



SURGICAL OUTCOMES OF ACUTE EPIDURAL HEMATOMA EVACUATION: TIMING OF INTERVENTION AND PREDICTORS OF OUTCOME — A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIAL AND PRIMARY STUDIES

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ABSTRACT

Introduction: Acute epidural hematoma (EDH) is a time-critical neurosurgical emergency in which prompt evacuation can convert a potentially lethal mass lesion into a fully recoverable injury. Outcomes nevertheless vary widely, particularly in low- and middle-income countries (LMICs) where computed tomography (CT), neurosurgeons, operating theatres and referral systems are unevenly distributed. This review aimed to quantify contemporary mortality and functional outcome after surgical evacuation of acute EDH, to estimate the association between delayed surgery and outcome, to identify pre-operative predictors of outcome, and to synthesise evidence on facility- and human resource-related causes of delay.

Methods: The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines. Randomized controlled trials and prospective, retrospective, cohort, case-control and cross-sectional studies of

patients undergoing surgical evacuation of traumatic acute EDH were eligible. Risk of bias was assessed with the Quality In Prognosis Studies (QUIPS) tool and the Newcastle–Ottawa Scale. Proportions were pooled on the logit scale and odds ratios (ORs) with DerSimonian–Laird random-effects models; Mantel–Haenszel and Peto methods, leave-one-out analyses, subgroup analyses, meta-regression and funnel-plot tests were used for robustness. Certainty of evidence was graded with GRADE for prognosis.

Results: Thirty-one studies (3,368 patients; 24 from LMICs, two from Indonesia) met inclusion criteria; no randomized trial was identified. Pooled mortality after evacuation was 7.5% (95% CI 5.2–10.6; $k = 21$; $I^2 = 74\%$), rising to 21.1% in cohorts restricted to comatose patients, and favourable outcome was achieved in 78.9% (95% CI 72.8–84.0; $k = 15$). Delayed evacuation was associated with unfavourable outcome (OR 6.17, 95% CI 1.27–29.94; $k = 6$) and, for a 6-hour threshold, with mortality (OR 14.23, 95% CI 2.90–69.78; $k = 4$), with marked heterogeneity driven by confounding by indication in high-income cohorts. Pre-operative Glasgow Coma Scale (GCS) ≤ 8 (mortality OR 9.26, 95% CI 3.68–23.33; unfavourable outcome OR 17.34, 95% CI 7.54–39.88), abnormal pupillary status (OR 5.85, 95% CI 3.10–11.05), associated intracranial lesions (OR 3.44, 95% CI 1.78–6.63) and older age (OR 2.85, 95% CI 1.33–6.08) predicted poor outcome. The proportion of comatose patients explained 38% of between-study heterogeneity in mortality. In LMIC cohorts, median injury-to-surgery intervals reached 15–78 hours, and logistical problems (28.1%) and resource constraints in staff, intensive care beds and equipment (22.5%) were the leading reported causes of delay.

Discussion: Surgical evacuation of acute EDH achieves low mortality and high rates of functional recovery, but outcome is governed chiefly by the neurological state at the time of surgery. Delay matters most where it allows neurological deterioration—a situation concentrated in referral-dependent LMIC systems lacking on-site CT, neurosurgeons and theatre capacity. In high-income systems with triage-driven prioritisation, crude time–outcome associations are attenuated or reversed.

Conclusion: Low pre-operative GCS, abnormal pupils, associated intracranial injury, older age and delayed evacuation identify patients at highest risk. Reducing facility- and workforce-related delay through regional neurotrauma networks, teleradiology, transfer protocols and credentialed damage-control craniotomy where neurosurgical transfer is not feasible is the most actionable lever for improving EDH outcomes in Indonesia and comparable settings.

Keywords: Epidural hematoma; Extradural hematoma; Craniotomy; Time-to-treatment; Glasgow Coma Scale; Prognosis; Traumatic brain injury; Low- and middle-income countries; Health services accessibility; Meta-analysis

INTRODUCTION

Background

Traumatic brain injury (TBI) is a leading cause of death and disability among young, economically productive adults worldwide. A global mapping of neurosurgical burden estimated that 22.6 million people each year sustain neurological conditions requiring the expertise of a neurosurgeon, of whom 13.8 million need surgery, and that roughly 23,300 additional neurosurgeons would be required to address more than five million essential cases that go untreated annually—all of them in LMICs. Neurotrauma alone accounts for almost 4.9 million operative cases each year in LMICs, and access to neurosurgical care within a reasonable travel time remains particularly limited in Africa and in East Asia and the Pacific, the latter including Indonesia.^{1–3}

Acute epidural (extradural) hematoma (EDH) is a collection of blood between the inner table of the skull and the dura mater, most often arising from laceration of the middle meningeal artery or its branches by a skull fracture, and less frequently from diploic veins or dural venous sinuses. A recent global meta-analysis estimated that EDH complicates 8.2% of TBI presentations and that approximately 3.1 million people require surgical evacuation for traumatic EDH every year, most of whom are in their prime working years. Because the underlying brain is frequently spared, EDH is regarded as one of the most rewarding lesions in neurotrauma: timely evacuation can restore full neurological function, whereas delayed decompression allows progressive intracranial hypertension, transtentorial herniation and secondary brainstem ischaemia.^{4–6}

The aspiration of “zero mortality” for EDH, first articulated in a European regional trauma system, is still unmet even in high-income settings. A 2026 reappraisal from the same institution reported an in-hospital mortality of 2.4% despite four decades of system improvements and attributed residual deaths to referral and triage delays. In Indonesia, a review of 268 surgically treated EDH patients at a national referral hospital in Surabaya documented a post-operative mortality of 11.6% and highlighted the specific problems and challenges of a developing health system.^{7,8}

The Brain Trauma Foundation surgical recommendations—evacuation of any EDH larger than 30 cm³ regardless of GCS, and urgent evacuation of acute EDH in comatose patients with anisocoria—have been widely adopted, but they rest on low-level evidence and do not specify a maximum acceptable interval from injury to surgery. Clinical series have

repeatedly identified pre-operative GCS, pupillary abnormalities, hematoma volume, midline shift, associated intracranial lesions, age and time to surgery as candidate prognostic factors, yet the direction and magnitude of these associations vary considerably between centres and health systems.^{6,9,10}

The timing of evacuation is the factor most directly modifiable by health-system organisation. In LMICs, delays arise at every step of the care continuum: the decision to seek care, transport and interfacility referral, and in-hospital access to CT, a neurosurgeon, an anaesthetist, an operating theatre and an intensive care bed. A systematic review of 55 studies from 18 LMICs identified the absence of in-house CT scanners (35%), limited theatre space (28%), absence of in-house neurosurgical facilities (28%) and absence of in-house neurosurgeons (28%) as major in-hospital causes of delay in TBI care. Indonesian observations similarly point to geographical constraints, a lack of organised emergency transport and a scarcity of neurosurgeons and CT scanners in rural regions as primary barriers to timely neurotrauma surgery.^{11–13}

Conversely, studies from high-income trauma systems frequently fail to show a time–outcome gradient, or even show worse outcomes with earlier surgery, because the sickest patients are operated on first. A 2026 meta-analysis in acute subdural hematoma found no association between time to intervention and mortality and explicitly attributed this to confounding by indication, while a 2024 meta-analysis of traumatic intracranial hematomas of all types reported equivocal results and lower mortality with evacuation within 4 hours. These contradictory signals have never been synthesised specifically for surgically treated acute EDH, the lesion in which the benefit of speed should theoretically be greatest.^{14–16}

Research gap

Existing syntheses address related but distinct questions. The global EDH meta-analysis by Rahimi and colleagues estimated incidence, operative rates and mortality by income group but did not examine surgical timing or prognostic factors. Merakis and colleagues pooled time-to-operation data across mixed traumatic intracranial hematomas, dominated by subdural lesions. Scotter and colleagues restricted their analysis to patients with bilateral fixed dilated pupils, Marhold and colleagues to the influence of additional intracranial injuries, Lee and colleagues to paediatric posterior fossa EDH, and a 2025 Spanish-language review to incidence and operative rates in LMICs. No previous review has quantitatively integrated (i) contemporary mortality and functional outcomes after EDH evacuation, (ii) the association between delayed surgery and outcome, (iii) the magnitude of

pre-operative prognostic factors, and (iv) the facility- and human resource-related determinants of delay, with explicit attention to LMIC and Indonesian settings.^{4,5,15,17–19}

Objectives

The primary objective was to estimate pooled mortality and favourable functional outcome after surgical evacuation of traumatic acute EDH. Secondary objectives were (a) to quantify the association between delayed versus early evacuation and mortality or unfavourable outcome; (b) to quantify the prognostic value of pre-operative GCS, pupillary status, associated intracranial lesions, age and paediatric status; (c) to explore sources of heterogeneity, including income setting, population and case mix; and (d) to describe time-to-care metrics and the reported facility- and human resource-related causes of surgical delay.^{20,21}

Research hypotheses

Hypothesis 1 (H1). Delayed surgical evacuation, defined by study-specific thresholds (6, 12 or 24 hours after injury), is associated with higher mortality and a higher proportion of unfavourable functional outcome than early evacuation. **Null hypothesis (H0₁):** there is no association between timing of evacuation and outcome. **Hypothesis 2 (H2).** Pre-operative GCS ≤ 8 , abnormal pupillary status, associated intracranial lesions and older age are independently associated with poor outcome. **Null hypothesis (H0₂):** these factors are not associated with outcome. **Hypothesis 3 (H3).** Outcome after EDH evacuation differs between income settings and is explained, at least in part, by differences in case mix and access to timely surgery.^{21,22}

Significance and benefits of the study

Clinical benefit. Pooled absolute risks stratified by GCS, pupillary status and timing provide bedside prognostic anchors for counselling families and for triaging scarce operating-theatre time in regional hospitals. **Health-system benefit.** Quantifying the cost of delay, and the facility- and workforce-related reasons for it, informs referral policy, the regionalisation of neurotrauma services, teleradiology and the training of non-neurosurgeons in damage-control cranial surgery, priorities that are directly relevant to Indonesia's archipelagic referral network. **Academic benefit.** The review identifies the methodological weaknesses of the current literature, particularly confounding by indication and inconsistent outcome definitions, and proposes a research agenda for registry-based, risk-adjusted studies.^{2,23,24}

Novelty

To our knowledge, this is the first systematic review and meta-analysis restricted to surgically evacuated acute EDH that simultaneously (i) pools contemporary mortality and

favourable outcome with subgroup analyses by income setting and population; (ii) meta-analyses delayed versus early evacuation using study-specific thresholds together with sparse-data sensitivity methods; (iii) quantifies five pre-operative prognostic factors and translates them into absolute risks; (iv) demonstrates by meta-regression that case mix explains a substantial part of between-study heterogeneity; (v) synthesises facility- and human resource-related causes of delay within a three-delay framework; and (vi) incorporates Indonesian data from Surabaya and Denpasar. The evidence base is dominated by LMIC cohorts (24 of 31 studies), giving the findings direct relevance to regional hospitals without on-site neurosurgical services.^{8,25,26}

