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ORIGINAL RESEARCH

Comparison of Remimazolam and Propofol on Post-Induction Hypotension in Elderly Hypertensive Patients: A Randomized Controlled Trial

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Purpose: Post-induction hypotension (PIH) is a common complication in elderly hypertensive patients, posing significant risks of inadequate organ perfusion and increased postoperative morbidity and mortality. This study evaluated the effectiveness of remimazolam in preventing PIH.

Patients and methods: In this randomized controlled trial, 196 elderly hypertensive patients undergoing elective general anesthesia surgery were randomly allocated to either the remimazolam group (Group R) or the propofol group (Group P). Group R received remimazolam at a dose of 0.15–0.2 mg/kg via intravenous infusion at a rate of 6.0 mg/kg/h, while Group P received propofol at a dose of 1.0–1.5 mg/kg via intravenous infusion at a rate of 60 mg/kg/h during induction. Primary outcome was the incidence of PIH. Secondary outcomes included the time-weighted average (TWA) of hypotension, norepinephrine usage, key time-point blood pressures from induction to skin incision, and postoperative quality of recovery-15(QoR-15) scale on postoperative day 1 and day 3 (POD1 and POD3).

Results: Among the 196 patients analyzed, Group R showed a significantly lower incidence of PIH compared to the Group P (46.5% vs 73.2%; $P < 0.001$). Additionally, Group R exhibited reduced frequency of hypotension (0 [0, 2] vs 2 [0, 3], $P < 0.001$), lower total time in hypotension (0 [0, 4] min vs 4 [0, 7] min, $P < 0.001$), lower TWA (0 [0, 0.67] mmHg vs 0.56 [0, 4.72] mmHg, $P < 0.001$), and decreased norepinephrine usage (0 [0, 16] μg vs 16 [0, 28] μg, $P < 0.001$). Hemodynamic stability was better maintained in Group R during anesthesia induction. No significant differences were observed in QoR-15 scores between the two groups on POD1 and POD3.

Conclusion: Compared with propofol, remimazolam significantly reduces the incidence of PIH in elderly hypertensive patients.

Keywords: post-induction hypotension, remimazolam, propofol, elderly hypertensive patients, time-weighted average

Introduction

Post-induction hypotension (PIH) is a common complication of general anesthesia, with an incidence ranging from 36.5% to 96.8%.[1,2] PIH can significantly compromise perfusion to critical organs, including the heart, brain, and kidneys, thereby elevating the risk of severe postoperative complications, such as acute kidney injury, myocardial injury, and the necessity for intensive care unit (ICU) admission.[3–6] In elderly patients, PIH is particularly concerning, as it may lead to postoperative cognitive decline, prolonged hospital stays, increased healthcare costs, and higher mortality rates.[7–9]

Elderly patients are at higher risk for PIH due to age-related structural arterial changes, reduced cardiac function, relative hypovolemia, and impaired physiological regulation, which collectively exacerbate the hemodynamic effects of anesthetic agents.[10] Additionally, elderly patients exhibit poorer tolerance to PIH and are more likely to experience related complications.[11] Studies have shown that PIH is more common in individuals with hypertension, with incidence

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rates as high as 47.6% to 96.8%.[1,2,12] Therefore, it is critical to prioritize the reduction and prevention of PIH in elderly hypertensive patients.

Patient-related risk factors for PIH include advanced age, high American Society of Anesthesiologists (ASA) classification, long-term use of angiotensin receptor blockers (ARBs) or angiotensin-converting enzyme inhibitors (ACEIs), presence of type II diabetes, and a history of hypertension.[12,13] Anesthesia management-related risk factors include the use of opioids and propofol.[13] As these risk factors are difficult to modify, preventive strategies primarily focus on optimizing anesthesia management.

Remimazolam is a novel ultra-short-acting benzodiazepine that acts on γ-aminobutyric acid type A receptors ($GABA_A$) and is rapidly metabolized by tissue esterases into an inactive carboxylic acid metabolite.[14] It has a quick onset of action and rapid recovery, does not rely on liver or kidney function for metabolism, exerts minimal effects on hemodynamics and respiration, and can be reversed by flumazenil.[15] Previous studies have demonstrated that remimazolam effectively reduces the incidence of PIH in patients with ASA physical status III or IV, or undergoing urological surgery, as compared to propofol.[16,17] However, there remains a significant gap in research regarding the use of remimazolam for the prevention of PIH specifically in elderly hypertensive patients, a group particularly at high risk for this complication. Therefore, we conducted a randomized controlled trial to compare the incidence of PIH between remimazolam and propofol in elderly hypertensive patients.

