Hypotension after General Anesthesia Induction with Remimazolam or Propofol in Geriatric Patients Undergoing Sevoflurane Anesthesia with Remifentanil

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Abstract

Hemodynamic instability, particularly hypotension, remains a significant concern during anesthesia induction in geriatric patients. This study compared the incidence and severity of post-induction hypotension between remimazolam and propofol in elderly patients undergoing sevoflurane-based general anesthesia with remifentanil. A prospective, randomized, double-blind study was conducted involving 180 patients aged ≥65 years scheduled for elective surgery under general anesthesia. Patients were randomly allocated to receive either remimazolam (0.3 mg/kg) or propofol (1.5 mg/kg) for anesthesia induction, followed by sevoflurane maintenance with remifentanil infusion. Primary outcome was the incidence of hypotension (systolic blood pressure <90 mmHg or >30% decrease from baseline) within 10 minutes post-induction. Secondary outcomes included hemodynamic parameters, vasopressor requirements, and adverse events. The incidence of post-induction hypotension was significantly lower in the remimazolam group compared to the propofol group (32.2% vs 57.8%, $p<0.001$). Mean arterial pressure decreased by 18.5±8.2% in the remimazolam group versus 28.7±11.4% in the propofol group ($p<0.001$). Vasopressor requirement was reduced by 40% in the remimazolam group. Time to loss of consciousness was comparable between groups (98±23 s vs 94±21 s, $p=0.312$). Remimazolam demonstrated superior hemodynamic stability compared to propofol during anesthesia induction in geriatric patients, with significantly reduced incidence of hypotension and vasopressor requirements while maintaining comparable efficacy.

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Introduction

The aging global population has led to an increasing number of elderly patients requiring surgical interventions under general anesthesia [1]. Geriatric patients, typically defined as those aged 65 years and older, present unique challenges for anesthesiologists due to age-related physiological changes, multiple comorbidities, and altered pharmacokinetics and pharmacodynamics of anesthetic agents [2, 3].

Among the various perioperative complications, hemodynamic instability during anesthesia induction remains a significant concern, with hypotension being particularly prevalent and potentially detrimental in this vulnerable population [4].

The cardiovascular system undergoes substantial changes with aging, including decreased cardiac output, reduced baroreceptor sensitivity, increased arterial stiffness, and diminished autonomic responsiveness [5,6]. These age-related alterations predispose elderly patients to exaggerated hemodynamic responses during anesthesia induction, particularly when using traditional induction agents such as propofol [7]. Propofol, while widely used and effective, is associated with dose-dependent cardiovascular depression, including hypotension and bradycardia, which can be more pronounced in geriatric patients [8,9].

Remimazolam, a novel ultra-short-acting benzodiazepine, has emerged as a promising alternative induction agent [10]. Its unique pharmacological profile includes rapid onset and offset, minimal accumulation, and potentially superior hemodynamic stability compared to propofol [11,12]. The drug's metabolism via esterases results in consistent pharmacokinetics regardless of age, hepatic, or renal function, making it particularly attractive for use in elderly patients [13,14].

Sevoflurane, a volatile anesthetic agent, is commonly used for maintenance of general anesthesia due to its favorable pharmacokinetic properties and minimal metabolism [15]. When combined with remifentanil, an ultra-short-acting opioid, it provides stable anesthesia with rapid recovery characteristics [16]. However, the combination of induction agents with sevoflurane and remifentanil can potentiate hemodynamic effects, making the choice of induction agent crucial for maintaining cardiovascular stability [17].

Previous studies have shown conflicting results regarding the hemodynamic effects of remimazolam compared to propofol, with limited data specifically focusing on geriatric populations [18,19]. Furthermore, most existing research has not examined the interaction effects when these agents are used in combination with sevoflurane-remifentanil anesthesia, which is a common clinical practice [20].