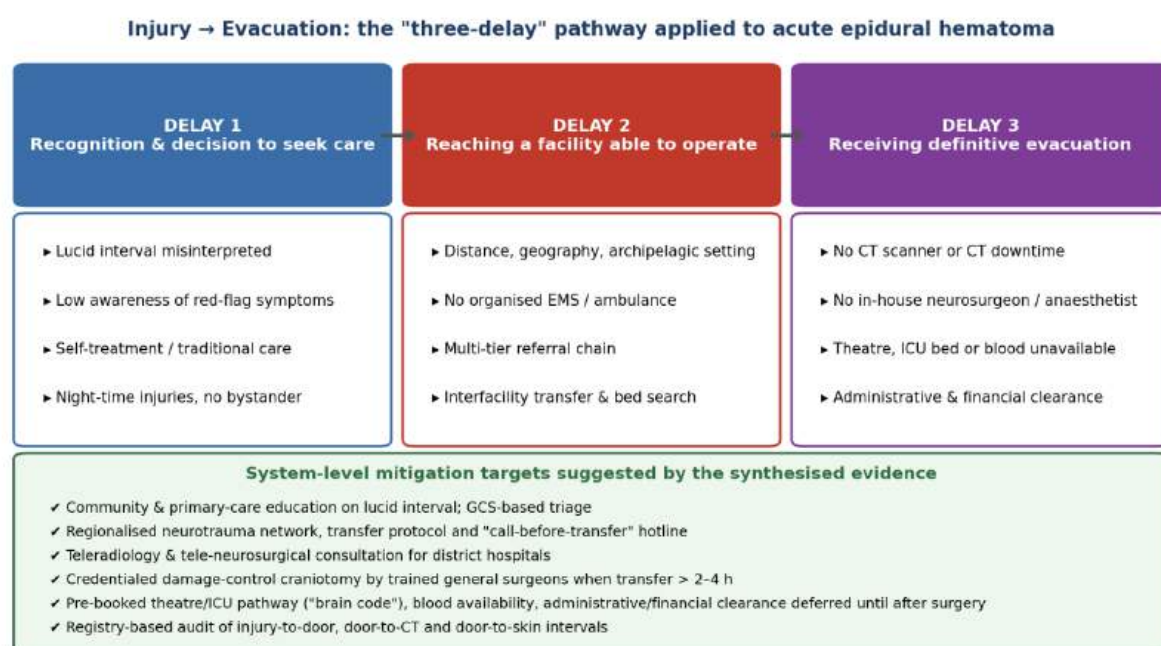


Figure 1. Conceptual framework: the “three-delay” pathway from injury to evacuation of acute epidural hematoma, showing facility- and human resource-related bottlenecks and the system-level mitigation targets examined in this review. The framework adapts the three-delay model used in LMIC neurotrauma research to the EDH care pathway.^{11,12}

METHODS

Protocol, reporting standard and registration

This review was designed and reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement. Because the review addresses prognosis rather than the effect of an intervention, methodological choices for risk-of-bias assessment and certainty grading followed guidance specific to prognostic factor research. The protocol was specified before data extraction (eligibility criteria, outcomes, effect measures and planned subgroup analyses).^{20–22}

Eligibility criteria

Eligibility was defined using a PECOS framework. Studies were eligible if they enrolled patients of any age with CT-confirmed traumatic acute EDH treated by surgical evacuation (craniotomy, craniectomy or burr-hole/trephination evacuation) and reported mortality, functional outcome (Glasgow Outcome Scale [GOS], extended GOS [GOSE] or equivalent) or the association between a pre-operative factor or surgical timing and outcome. In line with the review brief, eligible designs were randomized controlled trials, cohort studies (prospective or retrospective), case-control studies, cross-sectional studies and other observational designs. Publication was restricted to January 2011 – October 2026 to reflect contemporary CT-based diagnosis, resuscitation and neurocritical care. Systematic reviews and meta-analyses were not included as primary data but were retained for the Discussion.^{4,20}

Table 1. Eligibility criteria (PECOS framework)

Element	Inclusion criteria	Exclusion criteria
Population	Patients of any age with CT-confirmed traumatic acute EDH undergoing surgical evacuation	Spontaneous/non-traumatic EDH; spinal EDH; chronic EDH; cohorts mixing EDH with SDH/ICH without separable EDH data
Exposure / prognostic factor	Time from injury (or admission) to surgery; pre-operative GCS; pupillary status; associated intracranial lesions; age; hematoma volume; midline shift; paediatric status	Factors measured only post-operatively
Comparator	Early vs delayed evacuation (study-specific threshold); absence vs presence of the prognostic factor	—
Outcomes	Primary: mortality (in-hospital or study-defined) and favourable functional outcome (GOS 4–5 / GOSE 5–8). Secondary: unfavourable outcome (GOS 1–3 or study definition), time-to-care metrics, reported causes of delay	Outcomes not separable for operated EDH patients
Study	RCTs; prospective or retrospective	Case reports, technical notes,

design	cohort, case-control, cross-sectional and other observational primary studies	editorials, conference abstracts/posters, narrative reviews; systematic reviews/meta-analyses (Discussion only)
Time frame & language	Published January 2011 – October 2026; English (abstract or full text)	Published before 2011
Record integrity	Bibliographic record verifiable in Crossref or a recognised index	Unverifiable records/DOIs; duplicate or overlapping cohorts (larger/most complete report retained)

Search Strategy

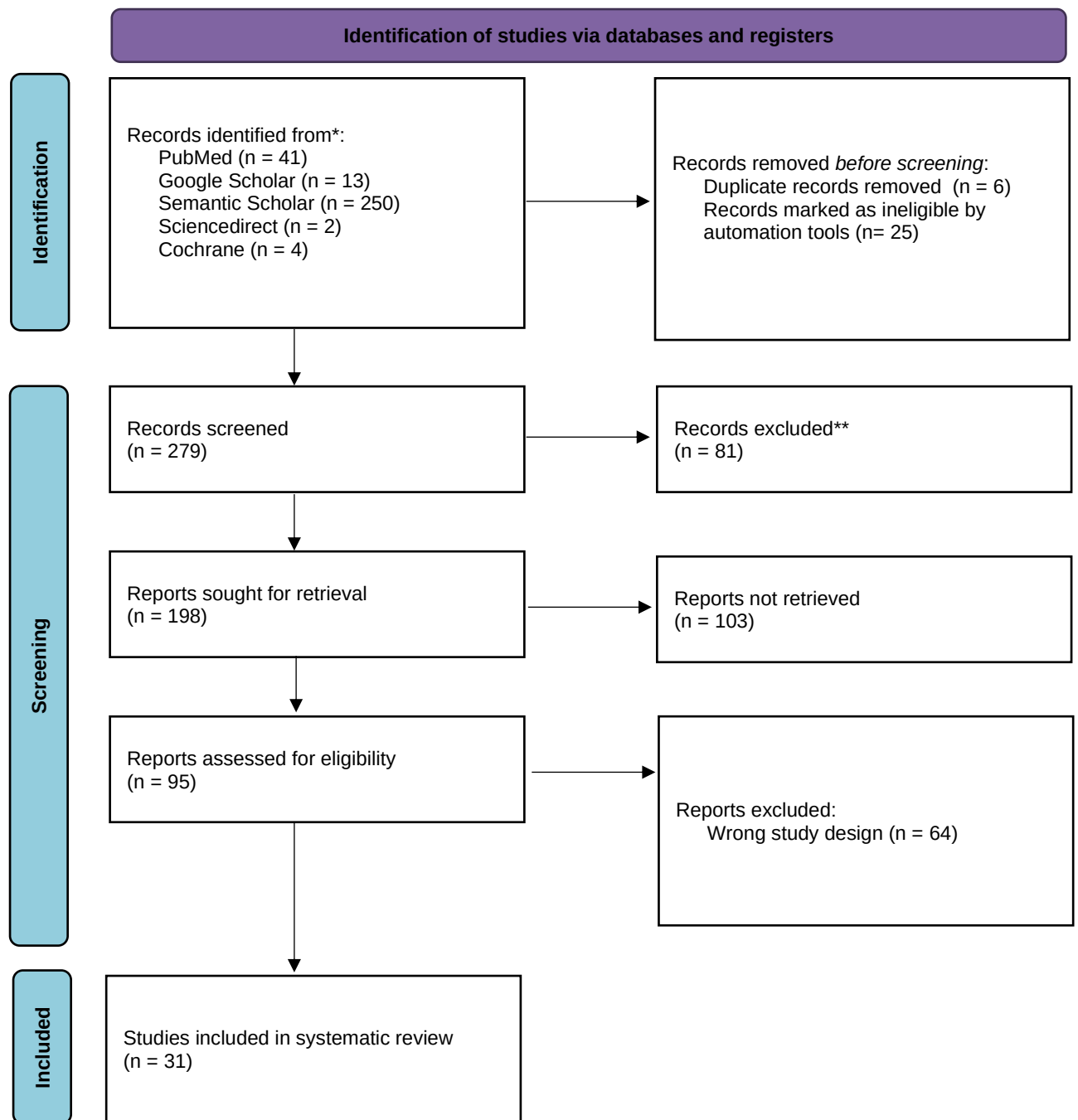
The keywords used for this research based PICO :

PICO Element	Keyword 1	Keyword 2	Keyword 3
P — Population	Acute epidural hematoma (EDH)	Traumatic brain injury (TBI)	Surgically treated EDH patients
I — Intervention	Surgical evacuation (craniotomy/craniectomy)	Early surgical evacuation	Damage-control craniotomy
C — Comparison	Delayed surgical evacuation	Conservative management	Non-neurosurgical care
O — Outcome	Mortality	Functional outcome (GOS/GOSE)	Time-to-surgery interval

The Boolean MeSH keywords inputted on databases for this research are: ("*Acute epidural hematoma (EDH)*") OR ("*Traumatic brain injury (TBI)*") OR ("*Surgically treated EDH patients*") AND ("*Surgical evacuation (craniotomy/craniectomy)*") OR ("*Early surgical evacuation*") OR ("*Damage-control craniotomy*") AND ("*Delayed surgical evacuation*") OR ("*Conservative management*") OR ("*Non-neurosurgical care*") AND ("*Mortality*") OR ("*Functional outcome (GOS/GOSE)*") OR ("*Time-to-surgery interval*")

Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Acute epidural hematoma (EDH)" AND "Surgical evacuation (craniotomy/craniectomy)" OR "Early surgical evacuation" OR "Delayed surgical evacuation" AND "Mortality" OR "Functional outcome (GOS/GOSE)" OR "Time-to-surgery interval")</i>	41
Google Scholar	<i>("Acute epidural hematoma (EDH)" OR "Traumatic brain injury (TBI)" OR "Surgically treated EDH patients") AND ("Surgical evacuation (craniotomy/craniectomy)" OR "Early surgical evacuation" OR "Damage-control craniotomy") AND ("Delayed surgical evacuation" OR "Conservative management" OR "Non-neurosurgical care") AND ("Mortality" OR "Functional outcome (GOS/GOSE)" OR "Time-to-surgery interval")</i>	13
Semantic Scholar	<i>("Acute epidural hematoma (EDH)" OR "Traumatic brain injury (TBI)" OR "Surgically treated EDH patients") AND ("Surgical evacuation (craniotomy/craniectomy)" OR "Early surgical evacuation" OR "Damage-control craniotomy") AND ("Delayed surgical evacuation" OR "Conservative management" OR "Non-neurosurgical care") AND ("Mortality" OR "Functional outcome (GOS/GOSE)" OR "Time-to-surgery interval")</i>	250
Science-direct	<i>("Acute epidural hematoma (EDH)") AND ("Surgical evacuation (craniotomy/craniectomy)" OR "Early surgical evacuation" OR "Delayed surgical evacuation") AND ("Mortality" OR "Functional outcome (GOS/GOSE)" OR "Time-to-surgery interval")</i>	2
Cochrane	<i>("Acute epidural hematoma (EDH)" AND "Surgical evacuation (craniotomy/craniectomy)" OR "Early surgical evacuation" OR "Delayed surgical evacuation" AND "Mortality" OR "Functional outcome (GOS/GOSE)" OR "Time-to-surgery interval")</i>	4



Article search flowchart

Study selection

Titles and abstracts of all de-duplicated records were screened against the eligibility criteria, followed by full-text (or, when the full text was behind an access barrier, abstract-plus-metadata) assessment of potentially eligible reports. Reasons for exclusion at the full-text stage were recorded. When several reports described the same or overlapping cohorts, the most complete report was retained and the companion report was used only for supplementary information. Two specific integrity checks were applied: identical outcome

distributions across reports from different institutions were flagged as suspected duplicate publication, and cohorts from the same institution and overlapping periods were not pooled together in the same meta-analysis.^{20,27,28}

Data extraction

A standardised, piloted extraction form captured bibliographic details, country and World Bank income group, design, recruitment period, sample size, population and age, surgical procedure, outcome instrument and time point, deaths, favourable/unfavourable outcomes, time-to-care metrics, reported causes of delay, and two-by-two outcome data for each candidate prognostic factor. Numerical data were extracted from tables and text of full-text articles (16 studies) or from abstracts and indexed metadata when full texts were inaccessible (15 studies); every numerical entry was re-verified against the source in a second pass. Where only percentages were reported, counts were back-calculated and rounded to the nearest integer (for example, 6.8% of 131 patients = 9 deaths). Internal inconsistencies in source data were recorded and resolved conservatively by using the outcome total that reconciled with the reported overall figures.^{20,22}

Table 2. Data items, outcome definitions and harmonisation rules

Domain	Definition used in this review	Harmonisation rule
Mortality	Death before discharge or at the earliest reported time point after surgery	In-hospital mortality preferred; follow-up mortality used only when no in-hospital figure was reported
Favourable outcome	GOS 4–5 (moderate disability or good recovery) or GOSE 5–8	Studies reporting only GOS 5 (good recovery) were included and removed in sensitivity analysis
Unfavourable outcome	GOS 1–3 or GOSE 1–4 (death, vegetative state, severe disability)	Where studies combined GOS 2–4 as "residual disability", the study definition was retained and flagged
Early vs delayed surgery	Study-specific cut-off from injury to surgery (6 h, 12 h or 24 h)	Delayed = above threshold; subgroup analysis by threshold
Low GCS	Pre-operative (or last pre-operative) GCS $\leq$ 8	GCS > 8 as reference

Abnormal pupils	Anisocoria, unilateral or bilateral unreactive/dilated pupil	Normal, equal and reactive pupils as reference
Associated lesion	Any additional intradural lesion (contusion, SDH, tSAH, ICH) on CT	Isolated EDH as reference
Older age	Study-specific threshold (≥ 40 , ≥ 46 or ≥ 50 years)	Younger patients as reference
Income setting	World Bank classification (LIC, LMIC, UMIC, HIC)	LIC/LMIC/UMIC grouped as "LMIC" for subgroup analysis

Risk-of-bias and quality assessment

Risk of bias was assessed at study level with the Quality In Prognosis Studies (QUIPS) tool, which evaluates six domains: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. Each domain was rated as low, moderate or high risk. An overall rating was assigned a priori as low (no high-risk domain and at most one moderate domain), moderate (two or three moderate domains without any high-risk domain) or high (any high-risk domain or four or more moderate domains). Confounding was judged high when timing or prognostic factor associations were reported without consideration of injury severity in a setting where severity clearly drove surgical prioritisation. Methodological quality was additionally scored with the Newcastle–Ottawa Scale (NOS; selection 0–4, comparability 0–2, outcome 0–3), with ≥ 7 considered good, 5–6 fair and ≤ 4 poor.^{22,29,30}

Table 3. Risk of bias (QUIPS) and methodological quality (Newcastle–Ottawa Scale) of the 31 included studies

Study	D1	D2	D3	D4	D5	D6	QUIPS overall	NOS S/C/O = total
Javed 2013 ³¹	Low	Low	Low	Low	Moderate	Moderate	Moderate	4/0/3 = 7 (Good)
Ali 2016 ²⁷	Moderate	Low	Low	High	Moderate	Moderate	High	2/0/1 = 3 (Poor)
Niryana 2017 ²⁵	Moderate	Moderate	Low	Low	Low	Moderate	Moderate	3/1/2 = 6 (Fair)
Gutowski 2018 ³²	Low	Low	Low	Moderate	Low	Moderate	Moderate	4/1/2 = 7 (Good)
Ndumbe 2018 ³³	Moderate	Low	Low	Moderate	High	Moderate	High	3/0/2 = 5 (Fair)

	d	w	w	d	h	d		
Elsayed 2018 ³⁴	Mo d	Lo w	Mo d	Mo d	Hig h	Hig h	High	2/0/2 = 4 (Poor)
Rosyidi 2019 ⁸	Lo w	Lo w	Lo w	Mo d	Mo d	Mo d	Moderat e	4/1/2 = 7 (Good)
Kandregula 2019 ³⁵	Lo w	Mo d	Lo w	Lo w	Lo w	Mo d	Moderat e	4/2/2 = 8 (Good)
Onodera 2020 ³⁶	Lo w	Lo w	Lo w	Mo d	Lo w	Lo w	Low	4/2/2 = 8 (Good)
Ayogu 2021 ³⁷	Lo w	Mo d	Lo w	Lo w	Hig h	Mo d	High	4/0/2 = 6 (Fair)
Howlader 2021 ⁹	Hig h	Lo w	Lo w	Lo w	Hig h	Mo d	High	2/0/3 = 5 (Fair)
Vilcinis 2021 ³⁸	Mo d	Lo w	Lo w	Mo d	Hig h	Mo d	High	3/0/2 = 5 (Fair)
Choi 2022 ³⁹	Lo w	Lo w	Lo w	Lo w	Lo w	Mo d	Low	4/2/3 = 9 (Good)
Kapoor 2022 ⁴⁰	Mo d	Mo d	Lo w	Mo d	Hig h	Hig h	High	2/0/1 = 3 (Poor)
Echara 2023 ⁴¹	Lo w	Mo d	Lo w	Lo w	Mo d	Mo d	Moderat e	4/1/3 = 8 (Good)
Miao 2023 ⁴²	Mo d	Lo w	Lo w	Lo w	Mo d	Mo d	Moderat e	3/1/3 = 7 (Good)
Khalid 2023 ⁴³	Lo w	Lo w	Lo w	Mo d	Hig h	Mo d	High	4/0/2 = 6 (Fair)
Marhold 2023 ⁵	Lo w	Mo d	Lo w	Lo w	Mo d	Lo w	Moderat e	4/1/3 = 8 (Good)
Das 2024 ¹⁰	Mo d	Lo w	Lo w	Hig h	Hig h	Mo d	High	3/0/1 = 4 (Poor)
Jabbar 2024 ⁴⁴	Mo d	Lo w	Lo w	Lo w	Hig h	Mo d	High	3/0/3 = 6 (Fair)
Ullah 2024 ⁴⁵	Mo d	Lo w	Lo w	Mo d	Hig h	Mo d	High	3/0/2 = 5 (Fair)

Adalat 2024 ⁴⁶	Hig h	Lo w	Lo w	Lo w	Hig h	Hig h	High	2/0/3 = 5 (Fair)
Elkholy 2024 ⁴⁷	Mo d	Lo w	Lo w	Lo w	Mo d	Mo d	Moderat e	3/1/3 = 7 (Good)
Kebede 2025 ⁴⁸	Lo w	Lo w	Lo w	Mo d	Mo d	Mo d	Moderat e	4/1/2 = 7 (Good)
Khan Z 2025 ²⁶	Mo d	Lo w	Mo d	Mo d	Mo d	Hig h	High	2/1/2 = 5 (Fair)
Gmeiner 2025 ⁴⁹	Lo w	Lo w	Lo w	Mo d	Lo w	Mo d	Moderat e	4/2/2 = 8 (Good)
Tshiamala Ngalula 2025 ⁵⁰	Mo d	Lo w	Lo w	Mo d	Hig h	Mo d	High	3/0/2 = 5 (Fair)
Mercea 2026 ⁵¹	Mo d	Lo w	Lo w	Mo d	Lo w	Lo w	Moderat e	3/2/2 = 7 (Good)
Marchesini 2026 ⁷	Lo w	Lo w	Lo w	Mo d	Mo d	Lo w	Moderat e	4/1/2 = 7 (Good)
Khan MS 2026 ⁵²	Lo w	Lo w	Lo w	Mo d	Lo w	Mo d	Moderat e	4/2/2 = 8 (Good)
Taha 2026 ⁵³	Mo d	Lo w	Lo w	Lo w	Mo d	Hig h	High	3/1/3 = 7 (Good)

D1, study participation; D2, study attrition; D3, prognostic factor measurement; D4, outcome measurement; D5, study confounding; D6, statistical analysis and reporting. QUIPS ratings: Low, Mod (moderate), High. NOS: S, selection (0–4); C, comparability (0–2); O, outcome (0–3). Overall QUIPS rule: low = no high-risk domain and ≤ 1 moderate; moderate = 2–3 moderate domains without high risk; high = any high-risk domain or ≥ 4 moderate domains.