Methods

Study Design and Patient Enrollment

This study was a randomized controlled trial registered with the Chinese Clinical Trial Registry (ChiCTR2300068172, 02/09/2023). Approval was obtained from the Ethics Committee of Xuzhou Central Hospital (Ethics number: XZXY-LK-20230801-0133). The study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines. All patients signed a written informed consent form prior to enrollment. Our study complies with the Declaration of Helsinki.

Participants

This randomized controlled trial was conducted from August 2023 to September 2024. The trial ended after the follow-up of the last participant was completed. A total of 251 participants aged ≥ 60 years undergoing elective general anesthesia, with ASA physical status classification of grade II–III, who were previously diagnosed hypertension (diagnosed if three non-consecutive blood pressure measurements showed systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) were recruited. Exclusion criteria included: 1) History of cardiac surgery, cerebrovascular accidents, alcohol abuse, or heart failure; 2) Presence of severe organic diseases such as liver or renal dysfunction; 3) Coagulation disorders; 4) Severe visual or auditory impairments that hindered communication; 5) Pre-existing psychiatric disorders or long-term use of sedatives or antidepressants; 6) Allergy or contraindication to benzodiazepines, propofol, or their components; 7) BMI > 30 kg/m²; 8) Emergency surgeries, cardiac surgeries, gastrointestinal surgeries, gynecological surgeries, or pheochromocytoma surgeries; 9) Any other conditions deemed unsuitable for inclusion by the investigators (eg severe arrhythmias that significantly affect hemodynamics, poorly controlled hypertension: systolic blood pressure > 180 mmHg, hypovolemia: inferior vena cava (IVC) < 1cm, etc).

Randomization and Blinding

Patients were randomly assigned in a 1:1 ratio to either the remimazolam group (Group R) or the propofol group (Group P) using a computer-generated random sequence. The study personnel sequentially numbered the envelopes and sealed them in opaque envelopes. The surgical doctors, patients, data collectors, and data analysts were all blinded to the study group assignments. The primary anesthesiologist was not blinded.

Anesthesia Management

All patients were instructed to fast from midnight on the day of surgery. Patients continued their medications, including β-blockers, calcium channel blockers (CCBs), nitrates, ACEIs/ARBs, until the day of surgery. Diuretics were discontinued on

the day of surgery, and any compound formulations were stopped 1 week prior and replaced with other antihypertensives. Upon entering the operating room, peripheral venous access was established, and a loading dose of lactated Ringer's solution (6 mL/kg) was administered intravenously. The physiological needs of each patient from fasting until entry into the operating room were calculated based on the medical record system's surgical orders, and any deficits were replenished accordingly. Radial artery puncture and catheterization were performed, and invasive arterial pressure was recorded 5 minutes later as the baseline blood pressure (BP). Continuous monitoring of invasive arterial pressure, heart rate (HR), mean arterial pressure (MAP), blood oxygen saturation, bispectral index (BIS), and end-tidal carbon dioxide was conducted. Prior to anesthetic induction, ultrasound assessment of the inferior vena cava (IVC) was performed. The patient was positioned supine with the head of the bed elevated between 0°-30°, marking the point below the xiphoid process towards the head, and obtaining the long-axis view of the IVC. The IVC diameter was measured 1–3 cm from the entrance to the right atrium.

In Group R, remimazolam was administered for anesthetic induction at a dose of 0.15–0.2 mg/kg via intravenous infusion at a rate of 6 mg/kg/h.[18] Once the eyelash reflex was lost and there was no response to light pricking or shaking, indicating a sedation score of 1 on the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale, cisatracurium (0.15–0.3 mg/kg) was administered at 2 minutes and sufentanil (0.1–5 μg/kg) at 4 minutes. The MOAA/S scale helps medical staff assess the level of consciousness in patients under sedation by observing their responsiveness (Supplementary Figure 1). In Group P, propofol was administered for anesthetic induction at a dose of 1.0–1.5 mg/kg via intravenous infusion at a rate of 60 mg/kg/h, with the same criteria for administering cisatracurium and sufentanil as in Group R. Intubation was performed at 5 minutes, and all patients' anesthetic inductions was managed by the same anesthesiologist. After intubation, BIS was maintained at 45–55. If BIS exceeded 60, maintenance anesthetic drugs were administered early; otherwise, maintenance infusion began 1 minute before skin incision. If MAP decreased by more than 30% from baseline or MAP < 65 mmHg, and if HR > 45 beats/min, norepinephrine (4 μg) was administered; if HR < 45 beats/min, ephedrine (3–6 mg) was given, converted to an equivalent dose of norepinephrine (1 mg of ephedrine is equivalent to 1 μg of norepinephrine), with repeat dosing as necessary. Maintenance anesthesia for both groups consisted of propofol (4–10 mg/kg/h), cisatracurium (0.06–0.12 mg/kg/h), and remifentanil (0.03–0.12 mg/kg/h), adjusted according to surgical needs while maintaining BIS at 45–55. At the end of the surgery, patients were transferred to the PACU (Post-Anesthesia Care Unit) while still intubated. All patients received postoperative analgesia via patient-controlled intravenous analgesia (PCIA), with a formulation of hydromorphone (10 mg) and metoclopramide (30 mg) diluted in 0.9% sodium chloride solution to a total volume of 100 mL, with settings of a background infusion rate of 2 mL/h, a PCIA dose of 0.5 mL per use, and a lockout time of 15 minutes.