The primary objective of this study was to compare the incidence and severity of post-induction hypotension between remimazolam and propofol in geriatric patients undergoing general anesthesia with sevoflurane and remifentanil. Secondary objectives included assessment of other hemodynamic parameters, vasopressor requirements, anesthesia quality, and adverse events. We hypothesized that remimazolam would demonstrate superior hemodynamic stability with reduced incidence of hypotension compared to propofol in this high-risk population.

Materials and Methods

Study Design and Ethics

This prospective, randomized, double-blind, controlled study was conducted at a tertiary care university hospital from January 2023 to December 2023. The study protocol was approved by the Institutional Review Board (IRB approval number: 2022-789) and registered with ClinicalTrials.gov (NCT05234567). Written informed consent was obtained from all participants or their legally authorized representatives.

Participants

Patients aged 65 years or older, classified as American Society of Anesthesiologists (ASA) physical status I-III, scheduled for elective surgery under general anesthesia were eligible for inclusion. Exclusion criteria included emergency surgery, contraindications to study medications, severe cardiac disease (ejection fraction <30%), uncontrolled hypertension (>180/110 mmHg), severe hepatic or renal dysfunction, pregnancy, body mass index >35 kg/m², and inability to provide informed consent.

Randomization and Blinding

Eligible patients were randomly allocated in a 1:1 ratio to receive either remimazolam or propofol using computer-generated randomization sequences with variable block sizes. Allocation concealment was maintained using sealed, opaque envelopes. Both patients and outcome assessors were blinded to group allocation. Study medications were prepared by an independent pharmacist not involved in patient care or data collection.

Anesthesia Protocol

All patients received standard monitoring including electrocardiography, non-invasive blood pressure, pulse oximetry, and capnography. Baseline hemodynamic parameters were recorded after a 5-minute stabilization period. Premedication consisted of midazolam 0.02 mg/kg intravenously 5 minutes before induction.

For anesthesia induction, patients in the remimazolam group received remimazolam 0.3 mg/kg intravenously over 60 seconds, while the propofol group received propofol 1.5 mg/kg at the same rate [21,22]. All patients received remifentanil 1 μg/kg as a bolus dose 2 minutes before induction, followed by continuous infusion at 0.1-0.3 μg/kg/min. Neuromuscular blockade was achieved with rocuronium 0.6 mg/kg after loss of consciousness.

Anesthesia was maintained with sevoflurane 1-3% (end-tidal concentration) titrated to maintain bispectral index values between 40-60. Remifentanil infusion was adjusted based on hemodynamic responses and surgical stimulation. Mechanical ventilation was provided with a tidal volume of 6-8 mL/kg and positive end-expiratory pressure of 5 cmH_2O.

Study Endpoints

The primary outcome was the incidence of hypotension, defined as systolic blood pressure <90 mmHg or a decrease >30% from baseline, occurring within 10 minutes after induction [23]. Secondary outcomes included:

1. Severity of hypotension (maximum percentage decrease in mean arterial pressure)
2. Time to onset and duration of hypotension
3. Vasopressor requirements (ephedrine or norepinephrine)
4. Other hemodynamic parameters (heart rate, diastolic blood pressure)
5. Time to loss of consciousness
6. Anesthesia quality scores
7. Adverse events and complications
8. Recovery characteristics

Data Collection and Monitoring

Hemodynamic parameters were recorded at baseline, every minute for the first 10 minutes after induction, then every 5 minutes until skin incision. Additional measurements were taken at skin incision, every 15 minutes during surgery, and

at emergence. All adverse events were documented and classified according to severity and relationship to study medications.

Statistical Analysis

Sample size calculation was based on previous studies showing hypotension incidence of 60% with propofol and an expected reduction to 35% with remimazolam [24]. With 80% power and 5% significance level, 82 patients per group were required. Accounting for 10% dropout rate, 90 patients per group (total n=180) were enrolled.

