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Review Article

Volatiles Benefit on Postoperative Cognitive Outcomes in Older Patients with Cardiovascular Surgery: A Systematic Review and Meta-Analysis

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SUMMARY

Total intravenous anesthesia (TIVA) has a lower incidence of postoperative cognitive dysfunction (POCD) compared with inhalation agents in older patients undergoing non-cardiac surgery. This systematic review aimed to investigate the postoperative cognitive function in elderly patients following cardiac surgery with TIVA versus inhalation anesthesia. We searched the databases, Cochrane, MEDLINE, and EMBASE, up to May 2022 and selected relevant randomized controlled trials. For the meta-analysis, the random-effects model on the standardized mean difference for continuous outcomes and risk ratio for dichotomous outcomes were used. Five RCTs (590 participants) were included in the final analysis. The result showed that the cognitive score reduced less after the operation in patients receiving volatile anesthesia compared with those receiving propofol-based TIVA, three days (SMD -2.31, 95% CI: [-4.63, 0.01], I^2 = 96%, p < 0.01) and five days later (SMD -2.29, 95% CI: [-3.90, -0.68], I^2 = 97%, p < 0.01). In contrast, The POCD five days after the operation did not lower significantly in patient receiving volatile anesthesia (RR 2.25, 95% CI: [0.51, 10.02], I^2 = 61%, p = 0.11). Our findings indicated that for elderly patients undergoing elective cardiac surgery, the cognitive assessment score was reduced less with volatile anesthetics than with TIVA. The incidence of POCD was not significantly different. More studies to verify these results.

1. Introduction

Postoperative cognitive dysfunction (POCD) is a syndrome defined as a declined performance on neuropsychologic tests after the operation compared with baseline test results.[1] The decline may be observed across multiple domains, days to weeks after surgery, and may resolve within months. For some patients, the decline may be prolonged by up to five years or longer.[1] Cognitive function can be assessed using the mini-mental state examination (MMSE),[2] Montreal cognitive assessment (MoCA),[3] and the abbreviated mental test (AMT).[4,5] MMSE comprises 11 questions covering seven domains, is a widely used tool, with a sensitivity and specificity of 88.3% and 86.2%, respectively. Cognitive dysfunction is defined as a score less than or equal to 23 out of 30.[6–8] MoCA, with a total possible score of 0 to 30 in eight domains, detects mild cognitive impairment,[3] and is comparable to the MMSE.[9,10]

POCD is strongly associated with age.[11] Aging affects many molecular and cellular mechanisms of many organ systems, such as genomic instability, telomere attrition, epigenetic alteration, stem cell exhaustion, mitochondrial dysfunction, cellular senescence, and so on.[12] In the central nervous system, brain volume is decreased due to dendritic and synaptic losses, reduced neuronal transmission and firing, interfered calcium metabolism, and downregulated gene expression that results in impaired neuronal connectivity and plasticity. In turn, these may lead to cognitive decline.[13–15] Due to aging and a diminished cognitive reserve, elderly individuals are more sensitive to anesthetic medication and thus, more vulnerable to POCD and delirium.[16,17] Patients requiring cardiovascular surgery have an even poorer physiologic reserve. That, together with a longer duration of anesthesia and subsequent sedation, increases the risk of POCD among these patients, due to the cell effects-related changes that occur during the prolonged use of volatile anesthetics.[18,19] With the expanding life expectancy and the growing geriatric population globally,[20] this issue deserves more attention.

Several mechanisms of POCD have been proposed. For example, neuroinflammation, calcium dysregulation, tauopathy, amyloidopathy, and gut microbiota.[21,22] Although anesthetic itself is not associated with POCD in healthy human and animal studies,[23,24] anesthetics may exaggerate or ameliorate the development of POCD by involving different parts of these mechanisms. For example, in animal studies, downregulation of ACSL4 restrained ferroptotic cell death in the hippocampus of aged rats after sevoflurane exposure.[25] On the contrary, other studies have demonstrated an upregulation of apoptotic genes (e.g., Bax and Caspase-3) and downregulation of anti-inflammatory genes (e.g., miR-27b-3p) in the hippocampus of aged rats after sevoflurane exposure.[26,27] The apoptosis cascades can also be triggered by iron overload and downregulation of glucose transporter 1 in the hippocampus and cortex.[28] As to the isoflurane, decreased anti-apoptotic and anti-inflammatory AGGF1 ex-

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pression vias PI3K/AKT pathways and SETD7-activated NLRP3 inflammasomes, are possible mechanisms for neuroinflammation and pyroptosis.[29,30] In contrast, propofol anesthesia has fewer effects on spatial learning and memory in aged rats receiving cardiac surgery, and a relative reduction in activated microglia. Moreover, an increase in miR-223-3p expression has been associated with less inflammation.[24] Propofol is hypothesized to ameliorate POCD. The results of a Cochrane review analyzing studies of elderly patients undergoing non-cardiac surgery support this hypothesis.[31]

