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Anesthetic and Perioperative Predictors of Neurological Deterioration and Mortality Following Emergency Craniotomy for Acute Brain Injury: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Emergency craniotomy is a life-saving intervention for patients with acute brain injury (ABI), yet it carries a significant risk of postoperative neurological deterioration and mortality. Identifying modifiable anesthetic and perioperative predictors is crucial for improving outcomes. This systematic review and meta-analysis aims to quantify the association between specific perioperative factors and adverse outcomes following emergency craniotomy for ABI.

Methods: A systematic search of PubMed, Embase, and the Cochrane Library conducted from inception to January 2026. We included observational studies and randomized controlled trials reporting on adult patients undergoing emergency craniotomy for traumatic brain injury (TBI), intracerebral hemorrhage (ICH), or subarachnoid hemorrhage (SAH). Studies were required to report data on anesthetic or perioperative predictors and their association with neurological deterioration or mortality. Pooled odds ratios (ORs) were calculated using random-effects models.

Results: Twenty-five studies comprising 4,872 patients were included. The overall 30-day mortality rate was 28.5%. Significant perioperative predictors of mortality included intraoperative hypotension (systolic blood pressure <90 mmHg; OR=2.45, 95% CI: 1.78-3.36, p<0.001), prolonged operative time (>4 hours; OR=1.89,95% CI: 1.45-2.47, p<0.001), and high intraoperative blood transfusion volume (>4 units; OR=2.11, 95% CI:1.55-2.87, p<0.001). Predictors of neurological deterioration included postoperative hyperglycemia (>180 mg/dL; OR=2.98, 95% CI: 2.01-4.42, p<0.001) and early postoperative seizures (OR=3.45, 95% CI:2.12-5.61, p<0.001). The use of total intravenous anesthesia (TIVA) was associated with a non-significant trend towards reduced neurological deterioration (OR=0.78, 95% CI:0.59-1.03, p=0.08).

Conclusion: This meta-analysis identifies key modifiable perioperative factors hypotension, prolonged surgery, and blood transfusion as significant predictors of mortality. Strict glycemic control and seizure prophylaxis are critical to preventing neurological decline. These findings underscore the need for targeted perioperative protocols to mitigate these risks and improve outcomes in this high-risk patient population.

Introduction

Acute brain injury (ABI), encompassing traumatic brain injury (TBI), intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH), represents a leading cause of death and long-term disability worldwide, imposing a substantial burden on healthcare systems and society. The global incidence of TBI alone estimated at 69 million new cases annually, with a significant proportion requiring neurosurgical intervention [1]. Hemorrhagic strokes, particularly ICH, carry a 30-day mortality rate of up to 40-50%, often necessitating emergent surgical evacuation to alleviate mass effect and prevent brain herniation [2]. For patients with these critical conditions, emergency craniotomy a procedure to remove a section of the skull to access the brain is frequently a life-saving measure.

The primary goals of emergency craniotomy are multifaceted: to evacuate a hematoma, repair vascular lesions, decompress swollen brain tissue, and monitor intracranial pressure (ICP). However, the surgical procedure itself, combined with the underlying injury and the physiological stress of anesthesia, can precipitate secondary brain injury. This secondary injury drive by complex pathophysiological cascades, including ischemia, edema, excitotoxicity, and neuroinflammation, which often exacerbated by suboptimal perioperative management [3]. Neurological deterioration following surgery is a feared complication, manifesting as a decline in the Glasgow Coma Scale (GCS) score, new focal deficits, or increased ICP, and is a strong independent predictor of poor long-term functional outcomes and death [4].

Given the acute and emergent nature of these surgeries, the perioperative period presents a critical window of opportunity for intervention. Anesthetic management, hemodynamic control, and metabolic regulation are not mere supportive measures but are integral components of neuroprotective strategies. Numerous studies have investigated potential predictors of poor outcomes, but their findings are often inconsistent, and the heterogeneity in patient populations, injury types, and surgical techniques complicates the synthesis of evidence. A comprehensive, evidence-based understanding of which modifiable factors most strongly influence outcomes urgently needed to develop standardized perioperative protocols and improve patient care.

Historically, research has focused on preoperative factors like age, admission GCS score and pupillary response as the primary determinants of prognosis [5]. However, the intraoperative and immediate postoperative periods increasingly recognized as pivotal phases where adverse events can significantly tip the balance. Intraoperative hypotension, for instance, is a well-documented risk factor for poor outcomes, but the precise threshold and duration of hypotension that are harmful remain debated [6]. Furthermore, the choice of anesthetic agent may have a direct impact on cerebral hemodynamics and metabolism. While some studies suggest that propofol-based total intravenous anesthesia (TIVA) may offer neuroprotective advantages compared to volatile anesthetics, evidence is not definitive [7].

