

Comparison of Propofol-Based Total Intravenous Anesthetics Versus Volatile Anesthetics on Postoperative Cognitive Function and Delirium After Adult Cardiac Surgery: An Updated Systematic Review and Meta-Analysis

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ABSTRACT

Background and Objectives: Postoperative neurocognitive disorders including postoperative delirium (POD) and postoperative cognitive dysfunction (POCD) are frequent postoperative conditions related to cardiac surgery. It is uncertain whether the use of propofol-based total intravenous anaesthesia (TIVA) or volatile anaesthetics influences the occurrence of these conditions. This meta-analysis assessed the association between anaesthetic technique and postoperative neurocognitive outcomes in patients undergoing cardiac surgery.

Methods: This systematic review and meta-analysis was conducted according to PRISMA guidelines. PubMed, Google Scholar, and Cochrane Central were searched from inception to August 6, 2025. RCTs with adult patients (>18) undergoing cardiac surgery in which propofol-based TIVA was compared to volatile anaesthetics were included. Studies involving non-cardiac surgery, paediatric population, or mixed modes of anaesthetics were eliminated. Three authors independently screened and excluded studies that did not fulfil the inclusion criteria.

Results: This meta-analysis included 15 RCTs involving 6973 patients. No significant difference was found between anaesthetic approaches in POCD (RR 0.91, 95% CI 0.58-1.42) and POD (RR 0.98, 95% CI 0.81-1.18). Cognitive performance assessed at 24 hours with the Mini-Mental State Examination showed no significant difference between the two groups. No significant differences were observed in the secondary outcomes i.e. ICU stay, hospital stay.

Conclusion: TIVA using propofol and volatile anaesthetics have an equivalent postoperative neurocognitive and clinical outcome in adults undergoing cardiac surgery. Existing evidence does not show a clinically significant advantage of either anaesthetic approach on postoperative cognitive function.

KEY WORDS: Postoperative cognitive dysfunction (POCD), Postoperative delirium (POD), Cardiac surgery, Propofol / Total intravenous anaesthesia (TIVA), Volatile anaesthesia (VA)

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INTRODUCTION

Postoperative neurocognitive disorders (PNDs), encompassing postoperative delirium (POD) and postoperative cognitive dysfunction (POCD), are among the most common complications following cardiac surgery, as defined by the 2018 nomenclature consensus (1). The reported prevalence of POCD after cardiac surgery varies widely across studies, with overall estimates ranging from 40% to 70%. A recent cohort study reported POCD in approximately 47% of patients during the first postoperative week, which declined to 10–20% by three months (2,3,4). These disorders are associated with prolonged hospital stay, diminished quality of life, and an increased risk of mortality and morbidity (5).

Postoperative cognitive outcomes in patients undergoing cardiac surgery are often measured using standard neurocognitive tests. The most commonly used tests are the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) [13,27]. The impact of different anesthetics maintenance strategies on postoperative cognitive outcomes remains an area of ongoing research. Volatile agents provide stable anesthesia for long procedures and have been associated with differences in early postoperative cognitive outcomes in some trials (37). In contrast, propofol-based total intravenous anesthesia (TIVA) has been proposed to have potential neuroprotective effects and faster recovery times. However, data regarding its effect on cognition are inconclusive (6,7). The underlying mechanisms of POCD and POD, including molecular specificity, patient-related risk factors, and dose dependency, are not fully understood (8). Several trials have compared the

association between these two agents and the prevalence of POD and POCD. A Randomized Controlled Trial (RCT) in elective Coronary Artery Bypass Graft (CABG) reported that patients receiving propofol-based TIVA had lower early POCD rates (32.3% vs 57.1%, OR 1.63, $p=0.038$) and delirium (8.8% vs 34.2%, OR 1.72, $p=0.027$) than those receiving sevoflurane (9). Another trial reported improved short-term outcomes with sevoflurane in patients with preexisting cognitive dysfunction. These contrasting results demonstrate the variability and inconsistency in the effect of different anesthetic agents on postoperative cognitive outcomes. (6).

Older meta-analyses mostly found no significant differences between volatile agents and TIVA in terms of POD or POCD (RR 1.10, 95% CI 0.81–1.50; SMD –0.06, 95% CI –0.81 to 0.69) (10). However, newer studies with larger sample sizes and more comprehensive outcome reporting provide an opportunity to further refine this understanding. Since PNDs are commonly encountered postoperatively and anesthetic choice is modifiable, it is necessary to update the existing evidence. This meta-analysis exclusively included adult patients undergoing cardiac surgery to compare volatile anesthetic agents with propofol-based TIVA in terms of postoperative delirium and cognitive decline.

METHOD

Literature Search

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A complete PRISMA checklist is provided in Figure S1B. The review protocol was registered in PROSPERO, (registration number CRD420251123366). The following

databases were systematically searched to identify relevant RCTs: PubMed, Cochrane Central, and Google Scholar. The following MeSH terms and keywords were used in the search strategy to identify studies evaluating the effects of anesthetic agents on postoperative delirium (POD) and cognitive dysfunction (POCD) in cardiac surgery: “Cardiac Surgical Procedures,” “cardiac surg,” “Anesthesia Intravenous,” “TIVA,” “sevoflurane,” “desflurane,” “isoflurane,” “anesthetics, intravenous,” and “propofol,” and “remifentanyl.” No restrictions were applied regarding language or year of publication. The detailed literature search strategies for each database are presented in Supplementary Table S1A. The last search was conducted on August 6, 2025, and included all eligible studies from databases inception to this date.