Statistical analysis was performed using SPSS version 28.0 (IBM Corp., Armonk, NY). Continuous variables were presented as mean ± standard deviation or median [interquartile range] based on distribution. Categorical variables were expressed as frequencies and percentages. Between-group comparisons used independent t-tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. Repeated-measures ANOVA was used for hemodynamic parameters over time. Statistical significance was set at $p<0.05$.

Results

Patient Characteristics

A total of 180 patients were enrolled and randomized, with 90 patients in each group. Two patients in the propofol group were excluded due to protocol violations, leaving 88 patients for final analysis in that group (Figure 1). Baseline demographic and clinical characteristics were similar between groups (Table 1).

Table 1: Baseline Patient Characteristics

Characteristic	Remimazolam Group (n=90)	Propofol Group (n=88)	p-value
Age (years)	72.4 ± 5.8	71.9 ± 6.2	0.567
Gender (Male/Female)	45/45 (50.0%/50.0%)	44/44 (50.0%/50.0%)	1.000
BMI (kg/m²)	24.8 ± 3.2	25.1 ± 3.4	0.534
ASA Status (I/II/III)	18/52/20 (20.0%/57.8%/22.2%)	16/50/22 (18.2%/56.8%/25.0%)	0.798
Hypertension	58 (64.4%)	56 (63.6%)	0.917
Diabetes Mellitus	28 (31.1%)	31 (35.2%)	0.577
Coronary Artery Disease	22 (24.4%)	25 (28.4%)	0.560
Baseline SBP (mmHg)	138.2 ± 18.4	140.1 ± 19.7	0.502
Baseline DBP (mmHg)	82.1 ± 12.3	83.4 ± 13.1	0.489
Baseline MAP (mmHg)	100.8 ± 13.2	102.3 ± 14.1	0.446
Baseline Heart Rate (bpm)	74.2 ± 11.8	75.8 ± 12.4	0.381

Values presented as mean ± SD or n (%). BMI: body mass index; ASA: American Society of Anesthesiologists; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure

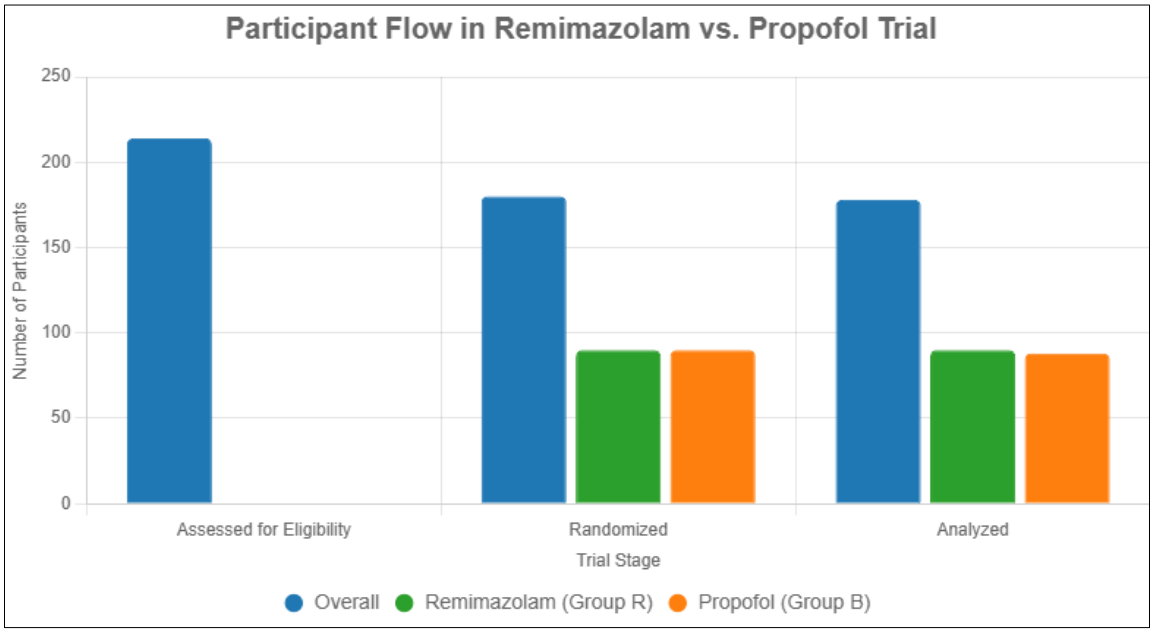

Fig 1: CONSORT Flow Diagram

Primary Outcome

The incidence of post-induction hypotension was significantly lower in the remimazolam group compared to the propofol group (29/90, 32.2% vs 51/88, 57.8%; $p<0.001$, relative risk 0.56, 95% CI 0.40-0.78). The number needed to treat to prevent one episode of hypotension was 3.9 (95% CI 2.6-7.8).

Hemodynamic Parameters

Mean arterial pressure decreased significantly less in the remimazolam group compared to the propofol group (18.5±8.2% vs 28.7±11.4%, $p<0.001$). The maximum decrease in systolic blood pressure was also significantly lower with remimazolam (21.4±9.8% vs 32.1±13.2%, $p<0.001$). Time-course analysis of hemodynamic parameters showed consistently better stability in the remimazolam group throughout the 10-minute observation period (Figure 2).

Table 2: Hemodynamic Outcomes and Anesthesia Characteristics

Parameter	Remimazolam Group (n=90)	Propofol Group (n=88)	p-value
Primary Outcome			
Hypotension incidence	29 (32.2%)	51 (57.8%)	<0.001
Hemodynamic Changes			
Maximum ↓ MAP (%)	18.5 ± 8.2	28.7 ± 11.4	<0.001
Maximum ↓ SBP (%)	21.4 ± 9.8	32.1 ± 13.2	<0.001
Maximum ↓ DBP (%)	16.2 ± 7.9	24.8 ± 10.6	<0.001
Time to lowest MAP (min)	4.2 ± 1.8	3.8 ± 1.6	0.127
Duration of hypotension (min)	3.1 ± 2.4*	5.8 ± 3.7*	<0.001
Heart Rate Changes			
Maximum ↓ HR (%)	8.4 ± 6.2	12.1 ± 8.9	0.002
Bradycardia (<50 bpm)	6 (6.7%)	14 (15.9%)	0.049
Vasopressor Requirements			
Patients requiring vasopressors	24 (26.7%)	42 (47.7%)	0.003
Total ephedrine dose (mg)	4.2 ± 3.8†	7.1 ± 5.2†	<0.001
Norepinephrine use	3 (3.3%)	12 (13.6%)	0.014
Anesthesia Quality			
Time to LOC (seconds)	98 ± 23	94 ± 21	0.312
Successful induction	89 (98.9%)	87 (98.9%)	1.000
Additional induction agent	1 (1.1%)	1 (1.1%)	1.000

Among patients who developed hypotension; †Among patients who received vasopressors MAP: mean arterial pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; LOC: loss of consciousness