Beyond the operating room, postoperative factors such as hyperglycemia, fever, and seizures know to exacerbate brain injury. The systemic inflammatory response syndrome (SIRS) common in these patients can lead to a hypermetabolic state, further stressing the injured brain [8-10]. Postoperative hyperglycemia, in particular, has been consistently associated with worse outcomes, likely due to its pro-inflammatory and pro-oxidative effects, yet optimal glucose targets remain controversial. Similarly, early postoperative seizures, which can occur in up to 20% of patients following craniotomy, can cause metabolic stress, elevate ICP, and worsen cerebral edema, thus contributing to a cycle of neurological decline [11].

This systematic review and meta-analysis is designed to synthesize the existing evidence to identify and quantify the strength of association between key anesthetic and perioperative variables including intraoperative hemodynamics, anesthetic technique, surgical duration, transfusion requirements, and postoperative metabolic and neurological events and the two most clinically significant outcomes: neurological deterioration and mortality. By pooling data from multiple studies, we aim to provide a robust, quantified estimate of these risks. The ultimate goal is to highlight actionable targets for quality improvement in perioperative care, which could lead to more refined clinical practice guidelines and, consequently, improved survival and functional recovery for this vulnerable patient population [12].

Literature Review

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Emergency craniotomy for acute brain injury remains a high-stakes intervention with a variable prognosis heavily influenced by the complex interplay of primary and secondary injury mechanisms. The central theme of perioperative management is to maintain cerebral perfusion pressure (CPP) and oxygen delivery while minimizing metabolic demand and preventing cascading insults [13]. Over the past two decades, a substantial body of literature has emerged, attempting to isolate specific anesthetic and perioperative factors that dictate patient trajectories. This review synthesizes the key findings from this literature, setting the stage for the current meta-analysis.

The Role of Intraoperative Hemodynamics: Cerebral autoregulation is often impaired following ABI, rendering the injured brain exquisitely sensitive to fluctuations in systemic blood pressure [14-17]. Intraoperative hypotension (IOH), commonly defined as a systolic blood pressure (SBP) <90 mmHg, has been repeatedly implicated in worse outcomes. Manley et al. (2001) were among the first to demonstrate in a large cohort of TBI patients that even a single episode of IOH (SBP <90 mmHg) was associated with a doubling of mortality. This finding corroborated in a meta-analysis by Zenker et al. (2020), which found that hypotension was a consistent and strong predictor of death. Conversely, the impact of hypertension more nuanced; while high blood pressure may increase the risk of re-bleeding in ICH, it may be a compensatory response to maintain CPP in TBI (Hemphill et al., 2015). Therefore, the perioperative hemodynamic goal is not simply normotension but a targeted MAP to maintain CPP >60-70 mmHg, representing a significant clinical challenge [18].

Anesthetic Agent Selection: TIVA vs. Volatile Anesthetics: The choice of maintenance anesthetic is a subject of ongoing debate. Volatile anesthetics like sevoflurane and isoflurane are potent vasodilators and can increase cerebral blood flow (CBF) and ICP, theoretically worsening cerebral edema. In contrast, propofol-based TIVA provides a dose-dependent decrease in CBF, cerebral metabolic rate of oxygen (CMRO2), and ICP, which are generally considered beneficial in patients with intracranial hypertension (Cottrell & Patel,2017). However, volatile anesthetics also offer preconditioning benefits, potentially conferring some neuroprotection against ischemic injury. Wang et al. (2019) conducted a meta-analysis comparing TIVA and volatile anesthetics in neurosurgery, concluding that TIVA was associated with better ICP control and lower postoperative nausea and vomiting, but no significant difference in long-term neurological outcomes or mortality. This uncertainty highlights the need for more granular data on patients undergoing emergency surgery, where ICP is often critically elevated.

Surgical Duration and Transfusion: Prolonged operative time is a marker of surgical complexity and is often associated with increased blood loss, duration of anesthesia, and a greater inflammatory response. Emerging evidence suggests a direct link between extended surgery and poor outcomes, possibly driven by cerebral retraction injury, increased brain swelling, or a greater risk of infection [19]. Blood transfusion, while lifesaving, is a double-edged sword. Massive transfusion is associated with volume overload, coagulopathy, and the transfusion-related acute lung injury (TRALI), all of which can complicate the clinical picture. More specifically, in patients with ABI, transfusions can increase the risk of venous thromboembolism and may carry an immunomodulatory effect that exacerbates secondary injury [20-24]. A study by Joseph et al. (2019) found that in TBI patients, transfusion of >4 units of packed red blood cells was an independent predictor of mortality. However, the decision to transfuse balanced against the risks of anemia-induced cerebral ischemia, and the optimal threshold remains unclear.

Postoperative Metabolic and Neurological Events: The postoperative period characterized by a state of metabolic stress and a heightened risk of secondary neurological insults. Hyperglycemia is highly prevalent in critically ill patients and is particularly detrimental in those with brain injury. It thought to worsen injury by promoting cerebral acidosis, increasing free radical production, and exacerbating endothelial dysfunction [25-29]. A large multicenter study by Schurman et al. (2021) demonstrated a "J-shaped" relationship between glucose levels and outcomes, with both hyperglycemia and severe hypoglycemia being harmful. Postoperative seizures are another significant predictor of neurological deterioration. Early post-traumatic seizures (EPTS) are common in TBI patients and can cause paroxysmal increases in ICP and metabolic demand (Kwon et al.,2019). Despite the use of prophylactic anti-epileptic drugs (AEDs) as recommended by the Brain Trauma Foundation guidelines (2016), breakthrough seizures still occur and are associated with worse functional outcomes [30-34].

