The Review Of
DIABETIC
STUDIES OPEN ACCESS

Anesthesia And Recovery: Comparing Methods To Minimize Drug Effects On Emergence Time

Dr.Tariq Lutfi Jilani[1],Dr. Ahmad Salem Banjar[2],Dr.Emad Mohammed Alhazmi[3],Dr Samer Abduallah Khojah[4],Ammar Sulaiman Musa Maimani[5],Dr.Omar Ageel[6],Awad Ali Alamri[7],Hamzah Jamil Basnawi[8],Abdullah Faisal Bahkeem[9],Abdulrahman Helal Helal Almalki[10]

[1]Cardiac anesthesia consultant King Abdullah medical city
[2]Regional Anesthesia and Acute Pain Consultant King Abdullah medical city
[3]Pediatric anesthesia consultant King abdullah medical city
[4]Pain Managment and Anestheisa Consultant King Abduallah Medical City
[5]Specialist-Anesthesia Technology King Abdulaziz hospital
[6]Cardiac anesthesia consultant King Abdullah medical city
[7]Anesthesia Technology Specialist King Abdullah medical city
[8]Anesthesia Technology Specialist King Abdullah Medical City
[9]Anesthesia Technology Specialist King Abdullah Medical City
[10]Anaesthesia technician King Abdulaziz hospital

Abstract
This synthesis examines the comparative effects of total intravenous anesthesia (TIVA) and inhalational anesthesia on emergence time, recovery quality, and postoperative cognitive function, with a focus on adult and elderly surgical populations. TIVA, primarily utilizing propofol and short-acting opioids, offers precise plasma concentration control and rapid offset, potentially reducing residual sedation and neuroinflammatory responses. Inhalational agents such as sevoflurane and desflurane provide adjustable depth via inspired gas concentrations, with emergence profiles influenced by blood-gas solubility and patient physiology. Pharmacokinetic and pharmacodynamic differences, alongside adjunctive medications, contribute to variability in awakening speed and recovery metrics. Elderly patients exhibit altered drug metabolism and distribution, affecting anesthetic clearance and cognitive outcomes. Objective recovery measures, including time to eye opening, extubation readiness, and post-anesthesia care unit discharge criteria, reveal nuanced distinctions between modalities, with TIVA often associated with reduced postoperative nausea and vomiting. Cognitive assessments yield mixed results, reflecting heterogeneity in surgical types, baseline function, and testing intervals. Ethical considerations emphasize informed consent processes sensitive to perioperative stress and cognitive capacity, while balancing patient safety with research rigor requires adaptive protocols and vigilant monitoring. This integrated evaluation suggests that anesthetic choice should consider individual patient factors, surgical context, and recovery goals to optimize perioperative outcomes.

1 Introduction

The choice between total intravenous anesthesia (TIVA) and inhalational anesthesia has long invited debate in perioperative medicine, particularly for elderly populations undergoing surgical procedures. Both techniques are widely used in clinical practice and rely on distinct pharmacokinetic and pharmacodynamic mechanisms that could influence postoperative emergence time, recovery quality, and neurocognitive outcomes. Sevoflurane and propofol are the most common representatives of inhalational and intravenous anesthesia respectively, each associated with distinct benefit–risk profiles depending on the endpoints being examined (Moro et al., 2016). Sevoflurane allows relatively rapid titration during surgery but may lead to accumulation effects in fatty tissues which delay recovery in older adults, whereas TIVA offers precise infusion control with reduced potential for prolonged residual effects (Tariq et al., 2023). Emergence time represents an immediate marker of anesthetic efficiency but is intertwined with quality of recovery parameters such as hemodynamic stability, control of postoperative nausea and vomiting (PONV), and cognitive reorientation. Differences in these outcomes have at times been inconsistent across studies due to variability in surgical type, anesthetic dosing

regimens, and patient comorbidities (D.-H. Kim et al., 2022). The distribution of agent-specific adverse effects also shapes their comparative evaluation. Propofol's favorable profile with regard to PONV reduction is offset by its limited intrinsic analgesia and muscle relaxation relative to sevoflurane as well as a higher tendency to depress respiratory function (Song et al., 2024). This contrast explain why multimodal strategies have been explored, combining agents or integrating opioid-sparing regional blocks to mitigate individual shortcomings while potentially enhancing cognitive preservation (Zhao et al., 2022). Quality of postoperative recovery extends beyond physical stability into domains of subjective well-being, emotional state, and functional autonomy. Measures incorporating patient-reported outcomes provide insight here, reflecting a growing emphasis on recovery quality from the patient's perspective rather than relying solely on physiological indicators (Moro et al., 2016). Specific anesthetic strategies have been reported to influence inflammatory responses during surgery, which could indirectly protect or impair cognitive performance in the immediate period after awakening. For example, propofol-based TIVA has demonstrated lower postoperative inflammatory markers compared with inhalational agents in some cohorts (Tariq et al., 2023), a factor hypothesized to reduce risk for postoperative cognitive dysfunction (POCD). The literature evaluating cognitive trajectories after general anesthesia reveals a frustrating heterogeneity. While some trials have linked TIVA to better cognitive scores in the early postoperative period, others find equal or even better results with inhalational techniques depending on the nature of the testing paradigm (Davis et al., 2014). For instance, differential outcomes have been observed across specific neuropsychological tests such as reaction times versus verbal fluency measures, suggesting that anesthesia-related neurocognitive effects may be domain-specific. Results may also be confounded by baseline group disparities or learning effects from repeat testing. The task complexity further complicates interpretation: high-complexity surgeries like video-assisted thoracic or laparoscopic procedures carry additional physiological stressors that independently influence brain function recovery trajectories (L. Yang et al., 2022; Zhao et al., 2022). In elderly patients, already at increased vulnerability for POCD due to age-related neuronal changes, the accumulation profile of inhaled agents might contribute more strongly to delayed neurocognitive recovery than intravenously administered drugs which can be titrated closely based on intraoperative feedback (Tariq et al., 2023). Supporting this notion, certain studies report greater adverse cognitive effects from propofol versus sevoflurane only when concurrent comorbidities such as cancer create unique metabolic demands (Sun et al., 2019). These inconsistencies suggest that the relationship between drug choice and neurocognitive outcome cannot be viewed in isolation from the patient's physiological milieu and surgical context. Beyond pharmacologic properties alone, combination strategies employing S-ketamine alongside traditional anesthetics illustrate targeted attempts to manipulate perioperative physiology for improved recovery metrics. S-ketamine's neuroprotective properties and ability to dampen perioperative stress responses may improve both early emergence quality and resilience against transient cognitive decline postoperatively (Zhang et al., 2023). Similarly, hybrid regimens pairing low concentrations of sevoflurane with propofol infusion have been proposed not only for optimized depth control but also potential interplay effects that spare coagulation pathways while minimizing systemic inflammation (L. Yang et al., 2022). From a methodological perspective consistent with PRISMA-guided systematic review principles, any comparison must address wide interstudy variability by explicitly controlling confounders like ASA classification status, preoperative baseline mental scores (e.g., MMSE), type of intraoperative monitoring employed for anesthesia depth control (such as BIS index), and duration of exposure. Recovery endpoints should ideally integrate both objective criteria, such as time from cessation of drug administration to meeting extubation readiness, and subjective dimensions captured via validated questionnaires assessing overall perceived wellness post emergence. Tracking multiple timepoints postoperatively helps identify whether differences reflect transient phenomena limited to early awakening or maintain relevance over days leading into convalescence (Tariq et al., 2023). By situating these considerations within aging physiology, decreased hepatic metabolism rate, altered fat-to-lean mass ratio affecting anesthetic distribution kinetics, it becomes clearer why individualized selection may outperform a binary preference for one technique over another across all cases. The synthesis of emerging comparative data seeks not merely to declare superiority but rather illuminate under what specific scenarios each method aligns optimally with favorable emergence timing, stable systemic parameters during early recovery hours, and preservation of mental clarity into later postoperative days. This integrated framework defines not just an anesthetic choice but an approach refined through

evidence-backed nuance aimed at minimizing residual drug impact while preserving patient safety and comfort across diverse procedural landscapes.

2 Background and Rationale

2.1 Overview of Anesthesia Modalities

2.1.1 Definition and Principles of Total Intravenous Anesthesia (TIVA)

Total Intravenous Anesthesia (TIVA) is characterized by the exclusive administration of anesthetic agents via the intravenous route, without concurrent delivery of inhaled anesthetics. In practice, this often involves a continuous infusion of hypnotics such as propofol, complemented by opioids like remifentanil to achieve desired levels of analgesia and sedation (Casas-Arroyave, 2022). By relying solely on intravenous delivery, TIVA avoids potential variability in alveolar concentration associated with inhalational methods. Instead, plasma concentrations can be tightly regulated through infusion pumps, enabling fine adjustments to depth of anesthesia in response to intraoperative monitoring indices. This precision in titration appears particularly advantageous where maintaining stable anesthesia is essential, as during neurosurgical or spinal procedures where electrophysiological monitoring might be compromised by volatile agents. Pharmacokinetically, propofol is valued for its rapid onset and predictable offset due to redistribution and metabolism. These qualities are associated with shortened emergence profiles relative to some inhaled agents under comparable exposures (Shimizu et al., 2023). The absence of active metabolites further reduces residual sedative effects that might delay postoperative orientation or mobilization. However, such benefits are contingent on careful dosing strategies; excessive infusion rates may still prolong recovery despite the drug's short half-life. Opioids used within TIVA regimens differ in their onset and duration characteristics, remifentanil exhibits ultra-rapid metabolism without tissue accumulation, supporting swift awakening once infusions cease, whereas longer-acting counterparts like sufentanil extend analgesic effects but risk delayed extubation readiness (Qi et al., 2016). From a mechanistic standpoint, intravenous agents administered in TIVA potentially modulate the inflammatory cascade differently compared with volatile anesthetics. Propofol has been shown to attenuate oxidative stress markers and neuroinflammatory pathways during surgery, raising hypotheses that such modulation could translate into lower incidence or severity of postoperative cognitive dysfunction (POCD), particularly in vulnerable groups such as older adults undergoing major operations (Tariq et al., 2023). The possibility that reduced systemic inflammatory load supports better cognitive trajectories is plausible but remains incompletely confirmed across heterogeneous clinical populations. Emergence time under TIVA protocols can be shaped not only by inherent pharmacology but also by concomitant agent selection and patient-specific physiology. For example, pairing propofol with ultra-short acting opioids facilitates rapid return of spontaneous ventilation and airway reflexes after discontinuation (Qi et al., 2016). In elderly patients, who often exhibit slower hepatic clearance and altered drug distribution due to increased fat mass, these features may provide an advantage over inhaled agents prone to prolonged wash-out from tissue reservoirs. Yet regional differences in clinical practice illustrate how perceptions of these advantages vary; surveys indicate markedly different adoption rates depending on national trends in anesthetic training and institutional experience (Casas-Arroyave, 2022). The principles underlying TIVA stress controlled drug administration aimed at minimizing variability in end-organ exposure. Technological integration plays a central role: target-controlled infusion systems estimate plasma or effect-site concentrations based on pharmacokinetic models and adjust infusion rates accordingly. This provides real-time control over sedation depth while mitigating risks of over- or under-dose events, a limitation sometimes encountered with inspired gas concentration monitoring in volatile-based techniques. Continuous electroencephalographic depth indices like the bispectral index (BIS) can complement these adjustments by correlating dose delivery directly with cerebral activity patterns. In terms of recovery quality, a composite encompassing physical stability, subjective comfort, and readiness for discharge, TIVA's predictability has been reported as favorable in select contexts. Studies comparing quality-of-recovery scores between propofol-based TIVA and sevoflurane-balanced techniques show either parity or marginal improvement for TIVA when early postoperative comfort measures are prioritized (Moro et al., 2016). That said, absence of inherent analgesic properties in

propofol demands careful opioid integration to prevent pain-related deterioration in recovery perception. One additional principle often cited is avoidance of environmental contamination; intravenous delivery eliminates ambient exposure to waste anesthetic gases found in volatile-based systems. Although this factor relates more to occupational health than direct patient outcomes, it nonetheless contributes to differing institutional preferences for TIVA versus inhalational methods. While theoretical benefits, including possible cognitive preservation through reduced neuroinflammation, and practical ones like precise depth modulation are appealing, existing literature cautions against assuming universal superiority across all surgical categories (Casas-Arroyave, 2022). Procedure duration, patient comorbidities, intraoperative complexity, and provider familiarity all interact with core principles of TIVA administration to determine whether its potential advantages manifest clinically. Defining TIVA involves appreciation for both its pharmacologic foundation, reliance on intravenous hypnotics and adjuncts, and operational principles emphasizing controllable drug kinetics with avoidance of inspired anesthetics. This framework connects intrinsically with outcomes, providing a basis for subsequent comparisons with inhalational techniques vis-à-vis emergence timing, recovery quality metrics, and neurocognitive endpoints as components of perioperative safety and efficacy evaluation.