One previous systematic review evaluated the effect of volatile anesthesia and total intravenous anesthesia (TIVA) on mortality, duration of intensive care unit (ICU) and hospital stays, and cardiovascular morbidities after cardiac surgery, and found that patients who received volatile anesthesia were discharged significantly earlier from ICU and the hospital, with a standardized mean difference of 0.29 (95% CI 0.01, 0.57) and 0.42 (95% CI 0.10, 0.75), respectively.[32] Another systematic review on patients who underwent cardiopulmonary bypass during cardiac surgery (e.g., coronary artery bypass graft (CABG) or valve surgery) using volatile anesthetics reported a non-significant difference in short-term mortality and incidence of acute kidney injury, but a significantly lower one-year mortality (OR 0.76, 95% CI 0.60–0.96), lower incidence of myocardial infarction (OR 0.63, 95% CI 0.41–0.95), lower troponin level (SMD -0.39, 95% CI -0.59–-0.19), less inotrope (OR 0.46, 95% CI 0.29–0.72), and higher cardiac index (SMD 0.71, 95% CI 0.40–1.02).[33] However, these two articles did not address the effect of anesthetics on cognition. Most available studies evaluated the effect of anesthetics on the brain via surrogate endpoints, such as S100β protein, arteriovenous oxygen saturation, but seldom obtain a cognitive assessment. One systematic review, published in 2017, included three randomized controlled trials that assessed the cognitive function of patients, 24 hours after cardiac surgery with volatile anesthetics, using the MMSE, and found a higher MMSE score (MD 1.00, 95% CI 0.37–1.63).[34] Still another systematic review, released in 2019, reported a non-significant incidence of postoperative cognitive impairment by combining the results of 8 randomized controlled trials comparing volatile anesthetics to TIVA (RR 1.2, 95% CI 0.74–1.94).[35] Nevertheless, the studies mostly enrolled patients with a mean age younger than 50 years, which may not reflect the vulnerability of the elderly. Furthermore, these studies assessed only short-term cognitive functions, which may improve further with time.[23]

This systemic review aimed to compare the effect of inhalation anesthesia to TIVA on the POCD of geriatric patients who underwent cardiovascular surgery.

2. Methods

This systematic review and meta-analysis followed the principles in the Cochrane Handbook. The pre-written protocol was registered in PROSPERO (PROSPERO CRD 42022315946). According to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, evidence selection, quality assessment, evidence synthesis, and research results were reported.[36]

2.1. Databases, search strategy, and study selection

Eligibility criteria were defined before conducting a comprehensive literature search. The inclusion criteria were: (1) randomized controlled trials, (2) elective cardiovascular surgery, (3) volatile anesthetics maintenance and TIVA compared, (4) POCD assessed with cognitive assessment tools, (5) aged population with a mean age over 55 years, (6) peer-reviewed article, (7) published data, and (8) written in English. No limitation to the published date was set. Based on these criteria, the relevant terms included "aged", "intravenous anesthesia", "total intravenous anesthesia", "propofol", "volatile", "desflurane", "sevoflurane", "isoflurane", and "cognition" in free text and medical subject headings (MeSH in PubMed and Emtree in EMBASE) were used for the literature search. Boolean operators were used to combine the keywords, and a primary search strategy without limitations on the language and publication date was generated. The primary search strategy was developed for PubMed and was adjusted for the Cochrane Library (including Cochrane CENTRAL and Cochrane CDSR), and Embase. Furthermore, ClinicalTrials.gov was searched for ongoing trials. The citations of the relevant trials and reviews were also screened. The final search was completed on May 1, 2022. Two authors (YJY and YCL) independently screened all searched articles according to the predetermined criteria. A third author (JYC) was consulted to reach a consensus on study selection when disagreement occurred between the two authors.

2.2. Data extraction and quality assessment

Two authors (YJY and YCL) independently reviewed all selected trials for data extraction and risk of bias assessment. The characteristics and outcome data were extracted for every included study. Trial and patient characteristics, including author name, publication year, country, patient number, age, gender, type of cardiovascular surgery, anesthetics administration, outcomes, and other important information were enumerated. The quality of the selected studies was assessed using the Risk-of-Bias 2.0 tool (RoB 2.0).[37] Any disagreement on the risk of bias assessment between the two authors was considered by the third author (JYC) who made the final judgment.