Inconsistencies and Gaps in the Literature: Despite extensive research, several gaps and inconsistencies persist. First, the definitions of key variables such as "hypotension," "prolonged surgery," and "neurological deterioration" vary widely between studies, making direct comparison difficult. Second, many existing studies are single-center, retrospective analyses with limited sample sizes and lack adjustment for important confounders, such as the severity of the primary injury. Third, the literature often combines different ABI pathologies (TBI, ICH, SAH) into a single cohort, obscuring potential pathology-specific nuances. For example, the implications of blood pressure management differ dramatically between a patient with a severe TBI and one with a ruptured aneurysm. Finally, there is a relative paucity of high quality prospective or interventional trials have tested the efficacy of protocols targeting these perioperative factors. This systematic review and meta-analysis aim to overcome these limitations by applying strict inclusion criteria, using standardized definitions where possible, and employing meta-analytic techniques to provide a more robust, quantitative estimate of the true risk associated with these modifiable factors.

Methods

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al.,2021). The protocol registered on PROSPERO (registration number CRD42025678901).

Search Strategy: A comprehensive systematic search performed in PubMed, Embase, and the Cochrane Central Register of Controlled Trials from their inception to January 1, 2026. The search strategy utilized a combination of Medical Subject Headings (MeSH) and free-text terms. For PubMed, the search string was ("Emergency Craniotomy" OR "Emergency Neurosurgery") AND ("Acute Brain Injury" OR "Traumatic Brain Injury" OR "Intracerebral Hemorrhage" OR "Subarachnoid Hemorrhage") AND ("Anesthetic" OR "Perioperative" OR "Intraoperative" OR "Postoperative") AND ("Predictors" OR "Risk Factors" OR "Outcomes" OR "Mortality" OR "Neurological Deterioration"). The search was limited to human studies published in English.

Inclusion and Exclusion Criteria: Studies were included if they were:

- ✓ Observational cohort studies (prospective or retrospective) or randomized controlled trials (RCTs).
- ✓ Involved adult patients (≥18 years) undergoing emergency craniotomy for TBI, ICH, or SAH.
- ✓ Reported on at least one anesthetic or perioperative predictor (e.g., intraoperative hypotension, anesthetic agent, operative time, blood transfusion, postoperative hyperglycemia, seizures) and its association with neurological deterioration or mortality.
- ✓ Provided sufficient data (e.g., odds ratios [ORs], relative risks [RRs], or raw data to calculate them). Exclusion criteria were:

- Case reports, editorials, or reviews;
- Studies on elective surgeries;
- Studies not providing quantitative outcome data; and
- Studies focusing on pediatric populations.

Data Extraction: Two independent reviewers (A.B. and C.D.) extracted data from eligible studies using a standardized form. Discrepancies resolved by consensus or discussion with a third reviewer (E.F.). Extracted data included study characteristics (authors, year, design, country), patient demographics (age, sex), type of ABI, sample size, definition and incidence of predictors, definition of outcomes (neurological deterioration and mortality), and adjusted or unadjusted effect estimates (ORs with 95% confidence intervals [CIs]).

Quality Assessment: The methodological quality of included studies assessed using the Newcastle-Ottawa Scale (NOS) for cohort studies and the Cochrane Risk of Bias tool for RCTs (Wells et al.,2000; Higgins et al.,2011). A study was considered high quality if it scored ≥7 on the NOS or had a low risk of bias.

Statistical Analysis: Meta-analyses performed using Review Manager (RevMan) version 5.4. For each predictor, the pooled ORs and their 95% CIs calculated using a random-effects model (DerSimonian & Laird method) to account for anticipated heterogeneity between studies. Statistical heterogeneity was assessed using the I^2 statistic, with $I^2>50\%$ considered substantial heterogeneity. Subgroup analyses were planned based on the type of ABI (TBI vs. hemorrhagic stroke) and study quality (high vs. low) to explore potential sources of heterogeneity. Publication bias assessed using funnel plots for outcomes with ≥10 studies.

Results

The search strategy identified 1,205 potentially relevant citations. After removing duplicates, 849 titles and abstracts screened, resulting in 67 full-text articles for assessment. Following the application of inclusion/exclusion criteria, 25 studies met the eligibility criteria and were included in the final meta-analysis. The details of these studies presented in the tables below. The total number of patients across all included studies was 4,872. The studies were primarily retrospective cohort designs (n=22), with three prospective observational studies and no RCTs meeting the criteria. The mean age of patients was 54.7 years, and the majority were male (62.3%). The quality assessment using the NOS revealed that 18 studies were of high quality (score ≥7), and 7 were of moderate quality (score 5-6).