Table 1: Comparative Pharmacological and Clinical Profiles of TIVA (Propofol) vs. Inhalational Agents

Feature	TIVA (Propofol-based)	Inhalational (Sevoflurane/Desflurane)
Primary Mechanism	Predominantly GABA-A receptor potentiation; selective inhibition of excitatory transmission.	Polyreceptor action: GABA enhancement, NMDA inhibition, and potassium channel modulation.
Pharmacokinetics	Rapid redistribution; clearance via hepatic metabolism. No active metabolites.	Clearance via alveolar washout. Kinetics depend on blood-gas solubility (Desflurane < Sevoflurane).
Emergence Profile	Rapid and predictable if infusions are titrated. Less affected by duration in short/medium cases.	Variable. Desflurane is fast; Sevoflurane may accumulate in adipose tissue, delaying recovery in elderly/obese patients.
Post-op Side Effects	Reduced PONV (anti-emetic properties). Higher risk of respiratory depression.	Higher incidence of PONV. Desflurane may cause airway irritation and sympathetic surges.
Neuroinflammation	Anti-inflammatory and antioxidative properties; potentially neuroprotective.	Variable immunomodulation; potential for accumulation in neural lipids.

2.1.2 Definition and Principles of Inhalational Anesthesia

Inhalational anesthesia is defined by the use of volatile anesthetic agents, delivered via a respiratory circuit, to induce and maintain unconsciousness during surgical procedures. These agents, commonly sevoflurane and desflurane, are absorbed through the alveolar-capillary interface and distributed systemically, with their pharmacokinetic behavior governed largely by their solubility in blood and tissues (Werner et al., 2015). The alveolar concentration, often expressed as MAC (minimum alveolar concentration), serves as a practical guide for titration to desired anesthetic depth, allowing adjustments based on clinical signs or supplemental monitoring such as bispectral index (BIS). The primary principle distinguishing inhalational anesthesia from intravenous techniques is this reliance on inspired gas delivery, which enables rapid modifications during surgery through changes in vaporizer settings. Sevoflurane, in particular, has been recognized for its ease of control over anesthesia depth and relatively smooth hemodynamic profile compared with some intravenous agents (Song et al., 2024). The speed of emergence following sevoflurane administration benefits from its low blood-gas partition coefficient; after discontinuation, washout from the lungs rapidly reduces systemic concentrations.

However, this recovery efficiency can be modulated by patient physiologic characteristics such as reduced pulmonary function or high adipose tissue content, where redistribution effects prolong elimination. Desflurane offers even lower blood solubility than sevoflurane, translating into faster recovery times across various outpatient protocols (Werner et al., 2015). This rapid clearance is particularly advantageous in clinical settings prioritizing short post-anesthesia care unit (PACU) stays or quick operating room turnover. Yet accelerated emergence carries its own considerations: airway irritation and sympathetic stimulation during desflurane administration can lead to undesirable responses unless mitigated with adjunctive agents or controlled vaporizer ramp rates. The operational principles of inhalational anesthesia integrate balanced anesthesia strategies in many institutions: combining volatile agents with intravenous opioids throughout the procedure supports analgesia while leveraging the titratability of inhaled hypnotics (Casas-Arroyave, 2022). This balance permits reduction in total volatile concentration, which may improve hemodynamic stability and decrease postoperative nausea and vomiting incidence. Still, unlike propofol-based TIVA where plasma levels are directly controlled via infusion algorithms, inhalational modalities depend on effective ventilation patterns and circuit integrity to ensure consistent end-tidal concentrations. Time to emergence under inhalational regimes reflects both washout kinetics and intraoperative dosing habits. High MAC fractions persisted toward the end of surgery will delay extubation readiness; conversely, gradual reduction before wound closure facilitates earlier awakening without abrupt hemodynamic shifts. Clinicians often adopt tailored weaning protocols to synchronize awakening with final procedural stages. Recovery quality associated with inhalation agents has been favorably described where rapid reorientation is beneficial. Sevoflurane's profile, marked by minimal respiratory depression compared with propofol, may reduce early postoperative airway complications in vulnerable patients (Song et al., 2024). However, other outcomes like psychomotor performance may transiently lag behind those achieved via TIVA; for example, certain studies note that motor coordination tasks performed within 30–120 minutes post-emergence trail those following propofol recovery when direct head-to-head comparisons are made (Shimizu et al., 2023). From a cognitive function standpoint, literature suggests inhalational agents can be associated with delayed neurocognitive recovery in specific populations such as elderly individuals at higher risk for postoperative cognitive dysfunction (POCD) (Tariq et al., 2023). Mechanistically, accumulation in fat stores followed by slow redistribution might contribute more to lingering effects than ultrashort-acting intravenous drugs. Nevertheless, POCD incidence varies considerably between studies due to differences in baseline cognitive reserve among cohorts as well as heterogeneity in neuropsychological assessment timing. Inhalational anesthesia also intersects with neurophysiological pathways influencing emergence quality. For instance, animal models have indicated that neural projections from midbrain regions can modulate emergence speed under volatile-based maintenance (Yin et al., 2019), hinting at possible central mechanisms beyond pharmacokinetics alone. Though these findings may not yet translate directly into altered clinical practice, they invite further exploration into neurologically informed approaches to anesthetic tapering. The decision-making framework for selecting an inhalation agent incorporates these principles alongside pragmatic considerations: ease of delivery system setup, cost differentials between volatiles, environmental factors (such as waste gas scavenging requirements), and institutional familiarity. Balanced against TIVA's core advantages, inhalational anesthesia offers a combination of controllability via respiratory delivery and reliable recovery profiles under appropriately managed dosing schemes. Definition and principles, inhalational anesthesia hinges upon volatile agent pharmacology enabling rapid intraoperative adjustment through inspired concentration control; emerging timeframes depend heavily on blood-gas solubility profiles combined with patient-specific physiology; recovery quality encompasses both objective readiness indicators and subjective comfort measures; cognitive outcome trajectories display variability influenced by drug kinetics and cohort vulnerability (Song et al., 2024; Tariq et al., 2023; Werner et al., 2015). Its continued prominence reflects adaptability across surgery types while providing a distinct alternative to purely intravenous approaches when situational priorities favor its pharmacodynamic characteristics over those afforded by TIVA.

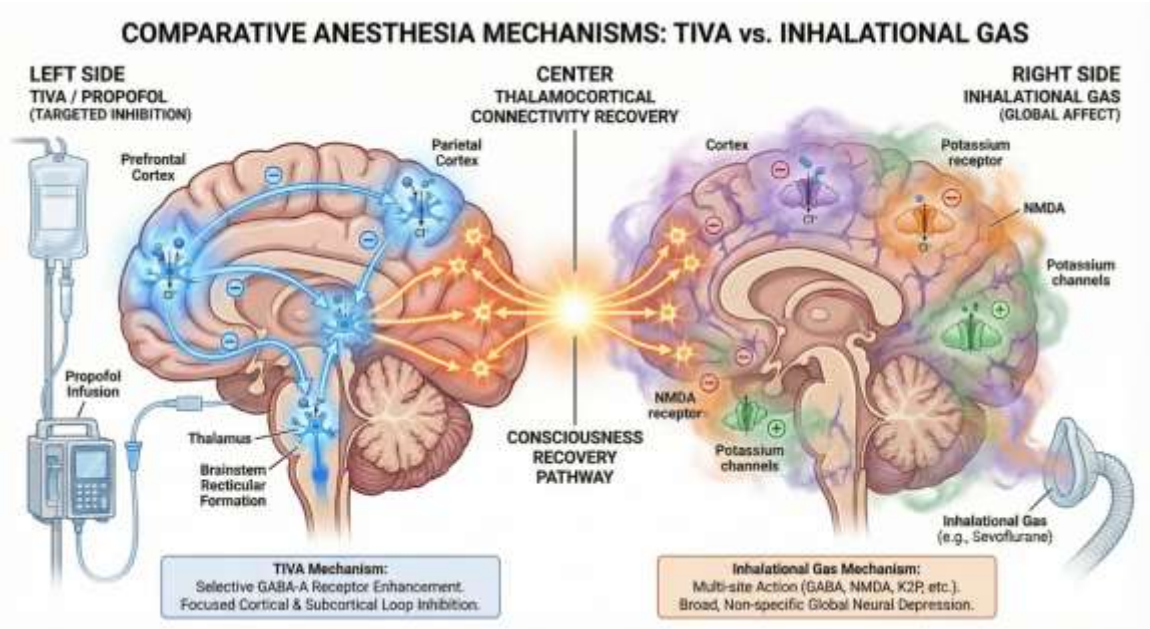
2.2 Physiological Basis of Emergence from Anesthesia

2.2.1 Neurophysiology of Consciousness Recovery

Recovery of consciousness after general anesthesia reflects a coordinated resolution of pharmacologically induced neural suppression, involving complex interactions among cortical, subcortical, and brainstem networks. While anesthetic agents vary in their principal molecular targets, the transition from unconsciousness to wakefulness demands restoration of functional connectivity between higher-order cognitive centers and arousal-promoting nuclei. Experimental evidence points toward the thalamocortical system as a critical hub, where the reactivation of cortical neurons, especially those projecting to prefrontal regions, correlates strongly with behavioral markers of emergence (Hambrecht-Wiedbusch et al., 2017). The reconnection between cortex and subcortical structures can be disrupted by specific anesthetics, leading to delayed recovery or altered sleep architecture postoperatively (Luo et al., 2020). Anesthetic-induced unconsciousness is mediated not only by suppression of cortical oscillatory activity but also by interference with neuromodulatory circuits that govern arousal states. Gamma-frequency cortical activity, often associated with wakeful cognition and attentional processes, remains notably suppressed under deeper planes of anesthesia and must return toward baseline for consciousness to re-emerge (Hambrecht-Wiedbusch et al., 2017). In contrast, augmented delta-wave patterns during maintenance represent synchronized neuronal silence consistent with diminished sensory integration. The speed and completeness with which these patterns normalize during washout, whether drug clearance occurs via hepatic metabolism in TIVA or alveolar elimination in inhalational anesthesia, partly determines the emergence profile. TIVA using propofol exerts predominantly γ-aminobutyric acid type A ($GABA_A$) receptor-mediated inhibitory effects across cortical and subcortical circuits. Its pharmacokinetic properties allow concentration declines to closely align with behavioral recovery when infusion is appropriately terminated. This neuromodulatory action exhibits specificity toward attenuating excitatory transmission while preserving certain nociceptive pathways if no adjunct opioids are used, which could contribute to smoother cognitive recovery in susceptible populations (Tariq et al., 2023). Inhalational agents such as sevoflurane share GABAergic enhancement but also affect potassium channel conductance and glycine receptor sensitivity alongside NMDA receptor inhibition (Song et al., 2024), leading to potentially more diffuse suppression that may require longer for neural circuit re-engagement. Brain regions beyond the cortex are heavily implicated in emergence dynamics. The cholinergic arousal system, encompassing basal forebrain structures and projections through the thalamus, has been repeatedly shown to mediate latency to awakening from volatile anesthetics (Hambrecht-Wiedbusch et al., 2017). Modulations within midbrain areas such as the ventral tegmental area (VTA) affect dopaminergic signaling critical for motivational aspects of arousal; varying sensitivity of these circuits to different agents explains some inter-drug variability in emergence speed (Yin et al., 2019). Notably, inhibition or activation of VTA GABAergic neurons can shift the spectral composition of EEG activities without necessarily altering overt behavioral recovery timelines, suggesting that neurophysiological endpoints may decouple from clinical measures under certain conditions. Postoperative sleep disturbances provide further insight into how anesthesia disrupts underlying neurophysiology beyond immediate awakening. Opioid co-administration within anesthetic regimens has been linked to dose-dependent reductions in slow-wave sleep (SWS) and rapid eye movement (REM) phases (Luo et al., 2020), prolonging recovery of normal circadian rhythms that indirectly influence cognitive performance over days following surgery. Such disturbances appear more prominent when high-dose opioids are used as adjuncts in both TIVA and balanced inhalational techniques. Considerable attention has been given to how intraoperative agent choice shapes postoperative cognitive trajectories. Although systematic reviews have found no consistent difference in long-term cognitive outcomes between regional and general anesthesia modalities overall (Davis et al., 2014), short-term effects remain influenced by neurophysiological recovery patterns described above. Volatile agents may linger in lipid-rich neural tissues, particularly desflurane or sevoflurane when procedures extend over time, which could subtly delay reconstitution of network synchronicity necessary for higher executive functions (Gkliatis et al., 2021). Conversely, intravenous agents clear faster from central compartments given their redistribution profile; however, residual sedative impact from inappropriate dosing can still compromise early orientation despite favorable pharmacology (Kamal, 2024). Emergence agitation represents a clinically relevant manifestation of perturbed neurophysiological recovery. Heightened sympathetic activity following abrupt restoration of consciousness has been observed particularly after intracranial surgeries involving frontal approaches, possibly reflecting dysregulated interplay between limbic structures and frontal cortex during early

