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CLINICAL TRIAL REPORT

Effects of Ciprofol and Propofol General Anesthesia on Postoperative Recovery Quality in Patients Undergoing Ureteroscopy: A Randomized, Controlled, Double-Blind Clinical Trial

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Objective: This study compares postoperative recovery quality between Ciprofol and Propofol, providing a reference for the clinical application of anesthetics.

Methods: We randomized 112 patients undergoing ureteroscopic surgery into two groups: the Ciprofol group (Group C), with an induction dose of 0.4 mg/kg and a maintenance dose of 0.8–1.5 mg/(kg·h), and the Propofol group (Group P), with an induction dose of 2 mg/kg and a maintenance dose of 4–10 mg/(kg·h). Both groups received sevoflurane at a concentration of 1%. The Bispectral Index (BIS) was maintained between 40 and 60. The primary outcomes were the Quality of Recovery-15 (QoR-15) scores on postoperative day 1 (POD1). Secondary outcomes included hemodynamic parameters, vasopressor use, timing indicators, sedative consumption, BIS values, Riker Sedation-Agitation Scale (R-SAS) scores, urinary tract symptoms, patient satisfaction, and adverse events.

Results: No significant differences were observed in QoR-15 scores between the two groups. Although Group C had higher pain ($P = 0.004$) and comfort ($P = 0.002$) scores on POD1, these differences were not clinically significant. The incidence of hypotension and vasopressor use was lower in Group C, which had more stable hemodynamics. Additionally, the time from induction to BIS ≤ 60 was shorter in Group P ($P = 0.001$), while Group C had lower BIS values from drug discontinuation to full recovery of consciousness ($P = 0.001$). The incidence of urinary tract symptoms on POD1 was lower in Group C ($P = 0.043$). There were no significant differences in time to spontaneous breathing recovery, extubation, recovery room stay, time to first ambulation, hospital stay, patient satisfaction, or other adverse events.

Conclusion: Ciprofol provides comparable early postoperative recovery to Propofol during ureteroscopy and may be a preferable alternative for urological procedures, especially in patients with blood pressure concerns.

Trial Registration: Chinese Clinical Trial Registry (ChiCTR2400082736).

Keywords: ciprofol, propofol, postoperative recovery quality, ureteroscopic surgery

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Introduction

Ureteroscopic surgery, a common minimally invasive procedure for urinary tract stones, involves minimal tissue damage, faster recovery, and fewer complications, leading to a significant improvement in early postoperative recovery quality.[1] However, despite its minimally invasive nature, potential issues remain, such as urinary tract infections,[2,3] obstruction,[4] fasting requirements,[5,6] and the use of anesthetic agents,[7] which can contribute to intraoperative hypotension. Previous studies have also indicated that patients undergoing ureteroscopic treatment often experience bothersome urinary symptoms, including pain, urgency, frequency, hematuria, and incontinence.[8–10] These factors place higher demands on anesthesia management.

The choice of anesthetic agents is crucial for the successful conduct of surgery and the quality of postoperative recovery. Although a variety of sedatives and hypnotics are available, finding an ideal general anesthetic remains challenging. Even widely used classic general anesthetics like Propofol have drawbacks, such as injection pain, cardiopulmonary suppression, metabolic acidosis, hyperlipidemia, and hepatic enlargement.[11,12] For general anesthesia, an ideal intravenous anesthetic should exhibit rapid onset, good controllability, stable respiratory and circulatory function, minimal local irritation, and high safety.

Recently, a new short-acting sedative and hypnotic agent, Ciprofol, has been approved for clinical use. Ciprofol is a 2.6-disubstituted phenol derivative and acts as a short-acting GABA receptor agonist. Its mechanism is based on the introduction of a cyclopropyl group into the chemical structure of Propofol, enhancing Gamma-aminobutyric Acid (GABA) -mediated chloride influx to produce sedative or anesthetic effects.[13] Studies have shown that Ciprofol's potency is 4–5 times greater than that of Propofol, with 0.4 mg/kg of Ciprofol achieving anesthetic effects comparable to 2 mg/kg of Propofol.[14,15] During the maintenance phase of anesthesia, infusion of 0.8–1.5 mg/kg of Ciprofol has demonstrated a 100% success rate and a lower incidence of drug-related adverse effects.[15] Although existing research has confirmed the efficacy and safety of Ciprofol in general anesthesia induction,[16,17] there is limited research on post-operative recovery. It remains unclear whether Ciprofol offers superior postoperative recovery quality compared to Propofol, which is crucial for patient outcomes.

Therefore, we hypothesize that Ciprofol may provide better postoperative recovery quality compared to Propofol following general anesthesia. To test this hypothesis, we used the Quality of Recovery-15 (QoR-15) questionnaire to assess postoperative recovery quality in patients undergoing ureteroscopic surgery with Ciprofol-based general anesthesia, with Propofol-based general anesthesia as the control.

