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Research Article

Comparison of Propofol and Inhalational Anaesthetics for Brain Relaxation in Neurosurgery: A Network Meta-Analysis

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ABSTRACT

Background: In neurosurgery, relaxation of the brain is a key factor in surgical exposure and outcome in the case of intracranial surgery. The theoretical advantages and disadvantages of total intravenous anaesthesia (TIVA) (propofol) and volatile inhalational agents (sevoflurane, isoflurane, desflurane) are both present and absent with the available evidence split over dozens of small, heterogeneous randomized controlled trials (RCTs). A current (2022-2026) review of the literature that compares the pros and cons of propofol and inhalational anaesthetic for brain relaxation and related peri-operative outcomes in neurosurgery, integrating the existing network of pairwise and multiple treatment meta-analytic evidence.

Methods: A systematic literature search (Scopus, PubMed/MEDLINE, Cochrane Library, Embase) was performed from January 2022 to July 2026, which compared propofol to sevoflurane, isoflurane or desflurane in adult patients undergoing craniotomy or other intra-cranial neurosurgical procedures within RCTs, cohort studies and meta-analyses. Intraoperative brain relaxation score, ICP, haemodynamic stability, emergence and recovery times, postoperative nausea and vomiting (PONV), postoperative cognitive dysfunction (POCD)/delirium, biomarkers of neuronal injury and mortality/morbidity were extracted from the data. Findings were presented in a narrative synthesis and combined with previously published pairwise and network meta-analyses to create a network of treatments between propofol, sevoflurane, isoflurane and desflurane as per the general principles of the PRISMA-NMA reporting framework.

Results: Sixteen primary studies and meta-analyses were included, including RCTs, retrospective and nationwide cohort studies, and systematic reviews in a number of thousands of patients. In most head to head trials and meta analyses, scores for brain relaxation were equally comparable between propofol and volatile agents. Propofol-based anaesthesia was associated with a modestly lower risk of intraoperative brain swelling (risk ratio [RR] 0.85), lower ICP (mean difference [MD] approximately −4 mmHg), less tachycardia (RR 0.54) and less PONV compared with volatile anaesthesia in pooled meta-analytic data. For recovery, desflurane was the fastest emerging/extubating of the inhalational agents but in at least one study was associated with more PONV and more tachycardia than TIVA. There was inconsistent evidence for postoperative cognitive dysfunction and delirium; a large multicentre randomised controlled trial (RCT) and a global observational cohort study produced partially opposing results. There was no significant difference in 90-day death rates among large national cohort data for patients undergoing cranial neurosurgery, although a small effect favoring TIVA was seen on similar spine-surgery data.

Conclusion: Both propofol and volatile inhalational agents have similar effects on brain relaxation during surgery, but propofol has slight benefits for ICP control, haemodynamic stability and for PONV, and desflurane has the best recovery times of the volatile agents across the current evidence network. There is no clear and consistent benefit for either technique regarding long-term neurologic outcomes and death. Until the results of larger and well powered individual patient data network meta-analysis, selection of the anaesthetic should be individualised, and based on patient comorbidities, monitoring needs and institutional experience..

Keywords: Propofol; Total intravenous anaesthesia; Sevoflurane; Isoflurane; Desflurane; Brain relaxation; Neurosurgery; Craniotomy; Network meta-analysis; Systematic review

Introduction

In intracranial surgery, sufficient brain relaxation is one of the main factors that affect surgical access, resection quality and incidence of surgical complications, which is defined by the lack of bulging on the surface of the brain at the opening of the dura. A brain with a convex surface gives the surgeon more difficulty to retract it, longer operating time and has been associated with poor surgical and neurologic results. The mode of anaesthetic administration is a material determinant of brain bulk, most importantly cerebral blood flow (CBF), cerebral blood volume (CBV) and intracranial pressure (ICP) with general anaesthesia. In present day neuroanaesthetic practice, two broad anaesthetic approaches are in vogue: total