2.3. Statistical synthesis and analysis

The data were synthesized using R version 4.1.2 (R Core Team, 2021). For the quantitative synthesis, the mean difference (MD) was adopted for continuous data the standardized mean difference (SMD) for continuous data with different assessment scales, and the risk ratio (RR) for binary outcomes. The common effect model was used when heterogeneity of the study designs was trivial, whereas a random-effects model was selected when heterogeneity was present. The results are presented as MD, SMD, or RR and 95% confidence intervals (CIs). If the outcomes were only presented in figures and the primary data cannot be obtained by direct contact with the authors and other ways, the data was extracted from the figures using the Engauge Digitizer Software.[38] For studies that failed to report standard deviation (SD), standard error (SE), or interquartile ranges (IQRs), data imputed from other studies were used as suggested in the Cochrane handbook. The quantitative synthesis results were presented as forest plots. A p-value < 0.05 was considered statistically significant.

To investigate the heterogeneity of the pooled results, the I-square, p-value of Cochran's Q statistic, and tau-square were used. In this study, high heterogeneity was defined as an I-square $> 50\%$ and Cochran's Q p-value < 0.10. Sensitivity analysis was adopted by repeating the analysis after removing the only trial on carotid endarterectomy, then again after removing a study that did not provide standard deviations. A small-study effect was demonstrated in the funnel plot. The Egger's test was planned for outcomes with more than ten studies. An asymmetric distribution on the funnel plot, or the p-value of Egger's test < 0.05 suggested the existence of publication bias.

3. Results

3.1. Evidence selection

A total of 764 studies were available from biomedical databases, reference screening, and manual search results. Of these, 343 duplicates were automatically removed. Another 381 studies were removed from the remaining 421 studies after screening the titles and abstracts owing to incorrect study type, population, or intervention. We retrieved the full text of the remaining 39 articles. And 34 studies were excluded for the following reasons: duplicates (n = 2), trial protocols (n = 14), surgery other than cardiovascular surgery (n = 8), anesthetics used outside of an operating theater (n = 1), incorrect study designs (n = 2), and written in Chinese only (n = 8). Finally, 5 RCTs[39–43] were included for qualitative and quantitative analysis. The selection process is shown in Figure 1.

3.2. Characteristics of included studies

The five eligible RCTs from five different countries included 590 participants who underwent either CABG,[39–41,43] valve surgery,[40] or carotid endarterectomy.[42] Table 1 shows the detailed information of these RCTs. Most studies were male predominant,[40–43] with a mean age over 55 years. All studies used propofol for TIVA. Regarding volatile anesthetics, three studies adopted sevoflurane,[40,42,43] one desflurane,[41] and one isoflurane.[39] Three studies used bispectral index monitoring to adjust the depth of anesthetics.[39–41] Cognitive function was assessed with MMSE in two studies,[39,43] AMT in one[40] and MoCA in another;[42] and the incidence of cognitive dysfunction was only reported in two trials.[41,42]

3.3. Quality assessment

The RoB 2.0 quality assessment of all the outcomes is presented in Figure 2. Most outcomes had low or some concerns regarding the risk of bias due to the lack of detailed description of the allocation sequence, randomization generation, blinding, and cases analyzed.

Forest plots of all the analyzed outcomes, including sensitivity analysis, are shown in Figure 3 to Figure 8. Funnel plots showed an asymmetric distribution in the cognitive score changes (Figure 9A and 9B) and the incidence of cognitive dysfunction (Figure 9C).

4. Outcomes

4.1. Cognitive score changes

The quantitative results of the random-effects model showed that the cognitive score was reduced significantly less in patients who received volatile anesthesia than those who received propofol-based TIVA three days (SMD -2.31, 95% CI: [-4.63, 0.01], I^2 = 96%, $p < 0.01$) (Figure 3)[39,40,42] and five days (SMD -2.29, 95% CI: [-3.90, -0.68), I^2 = 97%, $p < 0.01$) (Figure 4).[39,40,42,43] Both results showed significantly high heterogeneity.

