¹, Yongyi Pan¹, Yong Zhou¹, Wei Jiang¹, Feng Li¹, Bin Qian¹

¹Department of Anesthesiology, The First People's Hospital of Yancheng, The Yancheng Clinical College of Xuzhou Medical University, Yancheng, Jiangsu, People's Republic of China; ²Jiangsu Province Key Laboratory of Anesthesiology, Jiangsu Province Key Laboratory of Anesthesia and Analgesia Application Technology, NMPA Key Laboratory for Research and Evaluation of Narcotic and Psychotropic Drugs, Xuzhou Medical University, Xuzhou, Jiangsu, People's Republic of China

*These authors contributed equally to this work

Correspondence: Feng Li; Bin Qian, Department of Anesthesiology, The First People's Hospital of Yancheng, No. 166 West Yulong Road, Yancheng, Jiangsu, 224001, People's Republic of China, Email 1226637852@qq.com; qbmzk19@sina.com

Background: Ciprofol, a recently developed intravenous anesthetic, whereas sufentanil is a widely used adjuvant for gastroenteroscopy sedation. The recommended dosage of ciprofol for obese patients remains unclear. Our study aimed to determine the median effective dose (ED₅₀) of ciprofol in combination with sufentanil for obese patients undergoing gastroscopy sedation.

Methods: A total of 70 patients undergoing painless gastroscopy from July 2024 to September 2024 were recruited. Patients were assigned to the obese group (body mass index [BMI] ≥ 28 kg/m², n=34) and non-obese group (18.5 kg/m² ≤ BMI < 24 kg/m², n=36). All patients received 0.1 µg/kg of sufentanil, and the ciprofol dose was determined by the modified Dixon sequential method with an initial dose of 0.4 mg/kg and a dose gradient of 0.01 mg/kg. The dose of ciprofol administered to the subsequent patient was determined by the response of the preceding patient. The response referred to the patient's cough, swallowing, and body movement during gastroscope insertion. The primary outcome was the ED₅₀ of ciprofol in each group, while the secondary outcomes comprised the incidences of hypoxemia, hypotension, bradycardia, postoperative nausea and vomiting (PONV), and hemodynamic parameters.

Results: The ED₅₀ of ciprofol was 0.278 mg/kg (95% confidence interval [CI]: 0.226–0.297 mg/kg) in the obese group and 0.347 mg/kg (95% CI: 0.329–0.360 mg/kg) in the non-obese group for gastroscopy sedation. The ED₅₀ of ciprofol in the obese group was significantly lower than that in the non-obese group ($P < 0.05$). The incidence of hypoxemia in the obese group was significantly higher than that in the non-obese group ($P < 0.05$).

Conclusion: Obesity affected the ED₅₀ of ciprofol, suggesting that the ciprofol dosage should be adjusted in obese patients.

Keywords: obesity, ciprofol, median effective dose, painless gastroscopy

Introduction

Gastroscopy is the most common method to diagnose and treat upper gastrointestinal tract diseases.¹ While sedation or anesthesia during a gastroscopy might reduce the patients' anxiety and discomfort, there are some sedation-related adverse events to be aware of, including hypotension, respiratory depression, and a prolonged recovery time.^{2,3} The global obesity rate has been steadily rising in recent years,⁴ and obesity is frequently associated with elevated oxygen demand, decreased expiratory reserve volume and functional residual volume.^{5,6} The incidence of hypoxemia in obese patients under sedation was higher than that in non-obese patients, and airway modifications (AMs) were often required,

such as chin lift maneuver, nasopharyngeal airway, modified mask airway, mask ventilation, or endotracheal intubation.^{7–9}

The most commonly used anesthetic for gastrointestinal endoscopic sedation is propofol, but it is associated with adverse effects including respiratory depression, hypotension, and injection pain.¹⁰ Based on the molecular structure of propofol, which exhibits mild inhibitory effects on respiratory and circulatory functions, ciprofol incorporates a cyclopropyl group.¹¹ During the sedation of gastroenteroscopy, the ciprofol group experienced a significantly decreased incidence of injection pain, hypotension, and respiratory depression compared to the propofol group.¹² Opioids are commonly used for gastrointestinal sedation to alleviate patients' discomfort while simultaneously reducing the required dosage of anesthetic drugs.¹³ Sufentanil is a widely used adjuvant for gastroenteroscopy sedation in China, and a multicenter trial on sedated gastrointestinal endoscopy in obese patients also selected sufentanil as an adjuvant.¹⁴ Currently, the combination of ciprofol and sufentanil is widely used in various types of day surgery, including bronchoscopy and gastroenteroscopy sedation.^{15,16}

However, at present, there are few studies on the sedation of gastroscopy using ciprofol combined with sufentanil in obese patients, and the individualized dose of ciprofol combined with sufentanil has not been determined. In order to provide guidelines for the safe administration of ciprofol, the aim of this study was to investigate the ED₅₀ of ciprofol combined with sufentanil for the sedation during gastroscopy in obese individuals.

Materials and Methods

Ethical Approval

This prospective, single-center study was approved by the Ethics Committee of The First People's Hospital of Yancheng (2024-k-141), and the clinical trial was registered in the Chinese Clinical Trial Registry (No: ChiCTR2400086298). The data for this trial were collected at the Endoscopy Center of the First People's Hospital of Yancheng between July and September 2024. The written informed consents were provided by all participants prior to enrollment, and our present research followed the Helsinki Declaration.

Design and Patients

Inclusion Criteria

1) Age: 18–64 years old; 2) $18.5 \leq \text{BMI} < 24.0 \text{ kg/m}^2$ or $\text{BMI} \geq 28 \text{ kg/m}^2$; 3) American Society of Anesthesiologists (ASA) grade I–II and stable grade III patients undergoing sedation for gastroscopy.

