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CLINICAL TRIAL REPORT

Induction of General Anesthesia with Fospropofol in Elderly Patients Undergoing Hip Surgery: An Efficacy and Safety Analysis

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Purpose: To compare fospropofol with etomidate for the induction of anesthesia in elderly patients undergoing hip surgery, with a focus on safety and efficacy.

Patients and Methods: A prospective, single-blind, randomized, controlled study that enrolled 120 elderly patients, who were randomly assigned to a fospropofol group (10 mg/kg, group P, n = 60) or an etomidate group (0.3 mg/kg, group E, n = 60). The main outcome was the time to loss of consciousness (LOC). The secondary endpoints were the success rate of anesthesia induction, hemodynamic parameters, adverse reactions, dosage of anesthetic maintenance drugs and postoperative recovery conditions.

Results: The study was completed by all enrolled patients in both groups. The success rate for induction of general anesthesia in both groups was 100% (P=1.000). The LOC time was greater in group P compared to group E (98.50 vs. 40.00 s, P<0.001). Compared to group E, group P had better control of systolic blood pressure (SBP) and heart rate at intubation (P<0.001) and required less remifentanil (6.7% vs. 20.0%, P=0.032). In the 10 min post-intubation, group P showed smaller increases in SBP and lower heart rates at most time points (P<0.001), along with lower propofol consumption (3.40 [2.50, 4.25] vs. 4.18 [3.83, 4.62] mg/min, P<0.001). The incidence of myoclonus was less in group P (1.7% vs. 31.7%, P<0.001), but paresthesia (primarily pruritus) was more frequently observed in group P (15.0% vs. 0.0%, P=0.002). The incidence of postoperative nausea and vomiting (PONV) at 0–24 h was lower in group P (11.67% vs. 26.67%, P=0.038), while no significant difference was observed at 24–48 h (5.0% vs. 1.67%, P=0.355) or during recovery (11.67% vs. 21.67%, P=0.149). The incidence of other adverse events was similar between the two groups.

Conclusion: Fospropofol provides better suppression of the stress response during tracheal intubation and positioning. It also significantly reduces the incidence of myoclonus and demonstrates favorable hemodynamic stability though its slower onset and higher incidence of pruritus require clinical consideration.

Clinical Trial Registration: Registered at: https://www.isrctn.com/, ISRCTN12170320, registration date: 24/06/2025.

Keywords: fospropofol disodium, etomidate, elderly patients, hip surgery, anesthesia

Introduction

Hip diseases, including proximal femoral fractures, osteoarthritis, and femoral head necrosis, significantly impact the quality of life of the elderly. Among these, hip fractures are often referred to as "the last fracture in the elderly" because of the high disability and incidence rates, and mortality.[1] With the accelerated global aging population, the disease burden is increasingly severe. Currently, surgical treatment is the preferred approach to restore function and reduce complications.[2] The American Academy of Orthopaedic Surgeons guidelines emphasize that surgery should be completed within 48 hours of injury to improve outcomes.[3]

However, elderly patients often have multiple underlying medical conditions and reduced physiological reserve, significantly lowering their tolerance for surgery and anesthesia. During the anesthesia induction phase, particularly from loss of consciousness (LOC) to the start of surgery, strong noxious stimuli (such as tracheal intubation and positioning) combined with drug effects

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can easily trigger severe hemodynamic fluctuations.[4] This unstable hemodynamic state has been proven to be closely linked to an increase in the risk for serious perioperative cardiovascular complications including stroke and myocardial injury. Therefore, the American Society of Anesthesiologists (ASA) guidelines for the perioperative management of elderly patients explicitly states that optimizing anesthesia induction strategies to maintain hemodynamic stability is a key component in reducing perioperative risks for this population.[5]

Etomidate has a minimal impact on hemodynamics and is therefore often preferred over propofol for anesthetic induction in elderly patients, especially in those who are very old, have cardiovascular diseases, or are otherwise hemodynamically unstable It is currently the first-choice induction agent for this patient population at our center.[6] However, its application is limited by a series of inherent drawbacks, including a high incidence of myoclonus, injection pain, and inhibitory effects on adrenocortical function.[7] These factors may compromise the smoothness of anesthesia and patient safety.

Fospropofol disodium (Lusedra) is a water-soluble propofol prodrug originally developed by Eisai Co., Ltd. It received FDA approval in the United States for monitored anesthesia care (MAC) sedation in adult patients undergoing diagnostic or therapeutic procedures. However, due to safety concerns in outpatient use and poor sales, it was withdrawn from the market four years later. The newly approved fospropofol disodium is a water-soluble propofol prodrug independently developed in China. Although both drugs share the same primary chemical component ($C_{13}H_{19}O_5PNa_2$), they differ in excipients, dosage forms, and manufacturing processes. This drug was approved for clinical use in China in 2021 and is currently used as a Class I chemical drug for the induction of general anesthesia in adults.[8] Its unique pharmacological characteristic of slow enzymatic release of the active component in vivo theoretically allows for a smoother induction process. While avoiding metabolic adverse effects associated with lipid emulsions (such as hypertriglyceridemia and fat overload).[9] The aqueous formulation also reduces the risk of bacterial contamination and eliminates injection site burning pain. These features make fospropofol particularly suitable for elderly patients with diminished physiological reserves. Previous studies suggest that fospropofol disodium is associated with fewer respiratory and circulatory adverse events when used for anesthesia induction.[10] The present study was designed to systematically evaluate the efficacy and safety of fospropofol versus etomidate for the induction of general anesthesia in elderly patients undergoing hip surgery, with the aim of providing evidence-based guidance for precise anesthesia management in this vulnerable patient population.

