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The impact of remimazolam on postoperative neurocognitive disorder in surgical patients: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - No funding.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 April 2026 and was last updated on 10 April 2026.

INTRODUCTION

Review question / Objective (P) Population: Adult patients aged 18 years or older undergoing elective surgery who underwent general anesthesia or spinal anesthesia, regardless of sex or nationality. We excluded studies involving individuals with pre-existing brain diseases. (I) Intervention: Remimazolam was used as the sedative for induction and maintenance of anesthesia in the intervention group, and other sedative drugs or saline was used in the control group. (C) Comparator: Studies that compared remimazolam with other sedation drugs (propofol, dexmedetomidine, midazolam or normal saline), combined with the same inhalation anesthetics in both groups, are included. (O) Outcomes: The outcome included the incidence of PND, POD or POCD.

Condition being studied Postoperative neurocognitive disorder (PND), including postoperative delirium (POD), and postoperative cognitive dysfunction (POCD) are prevalent and debilitating complications in elderly surgical patients. remimazolam, a novel ultra-short-acting benzodiazepine, has shown favorable hemodynamic and sedative properties, but its effects on PND remain incompletely elucidated.

METHODS

Participant or population Adult patients aged 18 years or older undergoing elective surgery who underwent general anesthesia or spinal anesthesia, regardless of sex or nationality.

Intervention Remimazolam was used as the sedative for induction and maintenance of anesthesia in the intervention group, and other sedative drugs or saline was used in the control group.

Comparator Studies that compared remimazolam with other sedation drugs (propofol, dexmedetomidine, midazolam or normal saline), combined with the same inhalation anesthetics in both groups, are included.

Study designs to be included RCT.

Eligibility criteria RCTs meeting the following criteria were included in our meta-analysis: (P) Population: Adult patients aged 18 years or older undergoing elective surgery who underwent general anesthesia or spinal anesthesia, regardless of sex or nationality. We excluded studies involving individuals with pre-existing brain diseases. (I) Intervention: Remimazolam was used as the sedative for induction and maintenance of anesthesia in the intervention group, and other sedative drugs or saline was used in the control group. (C) Comparator: Studies that compared remimazolam with other sedation drugs (propofol, dexmedetomidine, midazolam or normal saline), combined with the same inhalation anesthetics in both groups, are included. (O) Outcomes: The outcome included the incidence of PND, POD or POCD.

Information sources PubMed, Embase, Web of science and Cochrane Library databases, from published through February 5, 2026, to identify relevant studies.

Main outcome(s) The primary outcome was the incidence of PND, POD or POCD.

Additional outcome(s) The secondary outcomes included postoperative MMSE scores at different time points, Intraoperative opioids consumption (remifentanil and sufentanil), duration of post-anesthesia care unit (PACU) and hospital stay, and perioperative complications [postoperative nausea and vomiting (PONV), post-induction hypotension, intraoperative bradycardia, postoperative respiratory depression, and intra-operative awareness].

Quality assessment / Risk of bias analysis Cochrane risk of bias tool was completed independently by two researchers, with disagreements resolved by discussion. We assessed the certainty of the evidence for each outcome using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) tool, which evaluates the following parameters: (i) risk of bias of included studies; (ii) indirectness, inconsistency, and imprecision of the effect estimate; and (iii) other considerations, including the risk of publication bias. For each finding, we rated the certainty of the evidence as 'high,' 'moderate,' 'low,' or 'very low.

Strategy of data synthesis Data were analyzed using the random-effects model in RevMan 5.4.1 (The Cochrane Collaboration). Heterogeneity was assessed using the I^2 statistic. A random-effects model was applied if $I^2 > 50\%$, indicating substantial heterogeneity; otherwise, a fixed-effects model was used. For dichotomous variables, we extracted the number of occurrences and the total number of the sample. Continuous data were expressed as means and standard deviations (SD), and standard mean differences (SMD) with 95% confidence intervals (CI) were calculated. For studies reporting medians and interquartile ranges (IQR), these values were converted to means and SD using the method described by Hozo et al. Dichotomous data were analyzed as relative risks (RR) with 95% CIs using the Mantel-Haenszel method. Additionally, subgroup analysis was conducted among studies that assessed for POD based on different types of surgery.

Subgroup analysis Subgroup analysis was conducted among studies that assessed for POD based on different types of surgery.

Sensitivity analysis Sensitivity analyses were conducted using the leave-one-out approach to identify potential sources of heterogeneity for primary outcome.

Country(ies) involved China.

Keywords Propofol, Postoperative neurocognitive disorder, Postoperative delirium, Postoperative cognitive dysfunction.

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