Exclusion Criteria

1) Patients who were allergic to sedative/anesthetic drugs such as sufentanil and ciprofol or had a history of severe allergic reactions; 2) Patients who had contraindications to endoscopy or refused anesthesia; 3) Patients who were unaccompanied by family members; 4) Uncontrolled severe hypertension (systolic blood pressure [SBP] $\geq 180 \text{ mmHg}$, diastolic blood pressure [DBP] $\geq 110 \text{ mmHg}$); 5) Patients with a recent acute respiratory infection, an acute exacerbation of asthma, an acute exacerbation of chronic obstructive pulmonary disease (COPD), or preoperative hypoxemia; 6) Acute coronary syndrome, severe arrhythmia, or heart failure; 7) Massive hemoptysis during the active phase; 8) Severe anemia ($\text{Hb} < 6 \text{ g/dL}$); 9) Patients with mental health disorders and cognitive dysfunction who cannot communicate effectively; 10) Have a history of psychotropic and narcotic drug abuse; 11) Liver dysfunction (Child-Pugh grade C or higher); renal dysfunction (chronic kidney disease [CKD] stage 3 or higher); 12) Pregnant or lactating women; 13) Acute upper gastrointestinal bleeding accompanied by shock, pyloric obstruction, achalasia of the cardia, gastric emptying disorders, and a history of upper gastrointestinal surgery.

This study was a non-randomized controlled trial. Based on BMI values, the study was divided into two groups: an obese group ($\text{BMI} \geq 28 \text{ kg/m}^2$) and a non-obese group ($18.5 \leq \text{BMI} < 24.0 \text{ kg/m}^2$).

Interventions

Sufentanil ($0.1 \text{ } \mu\text{g/kg}$) was administered intravenously to each patient, and the modified Dixon up-down sequential method was used to calculate the ED₅₀ of ciprofol.¹⁶ The median effective dose is defined as the dose that is effective for

50% of the population, known as ED₅₀.¹⁷ During the endoscopy, patients who did not experience coughing, swallowing, or movement were classified as “successful sedation” while others were classified as “failed sedation”.¹⁸ The initial patient received a ciprofol dosage of 0.4 mg/kg, and the subsequent patient’s dosage, with a dose gradient of 0.01 mg/kg, was decided based on the prior patient’s reaction. The ciprofol dose was increased by 0.01 mg/kg for the subsequent patient if the prior patient experienced “failed sedation”; otherwise, it was decreased by 0.01 mg/kg. The modified DIXON sequential method required a minimum of six crossover points to calculate ED₅₀, and seven crossover points were chosen to improve the accuracy of the data, based on relevant literature.^{19,20} A crossover point was defined when patient’s responses were transformed from “successful sedation” to “failed sedation”.²¹ All anesthesia procedures were performed by an experienced anesthesiologist holding senior title. Follow-up data were collected by a different anesthesiologist who was not involved in the anesthesia administration. The gastroscopy was performed by the same gastroenterologist (working experience > 5 years).

Before the gastroscopy, all patients were required to fast for 8 h and refrain from drinking for 4 h. An intravenous access was established, and the patients’ heart rate (HR), respiration rate (RR), pulse oxygen saturation (SpO₂), non-invasive cuff blood pressure, and electrocardiogram (ECG) were all continuously monitored. Each patient had a nasal catheter with a 5L/min oxygen flow while in the left decubitus position. After administering an intravenous injection of 0.1 µg/kg of sufentanil over 30 seconds, ciprofol was administered according to the outcomes of the modified Dixon up-down sequential method, with the injection completed within 30 to 60 seconds. The patient’s Modified Observer’s Assessment of Alertness/Sedation (MOAA/S) score was assessed every ten seconds after the ciprofol injection, and the endoscopist inserted the gastroscope when the patient’s MOAA/S score was 1 or less.^{19,20} A rescue dose of 0.05–0.2 mg/kg of ciprofol (infusion time > 10s) was administered to patients who demonstrated “failed sedation” or a MOAA/S score ≥ 2 during gastroscopy. Ciprofol was administered no more than 5 times within a 15-minute period, with each infusion interval lasting at least 2 minutes.^{22,23} After the completion of endoscopy, patients had their MOAA/S scores measured every two minutes until they were fully awake (MOAA/S ≥ 4, measured consecutively 3 times).¹⁶ The modified Aldrete score was used to evaluate the recovery of patients. Patients with an Aldrete score of 9 or higher for three consecutive times could be discharged from the post-anesthesia care unit (PACU).¹⁶

The monitor was set to measure the non-invasive blood pressure every two minutes. Under sufficient anesthesia depth, if hypertension occurred (SBP increased by more than 20% or SBP > 160 mmHg), urapidil was injected intravenously at a dose of 5 mg per time. If the mean arterial pressure (MAP) was less than 20% of the baseline value or the SBP was < 90 mmHg, intravenous ephedrine was given at a dose of 5–10 mg. If the HR was < 50 beats/min, atropine 0.2–0.5 mg was administered intravenously. When hypoxia occurred (75% ≤ SpO₂ < 90% for < 60 seconds), oxygen flow was increased, and the jaw-thrust maneuver or nasopharyngeal airway insertion (male: 7.0 or 7.5; female: 6.5 or 7.0) was performed. If severe hypoxia occurred (SpO₂ < 75% or 75% ≤ SpO₂ < 90% for ≥ 60 seconds), the gastroscope was withdrawn, mask mechanical ventilation was administered, and endotracheal intubation was considered if necessary.²⁴ Intravenous tropisetron 5 mg was typically given when the patient experienced PONV.

Outcome Measures

Primary Outcome

The ED₅₀ of ciprofol during gastroscopy in both groups.

Secondary Outcomes

The incidences of adverse reactions, such as hypoxemia, hypotension, bradycardia were monitored both during gastroscopy and in the PACU; PONV was recorded in the PACU. Additionally, hemodynamic parameters including MAP, HR, RR, SpO₂ were monitored throughout the peri-gastroscopy period from T₀ to T₄. T₀, baseline; T₁, the insertion of gastroscope; T₂, at the end of gastroscopy; T₃, when the patients were awake; T₄, at the time of exiting PACU.

Other outcomes: Demographic data, including gender, age, BMI, ASA classification, comorbidities, surgery for malignant tumors, gastroscopy duration, PACU stay time, the Modified Mallampati (MMP) score and STOP-Bang score. The MMP score is closely associated with upper airway obstruction.²⁵ The STOP-Bang score is a simple and effective screening tool for the early identification of patients at risk for obstructive sleep apnea (OSA). It consists of 8 items, each worth 1 point: Snoring: Do you snore loudly? Tiredness: Do you often feel tired, fatigued, or sleepy during the daytime?

