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ORIGINAL RESEARCH

Impact of Remimazolam on Postoperative Delirium in Elderly Non-Cardiac Surgery Patients Admitted to the ICU: A Retrospective Propensity Score Matched Study

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Background: Postoperative delirium (POD) is a common complication. Remimazolam, a novel ultra-short-acting benzodiazepine, has been introduced in anesthesia practice, but its impact on the incidence of POD remains unclear. This study aims to evaluate the association between intraoperative use of remimazolam and the incidence of POD.

Methods: In this retrospective cohort study, patients aged 65 years and older who underwent elective non-cardiac surgery and were directly transferred to the ICU postoperatively were included. Based on intraoperative use of remimazolam, patients were categorized into the remimazolam group or the non-remimazolam group. The primary outcome was the incidence of POD within seven days postoperatively or until discharge (whichever occurred first), assessed using the CAM-ICU or the 3D-CAM. Propensity score matching (PSM) and multivariable logistic regression analyses were performed to adjust for potential confounders.

Results: After PSM, 826 pairs of patients were analyzed. The overall incidence of POD was 10.29%. The incidence of POD was 9.32% in the remimazolam group and 11.26% in the non-remimazolam group ($P = 0.225$). Multivariable logistic regression showed that remimazolam use was not significantly associated with POD incidence (aOR = 0.810, 95% CI = 0.588–1.113, $P = 0.196$). Intraoperative use of dexmedetomidine was associated with a reduced incidence of POD (aOR = 0.345, 95% CI = 0.236–0.511, $P < 0.001$), while postoperative administration of esketamine was an independent risk factor for POD (aOR = 2.644, 95% CI = 1.269–5.156, $P = 0.006$).

Conclusion: In elderly patients undergoing non-cardiac surgery, intraoperative use of remimazolam was not significantly associated with the incidence of postoperative delirium.

Keywords: remimazolam, postoperative delirium, intensive care unit, elder, non-cardiac

Introduction

Postoperative delirium (POD) represents a common complication subsequent to surgical interventions, particularly in geriatric populations, with incidence rates reported between 11% and 50%.[1,2] This condition not only extends the duration of hospitalization and increases healthcare expenditures but also has the potential to result in enduring cognitive deficits.[3] The emergence of POD is correlated with multiple factors, including advanced age, pre-existing medical conditions, and the selection of anesthetic agents, etc.[4] While some studies suggest a potential link between

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benzodiazepines (eg, midazolam) and POD,[5–7] recent studies and meta-analyses have reported no significant association.[8–10] The role of benzodiazepines in POD remains debated.

Remimazolam, a novel ultra-short-acting benzodiazepine, has attracted significant attention in the fields of anesthesia and sedation due to its rapid onset and swift metabolic clearance.[11] Remimazolam acts as a benzodiazepine agonist at the GABA_A receptor, enhancing GABAergic neurotransmission, which results in sedative, anxiolytic, and amnesic effects.[11]

Despite remimazolam's structural similarity to midazolam, it is characterized by a high clearance rate and a short half-life (terminal half-life of approximately 0.7–1.2 hours), undergoing rapid hydrolysis by nonspecific tissue esterases into an inactive metabolite (CNS7054).[12,13] This unique metabolism is independent of hepatic cytochrome P450 enzymes, which contributes to its predictable pharmacokinetic profile and minimal risk of drug accumulation even after prolonged infusion.[12,13]

The rapid decline in blood concentration allows for a quick recovery of cognitive function after cessation of administration. This is particularly important in the context of postoperative delirium, as benzodiazepines with longer half-lives may cause prolonged sedation and contribute to delirium. In contrast, remimazolam's rapid clearance may minimize the duration of GABA_A receptor overstimulation, reducing the risk of delirium associated with benzodiazepine use.

Current clinical studies have shown that remimazolam does not increase the incidence of POD in patients.[14–16] For example, Aoki et al reported no significant association between remimazolam and POD in elderly patients undergoing cardiovascular surgery,[14] while another randomized trial found similar POD rates between remimazolam and propofol groups in orthopedic surgery.[15] Additionally, Kaneko et al suggested a potential reduction in POD incidence with remimazolam in transcatheter aortic valve implantation.[16] However, these studies have certain limitations, such as small sample sizes, a focus on specific types of surgeries, and inconsistencies in the methods and timing of delirium assessments.[14–16] Therefore, our primary objective is to evaluate the relationship between the use of remimazolam during surgery and POD in elderly patients undergoing non-cardiac surgeries. This study specifically selected patients who were transferred to the ICU postoperatively for evaluation, as the enhanced monitoring in the ICU helps to identify more cases of POD, thereby improving the accuracy of the study results.