intravenous anaesthesia (TIVA) with propofol and volatile inhalational anaesthetic with sevoflurane, isoflurane or desflurane. Propofol decreases whole brain cerebral metabolic rate of oxygen (CMRO2), cerebral blood flow and ICP in a dose-dependent manner without affecting CO2 and autoregulatory responsiveness of cerebral perfusion. The latter are cerebral vasodilators, however, and at concentrations of over about 1 minimum alveolar concentrations (MAC) may cause dose-dependent increases in CBF despite decreasing CMRO2, a property which has historically caused concern regarding their use when intracranial compliance is lowered. Even though this is a pharmacological argument, there is not consistent clinical evidence comparing the effect of propofol to volatile agents on brain relaxation. Concurrently, there have been several recent randomised trials that have reported statistically similar scores for brain relaxation, while other physiological measures (ICP, brain-swelling risk) have demonstrated statistically significant, albeit small, benefits for propofol.[1-4] This apparent dichotomy between similar scores for brain relaxation and divergent scores for ICP and brain-swelling risk is one aim of this review. Adding to the confusion, there is clinical variability between neurosurgical indications. The lessons from elective supratentorial tumour surgery, aneurysm clipping after subarachnoid haemorrhage (SAH), emergency evacuation after traumatic acute subdural haematoma (tASDH) and endoscopic transsphenoidal pituitary surgery cannot be extrapolated or applied to all these very different pathophysiological considerations; they include baseline intracranial compliance, urgency, and monitoring requirements (e.g., intra-operative neuro-physiological monitoring, which volatile agents can affect). In parallel, a rapidly increasing body of large-scale, real-world cohort studies utilising national health-insurance databases has started to examine broader issues of outcomes at 90 days, and beyond, with an ability to detect outcomes that are typically underpowered in individual RCTs. [5-8] Another current debate is about post-operative neurocognitive outcomes. This 2026 global comparative-effectiveness cohort study suggested that maintenance anaesthesia with propofol was associated with a higher incidence of postoperative delirium, cognitive decline and mortality in older surgical patients than maintenance anaesthesia with sevoflurane, which seems to contradict several previous RCTs, including a large multicentre trial in older adults undergoing major cancer surgery, which did not report such a signal, [9-11] and the physiological arguments in favour of propofol for cerebral protection. This apparent paradox can only be resolved if the study design is designed carefully, as observational comparative-effectiveness data can be subject to residual confounding by indication, which cannot be in randomised trials. A mapping of the entire evidence network in the form of a structured synthesis would be ideal, especially because of the numerous single agent-pair RCTs (propofol vs sevoflurane; propofol vs isoflurane; propofol vs desflurane; desflurane vs sevoflurane) and a smaller number of pairwise and network-style meta-analyses.

METHODS

Protocol and Reporting Framework

This review followed the general structure recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Network Meta-Analyses (PRISMA-NMA). Given a de novo, individual patient data Bayesian network meta-analysis was not feasible in this synthesis, the review combines (a) direct evidence derived from primary RCTs and cohort studies published in the target window; and (b) indirect and mixed-treatment evidence from contemporaneous pairwise and network meta-analyses performed on multiple primary trials. This methodology, known as "evidence-network synthesis" or "meta-analysis of meta-analyses", enables the comparative performance of propofol, sevoflurane, isoflurane and desflurane to be mapped throughout the entire treatment network, and makes it transparent which comparisons are based on direct pairwise data and which on indirect evidence via a common comparator (typically propofol or sevoflurane) [12-18].

Eligibility Criteria

Studies were included if they (1) included adult patients who had undergone craniotomy or any other intracranial neurosurgical procedure (including supratentorial tumour resection, aneurysm clipping, traumatic intracranial haematoma evacuation or endoscopic transsphenoidal surgery); (2) compared propofol-based TIVA with an inhalational anaesthetic (sevoflurane, isoflurane or desflurane); or compared two inhalational agents; and (3) reported at least one outcome of interest (intraoperative brain relaxation/bulge score, ICP, cerebral or systemic haemodynamics, emergence/recovery time, PONV, postoperative cognitive function/delirium, neuronal injury biomarkers, or mortality/major morbidity); and (4) were published between 1 January 2022 and 31 July 2026. The question has a mixed evidence base and all types of RCTs, prospective and retrospective cohort studies, nationwide registry-based cohort studies and systematic reviews/meta-analyses (including network meta-analyses) were eligible for inclusion. Studies relating to paediatrics were excluded, as were non-neurosurgical and studies that did not report on an outcome of interest.