Risk of bias

Two studies were judged at low overall risk of bias, 14 at moderate risk and 15 at high risk. The confounding domain was the most frequently compromised: 12 studies (39%) were rated at high risk because they reported associations between timing or prognostic factors and outcome without accounting for injury severity, which is the principal determinant of surgical prioritisation. Outcome measurement was frequently rated moderate because outcome was assessed at 48 hours or at discharge rather than at three to six months. Specific concerns

included purposive sampling, exclusion of referred patients from a timing study, internally inconsistent outcome tables in two studies, implausible summary statistics in one paediatric study, and inclusion of non-operated patients in one cohort. Median NOS score was 7 (range 3–9); 16 studies were rated good, 11 fair and 4 poor.^{9,22,26,46,51,53}



Figure 2. Risk-of-bias traffic-light plot for the 31 included studies (QUIPS domains D1–D6 and overall judgement).²²

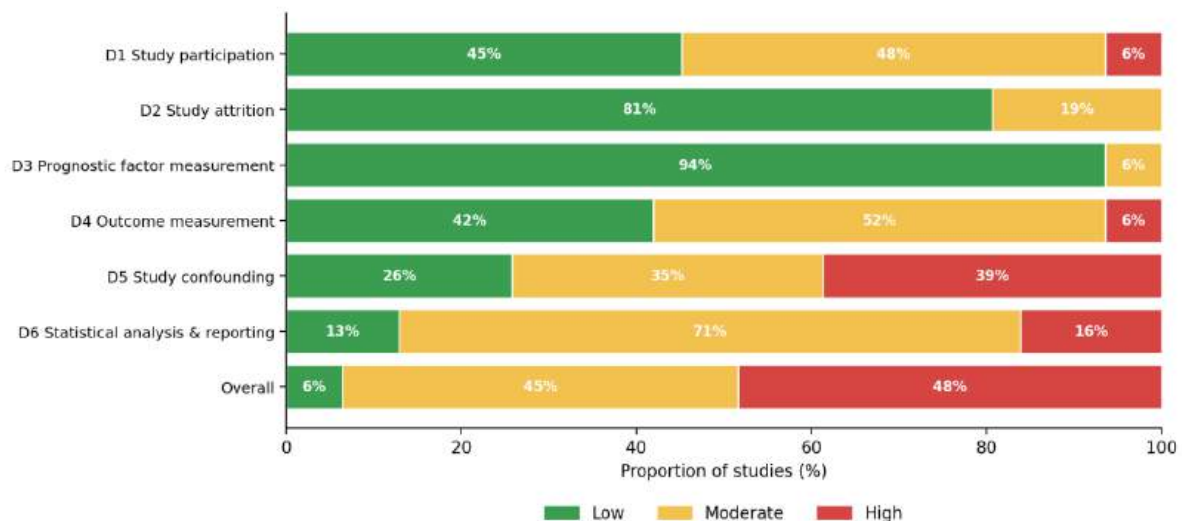


Figure 3. Risk-of-bias summary: proportion of studies at low, moderate and high risk in each QUIPS domain.^{22,29}

Effect measures and data synthesis

Single-arm proportions (mortality, favourable outcome) were transformed to the logit scale, with a continuity correction of 0.5 only for zero cells, pooled with a DerSimonian–Laird random-effects model and back-transformed; 95% confidence intervals (CIs) for individual studies were computed with the Wilson method. Associations between prognostic factors or timing and outcome were expressed as odds ratios (ORs) computed from two-by-two tables (continuity correction 0.5 for zero cells) and pooled with DerSimonian–Laird random-effects models. Meta-analysis was undertaken when at least two studies provided compatible data; estimates based on two or three studies are presented as exploratory. Ninety-five per cent prediction intervals were calculated for analyses with three or more studies. Pooled absolute risks in exposed and unexposed groups were also estimated to aid clinical interpretation, consistent with GRADE guidance for prognostic factors.^{21,54}

Heterogeneity was quantified with Cochran’s Q , I^2 and τ^2 . Pre-specified subgroup analyses examined income setting (LMIC vs HIC), study population (adult/mixed, paediatric, severe/comatose-only cohorts) and delay threshold (6 h, 12 h, 24 h). Sensitivity analyses included leave-one-out analysis; restriction to studies at low or moderate overall risk of bias; restriction to full-text-extracted studies; exclusion of the cohort that included non-operated patients; and, for sparse two-by-two data with zero cells, fixed-effect Mantel–Haenszel and Peto ORs. Random-effects meta-regression (method-of-moments estimator) explored whether case mix (proportion of patients with pre-operative GCS ≤ 8) and publication year explained

between-study variance in mortality, with the proportion of variance explained reported as an R^2 analogue.^{21,22}

Small-study effects were assessed visually with funnel plots and statistically with Egger's regression and Begg's rank-correlation tests when at least five studies were available; tests based on fewer than ten studies were interpreted as underpowered. Because funnel-plot asymmetry tests are known to perform poorly for single-arm proportions with low event rates, asymmetry in the pooled-mortality analysis was interpreted cautiously. All analyses were performed in Python (NumPy, SciPy) with purpose-written meta-analysis routines whose outputs were cross-checked against hand calculation; figures were drawn with Matplotlib.^{20,54}

Certainty of evidence

Certainty in pooled event rates and prognostic factor associations was rated with GRADE for prognosis. Following GRADE guidance, bodies of observational prognostic evidence started at high certainty and were rated down for risk of bias, inconsistency, indirectness, imprecision and publication bias, and rated up for a large magnitude of association or a dose-response gradient. Ratings were summarised in a summary-of-findings table.^{21,54,55}

Ethics

This review synthesised published, de-identified aggregate data and did not require ethical approval or informed consent.²⁰

RESULTS

Characteristics of included studies

The 31 included studies were published between 2013 and 2026 and enrolled 3,368 patients (sample size not reported in the accessible record of one study). Twenty-four studies originated from LMICs—Pakistan ($n = 7$), Bangladesh, Egypt and India ($n = 3$ each), Indonesia ($n = 2$), and Cameroon, China, the Democratic Republic of Congo, Ethiopia, Nigeria and South Africa ($n = 1$ each)—and seven from high-income countries (Austria [$n = 2$], Germany, Italy, Japan, Lithuania and South Korea). No randomized controlled trial was identified; the evidence comprised 20 retrospective cohort studies (including one multicentre national registry), eight prospective observational, interventional, cross-sectional or case-series studies, and three other cross-sectional or observational case series. Five studies were exclusively paediatric, two were restricted to comatose patients ($GCS\ 3-5$ and $GCS \leq 8$), and one was restricted to large hematomas (≥ 40 mL). Outcome was most commonly measured

with the GOS or GOSE at discharge, one month or three months; only three studies reported outcome at six months or later.^{5,35,38,39,47}

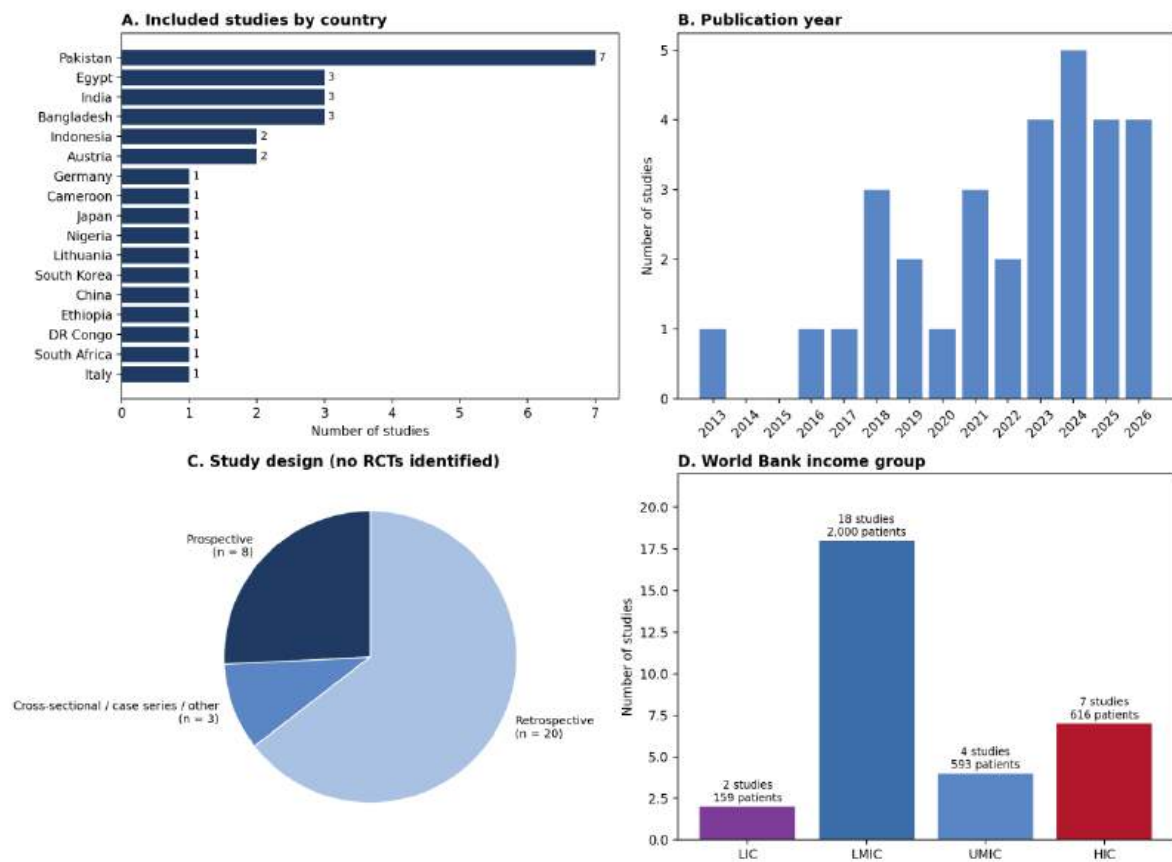


Figure 4. Overview of the included evidence: (A) country of origin, (B) publication year, (C) study design and (D) World Bank income group with number of studies and patients.⁴

Table 4. Characteristics of the 31 included primary studies (chronological order)