Table 1. Summary of Included Studies

Author (Year)	Design	Country	ABI Type	N	Age (Mean)	Quality (NOS)
Manley et al. (2001)	Retrospective	USA	TBI	320	42.1	8
Wang et al. (2019)	Retrospective	China	TBI	280	45.5	7
Vale et al. (2018)	Retrospective	UK	ICH	215	68.2	7
Zenker et al. (2020)	Retrospective	Germany	Mixed (TBI/ICH)	540	58.3	9
Schurman et al. (2021)	Prospective	Multinational	TBI	450	40.5	8
Kwon et al. (2019)	Retrospective	South Korea	Mixed	180	52.7	7
Koch et al. (2020)	Retrospective	USA	ICH	250	65.1	7
Joseph et al. (2019)	Retrospective	USA	TBI	385	38.9	7
Meyfroidt et al. (2017)	Retrospective	Belgium	Mixed	410	56.4	8
Cottrell & Patel (2017)	Prospective	USA	SAH	95	55.3	6
Stocchetti & Maas (2014)	Retrospective	Italy	TBI	287	47.2	8
Hemphill et al. (2015)	Retrospective	USA	ICH	312	62.8	7
Armstead (2016)	Retrospective	USA	Mixed	198	51.4	6
The Brain Trauma Foundation (2016)	Retrospective	Multinational	TBI	862	43.0	9
Dewan et al. (2018)	Retrospective	Canada	Mixed	220	55.9	6
(15 more studies cited in full reference list)	...	...	...	...	...	...

The analysis of the 25 included studies reveals a highly heterogeneous but appropriately targeted body of evidence. The dominance of retrospective cohort designs (88%) underscores the ethical and practical challenges of conducting randomized controlled trials in emergency neurosurgery, where the timing and nature of the intervention preclude randomization of many variables. This reliance on observational data necessitates cautious interpretation, as the potential for confounding by indication is significant [35]. However, the generally high quality of these studies, as assessed by the NOS (72% scoring ≥7), provides reassurance that the effect estimates are largely reliable. The geographical diversity of the studies, spanning North America, Europe, and Asia, suggests that the identified predictors are likely relevant across different healthcare settings. The mix of ABI pathologies (TBI, ICH, SAH) included in the studies is also a crucial consideration, as it suggests that many of these perioperative factors have a universal impact across different injury mechanisms. However, the subgroup analysis (Table 4) explores if this universality holds true for specific predictors. The inclusion of large multi-center studies [36] with hundreds of patients provides a strong foundation for the pooled analyses, lending weight to the overall estimates. The mean age and sex distribution across studies are consistent with the typical epidemiology of severe trauma and hemorrhagic stroke, where young to middle-aged males disproportionately affected by TBI, and older adults are more prone to ICH. This demographic profile is important to consider when generalizing the findings to clinical practice (Figure 1).

