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Effect of different doses of ciprofol on hemodynamics induced by general anesthesia in elderly diabetic patients undergoing spinal surgery: a double-blind, randomized, controlled study

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Abstract

Background To evaluate the safety and efficacy of different doses of ciprofol for the induction of general anesthesia in elderly patients with diabetes undergoing spinal surgery.

Methods Ninety elderly diabetic patients scheduled for elective single-level posterior lumbar interbody fusion (PLIF) under general anesthesia were enrolled and randomly assigned to three groups according to the induction dose of ciprofol: group A (0.2 mg/kg), Group B (0.3 mg/kg), and Group C (0.4 mg/kg). The safety and efficacy of anesthesia induction were compared among the three groups.

Case presentation The incidence of hypotension in Group C (46.4%) was significantly higher than that in Groups A (7.4%) and B (14.8%) ($P < 0.05$). The area under the time-mean arterial pressure curve (AUT_{MAP}) was significantly greater in Group C (176.39 ± 33.83 mmHg·min) than in Group B (158.44 ± 26.55 mmHg·min) and Group A (143.59 ± 19.52 mmHg·min) ($P < 0.05$). The incidence of intubation response was highest in Group A (77.8%, $P < 0.05$). Significant differences in bispectral index (BIS) values were observed at 3, 4, and 5 min post-administration among the groups

Conclusions The induction regimen of 0.3 mg/kg ciprofol combined with 0.4 μg/kg sufentanil and 0.7 mg/kg rocuronium provided superior hemodynamic stability and reduced the need for vasoactive drugs in elderly diabetic patients. This regimen was found to be more favorable compared to the 0.2 mg/kg and 0.4 mg/kg ciprofol dosing groups, demonstrating an optimal balance of safety and efficacy during anesthesia induction in this high-risk population. This trial was registered in the Chinese Clinical Trial Registry on February 26, 2024 (Registration Number: ChiCTR2400081164).

Keywords Older adults, Diabetes mellitus, Ciprofol, General anesthesia induction

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Background

With the aging population, an increasing number of elderly individuals require surgery under general anesthesia. Elderly patients often present with multiple comorbidities, which increase the risk of surgical complications [1]. Hypotension induced by general anesthesia is a common issue associated with poor prognosis [2]. Its risk factors include advanced age, history of hypertension, ASA III–V classification, type 2 diabetes, and propofol induction [3, 4].

Ciprofol, a novel sedative anesthetic independently developed in China, has a lower incidence of adverse effects, such as hypotension, bradycardia, and respiratory depression [5]. Currently, the commonly used dose is 0.4 mg/kg, which has been proven safe for short procedures, such as painless gastrointestinal endoscopy, bronchoscopy, and endoscopic retrograde cholangiopancreatography [6, 7]. Studies have demonstrated that ciprofol is also effective and safe for general anesthesia induction and maintenance, with a recommended dose range of 0.4–0.9 mg/kg. Compared with propofol, ciprofol significantly reduces cardiovascular adverse events, with smaller increases in blood pressure and heart rate. Li et al. [8] investigated the effects of dose and age on ciprofol's pharmacokinetics and safety, suggesting that 0.3 mg/kg is an appropriate dose for elderly patients. However, elderly patients with diabetes are more sensitive to anesthetic agents, have weaker compensatory mechanisms, and are more prone to cardiovascular and cerebrovascular complications. Therefore, further evaluation of the dose and safety profile of ciprofol in this patient population is warranted. This study aimed to investigate the safety and efficacy of different doses of ciprofol for general anesthesia induction in elderly patients with diabetes and to provide clinical reference data.