Data Collection

All patients underwent routine anesthesia follow-up on the day before the procedure. Baseline data recorded included age, gender, height, weight, ASA classification, hypertension grading, types of antihypertensive medications, left ventricular ejection fraction (LVEF), and history of diabetes. After entering the operating room, baseline measurements of BP, HR, peripheral oxygen saturation, the MOAA/S scale, and IVC diameter and total preoperative fluid intake were recorded. Following anesthesia induction, invasive arterial pressure was monitored in real time, and hemodynamic indicators were recorded at several key time points: baseline blood pressure (T0), before tracheal intubation (T1), immediately after intubation (T2), 5 minutes after intubation (T3), and just prior to skin incision (T4). The quality of postoperative recovery (QoR) was assessed using the QoR-15 scale on postoperative day 1 and day 3 (POD1 and POD3).[19] The QoR-15 scale consists of five dimensions: emotional state, physical comfort, psychological support, physical independence, and pain (Supplementary Figure 2).

The primary outcome measure is the incidence of PIH. This is defined as a MAP reduction of over 30% from baseline and/or a MAP of less than 65 mmHg during the first 20 minutes post-anesthesia induction or between anesthesia induction and the start of skin incision.[20] Previous studies have indicated that this threshold can trigger significant organ dysfunction.[21–23] Secondary outcome indicators include the time-weighted average (TWA) of hypotension,[24,25] frequency of hypotension, total time in hypotension, the usage of vasoactive drugs in both groups from induction to skin incision. Other secondary outcome indicators include blood pressure values at key time points, and scores from the QoR-15 recovery quality scale. Adverse outcome indicators included hemodynamic hyper-responsiveness, defined as an increase

of 30% in systolic blood pressure relative to baseline during anesthesia induction; tachycardia, defined as a HR > 120 beats per minute; hypoxemia, defined as blood oxygen saturation < 90%; coughing; movement reactions; muscle twitching; aspiration; allergic reactions; and malignant hyperthermia.

Sample Size Calculation

Our preliminary results indicated that the incidence of PIH in Group P was 65% (13/20), while in Group R, it was 45% (9/20). Based on these data, we calculated the sample size using PASS 11.0 with $\alpha = 0.05$ and $1 - \beta = 0.8$, resulting in a requirement of 96 patients per group. Given the short observation period for the primary outcome measures in this study and the ease of collecting patient data, we anticipated a lower-than-expected dropout rate. We aimed to enroll 100 patients in each group.

Statistical Methods

Statistical analysis was performed using SPSS 26.0 software. The Shapiro–Wilk test was employed to assess data normality, and Levene's test was used for variance homogeneity. Continuous variables with normal distribution were expressed as mean ± standard deviation (Mean ± SD) and compared between groups using independent two-sample *t*-tests. Non-normally distributed continuous variables were expressed as medians (25th and 75th percentiles) and compared using the Mann–Whitney *U*-test. Categorical variables were presented as counts (percentages) and analyzed using the χ^2-test or Fisher's exact probability method. Repeated measures analysis of variance (ANOVA) was used to compare continuous variables at different time points. All tests were two-tailed, with $P < 0.05$ considered statistically significant. The software used to create the graphs was GraphPad Prism version 10.1 for Windows.

Study Results

As illustrated in Figure 1, from August 2023 to September 2024, a total of 200 patients who met the inclusion criteria were randomly divided into two groups. Three patients were excluded from the group P (two due to difficult airways and one due to a surgery cancellation). One patient was excluded from the group R due to a difficult airway. Ultimately, 196 patients were included in the final analysis. There were no significant differences in demographic data or anesthesia-related characteristics (Table 1).