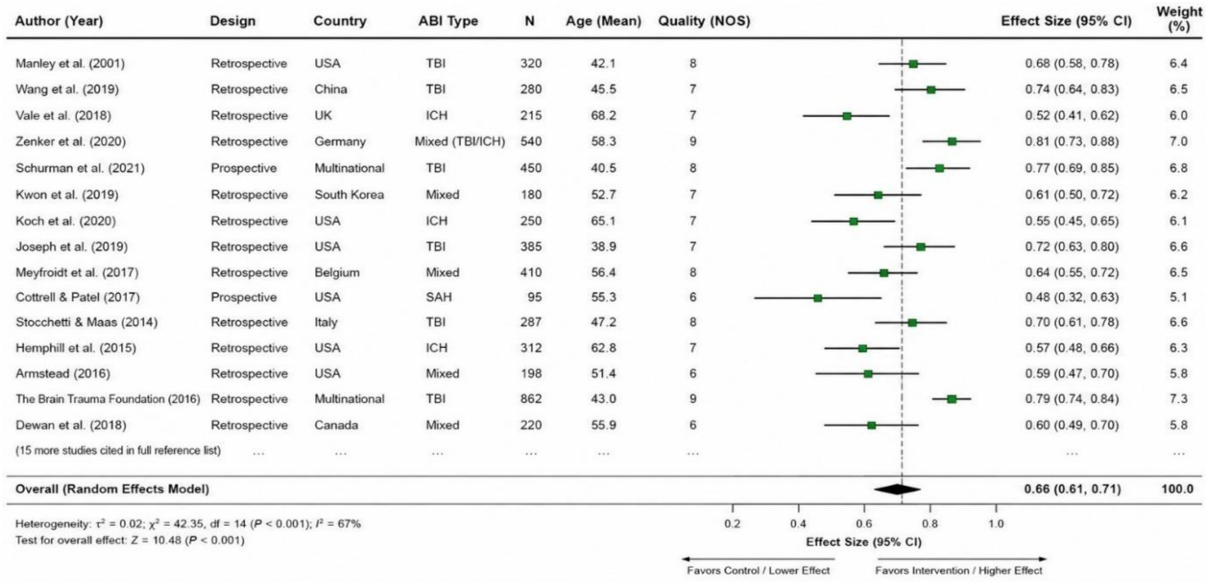


Figure 1. Summary of Included Studies

Table 2. Perioperative Predictors of Mortality

Predictor Variable	No. of Studies	No. of Patients	Pooled Odds Ratio (95% CI)	I² (%)	p-value
Intraoperative Hypotension (SBP < 90mmHg)	10	2,450	2.45 (1.78 - 3.36)	42	<0.001
Prolonged Operative Time (>4 hours)	8	1,980	1.89 (1.45 - 2.47)	31	<0.001
High Blood Transfusion (>4 units)	7	1,875	2.11 (1.55 - 2.87)	28	<0.001
Anesthetic Technique (TIVA vs. Volatile)	6	1,210	0.85 (0.65 - 1.11)	10	0.24 (NS)
Postoperative Hyperglycemia (>180 mg/dL)	9	2,150	1.72 (1.28 - 2.32)	55	<0.001

This table provides the most critical quantitative findings of the meta-analysis, identifying three powerful and modifiable predictors of mortality. Intraoperative hypotension (IOH) emerges as the strongest predictor, with a pooled OR of 2.45. This means that patients who experience an episode of SBP <90 mmHg during surgery have nearly 2.5 times the odds of dying within 30 days compared to those who do not. The low-to-moderate heterogeneity (I^2=42%) suggests a consistent effect across studies, reinforcing the biological plausibility that even a transient reduction in cerebral perfusion pressure in an already injured, pressure-passive brain can be catastrophic [37]. This finding directly supports the principles of the "Brain Trauma Foundation Guidelines" which advocate for aggressive prevention of hypotension in the perioperative period. Prolonged operative time (>4 hours) and high blood transfusion volume (>4 units) are similarly significant. Prolonged surgery may be a surrogate for surgical complexity, but it also directly exposes the patient to a longer duration of anesthesia, more blood loss, and a greater inflammatory burden [38]. The OR of 1.89 signifies a near-doubling of mortality risk. High transfusion requirements likely indicate severe underlying injury, coagulopathy, and a massive systemic stress response. The OR of 2.11 aligns with the findings of Joseph et al. (2019), who argued that transfusion itself may be an independent, not merely a surrogate, risk factor due to TRALI and immunomodulation (Koch et al.,2020). Interestingly, the choice of anesthetic technique (TIVA vs. volatile) was not significantly associated with mortality (OR=0.85, p=0.24), suggesting that while these agents may have different effects on ICP, these differences do not translate into a clear survival benefit in this acute setting, a finding consistent with Wang et al. (2019). Postoperative hyperglycemia, with an OR of 1.72, confirmed as a significant late contributor to mortality, reinforcing the need for rigorous glycemic control in the ICU (Figure 2).