Patients and Methods

Design of the Study and Enrolled Patients

It was a single-center, prospective, single-blind, randomized controlled study given approval by the Ethics Committee of The First People's Hospital of Changzhou/The Third Affiliated Hospital of Soochow University [Approval No. (2025) Teaching 042]. The study was registered on the ISRCTN platform under the registration number ISRCTN12170320 (registration date: 24/06/2025). It was carried out in strict accordance with the Declaration of Helsinki and the International Conference on Harmonization Guidelines for Good Clinical Practice. Written informed consent was obtained from all patients.

From July 21 to November 15, 2025, 120 elderly patients who underwent hip surgery under general anesthesia at the First People's Hospital of Changzhou were enrolled in the study. The inclusion and exclusion criteria of the study were as follows. Inclusion criteria were: patients scheduled for elective hip surgery under general anesthesia with endotracheal intubation; aged 65–74 years (young-old); body mass index (BMI) 18–27 kg/m^2; and American Society of Anesthesiologists (ASA) physical status I–III. Exclusion criteria were: patient refusal of general anesthesia; allergy to anesthetics; preoperative cognitive impairment; baseline blood pressure ≥ 180/110 mmHg or ≤ 90/60 mmHg; cardiac, pulmonary, hepatic, or renal impairment; multiple injuries or bilateral surgery; or receipt of regional or general anesthesia within the past 3 months.

Randomization and Blinding

A clinical coordinator who was not involved in the subsequent study used SPSS 26.0 statistical software to randomly assign the enrolled subjects into groups. The 120 patients were randomly assigned to the fospropofol (group P) or etomidate group (group E), with 60 per group. Due to differences in the appearance of the medications, blinding of the drug administrators was not feasible (Fospropofol disodium is a clear aqueous solution, whereas etomidate is a white fat emulsion). The patients, assessors of outcome and data analysts were blinded to the assignments of each group.

Interventions

All patients underwent an ultrasound-guided fascia iliaca compartment block on the affected side 20 minutes before the start of surgery to provide baseline analgesia. The administered drug was 0.25% ropivacaine at 0.6 mL/kg, with a total dose ≤ 100 mg. After entering the operating theatre, routine measurements were initiated, including ECG, BP, SpO_2, temperature, and the bispectral index (BIS). Both groups received flurbiprofen axetil (50 mg) and sufentanil (0.1 μg/kg intravenously) followed by rapid fluid infusion of 5 mL/kg. Group P received fospropofol (10 mg/kg) and group E etomidate (0.3 mg/kg). After LOC, sufentanil (0.3 μg/kg) and cisatracurium (0.15 mg/kg) were administered intravenously and 3 min later the patient received tracheal intubation. If systolic blood pressure (SBP) did not decrease by ≤ 20% of the baseline level before intubation, it was considered indicative of a high-risk stress response, and remifentanil 1 μg/kg was given intravenously. The time to LOC (defined as disappearance of the eyelash reflex and no response to two consecutive verbal calls) was recorded. Failure of induction was defined if LOC was not achieved within 20 min. Anesthesia was maintained using total intravenous anesthesia. When the BIS value reached 65, an additional bolus of propofol 1 mg/kg was given, followed by continuous infusion of propofol and remifentanil to ensure a BIS value in the 45–65. Intraoperative adjustments to analgesic dosage or the use of vasoactive agents were based on vital signs and the Surgical Pleth Index (SPI). Specifically, if the SPI value was in the range 20–50 and accompanied by a BP increase > 30% above the baseline measurement, urapidil (0.5 mg/kg) was given; if the SPI was ≥ 50, an additional bolus of remifentanil 1 μg/kg was given; if BP decreased by more than 30% below baseline or mean arterial pressure remained below 60 mmHg for 5 min, phenylephrine (40–80 μg) was administered; and if the heart rate (HR) fell below 50 beats per minute, the muscarinic antagonist atropine (0.3–0.5 mg) was given. All patients received a subcutaneous injection of 266 mg of liposomal bupivacaine for local infiltration of the wound at the time of skin closure. Postoperative pain intensity was assessed using the Visual Analog Scale (VAS). If the VAS score was ≥ 4, flurbiprofen axetil 50 mg was administered intravenously in the post-anesthesia care unit (PACU), and Diclofenac Sodium and Lidocaine Hydrochloride Injection (2 mL, containing diclofenac sodium 75 mg and lidocaine hydrochloride 20 mg [calculated as lidocaine]) was given intramuscularly in the ward as rescue analgesia.

Outcomes

The time to LOC was the primary outcome. The secondary outcomes were: success rate of induction of anesthesia; hemodynamic parameters (SBP and HR) at different time points; the incidence of paresthesia and myoclonus; the proportion of patients requiring supplemental remifentanil before intubation; the dosage of anesthetic maintenance drugs per unit time; postoperative recovery time; the incidence of postoperative nausea/vomiting and delirium (assessed using the Confusion Assessment Method); VAS scores at rest upon discharge from the PACU, at 24 hours postoperatively, and at 48 hours postoperatively, as well as the number of rescue analgesia administrations; and the high-sensitivity troponin T serum level 24 h postoperatively.