Search Strategy

A structured search was performed in the databases Scopus, MEDLINE/PubMed, Embase and the Cochrane Central Register of Controlled Trials, for the terms 'propofol', 'total intravenous anaesthesia', 'TIVA', 'sevoflurane', 'isoflurane', 'desflurane', 'volatile anaesthesia', 'brain relaxation', 'brain bulge', 'intracranial pressure', 'craniotomy' and 'neurosurgery' from January 2022 to July 2026. To find further eligible primary studies, the reference lists of retrieved systematic reviews and meta-analyses were hand-searched, as is common practice in systematic reviews.

Study Selection, Data Extraction and Risk of Bias

Titles and abstracts were screened for eligibility and potentially eligible reports were then reviewed for full text. For every study included, the following data were extracted if available: study design, sample size, indication for surgery, anaesthetic technique compared (including the use of 'adjunct' such as remifentanil, fentanyl or dexmedetomidine), main outcome and definition (most commonly a categorical brain relaxation/bulge score, e.g., a four-point scale ranging from 'relaxed' to 'bulging'), and effect estimates for secondary outcomes. The quality of the pooled evidence for each outcome domain was rated qualitatively (high/moderate/low/very low), broadly in line with the GRADE principles, taking into account

risk of bias, inconsistency, imprecision and the observational versus randomised nature of the included evidence in the underlying meta-analyses, as reported in the source RCTs.

Data Synthesis and Evidence-Network Construction

However, given the heterogeneity in the definitions of outcomes (especially for brain relaxation, which is reported on non-uniform 3- to 5-point scales across trials), there was no formal statistical pooling of raw trial level data, and instead, the pooled effect estimates (risk ratios [RR], mean differences [MD], odds ratios [OR] and surface-under-the-cumulative-ranking [SUCRA]-type rankings where published) derived from the included meta-analyses were reported and contextualised, along with directionally consistent findings from individual RCTs and cohort studies. If more than one meta-analysis used similar comparisons, for example comparing the use of propofol with volatile agents for brain relaxation, then results were compared for consistency of direction and size of the effect before being pooled for the comparison section of Results. This method is similar to that of a network meta-analysis whereby the common comparator, or 'hub' is propofol, and sevoflurane, isoflurane and desflurane are indirectly compared [1,19-24].

RESULTS

Study Identification and Characteristics

Sixteen studies and meta-analyses published between 2022 and 2026 were identified that fulfilled the inclusion criteria, including nine primary RCTs or cohort studies, five systematic reviews/meta-analyses (which included several dozen additional primary trials), and two large nationwide cohort studies. The primary and pooled studies combined encompass several thousand patients in whom a neurosurgical procedure was performed in the supratentorial compartment, in patients with aneurysm clipping following SAH, for emergency evacuation of the traumatic intracranial haematoma, the transsphenoidal endoscopic surgery of the pituitary, and in mixed

Table 1: Characteristics of included studies (2022–2026)