Observed Apnea: Has anyone observed you stopping breathing during your sleep? Pressure: Do you have or are you being treated for high blood pressure? BMI: Is your BMI over 35 kg/m²? Age: Are you older than 50 years? Neck Circumference: Is your neck circumference greater than 40 cm? Gender: Are you male? A total score of 5 or more indicates a higher risk for moderate to severe OSA.²⁶

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows (Version 22.0; IBM Corp., Armonk, NY, USA). Continuous data were tested for normality using Shapiro–Wilk test. Continuous variables in normal distribution such as MAP and HR were expressed as mean±standard deviation, and their differences were analyzed by the independent sample *t* test. Non-normally distributed continuous variables such as age, BMI, STOP-Bang score, gastroscopy time and PACU stay time were presented as median (interquartile range [IQR]) and compared using a Mann–Whitney *U*-test. Pearson χ^2 test, continuity correction χ^2 test or Fisher's exact test for categorical variables such as gender, ASA, MMP score, comorbidities, surgery for malignant tumors and the incidences of adverse events were used to compare between two groups. $P < 0.05$ was considered as statistically significant.

ED₅₀ and ED₉₅ were calculated using the Probit regression method. Sequential graphs and dose-response curves were generated with GraphPad Prism software (Version 8.0; GraphPad Software Inc., San Diego, CA, USA). The overlapping CI method was used to compare the ED₅₀ differences between the obese and non-obese groups. If the 95% CI of the two groups were overlap, the null hypothesis that the ED₅₀ was rejected at an approximate significance level of $\alpha = 0.05$.²⁷

Results

General Data

From July to September 2024, a total of 77 patients were enrolled. Of these, 2 patients were excluded due to poor preoperative blood pressure control, 1 patient had a history of upper gastrointestinal surgery, 1 patient had an acute respiratory infection, and 3 patients refused to participate. This resulted in a total of 70 patients being enrolled (Figure 1). The patients were divided into a non-obese group ($n=36$) and an obese group ($n=34$) according to their BMI, and the BMI of the obese group was significantly higher than that of the non-obese group ($P < 0.05$). No patients were lost to follow-up, and a total of 70 patients were included in the statistical analysis (Figure 1). The demographic data and clinical characteristics of the two groups are presented in Table 1. No statistically significant differences were observed between the two groups in terms of gender, age, ASA grading, incidence of diabetes mellitus (DM), surgical history of malignant tumors, gastroscopy duration, and PACU stay time. Additionally, the MMP score, prevalence of hypertension, and STOP-Bang score were higher in the obese group compared to the non-obese group ($P < 0.05$).

Dose–Response to Ciprofol for Anesthesia Induction

We performed probit regression analysis to demonstrate that the ED₅₀ of ciprofol during sedation in the non-obese group was 0.347 mg/kg (95% CI: 0.329–0.360 mg/kg), while the ED₅₀ of ciprofol in the obese group was 0.278 mg/kg (95% CI: 0.226–0.297 mg/kg). There was no overlap in the 95% CI between the two groups, suggesting that the ciprofol required for gastroscopy sedation in obese patients was significantly lower than that in patients with a normal BMI ($P < 0.05$). The ED₉₅ of ciprofol in the non-obese group was 0.384 mg/kg (95% CI 0.367–0.491 mg/kg), and the ED₉₅ of ciprofol in the obese group was 0.334 mg/kg (95% CI 0.309–0.537 mg/kg). The modified Dixon up-and-down plots for each group were shown in Figures 2 and 3. The dose–response curves of ciprofol induction in each group undergoing gastroscopy sedation were shown in Figures 4 and 5.

Adverse Events

During gastroscopy, the respiratory depression rate in the obese group was significantly higher than that in the non-obese group (44.1% vs 5.6%, $P < 0.05$) (Table 2). Among them, the incidence of hypoxemia in the obese group was 35.3%, compared to 5.6% in the non-obese group. Additionally, 3 patients (8.8%) in the obese group experienced severe hypoxemia. There were no significant differences in adverse events such as hypotension, bradycardia, and PONV (Table 2).

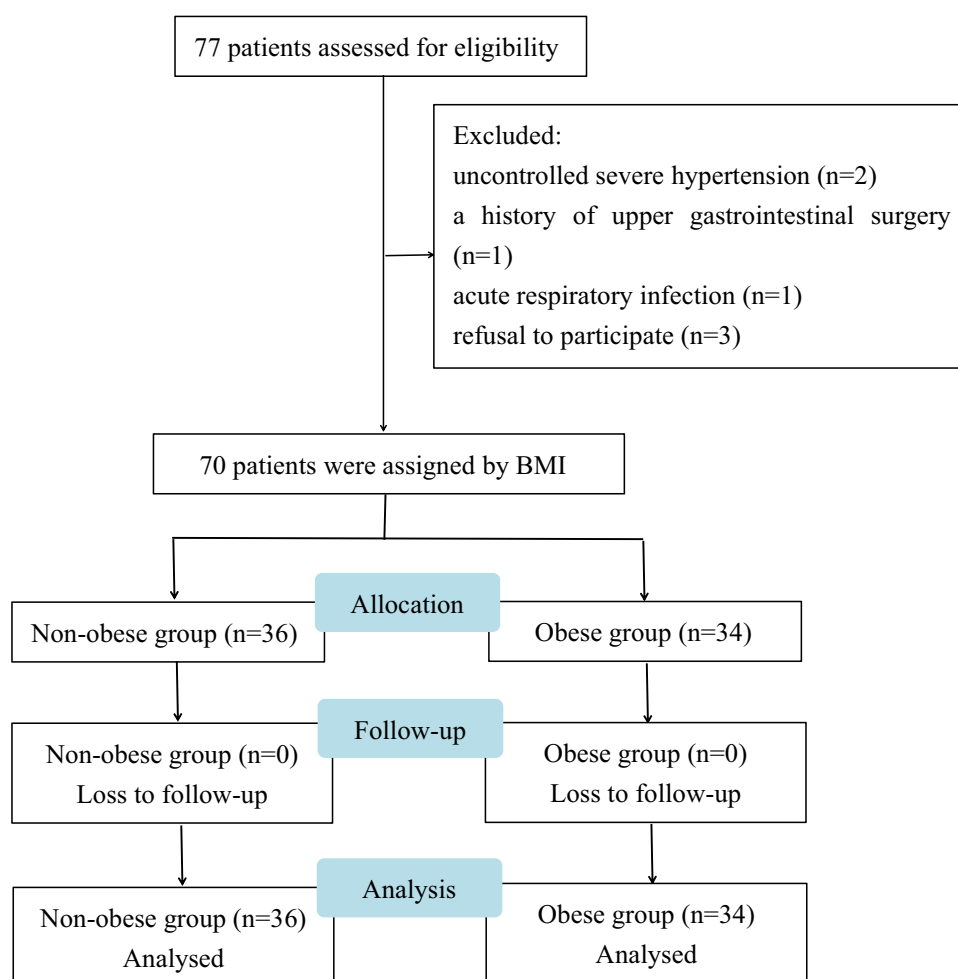


Figure 1 Flow diagram of included participants.