Methods

Study design

This prospective, double-blind, single-center study was conducted at the Second Hospital of Shanxi Medical University. Approval was obtained from the Ethics Committee of the Second Hospital of Shanxi Medical University (Review Board Number: [2024] YX 021), and informed consent was obtained from all patients or their families. Data and methods were collected between February 2024 and June 2024. The trial was registered with Chinese ClinicalTrials.gov on February 26, 2024 (Registration Number: ChiCTR2400081164). The study followed the Consolidated Standards of Reporting Trials statement and the Declaration of Helsinki. The report was prepared following the CONSORT checklist. Written informed consent was obtained from all participants.

Patients who underwent single-level posterior lumbar interbody fusion (PLIF) at the Second Clinical College of Shanxi Medical University between February 2024 and June 2024 and were scheduled for elective tracheal intubation under general anesthesia were enrolled in this study. Based on prior research [9], with a significance level (α) of 0.05, and a test power (1-β) of 0.9, the calculated sample size was 70. To account for potential loss to follow-up, the sample size was increased to 90.

Randomization was performed using SPSS software (version 26.0) to generate random numbers, and the participants were assigned to three groups accordingly. The induction dose of ciprofol was 0.2 mg/kg in Group A, 0.3 mg/kg in Group B, and 0.4 mg/kg in Group C. Nurse A prepared sealed envelopes containing the group allocation based on the randomization results, whereas Nurse B, blinded to the study design, prepared the medications by diluting them to 50 mL with saline and administered the experimental drug to the anesthesiologist. The anesthesiologist, patients, and postoperative evaluators were blinded to the group assignments.

The inclusion criteria were as follows: (1) diabetic patients with a confirmed diagnosis from secondary or higher public hospitals; (2) age ≥ 65 years; (3) ASA grade II–III; (4) BMI of 18–30 kg/m²; and (5) patients undergoing single-level posterior lumbar interbody fusion (PLIF) under general anesthesia with tracheal intubation. Exclusion criteria included known ciprofol allergy, abnormal liver or kidney function, bradycardia (heart rate < 60 beats/min), hypotension (mean arterial pressure < 55 mmHg), prolonged QT interval, or inability to cooperate with the research team. Eligible patients were informed of the study by the research team, and written informed consent was obtained from all patients.

Anesthesia procedure

Upon admission, peripheral venous access was established, and ECG monitoring was initiated. Parameters including heart rate (HR), blood pressure (BP), electrocardiogram (ECG), oxygen saturation (SpO_2), respiratory rate (RR), and bispectral index (BIS) were continuously monitored. A radial artery catheter was placed under local anesthesia with 2% lidocaine (2 mL) to enable invasive arterial pressure monitoring, and the blood glucose levels (T_0) were measured. Following invasive arterial pressure monitoring, oxygen was administered via a nasal catheter at a rate of 2 L/min. Midazolam (0.02 mg/kg) was then administered slowly via intravenous injection. Once the patient reached a Ramsay sedation score of 3, the mean arterial pressure (MAP) and heart rate (HR) were recorded as the basal mean arterial pressure (BMAP) and basal heart rate (BHR), respectively.

The patient was provided with oxygen via a face mask at 5 L/min for preoxygenation, followed by the administration of sufentanil (0.4 μg/kg over 10 s). Ciprofol was then administered for 30 s at doses specific to each group