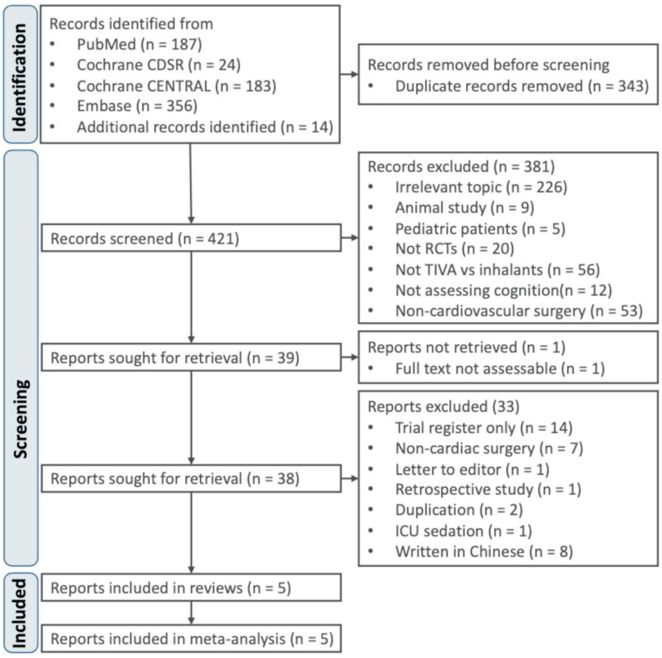

Figure 1. PRISMA flow diagram. ICU, intensive care unit; RCT, randomized controlled trial; TIVA, total intravenous anesthesia.

Table 1
Characteristics of the included studies.

	Study design	Type of surgery	Age (yo)	Sex (male, %)	Country	No.	Intervention	Control	Outcomes	Note
Kanbak et al., 2004	RCT	CABG	55 ± 6.8	-	Turkey	20	Propofol	Isoflurane	S-100β protein, MMSE, VADST	BIS monitor
Schoen et al., 2011	RCT	CABG, valve	64 ± 8.3	74%	Germany	128	Propofol + remifentanil	Sevoflurane + remifentanil	AMT, TMT, mStroop, WL-N, Sc_{O2}, S-100β protein, Cre, Tn-T, CRP	EuroScore 3.8 ± 3.0 BIS, both propofol infusion during CPB
Royse et al., 2011	RCT	CABG	63 ± 10.5	85%	Australia	182	Propofol + fentanyl	Desflurane + fentanyl	I_{POCD}, $I_{delirium}$, mortality, MI, arrhythmia…	EuroScore 3.0 ± 2.34 [0–14] BIS monitor
Kuzkov et al., 2018	RCT	Carotid endarterectomy	64 ± 6.7	100%	Russia	40	Propofol + fentanyl	Sevoflurane + fentanyl	$SctO_2$, MoCA score, $I_{cognitive\ dysfunction}$, MAP	Baseline cognitive impairment
Wang et al., 2021	RCT	CABG	67 ± 3.3	73%	China	220	Propofol + fentanyl	Sevoflurane + fentanyl	NRS, SIB, CIBIC, ADCS-ADL, MMSE, WHODAS, K-10	Baseline severe mental illness 10.5% Report means only

ADCS-ADL, Alzheimer's Disease Cooperative Study-activities of daily living; AMT, abbreviated mental test; BIS, bi-spectral index; CABG, coronary artery bypass graft; CIBIC, clinician interview-based impression of change; CPB, cardiopulmonary bypass; Cre, creatinine; CRP, C-reactive protein; I, incidence; K-10, Kessler K-10 Psychological Distress scale; MAP, mean arterial pressure; MI, myocardial infarction; MMSE, mini mental state examination; MoCA score, Montreal Cognitive Assessment score; mStroop, modified Stroop test; NRS, numeric rating scale (for pain); POCD, postoperative cognitive dysfunction; RCT, randomized controlled trials; Sc_{O2}, regional cerebral oxygen saturation; $SctO_2$, cerebral tissue oxygen saturation; SIB, severe impairment battery; TAVR, transarterial; TMT, trail-making test; Tn-T, troponin T; VADST, visual aural digit span test; WHODAS, World Health Organization disability assessment schedule; WL-N, Word List; yo, year-old.

Figure 2. Risk of bias assessment of included studies.

4.2. Incidence of POCD

Elderly individuals who received volatile anesthesia had a lower risk of POCD five days after the operation (RR 2.25, 95% CI: [0.51, 10.02], I^2 = 61%, p = 0.11), although the result were not significant.[41,42] No significant heterogeneity was found according to the Q-statistics.

4.3. Sensitivity analysis

The sensitivity analysis of studies on open-heart surgery with trivial heterogeneity showed that the cognitive score reduced significantly less in the volatile anesthetic group after three days (SMD -0.69, 95% CI: [-1.03; -0.34]) (Figure 6). However, the same result was not detected after five days (SMD -0.96, 95% CI: [-2.23; 0.31]) (Figure 7).

We excluded one RCT which did not provide standard deviations and then repeated the sensitivity analysis.[43] Using the random-effects model, the differences between the cognitive score from baseline to five days after the operation between the propofol-based TIVA group and the volatile anesthetics group was not significant (SMD -3.02, 95% CI: [-6.07; 0.04]) (Figure 8). Moreover, the heterogeneity of the studies was high.