Sample Size and Statistical Analysis

Based on previous literature, we conservatively estimated the difference in LOC time between the two groups. We assumed that the LOC time in group P would be 62.96 ± 13.32 seconds, and in group E, 55.8 ± 6.74 seconds.[11] The sample size was calculated using PASS 15.0 software, with α set at 0.05 and a power of 0.9. The ratio of sample sizes between the two groups was 1:1, requiring 48 patients per group. Considering a 20% dropout rate, a total of 120 patients were enrolled, with 60 patients in each group.

Statistical analyses were conducted using R software (ver. 4.1.5). For the descriptive analysis, continuous data that were normally distributed are given as the mean ± SD. Between-group comparisons were conducted using the independent samples *t*-test. Continuous data that did not follow a normal distribution are given as the median and interquartile range (Q1, Q3). Between-group comparisons were conducted using the Mann-Whitney *U*-test. Categorical data are given as number (%) and were analyzed by employing the χ^2 or Fisher's exact tests.

In addition, the success rate of induction was assessed according to the odds ratio (OR) and its 95% confidence interval (CI). For secondary outcomes, due to the low incidence of adverse events, the Firth regression model with penalization was applied, with the OR and its 95% CI reported as statistical measures. For non-normally distributed

quantitative data, which were not, the Mann–Whitney *U*-test was employed to calculate the median difference, and the Hodges-Lehmann estimator to estimate the CI. Repeated-measures data were analyzed using repeated-measures ANOVA; when Mauchly's sphericity test was not satisfied, the Greenhouse-Geisser correction was adopted. When an interaction effect was clearly present, simple effect analysis was conducted with the Bonferroni correction applied. Results are based on two-sided tests with a *P*-value ≤ 0.05 was deemed to be a significant finding.

Results

Trial Participants

Between July 2025 and November 2025, a total of 140 elderly patients scheduled for elective hip surgery under general anesthesia at The First People's Hospital of Changzhou were recruited for the study. Of these, 20 patients were excluded, including three with multiple trauma and compound fractures, three with preoperative systolic blood pressure exceeding 180 mmHg, twelve who declined participation (nine refused enrollment and three withdrew from surgical treatment), one with preoperative acute myocardial infarction, and one with suspected acute right heart failure. The remaining 120 patients were enrolled and randomly assigned to either the fospropofol group (Group P, n = 60) or the etomidate group (Group E, n = 60). All enrolled patients completed the study, and no cases were lost to follow-up (Figure 1).

Characteristics of the Patients

The two groups were comparable in terms of age, BMI, cognitive function, ASA classification, comorbidities, surgical etiology, baseline vital signs, and preoperative high-sensitivity troponin T levels ($P > 0.05$) (Table 1).

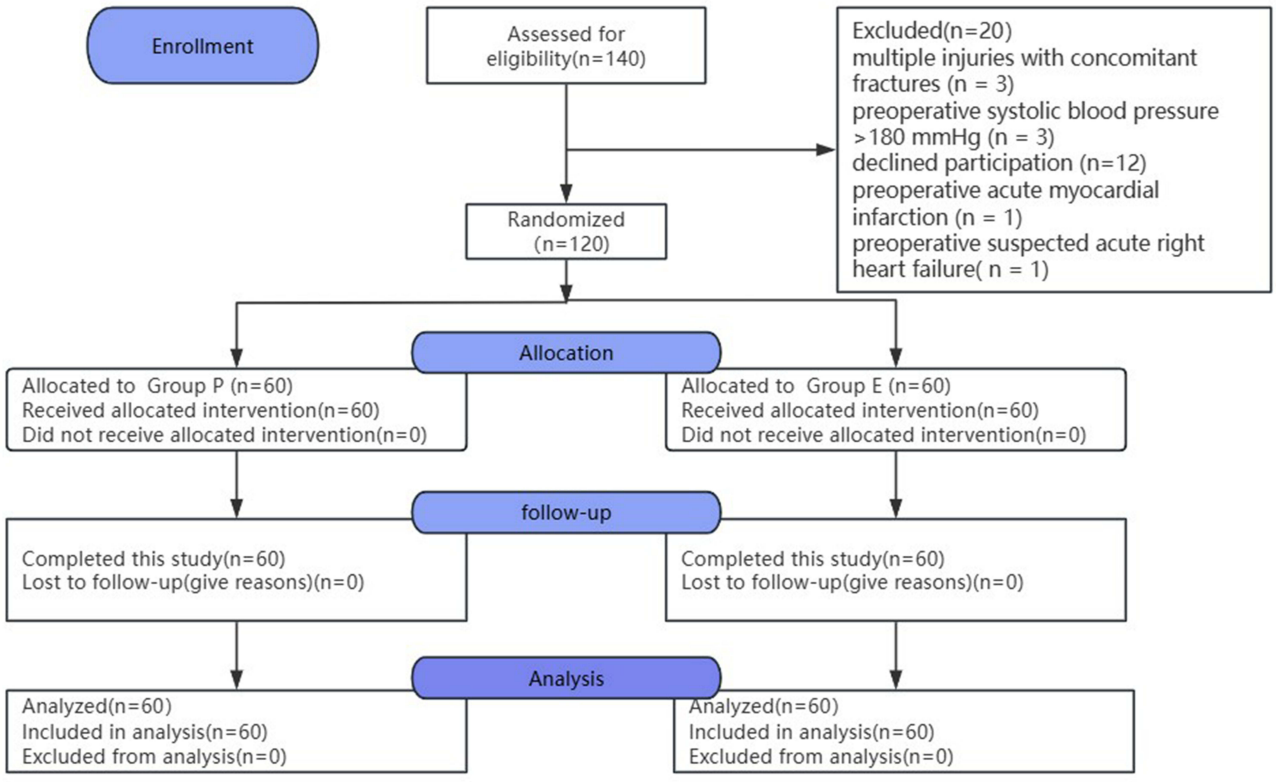

Figure 1 Flowchart of the study.
Abbreviations: Group P, fospropofol group; Group E, etomidate group.

