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CLINICAL TRIAL REPORT

Effects of Remimazolam-Propofol Anesthesia on Recovery and Sleep Quality in Older Adult Patients Undergoing Laparoscopic Colorectal Cancer Surgery: A Randomized Controlled Trial

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Purpose: Propofol and remimazolam monotherapy have their own limitations for general anesthesia in elderly patients. Optimizing anesthesia protocols is essential to enhance recovery and postoperative outcomes. This study aimed to evaluate the effects of combined sub-anesthetic doses of remimazolam and propofol on anesthesia recovery and sleep quality in this population.

Patients and Methods: This single-center, single-blind, prospective, randomized controlled trial enrolled 92 patients aged 65–80 years scheduled for elective laparoscopic colorectal cancer surgery. Patients were randomly allocated to either group P (propofol alone, 4–12 mg/kg/h) or group PR (propofol 2–4 mg/kg/h combined with remimazolam 0.3 mg/kg/h). The primary outcome was awakening time. The secondary outcomes included sedation scores, intraoperative hemodynamics, postoperative Pittsburgh Sleep Quality Index (PSQI) scores, Visual Analogue Scale (VAS) scores, Quality of Recovery-15 (QoR-15) scores, and the incidence of adverse events.

Results: Awakening time was significantly reduced in group PR compared with group P (14.8 ± 4.8 min vs 18.9 ± 5.1 min, $P < 0.001$). Group PR showed higher QoR-15 scores at 24 h postoperatively (129 [124.3–133] vs 121.5 [118–128], $P = 0.002$), a lower incidence of sleep disturbances on postoperative days 1 and 3 ($P < 0.001$), and more stable intraoperative hemodynamics with a lower incidence of hypotension (19.6% vs 54.4%, $P < 0.001$). No significant differences were observed in VAS scores or other adverse events.

Conclusion: Anesthesia maintenance using a sub-anesthetic dose of remimazolam combined with propofol was associated with shorter awakening time and improved postoperative recovery quality. This combination may represent a promising anesthetic strategy, but further research with objective sleep monitoring is warranted to confirm these findings.

Keywords: remimazolam, propofol, anesthesia maintenance, older adult patients, anesthesia recovery, sleep quality

Introduction

Colorectal cancer is the third most common malignancy and the second leading cause of cancer-related mortality, predominantly affecting individuals aged >50 years.[1,2] Laparoscopic surgical resection, the cornerstone of curative treatment for early-stage colorectal cancer, requires general anesthesia to ensure optimal surgical conditions. However, older adult patients—who exhibit diminished physiological reserves and a high prevalence of comorbidities—face elevated risks of perioperative hemodynamic instability, delayed recovery, and postoperative complications.[3] These vulnerabilities underscore the need to refine anesthetic strategies to enhance efficacy and safety in this population.

Propofol, a widely used intravenous anesthetic, is favored for its rapid onset, controllable sedation depth, and predictable recovery.[4] Nevertheless, dose-dependent cardiorespiratory depression, manifested as hypotension and impaired ventilation, poses significant challenges in older adult patients with compromised cardiopulmonary function.[5,6] Remimazolam, a novel

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benzodiazepine, shows potential as an alternative to propofol owing to its favorable pharmacological profile.[7] Unlike traditional benzodiazepines, remimazolam is metabolized via organ-independent hydrolysis by tissue esterases and can be rapidly reversed with flumazenil.[8] However, when used as a sole anesthetic agent, remimazolam has been associated with adverse outcomes, including paradoxical hypertension, delayed emergence, and intraoperative movement.[9–11] Theoretically, the co-administration of sub-anesthetic doses of remimazolam and propofol may achieve synergistic effects through the complementary modulation of γ-aminobutyric acid (GABA) type A receptors.[12] The balanced anesthesia strategy with combination therapy may reduce dose-dependent adverse effects by reducing reliance on high-dose monotherapy and accelerate patient recovery from anesthesia. However, robust clinical evidence supporting this strategy-particularly in older surgical populations-remains limited.

Furthermore, postoperative sleep disturbances (PSD) are commonly observed in most patients undergoing major abdominal surgery.[13] PSD can contribute to postoperative delirium (POD) and cognitive dysfunction, exacerbate acute postoperative pain, and delay recovery.[14] General anesthetics may modulate sleep phases by interacting with endogenous sleep-wake pathways or disrupting the circadian rhythm, potentially leading to either an improvement of or disturbance in sleep.[15] However, the impact of polypharmacy involving multiple general anesthetics on postoperative sleep remains unexplored.