Methods

Selection of Participants

This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University (Approval Number: 2024-KY-2213-001). A waiver of informed consent was granted by the Ethics Committee, as this research involved a retrospective analysis of anonymized medical records, and obtaining individual consent was deemed impractical without compromising the scientific validity of the study. All data were de-identified to ensure patient confidentiality. This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and adhered to the STROBE guidelines.[17] The study included patients who underwent general anesthesia between January 2021 and December 2023. The inclusion criteria were: age over 65 years; elective non-cardiac surgery; and direct transfer to the ICU postoperatively. The exclusion criteria were: patients who were unconscious prior to surgery; a history of stroke or neurodegenerative diseases (such as Parkinson's or Alzheimer's disease); second or subsequent surgeries; neurosurgical procedures, and data missing. Patients were divided into the remimazolam group and the non-remimazolam group based on whether remimazolam was used during the anesthesia process.

Primary Outcome

The primary outcome was the incidence of delirium within seven days postoperatively or until discharge (whichever occurred first). Patients were assessed twice daily (8:00–10:00 and 18:00–20:00), and all physicians and nurses involved in the assessments were trained. In the ICU, physicians used the Confusion Assessment Method for the ICU (CAM-ICU) to evaluate the patients' delirium status. A positive CAM-ICU result indicated that the patient had developed delirium. Additionally, during the two assessment periods, any fluctuations in the patient's level of consciousness were also

evaluated and recorded. After leaving the ICU, anesthesia nurses conducted delirium assessments using the 3D-CAM twice daily.

Secondary Outcome

Secondary outcomes included postoperative pain intensity, nausea and vomiting (PONV), ICU length of stay, total length of hospital stay, and in-hospital mortality rate. Postoperative complications were defined as the incidence of bradycardia, tachycardia, hypotension, hypertension, and hypoxemia within seven days. Pain intensity was assessed daily by nurses using a Numerical Rating Scale (NRS) to determine the highest pain score experienced by patients during activities. PONV was also routinely assessed daily by nurses. Bradycardia and tachycardia were defined as a heart rate of less than 60 beats per minute or greater than 100 beats per minute, sustained for at least one minute. Hypertension and hypotension were defined as a systolic blood pressure greater than 140 mmHg or less than 90 mmHg, respectively. Hypoxemia was defined as an oxygen saturation level below 90%. The patient's vital signs are monitored every 30 minutes to 1 hour in the ICU. When the patient is transferred to the ward, vital signs are monitored every 4–6 hours. Patient characteristics included age, gender, ASA grade, preoperative comorbidities, type of surgery, intraoperative fluid infusion, urine output, estimated blood loss, use of vasoactive drugs during surgery, and postoperative medication usage. Surgery types are divided into abdominal, chest, and other (ear, nose, throat, thyroid, oral and maxillofacial, etc).

Statistical Analysis

All statistical analyses were conducted using RStudio (RStudio 2023.06.0 Build 421, R version 4.4.1). Descriptive data are presented as mean ± SD or median (interquartile range) for continuous variables and as frequency (%) for categorical variables. The Chi-square test was used to compare categorical variables between the two groups. The Shapiro–Wilk test was employed to assess the normality of continuous variables. Normally distributed data were analyzed using the *t*-test, while non-normally distributed data were assessed with the Mann–Whitney *U*-test. Propensity scores were analyzed using the "MatchIt" package in R (version 4.5.5), with propensity scores calculated through generalized linear models. A greedy nearest-neighbor matching approach was applied at a 1:1 ratio, with a caliper set at 0.2. All patient characteristics were utilized to calculate propensity scores. The absolute standardized difference (ASD) was calculated for each variable to assess the balance before and after matching (an ASD below 0.1 after matching was considered good balance). To evaluate the effect of remimazolam on POD, we performed a logistic regression analysis. The logistic regression was further adjusted for potential confounders, including age, gender, preoperative comorbidities, etc. The logistic regression analysis was performed on the matched dataset. In a post hoc exploratory subgroup analysis, we investigated the effect of remimazolam on POD in specific subgroups: patients aged over 80 years, patients who did not receive dexmedetomidine, patients who received postoperative esketamine, and by type of surgery. As secondary outcomes were exploratory, no adjustments were made for multiple comparisons.

