

# Comparing Cognitive Recovery of Remimazolam versus Propofol in Elderly Patients Undergoing Colonoscopy: A Randomized Controlled Trial

Shuying Lin<sup>1,\*</sup>, Ying Wei<sup>2,\*</sup>, Yifen Zhuo<sup>3,\*</sup>, Shiqin Que<sup>4</sup>, Xuepeng Jin<sup>4</sup>, Yusheng Yao<sup>4</sup>, Bin Qian<sup>1</sup>

<sup>1</sup>Department of Anesthesiology, People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine, Fuzhou, People's Republic of China; <sup>2</sup>Department of Anesthesiology, Fujian Maternity and Child Health Hospital, College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, Fuzhou, People's Republic of China; <sup>3</sup>Department of Anesthesiology, Xiamen Haicang Hospital, Xiamen, People's Republic of China; <sup>4</sup>Department of Anesthesiology, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou, People's Republic of China

\*These authors contributed equally to this work

Correspondence: Yusheng Yao, Fujian Provincial Hospital, 134, Dongjie Street, Fuzhou, 350001, People's Republic of China, Email fjslyys@126.com; Bin Qian, People's Hospital Affiliated to Fujian University of Traditional Chinese Medicine, 602, Baiyiqi Road, Fuzhou, 350005, People's Republic of China, Email qianbin@fjtcu.edu.cn

**Background:** Remimazolam, a novel ultra-short-acting benzodiazepine, shows promise for procedural sedation. This study compared the cognitive recovery of remimazolam versus propofol in elderly patients undergoing colonoscopy.

**Patients and Methods:** In this prospective, randomized, double-blind, controlled trial, 228 patients aged  $\geq 65$  years undergoing outpatient colonoscopies were recruited. Patients received intravenous sufentanil 0.05  $\mu\text{g/kg}$ , followed by either remimazolam 0.2 mg/kg or propofol 1 mg/kg for sedation induction. The assigned study drug (remimazolam 0.1 mg/kg or propofol 0.5 mg/kg) was titrated to maintain a Modified Observer's Assessment of Alertness/Sedation scale score  $< 3$  during the procedure. The primary outcome was the incidence of cognitive recovery, assessed using the Postoperative Quality of Recovery Scale (PostopQRS) cognitive domain on postoperative day 3. Secondary outcomes included overall and other PostopQRS domains recovery, time to discharge, patient satisfaction, and adverse events.

**Results:** Cognitive recovery on day 3 was similar between remimazolam (84.2%) and propofol (85.1%) groups (risk ratio = 0.99; 95% CI: 0.89–1.11;  $p = 0.854$ ). No significant differences were observed in overall recovery, other domains, or discharge time. Remimazolam patients reported higher satisfaction ( $p = 0.001$ ) and experienced lower incidences of hypotension (21.9% vs 53.5%;  $p < 0.001$ ), hypoxemia (6.1% vs 16.7%;  $p = 0.024$ ), and injection site pain (15.8% vs 41.2%;  $p < 0.001$ ) compared to propofol.

**Conclusion:** In elderly patients undergoing colonoscopy, remimazolam demonstrated comparable cognitive recovery to propofol, with higher patient satisfaction and a more favorable safety profile. Remimazolam may be the preferred alternative to propofol for procedural sedation in this vulnerable population.

**Trial Registration:** The Chinese Clinical Trial Registry, ChiCTR2200066689.

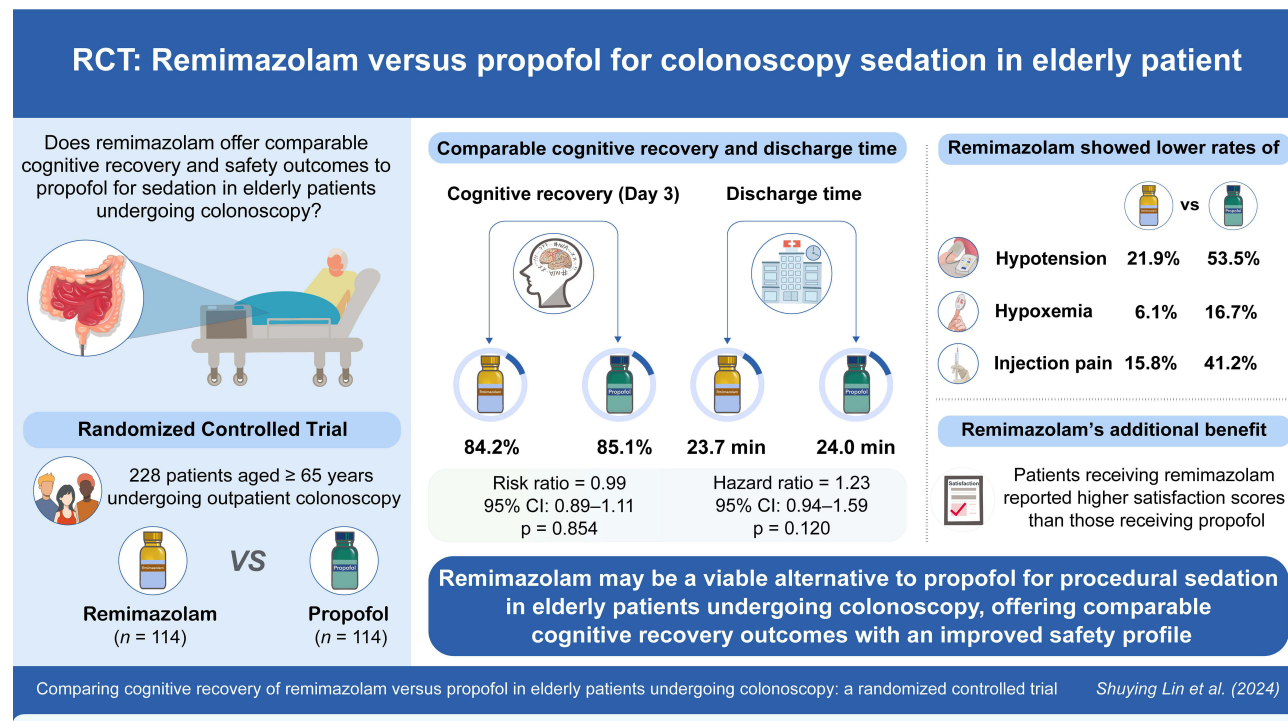
**Keywords:** cognitive recovery, colonoscopy, elderly patients, postoperative quality of recovery, propofol, remimazolam