To address this gap, a randomized controlled trial was conducted to evaluate the efficacy and safety of the remimazolam-propofol combination in older adult patients undergoing laparoscopic surgery for colorectal cancer.

Materials and Methods

Study Design and Participants

This single-center, prospective, randomized controlled clinical trial followed the Consolidated Standards of Reporting Trials (CONSORT) statement and the Declaration of Helsinki.[16] The study protocol was approved by the Ethics Committee of Shanghai Changhai Hospital (CHEC2024-126), and the trial was prospectively registered at the Chinese Clinical Trial Registry (ChiCTR2400083436). Written informed consent was obtained from all patients.

Patients aged 65–80 years, with an American Society of Anesthesiologists (ASA) physical status classification of I–III, with a body mass index of 18–28 kg/m^2, and who were scheduled for elective laparoscopic colorectal cancer surgery expected to last at least ≥1 h were included in the study. By contrast, patients with (1) severe cardiac disease (New York Heart Association > grade III), (2) renal insufficiency (serum creatinine >1.8 mg/dL or on dialysis) or hepatic impairment (Child-Pugh class C), (3) a known history of allergy to anesthetic drugs used in this study, (4) preoperative sleep disorders (Pittsburgh Sleep Quality Index [PSQI] score ≥ 7); (5) sedative or antidepressant dependence and alcoholism, (6) mental illness or cognitive impairment affecting compliance and cooperation, and (7) other contraindications to anesthesia or surgery were excluded.

Randomization and Blinding

Randomization was performed using block randomization (block size = 4) generated using SAS software 9.4 (SAS Inc., Cary, N.C., USA). Sequentially numbered, opaque, sealed envelopes were prepared by an independent statistician and opened by the attending anesthesiologist upon patient arrival in the operating room. Due to differences in drug formulation (remimazolam vs propofol), blinding of anesthesia providers was not feasible. However, the patients, outcome assessors, data analysts, and postoperative care teams remained blinded to group allocation.

Anesthesia Protocol

All procedures were performed by the same anesthesiologist. Upon entering the operating room, an intravenous line was established and vital signs were continuously monitored. The monitored parameters included electrocardiogram (ECG), mean arterial pressure (MAP), heart rate (HR), oxygen saturation (SpO_2), and bispectral index (BIS). Both groups received the same anesthesia induction protocol, which consisted of sequential intravenous administration of etomidate (0.3 mg/kg, Jiangsu Nhwa Pharmaceutical Co., Ltd., Xuzhou, China), sufentanil (0.4 μg/kg, YiChang HumanWell Healthcare Co., Ltd., Yichang, Hubei, China), cisatracurium (0.2 mg/kg, Nanjing King-Friend Biochemical Pharmaceutical Co., Ltd., Nanjing, China), and dexamethasone (8 mg, Henan Runhong Pharmaceutical Co., Ltd., Henan, China). Following induction, bilateral transversus

abdominis plane blocks were performed under ultrasound guidance, with 20 mL of 0.375% ropivacaine (AstraZeneca AB, Sweden) administered on each side.

During anesthesia maintenance, group PR received continuous intravenous infusions of propofol (2–4 mg/kg/h, Fresenius Kabi Austria GmbH, Austria) and remimazolam besylate (0.3 mg/kg/h, YiChang HumanWell Healthcare Co., Ltd., Yichang, Hubei, China). Group P only received continuous intravenous infusion of propofol (4–12 mg/kg/h). Both groups received remifentanil (YiChang HumanWell Healthcare Co., Ltd., Yichang, Hubei, China) at a rate of 0.2–0.3 μg/kg/min. Sufentanil was administered intraoperatively as needed based on hemodynamic parameters (0.1–0.2 μg/kg) with a final dose of 0.2 μg/kg given 30 minutes before the end of surgery, while cisatracurium was administered intermittently to maintain TOF ratio between 0–25% and discontinued 30 minutes before surgical completion. Based on established clinical guidelines and consensus statements, sedative infusion rates were adjusted to maintain BIS values between 40 and 60. If BIS exceeded 60 for >60 s, the propofol infusion was increased by 0.5 mg/kg/h. If BIS fell below 40, the infusion was decreased accordingly. Heart rate and blood pressure were maintained within 20% of the baseline values. Hypotension was defined as an MAP< 65 mmHg or a reduction of 20% from baseline and was treated with intravenous ephedrine (5–10 mg) or phenylephrine (50–100 μg), repeated as needed. Bradycardia, defined as an HR < 50 beats/min, was treated with intravenous atropine (0.5 mg). Tachycardia, defined as an HR > 100 beats/min, was treated with intravenous esmolol (10–20 mg). A PSQI score≥7 is considered indicative of sleep disturbance.[17]