Study (Year)	*Design / n*	*Comparison*	*Surgical setting*	*Key brain-relaxation / primary finding*
Kim et al. (2022)[1]	RCT, n=82	Sevoflurane–remifentanil vs propofol–remifentanil (TIVA)	Endoscopic transsphenoidal pituitary surgery	QoR-40 comparable; sevoflurane gave faster emergence, TIVA gave smoother emergence
Jiang et al. (2023)[2]	RCT, n=110 (mITT)	Desflurane vs propofol-based TIVA	Craniotomy, supratentorial tumours	Satisfactory relaxation 69% (desflurane) vs 73% (TIVA); RR 0.95 (95% CI 0.75–1.21)
Sailaja et al. (2023)[3]	RCT, elderly patients	Desflurane vs sevoflurane	Elective supratentorial craniotomy (elderly)	Recovery/haemodynamic profile compared; informs desflurane–sevoflurane arm of network
Liu et al. (2024)[4]	Meta-analysis, 17 RCTs, n=1976	Propofol-based vs volatile-based anaesthesia	Craniotomy (mixed pathology)	Brain-swelling RR 0.85 (p=0.03); ICP MD −4.06 mmHg favouring propofol
Jonathan et al. (2024)[5]	Meta-analysis, 17 RCTs, n=2135	Propofol-based vs volatile anaesthesia	Neurosurgery (mixed)	Lower ICP with propofol; brain-relaxation scores statistically comparable
Hariyanto et al. (2025)[6]	Meta-analysis, 14 RCTs, n=904	Desflurane vs sevoflurane	Neurosurgery (craniotomy, transsphenoidal, spine)	Faster emergence/extubation/recovery with desflurane; no difference in adverse events
Mahajan et al. (2024)[7]	RCT (long-term follow-up)	Propofol vs desflurane	Aneurysm clipping after SAH	Long-term postoperative cognitive dysfunction compared between agents
Esmaeeli et al. (2023)[8]	Retrospective comparative cohort	Propofol-supplemented vs volatile-only	Unruptured intracranial aneurysm repair	No added neurological benefit from propofol; longer ICU/hospital stay with combination
Oh et al. (2024)[9]	Nationwide cohort, n=144,506	Propofol-based TIVA vs inhalational	Cranial neurosurgery (Korea, all-comers)	90-day mortality 14.0% vs 14.2% (OR 0.97, ns); complications 47.1% vs 50.3%
Oh et al. (2025)[10]	Nationwide cohort	Propofol-based TIVA vs inhalational	Spine surgery (Korea)	TIVA associated with lower in-hospital mortality (OR 0.85) and fewer complications
Sun et al. (2026)[11]	Global comparative-effectiveness cohort	Propofol vs sevoflurane maintenance	Older surgical patients (mixed, incl. neurosurgery)	Propofol associated with higher delirium, cognitive decline and mortality risk (contested; see Discussion)
Cao et al. (2023)[12]	Multicentre RCT	Propofol vs sevoflurane	Major cancer surgery, older adults	Delirium incidence compared directly; informs debate on agent-related neurocognitive risk
Quan et al. (2025)[13]	Meta-analysis, 41 studies, n=4342	Sevoflurane vs propofol	Oncologic surgery (POCD outcome)	No overall POCD difference; time-point subgroup differences observed
Kampman et al. (2024)[14]	Systematic review/meta-analysis (evidence map)	TIVA vs inhalational anaesthesia	General/mixed surgical populations	Synthesised >100 RCTs across specialties, including neurosurgery subsets
Chinnarasan et al. (2024)[16]	RCT, n=100	Dexmedetomidine– vs fentanyl-adjunct propofol TIVA	Emergency craniotomy, acute subdural haematoma	ICP and brain-relaxation scores comparable; S100β lower with dexmedetomidine adjunct

elective neurosurgical populations. The information in the Table 1 is summarized in terms of the characteristics of the studies.

Risk of Bias and Certainty of Evidence

The main outcome was the brain relaxation (or 'brain bulge') score, primarily measured by the operating neurosurgeon on a categorical scale following opening of the dura. Two independent meta-analyses, one conducted in 2024 (pooled analysis of seventeen RCTs, n = 2135) and the other (seventeen RCTs, n = 1976) in 2024, both found no significant difference in brain relaxation scores between propofol, sevoflurane and desflurane at various time points during surgery in patients undergoing elective craniotomy for a tumour in the supratentorial region [1,26-34].

Primary Outcome: Intraoperative Brain Relaxation Score

The combined evidence from the treatments in this treatment network suggests that brain relaxation cannot be clinically distinguished between propofol and volatile agents in the general population of elective neurosurgical patients with normal or only slightly increased intracranial compliance. This equivalence should not however be blindly extended to patients with severely compromised intracranial compliance or raised ICP as a group that is often under-represented in RCTs due to ethical and practical considerations of randomising haemodynamically unstable or critically raised ICP patients.

Taken together, the weight of evidence across this treatment network indicates that, when brain relaxation is defined as a clinically g-raded categorical outcome, propofol and volatile agents are not reliably distinguishable in typical elective neurosurgical populations with normal or only modestly elevated intracranial compliance. This equivalence should not, however, be extrapolated uncritically to patients with severely reduced intracranial compliance or intracranial hypertension, a population that is systematically under-represented in the RCT literature because of ethical and practical constraints on randomising haemodynamically unstable or critically raised-ICP patients.

Intracranial Pressure and Risk of Brain Swelling

There was a more consistent, albeit small, propofol advantage in terms of physiological surrogates of brain relaxation. This is in line with the physiological basis that volatile agents cause dose-dependent cerebral vasodilatation, while propofol maintains flow–metabolism coupling, which is why the 2024 meta-analysis of 17 RCTs (n = 1976) showed a significantly lower risk of brain swelling with propofol compared with volatile agents (RR 0.85, p = 0.03, I^2 = 21%), with a corresponding lower ICP (mean difference −4.06 mmHg, p < 0.00001, I^2 = 44%, n = 409).[4] However, the overall ICP difference (about 4 mmHg) is a physiological benefit that is small compared with the threshold of ICP (>20–22 mmHg) to define clinically important intracranial hypertension, which could account for the fact that this physiological benefit is not always reflected as a measurable difference in the main surgical outcome measure of brain relaxation score, a categorical score.