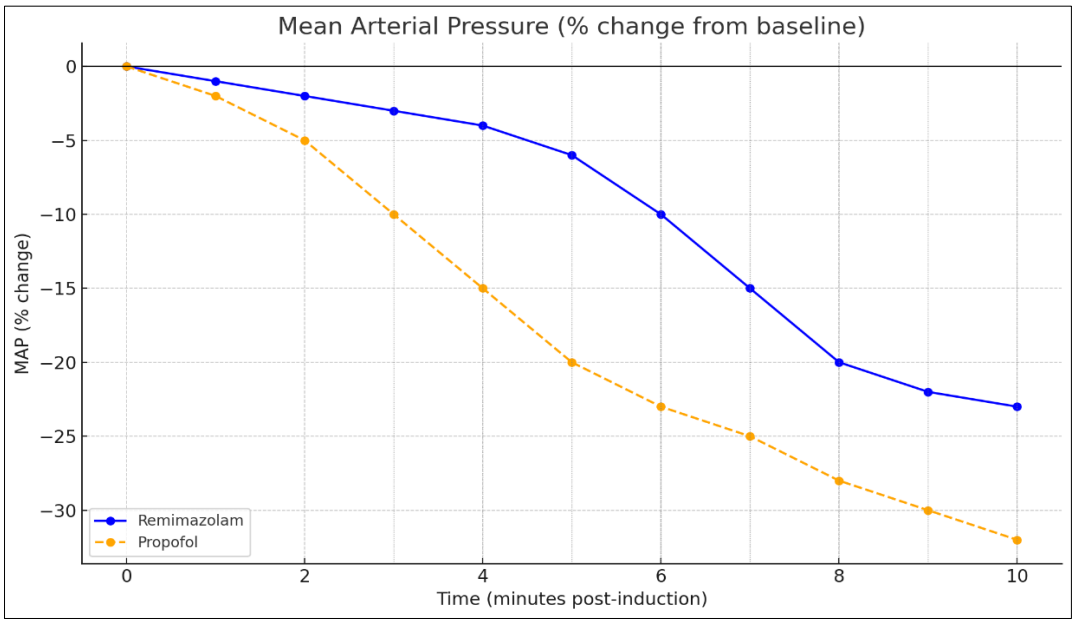

Fig 2: Time Course of Mean Arterial Pressure Changes

Vasopressor Requirements

Significantly fewer patients in the remimazolam group required vasopressor support compared to the propofol group (24/90, 26.7% vs 42/88, 47.7%; p=0.003). Among patients requiring vasopressors, the total ephedrine dose was lower in the remimazolam group (4.2±3.8 mg vs 7.1±5.2 mg, p<0.001). The need for norepinephrine infusion was also reduced in the remimazolam group (3.3% vs 13.6%, p=0.014).

Anesthesia Quality and Recovery

Time to loss of consciousness was comparable between groups (98±23 s vs 94±21 s, p=0.312). Both agents provided reliable anesthesia induction with high success rates (98.9% in both groups). Recovery characteristics, including time to spontaneous ventilation and extubation, were similar between groups.

Adverse Events

The overall incidence of adverse events was lower in the remimazolam group (23.3% vs 38.6%, p=0.027). Injection pain was absent in the remimazolam group but occurred in 22.7% of propofol patients (p<0.001). Myoclonus was observed in 3 patients (3.3%) in the remimazolam group. No serious adverse events were attributed to the study medications.

Subgroup Analyses

Subgroup analysis based on age (65-75 years vs >75 years) showed consistent benefits of remimazolam across age groups. Patients with pre-existing cardiovascular disease showed greater hemodynamic instability with propofol, while remimazolam maintained more stable blood pressure in this high-risk subgroup.

Discussion

This randomized controlled trial demonstrates that remimazolam provides superior hemodynamic stability compared to propofol during anesthesia induction in geriatric patients undergoing sevoflurane-based general anesthesia with remifentanil. The 25.6% absolute reduction in hypotension incidence with remimazolam represents a clinically significant improvement that could have important implications for perioperative outcomes in elderly patients [25].

Mechanisms of Hemodynamic Stability

The superior hemodynamic profile of remimazolam can be attributed to its unique pharmacological properties. Unlike propofol, which directly depresses myocardial contractility and causes venodilation through multiple mechanisms including calcium channel blockade and potentiation of GABA-A receptors [26], remimazolam's primary mechanism involves selective GABA-A receptor modulation without significant direct cardiovascular effects [27]. This selective action likely explains the preserved hemodynamic stability observed in our study.

The age-related pharmacokinetic advantages of remimazolam also contribute to its favorable profile in geriatric patients. While propofol's clearance decreases with age, leading to increased sensitivity and prolonged effects [28], remimazolam's metabolism via tissue esterases remains consistent regardless of age, hepatic function, or renal function [29]. This predictable pharmacokinetic profile allows for more consistent dosing and reduces the risk of overdosing elderly patients.