Hemodynamics

There was no significant difference in MAP and HR between the two groups at each time point. Compared to baseline MAP, the MAP in both groups decreased after anesthesia ($P<0.05$) (Figure 6). HR decreased after anesthesia in both

Table 1 Demographic Data and Clinical Characteristics (n=70)

	Non-obese group (n=36)	Obese group (n=34)	P value
Gender (male/female, n)	15/ 21	18 / 16	0.345
Age (years)	46 [34.5, 57]	51.5 [45, 58]	0.110
BMI (kg/m ²)	22 [20.5, 23.3]	30 [28.9, 31.1]	0.000***
ASA (I/II/III, n)	28 / 8 / 0	19 / 15 / 0	0.051
MMP score (I/II/III, n)	9 / 26 / 1	1 / 18 / 15	0.009**
Hypertension (n)	4	11	0.030*
DM (n)	0	2	0.232
Surgery for malignant tumors (n)	2	1	1.0
STOP-Bang Score	0 [0, 1]	3 [2, 4]	0.000***
Gastroscore duration (min)	3 [3, 4]	3 [3, 5]	0.577
PACU stay time (min)	16 [15, 21.5]	17.5 [15, 20]	0.520

Note: Data are presented as total number (n), median (interquartile range [IQR]). * $P<0.05$, ** $P<0.01$, *** $P<0.001$.

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; MMP, Modified Mallampati; DM, diabetes mellitus; PACU, post-anesthesia care unit.

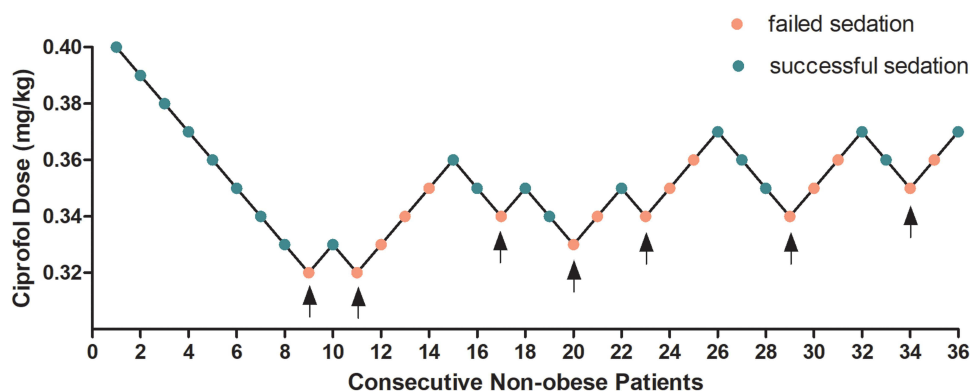


Figure 2 The up-and-down sequence of ciprofol dose for inhibiting responses to gastroscop insertion in non-obese patients. The black arrow represents crossover point (from "successful sedation" to "failed sedation").

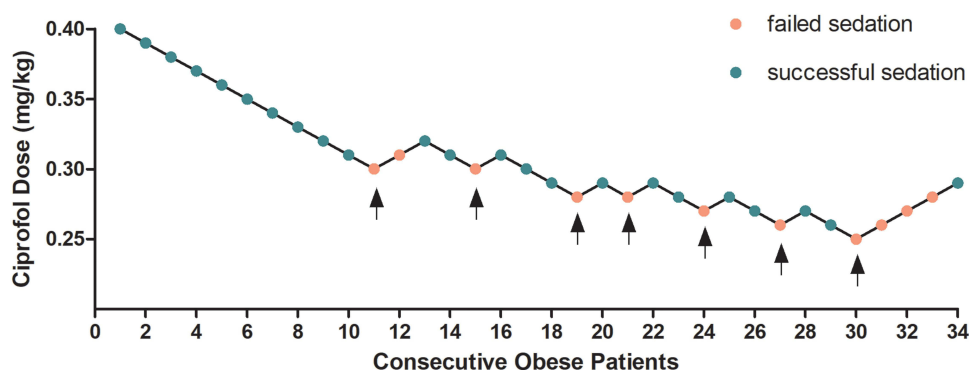


Figure 3 The up-and-down sequence of ciprofol dose for inhibiting responses to gastroscop insertion in obese patients. The black arrow represents crossover point (from "successful sedation" to "failed sedation").

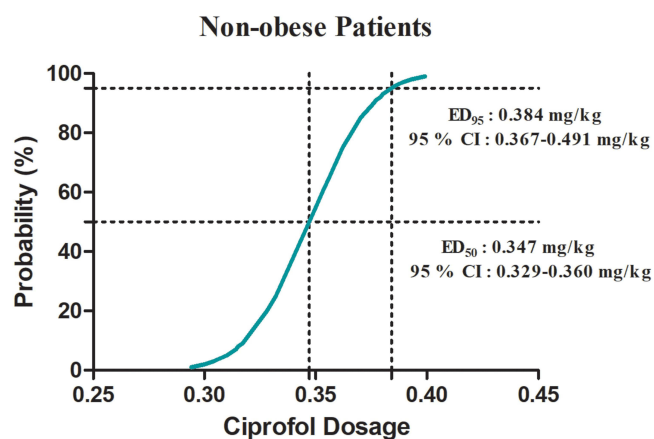


Figure 4 Dose-response curve of ciprofol for successful gastroscop insertion in non-obese patients.

groups. Compared to the baseline HR, statistical significance was observed in the obese group only at T₂ and in the non-obese group at both T₁ and T₂ ($P < 0.05$) (Figure 7).