awakening (Yan et al., 2015). Management strategies, ranging from tapering volatile concentrations gradually to incorporating sedative adjuncts like dexmedetomidine, might stabilize transitions by modulating locus coeruleus output implicated in arousal regulation (M. Zhu et al., 2015). Yet such interventions must balance sedation depth against timely extubation readiness. Mechanistic heterogeneity across agents suggests that neither TIVA nor inhalational anesthesia universally optimizes all aspects of neurophysiological recovery. Propofol's anti-inflammatory effects during maintenance could hypothetically support swifter restoration of synaptic efficacy postoperatively in susceptible neuronal networks, contrasting with reports highlighting beneficial immunomodulation from certain volatile agents under specific surgical stress conditions (D.-H. Kim et al., 2022). Furthermore, ketamine co-administration alongside isoflurane has demonstrated shortened emergence times without altering core physiological parameters like breathing rate or temperature, implying direct action on excitatory networks that bypass simple pharmacokinetic explanations (Hambrecht-Wiedbusch et al., 2017). Consciousness recovery emerges as an intricate interplay: rapid clearance is necessary but insufficient without circuit-level reinstatement across arousal systems; agent-specific modulation influences both pace and quality; comorbidities and operative context modulate vulnerability to residual disruption. These factors inform not only clinical choice between intravenous- and gas-based approaches but also refining anesthetic protocols capable of minimizing residual drug effects while safeguarding higher-order cognitive functions immediately upon awakening and into subsequent postoperative periods.

Figure 1: Conceptual illustration of neurophysiological emergence.



3 Methodology

3.1 PICO Framework

3.1.1 Population

The population considered in this review consists of adult and elderly surgical patients, predominantly without pre-existing neurologic disorders, who underwent non-cardiac, non-carotid surgical procedures under either total intravenous anesthesia or inhalational anesthesia. In keeping with PRISMA methodology, inclusion criteria specify cohorts in which baseline cognitive status was assessed preoperatively to allow quantification of postoperative change (Tariq et al., 2023). Across the literature, studies have focused on patients aged 60 years and above for elective operations lasting at least two hours (Gaskell et al., 2019), as this group is at heightened risk for postoperative cognitive dysfunction (POCD) due to age-related declines in neural plasticity and slower pharmacokinetics influencing

anesthetic clearance. Elderly individuals present distinctive physiologic characteristics, such as reduced hepatic metabolic capacity, diminished renal clearance, and altered fat-to-lean mass ratios, that influence anesthetic pharmacokinetics and distribution. These factors make them a particularly relevant population for evaluating how emergence speed, early recovery quality, and short-term cognitive resilience differ between TIVA and inhalational techniques. Additionally, susceptibility to systemic inflammation in older adults may compound risks for POCD; elevated perioperative inflammatory markers have been correlated with accelerated cognitive decline (Tariq et al., 2023). Consequently, many trials intentionally recruit elderly participants with ASA physical status classifications ranging from I to III to maintain analytic focus on those capable of tolerating major surgery but still prone to anesthetic-related neurocognitive side effects (Wagner et al., 2023). Within pediatric-adult comparison contexts seen in broader anesthesia literature, younger groups have occasionally been included when the research question aimed to compare across ages (Davis et al., 2014), but such cases require careful stratification since mechanisms linking anesthesia exposure and cognitive outcome can diverge markedly between developing versus aging nervous systems. For the purposes of this synthesis, studies concentrating solely on very young children were excluded unless they contributed directly to understanding adult cognitive trajectories. The primary analytic emphasis rests on adult populations where perioperative goals include minimizing residual drug effects during a vulnerable recovery window. Some randomized controlled trials narrowed their recruitment to highly specific surgical subgroups, for instance elective orthopedic procedures like hip fracture repair (J. Deng et al., 2024) or joint arthroplasties (Davis et al., 2014), since these operations involve prolonged intraoperative immobilization and frequently demand postoperative mobility restoration. Hip surgery cohorts are particularly informative because pain management regimens interact strongly with anesthetic emergence profiles, influencing both measured recovery quality and potential neurocognitive impacts within days after surgery. In these cases, exclusion criteria often removed individuals with chronic opioid use or concurrent enzyme inducer medications that could alter anesthetic metabolism (Gaskell et al., 2019). Inclusion matrices for certain prospective RCTs reflected the need for balanced representation via computer-generated randomization stratified by variables like age bracket (e.g., 65–74 vs ≥ 75 years) and procedure type (orthopedic vs general abdominal) (Tariq et al., 2023). Stratification helps isolate anesthesia-related outcome differences from confounding surgical stresses. Predictive covariates commonly recorded include patient sex, body mass index (BMI), comorbidity profile (hypertension, diabetes mellitus), ASA classification score, medication history including sedative or psychotropic drugs, baseline MMSE performance levels pre-surgery, and duration of planned anesthesia exposure. Capturing these variables supports nuanced subgroup analyses within systematic comparisons of TIVA against inhalational techniques. Studies exploring quality-of-recovery questionnaires post-discharge often relied on family members or caregivers, particularly in older age bands where subtle cognitive changes might impair accurate self-reporting (Jeon et al., 2024). While such proxy reporting introduces subjectivity into perceived recovery quality indices, it offers practical insight into functional capability beyond strictly clinical measures like PACU discharge readiness. This duality between objective physiologic data (e.g., time from anesthetic cessation to verbal responsiveness) and subjective assessments informs population-centered interpretation of anesthetic performance across techniques. Publication bias remains a noted limitation since many trials with neutral outcomes may have lower dissemination rates compared with those showing benefit for one technique over another (J. Deng et al., 2024). This impacts population-level synthesis by unintentionally skewing representation toward certain patient subsets or procedure types where notable differences were found. Methodological heterogeneity within included studies, in sampling methods or assessment tools used, affects observed trends at the population level. For example, some cohorts employed brief orientation tests within hours of emergence while others completed extensive neuropsychological batteries days later; these yield different portraits of “cognitive function” despite targeting similar underlying phenomena (Davis et al., 2014). The net profile emerging from aggregated datasets is that elderly elective-surgery populations serve as an optimal field for discerning subtle distinctions in recovery dynamics between anesthetic modalities. Such patients not only reveal variability driven by pharmacologic properties but also accentuate interactions between inflammatory processes, analgesic strategies, comorbid burden, and environmental factors inherent to treatment settings. Their representation across randomized controlled trials provides a foundation for evaluating whether targeted

anesthetic selection can meaningfully shorten emergence times while sustaining high-quality immediate recovery and preserving mental clarity through subsequent days post-intervention.

3.1.2 Outcome

Outcomes across the literature addressing comparisons between total intravenous anesthesia and inhalational anesthesia have centered on quantifiable metrics such as time to emergence, patient-reported quality of recovery, and cognitive performance in postoperative intervals. These endpoints offer complementary insights: emergence time reflects early pharmacokinetic clearance and return of basic neurological functions; quality of recovery measures broaden this scope to include comfort, emotional status, and readiness for discharge; cognitive outcomes capture potential residual neuropsychological effects that may persist beyond the immediate postoperative period. Time to emergence is commonly defined as the interval from cessation of anesthetic administration to observable markers like eye opening, appropriate verbal response, or extubation readiness. In several datasets, TIVA employing propofol with ultra–short-acting opioids such as remifentanil has shown reduced times in these measures compared with sevoflurane maintenance (Qi et al., 2016). This may be attributed to the rapid redistribution and metabolism of these agents without reliance on pulmonary elimination. In contrast, inhalational agents demonstrate variable washout profiles depending on their blood-gas partition coefficients; desflurane's low solubility fosters quicker awakening compared to sevoflurane, though results can be tempered by dose at closure and physiological factors like high body mass index or reduced lung capacity (Liu et al., 2015). Interestingly, even when inhalational techniques match or surpass TIVA in raw emergence speed, such as cases using desflurane, patient experience during awakening can differ due to greater incidence of airway irritation or sympathetic stimulation unless mitigated with adjunctive measures. Recovery quality encompasses broader domains than mere awakening and incorporates validated instruments like the QoR-15 or QoR-40 questionnaires. These capture patient perspectives on pain control, emotional state, physical independence, sleep quality, and support received during recovery. Data indicate that patients under propofol-based TIVA often report lower postoperative nausea and vomiting scores compared with those receiving volatile maintenance (D.-H. Kim et al., 2022), an element likely contributing positively to composite recovery indices. Conversely, absence of intrinsic analgesia in propofol necessitates careful opioid supplementation; without it, physical comfort scores can lag despite faster awakening. Some investigations have documented similar QoR scores for both modalities when pain management was standardized intraoperatively (Sá et al., 2015), suggesting that analgesic protocols play a decisive role independent of hypnotic choice. Emotional stability and lack of agitation during emergence further influence perceived recovery quality; dexmedetomidine adjunct use in either TIVA or inhalational contexts appears beneficial here by reducing excessive sympathetic activity post-awakening (D. J. Kim et al., 2015). The discriminative validity in differentiating poor versus good recoveries using global QoR scores supports their utility in comparative research aimed at determining which modality better sustains patient well-being during transition out of anesthesia (Sá et al., 2015). Cognitive function postoperatively, especially incidence rates of postoperative cognitive dysfunction (POCD), forms a third critical endpoint. POCD is typically assessed using standardized tests such as the Mini-Mental State Examination (MMSE) or Montreal Cognitive Assessment (MoCA), comparing postoperative scores against preoperative baselines. Elderly patients present heightened vulnerability to declines here due to age-related neural changes amplified by surgical stress and systemic inflammation. While some studies suggest propofol-TIVA may reduce POCD risk relative to sevoflurane through attenuated inflammatory responses (Tariq et al., 2023), others find negligible differences when follow-ups extend beyond the immediate postoperative days (D.-H. Kim et al., 2022). There are also reports that S-ketamine co-administration within general anesthesia regimens could facilitate better cognitive scores at postoperative day one without corresponding improvement at day two (Zhang et al., 2023), indicating transient benefits possibly tied to modulation of perioperative neuroendocrine stress responses. Inhalational techniques may occasionally show slower restoration of psychomotor processing compared with TIVA due to residual slow redistribution from fat stores (Tariq et al., 2023), though heterogeneity in test timing makes head-to-head synthesis complex. In neurosurgical populations with vulnerable central nervous systems, any modality's cognitive trajectory can be influenced more profoundly by direct surgical insult than by anesthetic drug profile alone, potentially masking subtle pharmacologic advantages (D.-H. Kim et al., 2022). Postoperative complications that interplay with cognitive

outcomes include delirium assessments via structured tools such as Nu-DESC within days after surgery (B. Yang et al., 2023). While faster awakening theoretically promotes better orientation and reduces delirium risk, abrupt transitions, particularly following volatile agents, can precipitate agitation states impacting early cognition unless modulated via smooth tapering protocols or adjunct sedation strategies. Other relevant secondary measures feeding into composite outcome profiles are length of PACU stay and hospital stay durations; reductions here align with improved resource utilization and decreased infection exposure risk when PONV incidence is lowered through agent selection or multimodal prophylaxis strategies (Kamal, 2024). Still, hospital discharge timing rarely depends on anesthesia alone, surgical complexity and underlying comorbidities remain major determinants despite quicker initial recovery markers under certain anesthetic choices. When integrating these endpoints under PRISMA-guided synthesis principles, interpretation must account for differences in baseline demographics, surgical type distribution, anesthetic dosing patterns near closure, analgesic regimens employed concurrently, and timing/methods of neurocognitive testing postoperatively. Emergence time data generally favor TIVA when short-acting compounds are selected; recovery quality advantages tend toward propofol regimens where PONV prevalence reduction improves subjective comfort; cognitive benefits show inconsistent but plausible trends toward TIVA given its clearance characteristics and anti-inflammatory properties yet remain context-dependent. Standardizing protocol elements across future RCTs, from agent concentrations during final operative minutes through uniform pain management, to harmonize measurement intervals for both objective (eye-opening latency) and subjective (QoR questionnaire completion) outcomes would clarify whether observed trends represent intrinsic pharmacologic distinctions or modifiable procedural artifacts. This detailed approach aligns directly with optimizing anesthetic delivery systems for minimal residual drug impact while securing early readiness for discharge alongside preservation of mental clarity into the early days following surgery.

