

Efficacy and safety of remimazolam besylate and ciprofol in painless gastrointestinal endoscopy in the elderly

Ziwei Zhu^{1*} 

1. The Fourth Affiliated Hospital of Soochow University  – Department of Anesthesiology – Suzhou, Jiangsu – China.

ABSTRACT

Purpose: This study aimed to ascertain the efficacy and safety of remimazolam besylate and ciprofol in elderly patients undergoing painless gastrointestinal endoscopy. **Methods:** Patients in the control group (n = 31) were anesthetized with ciprofol, and those in the observation group (n = 31) were anesthetized with remimazolam besylate. The anesthetic effect, analgesic effect, hemodynamics, cognitive function, and adverse reactions between the two groups were compared. **Results:** The observation group had shorter anesthesia onset time, recovery time, as well as anesthesia recovery room stay time and a higher effective rate of analgesia. At T₁, T₂, and T₃, the mean arterial pressure and heart rate of the observation group were higher versus the control group; at T₁ and T₂, SpO₂ in the observation group was higher versus the control group. The simple mental state scale score of the observation group was higher than that of the control group (all $p < 0.05$). The total incidence of adverse reactions exhibited no difference between the two groups ($p > 0.05$). **Conclusion:** Versus ciprofol, remimazolam besylate has better anesthetic and analgesic effects, more stable hemodynamics, less impact on patients' cognitive function, and good safety in elderly patients undergoing painless gastrointestinal endoscopy.

Key words: Endoscopy, Gastrointestinal. Hemodynamics. Cognition. Anesthetics.

■ Introduction

Elderly patients are representatives of a special group of patients with a higher incidence of co-morbid disorders and more susceptibility to endoscopic interventions¹. Dramatic elevations in life expectancy result in increasing utilization of gastrointestinal endoscopy in elderly patients². Advanced age is one of the significant risk factors for adverse reactions in the process of procedural sedation³. However, there are limited studies examining the risks, benefits, and utilization of common endoscopic procedures in the elderly group⁴. Therefore, our study focused on probing the safety and efficacy of remimazolam besylate and ciprofol in the elderly who undergo painless gastrointestinal endoscopy (PGE).

Propofol use is involved in risks such as hypo-tension, respiratory depression and pain at the injection site, and remimazolam and ciprofol attract the interest of researchers who are looking for alternatives to propofol⁵. Remimazolam and ciprofol are also new drugs tried to upgrade total intravenous anesthesia practice⁶. Remimazolam, a novel ultra-short-acting benzodiazepine, has been approved to be employed in procedural sedation, and this drug is also beneficial for both consistent sedation and quick recovery in PGE⁷. Remimazolam is also reported to have a minimal accumulative impact and reduced cardio-respiratory depression⁸. Remimazolam may serve as a viable alternative in elderly patients who undergo endoscopic procedures since it is linked to lower rates of hypo-tension in elderly patients undergoing upper gastrointestinal endoscopy under deep anesthesia or sedation versus propofol⁹. Moreover, remimazolam possesses not only sedative, amnestic, and anxiolytic properties, but also favorable hemodynamic stability¹⁰. Remimazolam tosylate, implemented in

*Corresponding author: zhuziwei6950@163.com

Received: Jul 14, 2024 | Accepted: Sept 30, 2024

Section editor: Everson Artifon 

Research performed at The Fourth Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China.

procedural sedation and general anesthesia, can be a safe and effective option for gastrointestinal endoscopy sedation in elderly patients, along with a lower incidence of sedation-relevant adverse reactions¹¹. Remimazolam tosylate is feasible and well tolerated for patients with superior safety profile than propofol¹².

