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ORIGINAL RESEARCH

Comparison of Ciprofol-Based and Propofol-Based Total Intravenous Anesthesia on Postoperative Recovery Quality in Patients Undergoing Hysteroscopic Surgery: A Randomized Non-Inferiority Trial

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Purpose: The 2,6-disubstituted alkylphenol ciprofol is a novel propofol analog for induction and maintenance of anesthesia. We aimed to compare the effects of ciprofol-based and propofol-based total intravenous anesthesia (TIVA) on postoperative recovery quality following hysteroscopic surgery.

Patients and Methods: In this randomized non-inferiority trial, women scheduled for hysteroscopic surgery at a tertiary hospital were randomly assigned to the ciprofol or propofol groups. The patients were administered intravenous injections of ciprofol (0.4 mg/kg) or propofol (2.0 mg/kg) for anesthesia induction before a maintenance infusion at initial rates of 0.8 or 5.0 mg/kg/h, respectively. The primary outcome was the Quality of Recovery-15 scale (QoR-15) score at 24 h post-surgery, and a non-inferiority margin of −8 was assumed. The secondary outcomes included hemodynamic changes, time to consciousness loss and recovery, incidences of injection pain, body movement, intraoperative respiratory adverse events, and postoperative adverse events.

Results: The trial included 120 participants (60 per group). The total QoR-15 score 24 h after surgery in the ciprofol group was comparable to that in the propofol group (median [interquartile range]: 113.5 [111.0, 117.0] vs 112.5 [108.0, 117.0]; median difference [95% confidence interval]: −1.0 [−3.0, 2.0]). There were no significant differences in the five QoR-15 dimensions between the groups. The mean arterial pressure and heart rate during anesthesia induction and surgery were significantly higher in the ciprofol group than in the propofol group, whereas the incidence of injection pain was lower. In addition, there were no significant between-group differences in the time to loss of consciousness or awakening, incidences of intraoperative hypoxemia or laryngospasm, or incidences of postoperative nausea, vomiting, headache, dizziness, and drowsiness.

Conclusion: Ciprofol is not inferior to propofol in terms of QoR score. Ciprofol administration is suitable for general anesthesia in female patients during hysteroscopic surgery.

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

Introduction

Hysteroscopic surgery is safe and effective for gynecological diseases, offering benefits such as reduced trauma and bleeding, rapid recovery, and fewer complications. Typically, hysteroscopy is performed in outpatient or ambulatory settings, often without general anesthesia, except for cases involving complex or large intrauterine abnormalities and for patients with high anxiety and low pain tolerance.[1,2] During the procedure, discomfort from cervical dilation, endoscope insertion, and electrical resection causes patient restlessness and body twisting, increasing operational difficulty.[3] Short-

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acting anesthetics are widely used in hysteroscopic surgery; however, their impact on postoperative recovery remains insufficiently understood.

The quality of anesthesia recovery is an ongoing concern, with efforts focusing on low postoperative pain, high comfort, minimal adverse reactions, and short recovery and extubation times.[4,5] The Quality of Recovery (QoR) score is an objective indicator of overall health status following surgery and anesthesia.[6–8] The latest version, the QoR-15 scale, has shown strong validity, reliability, and clinical feasibility and has been validated across various surgical procedures.[9,10] Moreover, early recovery quality based on the QoR-15 score is associated with postoperative complications 1 month after elective surgery.[11]

Total intravenous anesthesia (TIVA) with propofol is widely used in surgical and clinical scenarios and enhances QoR compared with balanced inhalational anesthesia. This effect likely reflects the ability of propofol to regulate perioperative stress, inflammatory responses, and physiological degradation.[12,13] However, propofol has certain drawbacks, including injection pain, cardiorespiratory depression, and the risk of rare but fatal metabolic derangements.[12–14] An option providing the benefits of propofol-based TIVA in terms of the QoR without the aforementioned side effects could improve anesthetic procedures.

Ciprofol, a novel 2,6-disubstituted phenol derivative, boasts a higher potency and stronger affinity for the γ-aminobutyric acid type A (GABAA) receptor and demonstrates faster onset and recovery profiles than propofol.[15] Moreover, ciprofol presents lower hypotension and respiratory depression risks and is devoid of injection pain or infusion syndrome.[15,16] Nevertheless, the effect of ciprofol on postoperative recovery following hysteroscopic surgery remains unexplored. Therefore, we compared postoperative recovery quality between ciprofol- and propofol-based TIVA in patients undergoing hysteroscopic surgery by assessing the QoR-15 score, hemodynamic changes, and adverse event frequency.

Patients and Methods

This randomized, controlled, double-blind trial was registered with the China Clinical Trial Centre under the registration number ChiCTR2500095274 (2025/01/04). The authors confirm that all ongoing and related trials for this drug/intervention are registered. The manuscript followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline for a randomized controlled trial.