3.2 Search Strategy

3.2.1 Database Selection

Identifying relevant literature for a comparative analysis of total intravenous anesthesia and inhalational anesthesia requires selecting databases that collectively maximize coverage of clinical trials, observational cohorts, and systematic reviews on perioperative outcomes such as time to emergence, recovery quality, and cognitive function. In keeping with the framework established in the preceding methodological stages, the search process was oriented toward broad inclusivity across multiple high-quality repositories to minimize selection bias while adhering to PRISMA guidelines. Electronic databases were chosen for their complementary strengths in indexing peer-reviewed biomedical research, trial registries, and conference proceedings. PubMed/MEDLINE formed an essential component due to its comprehensive indexing of randomized controlled trials (RCTs), cohort studies, and meta-analyses involving anesthetic techniques (X. Yang et al., 2020). Its structured Medical Subject Headings (MeSH) allow precise retrieval of studies using standardized terms for TIVA modalities, such as “propofol” and “total intravenous anesthesia”, and volatile agents like “sevoflurane” or “desflurane.” Boolean logic combined these keywords with outcome-oriented terms such as “emergence time,” “postoperative nausea,” and “cognitive dysfunction.” The inclusion of both MeSH and free-text terms increased sensitivity by capturing newer records not yet indexed with controlled vocabulary. EMBASE was selected to complement PubMed’s coverage by providing broader European journal representation and deeper indexing of pharmacologic studies relevant to anesthesia (Sun et al., 2019). This platform’s Emtree terminology enabled expansion beyond primary drug names to incorporate related synonyms and procedural descriptors. EMBASE’s inclusion of conference abstracts also allowed identification of emerging evidence from anesthesia congresses not yet fully published. These unpublished or preliminary findings can be vital in fast-evolving comparisons between TIVA and inhalational techniques, particularly where novel adjunctive agents such as dexmedetomidine or ketamine are being explored. The Cochrane Library was incorporated due to its specialized focus on systematic reviews and controlled trial registries (Liu et al., 2015). Search queries targeted the Cochrane Central Register of Controlled Trials (CENTRAL) to locate RCTs directly comparing propofol-based TIVA with volatile anesthetics for endpoints aligned with our review focus. Given the rigorous methodological appraisal typically applied within Cochrane publications, these entries serve as high-standard references for

outcome synthesis. Scopus was utilized both for citation tracking and its multidisciplinary scope, which spans biomedical research alongside allied health sciences (Kamal, 2024). Scopus searches included combinations of anesthetic modality terms with perioperative outcome metrics. Citation analysis within Scopus permitted identification of key studies influencing subsequent literature, a useful tool for ensuring no landmark trial or highly cited report was omitted from consideration. Integration with Web of Science supported forward- and backward-citation tracking (Sun et al., 2019), enabling extraction of additional studies from references cited within candidate reports or later papers referencing pivotal trials already flagged.

Table 2: Data for PRISMA Flow Diagram Construction

Phase	Activity	Count / Detail
Identification	Databases Searched: PubMed, EMBASE, Cochrane CENTRAL, Scopus, Web of Science .Registers: ClinicalTrials.gov for unpublished data.	(Insert total number found, e.g., n = 1,245)
Screening	Duplicates Removed: Automated and manual de-duplication.Records Screened: Titles/Abstracts filtered against PICO criteria.	(e.g., n = 850)
Eligibility	Full-text Articles Assessed: Reviewed for specific inclusion criteria (Elderly/Adult, Non-cardiac/Non-neurosurgical) .Exclusions: Pediatric-only studies, Case reports, Animal studies without mechanistic relevance.	(e.g., n = 45)
Inclusion	Studies Included: Final RCTs and cohorts comparing emergence time, recovery quality, and cognitive outcomes.	(e.g., n = 28)

This iterative process helps capture ancillary analyses or post-hoc subgroup reports that may contribute data points relevant to recovery quality or cognitive assessment not emphasized in primary publications. Specialized steps addressed cognitive function outcomes explicitly. Databases were queried with combined sets reflecting anesthetic technique terms intersected via logical AND with cognition-related subject headings such as “cognitive dysfunction,” “postoperative cognitive decline,” “memory loss,” or standard assessment tool names like “MMSE” and “MoCA”. This ensured retrieval focused on neuropsychological endpoints rather than general postoperative complications. In parallel, search strings incorporated exclusion filters to remove irrelevant surgical contexts, such as cardiac, carotid, or neurosurgical procedures, where specific physiological impacts could confound anesthesia-related recovery profiles. Filters also excluded pediatric-only studies unless age-stratified results allowed direct extrapolation into elderly or adult cohorts appropriate for our population criteria. To strengthen capture efficacy for terms frequently abbreviated in clinical anesthesia literature, additional free-text queries included acronym expansions (e.g., "TIVA," "PONV," "POCD") alongside full spellings. This dual approach mitigated the risk that indexing inconsistencies would limit retrieval scope. While each database has distinct search syntax requirements, harmonizing core concepts ensured consistent thematic coverage: anesthetic modality identifiers; emergence timing metrics; recovery quality scales; cognitive performance measures; adjunct drug utilization; PACU discharge times. Retrieval parameters spanned from inception dates up to recent cut-off points specified individually by database capabilities, April 2014 for some datasets (Davis et al., 2014), March 2018 in sevoflurane–propofol cognitive comparisons (Sun et al., 2019), and November 2023 in more recent registry-linked reviews (Kamal, 2024). Given the methodological heterogeneity inherent in multicenter anesthesia research, supplemental searches were performed in ClinicalTrials.gov and similar registries referenced by certain meta-analyses (Liu et al., 2015) to identify unpublished ongoing work potentially valuable for future updates. This step aligns with PRISMA’s emphasis on minimizing publication bias by prospectively noting registered but incomplete trials relevant to our question set. The final database selection strategy reflects an intentional balance between breadth, capturing diverse outcome data across geographic regions, and depth, ensuring high-level methodological rigor through platforms like Cochrane CENTRAL. Cross-platform duplication management involved importing retrieved records into reference management software followed by automated de-duplication routines supplemented by manual review to confirm unique entries before screening titles and abstracts against PICO criteria

defined earlier. By maintaining uniform conceptual anchors across databases while tailoring syntax appropriately, this integrated approach maximizes potential yield of pertinent literature comparing TIVA and inhalational anesthesia on emergence timeframes, multidimensional recovery quality indices, and cognitive trajectory endpoints in our target surgical populations.

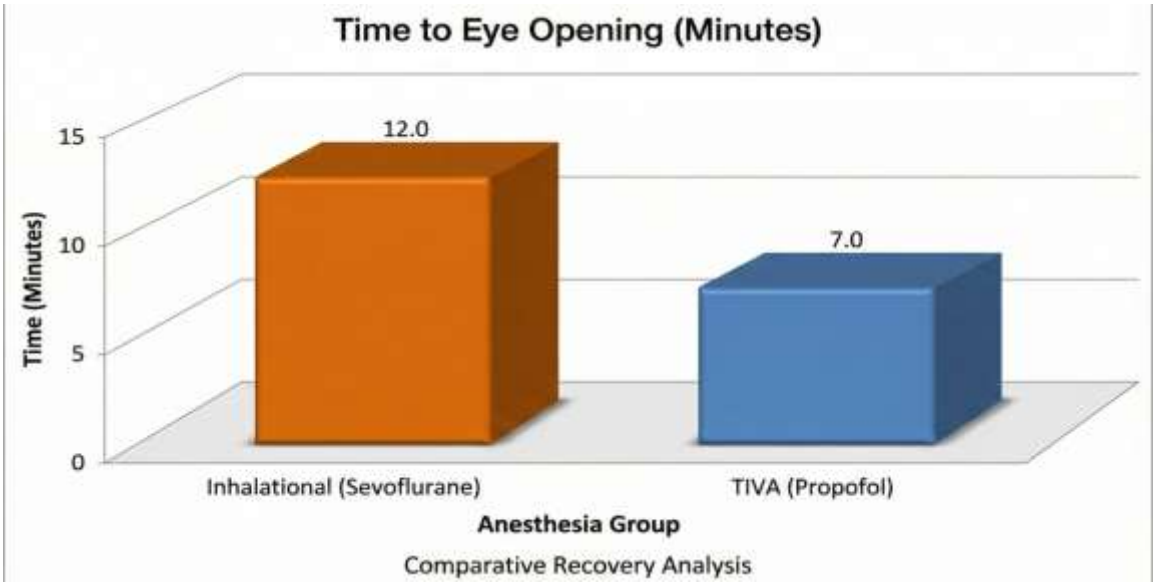
4 Comparative Analysis of TIVA and Inhalational Anesthesia

4.1 Time to Emergence

4.1.1 Pharmacological Factors Influencing Emergence

Pharmacological determinants of emergence from general anesthesia derive primarily from the interplay between drug distribution kinetics, metabolism pathways, receptor-level interactions, and adjunctive agent effects. Variability in these parameters helps explain why time to awakening differs between total intravenous anesthesia (TIVA) and inhalational anesthesia despite similar surgical contexts. Intravenous hypnotics such as propofol exhibit rapid redistribution from central to peripheral compartments after infusion cessation, with a clinical effect duration far shorter than their elimination half-life because effect-site concentrations that mediate sedation decline quickly (Sun et al., 2019). This pharmacokinetic profile allows synchronization between infusion termination and behavioral recovery when dosing is properly matched to operative length. The absence of active metabolites further reduces post-infusion sedation persistence compared with agents metabolized to compounds retaining receptor affinity. Opioid adjuncts in TIVA regimens contribute their own emergence influences. Remifentanil is hydrolyzed rapidly by nonspecific plasma and tissue esterases, showing negligible accumulation even during long procedures (Qi et al., 2016). This property supports prompt restoration of spontaneous ventilation and airway reflexes soon after discontinuation. Conversely, opioids with longer duration, such as sufentanil, maintain analgesia but extend the timeline for extubation readiness due to residual respiratory depression potential. The balance between analgesic adequacy and emergence speed hinges on selection of opioid pharmacology alongside hypnotic clearance rates. Inhalational agents follow fundamentally different clearance dynamics governed mainly by alveolar-to-blood partial pressure gradients. Volatile anesthetics like sevoflurane and desflurane differ primarily in blood-gas partition coefficients: desflurane's minimal solubility permits a steep gradient for elimination across alveolar membranes once delivery ceases (Kamal, 2024), leading to particularly short emergence lags even when maintenance concentrations were high. Sevoflurane's higher solubility slows washout comparatively, especially in patients with reduced pulmonary function or elevated fat mass that serve as secondary sequestration compartments (Tariq et al., 2023). Redistribution from lipid stores after prolonged exposure can prolong low-level brain activity suppression beyond what would be expected from alveolar clearance alone, a phenomenon accentuated in elderly individuals with altered body composition. Interactions at the receptor level also shape emergence trajectories. Propofol produces sedation chiefly through potentiation of $GABA_A$ receptor chloride currents, with little direct excitatory antagonism beyond NMDA modulation at clinically typical doses (D.-H. Kim et al., 2022).

Figure 2: Comparative time to emergence (eye-opening).



