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CLINICAL TRIAL REPORT

Effects of Sevoflurane Versus Propofol Total Intravenous Anaesthesia on Renal Function in Elderly Patients Undergoing Hip Fracture Surgery: A Randomised Controlled Trial

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Purpose: The impact of propofol-based total intravenous anaesthesia (TIVA) versus sevoflurane anaesthesia on renal function remains uncertain. We investigated the effect of anaesthetic type (propofol or sevoflurane) on renal function in elderly patients undergoing hip fracture surgery.

Patients and Methods: In this randomised controlled trial, 66 elderly patients scheduled for hip fracture surgery were randomly allocated to either propofol or sevoflurane maintenance anaesthesia. The primary outcome was estimated glomerular filtration rate (eGFR) 1 hour postoperatively.

Results: The mean age was 70 yr and 53% were female. Compared with the sevoflurane group, the propofol group exhibited significantly higher eGFR levels at 1 hour postoperatively (mean [SD]: 89.4 [13.4] vs 80.1 [17.3] mL min^{-1} $1.73m^{-2}$; difference=9.34 mL min^{-1} $1.73m^{-2}$; 95% CI, 1.88 to 16.80 mL min^{-1} $1.73m^{-2}$; P=0.017). In the secondary outcomes, the propofol group demonstrated significantly higher urine output during anaesthesia (difference=1.11 mL^{-1} kg^{-1} h^{-1}; 95% CI, 0.65 to 1.57 mL^{-1} kg^{-1} h^{-1}; q<0.001), as well as significantly greater urinary sodium excretion both during anaesthesia (difference=2.88 mmol h^{-1}; 95% CI, 2.02 to 3.75 mmol h^{-1}; q<0.001) and in the first 2 postoperative hours (difference=5.08 mmol h^{-1}; 95% CI, 3.20 to 6.97 mmol h^{-1}; q<0.001). Plasma renin levels were significantly lower in the propofol group both during anaesthesia (difference=−93.60 mIU L^{-1}; 95% CI, −108.32 to −78.87 mIU L^{-1}; q<0.001) and at 1 h postoperatively (difference=−27.90 mIU L^{-1}; 95% CI, −42.62 to −13.17 mIU L^{-1}; q<0.001). All other secondary and safety outcomes were comparable between groups. After adjustment for baseline covariates, the analysis yielded consistent results. In subgroup analyses, there was no significant difference in eGFR at 1 hour postoperatively between the propofol and sevoflurane groups.

Conclusion: Propofol-based TIVA was associated with higher eGFR at 1 hour postoperatively, along with increased urine output, greater urinary sodium excretion, and lower plasma renin levels during anaesthesia in elderly patients compared with sevoflurane anaesthesia. These findings warrant further investigation to determine their implications for long-term renal outcomes and intraoperative fluid management in this vulnerable population.

Trial Registration: Chinese Clinical Trial Registry (ChiCTR2300070049).

Keywords: Hip fracture surgery, propofol, renal function, renin, sevoflurane, sodium excretion

Introduction

Patients undergoing hip fracture surgery are at high risk of postoperative complications and mortality.[1,2] Acute kidney injury (AKI) is one of the most prevalent postoperative complications.[3] In elderly patients, age-related renal alterations,

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including reduced renal mass, vascular sclerosis, and a significant decline in functional renal reserve, predispose them to renal vulnerability.[4] Those changes, when compounded by anaesthesia-induced impairment of renal adaptation to haemodynamic fluctuations and diminished responsiveness to vasodilatory stimuli, further increase the risk of post-operative renal dysfunction.[5] The reported incidence of postoperative AKI in elderly populations ranges from 8% to 24%.[6–8] The development of AKI not only prolongs hospital stays but also elevates both short- and long-term mortality, while imposing significant burdens on healthcare systems.[9,10]

Anaesthetic agents significantly influence renal perfusion and functional regulation.[11] However, existing evidence remains inconsistent regarding the comparative renal effects of propofol-based total intravenous anaesthesia (TIVA) versus sevoflurane anaesthesia. A meta-analysis exclusively examining cardiac surgical patients reported significantly reduced incidence of postoperative AKI with volatile anaesthetic agents compared to propofol-based TIVA.[12] Conversely, a comprehensive meta-analysis encompassing all surgical types demonstrated an association between propofol use and decreased AKI occurrence.[13] Furthermore, a recent randomised controlled trial demonstrated no significant difference in postoperative renal function between propofol-based TIVA and volatile anaesthesia in patients undergoing nephrectomy.[14]

Given the uncertain effects of anaesthetic agents on renal outcomes, we conducted this randomised controlled trial to investigated the effects of propofol-based TIVA versus sevoflurane anaesthesia on estimated glomerular filtration rate (eGFR), renal excretory function, and plasma renin concentrations. We hypothesised that, compared with sevoflurane anaesthesia, propofol-based TIVA would lead to higher eGFR at 1 hour postoperatively, accompanied by increased urine output and urinary sodium excretion, as well as reduced plasma renin levels.

Methods

Ethics and Study Design

This single-centre, randomised controlled trial enrolled 66 elderly patients scheduled for hip fracture surgery. Ethical approval was granted by the Ethics Committee of the First Affiliated Hospital of Soochow University (Approval No. 2023–031), and the trial was prospectively registered in the Chinese Clinical Trial Registry (ChiCTR2300070049). The study was conducted in accordance with the Declaration of Helsinki and reported following the Consolidated Standards of Reporting Trials (CONSORT) guidelines (Supplementary material). Written informed consent was obtained from all participants before enrollment.