(Group A: 0.2 mg/kg, Group B: 0.3 mg/kg, Group C: 0.4 mg/kg, all diluted to 20 mL with 0.9% sodium chloride). The time to the disappearance of the eyelash reflex was observed. Once the eyelash reflex disappeared, rocuronium (0.7 mg/kg) was administered. Blood pressure, heart rate, and BIS values were recorded at 1, 2, 3, 4, and 5 min after propofol administration. At 5 min, if induction was successful (defined as a BIS < 60 and disappearance of the eyelash reflex), endotracheal intubation was performed using a video laryngoscope. Only cases of successful first-attempt intubation were included, and unsuccessful attempts were excluded. Blood glucose (T_1) and intubation complications were monitored for 2 min post-intubation. If induction failed, propofol (0.5 mg/kg) was administered as rescue therapy, and this case was excluded. After intubation, the patient was connected to a ventilator with the following parameters: oxygen flow rate, 2 L/min; tidal volume, 6–8 mL/kg; respiratory rate, 10–14 breaths/min; inspiration-expiration ratio 1:2, and $PetCO_2$ maintained at 30–40 mmHg. Anesthesia maintenance involved propofol (4–12 $mg{\cdot}kg^{-1}{\cdot}h^{-1}$) and remifentanil (8–15 $\mu g{\cdot}kg^{-1}{\cdot}min^{-1}$), adjusted to maintain a BIS of 40–60. Additional analgesics and muscle relaxants were administered as required. During anesthesia induction and maintenance, if the mean arterial pressure dropped below 55 mmHg for over 5 min, 6 mg ephedrine or 1 mg dopamine was administered, as determined by the anesthesiologist. If the heart rate dropped below 50 beats/min for more than 5 min, 0.3 mg of atropine was administered. Postoperatively, once the patient regained consciousness, the cough reflex recovered, and breathing normalized (VT > 6 mL/kg, respiratory rate > 10 breaths/min, and $ETCO_2$ <45 mmHg), the tracheal tube was removed, and the patient was transferred to the PACU. All procedures were performed by a professional anesthesiologist.

Primary outcome

The primary outcome was the incidence of hypotension during anesthesia induction, defined as a mean arterial pressure < 55 mmHg lasting for at least one minute.

Secondary outcome

Secondary outcomes included the area under the threshold of basal mean arterial pressure (AUT_{MAP}) during anesthesia induction, incidence of bradycardia (heart rate < 50 beats/min), area under the threshold of basal heart rate (AUT_{HR}) during anesthesia induction, time to disappearance of the eyelash reflex, time for BIS to drop to 60, intubation response (defined as systolic blood pressure, diastolic blood pressure, or heart rate exceeding 20% of baseline values within 3 min after intubation), number of intraoperative hypotension episodes, number and dosage of vasoactive drugs used, and blood glucose levels measured 2 min after operating room entry and intubation.

Statistical analysis

Statistical analysis was performed using SPSS software (version 26.0). Measurement data with a normal distribution were expressed as mean ± standard deviation, and inter-group comparisons were conducted using ANOVA. Non-normally distributed measurement data are presented as median (interquartile range), and inter-group comparisons were performed using the multiple local rank-sum test. Categorical data were expressed as rates (%), and comparisons between groups were analyzed using the chi-square test or Fisher's exact test. Statistical significance was set at $P < 0.05$.

Results

Patent and clinician characteristics

A total of 90 patients were included in this study, of which six were excluded due to unsuccessful first intubation and two were excluded due to the need for propofol rescue, leaving 82 patients who completed the study, as shown in Fig. 1. A comparison of the general conditions of the patients in the three groups revealed no statistically significant differences ($P > 0.05$), as shown in Table 1.

Hemodynamic comparison

Hemodynamic comparisons among the three groups showed that the incidence of hypotension was highest in Group C, with a statistically significant difference compared to Groups A and B, while the difference between Groups A and B was not statistically significant. The AUT_{MAP} values were highest in Group C, followed by Group B, and lowest in Group A statistically significant differences among the three groups. The incidence of bradycardia was also the highest in Group C, with a statistically significant difference compared to Group A. Regarding AUT_{HR}, Group C had higher values than Group B, and Group B had higher values than Group A, but only the difference between Groups A and C was statistically significant. The incidence of intubation reaction was the highest in Group A statistically significant difference compared to the other two groups (Table 2).