Eligibility Criteria

Studies were included based on the following criteria: (1) randomized controlled trials (RCTs) involving adult patients (≥ 18 years) undergoing cardiac surgery (CABG, valve replacement etc.); (2) interventions consisting of propofol-based TIVA. (3) the control group included sevoflurane, isoflurane, and desflurane volatile anesthetics. (4) studies available in full-text format. Eligible studies were required to report outcomes relevant to postoperative neurologic function. Exclusion criteria consisted of studies including pediatric patients (< 18 years). Studies involving non-cardiac surgical procedures (e.g., thoracic, abdominal, and pelvic) and patients undergoing major aortic surgeries requiring deep hypothermic circulatory arrest were excluded to limit clinical heterogeneity while allowing inclusion of cardiac surgical populations with shared perioperative pathophysiology.

Studies combining propofol and sevoflurane in the same intervention group were also excluded to preserve the integrity of different anesthesia treatments. Additionally, non-randomized studies, conference abstracts, and publications without sufficient outcome data or clarity were not considered in this study. Postoperative cognitive dysfunction (POCD) and delirium (POD) were defined based on the criteria used in the studies included. POCD was evaluated using validated screening tools, mainly the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). The MMSE is a common 30-point questionnaire that measures orientation, attention, memory, language, and visuospatial skills. The MoCA also scores out of 30 and includes tasks that assess executive function and visuospatial abilities. Higher values of both MMSE and MoCA indicate better cognitive performance. Lower postoperative scores therefore reflect worse cognitive function. The interpretation of changes in scores was made in the direction of lower scores that indicated a high level of cognitive impairment. POD was mainly diagnosed using the CAM-ICU, although some studies relied on the judgment of clinicians (i.e. assessment based on clinical evaluation rather than standardized tools) as documented. These definitions were accepted as reported in the original trials. No restriction was applied based on year of publication, and older studies meeting predefined eligibility and methodological criteria were not excluded.

Study Selection

Two independent authors (S.M.M. and S.H.H.) assessed all studies for primary screening using Rayyan, a web-based

application for systematic reviews. All the retrieved articles, including titles and abstracts, were screened against predefined eligibility criteria. If any discrepancy arose between the two reviewers regarding study eligibility, consensus was established through discussion with a third reviewer (S.U.S.)

Risk of Bias Assessment

The evaluation of study limitations and risk of bias was conducted independently by two reviewers (H.A. and U.S.S.) using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized controlled trials (<https://www.riskofbias.info/welcome/rob-2-0-tool/current-version-of-rob-2>). This tool examines five principal domains: the randomization procedure, deviations from the intended interventions, incompleteness of outcome data, accuracy of outcome measurement, and selective outcome reporting. Each domain is rated as either low risk, some concerns, or high risk. An overall judgement of risk of bias was derived from the domain-level assessments. Trials were classified as low risk only when all domains were rated low risk. If at least one domain raised some concerns, but none were judged high risk, the overall rating was some concerns. A high-risk judgment in any single domain resulted in the entire trial being categorized as high risk. Any discrepancies between reviewers were resolved through discussion with a third investigator (S.M.M.).

Data Extraction

The data were extracted by two authors (S.M.M. and S.H.H.) and organized in a Google spreadsheet. The following information was retrieved: author, study design, type of surgery, age, BMI, anesthetic agents, and tools for assessing postoperative neurologic outcomes and results; variations in surgical types were

recorded and considered during interpretation of pooled analysis. All the studies included were extracted into perioperative and procedural variables which included surgical method (CPB vs off pump), postoperative sedation guidelines and adjunct drugs use (dexmedetomidine, midazolam, ketamine, and benzodiazepines) to enable subgroup analysis and sensitivity analysis. When results were presented only in figures, the numerical data were digitized using a conversion program (Plot digitizer; <https://plotdigitizer.com/>). For studies presenting data as medians and interquartile ranges (IQR), values were converted to means and standard deviations (SD) using the method by Wan et al. (2014). SDs for mean changes were computed using standard formulas where changes were required. These conversions were performed using Meta-Analysis Accelerator, an online web-based tool (11). When only subgroup results were presented, the mean and SD values for each group were calculated using the same website. The limitations of assuming normal distribution for skewed data were acknowledged.

Outcomes and Statistical Analysis

Primary outcomes included postoperative cognitive function score, incidence of POCD, and incidence of POD. Secondary outcomes included length of ICU stay and length of hospital stay. All statistical analyses were performed using Review Manager (RevMan) version 5.4.1. For dichotomous outcomes, pooled risk ratios (RR) with 95% confidence intervals (CI) were calculated using the Mantel-Haenszel method. Continuous outcomes were analyzed using mean differences (MD) with 95% CI via the inverse variance method. In cases where different

assessment tools were used, standard mean difference (SMD) was taken rather than mean difference (MD). A random-effects model was used for all analyses unless heterogeneity was negligible ($I^2 < 50\%$ and $P > 0.05$), in which case a fixed effect model was applied; pooled estimates were interpreted as exploratory given clinical heterogeneity across cardiac surgical populations. Heterogeneity was assessed using the χ^2 test and I^2 statistic. I^2 values of 25%, 50%, and 75% were interpreted as low, moderate, and high heterogeneity, respectively. Minimal clinically important difference (MCID) of changes in postoperative MMSE or MoCA scores in cardiac surgery populations does not exist. It has been suggested in the prior literature that a shift of about 1-2 points of the MMSE or MoCA can indicate a statistically significant cognitive difference in the perioperative context; these values are dependent on population, baseline cognition, and timing of assessment. Accordingly, the interpretation of pooled differences was done with caution and emphasis was given to the direction, magnitude and consistency rather than clinical significance alone.