Gastrointestinal endoscopy can be a difficult experience and leave an unpleasant impression on patients. Remimazolam tosylate has mild inhibitory effects on the respiratory system and the circulatory system¹³. Ciprofol refers to an agonist of the γ -aminobutyric acid type A receptor¹⁴. Versus propofol, ciprofol possesses fewer effects on hemodynamics and is more suitable for painless gastroscopy¹⁵. Currently, ciprofol is employed in anesthesia induction and PGE, and ciprofol at an appropriate dose is more advantageous for PGE than propofol in hemodynamics along with respiratory stability, with diminished nausea and vomiting, as well as pain at the injection site¹⁶. Furthermore, ciprofol has pharmacodynamic characteristics of rapid onset and recovery rate in pre-clinical experiments¹⁷. As a novel intravenous anesthetic agent, ciprofol shows respiratory and hemodynamic stability and provides better sedative effects with raised recovery quality and satisfaction¹⁸. However, the effects of remimazolam besylate and ciprofol in PGE in the elderly are rarely discussed.

Therefore, this paper was aimed at unveiling the efficacy and safety of remimazolam besylate and ciprofol in elderly patients undergoing PGE.

■ Methods

Ethics statement

The study was under the approval of the Ethic Committee of the Fourth Affiliated Hospital of Soochow University (approval number: 20221215), and the patients and their families offered their written informed consent.

Study subjects

Sixty-two elderly patients who underwent PGE in the Fourth Affiliated Hospital of Soochow University from March 2023 to June 2023 were recruited as the study subjects, and the subjects were separated into the control and observation groups by random number table method ($n = 31$ cases). Patients in the control group were anesthetized with ciprofol, and those in the observation group were anesthetized with remazolam benzenesulfonate. Inclusion criteria:

- Patients whose age ≥ 60 years old;
- Those with American Society of Anesthesiologists (ASA) classification I-II;
- Those with complete medical records;
- Those with informed consent for the study.

Exclusion criteria were:

- Those with a previous history of adverse anesthesia;
- Those combined with severe cardiac, renal, and other organ failure or combined with multiple light failures;
- Those combined with psychiatric disorders or cognitive deficits who could not communicate normally;
- Those with allergies or contraindications to the anesthetic drugs in this study.

Methodology

Prior to the PGE operation, the patients were fasted for at least 6 hours and deprived of water for at least 2 hours. After the patients entered the examination room, a venous channel was established, and the patients' routine vital signs were monitored during anesthesia and examination. The patients were supine for oxygen inhalation for 3 minutes (5 L/min), and anesthesia induction was performed after the patient's vital signs were stable. Anesthesia was induced with sufentanil citrate injection (Yichang Humanwell Pharmaceutical Co., Ltd., H20054171, specification: 50 $\mu\text{g/mL}$) at 0.1 $\mu\text{g/kg}$ through intravenous injection. After 3 minutes of anesthesia induction, the patients were anesthetized. Patients in the control group

were anesthetized with ciprofol (Liaoning Haisco Pharmaceutical Co., Ltd., H20200013, specification: 50 mg/20 mL) at 0.4 mg/kg through slow intravenous injection; those in the observation group were anesthetized with remimazolam besylate (Yichang Humanwell Pharmaceutical Co., Ltd., H20200006, Specification: 25 mg) at 0.25 mg/kg through slow intravenous injection. PGE was performed when the Modified Observer's Assessment of Alertness/Sedation score was ≤ 2 . During the operation, if the patients showed body movement and obvious swallowing movements, additional anesthetic drugs (0.2–0.5 mg/kg of ciprofol or 3 mg/time of remazolam besilate) could be supplemented as needed until the patients recovered smoothly. After finishing PGE, the patients were sent to the anesthesia recovery room.

Observation indicators

Clinical data collection

Clinical data, including age, gender, body mass index (BMI), and ASA grade, of all subjects were collected.

Anesthesia effects

Anesthesia onset time, gastrointestinal endoscopy time, recovery time, as well as anesthesia recovery room stay time of the two groups, were recorded.

Analgesic effects

After 30 minutes of examination, the numerical rating scale (NRS)¹⁹ was employed to evaluate the analgesic effects of the patients. NRS was divided into 0–10 grades, with 0–3 for mild pain, 4–6 for moderate pain, and 7–10 for severe pain. Analgesic effective rate = (mild pain + moderate pain) cases/total cases $\times$ 100%.