Materials and Methods

Ethics and Registration

This study was a single-center, double-blind, randomized controlled clinical trial conducted in accordance with the Declaration of Helsinki. It was approved by the Ethics Committee of Lishui People's Hospital (Ethics Number: 2024041) and registered with the Chinese Clinical Trial Center (Approval Number: ChiCTR2400082736). All participants provided written informed consent.

Patient Inclusion and Exclusion Criteria

The study was conducted in the operating rooms of Lishui People's Hospital from April 2024 to August 2024. Research personnel, including anesthesiologists and nurses, received rigorous training. Potential participants were screened the day before the surgery.

Inclusion criteria were: inpatients scheduled for elective surgery who require general anesthesia for ureteroscopic lithotripsy and stone extraction; aged between 18 and 75 years; with a body mass index (BMI) ≥18 and ≤30 kg/m²; classified as American Society of Anesthesiologists (ASA) physical status I–III; and with vital signs during screening meeting the following criteria: respiratory rate (RR) ≥10 and ≤24 breaths per minute, Saturation of Peripheral Oxygen (SpO_2) ≥95% during breathing, systolic blood pressure (SBP) ≥90 mmHg and ≤160 mmHg, diastolic blood pressure (DBP) ≥60 mmHg and ≤100 mmHg, and heart rate (HR) ≥55 and ≤100 bpm.

Exclusion criteria included: anticipated difficult airway; BMI >30 or <18 kg/m²; use of benzodiazepines or opioids within the past month, or contraindications or allergic reactions to benzodiazepines, opioids, Propofol, or its components; significant preoperative respiratory or circulatory dysfunction, or abnormal blood and biochemical test results; pregnancy, lactation, or plans to conceive within the next three months (including male patients); cognitive impairment preventing cooperation; and any other condition deemed by the investigator as unsuitable for participation in the study.

Randomization and Masking

A total of 112 eligible participants were recruited for the study. An independent statistician used SPSS 27 to generate a random number table, assigning participants in a 1:1 ratio to either the Ciprofol group (Group C) or the Propofol group (Group P), with 56 participants in each group. The allocation was concealed in opaque envelopes numbered consecutively, and the study drugs were prepared and labeled by an anesthesiologist who was not involved in participant recruitment, data collection, or follow-up. Since both Ciprofol and Propofol are white emulsions, the group assignment was unknown to all participants, surgeons, and anesthesiologists. Blinding was maintained throughout the study, with unblinding permitted only in the event of severe adverse events (SAE). Unblinded cases were included in the intention-to-treat population but excluded from the safety analysis according to the study protocol. A SAE is any event during a clinical trial that requires hospitalization or its extension, causes disability or affects work capacity, leads to permanent organ damage, threatens life or results in death, or may cause cancer, congenital anomalies, or birth defects.

Technique

All patients in the study were instructed to fast for 6 hours and abstain from fluids for 2 hours prior to the procedure, and none of the participants received preoperative medication. Upon entering the operating room, patients were connected to a GE B650 monitor (GE Healthcare Finland Oy, Helsinki, Finland) for routine monitoring, including electrocardiogram (ECG), HR, non-invasive blood pressure (NIBP), pulse oximetry, and a Bispectral Index (BIS) sensor (Con View YY-106, Pearlcare, Zhejiang, China). Additionally, end-tidal carbon dioxide ($EtCO_2$) levels were measured using a Mindray iPM10 monitor (Mindray Medical International Limited, China).

Before anesthesia induction, baseline measurements were recorded for blood pressure, HR, pulse oximetry, BIS value, and preoperative QoR-15 scores. Anesthesia was administered by a certified anesthesiologist, and all surgeries were performed by experienced urologic surgeons. Assessment points included: T0 - baseline before anesthesia; T1 - 1 minute after anesthesia induction; T2 - 1 minute after intubation; T3 - immediately at the start of surgery; and T4 - immediately at the end of surgery. Postoperatively, patients were closely monitored in the post-anesthesia care unit until discharge.

Grouping and Intervention

During the anesthesia induction phase, patients were first administered either Ciprofol (0.4 mg/kg, Liaoning Haisheng Pharmaceutical Co., Ltd., Liaoning, China) or Propofol (2 mg/kg, Fresenius Kabi, Beijing, China). Deep sedation was defined by achieving a BIS value of ≤60, and only the experimental drug was used during this phase, with no other anesthetics administered. After intravenous injection of the experimental drug, the time required to achieve a BIS value of ≤60 was recorded. If the BIS value remained above 60 one minute after administration, an additional 50% of the initial dose was given until the BIS value reached ≤60. Following induction, sufentanil (0.4 μg/kg, Yichang Renfu Pharmaceutical Co., Ltd., Yichang, China) and cis-atracurium (0.15–0.2 mg/kg, Hangzhou AoYa Biotechnology Co., Ltd., Zhejiang, China) were administered intravenously.