Haemodynamic Stability

There was a difference between haemodynamic profiles by comparison. In contrast, there is some individual trial evidence that propofol may also cause hypotension or systemic haemodynamic change compared to sevoflurane (RR 2.88, p = 0.005, I^2 = 0%, n = 822).4 Haemodynamic risk is not necessarily universally greater with propofol than with sevoflurane. For supratentorial tumour surgery, the desflurane group had increased tachycardia during recovery (40% to 16%, p = 0.006), which occurred only at emergence, not during surgery. [9, 26-31]

Emergence and Recovery Profile

The greatest and most consistent differences between agents were observed in the recovery kinetics in the network, where desflurane was superior to the volatile agents, and TIVA was superior to desflurane in trials that directly compared the two agents. The longer emergence and extubation times, with the higher incidence of PONV and tachycardia during recovery (29% vs 11%, p = 0.017 and 40% vs 16%, p = 0.006, respectively) in the desflurane-versus-TIVA trial highlights a trade-off between the speed and quality of recovery, and neither emergence time alone nor recovery time is sufficient to capture the quality of recovery.

Postoperative Nausea and Vomiting

In the evidence network, propofol was consistently linked to reduced frequency of PONV as compared with volatile agents, which is thought to be due to the antiemetic activity that propofol possesses. In the desflurane-versus-TIVA trial, the risk of PONV was higher with desflurane than TIVA (29% vs 11%)², and in pooled meta-analytic data, the risk of PONV was also higher with desflurane, which has a shorter emergence time and less residual depth of anaesthesia at extubation than volatile agents in the brain-swelling meta-analysis.□

Postoperative Cognitive Function and Delirium

The domain with the least consistency in evidence was reported on postoperative cognitive dysfunction (POCD) and delirium. The results of this global comparative-effectiveness cohort study of older adults undergoing major cancer surgery under propofol vs sevoflurane maintenance anaesthesia must be interpreted with caution: it is an observational study, and is vulnerable to the confounding by indication that RCT-based studies are not, and the results contradict the trend found in the RCT-based evidence summarised above.

In apparent contrast, a 2026 global comparative-effectiveness cohort study using federated real-world electronic health record data reported that propofol maintenance anaesthesia was associated with higher rates of postoperative delirium, cognitive decline and mortality than sevoflurane in older adults.[11] This finding should be interpreted cautiously: as an observational comparative-effectiveness study, it is susceptible to confounding by indication (e.g., preferential propofol use in patients already at higher baseline risk of neurocognitive complications) in a way that randomised evidence is not, and its conclusions diverge from the pattern seen across the RCT-based evidence summarised above. This tension between a large observational signal and a more equivocal randomised evidence base is discussed further in Section 4. [7,36-38]

Long-Term Neurological Outcome, Mortality and Morbidity

There is little long-term neurological outcome data available but generally favourable for both techniques. However, a nationwide South Korean cohort study of 144,506 patients admitted for cranial

Table 2: Comparative synthesis of outcome domains across the propofol–volatile anaesthesia evidence network

Outcome domain	*Direction of effect (evidence base)*	*Approx. certainty*	*Key source(s)*
Brain relaxation score	No consistent superiority; scores statistically comparable across propofol, sevoflurane, isoflurane and desflurane in most head-to-head and pooled comparisons	Low–Moderate	2,5,6
Risk of brain swelling / tight brain	Propofol favoured (RR 0.85)	Moderate	4
Intracranial pressure (ICP)	Propofol favoured (MD ≈ −4 mmHg)	Moderate	4,5
Emergence / extubation time	Desflurane fastest; sevoflurane faster than isoflurane; propofol variable, often slower than desflurane	Moderate	2,6
Postoperative nausea/vomiting	Propofol favoured over volatile agents; desflurane more emetogenic than TIVA in some trials	Moderate	2,4
Haemodynamic stability (tachycardia)	Propofol favoured (RR 0.54)	Moderate	4
Postoperative cognitive function / POCD	Mixed; no consistent overall difference, some time-point-specific differences	Low	6,13
Postoperative delirium (older adults)	Conflicting: RCT evidence mixed; one large observational cohort favours volatile agents, contradicting several RCTs	Low (conflicting)	11,12
Neuronal injury biomarkers (S100□)	Adjunct/technique-dependent; limited direct propofol-vs-volatile head-to-head data in craniotomy	Very low	16
90-day mortality / major morbidity (real-world)	No significant difference in cranial neurosurgery cohort; TIVA favoured in spine-surgery cohort	Low (observational)	9,10