Results

Patient Cohort

A total of 2432 patients aged over 65 underwent non-cardiac surgery and were admitted to the ICU, with 960 patients receiving remimazolam. After performing propensity score matching (PSM), 826 pairs of patients were included in the analysis (Figure 1). Patient characteristics are summarized in Table 1. Before PSM, patients in the remimazolam group (R group) were significantly younger (ASD=0.144), had fewer female patients (ASD=0.144), exhibited fewer comorbidities (eg, liver disease: ASD=0.169), had lower ASA grades (ASD=0.126), and had greater fluid infusion (ASD=0.368) and urine output (ASD=0.236), with notable differences in intraoperative and postoperative medication (eg, antihypertension: ASD=0.410) and surgical types (ASD=0.117). After PSM, these variables were highly balanced, with all ASD < 0.1 (Figure 2).

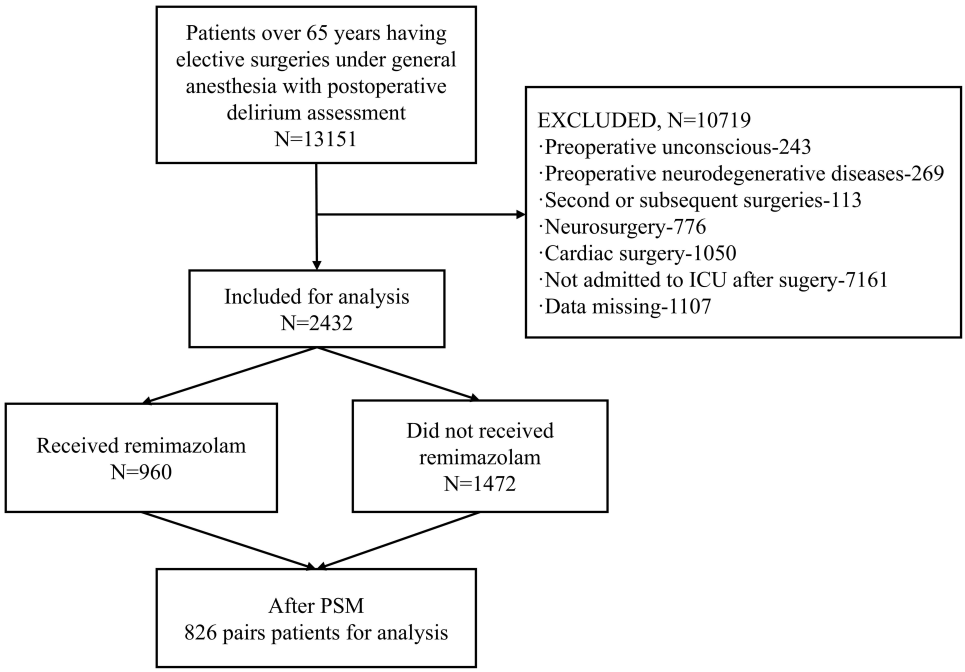

Figure 1 Flow diagram of patient recruitment.

Primary Outcomes

All patients included in the study underwent delirium assessments postoperatively, and we further reviewed the patients' electronic medical records to identify any fluctuations in consciousness beyond the assessment time points. Ultimately, after PSM, the overall incidence of POD was 10.29%. Remimazolam did not have a significant impact on the incidence of POD (R group 9.32% vs non-R group 11.26%, $P = 0.225$) (Table 2). Regression analysis also indicated that remimazolam was not associated with an increased incidence of POD, with an adjusted odds ratio (aOR) of 0.810 (95% CI 0.588–1.113; $P = 0.196$). The multivariate regression results for POD revealed that the intraoperative use of dexmedetomidine was associated with a reduced incidence of POD (aOR 0.345; 95% CI 0.236–0.511; $P < 0.001$). Conversely, the postoperative administration of esketamine was identified as an independent risk factor for POD (aOR 2.644; 95% CI 1.269–5.156; $P = 0.006$) (Table 3 and Figure 3, Supplementary Table 1).