RESULTS

3.1. Eligible Studies

Electronic database searches revealed a total of 436 articles. Out of these retrieved studies, duplicates were removed, and after careful title and abstract screening, 15 RCTs were included in this meta-analysis. The detailed search strategy is depicted in the PRISMA diagram (**Figure 1**). In studies included for comparison of volatile anesthetics, sevoflurane was used in 10 studies [6, 7, 9, 14, 19, 20, 21, 23, 24, 25]; isoflurane in one study [15]; desflurane in one study [16]; sevoflurane + desflurane in one study [26]; and a combination of

various volatile anesthetics (e.g., desflurane, isoflurane, sevoflurane) in one study [17]. One large multicenter randomized trial [17] compared a propofol-based total intravenous anesthesia approach with a combined anesthetic approach that included volatile agents during the surgery. Propofol was administered in both groups during surgery, and postoperative ICU sedation often involved propofol. Thus, this trial was considered a comparison of anesthetic strategies rather than a strict propofol-only versus volatile-only exposure, various drugs such as propofol, midazolam, etomidate, ketamine, and diazepam were used. For consistency, only the subgroup receiving propofol was used to determine the incidence of POCD and POD. The trial included various cardiac surgical procedures to make sample more inclusive of practice and hence real-world practice. Thus, clinical heterogeneity was taken into account when interpreting pooled results.

3.2. Baseline Characteristics

The pooled analysis included 6,973 participants, divided into two groups: patients receiving propofol-based TIVA and those receiving sevoflurane anesthesia. Of these, 5,301 were male and 1,672 were female. All the included studies reported the CPB status which shows that most of them were on-pump cardiac surgery except two studies [22, 17] where surgery was performed on off-pump basis and none of the studies described mixed CPB status. Regarding use of postoperative sedation protocols and adjunct drug, propofol and sevoflurane were most frequently used sedatives, but dexmedetomidine, midazolam, fentanyl, ketamine, remifentanyl, and etomidate were less frequently used. Further baseline and study-

level characteristics are summarized in **Tables 1 and Supplementary Figure S2, S3, S4 and S5.**

3.3. Risk of Bias Assessment

Risk of bias was assessed across five domains using the Cochrane RoB 2.0 tool. Eight of the fifteen studies were judged to have a low risk of bias, while eight raised some concerns during the randomization process. With respect to deviations from intended interventions, eleven studies were rated low risk and four showed some concerns. For missing outcome data all of the fifteen studies were rated low risk. Regarding the measurement of outcomes, eleven studies were low risk and four had some concerns. For selective reporting, twelve studies were low risk and three had some concerns. Overall, three studies were classified as low risk, twelve raised some concerns, and no study was found with high risk (Fig. 5A and 5B).

3.4. Primary Outcomes

3.4.1. Incidence of POCD

A total of 5 studies (Total patients=6,070; Propofol-based TIVA n=2985; VA n=3,085) reported the incidence of POCD. Pooled analysis showed no statistically significant difference in incidence of POCD between propofol-based TIVA and VA (RR 0.91, 95% CI [0.58-1.42], $P=0.66$, $I^2=77\%$). Heterogeneity was high ($I^2 = 77\%$) (random-effects model). To assess the impact of heterogeneity, we performed a sensitivity (leave one out) analysis, which showed that exclusion of any single study did not affect the overall effect size except when excluding [25] heterogeneity decreased from high to moderate i.e. 77% to 57% with full results presented in Supplementary figure S8.CPB-based sensitivity analysis (on-pump and off-pump) revealed no statistically significant difference,

subgroup analysis based on studies with unequal sedation protocols or significant adjunct drug use also revealed no statistically significant differences in the postoperative cognitive outcomes and this findings was consistent across POCD and POD analyses.

3.4.2. Postoperative cognitive function Score

The postoperative cognitive function was assessed using various tools, the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Abbreviated Mental Test (AMT), all scored such that higher values indicate better cognitive performance. Five studies used MMSE [14,15,19,20,22], one study used MoCA [9], one study used the AMT [6] and one study used both MMSE and MoCA [23].

3.4.2.1. Assessment at Day 1 (24hr)

Five RCTs, including a patient population of 414 patients (propofol-based TIVA n=207; VA n=207) were assessed at 24 hours postoperatively. Pooled analysis showed no statistically significant difference between propofol group compared to VA (MD 0.14, 95% CI [-1.90 to 2.17], $P=0.90$, $I^2=97\%$), Heterogeneity was high ($I^2 = 97\%$); (random-effects model). To examine the impact of heterogeneity, a leave-one-out sensitivity analysis was conducted, which showed that exclusion of any single study did not affect the overall effect size or heterogeneity with full results presented in Supplementary figure S9. Figure 3A. Postoperative MMSE and MoCA scores tended to be in the range of mild cognitive impairment across included studies and the differences between groups were small, expressed as absolute changes on a 30-point scale.