Postoperatively, the patients were transferred to the post-anesthesia care unit (PACU), where anesthetic recovery was managed by nurses who were blinded to the group assignments. The patients were awakened at regular intervals (once per minute). Additionally, all patients received the same patient-controlled intravenous analgesia (PCIA) protocol postoperatively. The PCIA solution contained sufentanil (2 μg/kg) diluted to a total volume of 150 mL with normal saline. The pump was set to a background infusion rate of 2 mL/h, with a 0.5 mL bolus dose and a lockout interval of 15 minutes. All postoperative assessments and follow-up evaluations were performed by a single blinded researcher using standardized assessment instruments at prespecified time points.

Outcome Measures

The primary outcome was awakening time, defined as the interval from discontinuation of sedatives to eye opening and response to verbal commands (nodding or shaking hands). The secondary outcomes were (1) post-extubation sedation scores evaluated using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) and Richmond Agitation-Sedation Scale (RASS) scales at T5 (post-extubation) and T6 (upon PACU discharge; (2) perioperative hemodynamic parameters (MAP, HR, and BIS) measured at predetermined intervals (T0: before induction; T1: 1 min post-intubation; T2: skin incision; T3: after pneumoperitoneum establishment; T4: end of surgery; T5: post-extubation; T6: PACU discharge); (3) time-related metrics, including extubation time, time to achieve a modified Aldrete score of >9, and length of PACU stay; (4) frequency of vasoactive drug use during the perioperative period; (5) postoperative assessments, including PSQI scores (postoperative days 1, 3, and 7), VAS scores (6, 12, and 24 h postoperatively), and QoR-15 scores at 24 h after surgery; and (6) perioperative adverse events.

Sample Size Calculation and Statistical Analysis

Based on the results of our preliminary pilot study with 20 cases, the mean awakening time in group P was 18.2 ± 4.2 min, whereas that in group PR was 15.6 ± 3.8 min. A total sample size of 92 patients (46 patients per group) was calculated using PASS software (version 21.0.9; LLC, Kaysville, UT, USA) (two-sided $\alpha = 0.05$, $\beta = 0.2$, group ratio 1:1, 10% dropout rate). Normally distributed quantitative variables were expressed as the mean ± standard deviation and were compared using Student's *t*-test. Non-normally distributed quantitative data were expressed as medians (interquartile range) and compared using the Mann–Whitney *U*-test. Qualitative variables were expressed as numbers (percentages) and analyzed using the chi-square test or Fisher's exact test, as appropriate. Repeated measures analysis of variance was applied for intra-group comparisons over time. All tests were two-sided, and a *P* value of <0.05 was considered significant.