Table 1 Baseline Characteristics of the Patients

	Group P (n = 60)	Group E (n = 60)	*P*-value
Age (years)	70.08 ± 3.26	70.80 ± 3.24	0.223
BMI (kg/m^2)	22.20 ± 3.55	22.92 ± 3.53	0.264
MMSE score	28.43 ± 1.20	28.50 ± 1.00	0.741
ASA I/II/III	0/41/19	0/45/15	0.544
Hypertension	33 (55.0)	28 (46.7)	0.465
Diabetes	12 (20.0)	9 (15.0)	0.632
Surgical etiology			
Fracture	37 (61.7)	43 (71.7)	0.333
Non-fracture	23 (38.3)	17 (28.3)	
Baseline vital signs			
HR (bpm)	77.28 ± 7.96	77.68 ± 7.00	0.770
SBP (mmHg)	136.53 ± 15.94	137.02 ± 16.53	0.871
DBP (mmHg)	81.25 ± 9.46	79.63 ± 9.53	0.353
MAP (mmHg)	99.68 ± 10.02	98.76 ± 10.65	0.628
SpO_2 (%)	96.07 ± 1.22	96.10 ± 0.95	0.868
Preoperative hs-TnT (pg/mL)*10^3	6.28 ± 6.40	8.06 ± 12.70	0.333
Operative time (min)	64.50 [60.00, 75.00]	67.50 [60.00, 78.50]	0.403

Notes: Data are given as the mean ± SD, n (%), or median [IQR]. Preoperative hs-TnT values were multiplied by 1000.

Abbreviations: ASA, American Society of Anesthesiologists; bpm, beats per minute; DBP, diastolic blood pressure; Group E, etomidate group; Group P, fospropofol group; HR, heart rate; hs-TnT, high-sensitivity troponin T; MAP, mean arterial pressure; MMSE, Mini-Mental State Examination; SBP, systolic blood pressure.

Primary Outcome

The time to reach LOC in group P was longer than for group E (98.50 [74.00, 127.50]s vs. 40.00 [34.00, 44.00]s, $P < 0.001$), with an approximately 2.5-fold delay in onset that is consistent with the prodrug nature of fospropofol, which requires hydrolysis by alkaline phosphatase to release active propofol (Table 2).

Secondary Outcomes

Despite the slower onset, the induction success rate was 100% in both groups, indicating that the delayed onset does not compromise the effectiveness of induction. The incidence of myoclonus in group P was significantly lower than that in group E (1.67% vs. 31.67%, P < 0.001), but the incidence of paresthesia (primarily itching) was higher in group P (15.00% vs. 0.00%, P = 0.001). The proportion of patients requiring additional remifentanil supplementation before intubation was lower in group P than in group E (6.67% vs. 20.00%, P = 0.033), and both propofol consumption per unit time and extubation time were also shorter in group P (P < 0.05). The incidence of postoperative nausea and vomiting within 0–24 hours was lower in group P than in group E (11.67% vs. 26.67%, P = 0.038). There were no significant differences between the two groups in the number of vasopressor administrations, atropine use, remifentanil consumption per unit time, incidence of PONV during the recovery period or at 24–48 hours, incidence of delirium at any time period, VAS scores and the number of rescue analgesia events at different time points, or hs-TnT level at 24 hours postoperatively (P > 0.05) (Table 2). Bradycardia (HR < 50 bpm) during intubation and positioning occurred in 3 patients in Group P and 2 patients in Group E, with no significant difference between the groups. All episodes were transient and resolved without sequelae following atropine administration (0.3–0.5 mg).

The results of repeated-measures ANOVA showed that the main effect of time was significant for both HR and SBP ($P < 0.001$), showing that both physiological parameters changed over time during the anesthesia induction process. The time × group interaction effect ($P < 0.001$) suggested that the effects of fospropofol and etomidate on HR and SBP differed during induction, with these differences varying over time (Table 3). The increase in SBP was significantly lower in group P than in group E, primarily occurring within the time range of immediately after tracheal intubation to 10 min after positioning (Table 4 and Figure 2). It is noteworthy that HR in group P was lower than in group E during most time