## Introduction

Colonoscopy is the gold standard for colorectal cancer screening and diagnosis, allowing for direct visualization, early detection, and potential removal of precancerous lesions.<sup>1</sup> Current screening guidelines recommend regular examinations beginning at age 45 for average-risk adults without personal or family history of colorectal neoplasia.<sup>2</sup> Despite 28 million eligible individuals in China, participation rates remain low at 14%,<sup>3,4</sup> largely due to procedural discomfort, leading to increased adoption of sedation protocols to improve patient acceptance and compliance.<sup>5</sup>

Propofol is widely preferred for colonoscopy sedation due to its rapid onset and recovery profile.<sup>6</sup> However, its use in elderly patients ( $\geq 65$  years) carries significant cardiovascular and respiratory risks.<sup>7,8</sup> Notably, propofol-induced

## Graphical Abstract



hypotension affects more than 50% of elderly patients, potentially compromising organ perfusion and cognitive function.<sup>9–11</sup> While midazolam presents an alternative, research shows a higher incidence of postoperative cognitive dysfunction compared to propofol in elderly patients, attributed to prolonged drug elimination.<sup>12–15</sup>

Remimazolam, a novel ultra-short-acting benzodiazepine, emerges as a promising alternative for procedural sedation.<sup>16–18</sup> Its unique metabolism by tissue esterases prevents drug accumulation, suggesting enhanced safety for elderly patients. However, data on remimazolam's post-discharge effects, particularly cognitive recovery, remain limited in this population. A direct comparison between remimazolam and propofol is crucial, given propofol's widespread use despite known risks in elderly patients. This comparison addresses a pressing clinical need for safer sedation options in elderly patients undergoing colonoscopy, as remimazolam may offer rapid onset and recovery comparable to propofol, with an improved safety profile.

To address this knowledge gap, we conducted a randomized controlled trial comparing remimazolam and propofol for colonoscopy sedation in elderly patients, focusing on cognitive recovery using the Postoperative Quality of Recovery Scale (PostopQRS).<sup>19</sup> We hypothesized comparable postoperative cognitive recovery between remimazolam and propofol in elderly outpatients undergoing colonoscopy.

## Methods

### Study Setting and Participants

This prospective, randomized, double-blind, parallel-group, active-controlled trial was conducted at the endoscopy center of Fujian Provincial Hospital, a tertiary care medical center in Fuzhou, China, from December 17, 2022, to January 26, 2024. The study protocol was approved by the Ethics Committee of Fujian Provincial Hospital (reference K2021-06-016) on June 24, 2021, and prospectively registered with the Chinese Clinical Trial Registry (<https://www.chictr.org.cn/bin/project/edit?pid=129595>, ChiCTR2200066689) on December 13, 2022. All patients provided written informed consent to

participate in the study and for their data to be published. The trial was carried out in accordance with the Code of Ethics of the World Medical Association Declaration of Helsinki for experiments involving humans. No protocol changes were made after trial commencement. We presented the research according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.<sup>20</sup>

Eligible participants were adults aged 65 years or older with an American Society of Anesthesiologists (ASA) physical status classification of I–III who were scheduled for elective outpatient colonoscopy. Patients were excluded if they met any of the following criteria: refusal to participate, allergy or hypersensitivity to study drugs, inability to ambulate independently, history of alcohol or substance abuse, pre-existing cognitive impairment, psychiatric or neurological disorders, body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup>, inability to communicate in Mandarin Chinese, or anticipated need for therapeutic endoscopic interventions (eg, endoscopic mucosal resection or submucosal dissection). Patients with severe cardiopulmonary, hepatic, or renal dysfunction were also excluded.

## Randomization and Masking

Participants were randomly allocated to receive either remimazolam or propofol in a 1:1 ratio using permuted block randomization with randomly selected block sizes of 4 or 6. The randomization sequence was generated by an independent statistician using R version 4.0.5 ('blockrand' package) and concealed using sequentially numbered, opaque, sealed envelopes. On the day of the procedure, a pharmacist not involved in patient care opened the envelopes and prepared the study drugs in identical syringes according to the assigned treatment group. Remimazolam (Jiangsu Hengrui Pharmaceutical Co., China) was diluted to 1 mg/mL, while long-chain/ medium-chain triglyceride propofol (Fresenius Kabi Deutschland GmbH, Germany) was prepared at 5 mg/mL, both using 0.9% saline. These concentrations ensured equal volumes to be administered on a weight-based basis. Consequently, participants, endoscopists, and study personnel responsible for data collection and analysis remained blinded to group assignments.