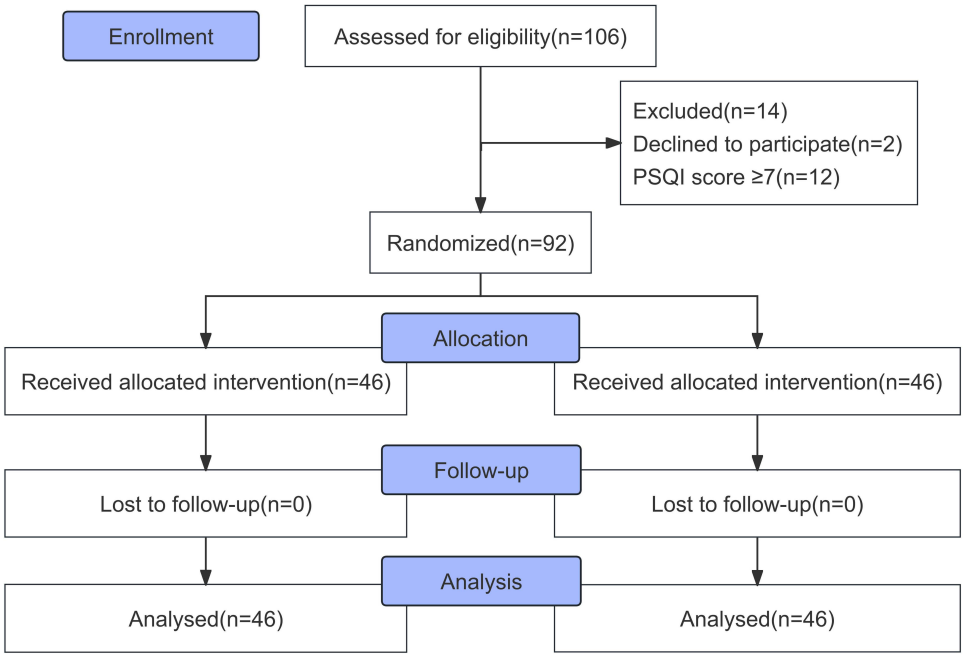

Figure 1 CONSORT flow diagram of the study.

Results

Of the 106 patients screened for eligibility, 92 were randomized and completed the study protocol, with no losses to follow-up or post-randomization dropouts (Figure 1). The baseline demographic and clinical characteristics were comparable between the two groups (Table 1). Compared to propofol alone, the propofol-remimazolam combination was associated with shorter awakening time and improved postoperative recovery quality. The detailed results are presented below.

Table 1 Demographic Characteristics of Patients in Each Group

	Propofol (n=46)	Propofol-Remimazolam (n=46)	*P*-value
Age, (years)	70±4	69±3	0.285
Sex, n(%)			0.182
Male	34 (73.9)	28 (60.9)	
Female	12 (26.1)	18 (39.1)	
BMI, (kg/m^2)	22.8±2.4	23.7±2.8	0.116
ASA, n(%)			0.414
I	2 (4.3)	6 (13.0)	
II	28 (60.9)	17 (37.0)	
III	16 (34.8)	23 (50.0)	
NYHA, n(%)			0.533
I	23 (50.0)	26 (56.5)	
II	23 (50.0)	20 (43.5)	
Baseline PSQI score	4.5(3–6)	4(3–6)	0.446
Propofol dosage, (mg)	840(700–1000)	500(450–637.5)	<0.001
Opioid dosage, (mg)	2(1.75–2.4)	2(1.6–2.5)	0.912
Anesthesia duration, (min)	201.8±47.1	200.0±41.4	0.844
Surgery duration, (min)	165.4±47.1	159.5±39.9	0.524

Notes: Data are presented as mean ± SD, median (IQR) or number (percentage).
Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association; PSQI, Pittsburgh Sleep Quality Index.

Table 2 Comparison of Outcome Measures

	Propofol (n=46)	Propofol-Remimazolam (n=46)	*P*-value
Awakening time (min)	18.9±5.1	14.8±4.8	<0.001*
Extubation time (min)	20.2±5.4	16.2±5.0	<0.001*
Time to modified Aldrete score>9 (min)	18.7±3.4	14.3±2.4	<0.001*
PACU stay duration (min)	21.5±3.2	17.0±2.1	<0.001*
MOAA/S score			
After extubation	4(3.8–4)	5(4–5)	<0.001*
Upon discharge from PACU	5(5–5)	5(5–5)	0.093
RASS score			
After extubation	−1(−2- −0.8)	0(−1-0)	<0.001*
Upon discharge from PACU	0(0–0)	0(0–0)	0.548

Notes: Data are presented as the mean ± SD or median (IQR). * $P < 0.05$, compared to Group P.
Abbreviations: PACU, post-anesthesia care unit; MOAA/S, modified observer's assessment of alertness/sedation scale; RASS, Richmond agitation and sedation scale.