Hemodynamics

Mean arterial pressure (MAP), heart rate (HR), and oxygen saturation (SpO_2) of the two groups were recorded before anesthesia induction (T_0), at the time of gastroscopy reaching the throat (T_1), 3 minutes after gastroscopy reached the throat (T_2), and at the end of gastroscopy (T_3).

Cognitive function

At 0.5 h after the patient awoke from anesthesia, mini-mental state examination (MMSE)²⁰ was implemented to evaluate the cognitive function of the patients after awakening. There were 30 questions in MMSE. The correct answer to each question scored 1 point, and the wrong answer or not knowing scored 0 point, with scores ranging from 0 to 30 points. The higher the MMSE scores, the better the cognitive function.

Adverse reactions

Adverse reactions including nausea and vomiting, hypotension, dizziness, injection pain, bradycardia, and respiratory depression of the two groups were recorded.

Statistics

GraphPad Prism 6.01 software (Graph Pad Inc., La Jolla, CA, United States of America) was utilized for data analysis. Measurement data were depicted as mean $\pm$ standard deviation ($\bar{x} \pm s$), and t test was conducted for comparison between groups. Numeration data were depicted in the form of rate (%), and the χ^2 test was implemented for comparison. $P < 0.05$ was considered statistically significant.

Results

Clinical data

No significant difference was found in age, gender, BMI, ASA grade and educational level between the two groups ($p > 0.05$) (Table 1).

Table 1 – Clinical data between two groups.

Indicators		The control group (n = 31)	The observation group (n = 31)	χ^2/t value	p-value
Age (years old)		69.84 ± 5.20	69.26 ± 5.38	0.432	0.667
Gender	Male	18 (58.06%)	17 (54.84%)	0.066	0.798
	Female	13 (41.94%)	14 (45.16%)		
Body mass index (kg/m ²)		25.00 ± 3.40	24.85 ± 3.90	0.167	0.868
American Society of Anesthesiologists grade	I grade	11 (35.48%)	14 (46.16%)	0.603	0.437
	II grade	20 (64.52%)	17 (54.84%)		
Educational level	Elementary school level	7 (22.58%)	9 (29.03%)	0.37	0.831
	Middle school level	6 (19.35%)	5 (16.13%)		
	High school and above level	18 (58.06%)	17 (54.84%)		

Source: Elaborated by the author.

Anesthesia effects

The anesthesia onset time, recovery time, as well as anesthesia recovery room stay time in the observation group, were shorter versus those in the control group ($p < 0.05$). The gastrointestinal endoscopy time and number of additional medications exhibited no difference between the two groups ($p > 0.05$). The results demonstrated that remimazolam besylate had a good anesthetic effect on PGE in the elderly (Table 2).

Table 2 – Anesthetic effects between the two groups.

Indicators	The control group (n = 31)	The observation group (n = 31)	t value	p-value
Anesthesia onset time (s)	49.58 ± 4.98	40.65 ± 4.92	7.106	< 0.001
Gastrointestinal endoscopy time (min)	18.45 ± 3.45	18.32 ± 3.71	0.142	0.888
Recovery time (min)	9.29 ± 1.04	8.00 ± 1.07	4.829	< 0.001
Anesthesia recovery room stay time (min)	30.97 ± 4.20	23.45 ± 5.14	6.303	< 0.001
Number of additional medications	0.61 ± 0.67	0.58 ± 0.72	0.183	0.855

Source: Elaborated by the author.

Analgesic effects

A higher effective rate of analgesia in the observation group (96.77%) was noted versus in the control group (80.65%) ($p < 0.05$). The results unraveled that remimazolam besylate had a good analgesic effect on PGE in the elderly (Table 3).

Table 3 – Analgesic effects between the two groups.

Indicators	The control group (n = 31)	The observation group (n = 31)	χ^2 value	p-value
Mild pain	10 (32.26%)	14 (45.16%)	-	-
Moderate pain	15 (48.39%)	16 (51.61%)	-	-
Severe pain	6 (19.35%)	1 (3.23%)	-	-
Analgesic effective rate	25 (80.65%)	30 (96.77%)	4.026	0.045

Source: Elaborated by the author.