After induction, a laryngeal mask was inserted, and the tidal volume was adjusted to 6–8 mL/kg, maintaining the $EtCO_2$ concentration between 35–45 mmHg. During the maintenance phase, anesthesia was maintained with Ciprofol (0.8–1.5 mg/kg/h),or Propofol (4–10 mg/kg/h). To optimize anesthesia depth, we adopted the commonly used anesthesia methods in our center and selected sevoflurane, known for its rapid elimination through the lungs, as an adjunct anesthetic. Both groups received sevoflurane at a fixed concentration of 1%. Anesthesiologists adjusted the doses of intravenous anesthetics (Ciprofol or Propofol) based on BIS monitoring data and the patients' clinical responses, while maintaining a constant concentration of sevoflurane to ensure that the BIS remained within the target range of 40–60. In cases of hypotension (defined as SBP <90 mmHg, DBP <50 mmHg, mean arterial pressure (MAP) <65 mmHg, or blood pressure fluctuations exceeding 20% of baseline), ephedrine (5–10 mg) was administered to raise blood pressure, with

repeated doses as necessary. For bradycardia (defined as HR <50 beats/min), atropine (0.5 mg) was given intravenously to increase the HR. To prevent postoperative nausea and vomiting, dexamethasone (5 mg) was administered before the start of surgery, and ondansetron (5 mg) was given 10 minutes before the end of the surgery.

Sevoflurane was discontinued 10 minutes before the end of the surgery, and residual sevoflurane in the lungs was eliminated by the end of the procedure. At the conclusion of the surgery, Ciprofol or Propofol was stopped, and the patient was transferred to the Post-Anesthesia Care Unit (PACU) for recovery. The laryngeal mask was removed after confirming the recovery of consciousness, defined as the ability to respond to verbal commands and demonstrate adequate spontaneous breathing (≥5 mL/kg). Postoperatively, 50 mg of Flurbiprofen Axetil Injection was administered for analgesia if the patient experienced significant pain in the PACU, with a VAS score of ≥3. The patient was discharged from the PACU and transferred back to the ward upon meeting the discharge criteria (Aldrete score ≥ 9). In the urology ward, urologists routinely administered 40 mg of Phloroglucinol injection daily to prevent spasmodic pain. If the patient continued to experience significant pain, rescue analgesia was provided as needed.

Outcomes

Primary Outcome

The primary outcome of our study was the QoR-15 questionnaire scores on the postoperative day 1 (POD1). Existing evidence supports that the QoR-15 is a reliable tool for measuring postoperative recovery quality.[18] The QoR-15 assesses recovery quality across five dimensions: physical comfort (5 items), emotional state (4 items), physical independence (2 items), psychological support (2 items), and pain (2 items). The total score for QoR-15 ranges from 0 (indicating the worst recovery quality) to 150 (indicating the best recovery quality).[19]

Secondary Outcomes

Secondary outcomes included perioperative hemodynamic changes, use of vasoactive drugs, time to achieve BIS ≤60 for Ciprofol or Propofol induction, time from discontinuation of the drug to the recovery of spontaneous respiration, BIS value at full recovery of consciousness, extubation time, duration of stay in the recovery room, time to ambulation, hospital stay duration, consumption of the study drug, Riker-Sedation Agitation Scale (R-SAS) scores, patient satisfaction scores, urinary tract irritation symptoms, and other adverse events such as nausea, vomiting, hypoxemia, hypotension, intraoperative awareness, drowsiness, and postoperative delirium. Additionally, we collected demographic information and clinical parameters from patients and used the age-adjusted Charlson Comorbidity Index (aCCI) and the Surgical Apgar Score to assess preoperative physical condition and surgical outcomes.

The duration of stay in the PACU was defined as the time from patient transfer to the recovery room until discharge from the PACU. After extubation in the PACU, the patient's consciousness was assessed using the R- SAS score, which ranges from 1 to 7, with higher scores indicating increasing levels of agitation. Hypoxemia was defined as SpO_2 <90% and managed by increasing oxygen flow, verbal and tactile stimulation, chin lift, or mask ventilation. Hypotension was defined as SBP <90 mmHg, DBP <50 mmHg, MAP <65 mmHg, or blood pressure fluctuations exceeding 20% of baseline, and was treated with ephedrine to raise blood pressure. Intraoperative awareness was assessed using the modified Brice interview;[20] drowsiness was defined as the state of feeling sleepy and falling asleep without stimulation; acute delirium was screened using the Nursing Delirium Screening Scale (Nu-DESC).[21] Additionally, the aCCI is an effective tool for identifying patients with multiple chronic diseases.[22] The Surgical Apgar Score, a 10-point system based on lowest heart rate, lowest mean arterial pressure, and estimated blood loss, effectively distinguishes between high and low-risk patients for major complications and postoperative mortality.[23]

Statistical Analysis

Sample Size and Statistical Analysis

The sample size was calculated based on the QoR-15 scores on POD1. Referencing prior studies, the minimal clinically important difference for QoR-15 is 8.[24] Additionally, based on our pilot data, the standard deviation for QoR-15 scores on POD1 was 14.1. Using PASS 15 software, it was determined that a sample size of 100 would provide an 80% power to detect this difference with a Type I error rate set at 0.05. To account for a 10% dropout rate, we included a total of 112 patients in the study.