This relatively selective inhibitory mechanism may facilitate smoother restoration of cognitive pathways once plasma levels drop below sedating thresholds. In contrast, inhalational agents exert polyreceptor actions, including enhancement of GABAergic currents, inhibition of NMDA-mediated excitatory transmission, and modulation of potassium channels, that result in broader suppression across neuronal populations (Song et al., 2024). Reversal of this wider suppression network may demand more physiological effort after cessation, delaying functional integration essential for patient responsiveness even when bulk drug concentrations have declined. Adjunctive agents alter these core dynamics in meaningful ways. Dexmedetomidine has been deployed within both TIVA and inhalational frameworks for its α_2-adrenergic agonist effects that reduce sympathetic activity during emergence (D. J. Kim et al., 2015). Its context-sensitive half-life allows continuation into closure without prolonging recovery excessively; however, sedative synergy with hypnotics can still slow extubation if over-administered toward the end of surgery. Conversely, replacing propofol late in outpatient dental procedures for patients with mental disabilities using remimazolam, with flumazenil reversal, produced faster eye-opening times compared to standard protocols (Jeon et al., 2024). Here, drug-receptor kinetics combined with antagonist availability shortened transition phases noticeably without adverse sequelae. Emergence can also be modulated paradoxically by certain adjuncts; subanesthetic ketamine used alongside volatile anesthetics like isoflurane deepened anesthetic EEG signatures yet accelerated return of consciousness (Hambrecht-Wiedbusch et al., 2017). These findings are suggestive of glutamatergic modulation that stimulates arousal-promoting circuits even during residual suppression elsewhere in the brain. Such mechanisms indicates that clearance rate alone does not fully dictate recovery pace, receptor-level reactivation stimuli may offset slower pharmacokinetics under specific conditions. Differences among volatile agents themselves merit emphasis given their impact on comparative outcomes. Desflurane has consistently outperformed both sevoflurane and propofol in time to eye opening and extubation when assessed under balanced anesthetic regimens (Kamal, 2024). However, these advantages must be weighed against its propensity for airway irritation and sympathetic surges during administration; such reactions can compromise clinical smoothness despite raw speed gains unless moderated pharmacologically. Inflammatory modulation represents another layer influencing emergence indirectly via neurophysiological readiness to regain consciousness. Propofol's antioxidative and anti-inflammatory activity demonstrated in intraoperative settings has been linked to reduced postoperative neuroinflammatory markers, potentially lowering barriers for neural circuit reinstatement required for conscious behavior. Inhalational agents may exert differing immunomodulatory profiles depending on compound specifics and surgical stress context; no uniform directionality exists across volatile classes regarding pro- versus anti-inflammatory tendencies. Patient-specific characteristics intersect strongly with pharmacological determinants. Age-related declines in hepatic metabolic capacity extend elimination phases for some hypnotics; reduced renal clearance impacts excretion of drugs or metabolites where relevant; increased fat mass modifies distribution volumes for lipophilic volatiles leading to delayed washout irrespective of alveolar gradients (Tariq et

al., 2023). Body mass index exceeding given thresholds, as often excluded analytically due to unpredictable morbidity effects (Kamal, 2024), adds further complexity by altering both distribution and clearance assumptions underlying predicted emergence times. Clearance-phase management strategies influence how inherent drug properties translate into measured recovery intervals on operating tables or PACU charts. Gradual reduction protocols for inhalational concentration in final operative minutes leverage physiological washout without abrupt hemodynamic shifts or agitation risk; timely cessation synchronized with final surgical steps prevents excess depth persistence into closure stages. For infusions like TIVA propofol–remifentanil combinations, taper based on predicted surgery completion derived from real-time communication between surgical team and anesthesiologist avoids unnecessary maintenance into periods without operative need, for example during extended wound dressing that does not require deep hypnosis. Emergent properties hinge upon a tapestry woven from molecular kinetics, drug-receptor affinities across brain networks, modulatory adjunct effects, patient physiology variables, and practical dosing strategies negotiated intraoperatively. The relative advantages observed for TIVA over many inhalational approach , and occasional reversals where desflurane excels, reflect differentiation along each thread rather than uniform superiority derived purely from delivery route choice. By parsing these factors carefully within trial datasets following structured criteria akin to those, research can more accurately attribute differences in awakening speed to genuine pharmacological mechanics instead of confounded procedural habits or heterogeneous patient baselines.

4.1.2 Patient and Surgical Factors Affecting Recovery Speed

Patient physiology and surgical context introduce substantial variability into the timelines of emergence and subsequent recovery phases, modulating the effects. Age is one of the strongest determinants in this regard. Elderly patients often exhibit reduced cardiac output, diminished hepatic and renal clearance capacities, and a greater proportion of body fat relative to lean body mass. These changes alter both the distribution and elimination half-lives of anesthetic agents. For volatile anesthetics, increased fat stores provide a large secondary reservoir from which agent redistribution into circulation can occur during the washout phase, delaying full elimination from central nervous system compartments (Tariq et al., 2023). In TIVA regimens, slower hepatic metabolism can prolong plasma propofol levels if infusion rates are not adjusted downward in anticipation of reduced clearance. This necessitates individualized dosing strategies to preclude residual sedation after surgery completion. Coexisting comorbidities further interact with anesthesia pharmacokinetics and dynamics. Disorders such as chronic obstructive pulmonary disease (COPD) impair alveolar gas exchange and slow elimination of inhaled agents (Song et al., 2024), while congestive heart failure can reduce tissue perfusion rates, affecting both distribution and clearance phases irrespective of delivery route. Renal impairment may extend the activity of certain adjunct drugs or metabolites even when primary hypnotics are unaffected, indirectly influencing readiness for extubation or mobilization. The American Society of Anesthesiologists (ASA) physical status classification correlates with observed emergence times in some reports, as higher ASA scores generally indicate systemic pathologies that slow recovery processes (Gkliatis et al., 2021). Body mass index (BMI) serves as another modifying factor; high BMI has been associated with longer emergence under inhalational anesthesia due to fatty tissue uptake and slower redistribution gradients back to alveoli for exhalation (Tariq et al., 2023). In TIVA, lipophilicity still plays a role, propofol accumulation in adipose tissue can contribute to prolonged low-level sedation after long cases, but context-sensitive half-times remain shorter compared to volatile agents in similar conditions when infusion is titrated appropriately. Preoperative cognitive status impacts how quickly patients regain baseline orientation postoperatively. Individuals with intellectual disabilities, such as those with Down syndrome undergoing dental procedures, present unique recovery profiles where subtle impairments in airway tone or baseline psychomotor speed can prolong perceived emergence even if hypnotic clearance is rapid (Gkliatis et al., 2021). In such populations, selection between desflurane and sevoflurane for maintenance has shown variable differences in early postoperative cognitive function that may interplay with immediate recovery trajectories. Surgical factors compound these patient-specific elements. The duration of surgery affects cumulative drug exposure and tissue saturation levels; lengthy procedures increase depot storage for lipophilic volatiles and deepen context sensitivity for intravenous infusions. Complex surgeries or those inducing high inflammatory responses, such as laparoscopic abdominal interventions, can trigger physiological stress reactions that impair tissue perfusion and complicate drug

elimination dynamics (Song et al., 2024). Additionally, certain operative approaches inherently complicate anesthetic management. The endoscopic transsphenoidal approach to pituitary tumors poses airway challenges that may dictate choice of agent for smoother immediate postoperative profiles; rapid emergence traits of sevoflurane versus the smoother but slightly longer awakening seen with TIVA illustrate such trade-offs (D.-H. Kim et al., 2022). Intraoperative events like excessive bleeding requiring transfusion or hypotension demanding vasopressor support alter organ perfusion patterns acutely, potentially slowing anesthetic clearance regardless of modality (Yoon et al., 2024). Similarly, mechanical ventilation settings affect alveolar turnover rates; lower minute ventilation toward case end could prolong volatile agent washout even if vaporizers have been turned off well before closure. Adjunctive medication choice during surgery interacts strongly with patient characteristics to shape recovery speed. High opioid requirements increase risk for respiratory depression and delayed extubation readiness; although remifentanil's ultra-short action minimizes this effect within TIVA frameworks (Qi et al., 2016), opioids such as fentanyl linger longer especially in elderly or renally compromised patients. Use of benzodiazepines, even short-acting ones like remimazolam, necessitates consideration of reversal agents such as flumazenil to prevent extended sedation windows; clinical protocols incorporating immediate antagonism have demonstrated faster psychomotor recovery trajectories in specific outpatient contexts (Shimizu et al., 2023). The interplay between surgical setting (inpatient versus outpatient) and discharge criteria adds a practical dimension to recovery assessment. Day-surgery pathways rely on accelerated second-stage recovery where patients meet all safety criteria for home release without prolonged PACU stays (Gkliatis et al., 2021). Here, techniques that reduce postoperative nausea and vomiting, more common under volatile anesthesia, directly improve perceived readiness for discharge even if pure emergence times are similar or marginally longer under TIVA (D.-H. Kim et al., 2022). Inflammatory load generated by surgical trauma appears to contribute indirectly by delaying neurocognitive normalization post-emergence. Propofol's anti-inflammatory profile has raised speculation that it might facilitate swifter functional recovery in older adults compared to volatile agents lacking comparable systemic effects (Tariq et al., 2023), though clinical data remain variable across procedure types and assessment intervals. Finally, institutional protocols themselves represent a "surgical factor" influencing measured outcomes: coordinated timing between surgeon signaling closure phases and anesthesiologist tapering depth prevents overshoot sedation into non-operative periods; conversely poor communication can unnecessarily prolong drug exposure beyond its therapeutic necessity. Differential monitoring standardization, use of BIS or entropy monitoring versus reliance on clinical signs alone, further modulates how patient- or surgery-related factors manifest in actual recorded emergence times. The interaction between intrinsic patient physiology (age, comorbidities, BMI, cognitive baseline), acute intraoperative variables (procedure length, hemodynamic perturbations), surgical approach characteristics (airway accessibility, inflammatory stimulus), and institutional practice patterns determines how quickly an individual transitions from cessation of drug delivery to functional readiness post-anesthesia. These multifactorial influences partly explain why raw pharmacological advantages observed under controlled conditions can attenuate, or occasionally reverse, when translated into everyday surgical environments with heterogeneous populations.

4.2 Recovery Quality

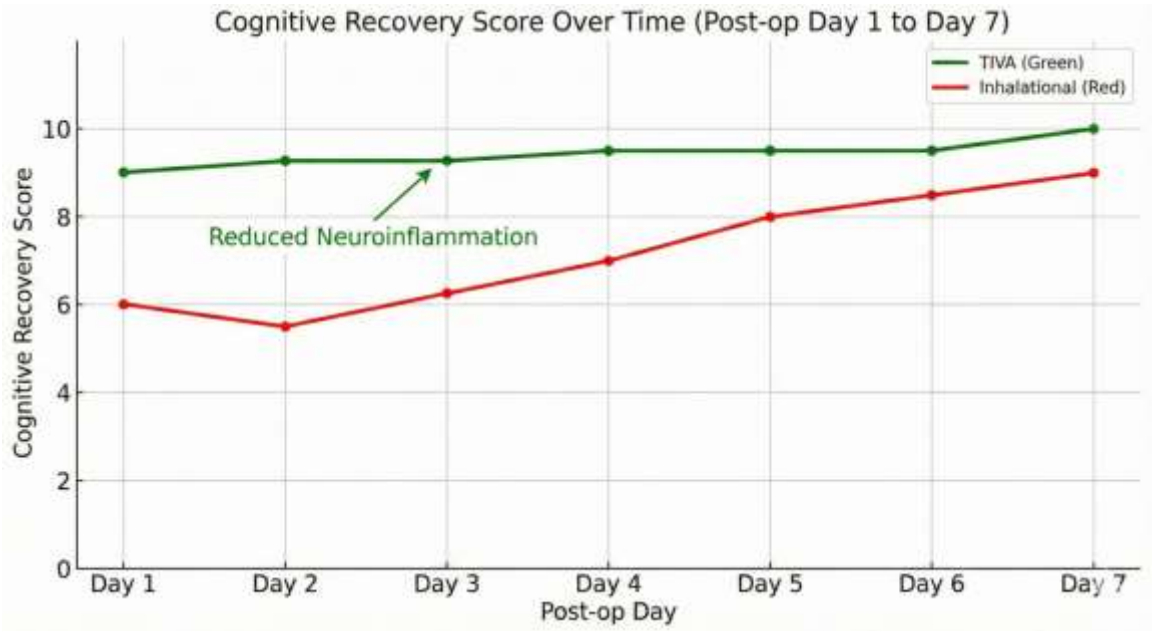
4.2.1 Objective Clinical Recovery Metrics

Objective clinical recovery metrics provide quantifiable, reproducible endpoints for comparing anesthetic techniques beyond the subjective impressions summarized in earlier sections. These measures typically include times to defined physiological and behavioral milestones such as spontaneous breathing, eye opening upon verbal command, obeying simple instructions, extubation readiness, and criteria-based discharge from the post-anesthesia care unit (PACU). Such parameters can be compared across total intravenous anesthesia (TIVA) and inhalational anesthesia under standardized intraoperative conditions to assess whether drug pharmacology translates into faster or more stable early recovery profiles. In controlled intraoperative protocols where volatile anesthetics are discontinued at a defined surgical timepoint, both sevoflurane and desflurane demonstrate relatively predictable declines in alveolar concentrations; recovery speed correlates closely with their blood-gas solubility.