Subjects

This study enrolled patients aged ≥ 60 years with ASA physical status I–III undergoing hip fracture surgery under general anaesthesia with endotracheal intubation. Exclusion criteria comprised: patient refusal, known hypersensitivity to propofol or sevoflurane, BMI > 37 kg m^{-2}, New York Heart Association (NYHA) class III–IV, insulin-treated diabetes mellitus, pre-existing renal or hepatic disease, and personal/family history of malignant hyperthermia.

Randomisation and Blinding

An independent researcher not involved in patient recruitment, anaesthetic procedures, data collection or outcome assessment generated the random allocation sequence (1:1 ratio) using the Sealed Envelope online randomisation tool (https://www.sealedenvelope.com/simple-randomiser/v1/lists) with variable block sizes of 2 and 4. The allocation sequence was concealed in sequentially numbered, opaque, sealed envelopes. On the day of surgery, the corresponding envelope was handed to the attending anaesthetist after the patient's arrival in the operating theatre. While the attending anaesthetist could not be blinded to the allocated intervention, participants, surgical teams and outcome assessors remained unaware of treatment allocation throughout the study period.

Anaesthesia and Study Interventions

All patients received standardised monitoring upon entry to the operating room, including electrocardiography, non-invasive blood pressure, pulse oximetry (SpO_2), and depth of anaesthesia monitoring (bispectral index [BIS]; Medtronic, Minneapolis,

MN, USA). Anaesthesia was induced with intravenous propofol (1.5–2 mg kg^{-1}), sufentanil (0.3–0.5 μg kg^{-1}), and cisatracurium (0.1–0.2 mg kg^{-1}), followed by tracheal intubation. After induction, invasive arterial blood pressure monitoring was established via arterial catheterization and a Foley catheter was inserted for urine output measurement. Anaesthesia was maintained using either target-controlled infusion of propofol (plasma target concentration: 3–6 μg mL^{-1}) or inhalation of sevoflurane (minimum alveolar concentration [MAC]: 0.7–1.3), according to group allocation. All patients received a continuous intravenous infusion of remifentanil (0.05–1 μg kg^{-1} min^{-1}) for intraoperative analgesia, and cisatracurium (4 mg every 50 minutes) to maintain muscle relaxation. Mean arterial pressure (MAP) was maintained within 20% of the preoperative baseline during surgery, and anaesthetic depth was kept within a BIS range of 40–60. Lactated Ringer's solution was infused intravenously during surgery to maintain fluid balance, and blood transfusion was administered if haemoglobin levels fell below 70 g L^{-1}. Thirty minutes before the end of surgery, sufentanil 10 μg was administered to control postoperative pain. Postoperative care in both groups was standardised according to routine hospital protocols.

Blood and Urine Collection and Analysis

Blood samples were collected at six predefined time points: (1) prior to anaesthesia induction, (2) immediately following anaesthesia cessation, (3) 1 hour postoperatively, (4) 24 hours postoperatively, (5) 72 hours postoperatively, and (6) 7 days postoperatively. Samples were drawn into two separate tubes: one lithium heparin tube and one ethylenediaminetetraacetic acid (EDTA) tube with Trasylol® 0.5 mL. Urine was collected continuously during anaesthesia, for 0–2 hours postoperatively, and for 2 hours at the 24-hour postoperative time point in the surgical ward, with pooled samples obtained for each period.

Blood and urine samples were collected for measurement of serum creatinine (SCr), estimated glomerular filtration rate (eGFR), blood urea nitrogen (BUN), cystatin C (Cys C), sodium, and potassium concentrations using standard laboratory methods. EDTA-anticoagulated blood samples were immediately placed on ice and centrifuged at 4 degrees Celsius (4000 rpm) for 10 minutes. The separated plasma was aliquoted and stored at −80 degrees Celsius until subsequent analysis of plasma renin concentration and arginine vasopressin (AVP) levels. Plasma renin concentration was quantified using a chemiluminescence immunoassay (Liaison XL analyzer; Diasorin, Saluggia, Italy) following the manufacturer's protocol (Enzo Life Sciences, Farmingdale, NY, USA). AVP concentrations were determined by competitive enzyme-linked immunosorbent assay (ELISA; ADI-900-017; Enzo Life Sciences) according to the manufacturer's instructions.

Study Outcomes

The primary outcome of this study was eGFR at 1 hour postoperatively. The eGFR was estimated using the Chronic Kidney Disease Epidemiology Collaboration equation (http://ckdepi.org/equations/gfr-calculator/).[15] The secondary outcomes included eGFR at 24 hours, 72 hours, and 7 days postoperatively; SCr, BUN, and Cys C at 1 hour, 24 hours, 72 hours, and 7 days postoperatively; urine output during anaesthesia, within 0–24 hours, and within 48–72 hours postoperatively; urinary sodium and potassium excretion, calculated as urinary concentration (mmol L^{-1}) multiplied by urine flow rate (mL h^{-1} ÷ 1000), was recorded during anaesthesia, and at 0–2 hours and 24–26 hours postoperatively; plasma renin and AVP levels during anaesthesia, and at 1 hour and 24 hours postoperatively; and the incidence of AKI within 7 days after surgery. AKI was identified using the Kidney Disease: Improving Global Outcomes (KDIGO) criteria (SCr: > 0.3 mg dL^{-1} increase within 48h or > 50% increase from baseline within 7 days).[16] Safety outcomes included postoperative nausea and vomiting (PONV), respiratory complications, postoperative delirium (POD), postoperative bleeding or thrombosis, stroke, postoperative admission to the intensive care unit (ICU), in-hospital need for renal replacement therapy (RRT), and in-hospital mortality.