## Procedures

Upon arrival at the endoscopy unit, all patients received standard monitoring, including pulse oximetry, noninvasive blood pressure, and electrocardiography. Supplemental oxygen was administered via nasal cannula at 2 L/min to maintain oxygen saturation above 90%. Sedation was initiated with an intravenous bolus of sufentanil 0.05 µg/kg, followed by either remimazolam 0.2 mg/kg or propofol 1 mg/kg administered over 30 seconds. The colonoscopy commenced once the patient reached a Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score  $< 3$ , indicating an adequate level of sedation.<sup>21</sup> If the target sedation level was not achieved within 2 minutes of the initial dose, a rescue dose of 0.1 mg/kg remimazolam or 0.5 mg/kg propofol was administered. The anesthesiologist maintained a MOAA/S score  $< 3$  throughout the procedure by titrating the assigned study drug with additional boluses of 0.1 mg/kg remimazolam or 0.5 mg/kg propofol as needed. The dosing regimens were based on our established clinical evidence.<sup>22</sup> A single experienced endoscopist performed the colonoscopy using standard techniques, aiming for cecal intubation and thorough examination of the colonic mucosa. After the procedure, patients were transferred to the post-anesthesia care unit (PACU) for observation and discharged upon reaching a Post-Anesthesia Discharge Scoring System (PADSS) score  $\geq 9$ , indicating readiness for discharge.<sup>23</sup>

## Outcomes

The primary outcome was the incidence of cognitive recovery on postoperative day 3, assessed using the cognitive domain of the PostopQRS. The PostopQRS is a validated, multidimensional tool that evaluates recovery in physiological, nociceptive, emotive, functional, and cognitive domains. Cognitive recovery was defined as a return to baseline function in all five tests of the PostopQRS cognitive domain (memory, attention, and executive function). Participants achieved cognitive recovery if their scores were equal to or better than baseline, allowing for a slight performance decrease (typically 2 points) to account for normal variability.<sup>24</sup>

Secondary outcomes included overall and other PostopQRS domain recovery at 30 minutes, 1 day, 3 days, and 7 days post-procedure; time to meet discharge criteria (time from colonoscopy completion until achieving a PADSS score  $\geq 9$ ); patient and endoscopist satisfaction using 5-point Likert scales (1 = very dissatisfied; 5 = very satisfied); induction time

(interval from initial sedative administration to achieving a MOAA/S score < 3); recovery time (interval from procedure completion to achieving a MOAA/S score = 5); and adverse events. Adverse events assessed included injection site pain (using an 11-point numeric rating scale), hypotension (mean arterial pressure < 65 mmHg or  $\geq 30\%$  decrease from baseline), bradycardia (heart rate < 50 beats/min), hypoxemia (oxygen saturation < 90% despite 2 L/min supplemental oxygen), postoperative nausea and vomiting (PONV), and postoperative dizziness. A blinded research assistant collected data in person during hospitalization and via telephone after discharge.

## Sample Size Calculation

Sample size calculation for the primary outcome was conducted using PASS 15.0 software (NCSS LLC, UT, USA). Based on prior research, we estimated that 80% of participants would achieve cognitive recovery by postoperative day 3, as measured by the PostopQRS. A 15% difference in cognitive recovery incidence between groups was clinically significant.<sup>25</sup> To detect this difference with 90% power using a two-sided Z test at a significance level of  $\alpha = 0.05$ , a sample size of 101 participants per group was required. Anticipating a 10% dropout rate, we set the target enrollment at 114 participants per group.

## Statistical Analysis

Continuous variables were assessed for normality using the Kolmogorov–Smirnov test. Normally distributed variables are presented as mean  $\pm$  SD, while non-normally distributed variables are shown as median (IQR). Categorical variables are summarized as  $n$  (%). Group comparisons were performed using the independent samples *t*-test for normally distributed variables, the Mann–Whitney *U*-test for non-normally distributed variables, and the chi-square or Fisher's exact test for categorical variables.

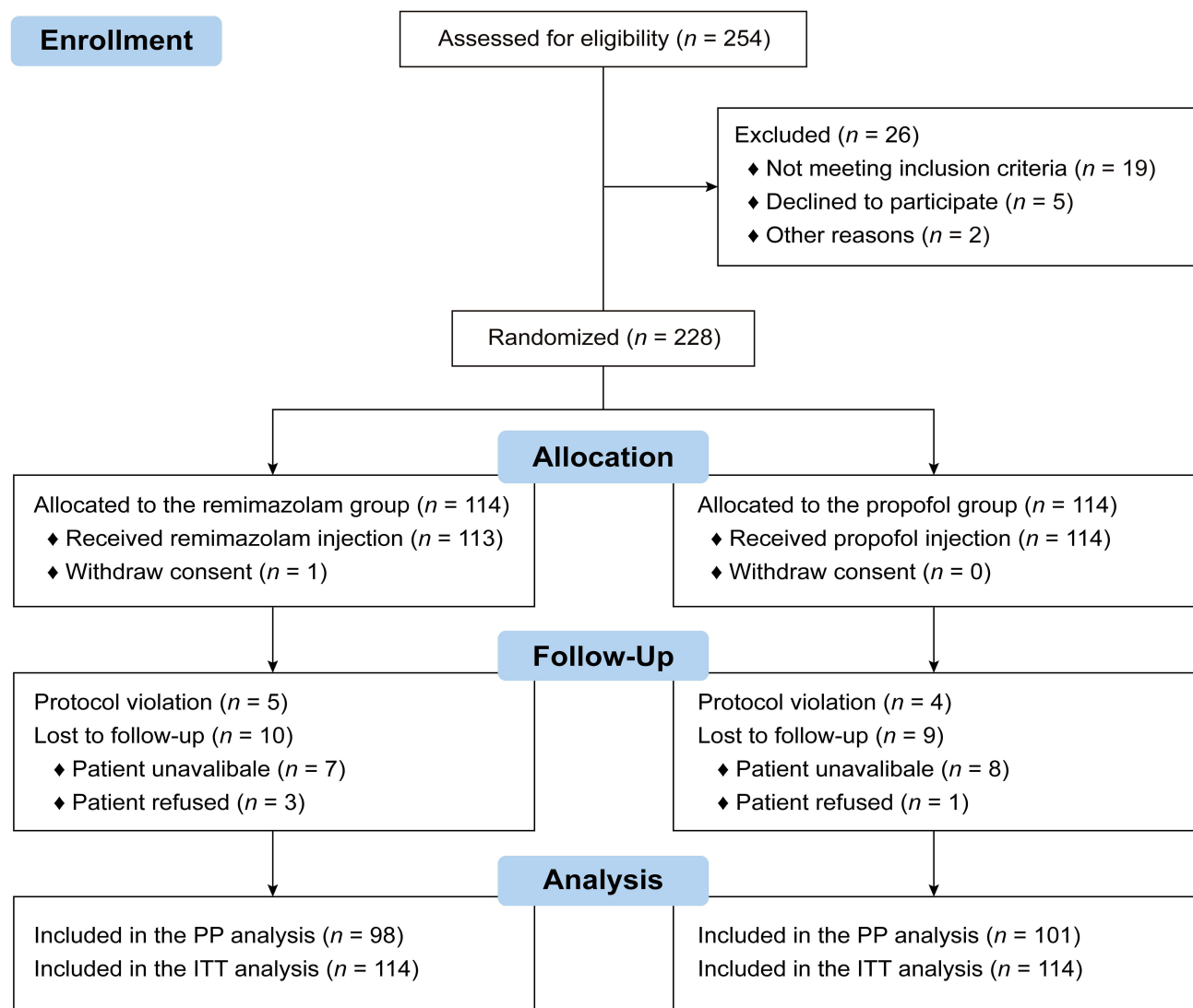
The incidence of cognitive recovery on postoperative day 3 was compared between groups using the chi-square test. Recovery trajectories over time were analyzed with a generalized linear mixed model (GLMM) using R version 4.3.3 ('lme4' package) with binomial distribution and a logit link function, including treatment group, time, and group-by-time interaction as fixed effects, and patient-specific random intercepts to account for within-subject correlation. Time to discharge readiness was analyzed using Kaplan–Meier survival analysis and Log rank test. A Cox proportional hazards model calculated hazard ratios with 95% CIs. Adverse event rates were compared using chi-square or Fisher's exact tests, with rate differences and 95% CIs visualized in a forest plot (R version 4.0.5, 'forest plot' package).