Table 3 Comparison of QoR-15, VAS and PSQI

	Propofol (n=46)	Propofol-Remimazolam (n=46)	*P*-value
QoR-15 score	121.5(118–128)	129(124.3–133)	0.002*
VAS score			
After extubation	1(0–2)	1.5(0–2)	0.785
Upon PACU discharge	2(0–2)	1(0–2)	0.062
6h postoperatively	2(1–2.3)	2(1–3)	0.848
12h postoperatively	2(1–2)	2(0.8–2)	0.330
24h postoperatively	1(0–2)	1(0–2)	0.612
PSQI score≥7, n(%)			
Postoperative day 1	44(95.7)	31(67.4)	<0.001*
Postoperative day 3	36(78.3)	16(34.8)	<0.001*
Postoperative day 7	2(4.3)	3(6.5)	1.000

Notes: Data are presented as medians (IQR) or number (percentage). * $P < 0.05$, compared to Group P.
Abbreviations: QoR-15, quality of recovery-15; VAS, visual analog scale; PSQI, Pittsburgh Sleep Quality Index.

The primary outcome, awakening time, was significantly shorter in group PR compared with group P (14.8 ± 4.8 min vs 18.9 ± 5.1 min, $P < 0.001$). Similarly, extubation time, time to achieve a modified Aldrete score of >9, and length of PACU stay were all significantly reduced in the group PR ($P < 0.001$). Additionally, post-extubation sedation scores were improved in group PR (MOAA/S: 5 [4 to 5] vs 4 [3.8 to 4], $P < 0.001$; RASS: 0 [−1 to 0] vs −1 [−2 to −0.8], $P < 0.001$) (Table 2).

Group PR obtained higher QoR-15 scores at 24 h after surgery (129 [124.3 to 133] vs 121.5 [118 to 128], $P = 0.002$) and a lower incidence of sleep disturbances on postoperative days 1 and 3 ($P < 0.001$) (Table 3). The trends in sleep quality and PSQI scores are represented in Figure 2. VAS pain scores did not differ significantly between the groups ($P > 0.05$) (Table 3).

Intraoperatively, the incidence of hypotension was significantly higher in group P than in group PR (54.4 vs 19.6%, $P < 0.001$). No significant differences were observed in other adverse events (Table 4). Detailed hemodynamic data are provided in Figure 3.

Discussion

The primary finding of this study is that the combination of sub-anesthetic doses of remimazolam and propofol resulted in shorter awakening times and improved postoperative recovery quality. A reduced emergence time may lower the risk of early postoperative complications.[18] Furthermore, the decreased anesthesia time may substantially enhance operating room turnover efficiency. Its cumulative impact in high-volume surgical settings could lead to increased throughput, optimized resource utilization, and potential cost savings.[19]

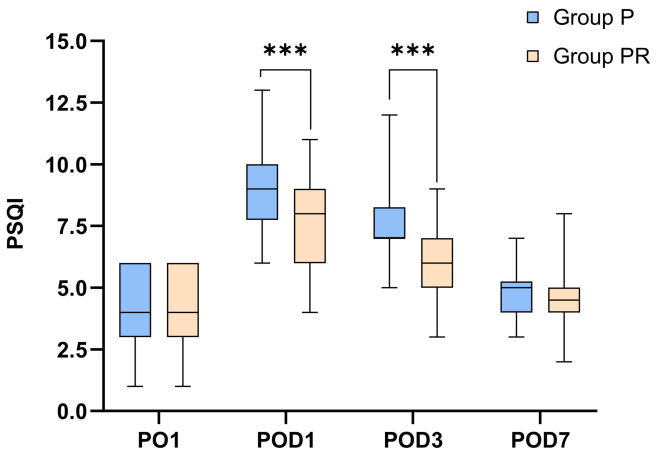

Figure 2 Comparison of PSQI scores between the groups. Box plots shows median (middle line), interquartile rang (box), and minimum and maximum value (whiskers) for Group P and Group PR; ***Indicates $P < 0.001$ between the groups.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; PO1, Preoperative day 1; POD1, Postoperative day 1; POD3, Postoperative day 3; POD7, Postoperative day 7.