Statistical Analysis

We conducted a pilot study involving 20 elderly patients undergoing hip fracture surgery, all of whom received sevoflurane inhalation anaesthesia. The results showed that the eGFR at 1 hour postoperatively was 78.2 ± 8.4 mL min^{-1} $1.73m^{-2}$. Based on previous literature, we anticipated that TIVA with propofol would lead to an 8% increase in

eGFR.[17] To achieve 80% statistical power at a significance level of 0.05, and accounting for a potential dropout rate of 10%, we calculated that 33 patients would be required in each group (PASS 11.0.7; NCSS, LCC, Kaysville, UT, USA).

The normality of data distribution was evaluated using the Kolmogorov–Smirnov test. Continuous variables are presented as mean (standard deviation [SD]) for normally distributed data, or as median (interquartile range [IQR]) for non-normally distributed data. Categorical variables are reported as number (%). Depending on the type and distribution of data, comparisons between groups were made using the independent *t*-test, Mann–Whitney rank-sum test, Chi-square test, or Fisher's exact test, as appropriate. The effect size of propofol vs sevoflurane was assessed using the odds ratio (OR) or difference with 95% confidence interval (CI). We used multivariable logistic regression or linear regression to adjust the primary and secondary outcomes for potential confounding factors, including hypertension, diabetes, type of surgery and preoperative eGFR. Subgroup analyses of the primary outcome were conducted based on sex, BMI, history of hypertension, history of diabetes and type of surgery.

Statistical analyses were conducted based on a modified intention-to-treat approach, which included all randomised patients who underwent surgery and for whom primary outcome data were available. No interim analyses were performed, and missing data were not imputed. All statistical analyses were carried out using R software (version 3.6.0; R Foundation for Statistical Computing). A two-sided P-value < 0.05 was considered statistically significant for the primary outcome. For secondary outcomes, the Benjamini-Hochberg procedure was applied to control for multiple comparisons, with a false discovery rate threshold set at $q < 0.05$. For the safety outcomes, multiple comparisons were not corrected; thus, these results should be interpreted as exploratory.

Results

From April 1, 2023 to July 31, 2024, a total of 87 patients were screened (Figure 1). Of these, 21 patients were excluded, and 66 patients were randomly assigned to the propofol group and the sevoflurane group. All randomised patients

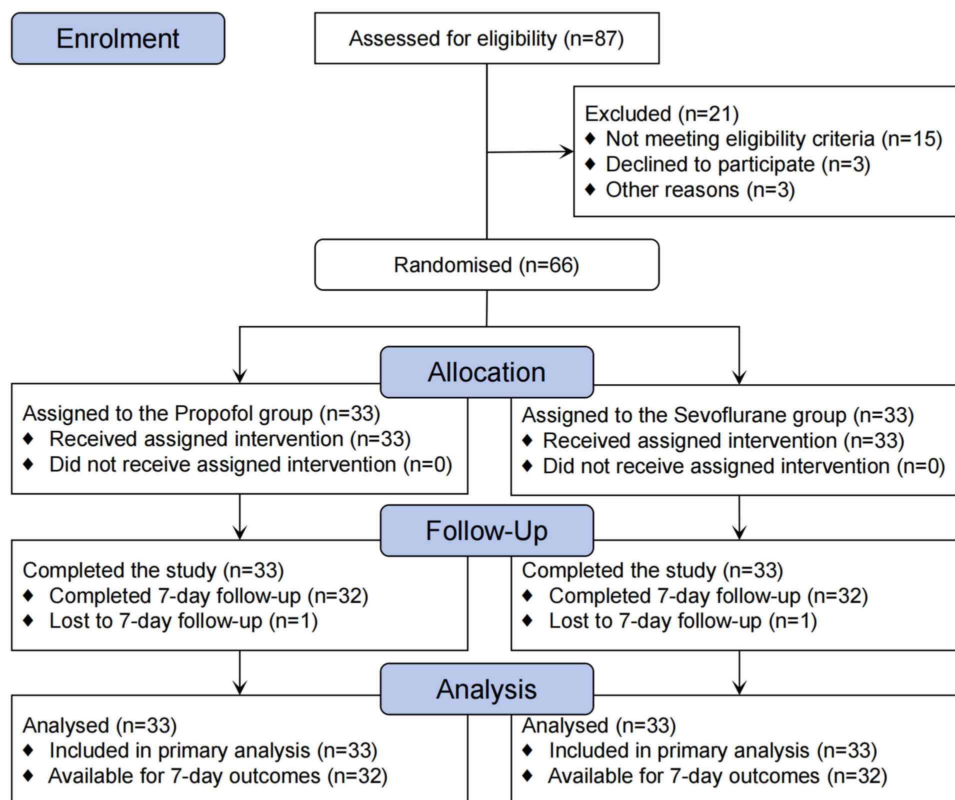

Figure 1 Trial flow diagram.

underwent surgery under their assigned anaesthesia regimens. Primary outcome data were complete for all patients, while secondary outcomes had one case of missing 7-day postoperative data in each group due to loss to follow-up.