Statistical analysis was performed using SPSS 27. Quantitative data were assessed for normality using the Shapiro–Wilk test. For data that followed a normal distribution, results are presented as means ± standard deviations and compared between groups using independent samples t-tests. For data that did not follow a normal distribution, results are presented as Medians (Interquartile Ranges) and compared between groups using the Mann–Whitney *U*-test. Categorical data are described using frequencies (percentages) and analyzed with chi-square tests or Fisher's exact tests. Hemodynamic values were compared using repeated measures Analysis of Variance (ANOVA). All tests were two-tailed, with $P < 0.05$ considered statistically significant.

Results

Between April and August 2024, we initially screened 117 patients. Exclusion criteria included BMI > 30 kg/m² (3 patients) and severe renal impairment (2 patients). Consequently, 112 patients were included and randomly assigned to either Group C (n=56) or Group P (n=56). Due to changes in surgical procedures during the operation (1 patient in Group C and 2 patients in Group P), the final analysis included 109 patients. The detailed flowchart is shown in Figure 1. Demographic and clinical characteristics of the two groups are presented in Table 1. There were no statistically significant differences between the groups in terms of gender, age, BMI, education level, smoking history, ASA classification, surgery time, anesthesia time, comorbidities, baseline BIS values, aCCI scores, surgical Apgar scores, or preoperative QoR-15 scores.

Table 2 displays the total QoR-15 scores and scores for each dimension for both groups. QoR-15 scores are presented as medians (interquartile ranges). On POD1 and POD3, there were no significant differences in the total QoR-15 scores between Group C and Group P (P > 0.05). On POD1, there were significant differences between Group C and Group P in the pain dimension (Median 20, IQR 20–20 vs Median 20, IQR 18–20; P = 0.004) and the comfort dimension (Median 44, IQR 42–45 vs Median 43, IQR 40.75–44; P = 0.002). There were no significant differences between the groups in the dimensions of physical independence, psychological support, or emotional state on either POD1 or POD3.

Secondary outcomes are detailed in Table 3. The time from induction to BIS ≤ 60 was significantly longer in Group C (0.88 ± 0.26 minutes) compared to Group P (0.67 ± 0.19 minutes; P = 0.001). At full recovery of consciousness, the BIS values in Group C were lower than in Group P (84.3 ± 7.2 vs 89.5 ± 6.3; P = 0.001). On the first postoperative day, a lower proportion of patients in Group C experienced urinary irritation symptoms compared to Group P (43.6% vs 63%;

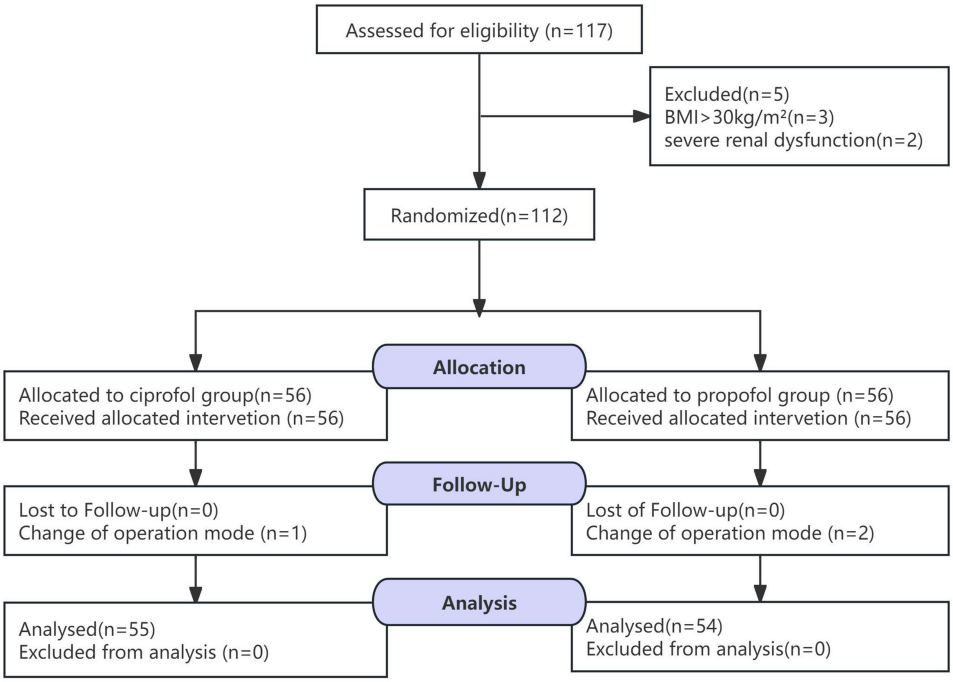

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) Flowchart describing patients progress through the study.