3.4.2.2. Assessment at Day 2 (48 hr)

Two RCTs out of 15 studies (Total patients =200 propofol based TIVA n=101; VA n=99) were assessed postoperatively at Day 2 (48 hr). Pooled analysis showed no statistically significant difference between propofol group compared to VA (SMD -0.13,95% CI: [-0.41 to 0.15], P=0.35, $I^2=0\%$). There was no observed heterogeneity across studies ($I^2 = 0\%$) (Fixed-effect model). Figure 3B

3.4.2.3. Assessment at Day 3-Day 4 (72-96hr)

Out of 15 studies, a total of 2 RCTs (Total patients =132; propofol-based TIVA n=66; VA n=66) were assessed from Day 3 (72 hr) to Day 4 (96 hr). Pooled analysis showed no significant difference between the two agents used (SMD 0.08,95% CI: [-0.26 to 0.42], P=0.66, $I^2=13\%$). There was mild heterogeneity observed ($I^2 = 0\%$) (Fixed-effect model). **Figure 3C**

3.4.2.4. Assessment at Day 6(144hr)-Day 7(168hr)

Three RCTs, including patients' population of 199 (propofol-based TIVA 100; VA 99), were assessed from Day 6(144hr) to Day 7 (168hr). Pooled analysis showed no statistically significant difference between propofol group compared to VA (SMD -0.97,95% CI: [-3.21 to 1.28], P=0.40, $I^2=97\%$). Heterogeneity was high ($I^2 = 97\%$) ;(Random-effect model). Figure 3D. Sensitivity analysis (leave-one-out) showed that no single study affected the overall effect size or heterogeneity.

3.4.3. Incidence of POD

Out of 15 studies, a total of 6 RCTs (Total patients =6805; propofol-based TIVA n=3457; VA n=3348) were assessed for POD. Patients' cognitive function was assessed using the Confusion Assessment Method for the ICU (CAM-ICU) [7, 9, 16, 26] and clinicians' judgment method [17]

and [21]. Pooled analysis showed no statistically significant difference between propofol group compared to VA (RR 0.98, 95% CI [0.81-1.18], P=0.82, $I^2=41\%$). Heterogeneity was moderate ($I^2 = 41\%$) ;(Fixed-effect model) Figure 4. Since most studies used CAM-ICU to assess delirium a subgroup analysis focused on these studies may help reduce variability in future updates of this review.

3.5. Secondary Outcomes**3.5.1. Length of Intensive Care Unit (ICU) stay**

A total of 4 RCTs (Total patients =6480; Propofol-based TIVA n = 3,196; VA n=3284) reported the length of ICU stay. Pooled analysis showed no statistically significant difference between propofol TIVA and VA (MD -0.00,95% CI: [-0.04 to 0.04], P=1.00, $I^2=0\%$). No heterogeneity was observed across studies ($I^2 = 0\%$) ;(Fixed-effect model).

3.5.2. Length of Hospital Stay

Six studies, including a patient population of 6,723 (propofol-based TIVA n=3353; VA n=3370) were assessed for the length of hospital stay. Pooled analysis showed no statistically significant difference between the two groups. (MD 0.23,95% CI: [-0.23 to 0.68], P=0.33, $I^2=90\%$). Heterogeneity was high ($I^2 = 90\%$) ;(random-effects model).

DISCUSSION:

A total of 15 RCTs, including more than 6,000 patients, were included in this systematic review and meta-analysis. This review compared postoperative cognitive and clinical outcomes of propofol-based total intravenous anesthesia (TIVA) and volatile anesthesia (VA) across multiple time points (day 1, day 2, days 3–4, day 6, and day 7). The pooled analysis did not demonstrate a significant statistical difference between the two anesthetic

choices in relation to POCD, POD, length of ICU and hospital stay. In contrast to previous meta-analyses that primarily focused on POD and POCD at 24 hours, the present study expands the available evidence. It includes cognitive scores at several postoperative intervals and adds more clinical and other relevant outcomes [10].

The pooled analysis of incidence of postoperative cognitive dysfunction revealed no statistical difference among TIVA and VA (RR = 0.91; 95% CI [0.58–1.42]) consistent with previous evidence that no clear differences were observed between the two anesthetic approaches in postoperative cognitive outcomes [1,12]. The effects of propofol and sevoflurane on neurocognitive outcomes may depend on factors like neuroinflammation, synaptic function, and mitochondrial signaling pathways; however, pooled analysis showed these influences are outweighed by patient-related factors, including baseline vulnerability and perioperative condition. These findings suggest that postoperative neurocognitive functions during cardiac surgery are also linked to embolic load, systemic inflammation, and preoperative management [28]. At 24 hours, postoperative neurocognitive dysfunction scores were assessed using the MMSE as an assessment tool reported no significant differences between the two groups (MD 0.14, 95% CI [-1.90 to 2.17], $P=0.90$, $I^2=97\%$) [19]. Similarly, some trials reported lower early postoperative cognitive scores among patients receiving administration of propofol [14,15]. Importantly, between-group differences dissipated by 48–96 hours, and the magnitude of early differences was small relative to the total scale range. In cardiac and major thoracic surgery, even early brief deficits may

influence mobilization, participation in rehabilitation, and safety planning; Guidelines therefore recommend routine early screening with sensitive tools in high-risk patients [28].

There were no statistical differences between TIVA and VA in the incidence of POD (RR=0.98; 95% CI [0.81-1.18]), consistent with large RCTs that report delirium rates across anesthetic strategies; however, mild heterogeneity was observed, likely related to the inclusion of different assessment time intervals [16,17]. Our results are consistent with the previous meta-analysis by Han et al., 2024 [10], who also showed no significant difference between TIVA and VA in terms of the incidence of POD. In our analysis, we included three additional RCTs [7, 9, 26] compared with [10] because their last search date was December 9, 2021, and these RCTs were published afterwards. The inclusion of these more recent studies expanded the overall sample size and produced a similar outcome. Therefore, our analysis provides a more current and comprehensive synthesis of the available evidence.