Hemodynamics

MAP, HR and SpO₂ levels in the two groups reduced first and then raised. No difference in MAP, HR and SpO₂ levels was exhibited between the two groups at T₀ ($p > 0.05$). At T₁, T₂, and T₃, MAP and HR in the observation group were higher versus in the control group ($p < 0.05$). At T₁ and T₂, SpO₂ in the observation group was higher in contrast with SpO₂ in the control group ($p < 0.05$). The results unearthed that remimazolam besylate could improve the hemodynamics of elderly patients undergoing PGE (Table 4).

Table 4 – Hemodynamics between the two groups.

Indicators		The control group (n = 31)	The observation group (n = 31)	<i>t</i> value	<i>p</i> -value
MAP (mmHg)	T ₀	87.52 ± 4.72	87.13 ± 4.28	0.338	0.736
	T ₁	70.23 ± 4.38	74.84 ± 3.39	4.639	< 0.001
	T ₂	74.06 ± 4.00	78.39 ± 3.20	4.698	< 0.001
	T ₃	81.48 ± 2.93	85.00 ± 3.00	4.668	< 0.001
HR (times/min)	T ₀	79.77 ± 4.75	80.23 ± 4.99	0.365	0.716
	T ₁	63.52 ± 4.46	66.39 ± 4.17	2.62	0.011
	T ₂	67.35 ± 5.10	70.77 ± 4.52	2.792	0.007
	T ₃	74.29 ± 3.46	79.61 ± 3.58	5.96	< 0.001
SpO ₂ (%)	T ₀	98.65 ± 0.84	98.61 ± 0.76	0.159	0.875
	T ₁	92.55 ± 2.77	94.97 ± 2.65	3.515	0.001
	T ₂	96.52 ± 1.34	98.35 ± 0.91	6.315	< 0.001
	T ₃	98.61 ± 0.62	98.87 ± 0.67	1.579	0.12

MAP: mean arterial pressure; HR: heart rate; SpO₂: oxygen saturation. Source: Elaborated by the author.

Cognitive function

MMSE scores of the observation group (28.42 ± 0.50) were higher versus those of the control group (25.19 ± 0.95) ($p < 0.05$). The results unraveled that remimazolam besylate had less effects on the cognitive function of elderly patients undergoing PGE.

Adverse reaction

The total incidence of adverse reactions exhibited no difference between the two groups ($p > 0.05$). The results unearthed that remimazolam besylate had good safety in PGE in the elderly (Table 5).

Table 5 – Adverse reactions between the two groups.

Indicators	The control group (n = 31)	The observation group (n = 31)	χ^2 value	<i>p</i> -value
Nausea and vomiting	2 (6.45%)	1 (3.23%)	-	-
Hypotension	2 (6.45%)	1 (3.23%)	-	-
Dizziness	3 (9.68%)	2 (6.45%)	-	-
Injection pain	2 (6.45%)	1 (3.23%)	-	-
Bradycardia	1 (3.23%)	1 (3.23%)	-	-
Respiratory depression	1 (3.23%)	0 (0.00%)	-	-
Total incidence rate	11 (35.48%)	6 (19.35%)	2.026	0.155

Source: Elaborated by the author.

■ Discussion

PGE is being increasingly and clinically utilized, and sedation management and options are important during the endoscopy procedures, which can not only reduce patient discomfort, but also facilitate high disorder detection rates¹⁴. This study focused on the efficacy and safety of remimazolam besylate and ciprofol in elderly patients undergoing PGE.

As previously reported, remimazolam is a safe and effective sedative drug with predictable sedative duration and rapid recovery in the process of gastrointestinal endoscopy²¹. It is demonstrated that remimazolam possesses better safety and efficacy for gastrointestinal endoscopy sedation, and remimazolam has an association with higher procedure success and lower need for rescue medication, as well as shorter total and delayed recalls²². Remimazolam tosylate can allow faster recovery from sedation, and patients who received remimazolam tosylate take shorter time to fully alert¹². It is also reported that remimazolam has the ability to achieve equivalent anesthetic and analgesic impact in elderly patients undergoing hip replacement²³.