Author, year	Country (WB income)	Design	Study period	n	Population / age	Outcome instrument and time point	Data source
Javed 2013 ³¹	Pakistan (LMIC)	Prospective cohort	NR	24	Paediatric (mean 8.6 y)	GOS, 1–3 mo	Full text
Ali 2016 ²⁷	Pakistan (LMIC)	Cross-sectional	May–Nov 2012	194	All ages	GOS, 48 h post-op	Abstract
Niryana 2017 ²⁵	Indonesia (UMIC)	Retrospective cohort	Jun 2015–Jun 2016	60	All ages (73% < 40 y)	GOS, 3 mo	Full text
Gutowski 2018 ³²	Germany (HIC)	Retrospective cohort	1997–2012	131	All ages	GOS, discharge	Abstract
Ndoumbe 2018 ³³	Cameroon (LMIC)	Retrospective cohort	Feb 2006–Dec 2013	46	All ages (mean 29.6 y)	GOS	Full text
Elsayed 2018 ³⁴	Egypt (LMIC)	Observational case series	NR	50	3–63 y (mean 38.5 y)	Clinical outcome at discharge	Abstract
Rosyidi 2019 ⁸	Indonesia (UMIC)	Retrospective (prospectively collected)	Jan 2009–May 2012	268	All ages (mean 27.1 y)	In-hospital mortality	Abstract
Kandregula 2019 ³⁵	India (LMIC)	Retrospective cohort	2011–2017	201	Paediatric	GOS, median 13.5 mo	Abstract

Onodera 2020 ³⁶	Japan (HIC)	Retrospective cohort	Sep 2011–2018	58	All ages (mean 49.8 y)	GOS	Full text
Ayogu 2021 ³⁷	Nigeria (LMIC)	Retrospective cohort	Jan 2015–Dec 2019	71	All ages (mean 30.3 y)	GOS, 3 mo	Full text
Howlader 2021 ⁹	Bangladesh (LMIC)	Prospective observational	Jan 2016–Dec 2017	98	4–55 y (mean 25.2 y)	GOS, discharge & 1 mo	Full text
Vilcinis 2021 ³⁸	Lithuania (HIC)	Retrospective cohort	12-year period	60	Comatose (GCS 3–5) adults	Mortality, GOS at discharge	Abstract
Choi 2022 ³⁹	South Korea (HIC)	Multicentre registry (KNTDB)	Jan 2018–Jun 2021	79	Severe TBI (GCS $\leq$ 8)	GOSE, 6 mo	Full text
Kapoor 2022 ⁴⁰	India (LMIC)	Observational	NR	35	All ages	GOS	Full text
Echara 2023 ⁴¹	India (LMIC)	Retrospective cohort	Jan 2016–Dec 2021	350	Paediatric ($\leq$ 18 y)	GOS discharge; GOS-E Peds 3 mo	Abstract
Miao 2023 ⁴²	China (UMIC)	Retrospective cohort	NR	40	Paediatric posterior fossa EDH	GOS	Abstract
Khalid 2023 ⁴³	Pakistan (LMIC)	Retrospective cohort	Jan 2019–Dec 2021	116	All ages (52.6% $\leq$ 15 y)	GOS, discharge	Full text
Marhold 2023 ⁵	Austria (HIC)	Retrospective cohort, long-term F/U	Apr 2002–Dec 2014	72	All ages (mean 39 y)	eGOS, discharge & > 6 y	Full text
Das 2024 ¹⁰	Bangladesh	Prospective	Jan 2017–Dec	NR	All ages	GOS, 48 h &	Abstract

	(LMIC)	interventional	2019			discharge	
Jabbar 2024 ⁴⁴	Bangladesh (LMIC)	Prospective interventional	Sep 2022–Feb 2024	81	1.5–60 y (median 22 y)	GOS, 3 mo	Abstract
Ullah 2024 ⁴⁵	Pakistan (LMIC)	Prospective case series	Apr–Nov 2021	78	All ages	GOS, discharge	Full text
Adalat 2024 ⁴⁶	Pakistan (LMIC)	Prospective observational	Jun–Dec 2023	51	Adults 18–60 y	GOS, 3 mo	Full text
Elkholy 2024 ⁴⁷	Egypt (LMIC)	Retrospective comparative cohort	Jul 2020–Dec 2022	93	Large EDH (≥ 40 mL), GCS 4–13	GOS, discharge & 1 mo	Abstract
Kebede 2025 ⁴⁸	Ethiopia (LIC)	Prospective cross-sectional (2 centres)	Feb 2020–Sep 2022	132	All ages (mean 30.8 y)	GOS-E, discharge	Abstract
Khan Z 2025 ²⁶	Pakistan (LMIC)	Retrospective cohort	Jan 2022–Dec 2023	178	Adults	Survival, 3-mo recovery	Full text
Gmeiner 2025 ⁴⁹	Austria (HIC)	Retrospective cohort	2009–2020	131	All ages	GOS	Abstract
Tshiamala Ngalula 2025 ⁵⁰	DR Congo (LIC)	Retrospective cohort (EDH subgroup)	Jan 2021–Apr 2024	27	≥ 2 y (EDH subgroup)	GOS, discharge	Full text
Mercea 2026 ⁵¹	South Africa (UMIC)	Retrospective cohort	Jan 2011–Jan 2022	225	Adults (median 28 y); 78.7% operated	GOSE, discharge	Full text

Marchesini 2026 ⁷	Italy (HIC)	Retrospective cohort + historical controls	2011–2021	85	All ages (mean 39.8 y)	GOS, discharge	Full text
Khan MS 2026 ⁵²	Pakistan (LMIC)	Retrospective cohort	24-month period	289	158 adults + 131 children	In-hospital mortality	Abstract
Taha 2026 ⁵³	Egypt (LMIC)	Prospective observational	Dec 2021–Dec 2023	45	Paediatric (median 15 y)	GOS, 3 mo	Abstract

WB, World Bank; LIC, low-income; LMIC, lower-middle-income; UMIC, upper-middle-income; HIC, high-income; GOS, Glasgow Outcome Scale; GOSE, extended GOS; GOS-E Peds, paediatric GOSE; eGOS, extended GOS; F/U, follow-up; KNTDB, Korean Neuro-Trauma Data Bank; NR, not reported. Data source indicates whether extraction used the full text or the abstract plus Crossref-verified metadata.

Table 5. Outcomes, time-to-surgery findings and prognostic factors reported by each included study

Author, year	Mortality / poor outcome, n (%)	Time-to-surgery data and finding	Prognostic factors reported as significant
Javed 2013 ³¹	3 (12.5%)	Median injury-to-surgery 10 h; delay → poorer GOS (p = 0.021)	GCS, age, injury-to-surgery time, anisocoria, basal cisterns
Ali 2016 ²⁷	Good outcome 157 (80.9%)	Surgery ≤ 6 h associated with good outcome	GCS, anisocoria, volume < 60 mL, associated lesions, time
Niryana 2017 ²⁵	3 (5.0%)	≥ 12 h independent predictor (adjusted RR 4.66)	GCS ≤ 8, pre-operative duration ≥ 12 h
Gutowski 2018 ³²	9 (6.8%)	NR	Associated intracranial injury, midline shift, ISS, alcohol

Ndoumbe 2018 ³³	6 (13.0%)	Mean trauma-to-surgery 78 h (companion report)	GCS $\leq$ 8
Elsayed 2018 ³⁴	4 (8.0%)	Most operated within 5 h of trauma	GCS < 8, size, time, posterior fossa site
Rosyidi 2019 ⁸	31 (11.6%)	Trauma–operation interval reported as outcome determinant	Interval, age, pre-operative status, extracranial injury
Kandregula 2019 ³⁵	1 (0.5%)	Median injury-to-diagnosis 14.7 h	Pupillary asymmetry, pyramidal signs, GCS, parenchymal injury
Onodera 2020 ³⁶	NR (poor outcome 50%)	Onset-to-operation 441 $\pm$ 308 min; not associated	Age < 55 y and GCS > 12 (independent)
Ayogu 2021 ³⁷	12 (16.9%)	Median injury-to-presentation 15 h; time not associated (p = 0.947)	GCS severity
Howlader 2021 ⁹	3 (3.1%)	Only 3.1% operated $\leq$ 6 h; 30.6% > 24 h	GCS, pupils, focal deficit
Vilcinis 2021 ³⁸	18 (30.0%)	NR	Decompressive craniectomy vs osteoplastic craniotomy
Choi 2022 ³⁹	11 (13.9%)	Admission-to-surgery 156–172 min; not associated	Age, bilateral unreactive pupils (independent)
Kapoor 2022 ⁴⁰	1 (2.9%)	NR	GCS
Echara 2023 ⁴¹	NR	Trauma-to-surgery interval correlated with GOS (supratentorial)	GCS, volume, mass effect, anisocoria, hypotension
Miao 2023 ⁴²	Poor outcome 8 (20%)	NR	GCS, convex hematoma morphology

Khalid 2023 ⁴³	5 (4.3%)	64.7% $\leq$ 6 h; all deaths operated > 6 h	GCS, pupils, associated lesions, delay, sex, age < 5 y
Marhold 2023 ⁵	1 in-hospital; 7 at F/U (10%)	NR	Additional intracranial injuries
Das 2024 ¹⁰	NR	Surgery $\leq$ 12 h associated with good outcome	GCS > 8, volume < 40 mL, anisocoria, associated injury, time
Jabbar 2024 ⁴⁴	Poor/death 5 (6.2%)	NR	GCS 3–8, mydriasis, volume > 50 mL, MLS, basal cisterns
Ullah 2024 ⁴⁵	4 (5.1%)	59.0% $\leq$ 6 h	Time from injury to surgery
Adalat 2024 ⁴⁶	8 (15.7%)	70.6% $\leq$ 6 h; mean 5.7 $\pm$ 3.3 h	Time from injury to surgery
Elkholy 2024 ⁴⁷	NR (higher if > 6 h; p = 0.014)	53.8% $\leq$ 6 h	Time from injury to surgery
Kebede 2025 ⁴⁸	4 (3.0%)	NR	Post-resuscitation GCS, cisterns, hemiparesis, SpO ₂ , pupils
Khan Z 2025 ²⁶	8 (4.5%)	Delay 7.9 h (survivors) vs 16.4 h (deaths); OR 1.16/h	Delay, volume, location, age, HTN, DM, logistics, resources
Gmeiner 2025 ⁴⁹	NR	Median time to surgery 4 h; transfer & time not associated	Interhospital transport pattern
Tshiamala Ngalula 2025 ⁵⁰	4 (14.8%)	Time > 24 h associated with death (whole cohort)	GCS < 8, time > 24 h
Mercea 2026 ⁵¹	11 (4.9%)	Median injury-to-surgery 32 h; not	TBI severity (independent); age, pupils

		independently associated	
Marchesini 2026 ⁷	2 (2.4%)	Median trauma-to-surgery 4.9 h; 68% ≤ 6 h	Last GCS, pupils, age, associated lesion
Khan MS 2026 ⁵²	26 (9.0%)	Children: OR 0.78 per hour earlier surgery; adults U-shaped	MLS, ASDH, tSAH, volume ≥ 33.5 mL (children)
Taha 2026 ⁵³	3 (6.7%)	Median injury-to-diagnosis 5.8 h	LOC, GCS, pupillary asymmetry, deficit, abdominal injury

h, hours; min, minutes; MLS, midline shift; ASDH, acute subdural hematoma; tSAH, traumatic subarachnoid haemorrhage; ISS, Injury Severity Score; HTN, hypertension; DM, diabetes mellitus; LOC, loss of consciousness; SpO₂, peripheral oxygen saturation; NR, not reported.