Current perioperative guidelines [25] emphasize a multicomponent team-based prevention (risk stratification, orientation and sleep protocols, early mobilization, adequate analgesia with opioid-sparing strategies, and minimal benzodiazepine exposure) rather than selection of a specific anesthetic to reduce POD. In cardiac cohorts, POD remains common and prognostically important (higher mortality, complications, and non-home discharge), reinforcing the need for system-level prevention regardless of anesthetic choice [23, 24, 25]. Notably, a recent Bayesian network meta-analysis with 79 RCTs encompassing over 24,000 patients

undergoing cardiac surgery showed that combining dexmedetomidine and melatonin is significantly associated with a reduced rate of POD [30]. These results emphasize that a combination of pharmacologic approaches might be associated with a greater reduction in delirium risk than changes in anesthetic regimen alone. Future studies should therefore place more emphasis on the evaluation of adjunctive agents and overall perioperative strategies aimed at minimizing delirium risk.

Despite the fact that POCD and POD are linked to higher rates of morbidity and mortality, only a small number of trials in our review reported these outcomes. Emerging data from studies outside the scope of this meta-analysis suggests potential associations between anesthetic type and survival outcomes. One randomized clinical trial reported an association between sevoflurane anesthesia and shorter hospital stay, as well as lower one-year mortality, compared with propofol-based TIVA [31]. Additionally, a recent meta-analysis has reported that patients receiving propofol have a higher overall mortality risk across a variety of surgical populations [32]. These observations are biologically plausible and have been explored in mechanistic studies [33], which indicate that propofol may inhibit remote ischemic preconditioning or organ-protective properties of other interventions, such as volatile anesthetics. Regarding the length of ICU and hospital stay, there was no significant difference between the two groups, supporting prior meta-analysis; nevertheless, heterogeneity was significantly high due to different time intervals being incorporated in the analysis [18]. Analyses of secondary outcomes such as ICU stay and hospital stay were limited

to trials that concurrently reported cognitive outcomes. Owing to the small number of available studies and the heterogeneity in reporting formats and timing, these findings should be interpreted as exploratory. Although our review showed no consistent differences between anesthetic groups, previous research has shown that volatile agents are associated with shorter length of hospital stay [31, 35, 36].

While this analysis focuses on the type of anesthetic agent, it is important to recognize that postoperative cognitive outcomes are affected by several perioperative factors. These include hemodynamic management, pain control, sleep protocols, and early mobilization. These various interventions likely have a bigger impact on cognitive recovery than merely the choice between TIVA and volatile anesthesia [38, 39, 40]

Postoperative sedation can significantly affect how we understand the impact of intraoperative anesthetic techniques on neurocognitive outcomes. In modern cardiac surgery, propofol and dexmedetomidine are the main drugs used for sedation in the ICU after surgery. Increasing evidence shows that sedation with dexmedetomidine leads to a lower occurrence of postoperative delirium compared to propofol [41, 43]. This difference may be due to its ability to reduce pain, promote sleep-like sedation, and limit the use of benzodiazepines and opioids [42]. Since the reports on postoperative sedation strategies in the studies included were inconsistent, and some studies involved both groups having exposure to propofol, the differences in postoperative cognitive outcomes might be more about sedation methods than just the intraoperative anesthetic choice. Therefore,

we should view these findings as reflecting the overall management of anesthesia during the entire perioperative period rather than just the effects of the intraoperative agents.

Large RCT population, follow-up at different time points, ICU and hospital stay, account for the strength of this meta-analysis.

Limitations

There are several limitations associated with this meta-analysis, including heterogeneity in surgical populations and cognitive assessment tools, limited follow-up durations (up to 7 days), and variation in type of volatile anesthetics used such as desflurane, isoflurane and sevoflurane. In addition, the quality of studies showed variation, exhibiting some concerns which may affect the reliability of these findings. Several trials focused on comparing anesthetic strategies instead of just anesthetic agents. In particular, some studies involved overlapping anesthetic exposure. This included the use of propofol during both the surgery and recovery periods across both comparison groups. Additionally, there were various practices for sedation after surgery. This overlap might have made it harder to identify differences in postoperative cognitive dysfunction and delirium between the groups. Another limitation of our study is that adjunct anesthetics, such as benzodiazepines, opioids, ketamine, paralytics, and reversal agents, as well as postoperative sedation regimens, like propofol and dexmedetomidine infusions, were not consistently reported in the included trials. Because of this, we could not assess their potential influence on postoperative cognitive outcomes in this analysis.

CONCLUSION

The findings of this study suggests that no significant differences were observed in the risk of POD/POCD between TIVA and VA. Future research should aim to address current limitations by :(i) follow-ups should extend to 3-12 months to better deal with PND (ii) standardize test batteries with executive-function measures; and (iii) evaluate precision strategies that tailor anesthetic and prevention bundles by frailty, cognitive reserve, and genetic risk (e.g., APOE ε4), ideally within ERAS frameworks and cardiac surgery pathways[30,32]. In conclusion, both anesthetic techniques appear comparable regarding postoperative cognitive outcomes.

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Declaration of interest

The authors have no conflict of interest.