Ethics Approval

This trial was performed in accordance with the Declaration of Helsinki and the Chinese Clinical Trial Specifications, and the study was approved by the Institutional Ethics Committee of the First Affiliated Hospital of the University of South China (No. 2024KS-MZ-54-01). All participants and their families signed an informed consent form before surgery.

Participants

The present study included eligible patients aged 18–60 years, classified with an American Society of Anesthesiologists (ASA) physical status of I–II, scheduled for hysteroscopic surgery under general anesthesia between January 10, 2025, and May 23, 2025. Patients with chronic alcoholism; pregnancy; a history of allergy to any drugs or sedative opioids used in the study; uncontrolled hypertension; severe heart, lung, liver, or kidney dysfunction; or psychiatric or neurological disorders were excluded.

Randomization and Blinding

Patients were randomly assigned to the ciprofol or propofol groups at a 1:1 ratio using a computer-generated random number table The allocations were concealed in sealed envelopes, which were opened on the day of surgery in the anesthesia preparation room by an anesthetist nurse who was not involved in participant recruitment, data collection, or follow-up. Given the distinct pharmacokinetic profiles and administration protocols of ciprofol and propofol, it was not feasible to blind the anesthesiologists who administered the drugs. However, they were independent from the investigators responsible for postoperative assessments, including the QoR-15 questionnaire, and the investigators who administered the QoR-15 questionnaire were not involved in drug administration or intraoperative management. All participants, data collectors, postoperative follow-up researchers, and clinical staff were unaware of group assignments.

Interventions

Based on previous studies,[17–19] patients in the ciprofol group were administered a single induction injection of 0.4 mg/kg, followed by an initial maintenance infusion of 0.8 mg/kg/h. In contrast, patients in the propofol group received a single induction injection of 2.0 mg/kg, followed by an initial maintenance infusion of 5.0 mg/kg/h. The infusion rates of ciprofol and propofol were adjusted to maintain a bispectral index (BIS) of 40–60 until the end of surgery.

All patients received standardized surgical and anesthetic care, with only the type of general anesthetic agent varying. No premedication was administered before anesthesia. The QoR-15 score was assessed 1 day before surgery. After entering the operating room, the mean arterial pressure (MAP), heart rate (HR), blood oxygen saturation (SpO_2), and BIS were monitored for each patient. Patients in both groups received an intravenous dose of 0.1 μg/kg sufentanil citrate (Yichang Humanwell Pharmaceutical Co., Hubei, China) for analgesia. Anesthesia induction was then initiated with either 0.4 mg/kg ciprofol (HSK3486; Haisco Pharmaceutical Group Co., Liaoning, China) or 2.0 mg/kg propofol (Fresenius Kabi AG, Graz, Austria), administered over 30s based on group assignment. A laryngeal mask was inserted for mechanical ventilation when loss of consciousness was confirmed, defined as the loss of verbal response and eyelash reflex. As reported in previous studies, no muscle relaxants were used before or after laryngeal mask insertion during hysteroscopic surgery.[20–22] For maintenance, ciprofol was initially administered at a rate of 0.8 mg/kg/h, and the infusion rate was adjusted to 0.1–0.4 mg/kg/h, with a maximum allowed rate of 2.0 mg/kg/h. Propofol was initially administered at a rate of 5.0 mg/kg/h, with the rate modified as needed, allowing for a minimum infusion rate of 4.0 mg/kg/h and a maximum of 10.0 mg/kg/h. In the case of body movement affecting the operation or the occurrence of an air leak of the laryngeal mask, extra ciprofol (0.1 mg/kg/time) or propofol (0.5 mg/kg/time) was injected, as appropriate. During surgery, BIS was maintained at 40–60. The MAP, HR, and SpO_2 values were recorded before anesthesia (T1), at the time of loss of consciousness (T2), 1 min after laryngeal mask insertion (T3), 10 min after surgery started (T4), 20 min after surgery started (T5), and when the laryngeal mask was removed (T6).

Outcome Assessment

The primary outcome was the global QoR-15 score at 24 h postoperatively. The QoR-15 instrument, consisting of 15 items, is a validated questionnaire designed to evaluate the quality of postoperative recovery. It comprises five dimensions related to recovery: physical comfort (five items), physical independence (two items), emotional state (four items), psychological support (two items), and pain (two items). Each item is assessed on an 11-point scale based on its frequency in the questionnaire. The overall score varies from 0 (representing the poorest recovery quality) to 150 (representing the best recovery quality).[6–8] The study used a Chinese-language version of the QoR-15 (Figure S1) that has been validated and shown satisfactory psychometric properties comparable to those of the original English version (Figure S2).[23] No modifications were made to this validated version. The patients completed the QoR-15 1 day preoperatively and 24 h postoperatively. The QoR-15 was administered by an anesthetist who was blinded to the study. The QoR-15 score at 24 h postoperatively was the primary outcome of interest.