In our paper, we compared the anesthesia and analgesic effects between the two groups, and found that the anesthesia onset time, recovery time, as well as anesthesia recovery room stay time in the observation group, were shorter versus the control group. Moreover, the effective rate of analgesia in the observation group was higher versus that in the control group. All these demonstrated that remimazolam besylate had a good anesthetic and analgesic effect on PGE in the elderly.

A previous study has revealed that the utilization of remimazolam tosylate leads to less frequent hemodynamic events¹¹. In addition, remimazolam possesses lower hemodynamic effects during general anesthesia, and a lower delta HR and delta MAP display more stable hemodynamic features of remimazolam⁷. Moreover, remimazolam besylate in combination with alfentanil is demonstrated to be a safe and effective sedation option for patients undergoing painless gastroscopy, which can not only avoid deep sedation and large hemodynamic fluctuations, but also have fewer adverse reactions and reduced HR and blood pressure²⁴. In our study, it was found that MAP, HR and SpO₂ levels of the two groups reduced first and then raised. At T₁, T₂, and T₃, MAP and HR in the observation group were higher; at T₁ and T₂, SpO₂ in the observation group was higher, in contrast with that in the control group. The results unearthed that remimazolam besylate could improve the hemodynamics of elderly patients undergoing PGE.

The MMSE scores of the remimazolam group are higher than the propofol group²³. Patients who received remimazolam are reported to have higher MMSE scores²⁵. In our paper, it was found that the MMSE scores of the observation group were higher in contrast with the control groups. The results unraveled that remimazolam besylate had less effects on the cognitive function of elderly patients undergoing PGE. A previous study has reported that remimazolam can lead to lower risks of bradycardia, hypoxemia, and injection pain, and there are no differences of statistical significance in other adverse reactions²⁶. In our paper, we unearthed that remimazolam besylate had good safety in PGE in the elderly, and the total incidence of adverse reactions presented no difference between the two groups.

However, this study has certain limitations, such as not considering whether the patients' educational level influences MMSE scores, not conducting a longer follow-up tracking (with follow-up ending upon hospital discharge, potentially missing post-discharge adverse reactions), and having a relatively small sample size.

■ Conclusion

In summary, this research demonstrated that, versus ciprofol, remimazolam besylate has better anesthetic and analgesic effects, more stable hemodynamics, less impact on patients' cognitive function, and good safety in elderly patients undergoing PGE. Additionally, this research lays a foundation for further exploration of the efficacy and safety of remimazolam besylate in elderly patients undergoing PGE. To enhance the robustness of these findings, a larger, multicenter, double-blind randomized controlled study is necessary in the future.

■ Conflict of interest

Nothing to declare.

■ Data availability statement

The data will be available upon request.

■ Funding

Not applicable.

■ About the authors

Zhu Z is a MM.

■ Acknowledgements

Not applicable.