The sedation effect

The sedation effects among the three groups were compared based on the disappearance time of the eyelash reflex, time required for the BIS to drop to 60, blood glucose levels at the two time points, and frequency of intraoperative hypotension, with no statistically significant differences observed (Table 2). However, the lowest BIS value was recorded in Group C, showing a statistically significant difference compared to Groups A and B. The BIS trend indicated that it reached its lowest point at

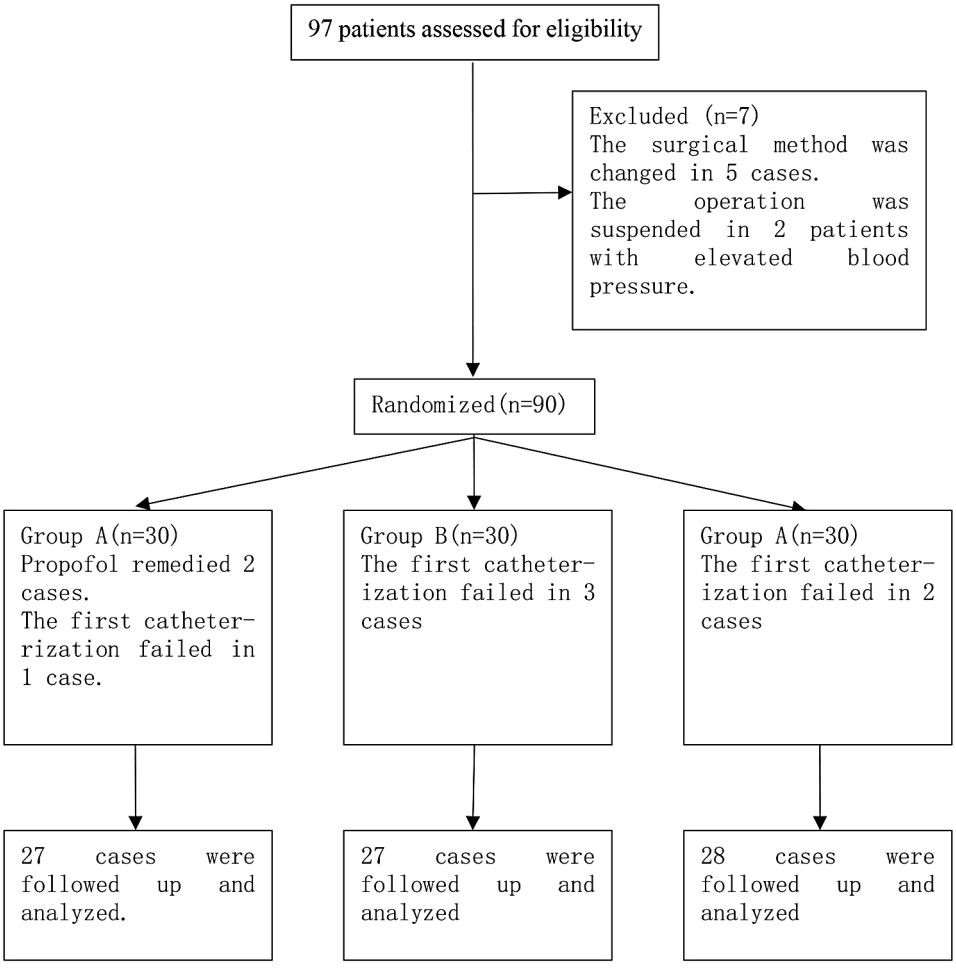

Fig. 1 CONSORT flow diagram of participants allocation

approximately 1 min and then gradually increased. While all BIS values remained below 60, the BIS values in Group A were significantly higher than those in Groups B and C at the 3rd, 4th, and 5th minutes, with the differences being statistically significant (see Fig 2).

Discussion

This study investigated the effects of different doses of ciprofol on hemodynamics and anesthetic outcomes during total intravenous anesthesia induction in elderly patients with diabetes. Single-stage spinal PLIF surgery was selected as the surgical model because of its standardized nature with a relatively fixed operation duration and blood loss, thus minimizing the potential impact of surgical factors on hemodynamic stability.