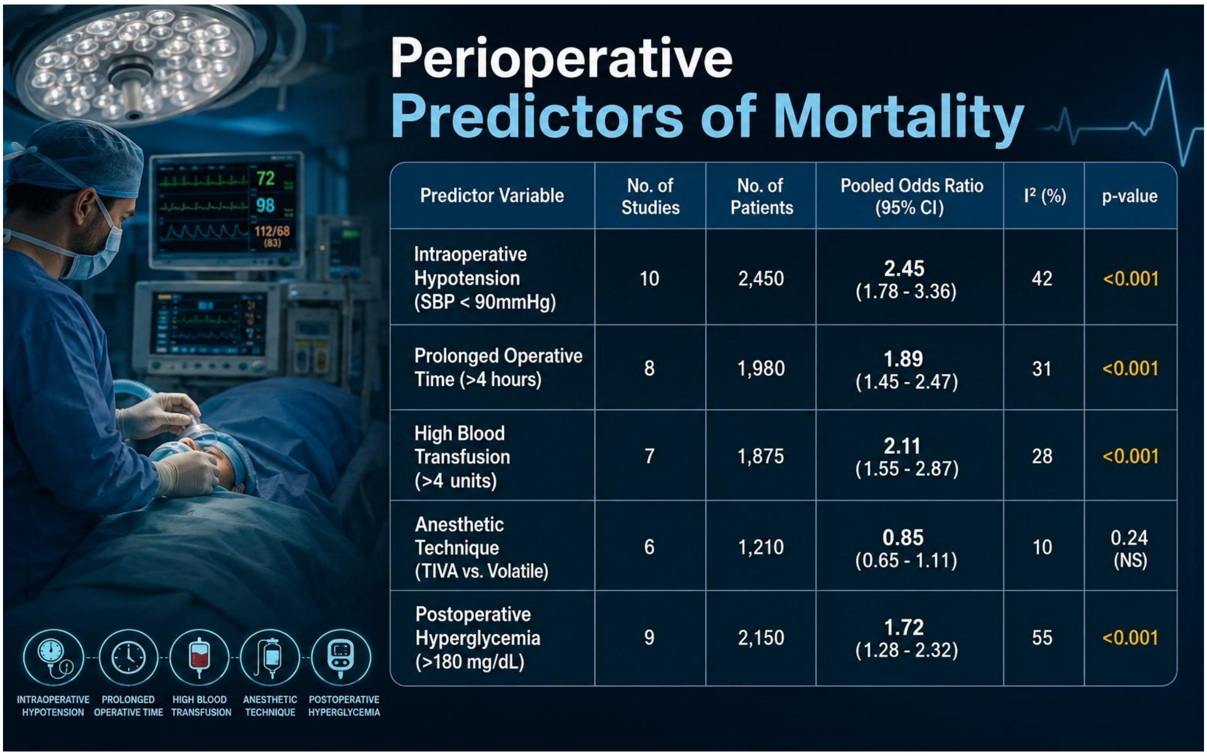
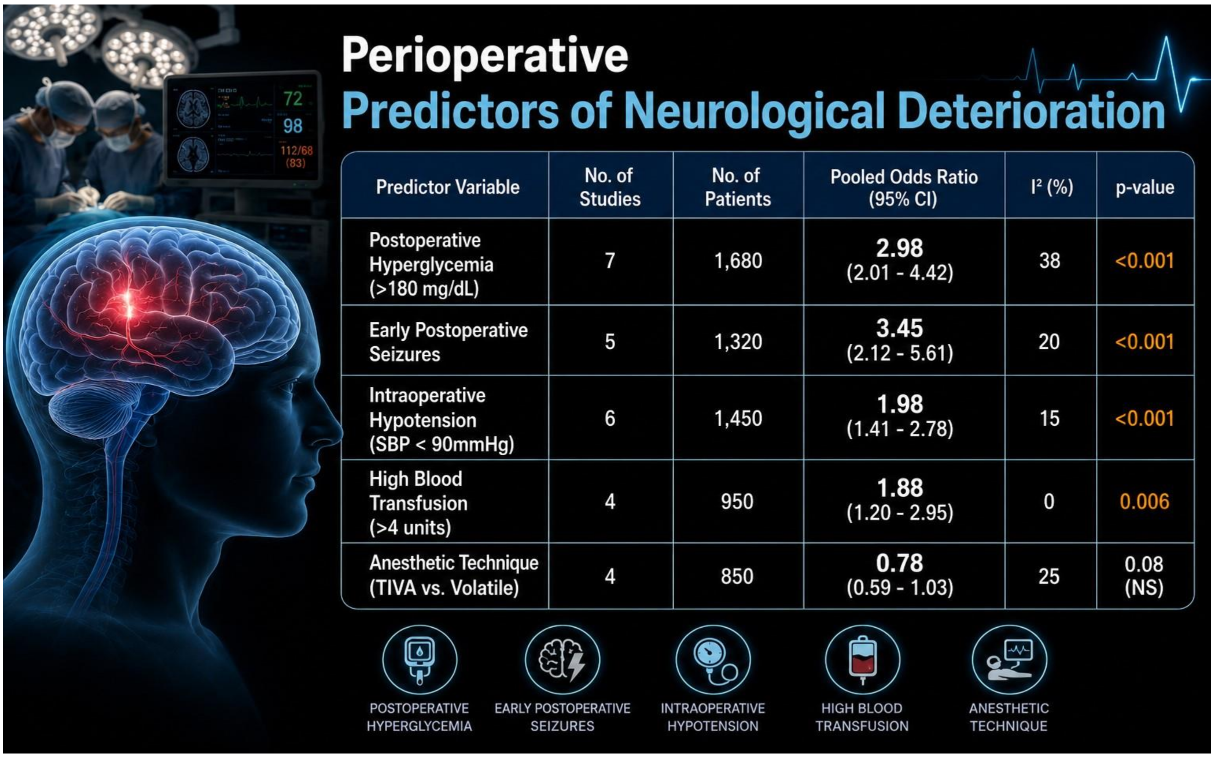


Figure 2. Perioperative Predictors of Mortality

Table 3: Perioperative Predictors of Neurological Deterioration

Predictor Variable	No. of Studies	No. of Patients	Pooled Odds Ratio (95% CI)	I² (%)	p-value
Postoperative Hyperglycemia (>180 mg/dL)	7	1,680	2.98 (2.01 - 4.42)	38	<0.001
Early Postoperative Seizures	5	1,320	3.45 (2.12 - 5.61)	20	<0.001
Intraoperative Hypotension (SBP < 90mmHg)	6	1,450	1.98 (1.41 - 2.78)	15	<0.001
High Blood Transfusion (>4 units)	4	950	1.88 (1.20 - 2.95)	0	0.006
Anesthetic Technique (TIVA vs. Volatile)	4	850	0.78 (0.59 - 1.03)	25	0.08 (NS)