The primary analysis followed the intention-to-treat (ITT) principle. A per-protocol (PP) analysis was also performed to assess the robustness of the primary outcome. Missing data were addressed using multiple imputations with the R version 4.3.1 ('mice' package). Statistical significance was set at a two-sided  $p < 0.05$ . All statistical analyses were performed using IBM SPSS version 27.0 (IBM Corp., Armonk, NY, USA).

## Results

The CONSORT diagram (Figure 1) illustrates the flow of participants through the study. Between December 17, 2022, and January 26, 2024, 228 outpatients were randomly assigned in a 1:1 ratio to receive either remimazolam or propofol sedation. In the remimazolam group ( $n=114$ ), 98 patients (86.0%) completed the protocol after one pre-intervention withdrawal, five protocol deviations, and ten losses to follow-up. In the propofol group ( $n=114$ ), 101 patients (88.6%) completed the protocol after four protocol deviations and nine losses to follow-up. Completion rates were comparable between groups ( $p = 0.551$ ). Baseline characteristics were balanced between the two groups (Table 1).

The recovery trajectories of the PostopQRS cognitive domain are illustrated in Figure 2A. In the ITT analysis, the incidence of cognitive recovery on postoperative day 3 was similar between the remimazolam (84.2%) and propofol (85.1%) groups (risk ratio, 0.99; 95% CI, 0.89–1.11;  $p = 0.854$ ). The PP analysis on day 3 yielded consistent results (risk ratio, 0.91; 95% CI, 0.80–1.04;  $p = 0.669$ ). Generalized linear mixed model analysis revealed no significant time-by-treatment interaction ( $p = 0.656$ ), indicating consistent treatment effects across all time points. The treatment group did not significantly affect recovery rates (remimazolam vs propofol: odds ratio, 0.72; 95% CI, 0.04–13.59;  $p = 0.829$ ;



**Figure 1** Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

**Abbreviations:** PP, per-protocol; ITT, intention-to-treat.

[Supplementary Table 1](#)). By day 7, 5.3% of remimazolam patients and 10.5% of propofol patients had not regained baseline cognitive function.

[Figure 2B–F](#) illustrate recovery trajectories for the overall and other PostopQRS domains (nociceptive, emotional, activities of daily living, and physiologic). No significant differences were observed between groups for any domain (all  $p > 0.05$ , [Supplementary Table 1](#)), suggesting comparable multidimensional recovery for both sedatives.

**Table 1** Demographic Characteristics of the Participants

	Remimazolam ( $n = 114$ )	Propofol ( $n = 114$ )	p value
Age, years	70 (67–75)	70 (68–75)	0.530
Sex, $n$ (%)			0.595
Male	59 (51.8%)	63 (55.3%)	
Female	55 (48.2%)	51 (44.7%)	

(Continued)

**Table 1** (Continued).

	<b>Remimazolam (n = 114)</b>	<b>Propofol (n = 114)</b>	<b>p value</b>
Weight, kg	62.5 (9.1)	61.3 (7.7)	0.252
Height, cm	165 (160–170)	164 (159–169)	0.325
BMI, kg m <sup>-2</sup>	22.9 (2.7)	22.7 (2.6)	0.477
Educational background, n (%)			0.656
Junior high school or below	63 (55.3%)	73 (64%)	
High school	38 (33.3%)	23 (20.2%)	
Associate degree or Bachelor's degree	13 (11.4%)	17 (14.9%)	
Master's degree or above	0 (0.0%)	1 (0.9%)	
ASA physical status, n (%)			0.648
I	8 (7.0%)	11 (9.6%)	
II	79 (69.3%)	73 (64.0%)	
III	27 (23.7%)	30 (26.3%)	
Comorbidities, n (%)			
Hypertension	50 (43.9%)	46 (40.4%)	0.592
Coronary artery disease	24 (21.1%)	28 (24.6%)	0.528
Diabetes mellitus	36 (31.6%)	32 (28.1%)	0.563
COPD	26 (22.8%)	33 (28.9%)	0.290