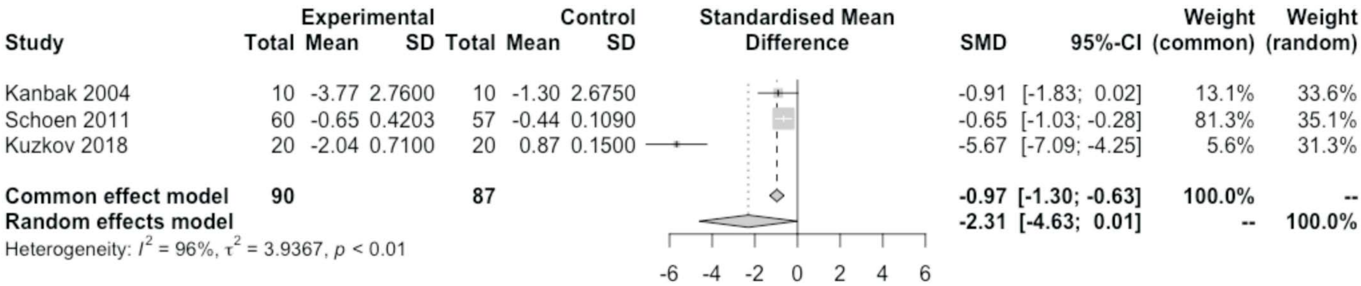

Figure 3. The forest plot shows the changes in scores as assessed by the cognitive assessment tools three days after the operation (Experimental group: propofol-based total intravenous anesthesia, control group: volatile anesthesia).

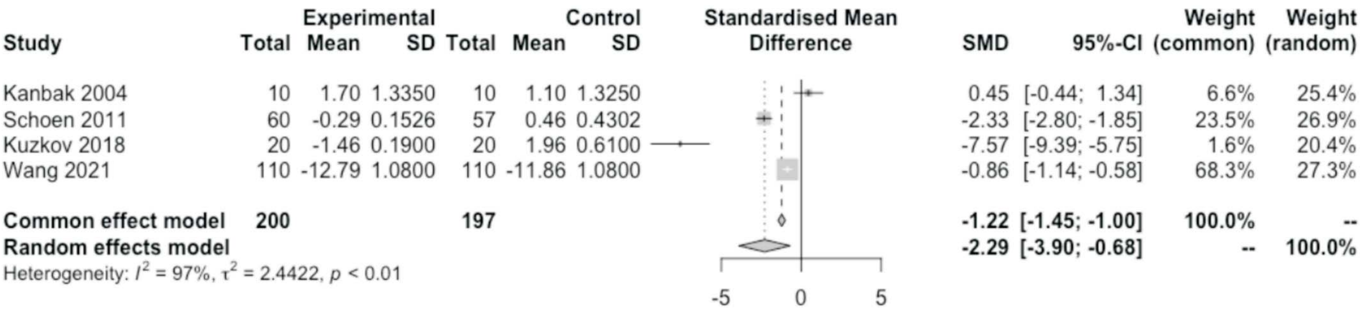

Figure 4. The forest plot shows the changes in scores as assessed by the cognitive assessment tools five days after the operation (Experimental group: propofol-based total intravenous anesthesia, control group: volatile anesthesia).

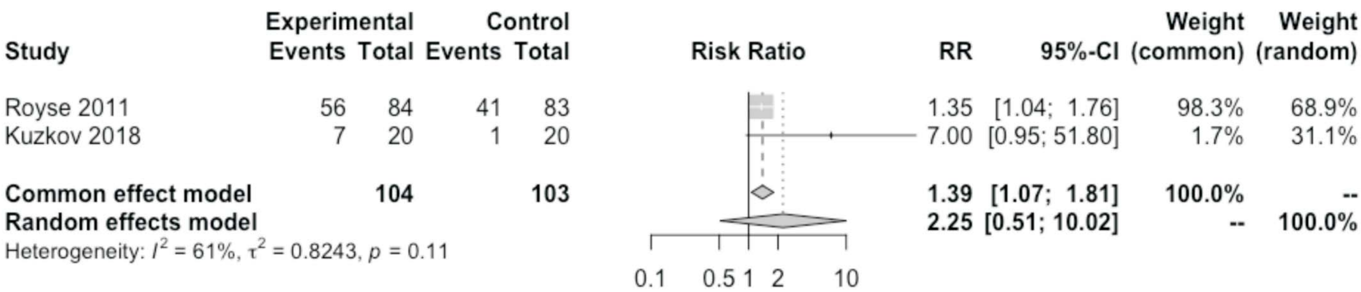

Figure 5. The forest plot shows the risks of postoperative cognitive dysfunction five days after the operation (Experimental group: propofol-based total intravenous anesthesia, control group: volatile anesthesia).