Patient characteristics and baseline data were well balanced between the two groups (Table 1). The mean (SD) age was 68.9 (6.7) yr in the propofol group and 71.0 (8.2) yr in the sevoflurane group. The propofol group included 17 (52%) female patients, compared with 18 (55%) in the sevoflurane group. 79% of patients in each group were classified as ASA physical status 1–2. Regarding surgical types, over 70% of patients in each group underwent total hip arthroplasty. Additionally, preoperative baseline renal function parameters were comparable between the two groups.

Perioperative Data

The median (IQR) infusion rate of propofol was 4.9 (4.6–5.1) mg kg^{-1} h^{-1}, while sevoflurane was dosed to give a median MAC (IQR) of 0.6 (0.6–0.7). No significant differences were observed between the two groups in intraoperative analgesic consumption, fluid administration, blood loss, or blood transfusion. The incidence of intraoperative haemodynamic events and the use of vasopressors were comparable between the two groups. MAP remained stable throughout anaesthesia and surgery, without significant differences between the groups. Additionally, the length of surgery, time to extubation, and length of post-anaesthesia care unit (PACU) stay were similar between the two groups (Table 2).

Table 1 Patient and Baseline Characteristics

	Propofol (n=33)	Sevoflurane (n=33)	*P* value
Age (years)	68.9 (6.7)	71.0 (8.2)	0.275
Sex			0.805
Female	17 (52%)	18 (55%)	
Male	16 (48%)	15 (45%)	
BMI (kg m^{-2})	23.5 (2.5)	24.1 (3.2)	0.463
ASA status			1.000
I	4 (12%)	5 (15%)	
II	22 (67%)	21 (64%)	
III	7 (21%)	7 (21%)	
Type of surgery			0.572
Total hip arthroplasty	26 (79%)	23 (70%)	
Hemiarthroplasty	3 (9%)	2 (6%)	
Cannulated screw internal fixation	4 (12%)	8 (24%)	
Comorbidities			
Hypertension	14 (42%)	15 (45%)	0.804
Diabetes mellitus	6 (18%)	5 (15%)	0.741
Coronary artery disease	2 (6%)	1 (3%)	1.000
Cerebrovascular disease	2 (6%)	3 (9%)	1.000
Chronic lung disease	1 (3%)	2 (6%)	1.000
Preoperative mean blood pressure (mmHg)	134.3 (11.4)	136.3 (10.2)	0.456
Preoperative heart rate (bpm)	69.5 (13.3)	67.5 (14.9)	0.568
Preoperative SCr (umol L^{-1})	63.4 (15.1)	63.6 (14.4)	0.969
Preoperative eGFR (mL min^{-1} $1.73m^{-2}$)	93.9 (16.8)	93.1 (16.9)	0.843
Preoperative BUN (mmol L^{-1})	6.55 (2.97)	6.37 (2.68)	0.800
Preoperative Cys C (mg L^{-1})	1.07 (0.38)	1.08 (0.33)	0.855
Preoperative plasma renin (mIU L^{-1})	14.6 (6.2–27.6)	13.9 (6.6–23.6)	0.577
Preoperative plasma AVP (pmol L^{-1})	9.6 (7.5–14.6)	10.4 (8.2–13.2)	0.847

Note: Data are median (inter-quartile range), mean (standard deviation), or n (%).
Abbreviations: ASA, American Society of Anesthesiologists; AVP, arginine-vasopressin; BUN, blood urea nitrogen; Cys C, cystatin c; eGFR, estimated glomerular filtration rate; SCr, serum creatinine.

Table 2 Perioperative Data

	Propofol (n=33)	Sevoflurane (n=33)	*P* value
Minimal alveolar concentration (MAC)	–	0.6 (0.6–0.7)	–
Propofol infusion (mg kg^{-1} h^{-1})	4.9 (4.6–5.1)	–	–
Sufentanil (μg)	35 (35–40)	35 (35–45)	0.166
Remifentanil (μg)	700 (600–770)	720 (560–800)	0.773
Intraoperative fluid (mL)	1150 (1080–1580)	1140 (1100–1640)	0.245
Intraoperative blood loss (mL)	150 (100–250)	200 (100–250)	0.768
Blood transfusion	2 (6%)	4 (12%)	0.669
Intraoperative hemodynamic events			
Hypotension	9 (27%)	7 (21%)	0.566
Bradycardia	5 (15%)	5 (15%)	1.000
Received vasopressors			
Ephedrine	6 (18%)	6 (18%)	1.000
Atropine	3 (9%)	2 (6%)	1.000
Phenylephrine	8 (24%)	7 (21%)	0.769
Mean arterial pressure (mmHg)			
Before induction of anaesthesia	102 (98–109)	101 (99–114)	0.533
Reduction at induction of anaesthesia	19 (14–23)	19 (15–26)	0.758
During surgery	83 (77–92)	85 (81–95)	0.223
After extubation[a]	88 (84–96)	91 (85–99)	0.133
Length of surgery (min)	120 (100–145)	113 (90–130)	0.211
Time to extubation (min)[a]	12 (10–13)	11 (8–16)	0.933
Length of PACU (min)[a]	27 (20–32)	28 (18–35)	0.653

Note: Data are median (inter-quartile range), or n (%). [a]One Propofol patient and two Sevoflurane patients were transferred to the ICU, leaving 32 and 31 patients for analysis, respectively.
Abbreviation: PACU, post-anesthesia care unit.