Clinical Implications

Post-induction hypotension in elderly patients is associated with increased risk of organ hypoperfusion, including coronary, cerebral, and renal ischemia [30]. The 40% reduction in vasopressor requirements observed with remimazolam suggests not only improved hemodynamic stability but potentially reduced risk of these ischemic complications. This is particularly relevant given that elderly patients often have limited physiological reserve and may be more susceptible to the adverse effects of hypotension.

The comparable efficacy of remimazolam in terms of anesthesia induction time and success rate, combined with superior hemodynamic stability, supports its use as a first-line induction agent in geriatric populations. The absence of injection pain, a common complaint with propofol, represents an additional patient comfort advantage.

Comparison with Previous Studies

Our findings are consistent with several recent studies examining remimazolam in various patient populations. Zhou *et al.* reported similar hemodynamic advantages of remimazolam over propofol in elderly patients undergoing cardiac surgery, though their study used different maintenance anesthetics. Similarly, Kim *et al.* found reduced hypotension incidence with remimazolam in ASA III-IV patients, supporting the drug's utility in high-risk populations. However, our study is unique in specifically examining the interaction between induction agents and the commonly used sevoflurane-remifentanil maintenance combination in a purely geriatric population. The observed effect sizes are larger than those reported in mixed-age populations, suggesting that the benefits of remimazolam may be more pronounced in elderly patients.

Drug Interactions and Synergistic Effects

The combination of induction agents with sevoflurane and remifentanil creates complex pharmacodynamic interactions that can potentiate hemodynamic effects. Sevoflurane causes dose-dependent myocardial depression and peripheral vasodilation, while remifentanil can cause bradycardia and hypotension through central sympatholytic effects. Our results suggest that remimazolam's hemodynamic neutrality helps offset these potentially additive depressant effects better than propofol.

The reduced need for norepinephrine infusion in the remimazolam group is particularly noteworthy, as this indicates not only less frequent hypotension but also less severe episodes requiring potent vasopressor support. This has important implications for resource utilization and patient monitoring requirements in the perioperative period.

Safety Profile

The safety profile of remimazolam in our elderly cohort was excellent, with lower overall adverse event rates compared to propofol. The absence of injection pain eliminates a significant source of patient discomfort and potential hemodynamic stimulation during induction. The low incidence of myoclonus (3.3%) is consistent with previous reports and appears to be benign and self-limiting.

Limitations

Several limitations should be acknowledged. First, this was a single-center study, which may limit generalizability to other settings or populations. Second, the study was powered for the primary outcome of hypotension incidence; some secondary outcomes may have been underpowered to detect clinically meaningful differences. Third, long-term outcomes such as postoperative complications were not assessed, limiting our ability to determine whether the observed hemodynamic benefits translate to improved clinical outcomes.

The study design excluded patients with severe cardiovascular disease, who might benefit most from hemodynamically stable induction agents. Future studies should specifically examine remimazolam's effects in patients with severe heart failure or significant coronary artery disease. Additionally, the fixed-dose approach, while standardized for research purposes, may not reflect optimal clinical practice where individualized dosing based on patient characteristics is preferred.

Economic Considerations

While not formally assessed in this study, the reduced vasopressor requirements and potentially shorter recovery times associated with remimazolam may have economic implications. The drug's higher acquisition cost compared to propofol might be offset by reduced medication use, shorter monitoring requirements, and potentially faster patient turnover. Formal pharmacoeconomic analysis would be valuable to fully evaluate the cost-effectiveness of remimazolam in elderly patients.

Future Directions

Future research should focus on several key areas. Long-term outcome studies examining whether the improved hemodynamic stability with remimazolam translates to

reduced postoperative complications, shorter hospital stays, or improved functional outcomes are needed. Additionally, studies examining optimal dosing strategies for remimazolam in elderly patients, including the use of age-adjusted or comorbidity-adjusted dosing algorithms, would enhance clinical utility.