**Note:** Data are shown as mean (SD), median (IQR), or n (%).

**Abbreviations:** ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; SD, standard deviation.

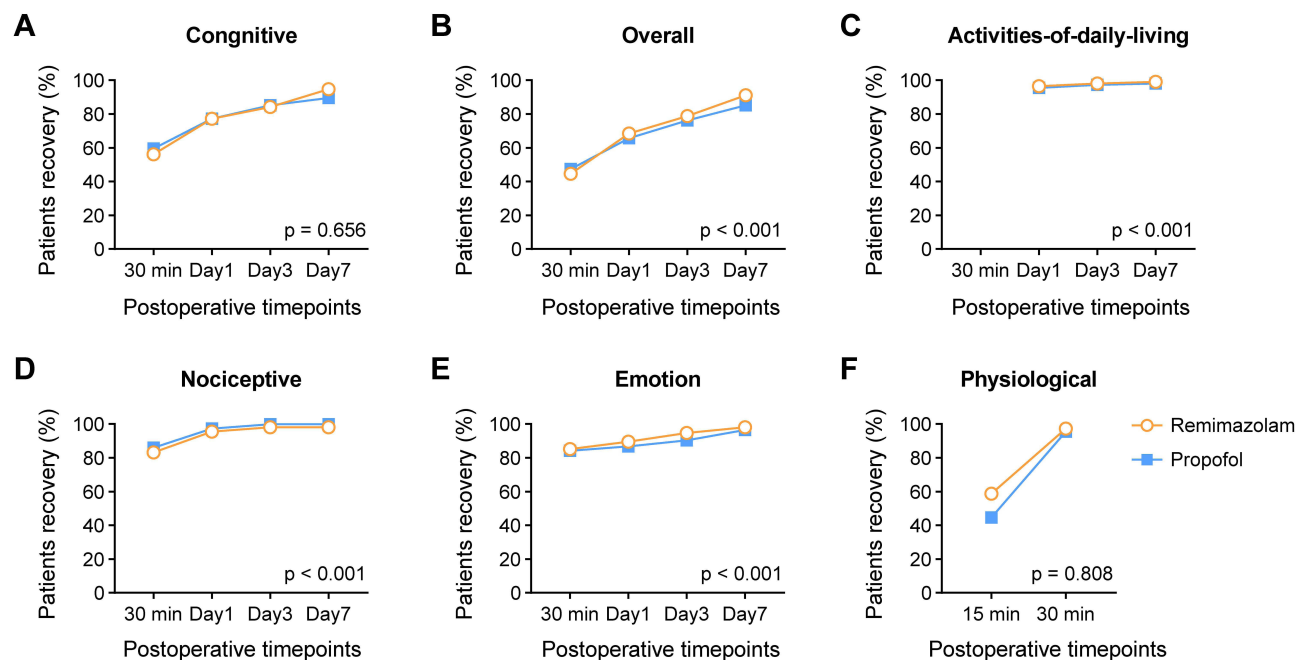
No significant differences between groups were found in induction time or colonoscopy duration (Table 2). Kaplan-Meier analysis revealed similar times to discharge readiness between the two groups, with a median of 23.7 minutes (95% CI: 23.0–24.0) for remimazolam and 24.0 minutes (95% CI: 23.0–25.0) for propofol (Hazard ratio: 1.23; 95% CI: 0.94–1.59; log-rank  $p = 0.120$ , [Supplementary Figure 1](#)). Remimazolam patients reported significantly higher satisfaction scores for sedation quality ( $p = 0.001$ ), while endoscopist satisfaction did not differ between groups ( $p = 0.531$ ).

Remimazolam was associated with significantly lower incidences of hypotension ( $p < 0.001$ ), hypoxemia ( $p = 0.024$ ), and injection site pain ( $p < 0.001$ ) compared to propofol. No significant differences were observed in other adverse events, including bradycardia, PONV, and dizziness (Figure 3).

## Discussion

Our results demonstrated comparable postoperative cognitive recovery profiles between remimazolam and propofol for sedation in elderly patients undergoing colonoscopy, as assessed by the PostopQRS. Discharge time was also similar between the two groups, suggesting that remimazolam does not prolong recovery compared to propofol. Furthermore, remimazolam was associated with lower incidences of hypotension, hypoxemia, and injection site pain. Notably, patients in the remimazolam group reported significantly higher satisfaction scores, indicating an improved overall experience. These findings support remimazolam as a suitable alternative to propofol for procedural sedation in elderly colonoscopy patients, offering comparable efficacy with potential advantages in safety and patient comfort.





**Figure 2** Recovery rates overall and by individual domains were measured using the Postoperative Quality of Recovery Scale (PostopQRS) following colonoscopy.

**Note:** (A) Proportion of patients recovered in the cognition domain. (B) Overall recovery across all PostopQRS domains. (C) Recovery of activities of daily living. (D) Nociceptive recovery (pain and nausea). (E) Emotional recovery (anxiety and depression). (F) Physiologic recovery. Data points represent the proportion of patients recovered in each domain. All p-values for group differences over time were derived from a generalized linear mixed model, reflecting the time-by-treatment interaction.