Primary Outcome

At 1 hour postoperatively, the propofol group demonstrated significantly higher eGFR compared to the sevoflurane group (mean [SD]: 89.4 [13.4] vs 80.1 [17.3] mL min^{-1} $1.73m^{-2}$; difference=9.34 mL min^{-1} $1.73m^{-2}$; 95% CI, 1.88 to 16.80 mL min^{-1} $1.73m^{-2}$; *P*=0.017) (Table 3). Even after adjustment for baseline covariates, the propofol group maintained significantly higher eGFR (difference=8.63 mL min^{-1} $1.73m^{-2}$; 95% CI, 1.48 to 15.79 mL min^{-1} $1.73m^{-2}$; *P*=0.021).

Secondary Outcomes

All secondary outcomes are presented in Table 3. No statistically significant differences in eGFR were found between the groups at 24h, 72h, or 7 days postoperatively, both in unadjusted and adjusted analyses. SCr, BUN, and Cys C levels remained comparable between the two groups at 1h, 24h, 72h, and 7 days postoperatively, in both unadjusted and adjusted analyses.

During anaesthesia, the propofol group exhibited significantly higher intraoperative urine output than the sevoflurane group in unadjusted (difference=1.11 mL^{-1} kg^{-1} h^{-1}; 95% CI, 0.65 to 1.57 mL^{-1} kg^{-1} h^{-1}; $q<0.001$) and adjusted analyses (difference=1.16 mL^{-1} kg^{-1} h^{-1}; 95% CI, 0.75 to 1.57 mL^{-1} kg^{-1} h^{-1}; $q<0.001$). There were no significant differences in urine output between the groups during either the 0–24h or 48–72h postoperative periods. Both unadjusted and adjusted analyses demonstrated significantly higher urinary sodium excretion in the propofol group versus sevoflurane group during anaesthesia and the 0–2h postoperative period, while no significant intergroup difference emerged at 24–26h post-surgery. Urinary potassium excretion showed no statistically significant intergroup differences at any time point in the study.

Both unadjusted and adjusted analyses demonstrated significantly higher plasma renin levels in the sevoflurane group during anaesthesia and the 0–2h postoperative period, with intergroup differences becoming non-significant by 24–26h postoperatively. Plasma AVP levels remained comparable between groups at all measured time points. During the 7-day postoperative period, AKI occurred in 2 patients (6%) in the propofol group and 3 patients (9%) in the sevoflurane group, with no statistically significant difference between groups.

Table 3 Trial Outcomes

	Propofol (n=33)	Sevoflurane (n=33)	OR or Difference (95% CI)	*P* value	*q* value	Adjusted OR or Difference (95% CI)[a]	Adjusted *P* value[a]	Adjusted *q* value[a]
Primary outcome								
eGFR at 1h (mL min^{-1} 1.73m^{-2})	89.4 (13.4)	80.1 (17.3)	9.34 (1.88 to 16.80)	0.017	–	8.63 (1.48 to 15.79)	0.021	–
Secondary outcomes[b]								
eGFR (mL min^{-1} 1.73m^{-2})								
at 24h	92.2 (14.7)	88.0 (17.0)	4.23 (−3.44 to 11.90)	0.284	0.547	3.77 (−0.99 to 8.54)	0.126	0.408
at 72h	93.7 (19.2)	90.6 (14.5)	3.09 (−5.11 to 11.28)	0.464	0.685	3.30 (−2.02 to 8.62)	0.229	0.431
at 7d[c]	94.4 (15.6)	94.2 (14.4)	0.20 (−7.03 to 7.43)	0.957	0.957	−0.07 (−3.97 to 3.83)	0.973	0.973
SCr (umol L^{-1})								
at 1h	65.1 (10.0)	73.2 (17.2)	−8.01 (−14.79 to −1.23)	0.024	0.124	−7.86 (−14.93 to −0.80)	0.033	0.171
at 24h	64.7 (13.7)	68.4 (15.4)	−3.61 (−10.63 to 3.42)	0.318	0.547	−3.61 (−9.88 to 2.67)	0.264	0.431
at 72h	64.4 (21.3)	65.3 (14.6)	−0.92 (−9.72 to 7.89)	0.839	0.897	−1.45 (−9.46 to 6.56)	0.724	0.831
at 7d[c]	63.3 (11.9)	64.0 (11.8)	−0.67 (−6.38 to 5.05)	0.820	0.897	−0.46 (−5.14 to 4.22)	0.848	0.906
BUN (mmol L^{-1})								
at 1h	6.8 (2.5)	7.6 (3.7)	−0.82 (−2.36 to 0.71)	0.296	0.547	−0.81 (−2.37 to 0.75)	0.314	0.464
at 24h	6.6 (3.0)	7.0 (3.0)	−0.40 (−1.84 to 1.04)	0.589	0.761	−0.25 (−1.48 to 0.97)	0.687	0.831
at 72h	6.5 (4.3)	6.7 (2.1)	−0.17 (−1.81 to 1.46)	0.837	0.897	−0.24 (−1.54 to 1.07)	0.723	0.831
at 7d[c]	6.5 (2.9)	6.5 (2.0)	−0.08 (−1.28 to 1.12)	0.898	0.928	−0.08 (−1.10 to 0.95)	0.885	0.915
Cys C (mg L^{-1})								
at 1h	1.19 (0.27)	1.33 (0.41)	−0.14 (−0.31 to 0.03)	0.104	0.403	−0.13 (−0.29 to 0.04)	0.133	0.408
at 24h	1.16 (0.38)	1.29 (0.36)	−0.13 (−0.31 to 0.05)	0.158	0.445	−0.13 (−0.28 to 0.02)	0.100	0.388
at 72h	1.13 (0.42)	1.20 (0.22)	−0.07 (−0.23 to 0.09)	0.402	0.623	−0.08 (−0.21 to 0.06)	0.262	0.431
at 7d[c]	1.10 (0.36	1.12 (0.27	−0.02 (−0.17 to 0.14)	0.834	0.897	−0.02 (−0.14 to 0.10)	0.775	0.858
Urine output (mL^{-1} kg^{-1} h^{-1})								
During anaesthesia	2.5 (1.9–3.2)	1.2 (0.8–1.7)	1.11 (0.65 to 1.57)	<0.001	<0.001	1.16 (0.75 to 1.57)	<0.001	<0.001
0–24h	1.0 (0.3–2.0)	0.7 (0.4–1.6)	0.27 (−0.22 to 0.75)	0.283	0.547	0.32 (−0.12 to 0.75)	0.161	0.408
48–72h	0.9 (0.5–1.7)	0.6 (0.3–1.1)	0.27 (−0.08 to 0.61)	0.137	0.425	0.25 (−0.09 to 0.59)	0.155	0.408
Urinary sodium excretion (mmol h^{-1})								
During anaesthesia	5.7 (4.8–7.1)	2.8 (2.2–4.1)	2.88 (2.02 to 3.75)	<0.001	<0.001	2.87 (1.98 to 3.75)	<0.001	<0.001
0–2h	9.4 (7.0–11.5)	4.4 (3.3–6.2)	5.08 (3.20 to 6.97)	<0.001	<0.001	5.09 (3.14 to 7.04)	<0.001	<0.001
24–26h	8.4 (7.6–11.4)	8.7 (7.3–10.7)	0.52 (−1.00 to 2.04)	0.504	0.710	0.49 (−1.05 to 2.03)	0.535	0.754
Urinary potassium excretion (mmol h^{-1})								
During anaesthesia	2.6 (2.0–3.2)	2.8 (2.3–3.6)	−0.22 (−0.66 to 0.22)	0.335	0.547	−0.27 (−0.72 to 0.17)	0.238	0.431
0–2h	3.7 (3.1–4.7)	4.0 (3.4–5.2)	−0.23 (−0.97 to 0.50)	0.538	0.725	−0.15 (−0.86 to 0.57)	0.686	0.831
24–26h	3.9 (3.3–4.6)	4.2 (3.8–4.7)	−0.43 (−0.99 to 0.13)	0.135	0.425	−0.34 (−0.88 to 0.21)	0.228	0.431