Table 2 Primary and Secondary Outcomes

	Group P (n = 60)	Group E (n = 60)	*P*-value
Primary outcome			
Time to LOC (s)	98.50 [74.00, 127.50]	40.00 [34.00, 44.00]	< 0.001
Secondary outcomes			
Induction success rate	60 (100%)	60 (100%)	1.000
Number of vasopressor administrations	1.00 [0.00, 2.00]	0.00 [0.00, 2.00]	0.217
Atropine	3 (5.0)	2 (3.3)	1.000
Injection pain or paresthesia	9 (15.00)	0 (0.00)	0.001
Myoclonus	1 (1.67)	19 (31.67)	< 0.001
Remifentanil supplementation	4 (6.67)	12 (20.00)	0.033
Propofol consumption per unit time (mg/min)	3.40 [2.50, 4.25]	4.18 [3.83, 4.62]	< 0.001
Remifentanil consumption per unit time (μg/min)	5.08 [4.07, 8.08]	5.95 [4.81, 7.04]	0.339
Extubation time (min)	20.00 [12.75, 28.00]	27.00 [19.75, 30.25]	0.020
PONV			
During recovery	7 (11.67)	13 (21.67)	0.149
0–24 h	7 (11.67)	16 (26.67)	0.038
24–48 h	3 (5.00)	1 (1.67)	0.355
Delirium			
During recovery	3 (5.00)	2 (3.33)	0.675
0–24 h	1 (1.67)	0 (0.00)	0.466
24–48 h	1 (1.67)	1 (1.67)	1.000
VAS score			
Before discharge from the PACU	2.00 [0.00, 2.00]	2.00 [0.00, 2.00]	0.502
0–24 h	2.00 [2.00, 3.00]	3.00 [2.00, 3.00]	0.350
24–48 h	3.00 [2.75, 3.00]	3.00 [3.00, 4.00]	0.222
Rescue analgesia			
During recovery	4 (6.7)	2 (3.3)	0.675
0–24 h	8 (13.3)	11 (18.3)	0.617
24–48 h	11 (18.3)	21 (35.0)	0.063
hs-TnT level at 24 h postoperatively (pg/mL)*10^3	5.75 [4.08, 9.00]	5.60 [4.20, 8.40]	0.823

Note: Data are given as the mean ± SD, median [IQR], or n (%).
Abbreviations: Group E, etomidate group; Group P, fospropofol group; VAS score, Visual Analogue Scale; LOC, loss of consciousness; PONV, postoperative nausea and vomiting; hs-TnT, high-sensitivity troponin T.

Table 3 Repeated-Measures ANOVA for HR and SBP

	Effect	*F*-value	*P*-value	Ges
HR				
	Group	11.25	0.001	0.070
	Time	116.4	< 0.001	0.173
	Time × Group	19.39	< 0.001	0.034
SBP				
	Group	4.61	0.034	0.023
	Time	31.07	< 0.001	0.097
	Time × Group	17.44	< 0.001	0.057

Abbreviations: Group E, etomidate group; Group P, fospropofol group; HR, heart rate; SBP, systolic blood pressure.

periods (Table 5 and Figure 3). These findings indicate that group P demonstrated better control over both BP and HR during the early stages of induction, specifically during tracheal intubation and positioning, with the effects gradually converging with those of group E thereafter.

Table 4 Magnitude of Change in Systolic Blood Pressure Relative to Baseline at Each Time Point

Time	Group P (mmHg)	Group E (mmHg)	Statistic	Adjusted *P*-value
T1-T0	−6.77 ± 25.42	−5.42 ± 23.05	−0.32	0.748
T2-T0	−12.37 ± 23.95	14.40 ± 22.72	−6.5	< 0.001
T3-T0	−25.40 ± 23.98	−6.63 ± 23.37	−4.2	< 0.001
T3.5-T0	−34.88 ± 24.91	−14.43 ± 28.44	−4.02	< 0.001
T3.10-T0	−30.22 ± 22.78	−15.80 ± 26.25	−2.93	0.005
T4-T0	−18.40 ± 23.94	−10.50 ± 24.93	−1.55	0.127
T5-T0	−11.75 ± 24.06	−13.35 ± 23.39	0.345	0.731
T6-T0	−16.72 ± 22.08	−19.08 ± 23.72	0.517	0.607
T7-T0	−17.68 ± 20.75	−24.12 ± 23.96	1.45	0.154
T8-T0	−19.08 ± 20.83	−26.35 ± 23.03	1.69	0.096

Abbreviations: Group E, etomidate group; Group P, fospropofol group; T0, baseline level; T1, loss of consciousness; T2, immediately after tracheal intubation; T3, positioning; T3.5, 5 min after positioning; T3.10, 10 min after positioning; T4, skin incision; T5–T8, 5, 10, 15, and 20 min after skin incision.

Discussion

This study compared the safety and efficacy of fospropofol versus etomidate for the induction of general anesthesia in elderly patients undergoing hip surgery. The main findings indicate that fospropofol can be effectively used for anesthesia induction in this population and offers unique clinical advantages.

The loss of consciousness (LOC) time in the fospropofol group was significantly longer than that in the etomidate group (98.5 seconds vs. 40.0 seconds, $p < 0.01$), which is consistent with its nature as a water-soluble prodrug that slowly releases active propofol following hydrolysis by alkaline phosphatase, creating a "buffer effect".[12] Despite its slower onset, it is precisely this sustained-release characteristic that resulted in smaller fluctuations in blood pressure and heart rate in the fospropofol group immediately after tracheal intubation (T2) compared to the etomidate group, indicating a better inhibitory effect on intubation-induced sympathetic activation.

In contrast, although etomidate has minimal cardiovascular depressive effects, it fails to effectively inhibit intubation-induced sympathetic activation. In the present study, the additional remifentanil requirement in the fospropofol group was reduced by 66.65% compared with the etomidate group, further confirming its inherent anti-stress properties. This buffering effect also helps to effectively reduce the risk of intraoperative awareness during procedures such as deep venous puncture and repositioning, providing anesthesiologists with more operational time and ensuring patient comfort and safety during these critical steps.[13]

The findings of the present study differ from those of Li et al[14] The discrepancy may be attributed to patients receiving sufentanil (0.1 μg/kg) prior to the initial dose in the present study. Sufentanil not only improved the success rate of sedation but also reduced the incidence of post-injection pruritus from 62% as reported in previous clinical studies to 15% in this study, with a lower severity of pruritus.[10] Post-injection pruritus, as the most notable adverse reaction to fospropofol disodium, is described in the clinical application guidelines as generally mild to moderate and transient, without serious consequences.[9] Nevertheless, it may affect patient comfort during the induction period. Previous studies have indicated that interventions targeting opioid receptors may alleviate pruritus symptoms.[15] In the present study, the reduction in the incidence and severity of pruritus associated with sufentanil may be related to its agonist effect on opioid receptors.