In the primary outcome measure, 73.2% (71/97) patients in Group P experienced PIH, while 46.5% (46/99) of patients in the Group R experienced PIH during induction (RR, 0.318 [95% CI, 0.175, 0.578]; $P < 0.001$, Table 2). The secondary outcomes during anesthesia induction are depicted in Table 2, patients in Group R had a significantly lower frequency of PIH (0[0, 2] vs 2[0, 3], $P < 0.001$) and total time in PIH (0 [0, 4] vs 4 [0, 7], $P < 0.001$) compared with subjects in Group P. Additionally, the TWA for PIH was lower in the Group R compared to the group P (0 [0,0.67] vs 0.56[0, 4.72], $P < 0.001$). The amount of norepinephrine used in the Group R was also significantly lower than that in the Group P (0 [0, 16] vs 16 [0, 28], $P < 0.001$). There was no significant difference in postoperative recovery quality between the two groups. Adverse events related to anesthesia included high hemodynamic events during induction in the Group P (4 cases) and the Group R (3 cases), all occurring post-double-lumen bronchial intubation. Other adverse events, such as tachycardia, hypoxemia, coughing, movement reactions, muscle twitching, and aspiration, as well as allergic reactions and malignant hyperthermia, showed no significant differences between the two groups (4 cases in Group P and 6 cases in Group R) (Table 2).

Hemodynamic variables before and after induction are shown in Table 3 and Figure 2. The hemodynamic indicators demonstrated significant within-subject effects in SBP, DBP, MAP and HR in both Group P and the Group R ($P < 0.001$). This indicates that SBP, DBP, MAP, and HR all significantly changed over time. The group-time interactions were also statistically significant, suggesting that a cross-over effect was identified between the group and time ($P < 0.001$), with the Group P exhibiting a more rapid decline in blood pressure. The results demonstrated significant differences in SBP, DBP, MAP and HR between patients in the Group P and the Group R ($P < 0.01$), indicating differences between the groups in SBP, DBP, MAP, and HR. Further simple effects pairwise comparisons by Bonferroni correction indicated significant differences between the two groups in SBP, DBP, MAP, and HR at T1; SBP, MAP and HR at T2; and SBP, DBP, and MAP at T3, with significant differences in HR at T4.

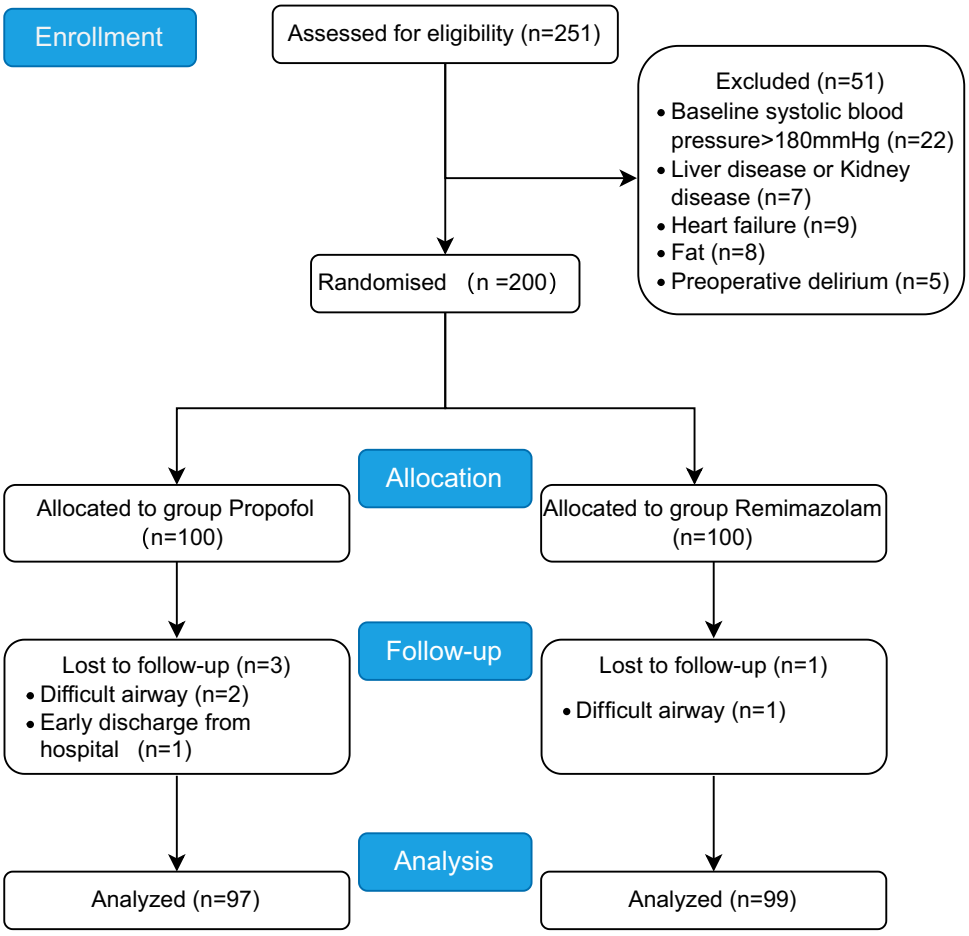

Figure 1 Flow diagram.