■ References

1. Monkemuller K, Fry LC, Malfertheiner P, Schuckardt W. Gastrointestinal endoscopy in the elderly: current issues. *Best Pract Res Clin Gastroenterol*. 2009;23(6):821–7. <https://doi.org/10.1016/j.bpg.2009.10.002>
2. García García de Paredes A, Mateos Muñoz B, Albillos A. Endoscopia digestiva en pacientes de edad avanzada Gastrointestinal endoscopy in patients of advanced age. *Rev Esp Geriatr Gerontol*. 2018;53(5):293–8. <https://doi.org/10.1016/j.regg.2018.02.006>
3. Ye E, Wu K, Ye H, Zhang W, Chu L, Zhang K, Xie G, Jin Y, Fang X. Comparison of 95% effective dose of remimazolam besylate and propofol for gastroscopy sedation on older patients: A single-centre randomized controlled trial. *Br J Clin Pharmacol*. 2023;89(11):3401–10. <https://doi.org/10.1111/bcp.15839>
4. Razavi F, Gross S and Katz S. Endoscopy in the elderly: risks, benefits, and yield of common endoscopic procedures. *Clin Geriatr Med*. 2014;30(1):133–47. <https://doi.org/10.1016/j.cger.2013.10.010>
5. Skiljic S, Budrovac D, Cicvaric A, Neskovic N, Kvolik S. Advances in analgosedation and periprocedural care for gastrointestinal endoscopy. *Life*. 2023;13(2):473. <https://doi.org/10.3390%2Flife13020473>
6. Bajwa SJS, Vinayagam S, Shinde S, Dalal S, Vennel J, Nanda S. Recent advancements in total intravenous anaesthesia and anaesthetic pharmacology. *Indian J Anaesth*. 2023;67(1):56–62. https://doi.org/10.4103/ija.ija_1022_22
7. Peng X, Liu C, Zhu Y, Peng L, Zhang X, Wei W, Zhu T. Hemodynamic Influences of remimazolam versus propofol during the induction period of general anesthesia: a systematic review and meta-analysis of randomized controlled trials. *Pain Physician*. 2023;26(7):E761–E773.
8. Yan L, Wang X, Chen Z, Wu N, Li H, Yang B. Safety and efficacy of remimazolam tosilate combined with low-dose fentanyl for procedural sedation in obese patients undergoing gastroscopy: study protocol for a single-centre, double-blind, randomised controlled trial. *BMJ Open*. 2023;13(12):e079095. <https://doi.org/10.1136/bmjopen-2023-079095>