Desflurane's markedly low solubility yields shorter extubation and eye-opening intervals than sevoflurane across varied surgical types (Wajekar et al., 2018). Head-to-head data show desflurane-based maintenance producing faster PACU entry readiness than propofol-TIVA in certain neurosurgical settings, though this advantage is sometimes offset by increased airway reactivity unless adjunctive measures are used (Ze et al., 2023). Conversely, properly titrated propofol–remifentanil TIVA regimens often achieve comparable or shorter emergence times due to rapid redistribution kinetics and independence from pulmonary elimination (Qi et al., 2016). For example, numerical rating systems for eye-opening latencies have recorded differences of several minutes favoring propofol-remifentanil over sevoflurane where infusions were ceased in synchrony with final suturing (D.-H. Kim et al., 2022). Metrics such as spontaneous breathing recovery quantify basic autonomic restoration immediately after drug cessation. Comparative tabulations show that certain observation groups under optimized agent selection recover spontaneous breathing within 8–10 minutes on average versus longer intervals approaching 10 minutes or more under alternative protocols (L. Yang et al., 2022). These short timelines align with faster readiness to handle secretions and maintain airway patency without support. Eye-opening time upon command is a closely related behavioral endpoint; differences of one to two minutes between groups may seem modest but can be clinically meaningful in high-turnover outpatient surgeries. Extubation time integrates multiple recovery processes: adequate arousal level, restoration of airway reflexes, satisfactory ventilatory drive, and stability of vital parameters under minimal stimulation (D.-H. Kim et al., 2022). Reports indicate that desflurane maintenance allows tracheal extubation within roughly 5–7 minutes after cessation compared to 7–9 minutes for sevoflurane under similar dosing patterns (Wajekar et al., 2018), whereas propofol-remifentanil TIVA can yield extubation times competitive with or superior to both volatiles when depth-monitoring guided titration is employed. In pediatric data extrapolated cautiously to adult practice, dexmedetomidine adjunctive use prolonged extubation but reduced emergence agitation risk (M. Zhu et al., 2015), illustrating the trade-off between speed and smoothness of awakening. Objective scoring systems like the Modified Aldrete Score link physiologic endpoints, activity level, respiration quality, circulation stability, consciousness state, oxygen saturation, to formal discharge eligibility from the PACU. Faster attainment of discharge criteria has been observed with desflurane relative to sevoflurane following bariatric or craniotomy procedures (Wajekar et al., 2018), yet comparable PACU times are achievable with TIVA if analgesia is well-managed to prevent movement-limiting pain on awakening. Postoperative nausea and vomiting (PONV), while often reported through patient questionnaires, also function as an objective determinant of recovery efficiency; fewer antiemetic interventions correlate with shorter monitored stays. Propofol-based TIVA frequently demonstrates a lower PONV incidence than volatile maintenance even when multimodal prophylaxis is applied equally (D.-H. Kim et al., 2022), leading directly to more rapid fulfillment of discharge criteria. Quantitative postoperative pain scores using standardized scales such as Numeric Rating Scales or Visual Analogue Scales figure centrally in recovery metrics since uncontrolled pain delays mobilization and discharge-readiness assessments (R. Zhu et al., 2020). Pain scores at early PACU timepoints can differ significantly between anesthetic modalities depending on perioperative opioid administration strategies; inadequate analgesia undermines otherwise favorable emergence timings by postponing functional criteria clearance. Therefore, comprehensive interpretation of objective metrics necessitates parallel recording of intra- and postoperative analgesic consumption so that delays attributed to "slower" modality recoveries are not confounded by protocol variance. Study designs employing repeated measurements post-extubation, for example at 15 and 30 minutes, capture dynamics in cognitive motor integration during immediate recovery phases. The Short Orientation Memory Concentration Test (SOMCT) applied at these intervals after neurosurgery has shown higher mean scores earlier in desflurane cohorts compared with TIVA despite similar gross emergence timings (Ze et al., 2023), suggesting that subtle neurobehavioral performance may resolve independently from simple motor criteria like eye opening. Physiological stability during emergence is another objective domain relevant to clinical quality assessment. Monitoring charts often include systolic blood pressure and heart rate trends during the transition from deep anesthesia to wakefulness. Volatile agents, particularly desflurane combined with nitrous oxide, can produce sharper sympathetic surges than intravenous regimens unless moderated pharmaceutically (Cho et al., 2024). Instances of transient hypertension or tachycardia are not uncommon; these perturbations may delay progression through standardized recovery protocols if they fail acceptable thresholds set for PACU transfer. In practice, objective clinical recovery metrics are sensitive not just

to the primary anesthetic chosen but also to adjunct drug profiles, intraoperative events influencing tissue perfusion and metabolism, patient comorbid context, and even environmental factors like OR-to-PACU transfer efficiency. When analyzed within PRISMA-compliant systematic frameworks ensuring comparable denominators across trials, in terms of definitions for "eye opening," "extubation," or "spontaneous breathing", these measurements form a robust base for drawing nuanced conclusions about relative modality performance. Real-world protocol variability means that differences measured in seconds or minutes need contextual framing within total perioperative workflow impact: an objectively shorter extubation interval may only translate marginally into actual bed turnover gains if other downstream bottlenecks remain unaffected. Properly interpreted alongside subjective indices explored elsewhere, these objective markers clarify how anesthetic pharmacodynamics intersect with operational efficiency and patient safety during the earliest stages of postoperative care.

Figure 3: Incidence of early Postoperative Cognitive Dysfunction (POCD).



The graph illustrates a trend toward lower POCD incidence with TIVA, hypothesized to be linked to reduced neuroinflammatory responses compared to inhalational anesthesia.

5 Ethical Considerations

5.1 Informed Consent in Comparative Anesthesia Trials

Conducting comparative trials between total intravenous anesthesia (TIVA) and inhalational anesthesia demands careful attention to informed consent procedures, as the interventions often involve nuanced risks and benefits that must be clearly communicated to participants. This imperative is heightened by the perioperative context, where patients may already face heightened anxiety, time constraints prior to surgery, and diminished capacity to absorb complex information due to stress or premedication. In such settings, ensuring valid consent entails more than obtaining a signature; it involves tailoring explanations to the patient's cognitive and emotional state while providing balanced detail about each anesthetic technique's profile in emergence timing, recovery quality, and potential cognitive sequelae. Prospective randomized controlled trials have emphasized compliance with established ethical frameworks such as the Helsinki Declaration-2013 when designing comparative anesthetic studies. These protocols typically require ethics committee or Institutional Review Board (IRB) approval before recruitment begins. In environments like university hospitals undertaking nasal surgery comparisons between remimazolam and desflurane/propofol regimens, written informed consent was systematically obtained from all participants or legal surrogates prior to enrolment (Cho et al., 2024). Such measures ensure that subjects understand they may receive either technique based on random assignment, that equivalent standards of intraoperative safety will be maintained across modalities, and that outcome measurements direct toward endpoints including speed of awakening, recovery comfort scores, and

neurocognitive testing. However, certain trial designs may obtain IRB waivers of informed consent under specific conditions, such as retrospective data reviews or pragmatic observational studies where standard clinical practices remain unaltered. In these cases, justification often rests on the absence of experimental interventions beyond routine care, thereby minimizing participant risk. For example, multicenter evaluations of recovery parameters using existing anesthesia records avoided direct patient involvement beyond customary clinical interactions; here the ethics boards at each hospital approved procedural waivers contingent upon robust data protection measures (Yan et al., 2015). While ethically permissible in select scenarios, omission of explicit consent limits potential for participants to voice preferences about inclusion in research focusing on anesthetic choices, a consideration relevant particularly when different modalities may impact subjective postoperative experiences. When comparing agents with distinct pharmacodynamic profiles, such as propofol within TIVA versus volatile agents like sevoflurane, the consent conversation ideally outlines possible differences not only in emergence speed but also in adjunctive medication needs (e.g., opioids) and variance in postoperative phenomena like nausea incidence or agitation patterns. Transparency extends further to acknowledging uncertainties highlighted in literature syntheses, for instance, mixed findings on cognitive outcomes beyond immediate recovery (Shimizu et al., 2023). Patients should know that cognitive follow-up tests (Mini-Mental State Examination or psychomotor tasks) form part of the protocol because subtle effects are possible even after apparently smooth awakenings. Operational realities in anesthesia trials also influence how consent is framed. Recruitment protocols for laparoscopic cholecystectomy RCTs screened out individuals with comorbidities likely to alter anesthetic metabolism, such as advanced hepatic or renal impairment, based on safety grounds (X. Deng & Zhu, 2014). Communicating such exclusion criteria during consent helps manage expectations among prospective participants who might otherwise expect eligibility. Likewise, for elderly cohorts where altered drug clearance could shape emergence times and cognitive trajectories (Tariq et al., 2023), disclosing age-related physiological variables strengthens comprehension of why individualized monitoring is incorporated into the study design. Standardizing informed consent materials across study sites is essential when multiple centers contribute data. Cochrane risk-of-bias appraisal domains list patient blinding status as a potential concern (Liu et al., 2015), which intersects ethically with how much detail participants receive about agent-specific characteristics without undermining randomization integrity. Balancing sufficient disclosure against preserving methodological validity remains challenging; for example informing patients that either agent “is known to be safe for routine use” avoids introducing bias toward perceived faster awakenings while still affirming equipoise. Consent processes must also address data usage beyond immediate clinical application. Dissemination plans outlined in certain multicenter protocols explicitly state intent to submit results to international peer-reviewed journals and present at conferences (Yan et al., 2015). Incorporating such statements into participant information sheets clarifies how anonymized results may enter public scientific discourse, an important ethical checkpoint, particularly if findings influence practice guidelines affecting future patient care. Some designs incorporate additional safeguards by seeking surrogate consent when patients cannot provide it themselves due to transient incapacity before surgery (for instance from sedation). Trials evaluating psychomotor recovery post-anesthesia occasionally delay enrollment until full capacity returns; however this risks logistical difficulties especially if intervention assignment needs confirmation well before drug administration. In contexts where surrogate input is used, as noted in inpatient nasal surgery datasets , ethical oversight ensures surrogates receive equivalent information depth so decisions reflect patient preferences faithfully. Finally, comparative anesthesia trials benefit from embedding feedback loops into the ethical process: post-study debriefings inform participants about their group assignment along with any relevant aggregate findings once analysis is complete. This fosters a sense of contribution and respect toward individuals whose participation helped clarify differences in outcomes like time-to-emergence intervals or postoperative comfort indices between TIVA and inhalational methods. In an era emphasizing patient-centered research culture, closing this loop aligns with broader transparency principles while respecting autonomy exercised during original consent interaction. Therefore, informed consent in this research domain navigates a delicate path between thorough disclosure tailored to individual circumstance and methodological neutrality needed for valid comparisons. By integrating structured ethics committee oversight (Cho et al., 2024), accommodating special-case waivers prudently (Yan et al., 2015), customizing content for physiologic subgroups (X. Deng & Zhu, 2014), and affirming dissemination plans upfront, investigators uphold participant rights

while enabling systematic evaluation of anesthetic modality impacts on emergence times, recovery quality metrics, and postoperative cognitive function.