Discussion

According to several clinical trials of ciprofol, the initial loading dose for gastrointestinal endoscopy in adults was 0.4 mg/kg.^{28–30} However, it was specifically noted that dosing should be individualized for special populations, such as

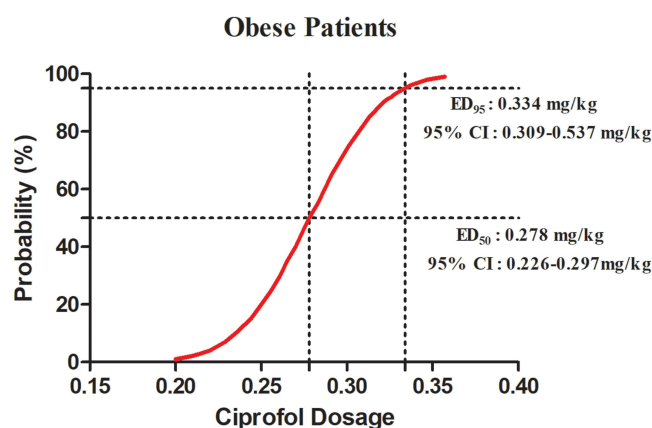


Figure 5 Dose-response curve of ciprofol for successful gastroscopy insertion in obese patients.

the elderly, whose induction dose of ciprofol should be reduced to 0.3 mg/kg.³¹ However, no specific adjustment guidelines of ciprofol have been provided for obese patients. A clinical study of elderly patients undergoing gastroscopy sedation suggested that when combined with 0.1 µg/kg sufentanil, the ED₅₀ of ciprofol was 0.23 mg/kg (95% CI: 0.09 to 0.30 mg/kg) in elderly patients aged 65–74 years; the ED₅₀ was 0.18 mg/kg (95% CI: 0.13–0.22 mg/kg) for elderly patients aged 75 years and older.¹⁶ Another single-arm study suggested that the median effective dose of ciprofol combined with 7 µg/kg of alfentanil to inhibit the gastroscopy insertion response in patients aged 18–64 years was 0.217 mg/kg (95% CI: 0.203–0.234 mg/kg).²² The opioid compatibility drug used in our study was 0.1 µg/kg sufentanil, and it was concluded that the ED₅₀ of ciprofol induction for gastroscopy sedation in obese patients was 0.278 mg/kg (95% CI: 0.226–0.297 mg/kg), while that of the non-obese group was 0.347 mg/kg (95% CI: 0.329–0.360 mg/kg). In summary, these findings indicated that the dosage of ciprofol should be adjusted for different subjects and various compatible opioids during anesthesia induction.

Both body fat and lean mass increase in obese patients, but the increase in adipose tissue is greater than that of lean mass. The fat solubility of anesthetic drugs affects the apparent distribution volume of these drugs, and hemodynamic changes associated with obesity can further influence the pharmacokinetics of anesthetic drugs.³² Dosing scalars other than total body weight (TBW), such as ideal body weight (IBW), body surface area (BSA), BMI, lean body weight (LBW), and corrected body weight (CBW) have been used.^{33,34} The pharmacokinetic properties of ciprofol are largely similar to those of propofol.³⁵ Studies have demonstrated that LBW was a more appropriate dosing scalar for propofol induction in morbidly obese patients, while the maintenance infusion should be based on TBW.^{36,37} Ciprofol is a lipophilic anesthetic, and very few studies have suggested which dosing scalar should be followed during the induction of anesthesia with ciprofol in obese patients. A recent study in 2025 suggested that CBW may be a reliable dosing scalar for the induction of ciprofol in obese patients.³⁸ However, it remains unclear whether CBW or LBW is more suitable for calculating the induction dose of ciprofol in obese patients, while TBW is considered unsuitable. Adjusting the ciprofol dosage in obese patients is essential to mitigate the risk of overdose.

Table 2 Adverse Events in Patients Treated With Gastroscopy (n=70)

	Non-obese group (n=36)	Obese group (n=34)	P value
Hypoxemia (n)	2 (5.6%)	15 (44.1%)	0.000***
75% ≤ SpO ₂ < 90%	2 (5.6%)	12 (35.3%)	
SpO ₂ < 75%	0	3 (8.8%)	0.225
Hypotension (n)	2 (5.6%)	6 (17.6%)	
Bradycardia (n)	0	0	
PONV (n)	1 (2.8%)	0	

Note: Data are presented as total number (n, %). ***P<0.001.

Abbreviations: PONV, postoperative nausea and vomiting.

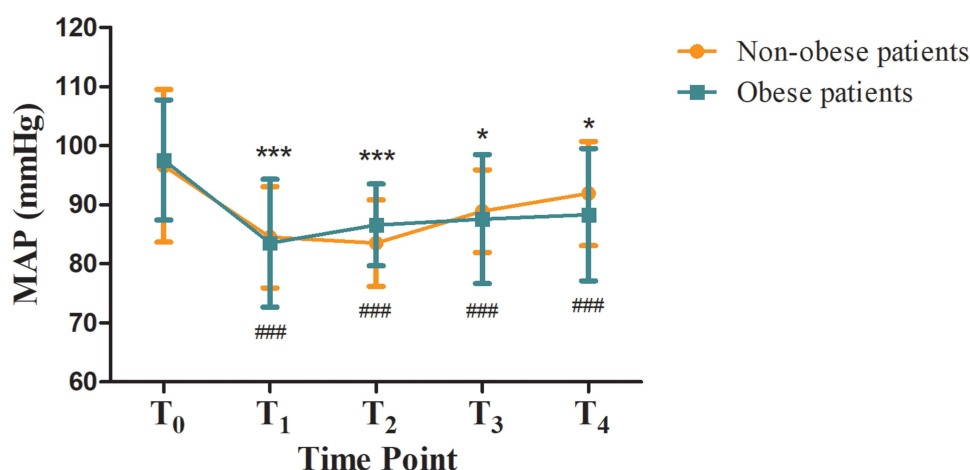


Figure 6 MAP from T₀ to T₄ in two groups. * $P < 0.05$ compared to T₀ in the non-obese patients. *** $P < 0.001$ compared to T₀ in the non-obese patients. ### $P < 0.001$ compared to T₀ in the obese patients.