9. Lu K, Wei S, Ling W, Wei Y, Ran X, Huang H, Wang M, Wei N, Liao Y, Qin Z, Pan M, Wei Q, Fu L, Xiong B, Ma C, Jiang J, Huang Y. Remimazolam versus propofol for deep sedation/anaesthesia in upper gastrointestinal endoscopy in elderly patients: A multicenter, randomized controlled trial. *J Clin Pharm Ther.* 2022;47(12):2230–6. <https://doi.org/10.1111/jcpt.13797>
10. Garrett A, Flowers J, Ng V, Tobias JD. Remimazolam for sedation during upper gastrointestinal endoscopy in an adolescent. *J Med Cases.* 2022;13(10):495–8. <https://doi.org/10.14740/jmc4013>
11. Guo J, Qian Y, Zhang X, Han S, Shi Q, Xu J. Remimazolam tosylate compared with propofol for gastrointestinal endoscopy in elderly patients: a prospective, randomized and controlled study. *BMC Anesthesiol.* 2022;22(1):180. <https://doi.org/10.1186/s12871-022-01713-6>
12. Chen SH, Yuan TM, Zhang J, Bai H, Tian M, Pan CX, Bao HG, Jin XJ, Ji FH, Zhong TD, Wang Q, Lv JR, Wang S, Li YJ, Yu YH, Luo AL, Li XK, Min S, Li L, Zou XH, Huang YG. Remimazolam tosylate in upper gastrointestinal endoscopy: A multicenter, randomized, non-inferiority, phase III trial. *J Gastroenterol Hepatol.* 2021;36(2):474–81. <https://doi.org/10.1111/jgh.15188>
13. Zhu H, Su Z, Huai X, Chen C, Zhang X, Zhou J, Su D. Efficacy and safety of remimazolam tosylate for sedation during upper gastrointestinal endoscopy: study protocol for a multicenter randomized controlled trial. *Trials.* 2022;23(1):995. <https://doi.org/10.1186/s13063-022-06935-0>
14. Qin X, Lu X, Tang L, Wang C, Xue J. Ciprofol versus propofol for sedation in gastrointestinal endoscopy: protocol for a systematic review and meta-analysis. *BMJ Open.* 2023;13(5):e071438. <https://doi.org/10.1136/bmjopen-2022-071438>
15. Liao J, Lv S, Wang X, Ye Y, Zhang Q, Zeng L, Dong S. Effect of ciprofol on swallowing function in patients undergoing painless gastrointestinal endoscopy. *Medicine.* 2023;102(35):e34422. <https://doi.org/10.1097%2FMD.00000000000034422>
16. Chen L, Xie Y, Du X, Qin W, Huang L, Dai J, Qin K, Huang J. The effect of different doses of ciprofol in patients with painless gastrointestinal endoscopy. *Drug Des Devel Ther.* 2023;17:1733–40. <https://doi.org/10.2147/DDDT.S414166>
17. Teng Y, Ou M, Wang X, Zhang W, Liu X, Liang Y, Li K, Wang Y, Ouyang W, Weng H, Li J, Yao S, Meng J, Shangguan W, Zuo Y, Zhu T, Liu B, Liu J. Efficacy and safety of ciprofol for the sedation/anesthesia in patients undergoing colonoscopy: Phase IIa and IIb multi-center clinical trials. *Eur J Pharm Sci.* 2021;164:105904. <https://doi.org/10.1016/j.ejps.2021.105904>
18. Zhang J, Liu R, Bi R, Li X, Xu M, Li L, Su Y, Yan W. Comparison of ciprofol-alfentanil and propofol-alfentanil sedation during bidirectional endoscopy: A prospective, double-blind, randomised, controlled trial. *Dig Liver Dis.* 2024;56(4):663–71. <https://doi.org/10.1016/j.dld.2023.09.016>
19. Lee HJ, Cho Y, Joo H, Jeon JY, Jang YE, Kim JT. Comparative study of verbal rating scale and numerical rating scale to assess postoperative pain intensity in the post anesthesia care unit: A prospective observational cohort study. *Medicine.* 2021;100(6):e24314. <https://doi.org/10.1097/md.00000000000024314>
20. Zhou Y, Wang X, Li Z, Ma Y, Yu C, Chen Y, Ding J, Yu J, Zhou R, Yang N, Liu T, Guo X, Fan T, Shi C. Development of a brief cognitive screening tool for predicting postoperative delirium in patients with parkinson's disease: a secondary analysis. *Clin Interv Aging.* 2023;18:1555–64. <https://doi.org/10.2147/CIA.S410687>
21. Dai G, Pei L, Duan F, Liao M, Zhang Y, Zhu M, Zhao Z, Zhang X. Safety and efficacy of remimazolam compared with propofol in induction of general anesthesia. *Minerva Anesthesiol.* 2021;87(10):1073–9. <https://doi.org/10.23736/s0375-9393.21.15517-8>
22. Zhang L, Li C, Zhao C, You Y, Xu J. The comparison of remimazolam and midazolam for the sedation of gastrointestinal endoscopy: a meta-analysis of randomized controlled studies. *Afr Health Sci.* 2022;22(2):384–91. <https://doi.org/10.4314/ahs.v22i2.44>
23. Zhang J, Wang X, Zhang Q, Wang Z, Zhu S. Application effects of remimazolam and propofol on elderly patients undergoing hip replacement. *BMC Anesthesiol.* 2022;22(1):118. <https://doi.org/10.1186/s12871-022-01641-5>
24. Xu C, He L, Ren J, Zhou J, Guo H, Chen N, Chen H, Lv Y. Efficacy and safety of remimazolam besylate combined with alfentanil in painless gastroscopy: a randomized, single-blind, parallel controlled study. *Contrast Media Mol Imaging.* 2022;2022:7102293. <https://doi.org/10.1155/2022/7102293>

25. Liao YQ, Min J, Wu ZX, Hu Z. Comparison of the effects of remimazolam and dexmedetomidine on early postoperative cognitive function in elderly patients with gastric cancer. *Front Aging Neurosci.* 2023;15:1123089. <https://doi.org/10.3389/fnagi.2023.1123089>
26. Ahmer W, Imtiaz S, Alam DM, Ahmed K, Sajid B, Yousuf J, Asnani S, Fahim MAA, Ali R, Mansoor M, Safdar MT, Anjum MU, Hasanain M, Larik MO. Remimazolam versus propofol for sedation in gastrointestinal endoscopy and colonoscopy within elderly patients: a meta-analysis of randomized controlled trials. *Eur J Clin Pharmacol.* 2024;80(4):493–503. <https://doi.org/10.1007/s00228-024-03624-6>