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Table 1 Demographic Characteristics and Clinical Data for Each Group

	Ciprofol(n=55)	Propofol(n=54)	P value
Sex, n(%)			0.615
Male	31 (56.4)	33(61.1)	
Female	24 (43.6)	21(38.9)	
Age (year)	56.3±11.0	55.1±11.7	0.600
BMI (kg/m^2)	24.0±2.8	24.0±3.2	0.869
Education level, n (%)			0.785
Elementary school and below	22(40.0)	24(44.4)	
Middle school	25(45.5)	21(38.9)	
College and above	8(14.5)	9(16.7)	
History of smoking, n (%)	20(36.4)	21(38.9)	0.786
Surgery time (min)	47(29–65)	40(24–65)	0.698
Anesthesia time (min)	53(37–70)	54(35–71)	0.941
ASA, n (%)			0.395
I	3(5.5)	3(5.6)	
II	49(89.1)	44(81.5)	
III	3(5.5)	7(13.0)	
Comorbidity, n (%)			0.318
Hypertension	12(21.8)	15(27.8)	
Diabetes	4(7.3)	6(11.1)	
Others	7(12.7)	2(3,7)	
CCI score	1 (0–2)	1 (0–2)	0.779
Surgical Apgar score	9(9–9)	9 (8–9)	0.623
Pre-anesthesia BIS value	95 (95–97)	96 (95–97)	0.063
Preoperative QoR15 score	143(142–146)	143(140–145)	0.151

Note: Data are presented as Mean ± SD, Numbers (Percentage) or Median (Interquartile Range).
Abbreviations: BMI, Body Mass Index; ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; BIS, Bispectral Index; QoR-15, the Quality of Recovery-15 scores; SD, Standard Deviation.

Table 2 Postoperative QoR-15 Scores

	Ciprofol(n=55)	Propofol(n=54)	Median Difference (95% CI)	P value
QoR-15 scores				
POD1	136 (133–138)	135 (132.75–137)	0.0 (1.0 to 3.0)	0.066
POD3	145 (144–146)	145 (143.75–147)	−1.0 (0.0 to 1.0)	0.782

(*Continued*)

Table 2 (Continued).

	Ciprofol(n=55)	Propofol(n=54)	Median Difference (95% CI)	P value
QoR-15 dimensions				
Pain				
POD1*	20 (20–20)	20 (18–20)	0.0 (0.0 to 1.0)	0.004
POD3	20 (20–20)	20 (20–20)	0.0 (0.0 to 0.0)	0.425
Physical comfort				
POD1*	44 (42–45)	43 (40.75–44)	1.0 (1.0 to 2.0)	0.002
POD3	48 (47–48)	48 (46–48)	0.0 (0.0 to 1.0)	0.142
Physical independence				
POD1	16 (15–16)	16 (14.75–16)	0.0 (0.0 to 1.0)	0.761
POD3	18 (18–19)	18 (18–20)	−10.0 (0.0 to 0.0)	0.457
Psychological support				
POD1	19 (19–19)	19 (19–19)	0.0 (0.0 to 0.0)	0.983
POD3	20 (19–20)	20 (19–20)	0.0 (0.0 to 0.0)	0.313
Emotional state				
POD1	38 (37–39)	38 (38–39.25)	−1.0 (0.0 to 0.0)	0.146
POD3	40 (39–40)	40 (39–40)	0.0 (0.0 to 0.0)	0.978

Notes: Scores of QoR-15 and its 5 dimensions. Data were presented as Median (Interquartile range); *Indicates *P< 0.05* between the groups.

Abbreviations: QoR-15, Quality of Recovery-15; POD1, Postoperative Day 1; POD3, Postoperative Day 3; CI, Confidence Interval.

Table 3 The Secondary Outcomes in This Study

	Ciprofol(n=55)	Propofol(n=54)	P value
BIS down to 60 time(min)*	0.88±0.26	0.67±0.19	0.001
Respiratory recovery time(min)	22.1±10.8	20.7±10.7	0.488
Extubation time(min)	26.3±10.6	24.9±10.4	0.461
Stay PACU time(min)	26.7±7.7	25.6±5.5	0.433
BIS value at recovery of consciousness*	84.3±7.2	89.5±6.3	0.001
Postoperative activity time(h)	13.7±4.6	14.6±4.7	0.403
Postoperative hospital stay(d)	2(1–2)	2 (1–2)	0.177
Consumption of sufentanil(ug)	25.8±4.0	26.6±4.4	0.334
Induced Consumption of ciprofol (mg)	25.4a±4.5	–	–
Maintenance Consumption of ciprofol (mg)	25 (24–29.5)	–	–
Induced Consumption of propofol (mg)	–	132.2±21.1	–
Maintenance Consumption of propofol (mg)	–	150(90–196.25)	–

(*Continued*)

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Table 3 (Continued).