Abbreviations: T₀, baseline; T₁, the insertion of gastroscope; T₂, at the end of gastroscope; T₃, when the patients were awake; T₄, at the time of exiting PACU; MAP, mean arterial pressure; PACU, post-anesthesia care unit.

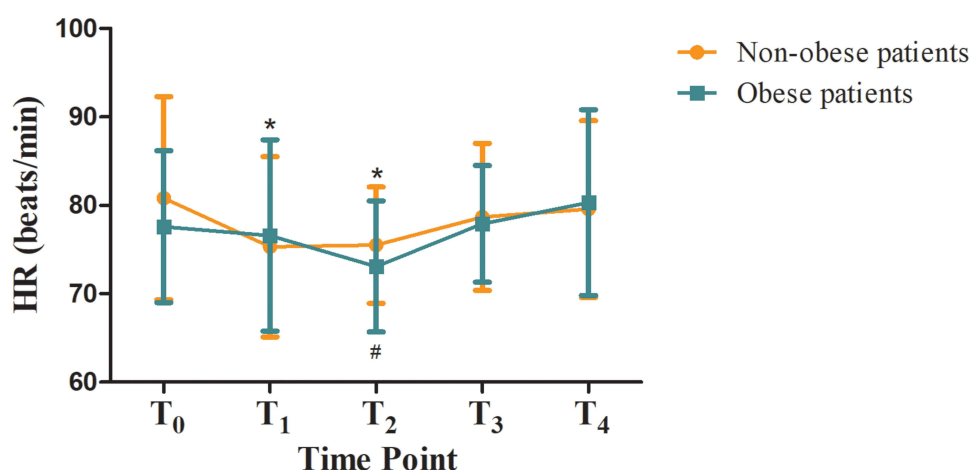


Figure 7 HR from T₀ to T₄ in two groups. * $P < 0.05$ compared to T₀ in the non-obese patients. # $P < 0.05$ compared to T₀ in the obese patients.

Abbreviations: T₀, baseline; T₁, the insertion of gastroscope; T₂, at the end of gastroscope; T₃, when the patients were awake; T₄, at the time of exiting PACU; HR, heart rate; PACU, post-anesthesia care unit.

Obese patients exhibit fat deposition in the oropharynx and chest wall. Additionally, some of these patients have varying degrees of upper respiratory tract obstruction and tongue sagging, which increases the risk of respiratory depression.³⁹ The MMP grade, STOP-Bang score, and the incidence of hypertension in the obese group were higher than those in the control group ($P < 0.05$). MMP can serve as a predictor of hypoxemia during endoscopic sedation.⁴⁰ In addition, the prevalence of hypertension and obesity ($\text{BMI} > 35 \text{ kg/m}^2$) was an independent risk factor for OSA, both of which increased the risk of OSA.²⁶ Furthermore, OSA was closely associated with the incidence of AMs and hypoxemia.⁴¹ These results suggested that rescue equipment, including nasopharyngeal airways, masks, or endotracheal tubes should be prepared in advance to prevent hypoxemia following the induction of anesthesia in obese patients with high STOP-Bang and MMP scores.

In our study, the incidence of hypoxemia was 35.3% in the obese group and 5.6% in the non-obese group, while the incidence of severe hypoxemia was 8.8% in the obese group and 0% in the non-obese group. Despite the patient's transient hypoxemia, their pulse oximetry quickly returned to normal following prompt treatment, and no adverse outcomes were observed. In a retrospective analysis, hypoxemia occurred in 13% of patients with a normal BMI, 18% of patients with class I obesity, 27% of patients with class II obesity, and 19% of patients with class III obesity during outpatient endoscopic sedation. The incidence of severe hypoxemia was 5.5% in patients with a normal BMI, and 7.2%,

12%, and 8.5% in patients with Class I–III obesity, respectively.⁷ The incidence of hypoxemia in obese patients in our study was slightly higher compared to the aforementioned study, which may be attributed to the following reasons: (1) The ciprofol dosage for each patient in our study was determined using the modified Dixon sequential method, rather than a uniform dose. The initial induction dose of ciprofol was relatively high, which may contributed to the increased incidence of respiratory depression in obese patients. (2) Different drug combinations in each study resulted in varying results. (3) Another important reason is that Laffin et al excluded patients with OSA,⁷ whereas our study did not exclude these potential patients. In fact, a total of six patients in the obese group had STOP-Bang score greater than or equal to 5, which strongly suggested that they had OSA.

Compared to propofol, ciprofol has the advantage of exerting less impact on the respiratory and circulatory systems.⁴² In this study, although the blood pressure and heart rate of both groups briefly decreased after anesthesia, they gradually increased following awakening. No bradycardia occurred in either group during anesthesia and resuscitation. The incidence of hypotension was 17.6% in the obese group, which was higher than the 5.6% observed in the non-obese group. This may be related to the higher prevalence of hypertension in the obese group ($P < 0.05$), whose vascular elasticity was poor. However, the incidence of hypotension was not statistically significant between the two groups.

Since there were few studies on the pharmacokinetics and pharmacodynamics of ciprofol in obese patients. However, using TBW and the dosage recommended by relevant studies to calculate the induction dose of ciprofol in obese patients may increase the risk of respiratory depression. Our results indicated that the median effective dose of ciprofol in obese patients undergoing painless gastroscopy was approximately 80% of that in non-obese patients. When obese patients undergo ciprofol sedation, the dosage should be adjusted to ensure personalized anesthesia.

Limitations of the study: (1) Firstly, our study was a non-randomized controlled trial, and a large-sample randomized controlled trial will be designed to investigate ciprofol induction in obese patients. (2) Secondly, only the modified Dixon sequential method was used to determine the ED_{50} of the ciprofol induction dose in obese patients, while the biased coin design (BCD) method was considered more accurate for ED_{95} .¹⁷ (3) In addition, we did not classify the severity of obesity among patients. (4) In a follow-up trial, patients with confirmed OSA or a STOP-Bang score ≥ 5 should be excluded to ensure their safety.