Discussion

Currently, it is believed that PIH results from the interplay of multiple factors. The potential pathophysiological mechanisms include preoperative fasting, intestinal preparation, or other bodily conditions that lead to inadequate blood volume;

Table 1 Demographic and Clinical Characteristic

Characteristics	Group Propofol (n=97)	Group Remimazolam (n=99)	P value
Age, median [IQR], years	68 [64, 74]	68 [64, 73]	0.879
Sex, n (%), male	40 (41.20)	49 (49.50)	0.246
Height, mean (SD), cm	162.22±8.17	162.76±8.31	0.646
Weight, mean (SD), kg	64.94±11.04	66.57±11.40	0.311
BMI, mean (SD), kg/cm^2	24.59±3.20	25.05±3.37	0.334
ASA(II/III), n (%)			
II	56 (57.73)	54 (54.55)	0.653
III	41 (42.27)	45 (45.45)	0.653
Type of antihypertensive drugs, n (%)			
ACEI/ARB	65 (67.01)	74 (74.74)	0.233
CCB	32 (32.99)	42 (42.42)	0.173
Diuretic	20 (20.62)	18 (18.19)	0.666
Others	2 (2.06)	3 (3.03)	0.667

(*Continued*)

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Table 1 (Continued).

Characteristics	Group Propofol (n=97)	Group Remimazolam (n=99)	P value
Combination antihypertensive drugs, n (%)	12 (12.37)	9 (9.09)	0.458
Irregularly medication	7 (7.22)	11 (11.11)	0.345
History of hypertension, mean (SD), years	11.71±6.15	11.75±5.94	0.967
Diabetes, n (%)	23 (23.71)	25 (25.26)	0.802
Duration of preoperative fasting, (h)	11.81±2.34	11.79±2.31	0.936
Perioperative fluid intake (mL)	1213.98±280.82	1235.64±267.78	0.581
Baseline hemodynamics, mean (SD), mmHg			
Systolic blood pressure	139.95±20.31	141.03±19.52	0.704
Diastolic blood pressure	73.23±11.76	72.78±10.10	0.774
Mean blood pressure	95.47±13.08	95.53±11.66	0.972
Heart rate	70.78±9.99	71.97±10.67	0.423
Type of surgery, n (%)			
Orthopedics	49 (50.52)	49 (49.50)	0.886
Lung surgery	16 (16.49)	25 (25.25)	0.132
Breast surgery	10 (10.31)	9 (9.09)	0.773
Urology	22 (22.68)	16 (16.16)	0.248

Note: There were no significant differences in the baseline characteristics.
Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiology; ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; CCB, calcium channel blockers.

Table 2 Primary and Secondary Outcomes

Variables	Group Propofol (n=97)	Group Remimazolam (n=99)	P value
Post-induction hypotension, n (%)	71 (73.20)	46 (46.50)	<0.001
Frequency of hypotension	2 [0, 3]	0 [0, 2]	<0.001
Total time in hypotension, (min)	4 [0, 7]	0 [0, 4]	<0.001
TWA, time-weighted average(mmHg)	0.56 [0, 4.72]	0 [0, 0.67]	<0.001
Norepinephrine (μg)	16 [0, 28]	0 [0, 16]	<0.001
Quality of Recovery-15			
Preoperative	118.75±9.53	117.35±9.78	0.310
Postoperative day 1	101.72±8.62	102.71±7.60	0.400
Postoperative day 3	112.32±7.59	113.73±8.39	0.220
Adverse events	8 (8.25)	9 (9.09)	0.834

Notes: Hypotension after induction: Defined Mean blood pressure as less than 65 mmHg or a decrease of greater than 30% from baseline during the first 20 minutes post-anesthesia induction or between anesthesia induction and the start of skin incision.