(*Continued*)

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Table 3 (Continued).

	Propofol (n=33)	Sevoflurane (n=33)	OR or Difference (95% CI)	*P* value	*q* value	Adjusted OR or Difference (95% CI)[a]	Adjusted *P* value[a]	Adjusted *q* value[a]
Perioperative plasma renin (mIU L^{-1})								
During anaesthesia	25.3 (15.4–40.7)	115.8 (97.3–148.9)	−93.60 (−108.32 to −78.87)	<0.001	<0.001	−93.63 (−108.05 to −79.21)	<0.001	<0.001
at 1h	19.7 (9.8–35.1)	44.5 (26.0–77.6)	−27.90 (−42.62 to −13.17)	<0.001	<0.001	−27.93 (−42.35 to −13.51)	<0.001	<0.001
at 24h	11.0 (8.3–24.5)	18.3 (10.3–27.3)	−3.17 (−9.35 to 3.01)	0.318	0.547	−4.13 (−9.97 to 1.71)	0.171	0.408
Perioperative plasma AVP (pmol L^{-1})								
During anaesthesia	10.1 (5.0–17.7)	12.9 (7.9–24.0)	−4.33 (−9.81 to 1.16)	0.127	0.275	−4.44 (−10.11 to 1.24)	0.131	0.288
at 1h	13.4 (4.6–22.7)	17.6 (7.9–28.8)	−4.23 (−11.02 to 2.57)	0.227	0.547	−3.58 (−10.41 to 3.26)	0.309	0.464
at 24h	12.7 (9.3–20.3)	15.5 (8.9–28.0)	−2.37 (−7.38 to 2.65)	0.358	0.547	−2.89 (−7.94 to 2.16)	0.266	0.425
AKI 0–7d after surgery[c]	2 (6%)	3 (9%)	0.65 (0.10 to 4.14)	0.644	0.799	0.59 (0.08 to 4.13)	0.595	0.802

Note: Data are median (inter-quartile range), mean (standard deviation), or n (%). [a]Adjusted for baseline covariates (hypertension, diabetes, type of surgery, eGFR) using multivariate logistic regression or generalized linear model. [b]For secondary outcomes, multiple comparisons were corrected using the Benjamini-Hochberg approach to control for false discovery ($q < 0.05$ was applied). [c]n=32.

Abbreviations: AKI, acute kidney injury; AVP, arginine vasopressin; BUN, blood urea nitrogen; CI, confidence interval; Cys C, cystatin c; eGFR, estimated glomerular filtration rate; OR, odds ratio; SCr, serum creatinine.