Superscript numbers refer to the reference list. RR = risk ratio; MD = mean difference; OR = odds ratio.

neurosurgery did not see any significant difference in 95% 90-day mortality between propofol-based TIVA and volatile anaesthesia (14.0% vs 14.2%, OR 0.97, 95% CI 0.94–1.01, p = 0.188) but a numerical advantage for TIVA was seen in terms of postoperative complications (47.1% vs 50.3%).[11] A similar nationwide cohort study of 139,610 patients undergoing spine surgery showed that 95% 90-day mortality for propofol-based TIVA was significantly lower (13.8% vs 15.6%, OR 0.85, 95% CI 0.80–0.89, p < 0.001) than for volatile anaesthesia, suggesting a procedure-specific, rather than general, mortality benefit for TIVA anaesthesia

Neuronal Injury Biomarkers

The direct head-to-head biomarker data comparing propofol to volatile agents specifically in the craniotomy patient population have been limited in the 2022-2026 time frame. The evidence available, however, is derived mainly from research on anaesthetic adjuncts used in conjunction with TIVA involving propofol. This is confounded by the fact that ICP and brain relaxation scores were similar between the two TIVA based anaesthetic combinations, and reflects the state of the evidence: strong, well powered comparisons of biomarkers directly between propofol-based TIVA and volatile anaesthetic for craniotomy patients are lacking.

Synthesis Across the Treatment Network

Integrating direct and indirect evidence across the propofol–sevoflurane–isoflurane–desflurane network, a consistent pattern emerges: differences between agents are more reliably detected in physiological and recovery-kinetic outcomes (ICP, brain-swelling risk, emergence time, PONV, tachycardia) than in the primary categorical brain relaxation score itself, for which the treatment effect is small and frequently non-significant. Table 2 summarises the direction and approximate certainty of evidence for each outcome domain evaluated in this review.

DISCUSSION

The aim of this study was to compare the current evidence (from 2022 to 2026) of TIVA using propofol versus volatile inhalational anaesthesia for brain relaxation and associated perioperative outcomes in neurosurgery. There are three general conclusions to draw. This clinical equivalence is an important and somewhat paradoxical finding, and applies to a majority of the available modern RCTs and pooled analyses across several clinical scenarios, including supratentorial tumour resection, aneurysm surgery and emergency haematoma evacuation. [1-4] This is a remarkable clinical result, especially in the context of the physiologic rationale that would dictate an advantage for propofol, based on the cerebral vasodilatory pharmacology of the two. Second, this apparent equivalence of primary categorical outcome exists alongside statistically significant but modest, physiological advantages for propofol on secondary surrogates, such as lowering ICP, lowering the risk of brain swelling, lowering the risk of tachycardia, and lowering the risk of PONV, which is plausible because the categorical scales of brain relaxation that are typically used are relatively coarse (three to five ordinal categories) and may lack sensitivity to detect differences on the order of a few mmHg, particularly in patients with near normal baseline intracranial compliance who make up the majority of elective RCT patient samples. This suggests that the physiological benefit of propofol may be more evident — and more likely to result in a change in the categorical brain relaxation score — in individuals who are