5.2 Balancing Patient Safety with Research Aims

Balancing patient safety with the objectives of comparative anesthesia research involves navigating a tension between generating rigorous, generalizable data and ensuring that no participant experiences undue risk or compromised care because of trial protocols. This balance is especially relevant for studies comparing total intravenous anesthesia (TIVA) and inhalational anesthesia, where differences in pharmacologic profiles may influence immediate postoperative outcomes such as time to emergence, recovery quality, and cognitive function. While research aims require standardized interventions, fixed dosing regimens, and predefined outcome collection intervals to reduce variability, patient safety considerations often demand tailoring of anesthetic administration to individual physiological states. One core aspect of maintaining this equilibrium is designing protocols that adhere to established standards of care independent of randomization group (R et al., 2023). For example, both TIVA and volatile-based maintenance techniques in many trials are implemented using agent concentrations or infusion targets within accepted clinical ranges, often guided by bispectral index (BIS) monitoring to prevent intraoperative awareness. Such monitoring not only serves a methodological role, ensuring comparability in depth of anesthesia across groups, but also functions as a direct safeguard against adverse intraoperative events like awareness or excessively deep sedation (Zhou et al., 2018). Incorporating BIS targets between 40–60 has been shown to minimize anesthetic drug load while maintaining adequate hypnosis; this dual effect aligns closely with patient safety priorities while enabling investigation into whether reduced exposure improves early cognitive recovery. Collateral safety mechanisms described in multicentre feasibility trials include structured adverse event reporting frameworks staffed by independent oversight boards (R et al., 2023). These frameworks capture both anticipated complications, such as postoperative nausea and vomiting (PONV), hypotension episodes meeting specific mean arterial pressure thresholds, or prolonged QTc intervals, and unanticipated phenomena potentially linked to study participation. Continuous intraoperative monitoring complemented by rapid access to rescue medications allows clinicians to respond promptly without breaking trial blinding unless absolutely necessary. Thus the research objective of clean comparative data remains intact while still operating within vigilant clinical guardrails. When choosing maintenance drugs for each arm, careful consideration must be given to agents' side-effect profiles relative to study population characteristics. Elderly patients, for instance, may face heightened risks from lingering sedative effects due to slower clearance rates (Tariq et al., 2023). In these cases protocolized dose adjustments based on corrected body weight or ideal body weight aim to harmonize exposures across participants without imposing excessive drug burdens. Closed-loop delivery systems like CLADS programmed to a target BIS have demonstrated ability to modulate propofol administration dynamically according to patient response (Kamal, 2024); inclusion of such technology strengthens safety assurance while preserving methodological fidelity. Certain measurable risks specific to one modality necessitate precise mitigation strategies in trial design. For inhalational agents like desflurane, increased incidence of sympathetic stimulation during emergence carries cardiovascular implications if uncontrolled. Protocol provisions may require concurrent opioid titration or beta-blocker availability if heart rate surges exceed pre-set thresholds. Similarly, prolonged QTc observed in some desflurane cohorts compared with TIVA patients (S. H. Kim et al., 2022) emphasize the importance of preoperative ECG screening and intraoperative rhythm monitoring within study frameworks, mitigation steps directly grounded in participant safety yet preserving integrity of comparative endpoints. Avoiding excessive inflammatory responses represents another point where patient welfare intersects with research measurement goals. Trials exploring propofol's neuroprotective potential through reduced postoperative S100β protein levels (Sun et al., 2019) must ensure operative conditions do not inadvertently exacerbate inflammatory triggers unrelated to anesthetic choice. Temperature control, hemodynamic stabilization, and minimization of surgical trauma where feasible protect participants' systemic milieu while preventing confounding influences on biomarker outcomes. The ethical requirement for robust postoperative follow-up also dovetails with analytic rigor. Patients assessed for neurocognitive trajectories via tools like MMSE at multiple intervals post-surgery benefit clinically from early detection of concerning deficits; concurrently researchers collect richer longitudinal datasets. This symmetry between direct patient benefit and investigational yield illustrates the ideal scenario

wherein safety monitoring doubles as outcome assessment. In cases where study objectives involve secondary physiological markers, for example evaluating bispectral index-guided dosing impact on elderly attention networks (Zhou et al., 2018), it is imperative that protocol pressures do not override individualized care cues during surgery. An anesthesiologist must reserve authority to deviate from preset infusion rates or vaporizer settings should early signs indicate impending hemodynamic instability. Documenting these deviations transparently ensures that resultant data can still inform conclusions without compromising ethical obligations. Trial operational logistics further influence how well safety is balanced alongside data quality ambitions. Efficient perioperative workflows help avoid extended pre-anesthesia waiting times that increase anxiety or fatigue before baseline measurement sessions; conversely post-surgical transport routes designed for continuous observation until PACU admission reduce risk during highest-vulnerability emergence phases. Coordination between surgical teams and anesthesia providers ensures timing of drug discontinuation aligns appropriately with procedure closure rather than rigid schedule adherence that could misalign depth recovery trajectories purely for standardization purposes. Some designs entail additional protective layers such as interim analyses screened by Data Safety Monitoring Boards (DSMBs) (R et al., 2023) which can halt recruitment early if excess adverse events cluster disproportionately in one modality arm, thereby prioritizing patient welfare over full statistical power attainment. PRISMA-aligned systematic examinations incorporating such details tend toward pragmatic realism acknowledging that certain aims may need scaling back under emergent clinical realities encountered mid-trial. Achieving this balance requires iterative dialogue between investigators aiming for methodological purity and clinicians charged with intraoperative stewardship under live conditions. Protocol rigidity yields internally valid comparisons only insofar as it leaves room for dynamic response when patient physiology diverges from model predictions, a lesson consistently reinforced where older adults experience slower emergence than anticipated despite optimal theoretical dosing (Tariq et al., 2023). Embedding flexible yet precisely documented deviation pathways into comparative anesthesia trial designs emerges as the most viable mechanism for safeguarding health without undermining scientific hypothesis testing on outcomes from awakening speed through early recovery metrics and cognitive performance profiles.

6 Conclusion

The comparative evaluation of total intravenous anesthesia (TIVA) and inhalational anesthesia reveals a nuanced landscape shaped by pharmacological properties, patient physiology, surgical factors, and adjunctive interventions. TIVA, primarily utilizing propofol and short-acting opioids, offers precise control over plasma drug concentrations, facilitating rapid emergence and potentially smoother cognitive recovery, especially in elderly populations with altered metabolic and distribution profiles. Inhalational agents such as sevoflurane and desflurane provide advantages in titratability through inspired gas concentration adjustments, with desflurane demonstrating particularly swift washout kinetics, though sometimes accompanied by airway irritation and sympathetic stimulation that may affect recovery quality.

Emergence time is influenced by a constellation of factors including drug solubility, receptor interactions, and patient-specific variables such as age, comorbidities, and body composition. The interplay between these elements explains why neither anesthetic modality universally outperforms the other across all clinical scenarios. Recovery quality encompasses objective clinical milestones, such as spontaneous breathing, eye opening, and extubation readiness, as well as subjective patient-reported outcomes including comfort, nausea incidence, and emotional stability. Propofol-based TIVA often correlates with reduced postoperative nausea and vomiting, contributing to enhanced patient comfort, though adequate analgesic supplementation remains essential to optimize overall recovery.

Cognitive outcomes following anesthesia exhibit heterogeneity, with some evidence suggesting that TIVA's anti-inflammatory effects may mitigate postoperative cognitive dysfunction in vulnerable elderly cohorts. However, variability in study designs, neuropsychological assessment timing, and surgical contexts complicate definitive attribution of cognitive benefits to anesthetic choice alone. Adjunctive agents like dexmedetomidine and S-ketamine show promise in modulating emergence quality and neurocognitive resilience, highlighting the potential of combination strategies to address individual agent limitations.

Ethical considerations in comparative anesthesia research emphasize the importance of informed consent that balances comprehensive disclosure with methodological neutrality, ensuring participant

autonomy without compromising study integrity. Patient safety remains paramount, with protocols incorporating real-time monitoring, dose adjustments, and contingency plans to manage adverse events while preserving the validity of comparative data. The integration of advanced delivery systems and monitoring technologies supports individualized anesthetic administration within standardized research frameworks.

Figure 4: Integrated decision framework for anesthetic selection.

The selection between TIVA and inhalational anesthesia should be informed by a synthesis of pharmacologic characteristics, patient-specific factors, surgical demands, and institutional expertise. Recognizing that emergence speed, recovery quality, and cognitive outcomes are influenced by a dynamic interplay of variables encourages a personalized approach rather than a one-size-fits-all preference. Continued investigation with harmonized methodologies and comprehensive outcome measures will further clarify optimal anesthetic strategies that balance efficiency, safety, and patient-centered recovery across diverse surgical populations.

References :

1. Atlee, J. L. (2006). Complications in anesthesia e-book. Elsevier Health Sciences. https://2cm.es/1l4qa
2. Casas-Arroyave, F. D. (2022). Total intravenous anesthesia vs inhalational anesthesia in patients undergoing surgery under general anesthesia. Cost-minimization study. Colombian Journal of Anesthesiology, 50, e1023. https://doi.org/10.5554/22562087.e1023
3. Cho, S.-A., Ahn, S., Kwon, W., & Sung, T.-Y. (2024). Comparison of remimazolam and desflurane in emergence agitation after general anesthesia for nasal surgery: A prospective randomized controlled study. Korean J Anesthesiol, 77(4), 432–440. https://doi.org/10.4097/kja.23953
4. Cote, C. J., Lerman, J., & Anderson, B. (2018). A practice of anesthesia for infants and children E-book. Elsevier Health Sciences. https://2cm.es/1l4rM
5. Davis, N., Lee, M., Lin, A. Y., Lynch, L., Monteleone, M., Falzon, L., Ispahany, N., & Lei, S. (2014). Post-operative cognitive function following general versus regional anesthesia, a systematic review. J Neurosurg Anesthesiol, 26(4), 369–376. https://doi.org/10.1097/ANA.0000000000000120
6. Deng, J., Li, J., & Cai, Y. (2024). Effects of intrathecal versus general anesthesia on postoperative cognitive function in elderly hip fracture patients: A system review and meta analysis protocol. Journal of Clinical Medicine Research, 5(2), 251. https://doi.org/10.32629/jcmr.v5i2.2322