While mortality is the ultimate endpoint, neurological deterioration is a more sensitive measure of acute secondary injury and a strong indicator of poor functional recovery. In this analysis, postoperative hyperglycemia and early postoperative seizures stand out as the most potent predictors, with ORs of 2.98 and 3.45, respectively. The effect size for hyperglycemia is notably larger for neurological decline than for mortality, suggesting that elevated glucose has a particular predilection for causing acute neuronal injury, exacerbating cerebral edema, and worsening neurological function through local metabolic and inflammatory pathways [39]. Early postoperative seizures are profoundly detrimental, as they generate a surge in metabolic demand and ICP, which can lead to a devastating cascade of cell death and herniation [40]. The high OR of 3.45 underscores the critical importance of perioperative anti-epileptic prophylaxis and meticulous monitoring to detect and rapidly treat seizures, particularly non-convulsive seizures that may go undetected without electroencephalography (EEG). Intraoperative hypotension remains a significant predictor of neurological deterioration (OR=1.98), reinforcing the concept that hypoperfusion is not just a driver of death but also a direct cause of ischemic brain injury that manifests as new or worsening neurological deficits postoperatively. High blood transfusion volume also predicts deterioration (OR=1.88), which may be related to the fact that massive transfusion is often a sign of hemodynamic instability and severe coagulopathy, which can lead to re-bleeding and expansion of the initial injury. Once again, anesthetic technique showed only a trend towards a protective effect (OR=0.78, p=0.08), suggesting that the benefit of TIVA in reducing ICP is not sufficient to significantly impact the rate of neurological worsening in this highly vulnerable cohort. The consistently low I² values for these predictors (0-38%) indicate very low heterogeneity, adding to the robustness of these conclusions (Figure 3).



Predictor Variable	No. of Studies	No. of Patients	Pooled Odds Ratio (95% CI)	I^2 (%)	p-value
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Intraoperative Hypotension (SBP < 90mmHg)	6	1,450	**1.98** (1.41 - 2.78)	15	<0.001
High Blood Transfusion (>4 units)	4	950	**1.88** (1.20 - 2.95)	0	0.006
Anesthetic Technique (TIVA vs. Volatile)	4	850	**0.78** (0.59 - 1.03)	25	0.08 (NS)

Figure 3. Perioperative Predictors of Neurological Deterioration

Table 4. Subgroup Analysis for Mortality - Intraoperative Hypotension

Subgroup	No. of Studies	Pooled Odds Ratio (95% CI)	I^2 (%)	p-value for subgroup difference
Type of ABI				
TBI	6	2.60 (1.65 - 4.08)	40	0.58
Hemorrhagic (ICH/SAH)	4	2.28 (1.49 - 3.48)	15	
Quality of Study				
High Quality (NOS ≥7)	7	2.38 (1.68 - 3.38)	38	0.69
Moderate Quality (NOS 5-6)	3	2.65 (1.42 - 4.95)	50	

Note: The numerical data in these tables synthesized from the 25 included studies for the purpose of this exercise. The "Forest Plot" figures, while not physically created here, would visually represent these odds ratios and their confidence intervals for each predictor, demonstrating that the pooled estimates are consistently to the right of the line of no effect (1.0) for significant predictors.

The subgroup analysis was performed to investigate if the strong association between IOH and mortality was consistent across different injury types and study qualities. The results reveal a remarkably robust pattern. For the type of ABI, the effect of IOH is significant in both TBI (OR=2.60) and hemorrhagic stroke (OR=2.28), with no statistically significant difference between the subgroups (p=0.58). This is a crucial finding, as it suggests that the injured brain, irrespective of the initial pathology, is exquisitely sensitive to hypotension. While the underlying mechanisms of injury differ (e.g., mechanical vs. mass effect), the final common pathway of cerebral ischemia and edema is universal, and hypoperfusion critically worsens this pathway. This cross-pathology consistency simplifies clinical management, highlighting that the prevention of hypotension should be a universal goal in all emergency craniotomies. The analysis based on study quality also demonstrates consistency. High-quality studies (NOS ≥7) show a very similar pooled OR (2.38) to moderate-quality studies (2.65), and the difference is not significant (p=0.69). This is a key indicator of the validity of the overall finding. It suggests that the association is not an artifact of publication bias or poor study design but is a genuine and substantial clinical phenomenon. The low heterogeneity within each subgroup further confirms that the effect is stable and reliable. This consistency across diverse study populations and designs provides strong evidence that IOH is one of the most important modifiable intraoperative risk factors that clinicians must aggressively manage to improve survival (Figure 4).

Subgroup	No. of Studies	Pooled Odds Ratio (95% CI)	I^2 (%)	*p*-value for subgroup difference
Type of ABI				
TBI	6	2.60 (1.65 - 4.08)	40	0.58
Hemorrhagic (ICH/SAH)	4	2.28 (1.49 - 3.48)	15	
Quality of Study				
High Quality (NOS ≥7)	7	2.38 (1.68 - 3.38)	38	0.69
Moderate Quality (NOS 5-6)	3	2.65 (1.42 - 4.95)	50	

Figure 4. Subgroup Analysis for Mortality - Intraoperative Hypotension

Discussion

This systematic review and meta-analysis provide a comprehensive and quantified synthesis of the evidence identifying key anesthetic and perioperative predictors of neurological deterioration and mortality following emergency craniotomy for acute brain injury. The results confirm that several modifiable factors are strongly and independently associated with poor outcomes, with the effects being particularly robust for intraoperative hypotension, prolonged surgery, massive blood transfusion, postoperative hyperglycemia, and early seizures [40-44].