This study found that 0.4 mg/kg ciprofol combined with 0.4 μg/kg sufentanil and 0.7 mg/kg rocuronium resulted in a significantly higher incidence of hypotension during induction compared to the 0.3 mg/kg and 0.2 mg/kg groups. Previous studies [9] also reported a high incidence of hypotension (57%) with 0.4 mg/kg ciprofol, which was higher than the 46.4% observed in this study. This discrepancy may be attributed to differences in the definition of hypotension, which was defined as a MAP < 55 mmHg lasting for 1 min, whereas prior studies defined it as MAP < 60 mmHg or a 30% drop from baseline. Retrospective studies [10, 11] have shown that an intraoperative MAP < 55 mmHg, even for short durations, is associated with AKI and myocardial injury, supporting the stricter definition used in this study. The subthreshold area method [12] was applied to account for both the duration and severity of MAP reduction, providing a more comprehensive assessment of blood pressure during induction. Comparisons of the area under the threshold for MAP (AUT_{MAP}) revealed that the 0.4 mg/kg group had significantly higher values than the 0.3 mg/kg and 0.2 mg/kg groups, and the 0.3 mg/kg group had higher values than the 0.2 mg/kg group, with all differences being statistically significant. Although there was no statistically significant difference in the incidence of hypotension between the 0.3 mg/kg and 0.2 mg/kg groups, the AUTMAP in the 0.2 mg/kg group

Table 1 Comparison of general conditions among the three groups

Variables	Group A (*n* = 27)	Group B (*n* = 27)	Group C (*n* = 28)	*P* value
Gender (Male)	14(51.8%)	16(59.3%)	14(50.0%)	0.768
Age (years)	71.33 ± 4.09	69.59 ± 3.87	71.96 ± 3.87	0.076
BMI(km/m^2)	22.72(2.66)	22.68(2.41)	23.29(1.66)	0.575
ASA(II)	13(48.1%)	17(63.0%)	14(50%)	0.492
Duration of diabetes (years)	6.00(8.00)	7.00(8.00)	6.50(10.00)	0.931
HbA1c	8.33(2.32)	8.36(2.04)	7.70(2.30)	0.774
Mean value of blood glucose	8.96 ± 0.68	9.05 ± 0.84	9.14 ± 0.69	0.658
Standard deviation of blood glucose	2.07 ± 0.63	2.19 ± 0.65	2.06 ± 0.58	0.674
Combined hypertension	18(27)	13(27)	16(28)	0.370
Combined coronary heart disease	12(27)	12(27)	8(28)	0.377
Fasting time	4(2.5)	4(2.5)	3.75(1.38)	0.918
fluid intake in the ward	600(500)	600(350)	600(462.5)	0.892
preoperative fluid intake	300(200)	300(100)	350(150)	0.516
BMAP(mmHg)	98.37 ± 4.84	97.63 ± 4.72	99.64 ± 6.71	0.396
BHR (times/min)	68.93 ± 4.92	71.67 ± 5.48	72.29 ± 5.45	0.051
Blood sugar level (T_0)	6.34 ± 0.79	6.06 ± 0.72	6.15 ± 0.58	0.320
Operation duration (min)	138.78 ± 13.23	139.37 ± 17.40	143.32 ± 17.22	0.524
Anesthesia duration (min)	188.96 ± 14.73	186.78 ± 13.82	188.32 ± 16.55	0.861
Liquid intake (ml)	1600(500)	1750(500)	1750(500)	0.764
Amount of bleeding (ml)	190(40)	210(60)	190(50)	0.921

Continuous data are presented as mean ± SD or median [interquartile range (IQR); range], Categorical data are presented as number (proportion)