The secondary outcomes included hemodynamic changes during anesthesia; time to consciousness loss and recovery; injection pain; body movement; respiratory adverse events, such as laryngospasm and hypoxemia; and incidences of postoperative adverse effects, including nausea, vomiting, headache, dizziness, and drowsiness. Time to loss of consciousness refers to the duration from the completion of drug administration to the onset of unconsciousness. Recovery time was defined as the time from anesthetic cessation until the patient could respond to verbal commands and had sufficient spontaneous breath. Injection pain was defined as the self-reported presence of pain (yes vs no) after receiving the initial injection. Body movement was defined as any visible limb bending or head movements during hysteroscopy. Intraoperative hypoxemia was defined as a decrease in SpO_2 <95% or the requirement for airway management. Postoperative nausea and vomiting, headache, dizziness, and drowsiness were recorded when patients achieved anesthesia recovery.

Sample Size and Statistical Analysis

Since propofol has been shown to provide better QoR-15 scores than other anesthetics in various surgeries,[24–26] we selected it as the positive control for our non-inferiority study comparing the effects of ciprofol with propofol based on QoR-15 scores. Based on previous studies, an 8-point variation in QoR-15 scores is considered the minimal clinically important difference for perioperative interventions.[27,28] Therefore, a non-inferiority margin of −8 was assumed in the current study. The preliminary data used for power calculation were obtained from a pilot study conducted before the main trial. The pilot study included a smaller patient cohort (12 per group) to estimate variability in QoR-15 scores.[29,30] The mean ± standard deviation of QoR-15 scores in the pilot study was 114.9 ± 9.9 for ciprofol and 112.2 ± 9.4 for propofol. To identify a difference with a non-inferiority margin of −8, a sample size of 108 patients (54 per group) was required, ensuring 80% power and a one-sided significance level of 2.5%. A sample size of 120 patients was projected, considering a dropout rate of 10%. The sample size was calculated using PASS software for Windows (version 19.0; NCSS, Kaysville, UT).

Statistical analyses were conducted using SPSS (version 25, IBM Statistics, Chicago, IL, USA) and SAS (version 9.4; SAS Institute, Cary, NC) for Windows. P<0.05 was considered statistically significant. Continuous variables are presented as mean ± standard deviation or median (interquartile range) and were compared using two-sample t-tests or the Mann–Whitney U-test depending on the normality distribution. Categorical variables are presented as percentages of the overall patient count and were compared between groups using chi-squared or Fisher's exact tests, as appropriate. The 95% confidence intervals (CIs) for differences in means or medians (continuous outcomes) or relative risks (categorical outcomes) were calculated. We calculated 95% CIs for the difference in mean QoR-15 scores between the ciprofol and propofol groups. The hypothesis tested was the non-inferiority of ciprofol to propofol in terms of the QoR-15 score 24 h after surgery. If the lower limit of the 95% CI for the difference in mean QoR-15 scores was greater than the predefined non-inferiority margin (−8), the null hypothesis was rejected, indicating that ciprofol is non-inferior to propofol. Non-superiority testing was performed using SAS.

Results

Disposition and Demographics

A total of 140 patients were assessed for eligibility; 14 patients did not meet the inclusion criteria, 3 declined to participate, and another 3 did not participate for other reasons. The remaining 120 patients were enrolled in this study and randomly assigned to the ciprofol or propofol group in a 1:1 ratio. All data collected from these patients were analyzed. The allocation process, according to the CONSORT guidelines, is presented in Figure 1.

Patient Characteristics

Table 1 shows patient demographics and surgical data. The groups showed no significant differences in age (P=0.502), height (P=0.812), weight (P=0.398), body mass index (P=0.363), parity (P=0.626), or ASA classification (P=0.999). Additionally, hysteroscopic surgery types (P=0.820), the length of surgery (P=0.133), and anesthesia duration (P=0.136) did not differ significantly between the groups.

Primary Outcome

QoR-15 Scores 24 h Postoperatively

The QoR-15 scores are shown in Table 2. In the primary analysis, the median global QoR-15 score measured 1 day before surgery was 126.0 (121.3, 130.8) in the ciprofol group and 126.0 (122.0, 129.0) in the propofol group, with a between-group difference of 0.0 (95% CI: −3.0, 2.0). Preoperatively, the total score or the individual QoR-15 dimensions did not differ significantly between the groups (P=0.600).