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Table 1: PATIENTS CHARACTERISTICS

Studies	Number of Patients			Age		Weight in kgs		Gender(male%)	Intervention Group	Control Group	Type of Surgery
	Total randomised	Propofol analysed	Volatile analysed	propofol	volatile	Propofol	Volatile				
kanbak et al, 2004	20	10	10	56 ± 7.6	54.5 ± 5.9	Propofol	volatile	100%	Propofol	Isoflurane	Cabg
schoen et al, 2011	128	60	57	64 ± 8.3	64 ± 8.3	68.36 ± 9.54	71.23±8.78	74%	Propofol + Remifentanyl	Sevoflurane + Remifentanyl	Cabg, valve
royse et al., 2011	182	87	90	63.8 ± 10.6	61.8 ± (10.4)	NR	NR	85%	Propofol + Fentanyl	Desflurane + Fentanyl	Cabg
koc et al 2014	40	20	20	52.05 ± 7.2	58.15 ± 6.37	76.2±12.7	75.9±11.8	100%	Propofol	Sevoflurane	Cabg
landoni et al 2014	200	100	100	70	68	77.25±15.67	73.85±9.78	68%	Propofol	Sevoflurane	Cabg, valve
hou et al 2017	90	45	45	54.2 ± 3.7	53.7 ± 4.3	NR	NR	65.56%	Propofol	Sevoflurane	Cabg, valve
ozer and yilmaz 2017	80	40	40	66±4*	69±3	80.67±14.83	81.67±15.58	56.25%	Propofol-remifentanyl	Isoflurane	Cabg
shi and wang 2018	94	47	47	28.9	29.5	78.3 ±9	77.6 ±8	59.57%	Propofol-fentanyl	Sevoflurane	Cabg
landoni et al 2019	5400	2668	2685	62.3 ± 8.41	62.2 ± 8.37	75 ± 15.2	72 ±11.6	81.19%	intravenous anesthesia	Des Flurane, isoflurane,	Cabg
tang et al 2019	110	55	55	64.5	64.1	NR	NR	50%	Propofol.	Sevoflurane	Cardiac surgery
wang et al., 2021	220	110	110	67.4 ± 2.2	67.3 ± 4.1	81.67±18.35	78 ±12.77	73%	Propofol + Fentanyl	Sevoflurane + Fentanyl	Cabg
duan et al 2022	300	145	144	47 (9)	48 (9)	NR	NR	40.83%	Propofol	Sevoflurane	Valve surgery
jiang Et al 2023	698	343	341	53.4 ± 11.2	54.1 ± 11.0	59.3 ± 10.2	60.4 ± 9.1	44.19%	Propofol	Sevoflurane or des Flurane	Valve, cabg
varsha Et al 2024	72	34	35	59.34± 6.87	59.46 ± 10.08	NR	NR	84.06%	Propofol	Sevoflurane	Cabg
zhao Et al 2025	113	58	55	54.43± 11.44	56.40± 11.13	NR	61.05±7.26	43.36%	Propofol	Sevoflurane	Cpb , cabg, valve

Abbreviations: RCT, randomized controlled trial; NR, not reported; CABG, Coronary Artery Bypass Grafting; CPB, Coronary Artery Bypass Grafting.