Secondary Outcomes

There was no significant association between remimazolam and the following outcomes: postoperative pain intensity (aOR 0.974; 95% CI 0.869–1.091; $P = 0.643$), PONV (aOR 1.054; 95% CI 0.767–1.449; $P = 0.746$), bradycardia (aOR 0.807; 95% CI 0.608–1.068; $P = 0.134$), tachycardia (aOR 0.985; 95% CI 0.698–1.388; $P = 0.930$), hypotension (aOR 0.825; 95% CI 0.661–1.030; $P = 0.090$), hypertension (aOR 1.036; 95% CI 0.766–1.402; $P = 0.817$), hypoxemia (aOR 0.926; 95% CI 0.630–1.360; $P = 0.696$), ICU length of stay (aOR 1.002; 95% CI 0.996–1.009; $P = 0.524$), hospital length of stay in the general ward (aOR 1.003; 95% CI 0.995–1.012; $P = 0.492$), and mortality rate (aOR 1.763; 95% CI 0.751–4.435; $P = 0.204$).

Subgroup Analysis

Post-hoc subgroup analysis showed that no significant interaction was observed between the remimazolam group and the non-remimazolam group in all strata (all P for interaction were > 0.05). Specifically, patients over 80 years of age (aOR 0.860; 95% CI 0.470–1.570; $P = 0.631$), those who did not receive dexmedetomidine (aOR 0.940; 95% CI 0.480–1.830; $P = 0.848$), patients administered esketamine postoperatively (aOR 2.100; 95% CI 0.550–7.960; $P = 0.275$), and different types of surgery ($P = 0.383$) (Figure 4).

Table 1 Baseline Variables

Variables	Before PSM			After PSM		
	No Remimazolam (n=1472)	Remimazolam (n=960)	ASD	No Remimazolam (n=826)	Remimazolam (n=826)	ASD
Age, years	71 [68, 75]	70 [67, 74]	0.144	71.62±4.96	71.23±4.79	0.083
Gender			0.144			0.005
Male, n (%)	1045 (70.99)	615 (64.06)		545 (65.98)	547 (66.22)	
Female, n (%)	427 (29.01)	345 (35.94)		281 (34.02)	279 (33.78)	
Preoperative comorbidity, n (%)						
Diabetes	172 (11.68)	148 (15.42)	0.103	110 (13.32)	111 (13.44)	0.003
Cancer	588 (39.95)	444 (46.25)	0.126	340 (41.16)	358 (43.34)	0.044
Cardiovascular diseases	332 (22.55)	256 (26.67)	0.093	208 (25.18)	211 (25.54)	0.008
Liver disease	608 (41.30)	320 (33.33)	0.169	313 (37.89)	299 (36.20)	0.036
Renal disease	120 (8.15)	76 (7.92)	0.009	63 (7.63)	67 (8.11)	0.018
Respiratory disease	220 (14.95)	132 (13.75)	0.035	122 (14.77)	119 (14.41)	0.011
ASA grade, n (%)			0.126			0.016
I	20 (1.36)	20 (2.08)		11 (1.33)	16 (1.94)	
II	472 (32.07)	344 (35.83)		279 (33.78)	270 (32.69)	
III	632 (42.93)	412 (42.92)		354 (42.86)	367 (44.43)	
IV	348 (23.64)	184 (19.17)		182 (22.03)	173 (20.94)	
Dexmedetomidine, n (%)	1188 (80.71)	852 (88.75)	0.255	730 (88.38)	725 (87.77)	0.019
Vasopressors, n (%)	1332 (90.49)	880 (91.67)	0.043	758 (91.77)	753 (91.16)	0.022
Antihypertension, n (%)	380 (25.82)	444 (46.25)	0.410	295 (35.71)	325 (39.35)	0.073
Infusion volume (mL)	2300 [1700, 3150]	2750 [2050, 3650]	0.368	2756.97±1190.77	2774.04±1106.01	0.014
Urine volume (mL)	400 [200, 800]	500 [300, 1000]	0.236	713.32±616.29	712.46±652.83	0.001
Blood loss (mL)	343.64±461.91	378.26±516.27	0.067	360.47±533.01	355.16±428.05	0.010
Postoperative drugs, n (%)						
Dexmedetomidine	48 (3.26)	56 (5.83)	0.110	42 (5.08)	45 (5.45)	0.015
Hydromorphine	1272 (86.41)	896 (93.33)	0.277	777 (94.07)	769 (93.10)	0.039
Dezocine	1080 (73.37)	784 (81.67)	0.214	674 (81.60)	672 (81.36)	0.006
Palonosetron	816 (55.43)	540 (56.25)	0.016	495 (59.93)	471 (57.02)	0.059
Esketmine	32 (2.17)	32 (3.33)	0.065	26 (3.15)	21 (2.54)	0.034
Flurbiprofen axetil	104 (7.07)	128 (13.33)	0.184	83 (10.05)	91 (11.02)	0.028
Dexamethasone	32 (2.17)	56 (5.83)	0.156	32 (3.87)	37 (4.48)	0.026
Type of surgery, n (%)			0.117			0.076
Abdominal	1144 (77.72)	696 (72.50)		665 (80.51)	637 (77.12)	
Chest	248 (16.85)	92 (9.58)		86 (10.41)	89 (10.77)	
Other	80 (5.43)	172 (17.92)		75 (9.08)	100 (12.11)	