At 24 h after surgery, the global QoR-15 score in the ciprofol group was comparable to that in the propofol group (median [interquartile range]: 113.5 [111.0, 117.0] vs 112.5 [108.0, 117.0]). The median difference in QoR-15 scores was −1.0 (95% CI: −3.0, 2.0), and global QoR-15 scores did not significantly differ between the groups (P=0.633). Furthermore, the effect sizes are shown as median ± 95% CI, and the lower limit was higher than the non-inferiority

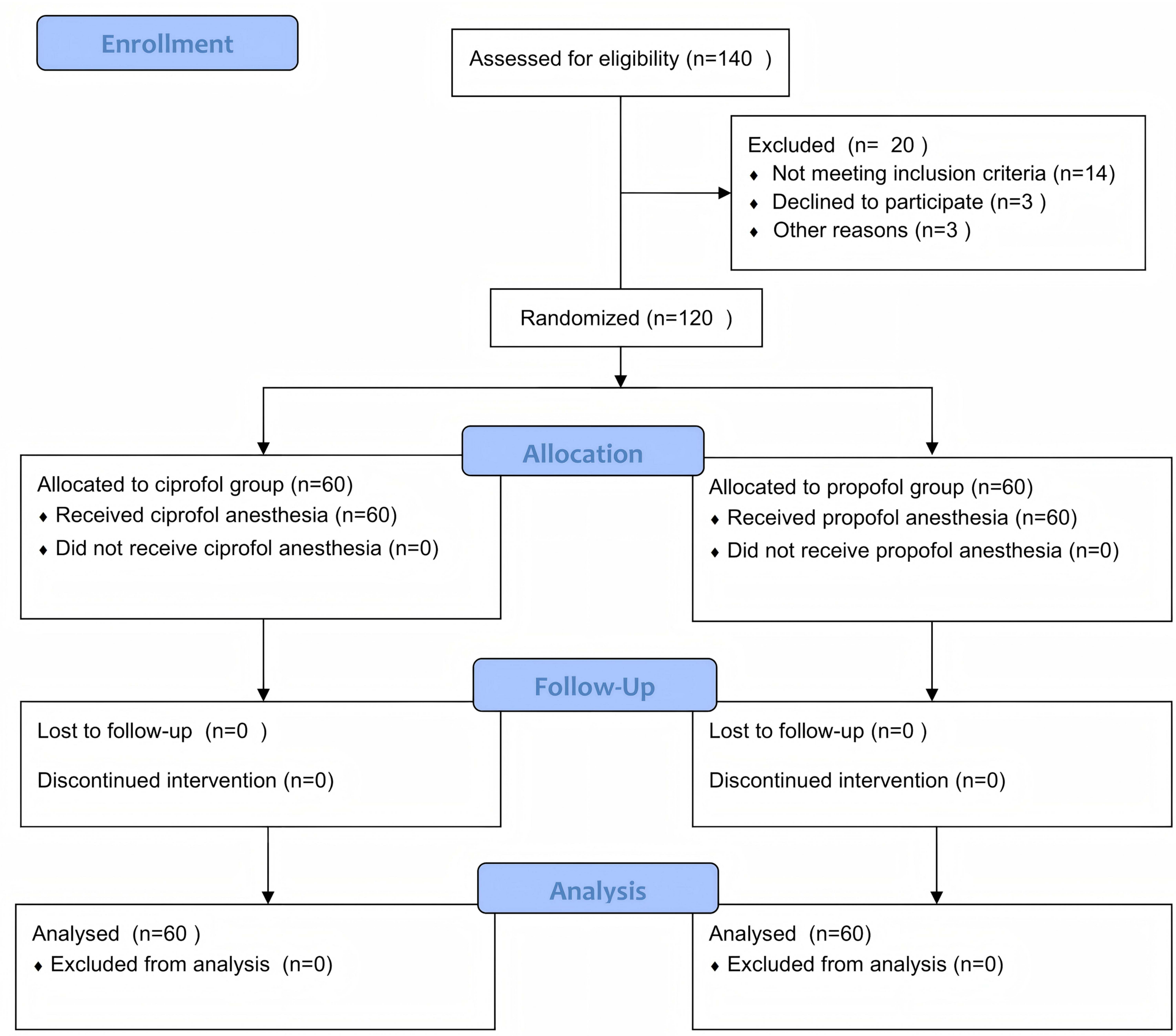

Figure 1 Flow chart of the study.

margin of −8 ($P<0.001$ for non-inferiority; Figure 2), indicating that ciprofol is non-inferior to propofol in terms of postoperative recovery quality as measured by the QoR-15 score. The scores for the five dimensions of the QoR-15 did not significantly differ between the groups (all $P>0.05$).