	Ciprofol(n=55)	Propofol(n=54)	P value
Number of vasoactive drugs, n (%)*	20 (36.4)	31 (57.4)	0.028
R-SAS	4 (4–4)	4 (4–4)	0.981
Satisfaction of patients	9 (9–10)	9 (9–10)	0.299
Urinary irritation symptoms on POD1, n (%)*	24 (43.6)	34 (63.0)	0.043
Urinary irritation symptoms on POD3, n (%)	7 (12.7)	14 (25.9)	0.081

Notes: Data are presented as Mean±SD, Numbers (Percentage) or Medians (Interquartile Range). *Indicates *P< 0.05* between the groups.
Abbreviations: BIS, Bispectral Index; PACU, Postanesthesia Care Unit; R-SAS, Riker Sedation-agitation scale; POD, Postoperative Day; SD,Standard Deviation.

Table 4 Adverse Events

	Ciprofol(n=56)	Propofol(n=56)	P value
Hypotension, n (%)*	18 (32.7)	31 (57.4)	0.01
PONV, n (%)	7 (12.7)	8 (14.8)	0.752
Hypoxemia, n (%)	0	0	–
Intraoperative awareness, n (%)	0	0	–
Somnolence, n (%)	11 (20.0)	6 (11.1)	0.201
Postoperative delirium, n (%)	0	0	–

Notes: Data are presented as Numbers (Percentage), * Indicates *P< 0.05* between the groups.
Abbreviation: PONV, postoperative nausea and vomiting.

P = 0.043). Additionally, no significant differences were observed between the groups regarding extubation time, PACU stay duration, time to ambulation, hospital stay, opioid consumption, R-SAS scores, or patient satisfaction.

Table 4 presents the incidence rates of adverse events. The incidence of intraoperative hypotension was significantly lower in Group C compared to Group P (32.7% vs 57.4%; P = 0.01), and the proportion of patients requiring vasoactive drugs was also lower in Group C (36.4% vs 57.4%; P = 0.028). Perioperative hemodynamic parameters are illustrated in Figure 2. The incidence rates of postoperative nausea and vomiting, drowsiness, hypoxemia, intraoperative awareness, and postoperative delirium were comparable between the groups.

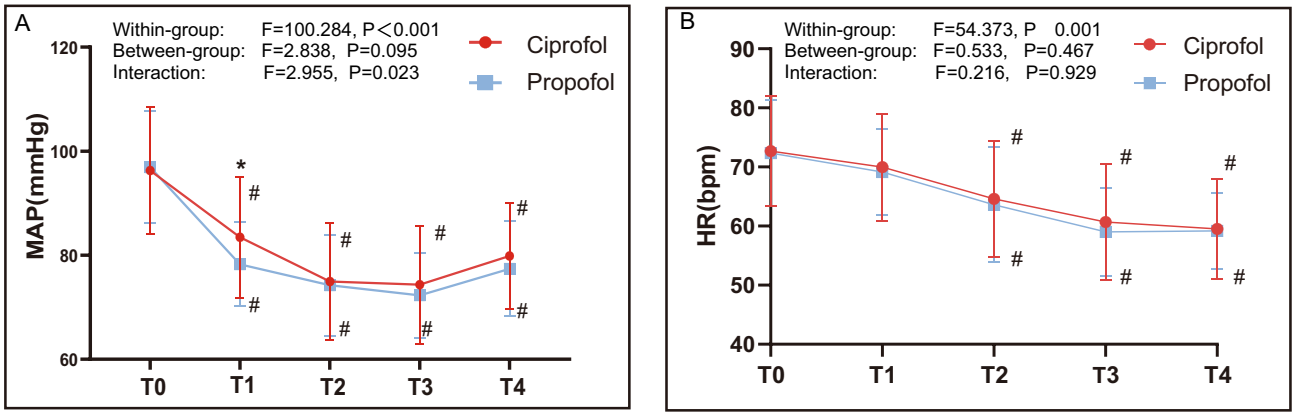

Figure 2 Comparisons of (**A**) MAP, (**B**) HR between the ciprofol and propofol groups. Data are presented as Mean ± SD, *Indicates P< 0.05 between the groups, #Indicates P< 0.05 compared with T0 within the same group.
Abbreviations: T0, before induction; T1, 1 minute after induction; T2, 1 minute after intubation; T3, At the beginning of surgery; T4, At the end of surgery; MAP, Mean Arterial Pressure; HR, Heart Rate; SD, Standard Deviation.