Table 3 Comparison of Hemodynamics

		T0	T1	T2	T3	T4
SBP	Propofol	139.95±20.31	94.51±14.14	111.55±24.43	103.24±16.74	101.41±13.67
	Remimazolam	141.03±19.52	106.21±18.83[a]	121.90±20.22[a]	111.69±15.79[a]	104.66±13.98
DBP	Propofol	73.23±11.76	53.82±6.32	64.31±12.20	58.40±9.10	59.27±7.11
	Remimazolam	72.78±10.10	58.37±9.93[a]	66.47±9.98	62.28±7.67[a]	58.89±7.88
MAP	Propofol	95.47±13.08	67.86±7.94	80.05±15.61	73.35±10.89	73.32±8.49
	Remimazolam	95.53±11.66	72.07±9.58[a]	84.95±12.34[a]	78.75±9.67[a]	74.14±8.87
HR	Propofol	70.78±9.99	57.62±6.68	62.81±7.34	61.48±5.87	58.54±5.85
	Remimazolam	71.97±10.67	62.48±7.92[a]	66.05±6.99[a]	62.72±5.67	60.21±5.03[a]

Notes: Comparison with groups Propofol, [a]P < 0.05; Bonferroni correction was applied for each variable.
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, Mean arterial pressure; HR, Heart rate; T0, before anesthesia induction (baseline blood pressure); T1, before tracheal intubation; T2, immediately after intubation; T3, 5 minutes after intubation, T4, just prior to skin incision.

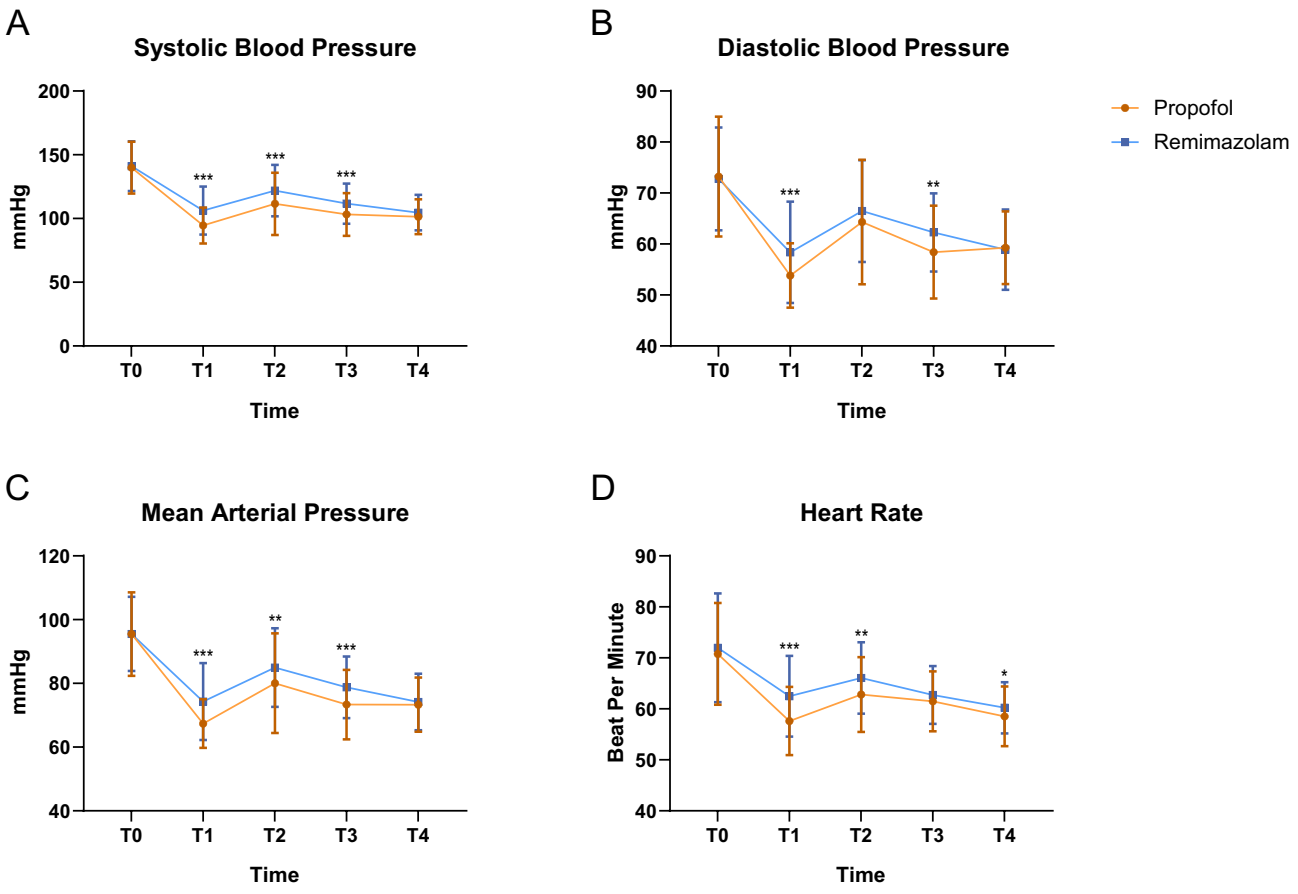

Figure 2 Vital signs at different time points between the two groups; (**A**) SBP at different time points between the two groups; (**B**) DBP at different time points between the two groups; (**C**) MAP at different time points between the two groups; (**D**) HR at different time points between the two groups. *: P<0.05; **: P<0.01; ***: P<0.001.