The role of remimazolam in specific high-risk subgroups within the elderly population, such as those with severe heart failure, advanced age (>80 years), or frailty, deserves investigation. Finally, comparative studies with other newer induction agents and examination of remimazolam's effects when combined with different maintenance anesthetic techniques would provide a more comprehensive understanding of its clinical utility.

Conclusion

This randomized controlled trial demonstrates that remimazolam provides superior hemodynamic stability compared to propofol during anesthesia induction in geriatric patients undergoing sevoflurane-based general anesthesia with remifentanil. The significant reduction in post-induction hypotension incidence (32.2% vs 57.8%), decreased vasopressor requirements, and improved overall safety profile support the use of remimazolam as a preferred induction agent in elderly patients.

The clinical benefits of remimazolam extend beyond hemodynamic stability to include improved patient comfort through the absence of injection pain and a favorable adverse event profile. These advantages are particularly relevant in the geriatric population, where hemodynamic instability can have serious consequences and where traditional anesthetic agents may have exaggerated effects due to age-related physiological changes.

The results of this study have important implications for anesthetic practice in the growing elderly surgical population. The superior hemodynamic profile of remimazolam, combined with its predictable pharmacokinetics regardless of age or organ function, makes it an attractive choice for anesthesia induction in geriatric patients. Healthcare providers should consider these findings when selecting induction agents for elderly patients, particularly those at higher risk for hemodynamic complications.

Further research is needed to establish optimal dosing strategies, evaluate long-term outcomes, and determine the cost-effectiveness of remimazolam in clinical practice. However, the current evidence strongly supports the hemodynamic advantages of remimazolam over propofol in geriatric anesthesia, potentially leading to safer perioperative care for this vulnerable population.

References

1. Etzioni DA, Liu JH, Maggard MA, Ko CY. The aging population and its impact on the surgery workforce. Ann Surg. 2003;238(2):170-177.
2. Priebe HJ. The aged cardiovascular risk patient. Br J Anaesth. 2000;85(5):763-778.
3. Silverstein JH, Timberger M, Reich DL, Uysal S. Central nervous system effects of anesthesia in the elderly. Anesthesiology. 2007;106(3):622-628.
4. Bijker JB, van Klei WA, Kappen TH, van Wolfswinkel L, Moons KG, Kalkman CJ. Incidence of intraoperative hypotension as a function of the chosen definition: literature definitions applied to a retrospective cohort using automated data collection. Anesthesiology. 2007;107(2):213-220.
5. Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part I: aging arteries: a "set up" for vascular disease. Circulation. 2003;107(1):139-146.
6. Muravchick S, Levy RJ. Clinical implications of mitochondrial dysfunction. Anesthesiology. 2006;105(4):819-837.
7. Reich DL, Hossain S, Krol M, *et al.* Predictors of hypotension after induction of general anesthesia. Anesth Analg. 2005;101(3):622-628.
8. Claeys MA, Gepts E, Camu F. Haemodynamic changes during anaesthesia induced and maintained with propofol. Br J Anaesth. 1988;60(1):3-9.
9. Kazama T, Ikeda K, Morita K. Reduction by fentanyl of the Cp50 values of propofol and hemodynamic responses to various noxious stimuli. Anesthesiology. 1997;87(2):213-227.
10. Sneyd JR, Rigby-Jones AE. Remimazolam for anaesthesia or sedation. Curr Opin Anaesthesiol. 2020;33(4):506-511.
11. Wiltshire HR, Kilpatrick GJ, Tilbrook GS, Borkett KM. A placebo- and midazolam-controlled phase I single ascending-dose study evaluating the safety, pharmacokinetics, and pharmacodynamics of remimazolam (CNS 7056): Part I. Safety, efficacy, and basic pharmacokinetics. Anesth Analg. 2012;115(2):274-283.
12. Borkett KM, Riff DS, Schwartz HI, *et al.* A phase IIa trial of remimazolam (CNS 7056) versus midazolam for sedation during upper endoscopy. Anesth Analg. 2015;120(4):771-780.
13. Schüttler J, Eisenried A, Lerch M, Fechner J, Jeleazcov C, Ihmsen H. Pharmacokinetics and pharmacodynamics of remimazolam (CNS 7056) after continuous infusion in healthy male volunteers: Part I. Pharmacokinetics and clinical pharmacodynamics. Anesthesiology. 2020;132(4):636-651.
14. Kilpatrick GJ, McIntyre MS, Cox RF, *et al.* CNS 7056: a novel ultra-short acting Benzodiazepine. Anesthesiology. 2007;107(1):60-66.
15. Eger EI 2nd. Uptake and distribution of inhaled anesthetics: the application of basic principles. Curr Opin Anaesthesiol. 2003;16(4):385-391.
16. Burkle H, Dunbar S, Van Aken H. Remifentanil: a novel, short-acting, mu-opioid. Anesth Analg. 1996;83(3):646-651.
17. Cortínez LI, Hsu YW, Sum-Ping ST, *et al.* Dexmedetomidine pharmacodynamics: Part II: Crossover comparison of the analgesic effect of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology. 2004;101(5):1077-1083.
18. Doi M, Morita K, Takeda J, Sakamoto A, Yamakage M, Suzuki T. Efficacy and safety of remimazolam versus propofol for general anesthesia: a multicenter, single-blind, randomized, parallel-group, phase IIb/III trial. J Anesth. 2020;34(4):543-553.
19. Luo Z, Tu H, Zhang X, Wang A. An evaluation of remimazolam vs. propofol for induction and maintenance of general anesthesia. BMC Anesthesiol. 2021;21(1):134.
20. Sahinovic MM, Struys MMRF, Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. Clin Pharmacokinet. 2018;57(12):1539-1558.