Pooled mortality after surgical evacuation

Twenty-one studies (1,907 patients, 141 deaths) contributed to the pooled mortality analysis. Pooled mortality was 7.5% (95% CI 5.2–10.6), with substantial heterogeneity ($I^2 = 74\%$, $\tau^2 = 0.519$) and a 95% prediction interval of 1.7–27.8%, meaning that a new centre could plausibly observe anything from near-zero to more than one-quarter mortality. Mortality did not differ between LMIC (7.2%, 95% CI 5.0–10.2; $k = 16$) and HIC settings (8.2%, 95% CI 3.1–20.0; $k = 5$; test for subgroup differences $p = 0.81$), but this comparison was distorted by the two HIC cohorts restricted to comatose patients. When analyses were restricted to adult or mixed-age, all-comer cohorts, mortality was 7.7% (95% CI 5.3–10.9; $k = 13$) in LMICs and 3.7% (95% CI 1.4–9.7; $k = 3$) in HICs.^{5,7,8,32,37}

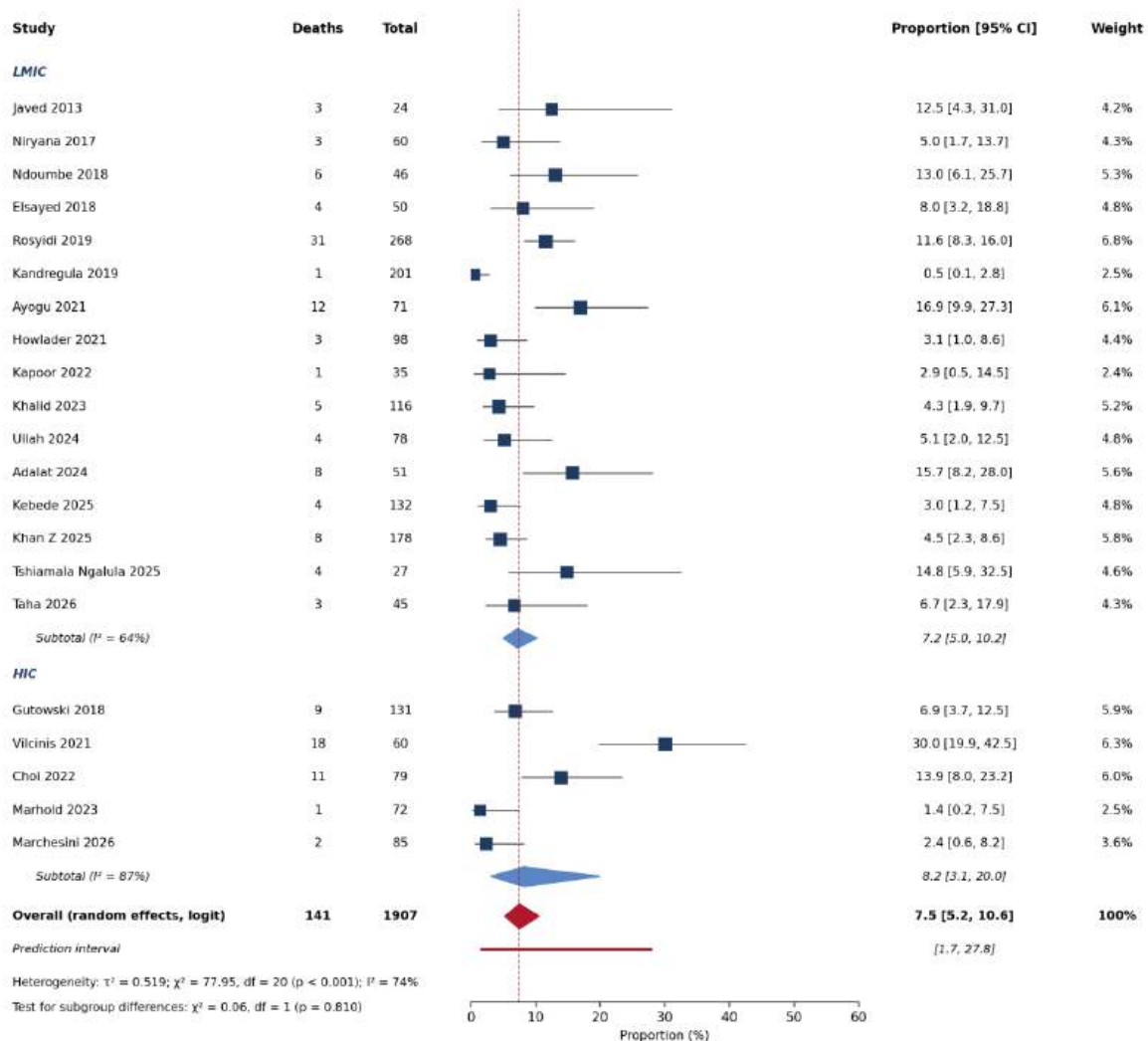


Figure 5. Forest plot of pooled in-hospital/short-term mortality after surgical evacuation of acute EDH, stratified by income setting (random effects, logit transformation). Squares are proportional to study weight; horizontal lines are Wilson 95% CIs; diamonds are pooled estimates; the red bar is the 95% prediction interval.⁵⁴

Stratification by population explained part of the heterogeneity (test for subgroup differences $p = 0.036$; Figure 7). Mortality was 6.9% (95% CI 4.9–9.6; $k = 16$) in adult or mixed-age cohorts, 4.2% (95% CI 0.9–18.6; $k = 3$) in paediatric cohorts and 21.1% (95% CI 9.3–40.9; $k = 2$) in cohorts restricted to comatose patients (Korean national data bank, $GCS \leq 8$; Lithuanian

cohort, GCS 3–5). Excluding comatose-only cohorts, pooled mortality was 6.6% (95% CI 4.7–9.2; $k = 19$). The two Indonesian cohorts (Denpasar and Surabaya) yielded a pooled mortality of 9.0% (95% CI 4.1–18.4).^{8,25,35,38,39}

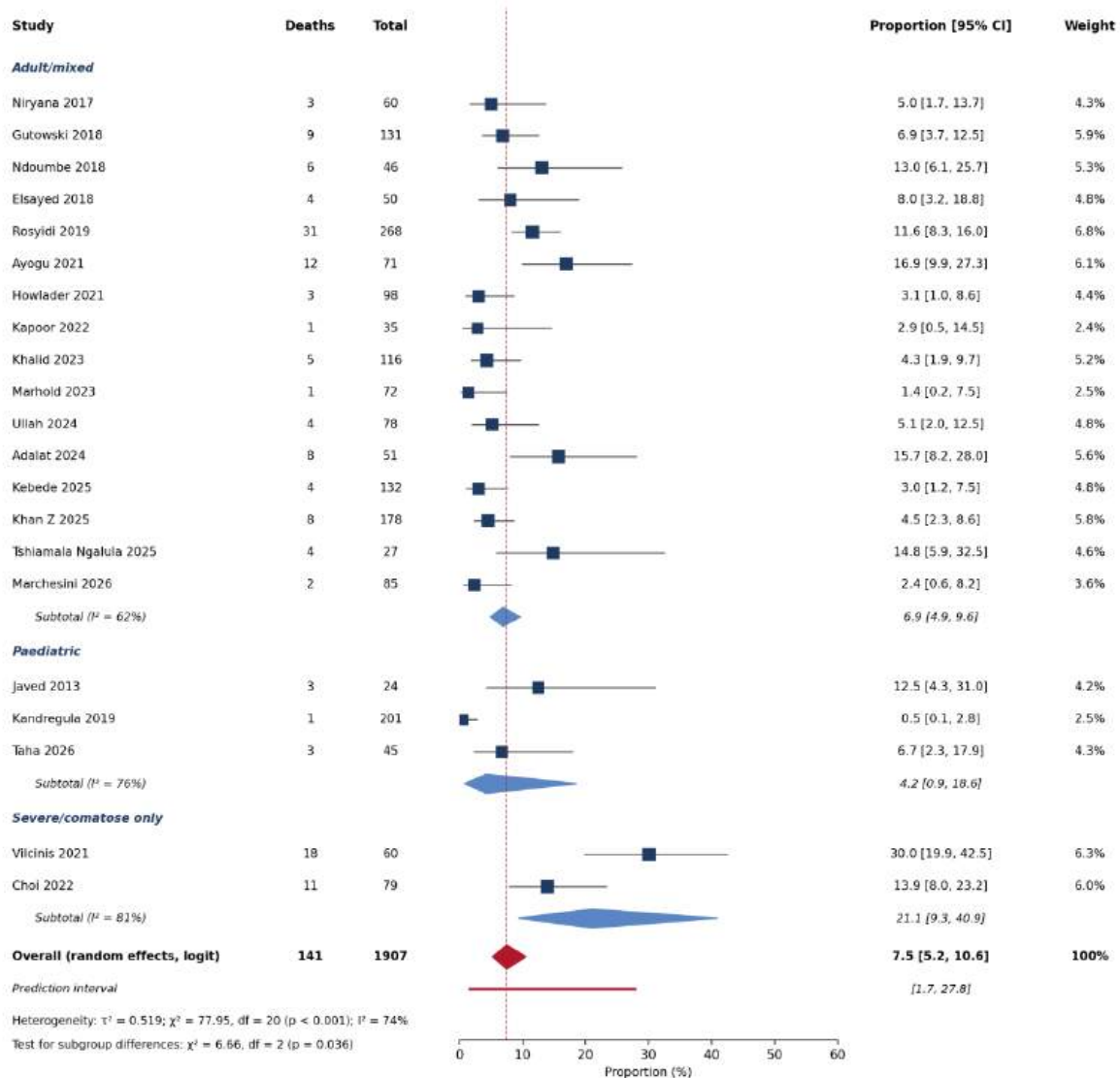


Figure 6. Forest plot of pooled mortality stratified by study population: adult/mixed-age, paediatric and severe/comatose-only cohorts.⁵⁴

Random-effects meta-regression in 13 studies that reported the proportion of patients with pre-operative GCS ≤ 8 showed that case mix was a significant moderator of mortality: each 10-

percentage-point increase in the proportion of comatose patients was associated with a 20% increase in the odds of death (OR 1.20, 95% CI 1.05–1.37; $p = 0.008$), explaining 38% of between-study variance (Figure 8). Publication year was not associated with mortality (slope -0.055 logit units per year; $p = 0.35$; Figure 9), indicating no detectable temporal trend within the 2013–2026 window.^{9,26,39,43}