Several factors influenced our study outcomes. Patient-related factors included advanced age and comorbidities, which we controlled by selecting patients aged  $\geq 65$  years with ASA I–III status and excluding pre-existing cognitive impairment. Procedural factors, notably the standardized use of sufentanil, may have confounded effects attribution, though reflecting standard practice. Assessment-related factors included cognitive evaluation timing, with day 3 chosen to balance residual sedation effects with short-term cognitive impact detection. A key strength was using the PostopQRS,

**Table 2** Anesthesia, Procedure, and Recovery Details

	Remimazolam (n = 114)	Propofol (n = 114)	p value
Induction time, sec	91 (84–102)	89 (77–103)	0.230
Duration of colonoscopy, min	22 (18–28)	23 (18–28)	0.841
Time to fully alertness, min	15 (12–18)	16 (12–20)	0.129
Time to discharge, min	24 (20–25)	24 (20–28)	0.148
Endoscopist satisfaction, n (%)			0.531
Very satisfied	48 (42.1%)	54 (47.4%)	
Satisfied	55 (48.2%)	48 (42.1%)	
Neutral	8 (7.0%)	11 (9.6%)	
Dissatisfied	3 (2.6%)	1 (0.9%)	
Very dissatisfied	0 (0.0%)	0 (0.0%)	

(Continued)

**Table 2** (Continued).

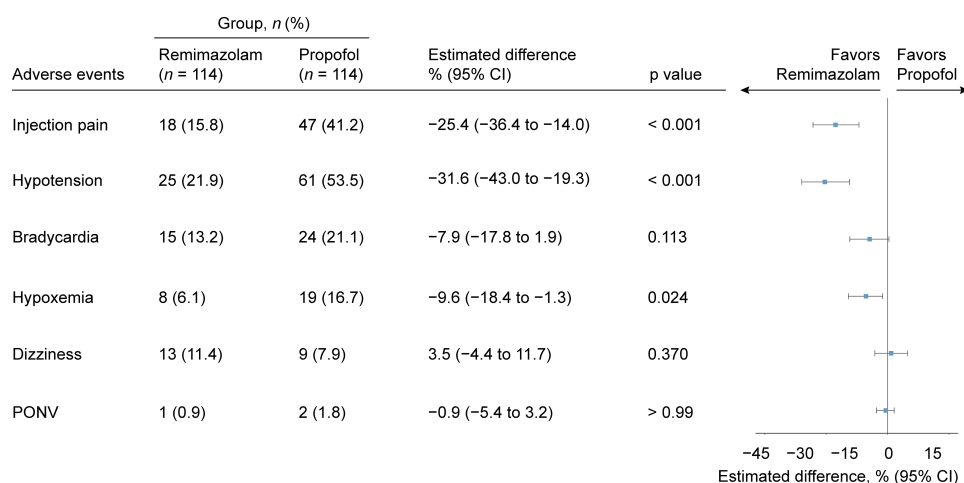
	Remimazolam (n = 114)	Propofol (n = 114)	p value
Patient satisfaction, n (%)			0.001
Very satisfied	62 (54.4%)	38 (33.3%)	
Satisfied	43 (37.7%)	46 (40.4%)	
Neutral	8 (7.0%)	22 (19.3%)	
Dissatisfied	1 (0.9%)	8 (7.0%)	
Very dissatisfied	0 (0.0%)	0 (0.0%)	

**Note:** Data are summarized as median (interquartile range [IQR] or n (%)).

which evaluates recovery relative to individual baselines, enabling personalized assessment and enhanced precision by accounting for individual variability.

Our results demonstrated comparable cognitive recovery profiles between remimazolam and propofol in elderly patients undergoing colonoscopy, contrasting with Tan et al<sup>26</sup> who reported inferior cognitive outcomes with remimazolam during upper gastrointestinal endoscopy. This discrepancy likely stems from methodological differences: We assessed cognitive recovery on day 3 using the PostopQRS with baseline comparisons, whereas Tan et al evaluated outcomes within 5 minutes of alertness using neuropsychological tests. Moreover, our study involved colonoscopy, which has different sedation requirements from upper endoscopy. The rapid reversibility of remimazolam with flumazenil suggests potential advantages for procedural sedation safety and efficiency,<sup>27</sup> further research is needed to validate these benefits.

Time to discharge readiness is a crucial indicator of postprocedural recovery. Our findings demonstrate comparable times to discharge readiness between remimazolam and propofol for sedation in elderly colonoscopy patients, consistent with prior studies.<sup>28</sup> Remimazolam's rapid onset, organ-independent metabolism, and non-reliance on hepatic or renal elimination likely facilitate timely discharge compared to other anesthetic agents.<sup>29</sup> These pharmacokinetic properties suggest remimazolam may be a suitable alternative to propofol for procedural sedation in elderly patients, who are more vulnerable to adverse events related to prolonged sedation and delayed recovery. Achieving timely discharge is

**Figure 3** Forest plot of differences in adverse event rates between the remimazolam and propofol groups.

**Note:** Adverse event rates were compared between groups using chi-square or Fisher's exact tests. Rate differences and 95% confidence intervals (CIs) were calculated. Remimazolam was associated with lower incidences of hypotension, hypoxemia, and injection site pain compared to propofol.



particularly important in ambulatory procedures like colonoscopy, where efficient patient turnover and resource utilization are essential.

Remimazolam demonstrated a more favorable hemodynamic profile than propofol in our elderly cohort (aged 65–87 years). The incidence of hypotension was significantly lower with remimazolam compared to propofol (21.9% vs 53.5%,  $p < 0.001$ ). This finding is particularly noteworthy as it extends our previous observations in a younger population (mean age  $47 \pm 11$  years), where we also found remimazolam to be associated with less hemodynamic instability.<sup>22</sup> The consistency across age groups strengthens the evidence for remimazolam's favorable safety profile, especially in elderly patients more vulnerable to hemodynamic fluctuations. Additionally, hypoxemia rates were lower with remimazolam (6.1% vs 16.7%,  $p = 0.024$ ), potentially due to reduced respiratory depression. This further supports the improved safety profile of remimazolam in elderly patients undergoing colonoscopy. These safety advantages may be particularly beneficial when non-anesthesiologists administer sedation, such as endoscopy suites or ambulatory surgical centers. Moreover, the potential for rapid reversal with flumazenil provides an additional safety measure, which could be especially reassuring for non-anesthesiologist providers managing elderly patients with comorbidities.