Table 2 Comparison of induction conditions among the three groups

Variables	Group A	Group B	Group C	*P* value
Hypotension	2(7.4%)	4(14.8%)	14[ab](46.4%)	0.001
AUT_{MAP}	143.59 ± 19.52	158.44 ± 26.55[a]	176.39 ± 33.83[ab]	0.000
Bradycardia	5(18.5%)	8(29.6%)	15[a](53.6%)	0.019
AUT_{HR}	63.52 ± 19.24	80.26 ± 25.97[a]	96.25 ± 26.54[ab]	0.000
AUT_{BIS}	191.15 ± 11.39	204.67 ± 10.40[a]	208.43 ± 12.60[a]	0.000
Intubation reaction	21(77.8%)	4(14.8%)[a]	2(7.1%)[a]	0.000
Eyelash reflexes disappear time	57.85 ± 7.52	56.70 ± 6.58	57.25 ± 10.46	0.839
Time for BIS drop to 60	66.59 ± 8.52	67.07 ± 7.30	68.11 ± 9.14	0.790
Blood sugar level(T_1)	8.03 ± 0.52	7.88 ± 0.57	7.82 ± 0.48	0.322

Continuous data are presented as mean ± SD or median [interquartile range (IQR); range], Categorical data are presented as number (proportion). a vs. group A, ($P < 0.05$); b vs. group B, ($P < 0.05$)

was significantly lower, suggesting that induction in the 0.2 mg/kg group had the least impact on blood pressure. Additionally, heart rate changes across the groups mirrored the changes in blood pressure, further indicating that the 0.2 mg/kg group had a minimal effect on both blood pressure and heart rate during induction.

This study also found that, although there were no statistically significant differences in the disappearance time of the eyelash reflex or the time for BIS to drop below 60 in the 0.2 mg/kg group compared to the other two groups, and BIS consistently remained below 60, the incidence of intubation response in the 0.2 mg/kg group was significantly higher than in the other groups. Additionally, the area under the threshold of BIS in Group A was lower than that in Groups B and C, and the BIS values at 3, 4, and 5 min after induction in Group A were significantly higher than those in the other groups. Hypertension and tachycardia caused by intubation responses are known risk factors for myocardial infarction and stroke [13, 14], particularly in elderly patients and those with a history of cardiovascular or cerebrovascular events [15–17]. Therefore, prevention of hemodynamic fluctuations during tracheal intubation is critical. While previous studies suggested that 0.2 mg/kg ciprofol could meet sedation requirements during induction, consistent with this study's findings, this study demonstrated a high incidence of intubation response in this group, making it unsuitable for elderly diabetic patients.

The blood glucose levels at 2 min after intubation were the highest in Group A, although the difference was not statistically significant, possibly due to the intubation response. The lack of statistical significance may also be attributed to the sample size. There was no significant difference in the incidence of hypotension and ephedrine use among the three groups during surgery; however, the use of atropine during induction was significantly higher in Group C than in Groups A and B. This indicates that 0.4 mg/kg of ciprofol is more likely to cause bradycardia, and the use of dopamine in the 0.4 mg group was significantly higher than in the other two groups (Table 3), which may reflect the medication habits of the