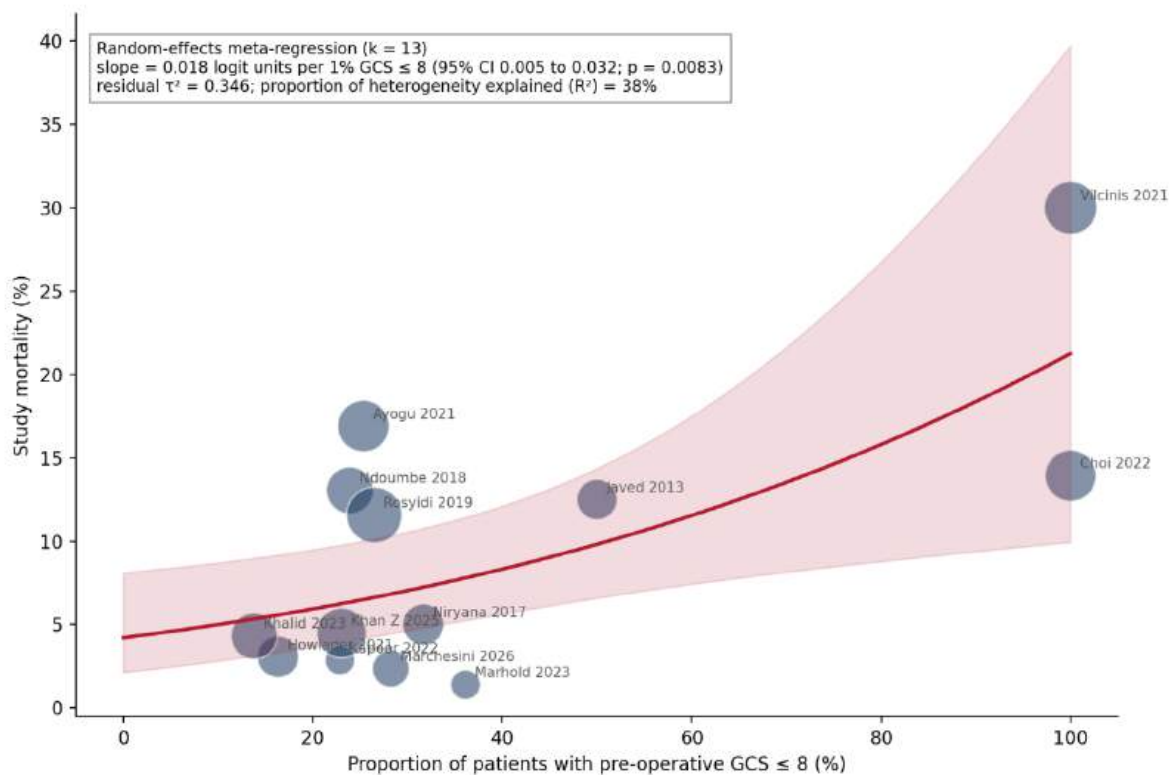


Figure 7. Bubble plot of random-effects meta-regression of study mortality on the proportion of patients with pre-operative $GCS \leq 8$ (bubble size proportional to weight; shaded band = 95% CI of the fitted line).⁵⁴

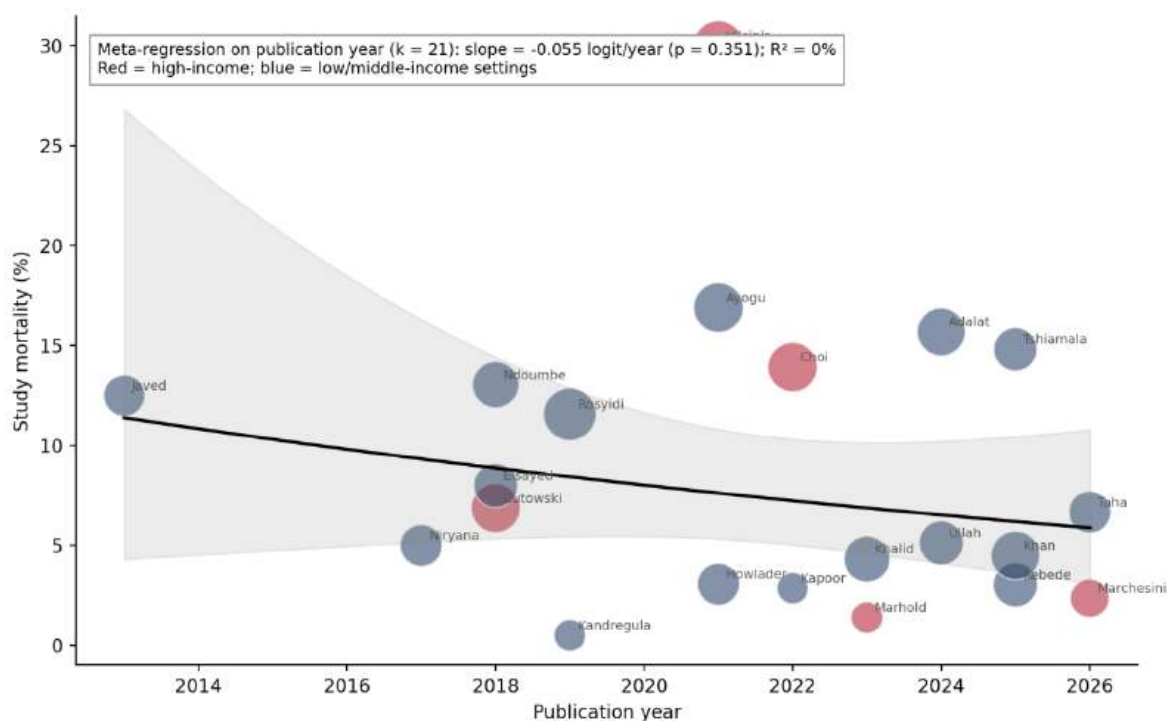


Figure 8. Bubble plot of study mortality by publication year (red = high-income, blue = low/middle-income settings).⁴

Favourable functional outcome

Fifteen studies reported the proportion of patients with favourable outcome (GOS 4–5 or GOSE 5–8). The pooled proportion was 78.9% (95% CI 72.8–84.0; $I^2 = 79\%$; prediction interval 50.5–93.2%; Figure 10). Excluding the study that defined favourable outcome as GOS 5 only did not change the estimate (79.8%, 95% CI 73.5–84.9). Restricting to studies at low or moderate risk of bias gave a lower estimate of 71.6% (95% CI 59.2–81.4; k = 6), reflecting longer follow-up and stricter outcome ascertainment in better-quality cohorts, and the larger share of comatose patients in two of them. The Korean registry of exclusively comatose patients still documented favourable recovery in 60.8% at six months, and the Austrian long-term cohort reported good recovery in 91% of isolated EDH versus 50% of EDH with additional intracranial injury at a mean follow-up of more than six years.^{5,36,37,39}

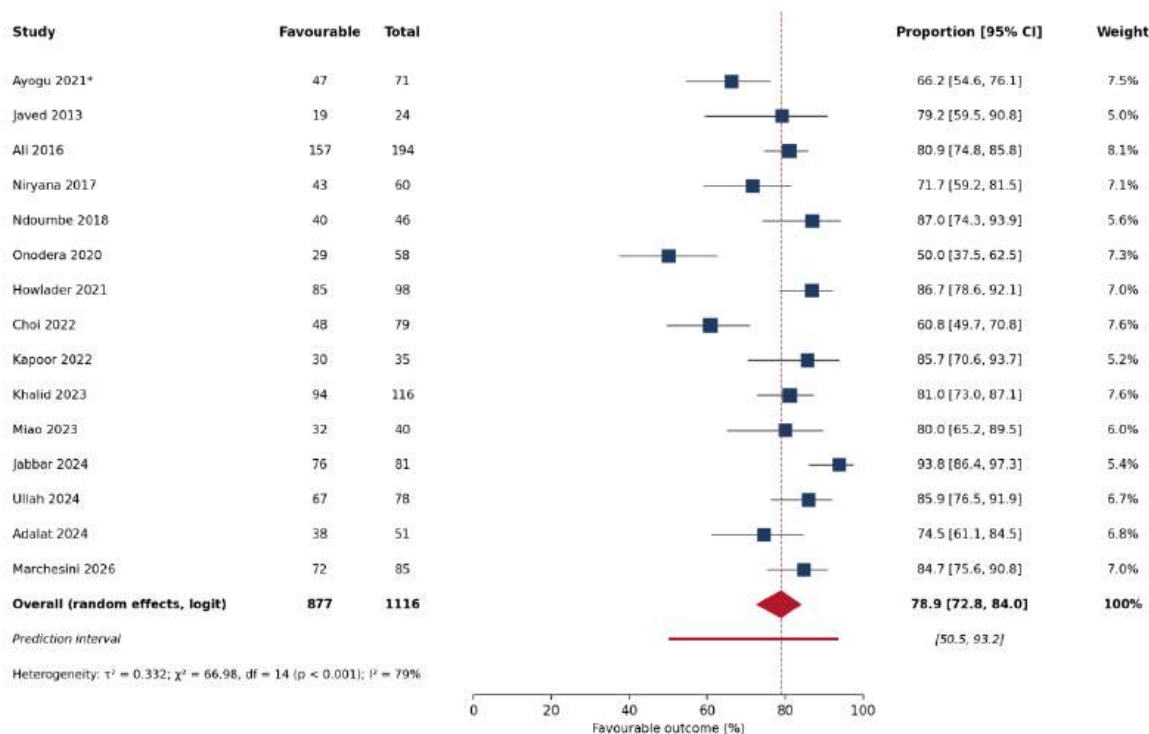


Figure 9. Forest plot of the pooled proportion of favourable functional outcome after surgical evacuation. *Ayogu 2021 defined favourable outcome as GOS 5 only.⁵⁴

Timing of evacuation

Delayed versus early evacuation and mortality

Five studies (387 patients) provided mortality data for delayed versus early evacuation: four used a 6-hour threshold and one a 24-hour threshold. The random-effects OR was 6.52 (95% CI 0.95–44.88; $p = 0.057$; $I^2 = 67\%$). Because three of the five studies recorded no deaths in the early group, sparse-data methods were applied: the Mantel–Haenszel OR was 4.60 (95% CI 1.98–10.68) and the Peto OR 5.69 (95% CI 2.60–12.46). For the 6-hour threshold, the association was strong and consistent (random-effects OR 14.23, 95% CI 2.90–69.78; $I^2 = 16\%$; Peto OR 18.84, 95% CI 7.00–50.72). In absolute terms, pooled mortality was 16.7% (95% CI 7.4–33.4) after delayed evacuation versus 2.8% (95% CI 0.5–13.5) after early evacuation.^{7,37,43,45,46}