vasodilation caused by anesthetic drugs, which decreases vascular resistance, alongside venous dilation that reduces venous return, pressure reflex inhibition, and direct cardiac suppression by anesthetic agents; an excessively deep level of anesthesia due to the absence of surgical stimulation from induction until the start of surgery; and patient-related risk factors, such as impaired autonomic regulation in diabetic or hypertensive patients, leading to inadequate cardiac response to low tissue perfusion.

There are several considerations regarding the efficacy of remimazolam compared with propofol in this study. Firstly, based on the ED95 estimates in the corresponding age group, in patients aged over 60 years undergoing endotracheal intubation, the recommended dosage range for remimazolam is 0.14–0.25 mg/kg.[18] According to the latest clinical guidelines, the appropriate dose of propofol for intubation in this age group is 1.0–1.5 mg/kg, which is consistent with our predetermined dosing protocol. To ensure precise drug administration, we employed continuous intravenous infusion via a syringe pump. The infusion was terminated immediately upon achieving the target sedation level, thereby minimizing potential confounding effects associated with variations in dosage and infusion rates on the study outcomes. Secondly, the optimal timing for endotracheal intubation is critical. The MAP decreased maximally at 180 seconds following the remimazolam bolus injection.[18] Previous studies have demonstrated that the decrease in SBP becomes greater and more prolonged with increasing age. In patients over 60 years of age, the half-times for SBP range from 8.87 to 10.22 minutes.[26] Adhering to the principle of patient benefit, the timing of tracheal intubation was determined based on the onset of the analgesic effect of sufentanil. Despite the potential confounding effect on outcome assessment, we observed significant statistical differences in SBP, MAP, DBP and HR between the two groups before tracheal intubation (T1). Furthermore, recent investigations have demonstrated that remimazolam exhibits significantly enhanced synergistic effect with opioids compared to propofol, as evidenced by pharmacodynamic analyses.[27,28] Although a standardized dose

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of sufentanil was administered in the present study, the precise pharmacokinetic and pharmacodynamic interaction models between the investigated agents remain to be fully elucidated in future studies.

In this study, the overall incidence of PIH was 56.69% (117/196), which aligns with previous findings. While there is currently no unified definition of PIH, we adopted diagnostic criteria of a MAP reduction of more than 30% from baseline and/or MAP < 65 mmHg. Previous studies suggested that even transient MAP < 60–70 mmHg can be harmful in non-cardiac surgeries.[29] Therefore, the criteria we selected are clinically significant. Propofol inhibits the release of the excitatory neurotransmitter glutamate and acts on the central inhibitory $GABA_A$ receptor, inducing systemic hypotension through direct myocardial suppression and peripheral vasodilation. Remimazolam shows a high clearance, small volumes of distribution, short half-lives, and a fast onset and recovery of sedation. It is therefore a drug with good controllability. The hemodynamic effects were moderate, and there is no clinically significant effect of remimazolam on cardiac repolarization.[30] We observed that compared to propofol, remimazolam significantly reduced the incidence of PIH during anesthetic induction (RR, 0.318 [95% CI, 0.175, 0.578]; P < 0.001). This may be attributed to remimazolam's superior ability to maintain systemic vascular resistance (SVR) compared to propofol.[31] In addition, a pharmacokinetic and pharmacodynamic study did not observe the impact of age on the pharmacokinetics of remimazolam, suggesting the benefits of remimazolam as an anesthetic induction agent for the elderly.[30] However, one study found that remimazolam did not reduce the incidence of PIH in patients aged 80 and above,[32] likely due to the concurrent use of remifentanil and sevoflurane, both of which significantly affect blood pressure and heart rate, hindering effective compensation during anesthetic induction.