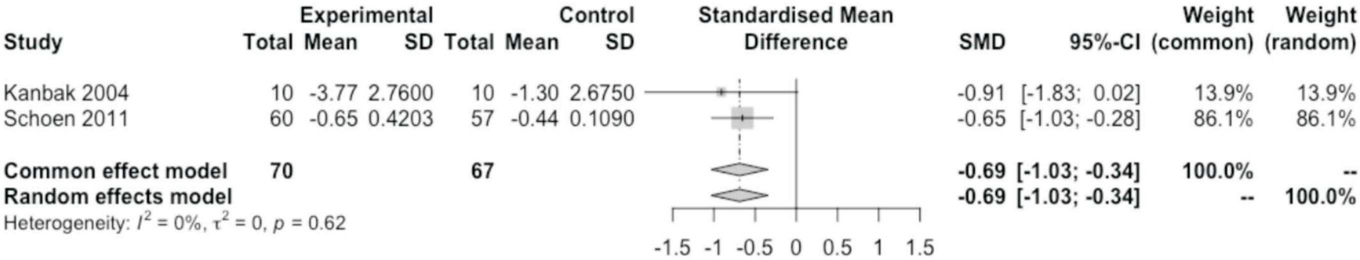

Figure 6. The forest plot shows the sensitivity analysis of open-heart surgery for the scores as assessed by the cognitive assessment tools three days after the operation (Experimental group: propofol-based total intravenous anesthesia, control group: volatile anesthesia).

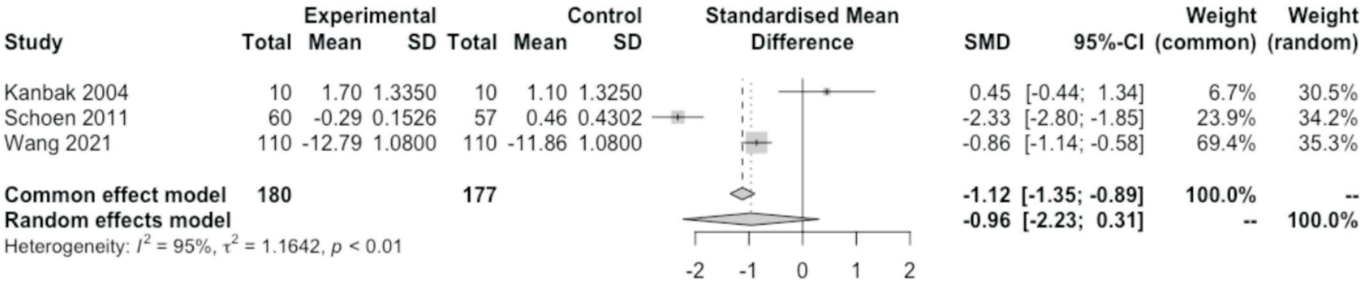

Figure 7. The forest plot shows the sensitivity analysis of open-heart surgery for the changes in scores as assessed by the cognitive assessment tools five days after the operation (Experimental group: propofol-based total intravenous anesthesia, control group: volatile anesthesia).

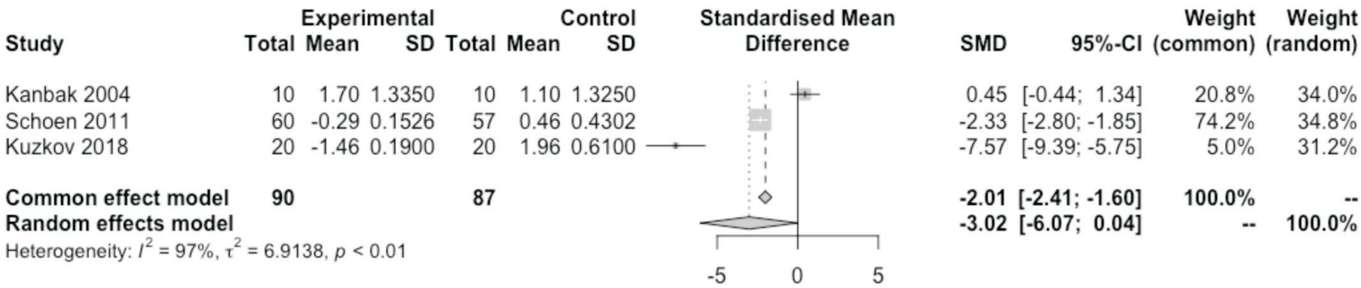

Figure 8. The forest plot shows the sensitivity analysis of complete reported data for the changes in scores as assessed by the cognitive assessment tools five days after the operation (Experimental group: propofol-based total intravenous anesthesia, control group: volatile anesthesia).