Patient satisfaction scores were higher with remimazolam, likely due to lower injection site pain incidence (15.8% vs 41.2%,  $p < 0.001$ ). While this incidence for propofol is lower than in some previous studies (up to 60%),<sup>30</sup> it remains clinically significant. The lower rate in our study may be due to cultural differences in pain reporting or our use of medium-chain/long-chain triglyceride propofol, which is associated with less pain.<sup>31</sup> Interestingly, endoscopist satisfaction did not differ significantly between groups. This may be because both agents provided adequate sedation for the procedure. The improved satisfaction with remimazolam represents an added benefit beyond its favorable respiratory and hemodynamic profiles in elderly colonoscopy patients.

This study has several limitations. The single-center design at a tertiary hospital and strict patient selection criteria restrict the broader application of our findings. The distinctive white appearance of propofol potentially compromised the double-blind design, though patients and outcome assessors remained blinded throughout the study. While the PostopQRS is validated for cognitive assessment, more comprehensive neurocognitive testing might have detected subtle changes, and repeated testing could have introduced learning effects. While reflecting clinical practice, the standardized use of sufentanil across both groups prevents attributing outcomes solely to the studied sedatives. Although our sample size was sufficient for the primary outcome, it may not have captured rare adverse events. Furthermore, our findings may not generalize to emergency procedures, other endoscopic interventions, or cases requiring different sedation depths.

This study addresses critical knowledge gaps by demonstrating remimazolam's comparable cognitive recovery to propofol with superior hemodynamic and respiratory stability in elderly colonoscopy patients. Given its advantages of improved safety margins and higher patient satisfaction, we recommend remimazolam (0.2 mg/kg induction, 0.1 mg/kg maintenance, with sufentanil 0.05 µg/kg) as a first-line sedative, especially for patients with cardiovascular risks, to optimize safety and efficiency in ambulatory settings.

## Conclusion

This randomized controlled trial demonstrates that remimazolam is a viable alternative to propofol for elderly colonoscopy patients, offering comparable cognitive recovery with an improved safety profile, including lower rates of hypotension, hypoxemia, and injection site pain. These findings support age-tailored sedation strategies in geriatric anesthesia, which is particularly relevant as colonoscopy demands increase in aging populations. Clinicians should consider patient characteristics, provider expertise, institutional guidelines, and cost-effectiveness factors when selecting sedation protocols to optimize safety and patient experience.

## Data Sharing Statement

The individual de-identified participant data supporting published results, the study protocol, and the statistical analysis plan are available from the corresponding author upon reasonable request.

## Acknowledgments

The authors thank Dr. Xiaoling Zheng and Dr. Wanyin Deng (Digestive Endoscopy Center, Fujian Provincial Hospital) for their generous support. We also thank Dr. Wenjun Lin (Fujian Medical University) for her valuable assistance and advice regarding the statistical analysis of this study.

## 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 all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

This study was funded by the Science and Technology Program of Haicang District of Xiamen, China (grant number 350205Z20232004), the Natural Science Foundation of Xiamen, China (grant number 3502Z202374068), National Natural Science Foundation Basic Research Enhancement Program Special Project (grant number JCZX202404), Fujian Strait Medical and Health Exchange Association Precision Anesthesia Research Project (grant number 2024HYHMZ04), Fujian Provincial Health Technology Project (grant number 2022CXA007), Fujian Provincial Natural Science Foundation (grant number 2022J01847), and Joint Funds for the Innovation of Science and Technology, Fujian province (grant number 2023Y9275). The funders had no role in study design, data collection and analysis, publication decisions, or manuscript preparation.

## Disclosure

The authors report no conflicts of interest in this work.

## References

1. Kanth P, Inadomi JM. Screening and prevention of colorectal cancer. *BMJ*. 2021;374:n1855. doi:10.1136/bmj.n1855
2. Davidson KW, Barry MJ; US Preventive Services Task Force. Screening for colorectal cancer: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2021;325(19):1965–1977. doi:10.1001/jama.2021.6238
3. Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015. *CA. Cancer J Clin*. 2016;66(2):115–132. doi:10.3322/caac.21338
4. Chen H, Li N, Ren J, et al. Participation and yield of a population-based colorectal cancer screening programme in China. *Gut*. 2019;68(8):1450–1457. doi:10.1136/gutjnl-2018-317124
5. Selva A, Mosconi G, Cacitti S, et al. Participants' satisfaction with colorectal cancer screening programs: a systematic review. *Prev Med*. 2023;175:107706. doi:10.1016/j.ypmed.2023.107706
6. Sahinovic MM, MMRF S, Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. *Clin Pharmacokinet*. 2018;57(12):1539–1558. doi:10.1007/s40262-018-0672-3
7. Sneyd JR, Absalom AR, Barends CRM, et al. Hypotension during propofol sedation for colonoscopy: a retrospective exploratory analysis and meta-analysis. *Br J Anaesth*. 2022;128(4):610–622. doi:10.1016/j.bja.2021.10.044
8. Kim SY, Moon CM, Kim MH, et al. Impacts of age and sedation on cardiocerebrovascular adverse events after diagnostic GI endoscopy: a nationwide population-based study. *Gastrointest Endosc*. 2020;92(3):591–602.e16. doi:10.1016/j.gie.2020.03.3864
9. Gregory A, Stapelfeldt WH, Khanna AK, et al. Intraoperative hypotension is associated with adverse clinical outcomes after noncardiac surgery. *Anesth Analg*. 2021;132(6):1654–1665. doi:10.1213/ANE.0000000000005250
10. Wang Y, Chen K, Ye M, Shen X. Intraoperative hypotension and postoperative delirium in elderly male patients undergoing laryngectomy: a single-center retrospective cohort study. *Braz J Anesthesiol*. 2024;75(1):844560. doi:10.1016/j.bjane.2024.844560
11. Xie X, Li J, Zhong Y, et al. A risk prediction model based on machine learning for postoperative cognitive dysfunction in elderly patients with non-cardiac surgery. *Aging Clin Exp Res*. 2023;35(12):2951–2960. doi:10.1007/s40520-023-02573-x
12. Prommer E. Midazolam: an essential palliative care drug. *Palliat Care Soc Pract*. 2020;14:2632352419895527. doi:10.1177/2632352419895527
13. Dossa F, Medeiros B, Keng C, Acuna SA, Baxter NN. Propofol versus midazolam with or without short-acting opioids for sedation in colonoscopy: a systematic review and meta-analysis of safety, satisfaction, and efficiency outcomes. *Gastrointest Endosc*. 2020;91(5):1015–1026.e7. doi:10.1016/j.gie.2019.12.047
14. Jafarian AA, Khatibi A, Mesbah Kiaei M, et al. Comparison of effects of stress and midazolam on retrograde and anterograde amnesia in patients undergoing general anesthesia. *Anesth Pain Med*. 2023;13(2):e134300. doi:10.5812/aapm-134300
15. Li WX, Luo RY, Chen C, et al. Effects of propofol, dexmedetomidine, and midazolam on postoperative cognitive dysfunction in elderly patients: a randomized controlled preliminary trial. *Chin Med J (Engl)*. 2019;132(4):437–445. doi:10.1097/CM9.000000000000098
16. Lee A, Shirley M. Remimazolam: a review in procedural sedation. *Drugs*. 2021;81:1193–1201. doi:10.1007/s40265-021-01544-8
17. Barbosa EC, Espirito Santo PA, Baraldo S, Meine GC. Remimazolam versus propofol for sedation in gastrointestinal endoscopic procedures: a systematic review and meta-analysis. *Br J Anaesth*. 2024;132(6):1219–1229. doi:10.1016/j.bja.2024.02.005