The effect of fospropofol on circulatory stability is complex. The significant interaction effect confirms that the two drugs exhibit distinct patterns of influence. Group P showed smaller fluctuations during the stress period, but a decrease in BP may occur 10 min after drug administration, particularly in elderly patients requiring repositioning, reflecting its cardiovascular depressant effect rather than a simple "stabilizing" action. A notable finding was that systolic blood pressure in the fospropofol group decreased by 25.40 mmHg from baseline during positioning (T3), whereas it decreased by only 6.63 mmHg in the etomidate group. This "positional hypotension" may result from a combination of cardiovascular depression induced by fospropofol and hemodynamic redistribution associated with hip positioning. Although

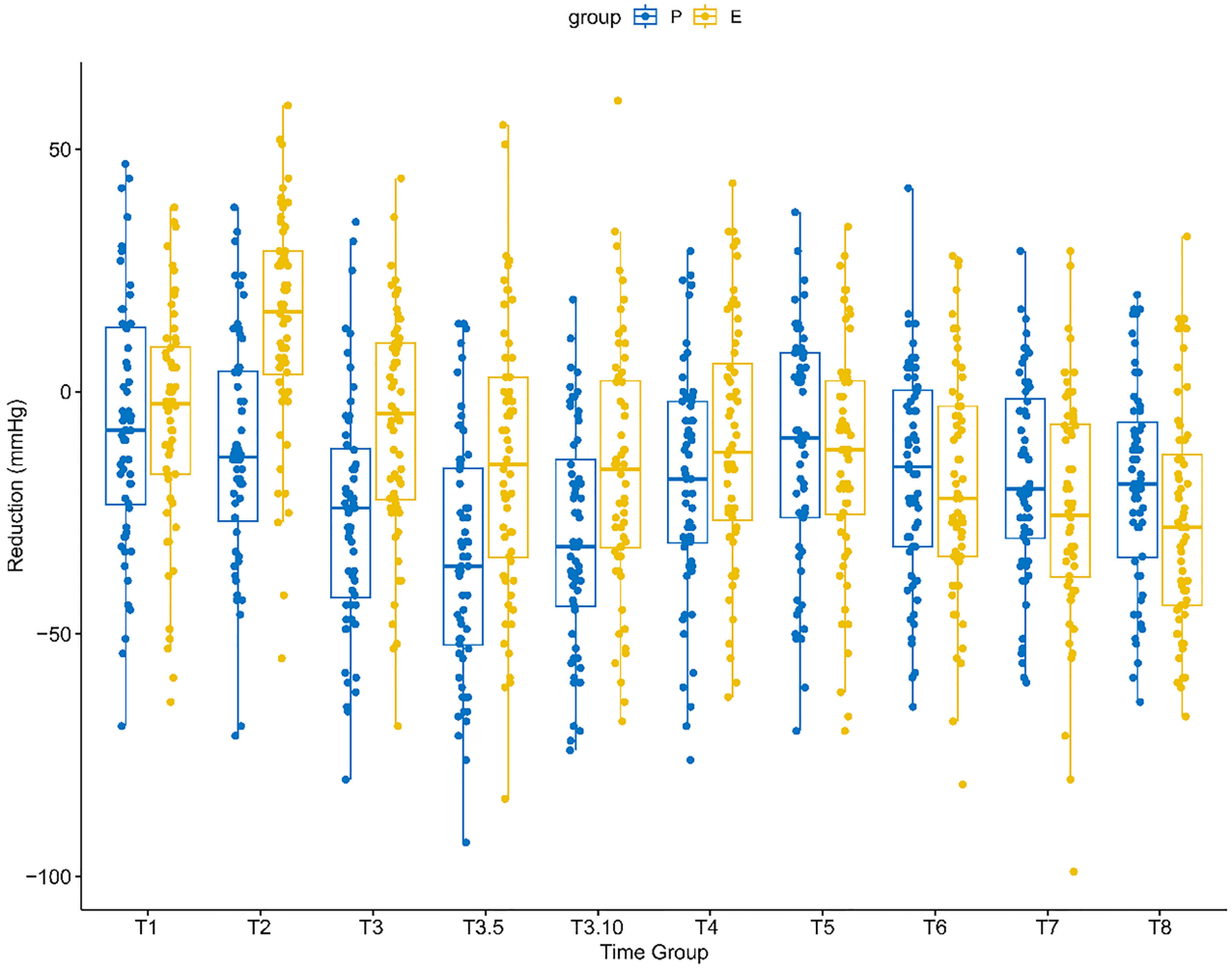

Figure 2 Box plot of systolic blood pressure changes from baseline at different time points. Reduction (mmHg) represents the magnitude of change in systolic blood pressure (SBP) from baseline (T0). Time Group represents the different time points for each group.
Abbreviations: Group P, fospropofol group; Group E, etomidate group; T0, baseline level; T1, loss of consciousness; T2, immediately after tracheal intubation; T3, positioning; T3.5, 5 min after positioning; T3.10, 10 min after positioning; T4, skin incision; T5–T8, 5, 10, 15 and 20 min after skin incision.