Notes: Data are presented as mean ± SD, numbers (%) or median (interquartile range).
Abbreviations: ASA, American Society of Anesthesiologists; ASD, absolute standardized difference; PSM, propensity score matching.

Discussion

In our retrospective study, we analyzed data from 1652 patients aged 65 and older, all of whom were treated at a large medical center in China. After adjusting for confounding factors, we found that the intraoperative use of remimazolam in elderly patients undergoing non-cardiac surgery was not associated with an increased incidence of POD. Although we employed PSM to adjust for confounding factors, which reduced the final number of patients included in the statistical analysis, this sample size far exceeded that of previous similar studies.

The overall incidence of POD in our cohort was 10.29%, which is slightly lower than that reported in some previous studies.[18,19] This discrepancy may be related to differences in the study populations and the types of surgeries performed. Additionally, a significant proportion of patients in our cohort received dexmedetomidine, and intraoperative monitoring

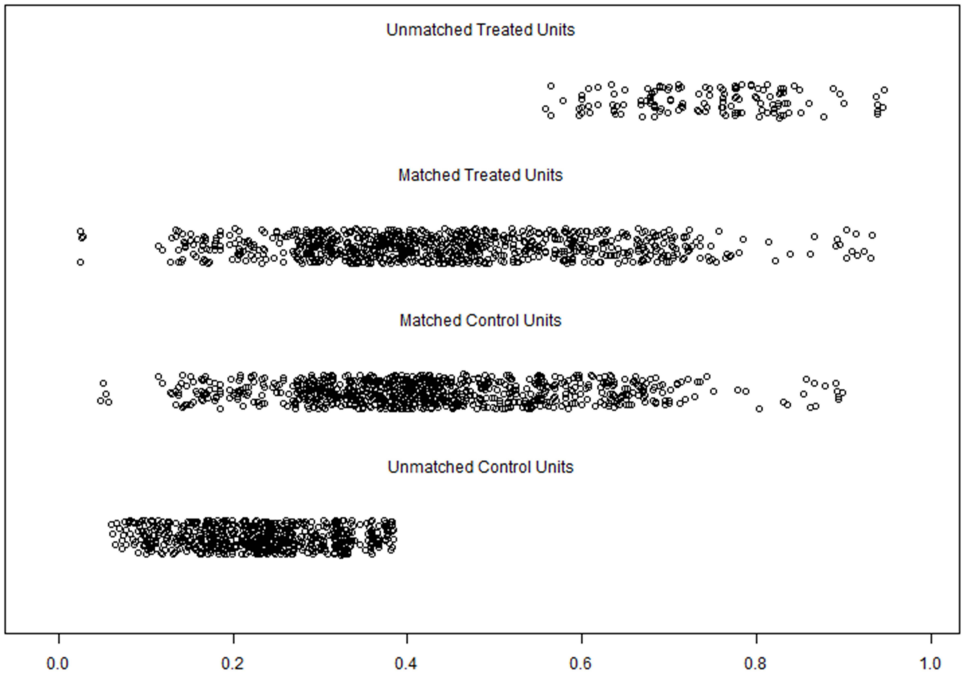

Figure 2 Scatter plot of propensity score distributions. The propensity scores of the two groups are similar after matching. The horizontal axis represents the propensity scores. The propensity score distributions for the treatment groups (those assigned a value of 1) and control groups (those assigned a value of 0) are presented in sequence, displaying the distributions before and after matching.

of the Bispectral Index (BIS) along with effective postoperative analgesia may have contributed to the reduction in the incidence of POD.