18. Zhao MJ, Hu HF, Li XL, Li XM, Wang DC, Kuang MJ. The safety and efficacy between remimazolam and propofol in intravenous anesthesia of endoscopy operation: a systematic review and meta-analysis. *Int. J Surg.* **2023**;109(11):3566–3577. doi:10.1097/JS9.0000000000000638
19. Royse CF, Newman S, Chung F, et al. Development and feasibility of a scale to assess postoperative recovery: the post-operative quality recovery scale. *Anesthesiology.* **2010**;113(4):892–905. doi:10.1097/ALN.0b013e3181d960a9
20. Schulz KF, Altman DG, Moher D, et al. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *BMJ.* **2010**;340:c332. doi:10.1136/bmj.c332
21. Chernik DA, Gillings D, Laine H, et al. Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: study with intravenous midazolam. *J Clin Psychopharmacol.* **1990**;10(4):244–251.
22. Yao Y, Guan J, Liu L, et al. Discharge readiness after remimazolam versus propofol for colonoscopy: a randomized, double-blind trial. *Eur J Anaesthesiol.* **2022**;39(12):911–917. doi:10.1097/EJA.0000000000001715
23. Chung F. Discharge criteria--A new trend. *Can J Anaesth.* **1995**;42(11):1056–1058. doi:10.1007/BF03011083
24. Royse CF, Newman S, Williams Z, et al. A human volunteer study to identify variability in performance in the cognitive domain of the postoperative quality of recovery scale. *Anesthesiology.* **2013**;119(3):576–581. doi:10.1097/ALN.0b013e318299f72b
25. Gurunathan U, Rahman T, Williams Z, et al. Effect of midazolam in addition to propofol and opiate sedation on the quality of recovery after colonoscopy: a randomized clinical trial. *Anesth Analg.* **2020**;131(3):741–750. doi:10.1213/ANE.0000000000004620
26. Tan Y, Ouyang W, Tang Y, et al. Effect of remimazolam tosylate on early cognitive function in elderly patients undergoing upper gastrointestinal endoscopy. *J Gastroenterol Hepatol.* **2022**;37(4):576–583. doi:10.1111/jgh.15761
27. Nobukuni K, Shirozu K, Maeda A, et al. Recovery of memory retention after anesthesia with remimazolam: an exploratory, randomized, open, propofol-controlled, single-center clinical trial. *JA Clin Rep.* **2023**;9(1):41. doi:10.1186/s40981-023-00635-7
28. Zhang J, Cairen Z, Shi L, et al. Remimazolam versus propofol for procedural sedation and anesthesia: a systemic review and meta-analysis. *Minerva Anesthesiol.* **2022**;88(12):1035–1042. doi:10.23736/S0375-9393.22.16817-3
29. Hu Q, Liu X, Wen C, et al. Remimazolam: an updated review of a new sedative and anesthetic. *Drug Des Devel Ther.* **2022**;16:3957–3974. doi:10.2147/DDDT.S384155
30. Jalota L, Kalira V, George E, et al. Prevention of pain on injection of propofol: systematic review and meta-analysis. *BMJ.* **2011**;342:d1110. doi:10.1136/bmj.d1110
31. Lee JS, Kim ES, Cho KB, Park KS, Lee YJ, Lee JY. Pain intensity at injection site during esophagogastroduodenoscopy using long- and medium-chain versus long-chain triglyceride propofol: a randomized controlled double-blind study. *Gut Liver.* **2021**;15(4):562–568. doi:10.5009/gnl20243

## Clinical Interventions in Aging

Dovepress

### Publish your work in this journal

Clinical Interventions in Aging is an international, peer-reviewed journal focusing on evidence-based reports on the value or lack thereof of treatments intended to prevent or delay the onset of maladaptive correlates of aging in human beings. This journal is indexed on PubMed Central, MedLine, CAS, Scopus and the Elsevier Bibliographic databases. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/clinical-interventions-in-aging-journal>