Secondary Outcomes

Changes in Hemodynamics

MAP and HR values at each timepoint are shown in Figure 3. The MAP and HR were similar between the groups at baseline (all $P>0.05$). Following anesthesia induction, both metrics significantly decreased; however, the ciprofol group exhibited notably higher MAP values than those in the propofol group at T2, T3, T4, and T5 ($P<0.001$, $P=0.004$, $P=0.001$, and $P=0.034$, respectively). The HR in the ciprofol group was significantly higher than that in the propofol group at T2, T3, T4, and T5 ($P<0.001$, $P=0.002$, $P=0.003$, and $P=0.002$, respectively). At the time of laryngeal mask removal (T6), the groups showed no notable differences in the MAP or HR (both $P>0.05$).

Table 1 Demographic and Surgical Characteristics of the Enrolled Patients

	Ciprofol (n=60)	Propofol (n=60)	*P*-value
Age (years)	47.7±6.8	48.6±7.6	0.502
Height (cm)	156.7±4.5	156.4±4.7	0.812
Weight (kg)	54.8±7.2	55.9±6.8	0.398
BMI (kg/m^2)	22.8±2.3	22.4±2.6	0.363
Parity	1.5±0.7	1.4±0.7	0.626
ASA physical status			0.999
I	20 (33.3)	22 (36.7)	
II	40 (66.7)	38 (63.3)	
Type of hysteroscopic surgery			0.820
Polypectomy	21	17	
Myomectomy	16	19	
Lysis of adhesions	19	21	
Mytroplast	4	3	
Length of surgery (min)	28.4±8.9	25.9±8.9	0.133
Duration of anesthesia (min)	31.2±9.0	28.8±8.7	0.136

Notes: Data are presented as mean ± standard deviation or n (%). Independent *t*-test was used for two normally distributed continuous outcomes, and Chi-square or Fisher Exact tests for binary outcomes.
Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index.

Table 2 Global and Five-Dimensional of QoR-15 Preoperatively and in the First 24 h After Surgery

	Ciprofol (n=60)	Propofol (n=60)	Difference in median (95% CI)	*P*-value
Global QoR-15 scores				
Preop	126.0 (121.3, 130.8)	126.0 (122.0, 129.0)	0.0 (−3.0, 2.0)	0.600
Post 24 h	113.5 (111.0, 117.0)	112.5 (108.0, 117.0)	−1.0 (−3.0, 2.0)	0.633
Emotional status				
Preop	29.0 (26.3, 31.0)	28.0 (25.00, 31.8)	−1.0 (−2.0, 1.0)	0.275
Post 24 h	29.0 (27.0, 30.0)	27.5 (26.00, 31.8)	−1.5 (−2.0, 1.0)	0.475
Physical comfort				
Preop	43.0 (42.0, 45.0)	43.0 (42.0, 44.8)	0.0 (−1.0, 1.0)	0.768
Post 24 h	41.0 (39.0, 42.0)	41.0 (40.0, 42.0)	0.0 (−1.0, 1.0)	0.721
Psychological support				
Preop	17.0 (16.3, 18.0)	17.0 (16.0, 18.0)	0.0 (−1.0, 0.0)	0.277
Post 24 h	17.0 (16.0, 18.0)	17.0 (16.0, 17.0)	0.0 (−1.0, 0.0)	0.120
Physical independence				
Preop	20.0 (14.0, 20.0)	20.0 (16.0, 20.0)	0.0 (0.0, 0.0)	0.482
Post 24 h	9.0 (8.0, 10.0)	9.0 (8.0, 10.0)	0.0 (−1.0, 0.0)	0.287
Pain				
Preop	20.0 (18.3, 20.0)	20.0 (19.0, 20.0)	0.0 (0.0, 0.0)	0.424
Post 24 h	18.0 (17.0, 19.0)	18.0 (17.0, 20.0)	0.0 (−1.0, 0.0)	0.786

Notes: Data are presented as median (interquartile range). Mann–Whitney *U*-test was used for nonparametric outcomes.
Abbreviations: QoR-15, Quality of Recovery-15; CI, confidence interval; Preop, 1 day preoperatively; Post 24 h, 24 h postoperatively.

Induction and Recovery Characteristics

The time to loss of consciousness and time to regain consciousness did not show significant differences between the groups (*P*=0.179 and *P*=0.708, respectively; Table 3).