under-represented in the randomised literature, such as those with low intracranial compliance, large mass lesions, and acute raised ICP, for practical and ethical reasons. Third, there is direct clinical relevance of the recovery-profile trade-offs that have been identified in this review in relation to anaesthetic selection. These considerations help to guide individual selection of anaesthetic techniques over use of a single technique for all treatments and patients, with the need for early postoperative neurological assessment in favour of desflurane and less emetogenic recovery in favour of propofol-based TIVA, and the requirement for intraoperative neurophysiology monitoring favours propofol-based TIVA, while reduced susceptibility to malignant hyperthermia favours propofol-based TIVA. There is a paradox between the 2026 global comparative-effectiveness cohort study, which linked propofol with poorer delirium, cognitive and mortality outcomes in older adults,[11] and the more varied literature from RCTs which did not consistently show a trend for worse outcomes,[12,13] as well. Large scale real world data have inherent external validity and statistical power that individual RCTs cannot compete with, but retrospective comparative-effectiveness designs are still subject to the hazard of confounding by indication: anaesthesiologists might be more likely to use propofol in patients who they believed to be at higher risk for postoperative complications, or, conversely, they might be more likely to use volatile agents in patients deemed more haemodynamically fragile. The existing RCT base for this outcome domain, though larger than is often believed, is more varied than recently noted (with the number of studies in the larger propofol versus inhalational base in the literature estimated at several hundred of studies that are likely relevant to this outcome domain) and does not uniformly reinforce a large causal disadvantage for propofol on postoperative neurocognitive outcomes. In this space, there is a need for future individual-patient-data meta-analysis to reconcile observations and randomised signals. By comparing the results of the two different subspecialty cohorts in the real world, the difference in real-world 90-day mortality (no difference in the cranial neurosurgery cohort, but modest difference in the spine-surgery cohort) and real-world mortality and complication benefit of TIVA (modest difference in the spine-surgery cohort, but not demonstrated in the cranial neurosurgery cohort) further conveys the message, that pooled statements like 'TIVA is safer than inhalational anaesthesia' or vice versa may not be uniformly applicable to all neurosurgical subspecialties, and that procedure-specific rather than general recommendations are likely to be more clinically useful. In terms of network-meta-analysis, propofol appears to be the natural anchor that links the sevoflurane, isoflurane and desflurane nodes, as the vast majority of modern RCTs employ propofol as the intravenous comparator arm. [5-9] This structure enabled reasonable confidence in the indirect comparison of volatile agents, e.g., desflurane is generally shown to have faster recovery than sevoflurane both from direct trials comparing the two agents and from the common propofol comparator; direct trials of isoflurane versus desflurane are relatively scarce in the 2022–2026 period and this specific node in the network is limited in precision due to the few studies available, which is a clear gap requiring future primary research.

LIMITATIONS

Firstly, it is not a de novo Bayesian network meta-analysis (DNA-BNM) utilising formally calculated pooled effect sizes and SUCRA rankings or inconsistency statistics, but it 'synthesises and cross-validates' effect estimates that have already been published in the individual meta-analyses included, in addition to a narrative integration of individual primary trial and cohort data. This method has the unavoidable consequence of using any methodologic drawbacks of the source meta-analyses, and of not allowing for the generation of new statistical estimates that are not reported in the literature. Second, there are differences in the definition and scoring of 'brain relaxation' across studies (three-, four- and five-point ordinal scales, different time points, different numbers of blinded assessors), which makes direct comparison difficult and could mask differences in actual brain relaxation between agents. Third, the evidence base of the RCT is heavily weighted towards elective, relatively low acuity neurosurgical populations with normal intracranial compliance, with those who do not fit this profile systematically under-represented and likely to be the most challenging scenarios where the anaesthetic technique used may have the greatest significance. Fourth, there is a possibility of publication and outcome-reporting bias, especially for smaller single-centre trials. Last, however, cohort data are useful for external validity, but cannot be used to establish causal inferences in the same way as randomised evidence and the differences in results between RCTs and cohorts highlight the need to be careful and not just take one piece of evidence at face value, especially when it comes to neurocognitive outcomes.

CONCLUSION

In most neurosurgical populations analysed in the contemporary 2022–2026 evidence network, TIVA with propofol and volatile inhalational anaesthetics have been found to be statistically equivalent in their ability to induce brain relaxation during surgery, with small physiological benefits found in favour of TIVA with propofol on ICP, brain-swelling risk, haemodynamic stability and postoperative nausea and vomiting. Desflurane has the quickest recovery time profile of the volatile agents and has reported to cause PONV and tachycardia during emergence. There is no current consensus in the literature regarding the role of postoperative cognitive dysfunction, delirium, long-term mortality, as measured by randomized vs. observational studies, and awaits further confirmation. Future studies should focus on the individual-patient-data network meta-analysis, preferably with sufficient study size and with a focus on patients with reduced intracranial compliance, and on prospective reconciliation of the conflicting randomised and real-world signals of postoperative neurocognitive outcomes; in the meantime, anaesthetic selection for neurosurgery should be tailored to the individual patient, based on his or her comorbidities, intracranial compliance, monitoring requirements and institutional expertise, and a uniformly superior technique has yet to be established.

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