Figure 1 showing Prisma flow chart

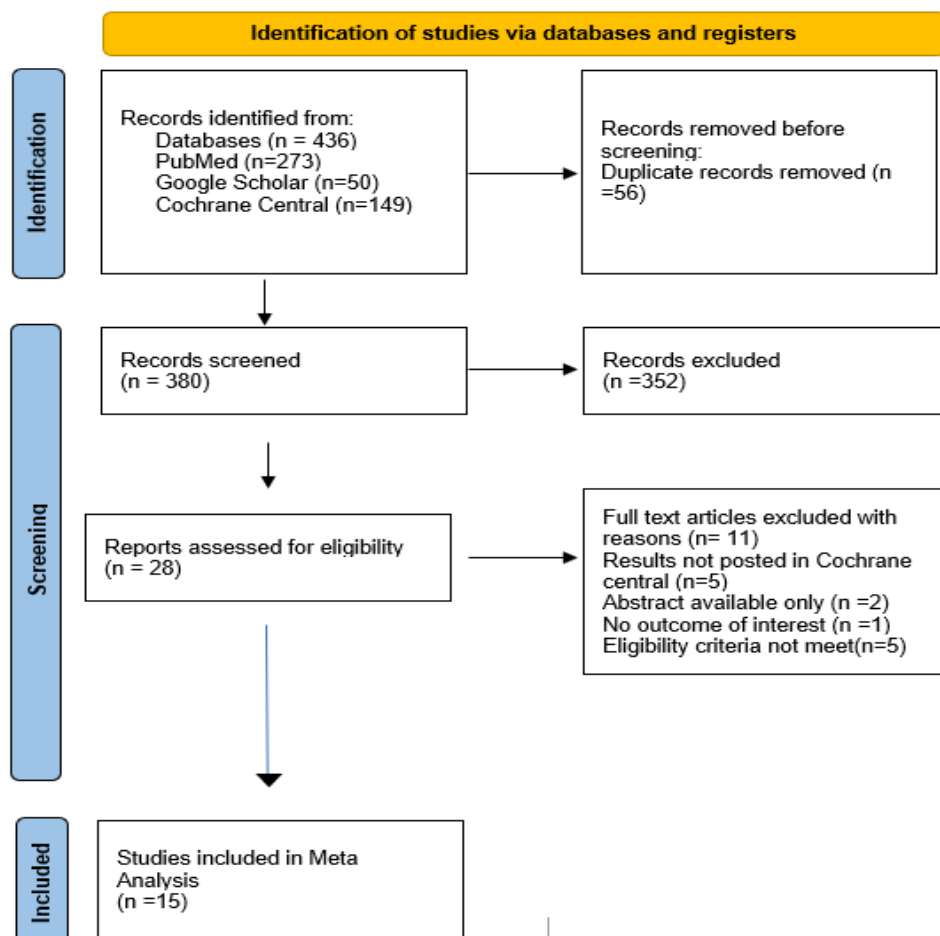


Figure 2. Forest plot showing incidence of POCD in propofol TIVA vs VA

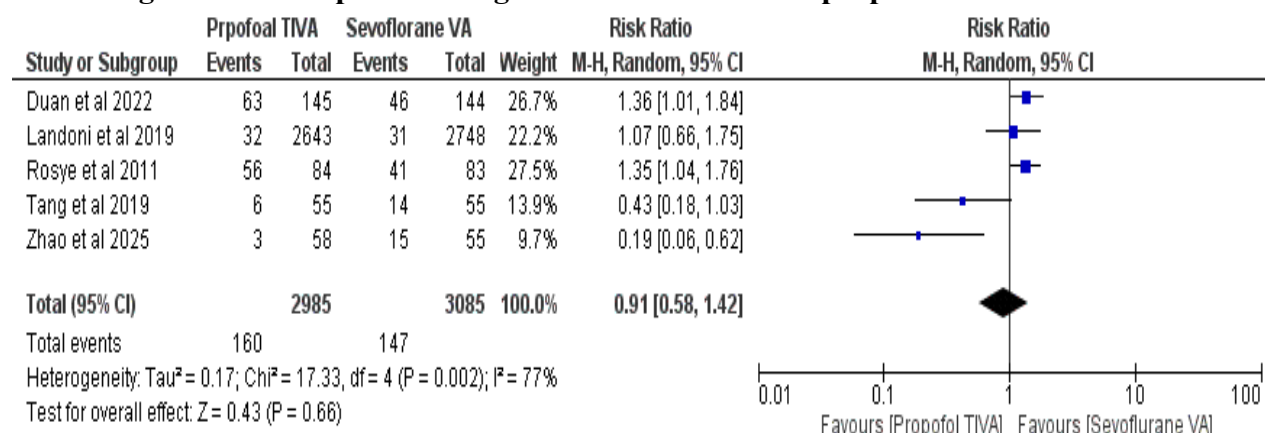


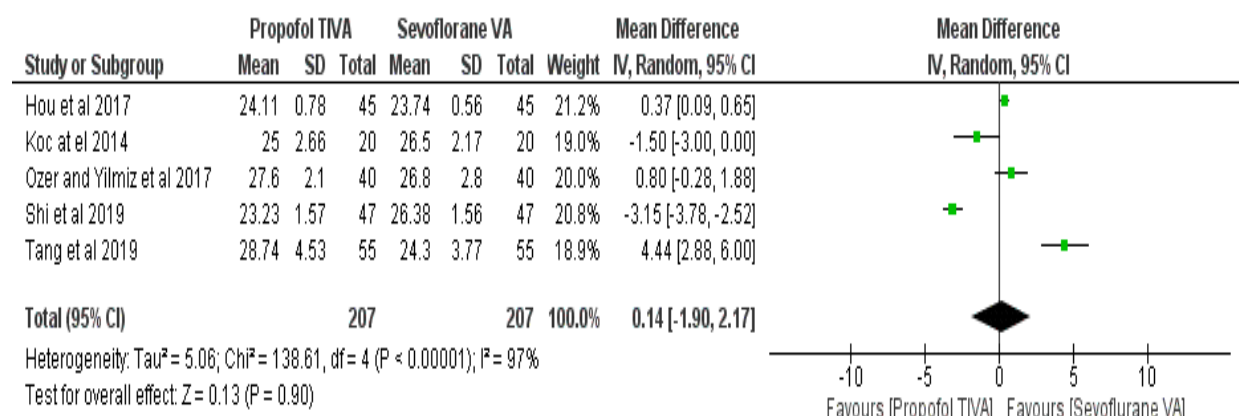
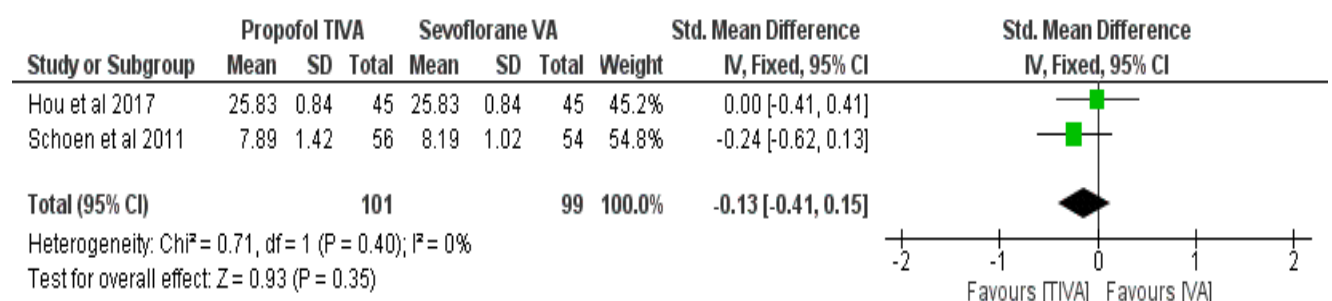
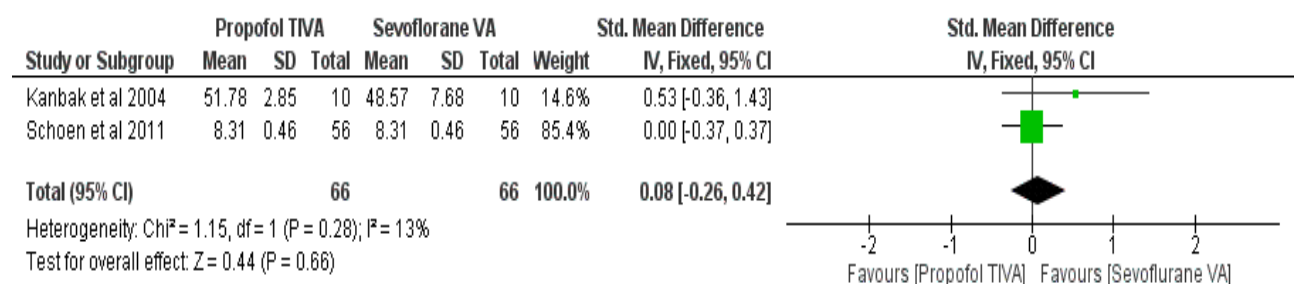
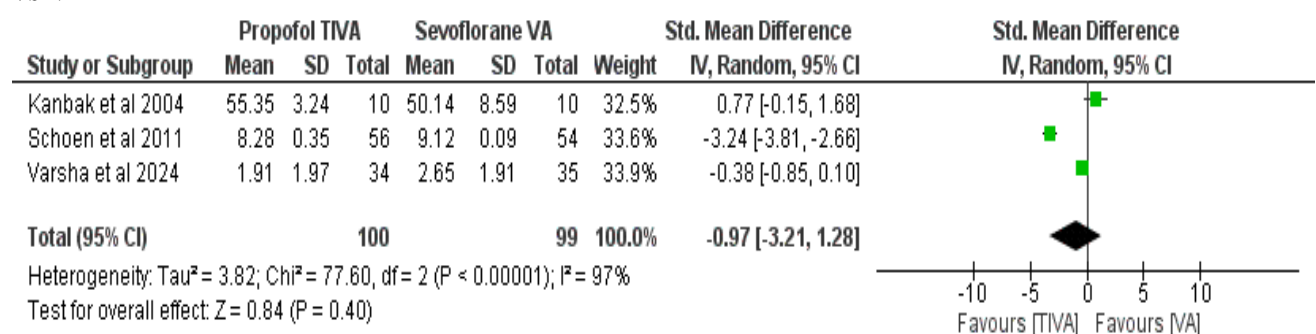
Figure 3A. Forest plot showing assessment scores of POCD at Day 1 in propofol TIVA vs VA**Figure 3B. Forest plot showing assessment scores of POCD at Day 2 in propofol TIVA vs VA****Figure 3C. Forest plot showing assessment score of POCD at Days 3-4 in propofol TIVA vs VA****Figure 3D. Forest plot showing assessment scores of POCD at Day 6-7 in propofol TIVA vs VA**