Conclusions

Our study demonstrated that the ED_{50} of ciprofol in obese patients undergoing painless gastroscopy was 0.278 mg/kg (95% CI: 0.226–0.297 mg/kg), whereas in non-obese patients, it was 0.347 mg/kg (95% CI: 0.329–0.360 mg/kg). The ED_{50} in the obese group was significantly lower than that in the non-obese group ($P < 0.05$), suggesting that ciprofol induction in obese patients required dose adjustment to minimize anesthetic-related adverse effects.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgments

We would like to express our sincere gratitude to the doctors and nurses of the Endoscopy Center of the First People's Hospital of Yancheng for their invaluable assistance.

Funding

This work was supported by the Key Laboratory Open Project of Colleges and Universities in Jiangsu Province (XZSYSKF2024010 to Xiang Liu) and the Medical Research Project of Yancheng Health Commission (YK2024077 to Zhouya Xue).

Disclosure

All authors declare that they have no competing interests.

References

- Kendall BJ. Post-endoscopy upper gastrointestinal cancer - identifying, understanding, and improving. *Endoscopy*. 2023;55(2):119–120. doi:10.1055/a-1961-7004
- Wadhwa V, Issa D, Garg S, Lopez R, Sanaka MR, Vargo JJ. Similar risk of cardiopulmonary adverse events between propofol and traditional anesthesia for gastrointestinal endoscopy: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2017;15(2):194–206. doi:10.1016/j.cgh.2016.07.013
- Cote GA, Hovis RM, Ansstas MA, et al. Incidence of sedation-related complications with propofol use during advanced endoscopic procedures. *Clin Gastroenterol Hepatol*. 2010;8(2):137–142. doi:10.1016/j.cgh.2009.07.008
- Gilden AH, Catenacci VA, Taormina JM. Obesity. *Ann Intern Med*. 2024;177(5):ITC65–ITC80. doi:10.7326/AITC202405210
- Zavorsky GS, Hoffman SL. Pulmonary gas exchange in the morbidly obese. *Obes Rev*. 2008;9(4):326–339. doi:10.1111/j.1467-789X.2008.00471.x
- Steier J, Lunt A, Hart N, Polkey MI, Moxham J. Observational study of the effect of obesity on lung volumes. *Thorax*. 2014;69(8):752–759. doi:10.1136/thoraxjnl-2014-205148
- Laffin AE, Kendale SM, Huncke TK. Severity and duration of hypoxemia during outpatient endoscopy in obese patients: a retrospective cohort study. *Can J Anaesth*. 2020;67(9):1182–1189. doi:10.1007/s12630-020-01737-x
- Wani S, Azar R, Hovis CE, et al. Obesity as a risk factor for sedation-related complications during propofol-mediated sedation for advanced endoscopic procedures. *Gastrointest Endosc*. 2011;74(6):1238–1247. doi:10.1016/j.gie.2011.09.006
- McVay T, Fang JC, Taylor L, et al. Safety analysis of bariatric patients undergoing outpatient upper endoscopy with non-anesthesia administered propofol sedation. *Obes Surg*. 2017;27(6):1501–1507. doi:10.1007/s11695-016-2478-4
- Ortega GH, Barbosa EC, Faria PC, et al. Ciprofol versus propofol for adult sedation in gastrointestinal endoscopic procedures: a systematic review and meta-analysis. *Minerva Anesthesiol*. 2024;90(11):1013–1021. doi:10.23736/S0375-9393.24.18203-X
- Zhong J, Zhang J, Fan Y, et al. Efficacy and safety of Ciprofol for procedural sedation and anesthesia in non-operating room settings. *J Clin Anesth*. 2023;85:111047. doi:10.1016/j.jclinane.2022.111047
- Chen L, Xie Y, Du X, et al. The effect of different doses of ciprofol in patients with painless gastrointestinal endoscopy. *Drug Des Devel Ther*. 2023;17:1733–1740. doi:10.2147/DDDT.S414166
- Zhou S, Zhu Z, Dai W, et al. National survey on sedation for gastrointestinal endoscopy in 2758 Chinese hospitals. *Br J Anaesth*. 2021;127(1):56–64. doi:10.1016/j.bja.2021.01.028
- Wang L, Zhang Y, Han D, et al. Effect of high flow nasal cannula oxygenation on incidence of hypoxia during sedated gastrointestinal endoscopy in patients with obesity: multicentre randomised controlled trial. *BMJ*. 2025;388:e080795. doi:10.1136/bmj-2024-080795
- Pan M, Liu W, Zhang Z, Li T, Xie W. ED50 of ciprofol combined with sufentanil for fiberoptic bronchoscopy of different patient populations with pulmonary tuberculosis. *BMC Anesthesiol*. 2024;24(1):197. doi:10.1186/s12871-024-02583-w
- Xiong H, Xu H, Yang Y, Hu B, Jiang K, Zou X. Median effective dose of ciprofol combined with sufentanil for inhibiting the upper gastrointestinal endoscopic placement reaction in elderly patients. *Dose Response*. 2024;22(2):15593258241248931. doi:10.1177/15593258241248931
- Oron AP, Souter MJ, Flournoy N. Understanding research methods: up-and-down designs for dose-finding. *Anesthesiology*. 2022;137(2):137–150. doi:10.1097/ALN.0000000000004282
- Hao PP, Tian T, Hu B, et al. Long-term high-risk drinking does not change effective doses of propofol for successful insertion of gastroscope in Chinese male patients. *BMC Anesthesiol*. 2022;22(1):183. doi:10.1186/s12871-022-01725-2
- Tang L, Lv W, Sun J, Chen L. Effect of intravenous lidocaine on the ED50 of propofol induction dose in elderly patients undergoing painless gastroscopy: a prospective, randomized, double-blinded, controlled study. *Perioper Med*. 2024;13(1):15. doi:10.1186/s13741-024-00370-2
- Yuan J, Liang Z, Geoffrey MB, et al. Exploring the median effective dose of ciprofol for anesthesia induction in elderly patients: impact of frailty on ED(50). *Drug Des Devel Ther*. 2024;18:1025–1034. doi:10.2147/DDDT.S453486
- Dixon WJ. Staircase bioassay: the up-and-down method. *Neurosci Biobehav Rev*. 1991;15(1):47–50. doi:10.1016/s0149-7634(05)80090-9
- Wu X, Liao M, Lin X, Hu J, Zhao T, Sun H. Effective doses of ciprofol combined with alfentanil in inhibiting responses to gastroscope insertion, a prospective, single-arm, single-center study. *BMC Anesthesiol*. 2024;24(1):2. doi:10.1186/s12871-023-02387-4
- Qin X, Lu X, Tang L, Wang C, Xue J. Ciprofol versus propofol for sedation in gastrointestinal endoscopy: protocol for a systematic review and meta-analysis. *BMJ Open*. 2023;13(5):e071438. doi:10.1136/bmjopen-2022-071438
- Lin Y, Zhang X, Li L, et al. High-flow nasal cannula oxygen therapy and hypoxia during gastroscopy with propofol sedation: a randomized multicenter clinical trial. *Gastrointest Endosc*. 2019;90(4):591–601. doi:10.1016/j.gie.2019.06.033
- Peng B, Chen M, Yang J, Lai Y, Zhang N. Development and validation of an oropharyngeal obstruction evaluation score. *Sleep Breath*. 2024;28(3):1145–1153. doi:10.1007/s11325-023-02978-y
- Chung F, Abdullah HR, Liao P. STOP-bang questionnaire: a practical approach to screen for obstructive sleep apnea. *Chest*. 2016;149(3):631–638. doi:10.1378/chest.15-0903
- Payton ME, Greenstone MH, Schenker N. Overlapping confidence intervals or standard error intervals: what do they mean in terms of statistical significance? *J Insect Sci*. 2003;3(34):34. doi:10.1093/jis/3.1.34
- Li J, Wang X, Liu J, et al. Comparison of ciprofol (HSK3486) versus propofol for the induction of deep sedation during gastroscopy and colonoscopy procedures: a multi-centre, non-inferiority, randomized, controlled Phase 3 clinical trial. *Basic Clin Pharmacol Toxicol*. 2022;131(2):138–148. doi:10.1111/bcpt.13761
- Gao SH, Tang QQ, Wang CM, et al. The efficacy and safety of ciprofol and propofol in patients undergoing colonoscopy: a double-blind, randomized, controlled trial. *J Clin Anesth*. 2024;95:111474. doi:10.1016/j.jclinane.2024.111474
- Teng Y, Ou M, Wang X, et al. Efficacy and safety of ciprofol for the sedation/anesthesia in patients undergoing colonoscopy: phase IIa and IIb multi-center clinical trials. *Eur J Pharm Sci*. 2021;164:105904. doi:10.1016/j.ejps.2021.105904