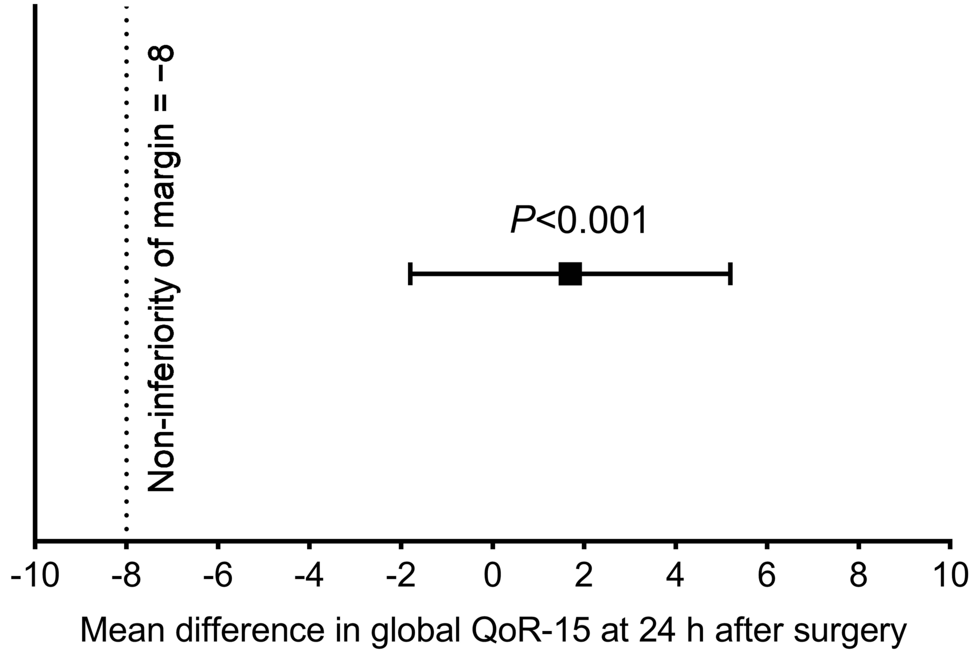

Figure 2 Median difference in global QoR-15 at 24 h after surgery. Data are presented as median ± 95% CI. Vertical line at −8 represents the margin of non-inferiority for the global QoR-15.
Abbreviations: QoR-15, Quality of Recovery-15; CI, confidence interval.

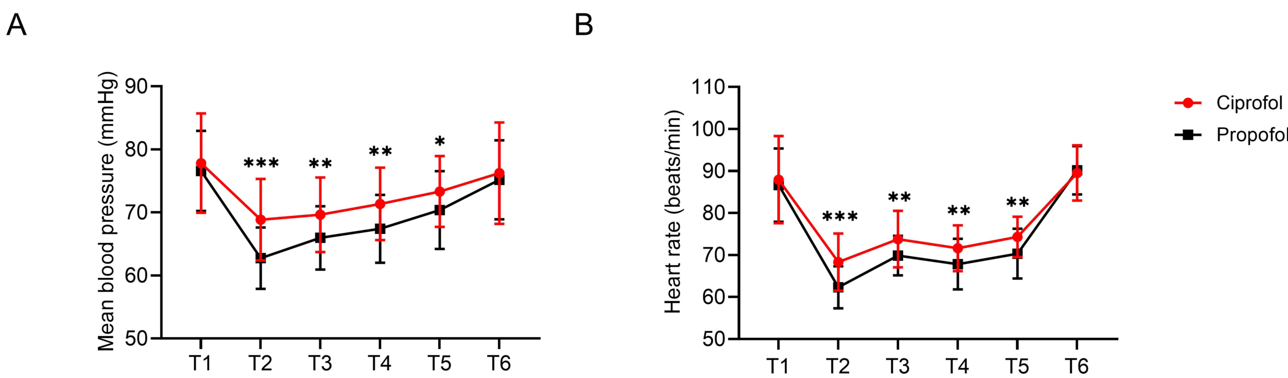

Figure 3 Comparison of MAP and HR at different time points between the two groups. (**A**) MAP at different time points in the two groups; (**B**) HR at different time points in the two groups. T1, baseline (before anesthetic induction); T2, at the time of loss of consciousness; T3, 1 min after laryngeal mask insertion; T4, 10 min after surgery started; T5, 20 min after surgery started; T6, immediately after the laryngeal mask removal. Data are presented as mean ± SD. **P*<0.01, ***P*<0.01, ****P*<0.001, compared with the propofol group.
Abbreviations: MAP, mean arterial pressure; HR, heart rate; SD, standard deviation.

Adverse Events

As depicted in Table 4, the incidence of injection pain was significantly higher in the propofol group compared with the ciprofol group (*P*<0.001). No significant between-group differences in the occurrence of body movements during the operation were revealed, and no intraoperative respiratory complications, including hypoxemia and laryngospasm, were detected in either group (all *P*=0.999). No significant differences were found in the incidence of postoperative adverse events; specifically, there was no significant difference in postoperative nausea (*P*=0.999) and vomiting (*P*=0.999), headache (*P*=0.439), dizziness (*P*=0.814), and drowsiness (*P*=0.619) between the two groups.

Table 3 Comparison of Anesthesia Induction and Recovery Characteristics Between the Two Study Groups

Characteristics	Ciprofol (n=60)	Propofol (n=60)	*P*-value
Time to loss of conscience (s)	46.7±2.6	46.0±2.9	0.179
Time to recovery of conscience (min)	9.3±1.3	9.2±1.1	0.708

Abbreviations: s, seconds; min, minute.