Previous studies have suggested that benzodiazepines may increase the risk of POD in patients; however, these studies primarily included high-dose or relatively long-acting benzodiazepines.[5–7,20] Recent studies have shown that the preoperative use of midazolam does not increase the incidence of POD in elderly patients[18,19] Remimazolam, on the other hand, is an ultra-short-acting benzodiazepine that is metabolized more rapidly in the body compared to traditional benzodiazepines. It can be quickly cleared from the system, and even with prolonged infusion, it does not lead to significant accumulation, thereby reducing the drug's inhibitory effects on the central nervous system. The rapid metabolism of remimazolam also allows patients to regain consciousness quickly after surgery, which is beneficial for the swift recovery of cognitive function, thereby lowering the risk of delirium.[21,22]

Table 2 Primary and Secondary Outcomes

Variables	No Remimazolam (n=826)	Remimazolam (n=826)	OR (95% CI)	*P*
POD, n (%)	93 (11.26)	77 (9.32)	0.81(0.588–1.113)	0.196
NRS pain scores	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]	0.974(0.869–1.091)	0.643
PONV, n (%)	83 (10.05)	87 (10.53)	1.054(0.767–1.449)	0.746
Bradycardia, n (%)	124 (15.01)	103 (12.47)	0.807(0.608–1.068)	0.134
Tachycardia, n (%)	72 (8.72)	71 (8.60)	0.985(0.698–1.388)	0.930
Hypotension, n (%)	225 (27.24)	195 (23.61)	0.825(0.661–1.03)	0.090
Hypertension, n (%)	94 (11.38)	97 (11.74)	1.036(0.766–1.402)	0.817
Hypoxemia, n (%)	58 (7.02)	54 (6.54)	0.926(0.63–1.36)	0.696
ICU stays (h)	28.00 [18.00, 37.00]	28.00 [18.00, 38.00]	1.002(0.996–1.009)	0.524
Hospital stays (day)	13.00 [11.00, 18.00]	14.00 [10.00, 20.00]	1.003(0.995–1.012)	0.492
Mortality, n (%)	8 (0.97)	14 (1.69)	1.763(0.751–4.435)	0.204

Notes: *P*: univariate regression analysis. Data are presented as numbers (%) or median (interquartile range).
Abbreviations: POD, postoperative delirium; NRS, numeric rating scale; PONV, postoperative nausea and vomiting; ICU, intensive care unit.

Table 3 Logistic Regression Analysis for POD

Variables	All (n = 1652)	No POD (n=1482)	POD (n=170)	Univariate Analysis		Multivariate Analysis	
				OR (95% CI)	*P*	OR (95% CI)	*P*
Dexmedetomidine	1455 (88.08)	1329 (89.68)	126 (74.12)	0.330 (0.226–0.487)	<0.001	0.345 (0.236–0.511)	<0.001
Remimazolam	826 (50.00)	749 (50.54)	77 (45.29)	0.810 (0.588–1.113)	0.196		
Postoperative drugs, n (%)							
Esketmine	47 (2.85)	35 (2.36)	12 (7.06)	3.140 (1.536–6.007)	0.001	2.643 (1.269–5.156)	0.006

Note: Data are presented as numbers (%).
Abbreviation: POD, postoperative delirium.

Our findings are consistent with those recent studies. For instance, in a prospective cohort study by Aoki et al,[14] which included 200 elderly patients undergoing cardiovascular surgery, the authors reported no significant association between continuous remimazolam infusion and POD (incidence: 12% in remimazolam group vs 15% in control, *P*=0.42). Similarly, Yang et al[15] conducted a randomized controlled trial in 120 elderly patients undergoing orthopedic surgery and found comparable rates of POD between remimazolam and propofol groups (10% vs 12.5%, *P*=0.75). In contrast, Kaneko et al[16] observed a lower incidence of POD with remimazolam (5.6% vs 21.4%, *P*=0.02) in a retrospective study of patients undergoing transcatheter aortic valve implantation. This discrepancy might be attributed to the use of flumazenil for reversal and shorter surgical duration (approximately 100 minutes) in their study, which could have minimized the sedative effects of benzodiazepines. Our study, with a larger sample size and broader inclusion of non-cardiac surgeries, provides further evidence that remimazolam does not increase the risk of POD in elderly ICU patients.