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Table 4 Safety Outcomes

	Propofol (n=33)	Sevoflurane (n=33)	OR (95% CI)	*P* value
Postoperative nausea and vomiting	4 (12%)	9 (27%)	0.37 (0.10 to 1.34)	0.130
Respiratory complications	2 (6%)	2 (6%)	1.00 (0.13 to 7.55)	1.000
Postoperative delirium	1 (3%)	2 (6%)	0.48 (0.04 to 5.62)	0.562
Postoperative bleeding or thrombosis	1 (3%)	1 (3%)	1.00 (0.06 to 16.69)	1.000
Stroke	0 (0%)	0 (0%)	–	1.000
Postoperative ICU admission	1 (3%)	2 (6%)	0.48 (0.04 to 5.62)	0.562
In-hospital need for RRT	0 (0%)	1 (3%)	0.00 (0.00 to 9.58)	0.997
In-hospital mortality	0 (0%)	0 (0%)	–	1.000

Note: Data are n (%).
Abbreviations: CI, confidence interval; ICU, intensive care unit; OR, odds ratio; RRT, renal replacement therapy.

Safety Outcomes

All safety outcomes were comparable between the two groups (Table 4). Four patients (12%) in the propofol group and nine patients (27%) in the sevoflurane group experienced postoperative nausea and vomiting. Furthermore, two patients (6%) in each group developed pulmonary complications, and one patient (3%) per group had postoperative bleeding or thrombosis. Postoperative delirium was observed in one patient (3%) receiving propofol compared with two patients (6%) receiving sevoflurane. Intensive care unit admission occurred in one propofol-treated patient (3%) versus two sevoflurane-treated patients (6%). No patients required renal replacement therapy in the propofol group, whereas one patient (3%) was recorded in the sevoflurane group. Neither group experienced strokes or in-hospital mortality.

Subgroup Analyses

In subgroup analyses, no significant differences in 1-hour postoperative eGFR were observed between propofol and sevoflurane groups across any strata, including sex (female vs male), BMI (<25 vs ≥25 kg m^{-2}), hypertension (no vs yes), diabetes (no vs yes), or surgical type (total hip arthroplasty vs hemiarthroplasty vs internal fixation) (Figure 2).

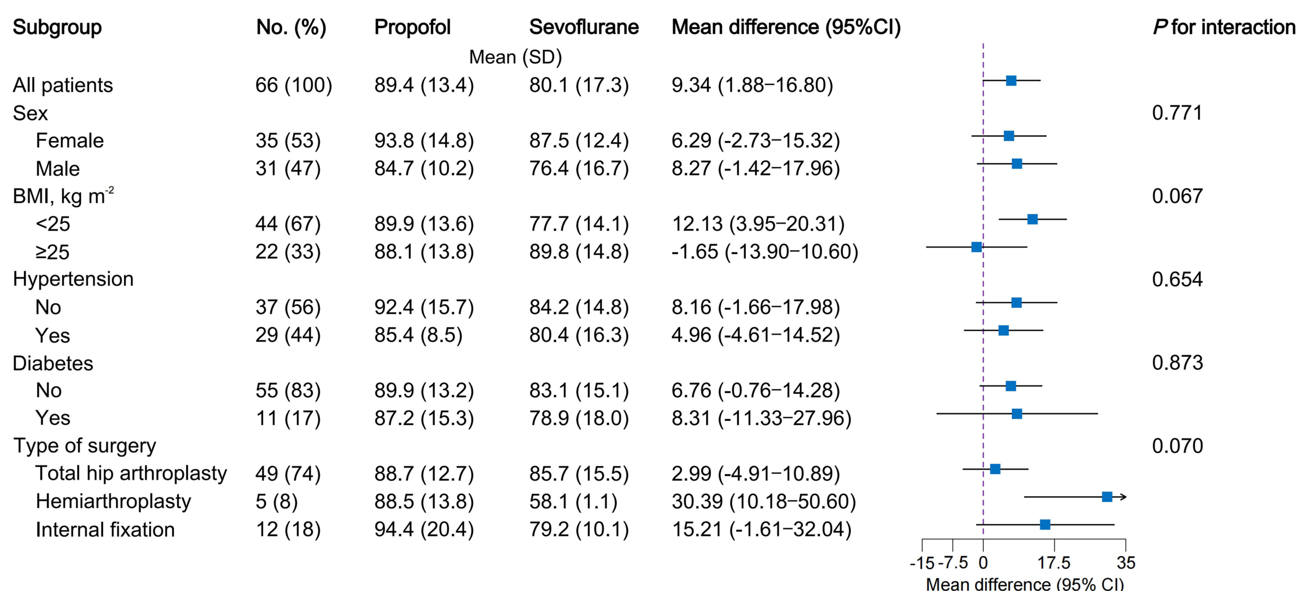

Figure 2 Subgroup analysis of 1-hour postoperative estimated glomerular filtration rate (eGFR).
Abbreviation: CI, confidence interval.

Discussion

In elderly patients undergoing hip fracture surgery, propofol-based TIVA was associated with higher eGFR at 1 hour postoperatively, along with greater urine output, higher urinary sodium excretion, and lower plasma renin levels during anaesthesia when compared with sevoflurane anaesthesia. The safety outcomes were comparable between the two anaesthesia regimens.

Previous studies comparing propofol-based TIVA with inhalational anaesthesia in relation to postoperative renal function have reported inconsistent results, with most focusing on postoperative AKI while giving limited consideration to early functional changes.[13,18,19] In our study, immediate postoperative eGFR at 1 hour was adopted as the primary outcome, and was significantly higher in the propofol group compared to the sevoflurane group. This finding is supported by a study in patients undergoing spinal surgery, in which renal function was assessed under pure anaesthetic conditions before surgical incision.[11] That study reported higher creatinine clearance in the propofol group compared with the sevoflurane group under pure anaesthetic conditions. Moreover, during the first 2 hours postoperatively, creatinine clearance remained higher in the propofol group, despite comparable rates of intraoperative hypotension between the groups. Similarly, in our study, the incidence of intraoperative hypotension did not differ significantly between groups. Given the well-established association between intraoperative hypotension and adverse postoperative renal outcomes,[20,21] the superior renal function associated with propofol is unlikely to be explained by differences in haemodynamic stability. Instead, the early inhibitory effect of sevoflurane on renal function may be attributable to the intrinsic properties of the anaesthetic agent itself.