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Discussion

In this randomized controlled trial, we used the QoR-15 questionnaire to compare the effects of general anesthesia with Ciprofol versus Propofol on the postoperative recovery quality of patients undergoing ureteroscopy. The results showed no significant difference in QoR-15 scores between Group C and Group P on POD1 and POD3. However, within the five dimensions of the QoR-15 scale, the Ciprofol group scored slightly higher than the Propofol group in the pain and physical comfort dimensions on POD1, with statistically significant differences, although these differences were not clinically meaningful. Additionally, our study showed that the time to achieve deep sedation after Ciprofol induction was longer compared to Propofol, and at full recovery, the BIS values were lower in the Group C. During anesthesia induction and surgery, the Ciprofol group exhibited more stable hemodynamics and required less medication. No significant differences in adverse drug reactions or perioperative complications were found between the two groups. This study is valuable as it evaluates the effectiveness of Ciprofol-based anesthesia induction and maintenance in ureteroscopy from the perspective of postoperative recovery.

Postoperative recovery is a multifaceted process influenced by several factors, including the patient's preoperative health status, the type of surgery, and the anesthesia technique used. In this study, the Charlson Comorbidity Index (CCI) was employed to evaluate the preoperative comorbidities in patients undergoing ureteroscopy. The CCI is a widely used tool that assigns weighted scores based on the type and severity of comorbidities, and it is commonly utilized to predict perioperative mortality risk. Its accuracy and reliability have been well established in clinical research.[25,26] Additionally, the surgical Apgar score was used to assess surgical outcomes. This score takes into account indicators such as blood loss, minimum mean arterial pressure, and lowest heart rate, providing a quick and objective measure of surgical quality that is closely correlated with postoperative outcomes.[27,28] The results revealed no significant differences between the Ciprofol and Propofol groups in terms of CCI, surgical Apgar scores, or other demographic characteristics, suggesting that the baseline characteristics and surgical conditions of the two groups were well matched.

This study utilized the QoR-15 to assess postoperative recovery quality in patients. The QoR-15 is an effective patient-reported outcome measure (PROM) used to assess postoperative recovery quality.[18] Research has demonstrated that the QoR-15 is both reliable and widely applicable in perioperative settings, and it is highly accepted in clinical practice. The scale includes five dimensions: physical comfort, emotional state, physical independence, psychological support, and pain.[19] Compared to the longer QoR-40, the QoR-15 offers superior validity and reliability, with the added advantage of requiring less time for patients to complete the assessment.[29,30] Previous studies have shown that propofol excels in improving postoperative recovery quality. Propofol reduces stress and excessive activation of pro-inflammatory cytokines, while also enhancing analgesia and antiemetic effects, contributing to better recovery outcomes.[31–33] Our study similarly demonstrated that, for patients undergoing ureteroscopy, general anesthesia with Ciprofol provided recovery quality comparable to that of Propofol. Although research on Ciprofol's impact on postoperative recovery remains limited, our findings offer valuable evidence for its use in anesthesia induction and maintenance.

Additionally, our study showed that the Ciprofol group had a slightly higher pain dimension score on POD1 compared to the Propofol group, particularly in terms of alleviating abdominal pain and urinary tract irritation. Although this difference was statistically significant, it did not reach clinical significance (the clinically minimal difference in QoR scores is 6 points).[34] As postoperative satisfaction and quality of life have become increasingly important, evaluating the impact of Ciprofol and Propofol on postoperative recovery is highly relevant. A previous study in elderly patients undergoing laparoscopic surgery found that postoperative recovery quality in the Ciprofol group was comparable to that in the Propofol group, which is consistent with our findings. However, this study also reported that on POD1 and POD3, the pain intensity and analgesic consumption were slightly higher in the Ciprofol group than in the Propofol group.[35] In contrast, our study demonstrated that Ciprofol provided slightly superior analgesia on POD1. We believe that, firstly, ureteroscopy itself is not typically a highly painful procedure, with the primary discomfort arising from smooth muscle spasms in the ureter or bladder and residual small stones causing urinary tract irritation. These symptoms are more influenced by intraoperative manipulation and residual stones.[36] Secondly, Ciprofol has a higher potency than Propofol, with a more prolonged sedative effect, and it can synergize with other analgesics to provide more

sustained pain relief. However, further research is needed to explore the pain management effects of Ciprofol across different surgical procedures.

Our study also found that on POD1, patients in Group C reported better physical comfort than those in Group P, particularly in terms of rest and sleep quality. Postoperative sleep quality is influenced by various factors, including the patient's age, pre-existing sleep habits, type of surgery, choice of anesthetic, and the level of postoperative pain. In a study utilizing a sleep assessment scale, researchers compared the effects of Ciprofol and Propofol on sleep quality following painless gastrointestinal endoscopy. The results indicated that both groups experienced similar improvements in sleep quality on POD1, with significant improvements in sleep quality on the day of surgery, suggesting that both anesthetics can facilitate good postoperative rest under certain conditions.[37] However, our study did not employ a specialized assessment scale to systematically evaluate sleep quality, relying more on patients' subjective reports. Nevertheless, all QoR-15 scores were based on patient-reported outcomes, which helped mitigate potential bias to some extent. Moreover, we noted that several ongoing clinical trials are specifically investigating the effects of Ciprofol on postoperative sleep quality. We look forward to the results of these studies, as they may provide more detailed insights and enhance our understanding of Ciprofol's potential benefits in improving postoperative sleep quality.