7. Deng, X., & Zhu, T. (2014). Clinical comparison of propofol-remifentanil TCI with sevoflurane induction/maintenance anesthesia in laparoscopic cholecystectomy. Pak J Med Sci, 30(5), 1017–1021. https://doi.org/10.12669/pjms.305.5196
8. Duke, J. (2015). Duke's Anesthesia Secrets E-Book: Duke's Anesthesia Secrets E-Book. Elsevier Health Sciences. https://2cm.es/1l4pR
9. Fleisher, L. A., & Rosenbaum, S. H. (2017). Complications in Anesthesia E-Book. Elsevier Health Sciences. https://2cm.es/1l4rd
10. Gaskell, A., Pullon, R., Hight, D., Termaat, J., Mans, G., Voss, L., Kreuzer, M., Schmid, S., Kratzer, S., Rodriguez, A., Schneider, G., Garcia, P., & Sleigh, J. (2019). Modulation of frontal EEG alpha oscillations during maintenance and emergence phases of general anaesthesia to improve early neurocognitive recovery in older patients: Protocol for a randomised controlled trial. Trials, 20(146), 146. https://doi.org/10.1186/s13063-019-3178-x
11. Gkliatis, E., Makris, A., & Staikou, C. (2021). The impact of inhalation anesthetics on early postoperative cognitive function and recovery characteristics in down syndrome patients: A randomized, double–blind study. BMC Anesthesiology, 21, 227. https://doi.org/10.1186/s12871-021-01447-x
12. Hambrecht-Wiedbusch, V. S., Li, D., & Mashour, G. A. (2017). Paradoxical emergence: Administration of subanesthetic ketamine during isoflurane anesthesia induces burst suppression but accelerates recovery. Anesthesiology, 126(3), 482–494. https://doi.org/10.1097/ALN.0000000000001512
13. Hall, B. A., & Chantigian, R. C. (2019). Anesthesia: A Comprehensive Review E-Book: Anesthesia: A Comprehensive Review E-Book. https://2cm.es/1gbdq
14. Heiner, J. S., Gabot, M., & Elisha, S. M. (2023). Emergency Management in Anesthesia and Critical Care-E-Book: Emergency Management in Anesthesia and Critical Care-E-Book. Elsevier Health Sciences. https://2cm.es/1gben
15. Hemmings, H. C., & Egan, T. D. (2012). Pharmacology and physiology for anesthesia e-book: foundations and clinical application. Elsevier Health Sciences. https://2cm.es/1l4pj
16. Jeon, S., Kim, J., Karm, M.-H., & Kim, J.-T. (2024). Effect of converting from propofol to remimazolam with flumazenil reversal on recovery from anesthesia in outpatients with mental disabilities: A randomized controlled trial. BMC Anesthesiology, 24(151), 151. https://doi.org/10.1186/s12871-024-02526-5
17. Kamal, L. Y. andDa. S., Faiza A. andFernet. (2024). Comparing perioperative outcomes of total intravenous anesthesia (TIVA) with volatile anesthesia in patients with obesity: A systematic review. Cureus, 16(2), e54094. https://doi.org/10.7759/cureus.54094
18. Kaplan, J. A. (2017). Kaplan's Essentials of Cardiac Anesthesia E-Book. Elsevier Health Sciences. https://2cm.es/1gbee
19. Kim, D. J., Kim, S. H., So, K. Y., & Jung, K. T. (2015). Effects of dexmedetomidine on smooth emergence from anaesthesia in elderly patients undergoing orthopaedic surgery. BMC Anesthesiology, 15, 139. https://doi.org/10.1186/s12871-015-0127-4
20. Kim, D.-H., Min, K. T., Kim, E. H., Choi, Y. S., & Choi, S. H. (2022). Comparison of the effects of inhalational and total intravenous anesthesia on quality of recovery in patients undergoing endoscopic transsphenoidal pituitary surgery: A randomized controlled trial. International Journal of Medical Sciences, 19(6), 1056–1064. https://doi.org/10.7150/ijms.72758
21. Kim, S. H., Lee, J. G., Ju, H. M., Choi, S., Yang, H., & Koo, B.-N. (2022). Propofol prevents further prolongation of QT interval during liver transplantation. Scientific Reports, 12, 4636. https://doi.org/10.1038/s41598-022-08592-4
22. Liu, F.-L., Cherng, Y.-G., Chen, S.-Y., Su, Y.-H., Huang, S.-Y., Lo, P.-H., Lee, Y.-Y., & Tam, K.-W. (2015). Postoperative recovery after anesthesia in morbidly obese patients: A systematic review and meta-analysis of randomized controlled trials. Canadian Journal of Anesthesia / Journal Canadien d'anesthésie, 62, 907–917. https://doi.org/10.1007/s12630-015-0405-0
23. Luo, M., Song, B., & Zhu, J. (2020). Sleep disturbances after general anesthesia: Current perspectives. Frontiers in Neurology, 11, 629. https://doi.org/10.3389/fneur.2020.00629
24. Malamed, S. F. (2019). Handbook of local anesthesia-E-book: handbook of local anesthesia-E-book. Elsevier health sciences. https://2cm.es/1l4ru

25. Miller, R. D., Eriksson, L. I., Fleisher, L. A., Wiener-Kronish, J. P., & Young, W. L. (2009). Anesthesia E-Book. Elsevier Health Sciences. https://2cm.es/1gbcA
26. Moro, E. T., Leme, F. C. O., Noronha, B. R., Saraiva, G. F. P., Leite, N. V. de M., & Navarro, L. H. C. (2016). Quality of recovery from anesthesia of patients undergoing balanced or total intravenous general anesthesia. Prospective randomized clinical trial. Journal of Clinical Anesthesia, 35, 369–375. https://doi.org/10.1016/j.jclinane.2016.08.022
27. Muir, W. W., & Hubbell, J. A. (2008). Equine Anesthesia E-Book: Monitoring and Emergency Therapy. elsevier Health sciences. https://2cm.es/1gbdW
28. Qi, Y., Yao, X., Zhang, B., & Du, X. (2016). Comparison of recovery effect for sufentanil and remifentanil anesthesia with TCI in laparoscopic radical resection during colorectal cancer. Oncology Letters, 11, 3361–3365. https://doi.org/10.3892/ol.2016.4394
29. R, T. P. B., A, C. D., D, N. M., C, P. M., M, J. A., Cathie, S., Steven, T.-P., Zhenke, W., S, K. S., H, G. S., S, A. M., Sachin, K., & THRIVE research group, for the. (2023). Feasibility pilot trial for the trajectories of recovery after intravenous propofol versus inhaled VolatilE anesthesia (THRIVE) pragmatic randomised controlled trial. BMJ Open, 13, e070096. https://doi.org/10.1136/bmjopen-2022-070096
30. Sá, A. C., Sousa, G., Santos, A., Santos, C., & Abelha, F. J. (2015). Quality of recovery after anesthesia: Validation of the portuguese version of the "quality of recovery 15" questionnaire. Acta Med Port, 28(5), 567–574. www.actamedicaportuguesa.com
31. Shehabi, Y., Stollings, J. L., & Girard, T. D. (Eds.). (2025). Optimizing Sedation & Analgesia in the ICU, An Issue of Critical Care Clinics: Optimizing Sedation & Analgesia in the ICU, An Issue of Critical Care Clinics, E-Book (Vol. 41, No. 4). Elsevier Health Sciences. https://2cm.es/1l4rZ
32. Shimizu, T., Takasusuki, T., & Yamaguchi, S. (2023). Remimazolam compared to propofol for total intravenous anesthesia with remifentanil on the recovery of psychomotor function: A randomized controlled trial. Adv Ther, 40(7), 4395–4404. https://doi.org/10.1007/s12325-023-02615-w
33. Song, T., Wu, L.-J., & Li, L. (2024). Comparison of combined intravenous and inhalation anesthesia and total intravenous anesthesia in laparoscopic surgery and the identification of predictive factors influencing the delayed recovery of neurocognitive function. Frontiers in Medicine, 11, 1353502. https://doi.org/10.3389/fmed.2024.1353502
34. Sun, H., Zhang, G., Ai, B., Zhang, H., Kong, X., Lee, W.-T., Zheng, H., Yan, T., & Sun, L. (2019). A systematic review: Comparative analysis of the effects of propofol and sevoflurane on postoperative cognitive function in elderly patients with lung cancer. BMC Cancer, 19, 1248. https://doi.org/10.1186/s12885-019-6426-2
35. Tariq, A., Iqbal, F., Younus, Z., & Chaudhary, W. A. (2023). The impact of total intravenous anesthesia versus inhalational anesthesia on postoperative cognitive dysfunction in elderly patients. Biol. Clin. Sci. Res. J., 2023, 580. https://doi.org/10.54112/bcsrj.v2023i1.580
36. Thompson, J., Moppett, I., & Wiles, M. (Eds.). (2025). Smith and Aitkenhead's Textbook of Anaesthesia-E-BOOK. Elsevier Health Sciences. https://2cm.es/1l4qo
37. Torsher, L. (Ed.). (2022). Advances in Anesthesia, E-Book 2022: Advances in Anesthesia, E-Book 2022 (Vol. 40, No. 1). Elsevier Health Sciences. https://2cm.es/1gbc-
38. Wagner, S., Breitkopf, M., Ahrens, E., Ma, H., Kuester, O., Thomas, C., Arnim, C. A. F. von, & Walther, A. (2023). Cognitive function in older patients and their stress challenge using different anesthesia regimes: A single center observational study. BMC Anesthesiology, 23(6), 6. https://doi.org/10.1186/s12871-022-01960-7
39. Wajekar, A., Shetty, A., Oak, S., & Jain, R. A. (2018). A prospective, randomized single-blind study of sevoflurane vs desflurane, with dexmedetomidine, on the intraoperative hemodynamics and postoperative recovery for transsphenoidal pituitary surgery. Research & Innovation in Anesthesia, 3(1), 13–17. https://doi.org/10.5005/jp-journals-10049-0041
40. Werner, J. G., Castellon-Larios, K., Thongrong, C., Knudsen, B. E., Lowery, D. S., Antor, M. A., & Bergese, S. D. (2015). Desflurane allows for a faster emergence when compared to sevoflurane without affecting the baseline cognitive recovery time. Frontiers in Medicine, 2, 75. https://doi.org/10.3389/fmed.2015.00075
41. Yan, L.-M., Chen, H., Yu, R.-G., Wang, Z.-H., Zhou, G.-H., Wang, Y.-J., Zhang, X., Xu, M., Chen, L., & Zhou, J.-X. (2015). Emergence agitation during recovery from intracranial surgery under

general anaesthesia: A protocol and statistical analysis plan for a prospective multicentre cohort study. BMJ Open, 5, e007542. https://doi.org/10.1136/bmjopen-2014-007542
42. Yang, B., Li, M., Liang, J., Tang, X., & Chen, Q. (2023). Effect of internal jugular vein catheterization on intracranial pressure and postoperative cognitive function in patients undergoing robot-assisted laparoscopic surgery. Frontiers in Medicine, 10, 1199931. https://doi.org/10.3389/fmed.2023.1199931
43. Yang, L., Chen, Z., & Xiang, D. (2022). Effects of intravenous anesthesia with sevoflurane combined with propofol on intraoperative hemodynamics, postoperative stress disorder and cognitive function in elderly patients undergoing laparoscopic surgery. Pak J Med Sci, 38(7), 1938–1944. https://doi.org/10.12669/pjms.38.7.5763
44. Yang, X., Hu, Z., Peng, F., Chen, G., Zhou, Y., Yang, Q., Yang, X., & Wang, M. (2020). Effects of dexmedetomidine on emergence agitation and recovery quality among children undergoing surgery under general anesthesia: A meta-analysis of randomized controlled trials. Frontiers in Pediatrics, 8, 580226. https://doi.org/10.3389/fped.2020.580226
45. Yentis, S. M., Hirsch, N. P., & Ip, J. (2013). Anaesthesia and Intensive Care AZ E-Book: an Encyclopedia of Principles and Practice. Elsevier Health Sciences. https://2cm.es/1l4pq
46. Yin, L., Li, L., Deng, J., Wang, D., Guo, Y., Zhang, X., Li, H., Zhao, S., Zhong, H., & Dong, H. (2019). Optogenetic/chemogenetic activation of GABAergic neurons in the ventral tegmental area facilitates general anesthesia via projections to the lateral hypothalamus in mice. Frontiers in Neural Circuits, 13, 73. https://doi.org/10.3389/fncir.2019.00073
47. Yoon, H.-K., Joo, S., Yoon, S., Seo, J.-H., Kim, W. H., & Lee, H.-J. (2024). Randomized controlled trial of the effect of general anesthetics on postoperative recovery after minimally invasive nephrectomy. Korean J Anesthesiol, 77(1), 95–105. https://doi.org/10.4097/kja.23083
48. Ze, J., Youxuan, W., Fa, L., Minyu, J., Haiyang, L., Hongxun, M., & Ruquan, H. (2023). Brain relaxation using desflurane anesthesia and total intravenous anesthesia in patients undergoing craniotomy for supratentorial tumors: A randomized controlled study. BMC Anesthesiology, 23, 15. https://doi.org/10.1186/s12871-023-01970-z
49. Zhang, J., Jia, D., Li, W., Li, X., Ma, Q., & Chen, X. (2023). General anesthesia with s-ketamine improves the early recovery and cognitive function in patients undergoing modified radical mastectomy: A prospective randomized controlled trial. BMC Anesthesiology, 23(214), 214. https://doi.org/10.1186/s12871-023-02161-6
50. Zhao, H., Han, Q., Shi, C., & Feng, Y. (2022). The effect of opioid-sparing anesthesia regimen on short -term cognitive function after thoracoscopic surgery: A prospective cohort study. Perioperative Medicine, 11, 45. https://doi.org/10.1186/s13741-022-00278-9
51. Zhou, Y., Li, Y., & Wang, K. (2018). Bispectral index monitoring during anesthesia promotes early postoperative recovery of cognitive function and reduces acute delirium in elderly patients with colon carcinoma: A prospective controlled study using the attention network test. Med Sci Monit, 24(33), 7785–7793. https://doi.org/10.12659/MSM.910124
52. Zhu, M., Wang, H., Zhu, A., Niu, K., & Wang, G. (2015). Meta-analysis of dexmedetomidine on emergence agitation and recovery profiles in children after sevoflurane anesthesia: Different administration and different dosage. PLoS ONE, 10(4), e0123728. https://doi.org/10.1371/journal.pone.0123728
53. Zhu, R., Du, T., & Gao, H. (2020). Effects of dezocine and ropivacaine infiltration anesthesia on cellular immune function indicators, anesthesia recovery time and pain factors in patients with open liver resection. Cellular and Molecular Biology, 66(3). https://doi.org/10.14715/cmb/2020.66.3.23