

Propofol versus inhalational general anesthesia in postoperative neurocognitive disorders in surgical patients: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION**Support** - 2024 Provincial cadre health care research project (2024-805).**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202650115**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 May 2026 and was last updated on 21 May 2026.**INTRODUCTION**

Review question / Objective P:Adult patients aged 18 to 80 years old; I: Anesthesia regimens consisting of propofol; C : Anesthesia regimens consisting of inhalation agents including desflurane, sevoflurane or isoflurane; S: Scheduled for various surgical operations under general anesthesia.

Condition being studied Postoperative neurocognitive disorders (PNDs), encompassing postoperative delirium (POD) and postoperative cognitive dysfunction (POCD), represent prevalent complications following anesthesia and surgical procedures. The differential impacts of propofol-based total intravenous anesthesia versus inhalational general anesthesia on PNDs and associated clinical outcomes have not yet been fully elucidated.

METHODS

Search strategy The strategy contained key words related to “volatile anesthetic”, “volatile anesthetics”, “sevoflurane”, “desflurane”, “isoflurane”, “propofol”, “surgery”, “postoperative cognitive complications”, “postoperative cognitive dysfunction”, and “postoperative neurocognitive disorders”.

Participant or population Adult patients aged 18 to 80 years old.

Intervention Anesthesia regimens consisting of propofol.

Comparator Anesthesia regimens consisting of inhalation agents including desflurane, sevoflurane or isoflurane.

Study designs to be included Randomized controlled trials.

Eligibility criteria The scope covered both induction and maintenance phases of anesthesia, with no restrictions imposed on the specific doses or administration regimens of propofol or inhalational anesthetics utilized. Studies involving perineural adjuvants or epinephrine were excluded. Furthermore, case reports, study protocols, conference abstracts, letters, non randomized cohort studies, and any non English publications translated via automated online tools were also excluded.

Information sources A database-specific search strategy was formulated by one author to ensure exhaustive retrieval. Searches were conducted across four databases: the Cochrane Library, PubMed, Web of Science, and Embase, with the time frame extending from inception to June 28, 2023. Furthermore, the reference lists of all potentially eligible studies were manually screened to identify additional trials satisfying the predefined inclusion criteria. For enhanced comprehensiveness, we also searched the Chinese Clinical Trial Register and ClinicalTrials.gov (United States) to locate ongoing or completed clinical trials that met the inclusion criteria.

Main outcome(s) The primary endpoint evaluated in this review was the incidence of PNDs (comprising POD and POCD) at various postoperative time intervals.

Additional outcome(s) Secondary outcomes assessed between the propofol and inhalational anesthesia groups included cognitive function scores, postoperative nausea and vomiting (PONV), pulmonary complications, postoperative hypotension, postoperative agitation (defined as acute agitation within 24 hours postoperatively), pain scores, serum S100 β concentrations (pg·mL⁻¹), ICU length of stay (LOS, hours), and hospital LOS.

Quality assessment / Risk of bias analysis The methodologic quality of outcomes aggregated across all included trials was evaluated in accordance with the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) guidelines. The strength of the evidence was subsequently categorized into four levels: high quality ($\oplus\oplus\oplus\oplus$), moderate quality ($\oplus\oplus\oplus\circ$), low quality ($\oplus\oplus\circ\circ$), and very low quality ($\oplus\circ\circ\circ$). All quality assessments were performed in duplicate by two independent reviewers.

Discrepancies arising during the assessment process were resolved through thorough discussion until a consensus was achieved. In cases where consensus could not be reached between the two primary reviewers, a third independent reviewer was consulted to make the final determination. Two independent reviewers evaluated the methodological quality of eligible studies using the Cochrane Risk of Bias Tool for randomized controlled trials. For studies lacking adequate descriptive details regarding blinding of participants, personnel and outcome assessors, we conservatively rated this domain as having an unclear risk of bias.

Strategy of data synthesis For continuous variables, including cognitive scores, pain scores, length of intensive care unit (ICU) stay, and length of hospital stay, standardized mean differences (SMD) with corresponding 95% confidence intervals (CI) were calculated using the inverse variance method with a random-effects model, given the clinical relevance of the effect sizes. For dichotomous variables, such as the number of patients who developed relevant postoperative complications (including postoperative nausea and vomiting, postoperative hypotension, and pulmonary complications)—risk ratios (RR) with 95% CI were computed via the Mantel-Haenszel method. Statistical heterogeneity for each analysis was assessed using Cochran's Q test and I² statistics, with an I² value of 50% designated as the cut-off for significant heterogeneity. A random-effects model was employed in our analysis due to the inherent heterogeneity among the different surgical procedures included in this meta-analysis.

Subgroup analysis Subgroup analyses were performed based on different inhalation anesthetics (sevoflurane, desflurane) compared with propofol-based general anesthesia. Additionally, a subgroup analysis was performed for the primary outcome stratified by different surgical procedures (noncardiac surgery or cardiac surgery).

Sensitivity analysis Sensitivity analyses were conducted by sequentially excluding one study at a time to evaluate the impact of each individual study on both primary and secondary outcomes.

Country(ies) involved China.

Keywords Inhalation anesthesia; propofol; perioperative neurocognitive disorders; postoperative delirium; postoperative cognitive dysfunction.

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