We performed radial artery puncture and catheterization to continuously monitor the patient's hemodynamic parameters. Compared to propofol, remimazolam significantly reduced the frequency of PIH (0 [0, 2] vs 2 [0, 3], P < 0.001), the total time in hypotension (0 [0, 4] vs 4 [0, 7], P < 0.001), the TWA for PIH (0 [0, 0.67] vs 0.56 [0, 4.72], P < 0.001), and the consumption of norepinephrine (0 [0, 16] vs.16 [0, 28], P < 0.001). The low blood pressure TWA reflects not only the severity and duration of hypotension but also minimizes the influence of the period from induction to skin incision (the first 20 minutes). According to our definition of PIH, the maximum occurrence time is 20 minutes. Despite early intervention with norepinephrine, the TWA remains statistically significant. We also analyzed hemodynamic parameters at specific time points. At T1, patients in the Group P had lower SBP, MAP, DBP, and HR compared to those in the Group R. At T2, following tracheal intubation, there were no statistically significant differences in DBP between the two groups. At T4, SBP, MAP, and DBP did not show significant differences, which may be related to the effect of vasopressors in correcting blood pressure.

In this study, we used the QoR-15 scale to measure the quality of postoperative recovery. There were no statistically significant differences in postoperative recovery quality between the two groups, which aligns with previous findings.[33] Recent studies have demonstrated that remimazolam exhibited a non-inferior postoperative recovery quality scores compared to propofol.[33,34] The observed advantage may be attributed to the anti-inflammatory properties of remimazolam, which potentially attenuate systemic inflammatory and stress responses, thereby enhancing postoperative recovery quality.[35,36] Discrepancies with findings of Choi et al, likely stem from demographic and surgical differences: our study focused on elderly hypertensive patients, who recover more slowly postoperatively, and involved surgeries with greater postoperative pain, both of which significantly influence QoR-15 scores. However, one study suggested that remimazolam temporarily impaired recovery quality in patients undergoing urological surgeries, primarily affecting physical comfort and emotional state.[37] We speculate that this may be due to both induction and maintenance of anesthesia using remimazolam in that study. When remimazolam is at the peak of its response curve, adverse desensitization effects and rebound phenomena such as anxiety may occur once it is discontinued.[38] This dose-response relationship potentially explains the absence of significant differences in postoperative recovery quality observed in our study. This finding highlights the importance of timely follow-up assessments to monitor cognitive and psychological status in patients receiving prolonged remimazolam infusion.

Other adverse reactions during anesthetic induction, such as high hemodynamic responses, hypoxemia, tachycardia, coughing, movement responses, reflux aspiration, malignant hyperthermia, and allergies, were not statistically significant. Remimazolam exhibits rapid and effective reversal with flumazenil administration, a pharmacological characteristic that is particularly critical for prompt airway re-establishment in patients with difficult airways. Specifically, there have not

been any observed effects on the ryanodine-1 receptor.[39] This lack of intervention may provide potential benefits for patients with a genetic predisposition to malignant hyperthermia.

However, this study has some limitations. First, the sample size is relatively small, as this is a single-center study that includes elderly patients from only one hospital in China. This limitation may restrict the generalizability of our findings. Second, the study encompasses a broad age range without stratification and lacks restrictions on surgical types. Future research should involve larger, multicenter, multi-ethnic patient populations to investigate whether remimazolam can effectively reduce hypotension during general anesthesia induction across various surgeries. Third, the study did not monitor objective indicators of blood flow perfusion in vital organs such as the heart, cerebral cortex, and kidneys—like brain oxygen saturation, glomerular filtration rate (GFR), fractional excretion of sodium (FENA), and markers of myocardial injury. This omission may overlook the beneficial effects of remimazolam's more stable hemodynamics compared to propofol during induction. Fourth, we did not follow up on patients' long-term outcomes, such as 30-day mortality rates. Lastly, during anesthetic induction, we monitored the depth of anesthesia using BIS values. Although some studies have demonstrated a relationship between remimazolam and BIS values, this relationship remains controversial.[40,41]

Conclusion

Remimazolam can be stably and effectively used in elderly patients with hypertension during general anesthesia induction. The total incidence of PIH was significantly lower among patients receiving remimazolam as the induction agent compared with propofol.

Data Sharing Statement

All data generated or analyzed during this study were not publicly available due to the privacy policies. Further inquiries about the datasets can be directed to the corresponding author on reasonable request. Any information we share will be deidentified.

Ethical Approval and Consent to Participate in the Study

This study was registered with the Chinese Clinical Trial Registry (ChiCTR2300068172, 02/09/2023). Approval was obtained from the Ethics Committee of Xuzhou Central Hospital (Ethics number: XZXY-LK-20230801-0133). All patients signed a written informed consent form prior to enrollment.

Consent for Publication

All the authors agreed to the publication of the article.

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Disclosure

The authors declare no competing interests in this work.

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