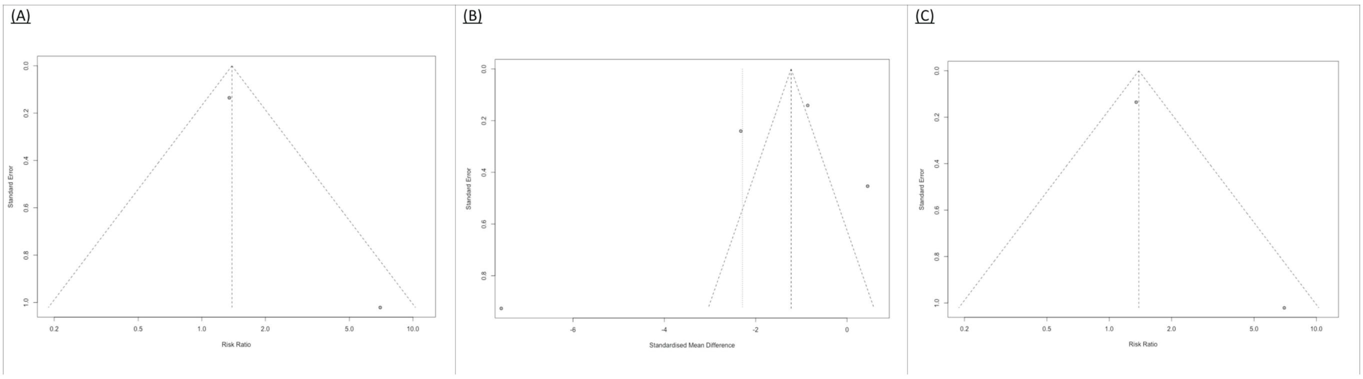

Figure 9. The funnel plot shows (A) the changes in the scores as assessed by the cognitive assessment tools three days after the operation, (B) the changes in the scores of cognitive assessment tools five days after the operation, and (C) the risks of postoperative cognitive dysfunction.

5. Discussion

This study aimed to compare the effect of TIVA and volatile anesthetics on POCD in elderly patients who underwent elective cardiovascular surgery. Compared with those who received TIVA, patients who received volatile anesthetics showed a significantly less reduction in their cognitive score five days after the operation. The slightly less reduction in cognitive score was also noted after three days but this was not significant. When the sensitivity analysis was conducted after eliminating an article without standard deviations, the significance reverted. Although volatile anesthetics have a lower risk for the occurrence of POCD, the result was not statistically significant.

There are several differences between the combined trials. Four studies provided original scores calculated from the cognitive assessment tools. However, the assessment tool used varied from study to study (MMSE in two studies,[39,43] AMT in one,[40] and MoCA in one[42]). There were also variations in the type of cardiovascular surgery. Two studies only enrolled patients for scheduled CABG,[39,43] one study included those patients who underwent CABG but also those who had isolated valve surgery,[40] and another study involved patients who underwent carotid endarterectomy.[42] Of note, Meral et al. did not report the gender ratio and demonstrated a younger mean age among the included studies. Moreover, Meral et al. and Schoen et al. adopted the bispectral index to guide the administration of anesthetics, which is believed to reduce POCD by avoiding a deep hypnotic state.[44,45] These study design differences justified the use of the random-effects model for analysis. Among the studies that used the same assessment tool (i.e. MMSE), the mean differences varied within both the TIVA group and the volatile anesthetic group.[39,43] This may be due to differences in the type of patients included. For example, Meral et al. excluded patients with baseline cognitive impairment, but Wang et al. included patients with baseline severe mental illness (10.5%). Vsevolod et al. reported the largest difference between the two anesthetic groups in patients who had carotid endarterectomy but not those who underwent open-surgery. Furthermore, even though the baseline MoCA score and numbers of severe cognitive impairment were not statistically significant, patients in the TIVA group had better MoCA scores and less severe cognitive impairment from the start. This result suggests that the differences between the two groups may be even bigger than what we reported. All of these factors may contribute to the heterogeneity observed.