Table 4 Summary of Secondary Outcomes Between the Two Study Groups

	Ciprofol (n=60)	Propofol (n=60)	*P*-value
Injection pain (n, %)	3 (5.0)	26 (43.3)	<0.001
Body movements (n, %)	4 (6.7)	3 (5.0)	0.999
Hypoxemia (n, %)	0 (0)	0 (0)	0.999
Laryngospasm (n, %)	0 (0)	0 (0)	0.999
Nausea (n, %)	0 (0)	0 (0)	0.999
Vomiting (n, %)	0 (0)	0 (0)	0.999
Postoperative headache	2 (3.3)	5 (8.3)	0.439
Postoperative dizziness	10 (16.7)	12 (20.0)	0.814
Postoperative drowsiness	1 (1.7)	3 (5.0)	0.619

Discussion

This single-center, randomized, controlled trial demonstrated that ciprofol-based TIVA was not inferior to propofol-based TIVA in terms of the global QoR-15 score assessed 24 h after surgery in patients who underwent hysteroscopic surgery. Moreover, the predefined non-inferiority margin was set at −8. Ciprofol- and propofol-based TIVA did not show significant differences in any of the five QoR-15 dimensions. Additionally, ciprofol-based TIVA resulted in lower injection pain and better maintenance of hemodynamic stability during hysteroscopic surgery under general anesthesia than did propofol-based TIVA. These findings suggest the potential of ciprofol as an option for general anesthesia, particularly in female patients undergoing hysteroscopic surgery.

Hysteroscopic surgery has the advantages of a short hospitalization time, safety, patient comfort, and rapid recovery after surgery for the treatment of various uterine diseases. However, the cervical sensory nerve is rich, and surgical procedures, such as cervical dilatation and intimal curettage, often cause pain and discomfort; coupled with fear and anxiety, patients often find these conditions unbearable, resulting in adverse complications.[1,31] Therefore, hysteroscopic surgery is generally performed under general anesthesia, and the effects of anesthetics on postoperative recovery warrant further investigation. TIVA is a commonly used anesthetic method for hysteroscopic surgery, for which intravenous and opioid analgesics are the most used. Among the intravenous anesthetic drugs, propofol is the most used; however, injection pain is a drawback. Ciprofol is a novel intravenous anesthetic characterized by rapid onset and recovery. It bears structural similarities to propofol while exhibiting a heightened binding affinity for the $GABA_A$ receptor.[15,16] The anesthetic method used in the present study was TIVA with sufentanil combined with ciprofol or propofol. The administered dose of ciprofol was 0.4 mg/kg, consistent with the safe dose range of ciprofol reported in a Phase I clinical study and the lowest effective dose recommended in a Phase II study.[17,18] All patients underwent hysteroscopic surgery, demonstrating that the depth of anesthesia required by hysteroscopic anesthesia can be met by 0.4 mg/kg ciprofol. Ciprofol offers similar efficacy and safety to propofol, with reduced injection pain, fewer adverse events, increased patient satisfaction, and more stable hemodynamics during hysteroscopy.[32,33] However, these findings were derived from studies conducted under sedation without laryngeal insertion. In contrast, recent research has found that ciprofol provided insertion conditions comparable to propofol during hysteroscopy when inserting laryngeal masks without a muscle relaxant agent.[20–22] Given these findings, we further investigated the QoR-15 score following ciprofol- and propofol-based TIVA in patients undergoing hysteroscopy under laryngeal mask anesthesia.

This study found no significant difference in QoR-15 scores between the ciprofol and propofol groups. To our knowledge, this study is the first to compare the impact of ciprofol- and propofol-based TIVA on QoR-15 scores in patients undergoing hysteroscopic surgery. Previous studies reported varying outcomes regarding differences in QoR-15 scores between propofol and other intravenous (remimazolam) and inhaled (desflurane) anesthetics.[24–26] For instance, intravenous propofol enhanced the quality of postoperative recovery compared with desflurane in patients undergoing robot-assisted or laparoscopic nephrectomy.[24] However, in another study, propofol-based TIVA provided only a transient improvement in postoperative recovery compared with desflurane anesthesia, with no significant differences in other outcomes.[25] Additionally, remimazolam-based total intravenous anesthesia provided a similar QoR to propofol, suggesting that these anesthetics can achieve comparable recovery quality.[26] In the present study, as expected, the QoR-15 score was lower at postoperative 24 h than on preoperative day 1, indicating that further recovery is needed after the initial postoperative period. Moreover, total QoR-15 scores were similar in the ciprofol and propofol groups, and both groups experienced good recovery in all dimensions of the QoR-15, including pain, physical comfort, physical independence, emotional distress, and psychological support. Three possible reasons may explain the failure of ciprofol-based TIVA to reach clinical significance for the QoR-15 at 24 h. First, as an indicator reflecting patient recovery, the minimum clinically important difference score of 8 in the QoR-15 was based on participants who underwent other surgeries.[27,28] Whether the QoR-15 can detect minor changes in the immediate postoperative period in patients undergoing hysteroscopic surgery remains unclear. Second, the understanding and comprehension of QoR-15 questionnaires partially depend on patient education. Finally, the data from the QoR-15 obtained preoperatively and early (24 h) after surgery may not completely reflect long-term outcomes. Other potential factors, such as the types of hysteroscopic surgeries and parity, could influence pain sensation and recovery. However, we found no significant differences between the ciprofol and propofol groups in these variables, suggesting that the observed outcomes are likely attributable to the anesthetic agents rather than other confounding factors.