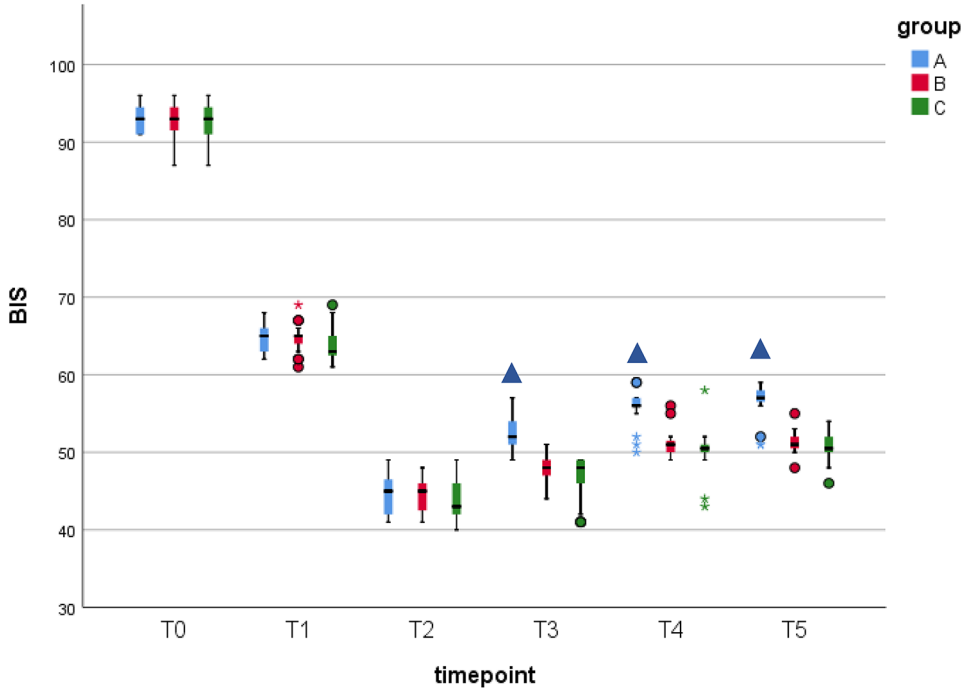

Fig. 2 Comparison of BIS at different time points among the three groups. Note ▲This indicates that the difference was statistically significant compared to groups B and C.

Table 3 Comparison of intraoperative hypotension among the three groups

Variables	Group A	Group B	Group C	*P* value
Frequency of intraoperative hypotension	5(2)	5(1)	4(2)	0.778
Vasoactive drugs were used during the operation				
ephedrine(mg)	18(6)	18(6)	12(6)	0.228
dopamine(mg)	3(4)	2.5(3.75)	5(3.75)[a]	0.012
atropine(mg)	0(0)	0(0)	0.15(0.3)[ab]	0.000

Continuous data are presented as mean ± SD or median [interquartile range (IQR); range]. a vs. group A, ($P < 0.05$); b vs. group B, ($P < 0.05$)

researchers. Ephedrine is typically used to treat hypotension, and dopamine is administered during follow-up when it is ineffective. This practice may explain the lower observed incidence of intraoperative hypotension in the 0.4 mg/kg group, suggesting that dopamine administration mitigated hypotension, further indicating that the 0.4 mg/kg dose had a greater impact on intraoperative blood pressure.

This was a single-center study with a small sample size, and clinical outcome indicators such as the incidence of postoperative cardiovascular and cerebrovascular events were not observed among the three groups. Further large-scale multi-center clinical trials are needed to draw more comprehensive conclusions.

Conclusions

In summary, 0.3 mg/kg ciprofol combined with 0.4 μg/kg sufentanil and 0.7 mg/kg rocuronium provided more stable hemodynamics and required less vasoactive drug intervention during induction in elderly diabetic patients, making it a superior choice compared to the 0.2 mg/kg and 0.4 mg/kg dosage groups.

Abbreviations

AUT	Area under the threshold
BMAP	Basal mean arterial pressure
BHR	Basal heart rate
BMI	Body mass index
PLIF	Posterior lumbar interbody fusion
PACU	Post anesthesia recovery unit

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-024-02881-3.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

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Author contributions
Jiang Xiaorui: Design paper, draft paper, write paper; Zhang Linzhong: experimental design, paper modification; Jiang Xiaorui, Jl Jiawei, Jing Yan: Research process implementation and data collection; Li Meiping: Data analysis. All authors read and approved the final manuscript and agreed to publish it.

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Data availability
The data that support the fndings of this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study followed the Consolidated Standards of Reporting Trials statement and the Declaration of Helsinki. This study was approved by the Ethics Committee of the Second Hospital of Shanxi Medical University (review board number: [2024] YX 021). Written informed consent was obtained from all patients before participation. The report was prepared following the CONSORT checklist.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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