In the multivariate regression analysis of delirium, we found that the intraoperative use of dexmedetomidine is associated with a reduced incidence of POD. This finding is consistent with several previous randomized controlled trials examining the relationship between dexmedetomidine and POD in elderly patients undergoing non-cardiac surgery.[23–25] Dexmedetomidine, a highly selective α_2-adrenergic receptor agonist, provides sedative, analgesic, and anxiolytic effects without causing significant respiratory depression.[25] The mechanisms by which it may reduce POD are believed to include the attenuation of perioperative inflammatory responses, the reduction in the consumption of other anesthetic agents, and the promotion of more stable hemodynamics.[23–25] In the present study, a high rate of dexmedetomidine utilization was observed in both groups (87.77% in the remimazolam group and 88.38% in the non-remimazolam group after matching). This may have influenced the overall incidence of POD and could partially account for the lower POD

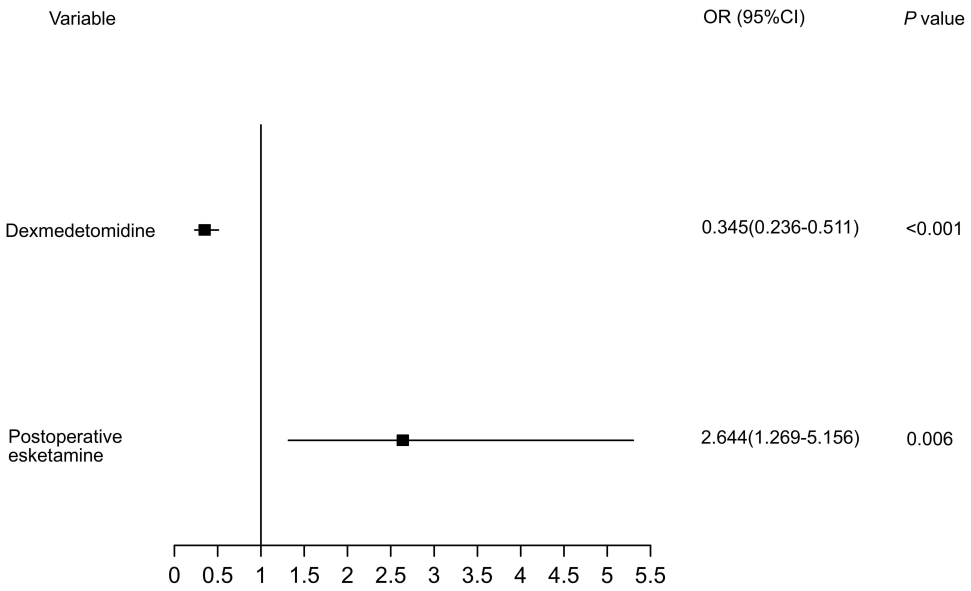

Figure 3 Forest plot of factors related to postoperative delirium.

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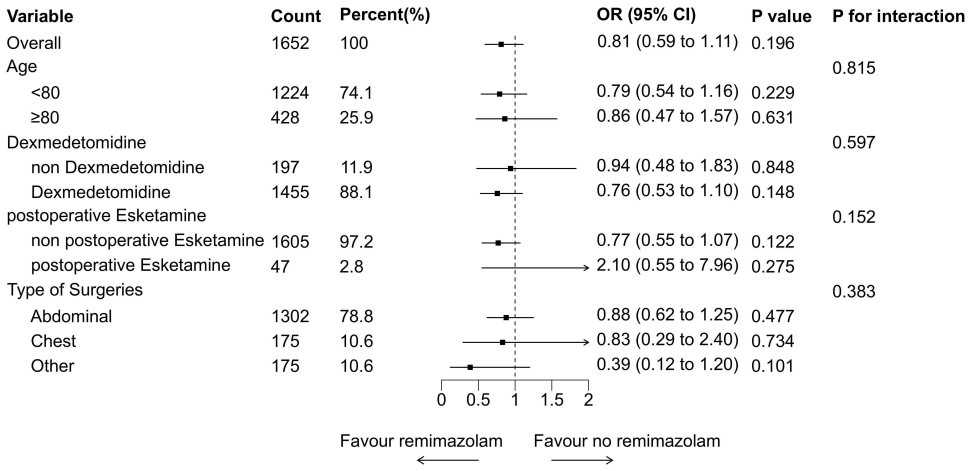

Figure 4 Forest plot of subgroup analysis.

rate observed in this study compared to previous reports. Therefore, in clinical practice, the use of dexmedetomidine may be considered for elderly surgical patients, particularly those at high risk for POD, in order to mitigate the risk of POD development.