The superior emergence profile observed in the combination group may be attributed to several factors. By excluding patients with significant hepatic or renal impairment, consistent drug metabolism was ensured. Moreover, the use of sub-anesthetic doses of remimazolam and propofol likely minimized the delayed recovery issues often associated with high-dose remimazolam monotherapy, as reported in previous studies.[20,21] Post-emergence sedation and agitation were assessed using both the MOAA/S and RASS scales. Although the group PR exhibited statistically superior scores compared with the propofol-only group, the clinical significance of these differences remains uncertain. This outcome may be attributed to the distinct sedative mechanism and pharmacokinetic properties of remimazolam. Moreover, its selective modulation of GABAA receptor pathways enables targeted sedation with minimal side effects, thereby avoiding excessive suppression of cortical and limbic functions. Consequently, remimazolam induces more physiological, sleep-like sedation that facilitates smoother emergence.[12] Moreover, in cases of delayed emergence, the availability of a specific antagonist, flumazenil, enables the rapid reversal of its sedative effects, further enhancing its safety and controllability.[22,23] This protocol may be more suitable for older adult patients, individuals with comorbidities, or those requiring prompt recovery of higher cognitive functions.

Perioperative sleep quality in older adult patients warrants particular attention, as postoperative sleep disturbances often result from a complex interplay of factors, including surgical stress, anesthetic agents, and environmental disruptions within clinical settings.[24] Propofol improves sleep architecture and mitigates circadian rhythm disruption. The underlying mechanisms may involve the activation of the ventrolateral preoptic nucleus and suppression of wakefulness-promoting systems, such as the lateral hypothalamic nucleus.[25] Benzodiazepines, commonly prescribed for the treatment of insomnia, may affect sleep regulation by modulating the GABAergic system, leading to reductions in extracellular acetylcholine and dopamine levels in the nucleus

Table 4 Perioperative Adverse Events

	Propofol (n=46)	Propofol-Remimazolam (n=46)	*P*-value
Use of vasoactive drugs, n(%)	27 (58.7)	12 (26.1)	0.002*
Intraoperative, n(%)			
Hypotension	25 (54.4)	9 (19.6)	<0.001*
Tachycardia	1 (2.2)	1 (2.2)	NS
Bradycardia	3 (6.5)	1 (2.2)	0.609
Postoperative, n(%)			
Agitation	4 (8.7)	0 (0)	0.125
Tachycardia	2 (4.4)	2 (4.4)	NS
Nausea and vomiting	6 (13.0)	4 (8.7)	0.738

Notes: Data are presented as numbers (percentages). NS; no significant differences were observed. * $P < 0.05$, compared to Group P.

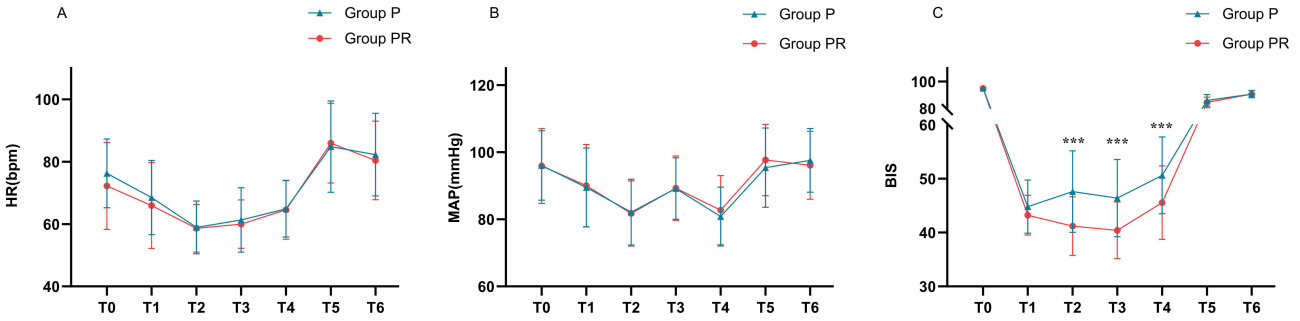

Figure 3 Comparison of HR(**A**), MAP(**B**), and BIS(**C**) between the two groups. Line graphs depict temporal trends of MAP, HR and BIS in Group P and Group PR; ***Indicates $P < 0.001$ between the groups.

Abbreviations: T0, before induction; T1, 1 min after intubation; T2, skin incision; T3, after successful establishment of pneumoperitoneum; T4, at the end of surgery; T5, after extubation; T6, upon PACU discharge; HR, Heart Rate; MAP, Mean Arterial Pressure; BIS, Bispectral index.

accumbens. This study demonstrated a lower incidence of PSD on postoperative days 1 and 3 in the PR group compared with the propofol-only group. However, the magnitude of this statistical difference may not reach the threshold for a minimal clinically important difference. Currently, research on the impact of remimazolam on perioperative sleep quality remains in the preliminary stages.[26,27] Future studies should adopt more robust evaluation methods, such as polysomnography, wearable sleep monitoring devices, and biological markers, to obtain a more comprehensive and objective assessment of the postoperative sleep quality.