Figure 4. Forest plot showing the incidence of POD in Propofol TIVA vs VA

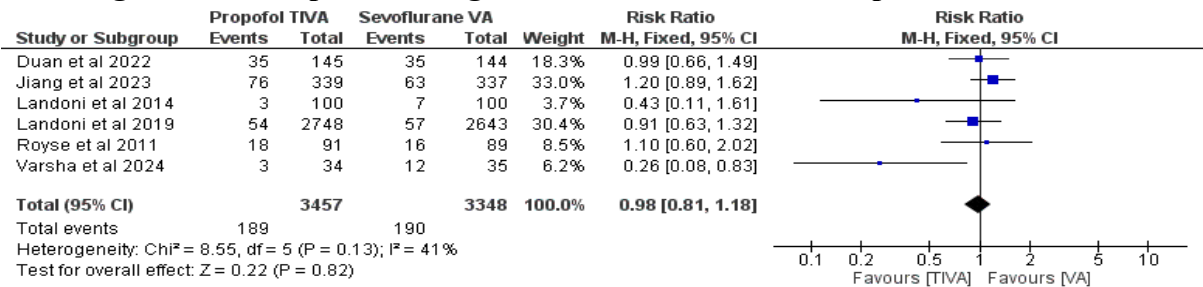


Figure 5A. Risk of bias summary

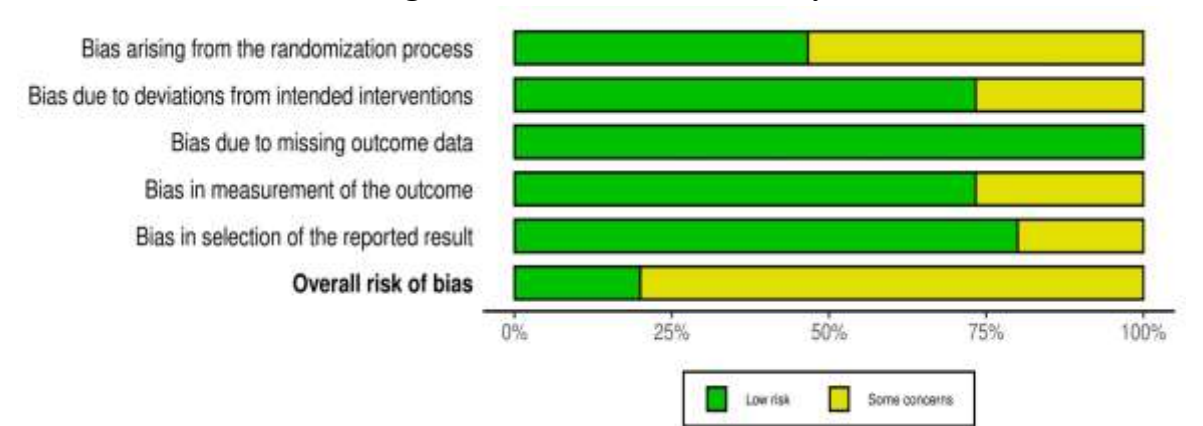


Figure 5B. Risk of bias graph