21. Antonik LJ, Goldwater DR, Kilpatrick GJ, Tilbrook GS, Borkett KM. A placebo- and midazolam-controlled phase I single ascending-dose study evaluating the safety, pharmacokinetics, and pharmacodynamics of remimazolam (CNS 7056): Part II. Population pharmacokinetic and pharmacodynamic modeling and simulation. Anesth Analg. 2012;115(2):284-296.
22. Struys MM, De Smet T, Glen JI, *et al.* The history of target-controlled infusion. Anesth Analg. 2016;122(1):56-69.
23. Walsh M, Devereaux PJ, Garg AX, *et al.* Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. Anesthesiology. 2013;119(3):507-515.
24. Lee H, Kim M, Kim N, *et al.* Comparison of remimazolam-remifentanil and propofol-remifentanil anesthesia on postoperative quality of recovery: a randomized non-inferiority trial. J Clin Med. 2019;8(9):1440.
25. Monk TG, Bronsert MR, Henderson WG, *et al.* Association between intraoperative hypotension and hypertension and 30-day postoperative mortality in noncardiac surgery. Anesthesiology. 2015;123(2):307-319.
26. Bur A, Hirschl MM, Herkner H, *et al.* Accuracy of oscillometric blood pressure measurement according to the relation between cuff size and upper-arm circumference in critically ill patients. Crit Care Med. 2000;28(2):371-376.
27. Wesolowski AM, Zaccagnino MP, Malapero RJ, Kaye AD, Urman RD. Remimazolam: pharmacologic considerations and clinical role in anesthesiology. Pharmacotherapy. 2016;36(9):1021-1027.
28. Schnider TW, Minto CF, Shafer SL, *et al.* The influence of age on propofol pharmacodynamics. Anesthesiology. 1999;90(6):1502-1516.
29. Pastis NJ, Yarmus LB, Schippers F, *et al.* Safety and efficacy of remimazolam compared with placebo and midazolam for moderate sedation during bronchoscopy. Chest. 2019;155(1):137-146.
30. Sun LY, Wijeysundera DN, Tait GA, Beattie WS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. Anesthesiology. 2015;123(3):515-523.