generally well tolerated, this finding suggests that for patients receiving fospropofol, particularly those with preexisting hypovolemia or low baseline blood pressure, careful patient positioning and adequate preload should be ensured. Although there was no difference in vasopressor use between the two groups, the high incidence of hypertensive events in group E contrasts sharply with the tendency toward hypotension in group P, indicating different risk profiles for the two drugs. Clinical application should be individualized, based on a patient's baseline condition: caution is warranted for hypovolemic patients regarding the risk of hypotension with fospropofol disodium, whereas hypertensive patients should avoid the sharp fluctuations associated with etomidate. At the same time, care should be taken to prevent termination of anesthesia and to avoid hemodynamic fluctuations caused by indiscriminate supplementation of maintenance anesthetic agents.[16,17]

Our study also confirms the absolute advantage of fospropofol in reducing myoclonus. The incidence of myoclonus with etomidate can be as high as one-third, which may lead to secondary injuries and increase surgical risks in patients with hip fractures, significantly limiting its clinical application.[18] Fospropofol disodium nearly eliminates this adverse reaction, representing one of its most critical clinical benefits. Although postoperative cortisol levels or adrenal function were not measured in this study, the absence of clinically apparent adrenal insufficiency in the etomidate group is reassuring.

Table 5 Magnitude of Change in Heart Rate Relative to Baseline at Each Time Point

Time	Group P (bpm)	Group E (bpm)	Statistic	Adjusted *P*-value
T1-T0	−9.60 ± 12.30	−1.97 ±11.66	−3.98	< 0.001
T2-T0	−5.90 ± 13.91	14.03 ±15.64	−7.91	< 0.001
T3-T0	−10.57 ± 11.54	−2.23 ±13.83	−3.78	< 0.001
T3.5-T0	−14.82 ± 11.71	−8.08 ±12.44	−3.19	0.002
T3.10-T0	−16.57 ± 11.60	−9.62 ±13.36	−3.17	0.002
T4-T0	−16.45 ± 12.27	−10.30 ±13.50	−2.81	0.007
T5-T0	−15.58 ± 12.69	−11.72 ±12.59	−1.69	0.096
T6-T0	−16.63 ± 13.11	−12.75 ±12.34	−1.64	0.106
T7-T0	−16.22 ± 13.22	−13.52 ±12.55	−1.21	0.230
T8-T0	−16.65 ± 12.21	−13.42 ±12.06	−1.51	0.136

Abbreviations: bpm, beats per minute; Group P, fospropofol group; Group E, etomidate group; T0, baseline level; T1, loss of consciousness; T2, immediately after tracheal intubation; T3, positioning; T3.5, 5 min after positioning; T3.10, 10 min after positioning; T4, skin incision; T5–T8, 5, 10, 15, and 20 min after skin incision.

The Expert Guidance on the Clinical Application of Fospropofol Disodium indicates that for general anesthesia induction, the recommended dose of fospropofol disodium should be between 10 and 15 mg/kg, which can be adjusted based on patient condition and surgical requirements.[9] Considering the reduced hepatic blood flow, decreased metabolic capacity, and slower drug clearance in elderly patients, a lower dose within the recommended range should be used. A review by Guan et al also reported that different doses of fospropofol can be used for the induction of anesthesia for various types of surgeries.[19] Wu et al[13] confirmed that 10 mg/kg is effective and safe for anesthesia induction in adults. Therefore, this study selected 10 mg/kg as the minimum effective starting dose for elderly patients, aiming to ensure anesthetic efficacy while reducing the risk of drug accumulation and adverse reactions.

Elderly patients undergoing hip surgery exhibit both "frailty" and "stress susceptibility".[20] This study provides evidence-based support for anesthetic selection in this population: for patients with hypertension, coronary heart disease, anticipated difficult intubation, or significant fracture displacement, fospropofol disodium is a preferable option; whereas for patients with hypovolemia or cardiac insufficiency, etomidate retains its value.[21]

This study has several limitations. First, due to the different physical appearances of fospropofol and etomidate, the personnel administering the drugs could not be blinded, representing a potential source of bias. Future studies may consider using identical opaque packaging or third-party blinding. Second, restricting the age range to 65–74 years (young-old) limits the generalizability of our findings to the "old-old" (≥75 years) and "oldest-old" (≥85 years) populations, who exhibit higher degrees of frailty, lower drug clearance, and greater perioperative risk. Clinical research on fospropofol is particularly limited in elderly patients, given its relatively short history of clinical use. Older adults represent a heterogeneous population, with distinct health status profiles among the young-old, old-old, and oldest-old individuals. We deliberately restricted the age range to a young-old cohort as an exploratory step, aiming to establish a foundation for future expansion to more advanced-age patient populations.[22,23] Third, patients with severe cardiac, pulmonary, hepatic, or renal insufficiency were excluded, which limits the generalizability of our findings to elderly patients with significant comorbidities. Fourth, postoperative delirium was assessed only up to 48 hours. Given that delirium can occur beyond this time window, our findings may underestimate the true incidence of postoperative cognitive dysfunction. Fifth, this was a single-center study, and the conclusions need to be validated through multicenter studies. Sixth, although the analysis of primary outcome measures was rigorous, post hoc pairwise comparisons of repeated measures data were not strictly corrected for multiple testing; therefore, the interpretation of some secondary findings should be cautious. Future research will focus on validating these findings in more fragile patient populations and exploring combination regimens to optimize the induction experience with fospropofol disodium (eg, how to effectively prevent pruritus).