Both groups exhibited good tolerability to their respective anesthesia maintenance protocols. However, group PR demonstrated a markedly lower incidence of hypotension compared with group P (19.6% vs 54.4%). Consequently, group P required significantly more frequent vasopressor support, consistent with the findings of previous studies.[28,29] These results highlight the superior hemodynamic stability provided by the combination of propofol and remimazolam. The observed differences were likely due to the myocardial depressant effects and peripheral vasodilatory properties associated with high-dose propofol.

The combination ratio of remimazolam and propofol implemented in the current study was determined based on previous titration studies. Under the established protocol, both groups achieved satisfactory sedation levels without any incidents of sedation failure or intraoperative awareness. Recent studies have shown that BIS values tend to remain high during remimazolam monotherapy.[30] In the current study, group PR exhibited significantly lower BIS values at three intraoperative time points (T2, T3, and T4), indicating that the combination group achieved deeper sedation. This observation can be attributed to the synergistic sedative effects of remimazolam and propofol. Both agents enhance GABAA receptor-mediated neurotransmission by suppressing central nervous system activity through distinct mechanisms. Propofol acts as a direct GABAA receptor agonist by facilitating chloride channel opening, whereas remimazolam binds to the benzodiazepine site on GABAA receptors, functioning as a positive allosteric modulator.[12] Certainly, the optimal dosage combination of remimazolam and propofol may also be one of the causes, and further research is needed.

Due to standardized pain management, there was no significant difference in postoperative VAS scores between the two groups. The QoR-15 questionnaire, a validated tool for assessing postoperative recovery, has demonstrated robust reliability and construct validity in clinical and research contexts.[31] In the current study, patients in group PR achieved significantly higher QoR-15 scores compared with those in group P ($P < 0.05$), meeting the minimal clinically important difference.[32] These findings align with those of previous research and suggest that remimazolam may provide superior benefits in terms of physical comfort and emotional well-being during the postoperative recovery period.[33]

This study has certain limitations. Firstly, as this was a single-center study with a relatively small sample size, the findings should be interpreted with caution. Secondly, the single-blind design of the study may introduce bias. We implemented multiple measures (standardized protocol, single anesthesiologist, BIS-guided sedation, objective primary outcome, blinded assessors) to mitigate this bias. Thirdly, given the critical role of sleep quality in postoperative recovery, further investigation should incorporate more comprehensive and objective measures. Finally, future research should focus on evaluating the efficacy of this anesthetic regimen in high-risk populations and determining the optimal dosing ratio between remimazolam and propofol to maximize the therapeutic benefits.

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Conclusion

This combination of sub-anesthetic doses of remimazolam and propofol, compared with propofol alone, was associated with shorter awakening times and better postoperative recovery quality. It also provided more stable intraoperative hemodynamics, suggesting its potential as a favorable alternative for anesthesia maintenance in older adult patients. Future large-scale, multi-center randomized trials are needed to confirm the generalizability and clinical impact of this anesthetic regimen.

Abbreviations

HR, Heart Rate; MAP, Mean Arterial Pressure; BIS, Bispectral Index; CRC, Colorectal Cancer; BMI, Body Mass Index; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association; MOAA/S, Modified Observer Assessment of Alertness/Sedation Scale; RASS, Richmond Agitation and Sedation Scale; PSQI, Pittsburgh Sleep Quality Index; VAS, Visual Analogue Scale; QoR-15, Quality of Recovery-15; PACU, Post-Anesthesia Care Unit; PCIA, Patient-Controlled Intravenous Analgesia; GABA, Gamma-aminobutyric Acid.

Data Sharing Statement

The datasets generated and/or analyzed during the current study are not publicly available due to institutional restrictions but are available from Lulong Bo upon reasonable request.

Ethics Approval and Consent to Participate

This study was registered at the Chinese Clinical Trials Registry (ChiCTR2400083436) on 04/25/2024, and the Ethics Committee of Shanghai Changhai Hospital approved the study (CHEC2024-126). All the participants provided written informed consent.

Consent for Publication

Individual consent was obtained from all participating patients.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest.

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