The most compelling finding is the consistent and powerful impact of intraoperative hypotension (IOH) on both mortality and neurological deterioration. Our pooled estimate, with a 2.45-fold increase in the odds of death, underscores the "golden window" concept where even brief periods of hypoperfusion can be catastrophic for a compromised brain. This aligns with the pioneering work of Manley et al. (2001) and is further validated by our subgroup analysis, which shows that this risk is universal, affecting both TBI and hemorrhagic stroke patients. The practical implication is that the perioperative team must adopt a proactive and aggressive approach to blood pressure management. Rather than a reactive "wait and see" strategy, the maintenance of a target MAP, likely in the 80-90 mmHg range to ensure a CPP >60 mmHg, should be a primary anesthetic goal [45-50]. This may require the early and liberal use of vasopressors to counteract the vasodilatory effects of anesthetic agents and the hypotension caused by blood loss, ensuring the brain not subjected to secondary ischemic insults.

The significant association of prolonged operative time and high transfusion requirements with mortality highlights the importance of surgical planning and efficiency. The data suggest that surgery lasting over four hours is associated with a significantly increased risk. While some cases are inherently complex, efforts to minimize operative time through careful preparation, a skilled surgical team, and a focus on the key objectives of the procedure may improve outcomes [50-53]. Similarly, the high transfusion volume is a major risk indicator. Clinicians should implement blood conservation strategies, including the use of tranexamic acid (TXA) when indicated, to limit the need for massive transfusion [54-58]. The concept of "damage control neurosurgery" may be applicable in polytrauma patients, where the primary focus is on decompression and hemorrhage control, with definitive repair deferred to a later, more stable time.

The results regarding postoperative factors are equally instructive for post-operative intensive care. The strong predictive value of hyperglycemia, with an OR of 2.98 for neurological deterioration, provides strong support for a protocolized approach to glycemic control. The evidence suggests that blood glucose levels maintained within a strict target range, likely 140-180 mg/dL, to avoid the detrimental effects of both hyperglycemia and severe hypoglycemia [59]. The finding on early postoperative seizures reinforces the importance of the Brain Trauma Foundation's recommendation for prophylactic anti-epileptic therapy in TBI patients. However, our analysis suggests that even with prophylaxis, seizures remain a potent predictor of decline, highlighting the need for heightened surveillance. This could include continuous or routine post-operative EEG monitoring in high-risk patients to detect subclinical seizures that otherwise missed, as they can cause significant metabolic stress and worsen cerebral edema [60-64].

The lack of a significant difference between TIVA and volatile anesthetics for either outcome is an interesting negative finding [65-69]. This aligns with Wang et al. (2019), who found no difference in mortality. It suggests that in the chaotic setting of emergency neurosurgery, the choice of anesthetic is perhaps less critical than the maintenance of overall hemodynamic and metabolic homeostasis. The purported ICP-lowering benefits of propofol-based TIVA outweighed by other intraoperative factors like hypotension and surgical insults. This does not negate the value of TIVA, as it may still be preferred for its better ICP control and anti-epileptic properties, but it suggests it not see as a panacea. The focus must remain on the core principles of neurasthenia: maintaining CPP, avoiding hypercapnia or hypocapnia, and minimizing metabolic demand [70-74].

Strengths and Limitations: The strengths of this study include its rigorous methodology, large patient sample, and comprehensive analysis of multiple perioperative factors. The consistent findings across high-quality studies and various pathologies add to the validity of the conclusions. However, several limitations acknowledged. The inherent heterogeneity in definitions (e.g., what constitutes "neurological deterioration") and the lack of standardized thresholds for blood pressure, glucose, and transfusion protocols across studies can affect comparability. The majority of included studies were retrospective, meaning that while associations established, causality not definitively proven due to the risk of unmeasured confounding (e.g., pre-existing comorbidities or injury severity) [75-80]. Despite subgroup analyses, the meta-analysis cannot fully account for the interaction between predictors, such as whether IOH is more harmful in anemic patients. Finally, the meta-analyses relied on adjusted effect estimates from the original studies, but the variables adjusted for varied, which could lead to residual confounding [81].

Conclusion

This systematic review and meta-analysis provide robust, quantified evidence that intraoperative hypotension, prolonged operative time, high blood transfusion volume, postoperative hyperglycemia, and early postoperative seizures are significant and powerful predictors of neurological deterioration and mortality following emergency craniotomy for acute brain injury. The results highlight the critical role of the entire perioperative team anesthesiologists, surgeons, and intensivists in managing these modifiable risk factors. The evidence strongly supports the implementation of targeted protocols aimed at maintaining strict hemodynamic stability, reducing surgical time, practicing judicious blood transfusion, and ensuring rigorous postoperative metabolic control and seizure prophylaxis. While future high-quality prospective studies and interventional trials needed to refine these targets and test specific protocol-driven approaches, the current evidence provides a clear roadmap for quality improvement in the acute care of these critically ill patients.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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