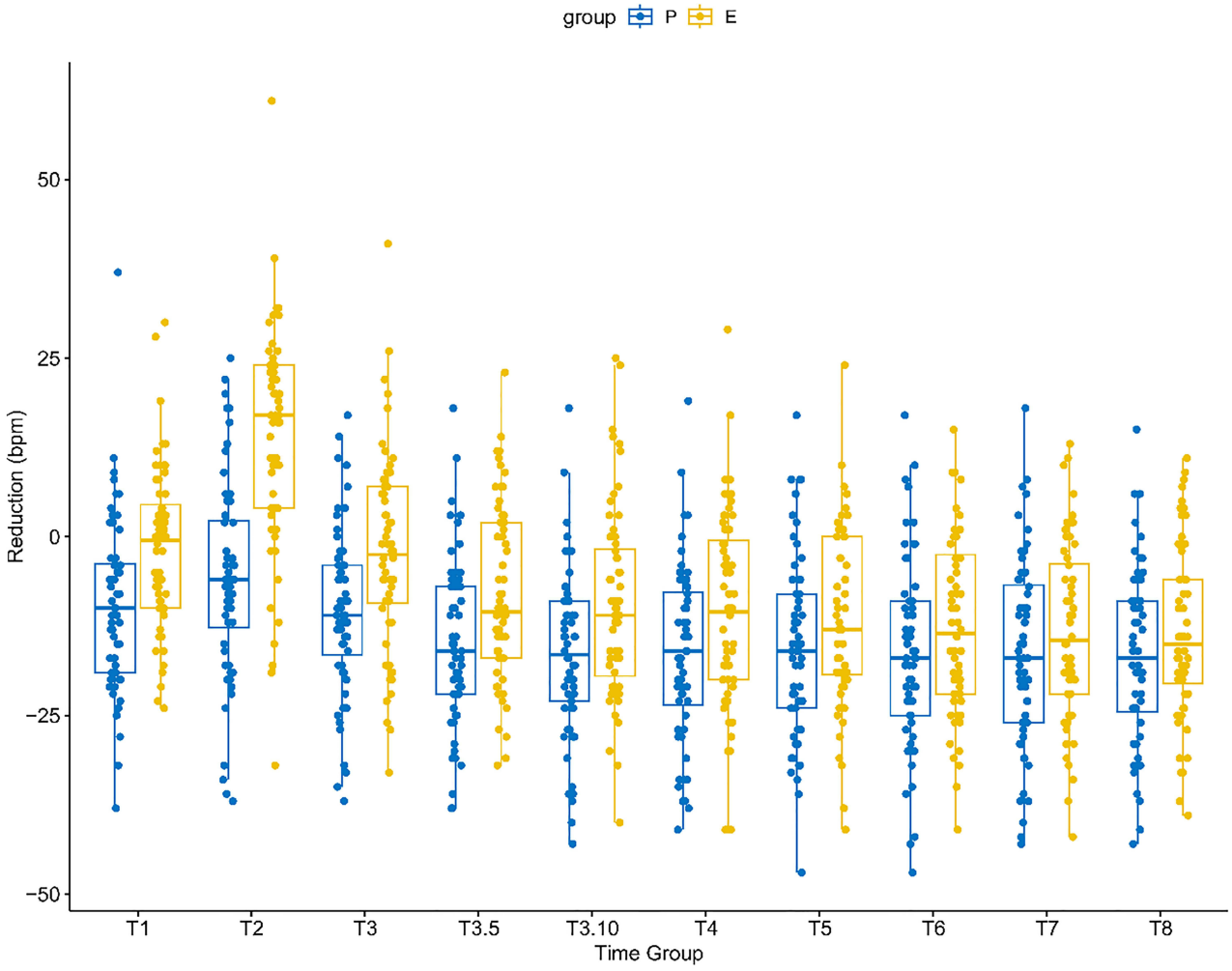

Figure 3 Box plot of heart rate changes from baseline at different time points. Reduction (bpm) represents the magnitude of change in heart rate (HR) relative to baseline (T0); Time Group represents the different time points for each group.
Abbreviations: bpm, beats per minute; Group P, fospropofol group; Group E, etomidate group; T0, baseline level; T1, loss of consciousness; T2, immediately after tracheal intubation; T3, positioning; T3.5, 5 min after positioning; T3.10, 10 min after positioning; T4, skin incision; T5–T8, 5, 10, 15 and 20 min after skin incision.

Conclusions

In elderly patients aged 65–74 years undergoing hip surgery, fospropofol disodium demonstrates comparable induction success rates to etomidate, with superior hemodynamic control during intubation and positioning, as well as a significantly lower incidence of myoclonus. However, its slower onset and higher incidence of pruritus represent factors that require individualized clinical trade-offs. These findings support fospropofol as a viable alternative to etomidate in this specific patient population, particularly for those with hypertension, anticipated difficult intubation, or risk of myoclonus-related injury.

Abbreviations

ASA, American Society of Anesthesiologists; BIS, bispectral index; BP, blood pressure; CI, confidence interval; group E, etomidate group; group P, fospropofol group; HR, heart rate; LOC, loss of consciousness; OR, odds ratio; PONV: Postoperative Nausea and Vomiting; SBP, systolic blood pressure; SPI, Surgical Pleth Index.

Data Sharing Statement

The individual participant data underlying this article were subject to ethical approval and cannot be shared publicly. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of The First People's Hospital of Changzhou/The Third Affiliated Hospital of Soochow University [Approval No. (2025) Teaching 042]. Written informed consent was obtained from all patients.

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An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified with PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR (www.parinc.com).

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.

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