Previous clinical studies have demonstrated that ciprofol causes less cardiovascular depression than propofol.[19,34] In the present study, the decrease in the MAP was significantly lower in the ciprofol group than in the propofol group. Patients in the ciprofol group experienced a minor decrease in HR during hysteroscopy; HR changes were relatively stable and did not require any particular intervention. In contrast, patients in the propofol group displayed a significant decrease in both the HR and MAP, indicating that propofol led to cardiovascular depression. The lower decrease in MAP and minor decrease in HR suggest that ciprofol maintains cardiovascular function more effectively, reducing the risk of significant cardiovascular depression. This is particularly important in clinical settings where maintaining stable hemodynamics is crucial for patient safety and recovery. Therefore, ciprofol-based anesthesia may offer better hemodynamic stability during hysteroscopic surgery.

Injection pain is a frequently reported side effect of propofol, with an incidence of 50–80%.[35] This pain can cause discomfort, increase tension and anxiety, and lead to body movement. In the current study, we found that the incidence of injection pain was significantly lower in the ciprofol group than in the propofol group, which is consistent with the results of a previous study.[33] As propofol is more soluble in the aqueous phase than ciprofol, pain is more obvious during propofol injection.[36] In the present study, the solubility of ciprofol in the oil-water emulsion was lower, and it had higher hydrophobicity and lower plasma concentration, thus resulting in lower injection pain.

In the present study, the duration of consciousness loss and time to recovery did not differ significantly between the ciprofol and propofol groups. In addition, no notable differences were observed in the prevalence of intraoperative body movements or postoperative adverse reactions. No discomfort, such as nausea or vomiting, occurred in either group; however, some patients experienced dizziness and drowsiness in the early postoperative stages. Considering the residual effect of the anesthetics, the dizziness and drowsiness symptoms improved after 30 min, showing no significant differences between the groups. Collectively, ciprofol greatly reduced the incidence of injection pain without causing adverse reactions during general anesthesia.

The present study has certain limitations. First, the procedures were conducted at a single center with a limited sample size, which may restrict the generalizability of the findings to broader populations. Therefore, future multicenter large-sample studies are required. Second, our study involved a relatively young patient cohort with ASA grades I and II. It is worth noting that the effects of ciprofol on QoR-15 scores in older patients and those with severe comorbidities remain unknown and require further investigation. Moreover, owing to the short hospitalization period for hysteroscopic surgery, our patient observation period and QoR questionnaires were limited to 24 h postoperatively, with no long-term (over 48 h) postoperative follow-ups. Another limitation was the lack of data on rescue medications needed for body movement and pain management during surgery. This could affect the interpretation of our results, as differences in these requirements between the ciprofol and propofol groups could reveal insights into their comparative effects on patient recovery and comfort. Future studies should include these outcomes for a more comprehensive assessment of anesthetic impact.

Conclusion

Our findings suggest that QoR after ciprofol-based TIVA was non-inferior to that after propofol-based TIVA in female patients undergoing hysteroscopic surgery. Hence, ciprofol may be considered a viable anesthetic option for hysteroscopy and other ambulatory surgeries, and a promising alternative for achieving QoR outcomes comparable to those experienced with propofol.

Abbreviations

ASA, American Society of Anesthesiologists; BIS, bispectral index; CIs, confidence intervals; CONSORT, Consolidated Standards of Reporting Trials; $GABA_A$, ɣ-aminobutyric acid type A; HR, heart rate; MAP, mean arterial pressure; QoR, Quality of Recovery scale; QoR-15, Quality of Recovery-15 scale; SpO_2, blood oxygen saturation; TIVA, total intravenous anesthesia.

Data Sharing Statement

We would like to share individual deidentified participant data, and researchers may contact the corresponding author to view raw data for scientific research purposes.

Ethics Approval and Informed Consent

The Institutional Ethics Committee of the First Affiliated Hospital of the University of South China approved the study (No. 2024KS-MZ-54-01). Written informed consent was provided from the patients enrolled in the study.

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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 report no conflicts of interest in this work.

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