31. Li X, Yang D, Li Q, et al. Safety, pharmacokinetics, and pharmacodynamics of a single bolus of the gamma-aminobutyric acid (GABA) receptor potentiator HSK3486 in healthy Chinese elderly and non-elderly. *Front Pharmacol.* **2021**;12:735700. doi:10.3389/fphar.2021.735700
32. Casati A, Putzu M. Anesthesia in the obese patient: pharmacokinetic considerations. *J Clin Anesth.* **2005**;17(2):134–145. doi:10.1016/j.jclinane.2004.01.009
33. Ingrande J, Lemmens HJ. Dose adjustment of anaesthetics in the morbidly obese. *Br J Anaesth.* **2010**;105(Suppl 1):i16–23. doi:10.1093/bja/aeq312
34. Hussain Z, Curtain C, Mirkazemi C, Zaidi STR. Peri-operative medication dosing in adult obese elective surgical patients: a systematic review of clinical studies. *Clin Drug Investig.* **2018**;38(8):673–693. doi:10.1007/s40261-018-0662-0
35. Lu M, Liu J, Wu X, Zhang Z. Ciprofol: a novel alternative to propofol in clinical intravenous anesthesia? *Biomed Res Int.* **2023**;2023:7443226. doi:10.1155/2023/7443226
36. Ingrande J, Brodsky JB, Lemmens HJ. Lean body weight scalar for the anesthetic induction dose of propofol in morbidly obese subjects. *Anesth Analg.* **2011**;113(1):57–62. doi:10.1213/ANE.0b013e3181f6d9c0
37. Dong D, Peng X, Liu J, Qian H, Li J, Wu B. Morbid obesity alters both pharmacokinetics and pharmacodynamics of propofol: dosing recommendation for anesthesia induction. *Drug Metab Dispos.* **2016**;44(10):1579–1583. doi:10.1124/dmd.116.071605
38. Li Y, Yuan M, Zhang P, Zhou T, Zhang M, Xu J. Efficacy and safety of ciprofol for anesthesia in painless colonoscopy with varying body mass indices patients: a prospective, single-center, observational study. *Drug Des Devel Ther.* **2025**;19:1–9. doi:10.2147/DDDT.S496783
39. Wang Y, Liu F, Zhang Y, Yang X, Wu J. The effect of capnography on the incidence of hypoxia during sedation for EGD and colonoscopy in mildly obese patients: a randomized, controlled study. *BMC Anesthesiol.* **2023**;23(1):188. doi:10.1186/s12871-023-02151-8
40. Li N, Wu J, Lu Y, et al. Predictive value of NoSAS questionnaire combined with the modified Mallampati grade for hypoxemia during routine sedation for gastrointestinal endoscopy. *BMC Anesthesiol.* **2023**;23(1):126. doi:10.1186/s12871-023-02075-3
41. Cote GA, Hovis CE, Hovis RM, et al. A screening instrument for sleep apnea predicts airway maneuvers in patients undergoing advanced endoscopic procedures. *Clin Gastroenterol Hepatol.* **2010**;8(8):660–665e661. doi:10.1016/j.cgh.2010.05.015
42. Curro JM, Santonocito C, Merola F, et al. Ciprofol as compared to propofol for sedation and general anesthesia: a systematic review of randomized controlled trials. *J Anesth Analg Crit Care.* **2024**;4(1):24. doi:10.1186/s44158-024-00159-1

Drug Design, Development and Therapy

Publish your work in this journal

Drug Design, Development and Therapy is an international, peer-reviewed open-access journal that spans the spectrum of drug design and development through to clinical applications. Clinical outcomes, patient safety, and programs for the development and effective, safe, and sustained use of medicines are a feature of the journal, which has also been accepted for indexing on PubMed Central. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/drug-design-development-and-therapy-journal>

Dovepress
Taylor & Francis Group