Meanwhile, this study demonstrated that the time required for the BIS to decrease to 60 after Ciprofol induction was longer than that for Propofol. Additionally, at full recovery of consciousness, the BIS values in the Ciprofol group were lower than those in the Propofol group. Our findings align with previous studies, indicating that Ciprofol provides a more prolonged and deeper sedative effect.[38,39] However, there were no significant differences between Ciprofol and Propofol in terms of time to regain consciousness, extubation time, recovery room stay duration, or hospital length of stay. Therefore, it can be concluded that, like Propofol, Ciprofol does not prolong hospital stay or increase the consumption of additional healthcare resources in patients undergoing ureteroscopy. Furthermore, the incidence of adverse reactions and complications was similar between the Ciprofol and Propofol groups in this study, suggesting that both anesthetics can be safely used for ureteroscopy anesthesia. Ciprofol's chemical structure is similar to that of Propofol, with the addition of a cyclopropyl group enhancing its affinity for GABA receptors.[13,14] Ciprofol is approximately 4–5 times more potent than Propofol, offering a broader therapeutic safety margin.[40] Our study also confirmed the dose relationship between the two anesthetics. Propofol-based general anesthesia is commonly associated with a reduction in heart rate and blood pressure, underscoring the importance of evaluating the hemodynamic effects of both Ciprofol and Propofol.[41,42] Throughout the trial, Ciprofol exhibited more stable hemodynamics.

This study has several limitations. First, it compared the use of Ciprofol and Propofol only in general anesthesia for ureteroscopy and did not evaluate their applications in other types of surgeries. Therefore, caution is advised when considering the use of Ciprofol in other surgical procedures. Second, the study relied on questionnaires, which lacked objective evaluation criteria and were influenced by patient subjectivity. However, since all scales were self-reported by patients, this approach helped mitigate bias to some extent. Third, a sub-anesthetic dose of sevoflurane was used as an adjunct during the maintenance phase, which could have introduced confounding factors. However, the concentration of sevoflurane was kept constant throughout the procedure and was rapidly eliminated 10 minutes before the end of surgery, ensuring that anesthesia depth remained at BIS ≤60, which helped minimize bias. Fourth, we did not compare the full intraoperative hemodynamic and BIS score changes over time. Future studies could focus on hemodynamic fluctuations and BIS score changes as primary outcome events. However, the time points we selected were typically critical moments when circulatory fluctuations were most significant, and we aimed to minimize confounding factors. Therefore, the data still reflect differences in circulatory fluctuations and BIS values at the time of complete recovery between the two groups. Finally, this was a small-scale, single-center clinical trial that only recorded short-term postoperative QoR-15 scores. Further research is needed to assess patients' long-term recovery outcomes.

Conclusion

The preliminary results of this study suggest that, during ureteroscopy, Ciprofol general anesthesia is comparable to Propofol general anesthesia in terms of overall postoperative recovery. Ciprofol is an appropriate alternative to Propofol in combined intravenous and inhalational anesthesia. It also offers certain advantages in reducing the risk of hypotension during both the induction and maintenance phases of anesthesia. For patients undergoing surgery via urological

physiological pathways, particularly those with blood pressure issues, Ciprofol should be considered as an alternative to Propofol in suitable clinical contexts.

Abbreviations

BIS, Bispectral Index; QoR-15, Quality of Recovery-15; R-SAS, Riker Sedation-Agitation Scale; GABA, Gamma-aminobutyric Acid; ASA, American Society of Anesthesiologists; SAE,severe adverse events; RR, Respiratory Rate; SpO_2, Saturation of Peripheral Oxygen; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MAP, Mean Arterial Pressure; HR, Heart Rate; ECG, Electrocardiogram; NIBP, Non-invasive Blood Pressure; $EtCO_2$, End-tidal Carbon Dioxide; PACU, Post-Anesthesia Care Unit; POD, Postoperative Day; ANOVA, Analysis of Variance; aCCI, age-adjusted Charlson Comorbidity Index; Nu-DESC, Nursing Delirium Screening Scale.

Data Sharing Statement

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

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Lishui People's Hospital (Ethical approval number: 2024041), and all participants signed written informed consent prior to the commencement of the study. The study was registered with the Chinese Clinical Trial Registry (ChiCTR2400082736) at http://www.chictr.org.cn.

Consent for Publication

Individual consent was obtained from all the participating patients.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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