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Efficacy of perioperative dexmedetomidine on postoperative delirium in elderly patients undergoing hip surgery: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - No support.

Review stage at the time of initial registration - Completed but not published.

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 16 November 2026 and was last updated on 16 November 2026.

INTRODUCTION

Review question / Objective Postoperative delirium (POD) is a frequent and serious complication in elderly patients undergoing hip surgery. Though dexmedetomidine has shown promise for delirium prevention in cardiac and other surgical cohorts, evidence specifically focused on geriatric hip surgery remains fragmented.

Condition being studied Postoperative delirium (POD) remains one of the most common and devastating neurocognitive complication in older adults undergoing hip fracture repair or arthroplasty, with reported incidences ranging from 15% to 50 depending on age, baseline cognition, and surgical urgency. POD is independently associated with prolonged hospitalization, increased mortality, accelerated functional decline, and substantial healthcare costs. Despite its clinical significance, pharmacological prevention strategies have yielded inconsistent results; benzodiazepines and deep general anesthesia are recognized risk factors, whereas the role of alternative sedatives remains incompletely defined. Dexmedetomidine, a highly selective α2-adrenergic receptor agonist, offers a mechanistically attractive profile for delirium prevention. Unlike GABAergic agents, it produces sedation resembling natural sleep via locus coeruleus-mediated pathways, preserves respiratory drive, and reduces the need for opioids and inhalational anesthetics. Preclinical and clinical evidence further suggests that dexmedetomidine attenuates neuroinflammatory cascades, modulates microglia activation, and stabilizes the blood barrier, all of which are implicated in the pathogenesis of POD. A recent network meta-analysis demonstrated that dexmedetomidine combined with melatonin constitutes an effective pharmacological strategy for preventing POD following cardiac surgery. Furthermore, a recent study conducted by D'Amico et al., investigated the interventions to prevent postoperative neurocognitive complications and found that dexmedetomidine was associated with reductions in these adverse outcomes. Over the past decade, numerous

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randomized controlled trials (RCTs) have examined perioperative dexmedetomidine across diverse surgical populations, yet evidence specifically focused on geriatric patients undergoing hip surgery remains fragmented. Notably, recent study indicate that hip fracture patients are frequently admitted with pre-existing delirium, underscoring the importance of interventions that target both prevention and severity reduction.
Existing meta-analyses have typically pooled data from cardiac, abdominal, and orthopedic cohorts, thereby obscuring procedure-specific and age-stratified effects. The optimal dosing regimen, timing of administration, and safety profile in this particularly vulnerable population, characterized by frailty, cardiovascular comorbidity, and altered pharmacokinetics, which remain unresolved. We therefore conducted this systematic review and meta-analysis to consolidate contemporary RCTs evidence on the efficacy and safety of perioperative dexmedetomidine for the prevention of delirium in older adults undergoing hip surgery.

METHODS

Participant or population Adults ≥ 60 years undergoing elective hip surgery under general or neuraxial anesthesia, regardless of sex or nationality.

Intervention Perioperative dexmedetomidine.

Comparator Active comparators (propofol, remimazolam, midazolam, or esketamine) or placebo (normal saline).

Study designs to be included Only RCT included.

Eligibility criteria The search strategy combined subject headings and free-text terms relating to postoperative delirium and dexmedetomidine. Exclusion criteria were: 1) emergency surgery, owing to uncontrolled confounders such as hemodynamic instability and incomplete preoperative assessment; and 2) studies involving participants with pre-existing brain diseases.

Information sources Two reviewers independently conducted a systematic literature search of PubMed, the Cochran library, and Web of science from databases inception through November 2, 2026.

Main outcome(s) The primary outcome was the incidence of POD, defined as occurrence between postoperative day1 andday7.

Additional outcome(s) The secondary outcomes included duration of surgery and hospital stay, and postoperative nausea and vomiting (PONV), hypotension, and bradycardia.

Quality assessment / Risk of bias analysis Two reviewers independently assessed risk for bias for each included study using the Cochrane risk-of-bias tool. Discrepancies were resolved through discussion. The certainty of evidence for each outcome was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, which considers risk of bias, inconsistency, indirectness, imprecision, and publication bias. The certainty of evidence for each outcome was classified 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). 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 (CIs) were calculated. For studies reporting medians and interquartile ranges (IQR), these values were converted to means and SD using the method described by previous study.
Statistical heterogeneity was evaluated using the I2 statistic, with values of 0-25%, 26-50%, and greater than 50% interpreted as low, moderate, and high heterogeneity, respectively.For dichotomous outcomes, we calculated relative risks (RRs) with 95% CIs under the different framework-based heterogeneity.To account for multi-arm trials without double-counting participants, we proportionally divided the sample size of shared intervention arms when conducting pairwise comparisons. Funnel plots were generated for outcomes with data from at least 10 included studies to visually appraise publication bias and small-study effects. $P < 0.05$ was considered statistically significant.

Subgroup analysis Subgroup analyses were conducted according to comparator type to examine whether the effect of dexmedetomidine on POD incidence varied across placebo, propofol, and other control conditions.

Sensitivity analysis For outcomes displaying substantial heterogeneity ($I2 > 50\%$), we performed leave-one-out sensitivity analyses to explore potential sources of inconsistency.

Country(ies) involved China.

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Keywords Dexmedetomidine, Postoperative delirium, Elderly patients, Hip surgery, Meta-analysis.

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