Many research studies have assessed the effect of TIVA versus volatile anesthetics in patients, aged over 60 years, who underwent non-cardiac surgery. A Cochrane review of these studies demonstrated a significantly lower odds ratio of POCD for TIVA (OR 0.52, 95% CI: [0.31; 0.87]).[31] A more recent study, focusing on cancer patients over 65 years old, also reported a significantly lower odds ratio of delayed neurocognitive recovery for propofol (OR 0.58, 95% CI: [0.34; 0.98]).[46] However, studies on patients who underwent cardiac surgery indicated a non-significant incidence of POCD and a significantly higher cognitive score when volatile anesthetics were used.[34,35] The reversed directionality may be due to the patient's age, surgery type, and surgical type-related characteristics, such as baseline cardiovascular risk factors and intraoperative cardiopulmonary bypass usage. For instance, patients receiving noncardiac surgery have a lower incidence of hypertension (44%–49%), hyperlipidemia (4%–5%), diabetes mellitus (20%–24%), previous stroke (8%–11%), and coronary artery disease (13%–19%).[46] On the contrary, patients receiving cardiac surgery have an incidence of hypertension as high as 45%–53%, diabetes mellitus 72%–80%, and previous transient ischemic attack or cerebrovascular accident 16%.[40,41,47] Our study also demonstrated a better score in the volatile group. Interestingly, the study by Chen et al. showed a smaller I-square than ours (84% and 96%, respectively). This may be due to the same assessment tool (i.e. MMSE) and the same patient ethnicity (i.e., all done in China) in the three included studies. In the systematic review published in 2019, the I-square was also smaller than ours (59% and 96%, respectively).[35] The relative risk, which was insignificant, was synthesized from seven randomized controlled trials written in Chinese and one in English. On the contrary, in this study, we searched for studies written in English only and collected articles from three main databases, namely, Cochrane, Embase, and Pubmed. In total, we included five studies conducted in five different countries. Furthermore, the patients had an average age older than 55 years in this systematic review. In contrast, previous studies gathered results from relatively younger patients.[34]

Another reason for the different results from this study relative to the studies on patients who underwent non-cardiac surgery may be the effect of volatile anesthetic-induced preconditioning. In both human and animal studies, volatile anesthetic agents have been shown to be preconditioning agents that protect the brain from ischemic events.[48–52] During cardiovascular surgery, hypoperfusion and hypoxia are major factors associated with CNS injury.[53] The preconditioning effect of volatile agents protects the brain against ischemic events during cardiovascular surgery and much more potent than the anti-inflammatory effect of propofol. The higher S100β protein level detected in patients who underwent cardiovascular surgery using propofol than those using isoflurane supports this opinion.[39] The benefits of preconditioning have also been documented in remote ischemic preconditioning, which is induced by repeated impairment of blood flow to a limb. The neuroprotective effects may result from altering peripheral immune responses and improving cerebral blood flow mediated by circulating nitrite and its associated nitrosylation complex.[54] Whether the two preconditioning share a similar mechanism warrant further studies.

It is believed that neuroinflammation plays a vital role in postoperative cognitive decline. Neuroinflammation is related to the surgery-induced systemic inflammatory response as well as peripheral inflammatory stress response and manifests as increased tumor necrosis factor-alpha (TNFα), C-reactive protein (CRP), and interleukin-6 (IL-6).[54] Activated by pro-inflammatory cytokines, microglia, astrocytes, and macrophages contribute further to neuroinflammation and neuronal apoptosis.[54] To evaluate postoperative neurological dysfunction, previous systematic reviews analyzed surrogate endpoints such as S100β protein, arteriovenous oxygen difference, cerebral oxygen extraction, and jugular bulb venous oxygen saturation.[34,35] Some studies have shown an association between astrocyte-expressed S100β protein and neuron-specific enolase with POCD.[55–57] However, an inconsistent relationship between regional cerebral oxygen saturation and cognitive outcomes after cardiac surgery has also been reported.[58] The possible baseline differences among the patients must also be considered.[59] Thus, these values may be evaluated for the development of prediction models for specific clinical outcomes, but are not appropriate as surrogate endpoints for POCD. Since there is no optimal risk stratifying method for POCD and no single preventive or therapeutic tool for neuroprotection, studies are needed before forming formal recommendations. Meanwhile, for patients with recognized risk factors and morbidities, such as increasing age, depression, underlying neurodegenerative disease, previous cerebrovascular accident, the use of sedative drugs, malnutrition, poor physical function, and frailty, the use of intraoperative electroencephalography monitoring can be considered.[60]

5.1. Limitations

This study has some limitations. First, only a few trials that investigated POCD in elderly patients who underwent cardiovascular surgery were identified. Thus, the results remain inconclusive. High-quality studies are needed to determine a more definitive conclusion. Second, discrepancies due to the use of different assessment tools and different definitions for POCD across studies limited the analyses. Third, the timing of cognitive function assessments differed among the studies. Therefore, combining the data for analysis was challenging. Fourth, due to the published data's varying format, some data had to be extracted from figures and some standard deviations had to be calculated based on estimations. Fifth, studies predominantly included males and CABG, the generalizability of the results to other cardiovascular surgery is doubtful.

6. Conclusion

In the elderly population, the cognitive assessment scores after elective cardiovascular surgery using volatile anesthetics were less reduced compared to those on TIVA five days post-surgery. Despite this, the incidence of POCD was not significantly different. Further research studies are needed to determine a more definitive conclusion.

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Conflicts of interest

None.

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