Conversely, our findings indicate that the postoperative administration of esketamine is an independent risk factor for POD. Esketamine, the S-enantiomer of ketamine, possesses enhanced analgesic properties and is utilized for post-operative pain management. However, the association between esketamine and POD remains unclear. The previous large randomized controlled trials have shown that a single subanesthetic dose of ketamine does not affect the incidence of POD in elderly patients undergoing major surgery.[26] Recently, a small-scale study[27] has suggested that low-dose esketamine may improve postoperative pain and mood without compromising early cognitive function, our results suggest a potential increase in POD risk. It should be noted that the number of patients receiving esketamine in our study was limited (n = 26 in the matched non-remimazolam group, and n = 21 in the remimazolam group), and stratified analysis based on varying dosages was not performed, which constrains the interpretation of these results. Therefore, this finding warrants further validation in prospective, large-sample studies to elucidate the role of esketamine on neurocognitive outcomes.

Age, preoperative comorbidities, and other factors were not significant in the multivariate regression, possibly because the strict matching of baseline characteristics in this study (all ASD < 0.1 after PSM) weakened these effects. Although surgical type (abdominal/thoracic) did not significantly influence POD, the POD rate was lower in thoracic surgery patients (8.82% vs overall 10.29%). Larger sample studies are suggested to verify the impact of surgical type.

Our study has several unique strengths. First, we included a substantial number of patients in a short period, mitigating the impact of advancements in anesthesia and surgical techniques, with a sample size far exceeding previous studies. Second, we controlled for postoperative medications as potential confounding factors, achieving a high degree of balance after employing PSM. Additionally, we conducted regression analyses and subgroup analyses, which further confirmed that exposure to remimazolam is not associated with POD.

Our study has certain limitations. First, like other retrospective studies, there may be unobserved confounding factors, such as the lack of preoperative cognitive function assessment. However, we excluded patients with preoperative consciousness disorders and adjusted for a sufficient number of perioperative confounding factors relevant to the study's objectives, including preoperative patient characteristics and postoperative medication. Second, we did not describe intraoperative patient parameters, such as the BIS and blood pressure. The primary reason for this is that the reliability of BIS in reflecting the depth of remimazolam anesthesia is still uncertain. Nevertheless, we did utilize BIS monitoring and maintained it within the range of 40–60. Additionally, some studies have reported that intraoperative hypotension may be associated with POD.[28] While we did not document blood pressure levels, we did record the use of vasoactive agents during surgery. Furthermore, patients admitted to the ICU postoperatively typically receive close monitoring, allowing

for the effective identification and documentation of severe fluctuations in consciousness. However, after leaving the ICU, we only assessed patients at two time points within a single day, which may have led to the omission of some positive cases. Fourth, this study did not capture neurological complications beyond POD (eg, stroke or seizures) due to the lack of standardized screening in the ward setting. Future research should incorporate comprehensive neurological assessments to evaluate potential interactions with POD. Fifth, although nutritional markers (eg, hemoglobin, albumin) and mechanical ventilation duration could provide additional insights, their retrospective collection would necessitate labor-intensive data extraction, which was not feasible within the framework of this study. Future prospective studies should prioritize standardized recording of these variables to further elucidate their role in postoperative outcomes. Finally, our study focused solely on the impact of remimazolam exposure on POD without recording the doses administered to patients. Therefore, further research is needed to explore the relationship between remimazolam dosage and POD.

Our findings suggest that remimazolam may be a favorable choice for anesthesia induction and maintenance in elderly patients at high risk of POD. Compared to other benzodiazepines or propofol, remimazolam's shorter context-sensitive half-time and milder cardiovascular effects may reduce the incidence of delirium in this vulnerable population. Clinicians should consider these advantages when selecting anesthetic agents for elderly patients undergoing procedures associated with a high risk of postoperative cognitive complications.

Conclusion

In conclusion, our study results indicate that for patients over the age of 65 who are admitted to the ICU postoperatively, the use of remimazolam during surgery does not have a significant impact on POD and can be applied safely. However, large-scale randomized controlled trials are still needed to further elucidate the relationship between remimazolam and POD, in order to better guide anesthetic medication for elderly patients.

Data Sharing Statement

All source data files are available upon request to the correspondence author.

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Disclosure

The authors report no conflicts of interest in this work.

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