A study in healthy non-surgical volunteers demonstrated that isoflurane anaesthesia reduced urine output and increased plasma renin concentrations.[22] Similarly, a retrospective cohort study in colorectal surgery patients reported significantly lower urine output with sevoflurane compared with propofol.[23] Furthermore, a randomised clinical trial in patients undergoing cardiac valve surgery found that those receiving sevoflurane required more postoperative diuretics than patients administered propofol.[17] Propofol appeared to exert renoprotection through multifaceted mechanisms, including suppression of connexin 32 activity, upregulation of bone morphogenetic protein-7, and attenuation of tumor necrosis factor-α and monocyte chemoattractant protein-1, mediated by its potent antioxidant and anti-inflammatory properties coupled with microRNA regulatory effects.[24,25] Consistent with these findings, our study showed that the propofol group had significantly greater urine output during anaesthesia, together with higher urinary sodium excretion both intraoperatively and during the first 0–2 hours postoperatively compared with the sevoflurane group. Collectively, these results suggest that propofol exerts less suppressive effect on renal excretory function than sevoflurane.

Reduced urine output may reflect decreased renal blood flow induced by sevoflurane. Recent studies demonstrated that increased renal sympathetic nerve activity is a principal mechanism underlying the reduction in urine output, sodium excretion and renal blood flow during sevoflurane anesthesia.[26,27] Renal sympathetic nerve activity induces both direct renal vasoconstriction and renin release via β-adrenergic receptors activation on the juxtaglomerular cells.[28] The secreted renin subsequently activates downstream effectors, including angiotensin and aldosterone, thereby further amplifying renal vasoconstriction, reducing renal blood flow, and promoting sodium and water retention.[29] In our study, the sevoflurane group had decreased eGFR, lower urine output and urinary sodium excretion, and higher plasma renin levels, findings consistent with the mechanism of sympathetic activation and suppression of renal filtration described above. In addition to renin, AVP represents another major regulatory hormone of renal function. Secreted primarily in response to hypernatremia or hypovolemia, AVP stimulates epithelial cells in the distal tubules and collecting ducts to reabsorb water, thereby promoting urinary concentration and water retention.[30] In our study, AVP concentration was similar between groups at each timepoint, which is in line with previous studies.[11,27] Moreover, the observation that decreased urine output was accompanied by a parallel reduction in sodium excretion further suggests that AVP was not a major contributor to the reduced urine output observed in this study.

In clinical practice, intraoperative oliguria is often interpreted as an indicator of hypovolaemia, with increased fluid administration being a common clinical response.[31] An implication of the present findings is that fluid resuscitation guided by urine output may be less reliable during sevoflurane anaesthesia compared with propofol anaesthesia. At 24 hours postoperatively, no significant differences were observed between the two groups in terms of eGFR, urine

output, urinary sodium excretion, or plasma renin concentration. These findings suggest that the reduction in renal blood flow and excretory function observed during sevoflurane anaesthesia was transient and did not result in sustained parenchymal renal injury. However, for patients with additional AKI risk factors, such as chronic kidney disease, diabetes mellitus, or heart failure, or in those undergoing more complex surgical procedures, sevoflurane exposure may increase the likelihood of renal impairment and potentially affect long-term outcomes.

In this study, safety outcomes showed no significant differences between the two groups. The incidence of PONV was lower in the propofol group compared with the sevoflurane group (12% vs 27%, difference=−15 percentage points), although this difference did not reach statistical significance. These findings align with previous studies showing lower rates of PONV with propofol anaesthesia compared with sevoflurane anaesthesia.[32,33] Moreover, a recent consensus guideline for PONV management recommends the use of propofol anaesthesia as a preventive strategy.[34]

This study has limitations. Firstly, the use of SCr-based eGFR equations may be confounded by muscle mass, nutritional status and non-steady-state creatinine metabolism, particularly in elderly trauma patients. Secondly, the limited sample size resulted in inadequate statistical power for secondary outcomes and subgroup analyses, increasing the risk of Type II errors. Thirdly, the absence of urinary creatinine measurements prevented calculation of fractional excretion of sodium and potassium, potentially missing early compensatory changes in tubular function when relying solely on absolute excretion values. Finally, this study only assessed short-term renal function, leaving the long-term effects uncertain. The generalizability of these single-center findings requires validation in larger future studies.

In conclusion, propofol-based TIVA was associated with higher eGFR at 1 hour postoperatively, along with increased urine output, greater urinary sodium excretion, and lower plasma renin levels during anaesthesia in elderly patients compared with sevoflurane anaesthesia. When considered together with experimental evidence of sevoflurane induced renal sympathetic nerve activation, the observed reductions in eGFR and excretory function may reflect impaired renal blood flow independent of hypotension or hypovolemia. These findings warrant further investigation to clarify their implications for long-term renal outcomes and intraoperative fluid management strategies in this vulnerable population.

Data Sharing Statement

Data are available to researchers on request for the purpose of reproducing the results or replicating the procedure by directly contacting the corresponding author, Xi-Sheng Shan.

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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