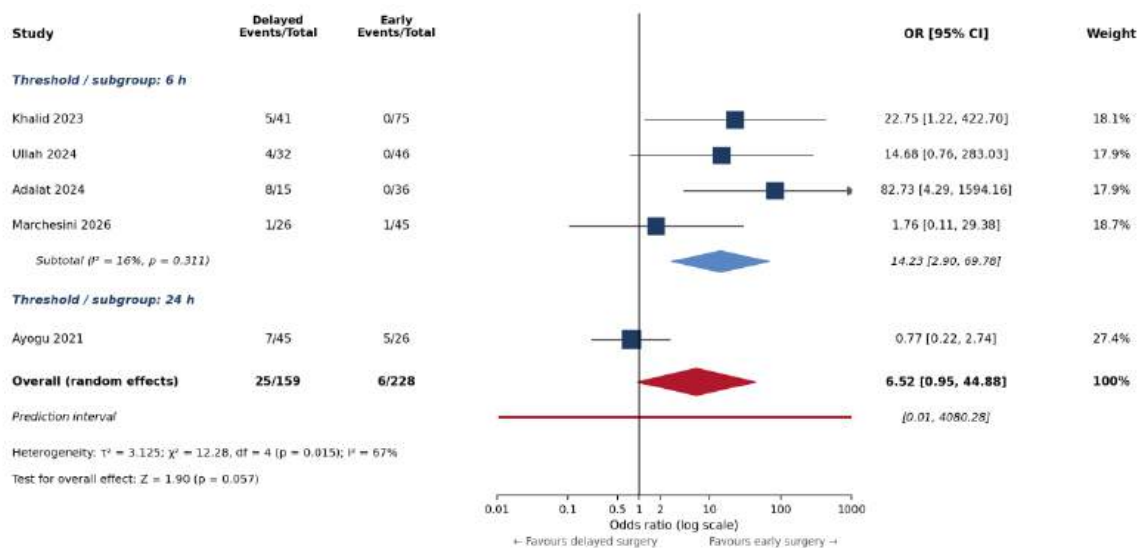


Figure 10. Forest plot of delayed versus early surgical evacuation and mortality, by study-specific delay threshold.^{37,43}

Delayed versus early evacuation and unfavourable outcome

Six studies (447 patients) contributed data on unfavourable outcome. Delayed evacuation was associated with unfavourable outcome (OR 6.17, 95% CI 1.27–29.94; $p = 0.024$), with considerable heterogeneity ($I^2 = 86\%$) and a prediction interval spanning harm and benefit (0.03–1396). The heterogeneity was structured rather than random. Four LMIC studies showed large harms of delay—the Indonesian cohort from Denpasar reported unfavourable outcome in 71.4% of patients operated ≥ 12 hours after injury versus 5.1% of those operated earlier (OR 46.25)—whereas the Italian cohort and the Nigerian cohort (24-hour threshold) showed no excess or an inverse association. Restricted to LMIC studies, the OR was 10.56 (95% CI 1.81–61.58; $k = 5$), and the Mantel–Haenszel OR across all six studies was 3.72 (95% CI 2.38–5.82). Pooled absolute risk of unfavourable outcome was 41.2% (95% CI 23.2–61.8) after delayed versus 11.4% (95% CI 5.0–23.9) after early evacuation.^{7,25,37,43,45,46}

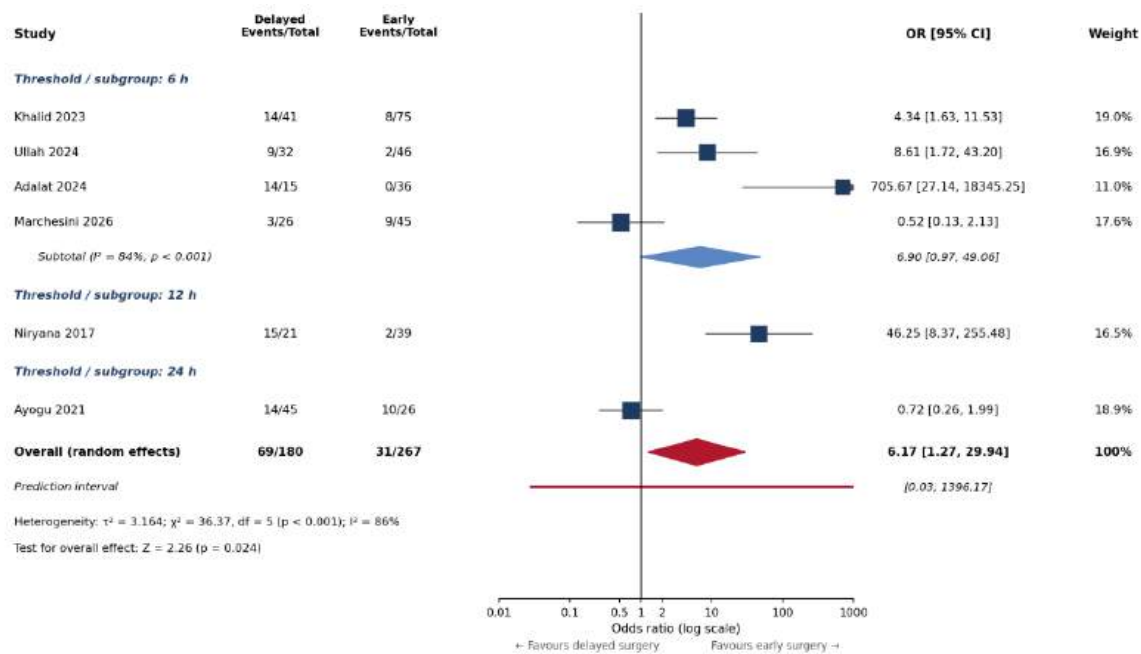


Figure 11. Forest plot of delayed versus early surgical evacuation and unfavourable functional outcome, stratified by delay threshold (6 h, 12 h, 24 h).^{25,37}

Studies not amenable to pooling

Several studies examined timing in ways that could not be pooled but were consistent with the meta-analytic pattern. In Egypt, among 93 patients with large hematomas (≥ 40 mL) and comparable baseline characteristics, surgery more than 6 hours after injury was associated with higher mortality ($p = 0.014$), worse functional recovery and longer hospital stay. In Peshawar, each additional hour of pre-surgical delay increased the odds of an adverse outcome (adjusted OR 1.16 per hour, 95% CI 1.10–1.23), and mean delay was 16.4 hours in patients who died versus 7.9 hours in survivors. In children, earlier surgery was linearly associated with lower mortality (OR 0.78 per hour), whereas adult mortality followed a U-shaped relationship with timing. A Bangladeshi cohort identified surgery within 12 hours, and a Pakistani paediatric cohort a shorter injury-to-surgery interval, as determinants of good outcome.^{10,26,31,47,52}

By contrast, four studies found no independent association. In South Africa, patients with unfavourable outcome were operated on sooner (median injury-to-surgery 19 vs 35 hours), and

neither injury-to-surgery nor admission-to-surgery interval was associated with outcome after adjustment for age and TBI severity. In Japan, mean onset-to-operation time was shorter in patients with poor outcome (383 vs 478 minutes), in Korea admission-to-surgery time did not differ by outcome, and in Austria neither time to surgery nor interhospital transport affected outcome. These four cohorts share a common feature: surgery was prioritised by neurological severity, so that crude time–outcome associations were confounded by indication.^{36,39,49,51}

Time-to-care metrics and facility- and human resource-related causes of delay

Reported time-to-care intervals differed by an order of magnitude between settings. In high-income cohorts, median admission-to-surgery or injury-to-surgery intervals ranged from 2.7 to 4.9 hours, and 68% of Italian patients were operated within 6 hours. In LMIC cohorts, the proportion operated within 6 hours ranged from 70.6% in Islamabad to only 3.1% in Dhaka, where 30.6% of patients waited more than 24 hours. Median injury-to-presentation was 15 hours in Abuja, median injury-to-surgery 32 hours in South Africa and mean trauma-to-surgery 78 hours in Yaoundé. Within the Italian system, referred patients had longer trauma-to-door (3.7 vs 1.2 hours) and trauma-to-surgery intervals (5.2 vs 3.4 hours) than direct admissions, and night-time arrivals had longer trauma-to-door times (2.9 vs 1.2 hours).^{7,9,37,46,51,56}

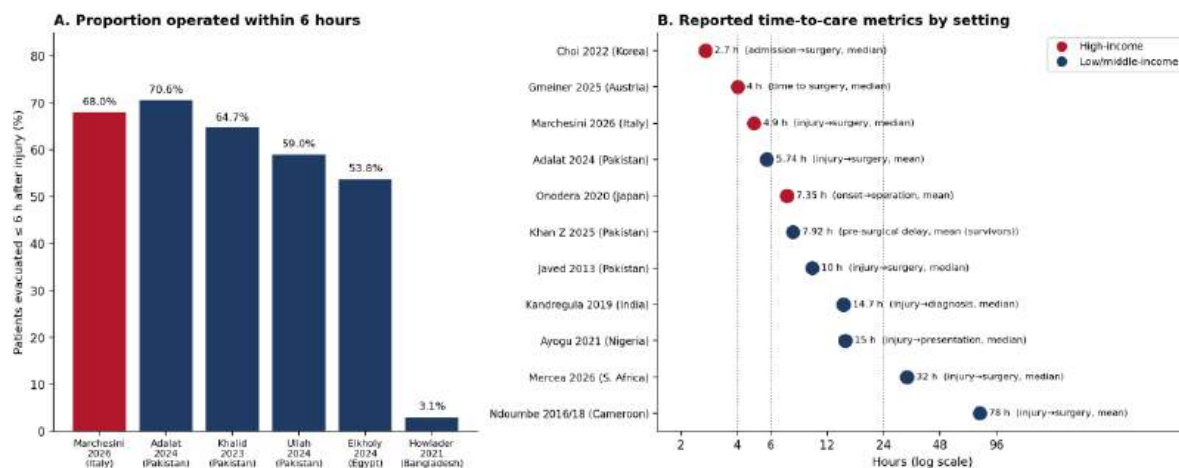


Figure 12. Time-to-care metrics: (A) proportion of patients evacuated within 6 hours of injury; (B) reported median or mean time intervals by study and income setting (log scale; dotted lines at 4, 6 and 24 hours).^{7,9,51}

Only one included study quantified the causes of pre-surgical delay directly. Among 178 adults operated for EDH at a tertiary hospital in Peshawar, delays were attributed to logistical issues (patient transport, bed availability and operating-room scheduling; 28.1%), the optimisation of comorbidities (25.3%), resource constraints (limited surgical staff, intensive care unit bed shortages and equipment unavailability; 22.5%), delayed diagnosis including delayed imaging (16.9%) and trauma complexity (7.3%). In multivariable analysis, both logistical issues (OR 1.28, 95% CI 1.01–1.63) and resource constraints (OR 1.35, 95% CI 1.05–1.74) were independently associated with adverse outcome.²⁶

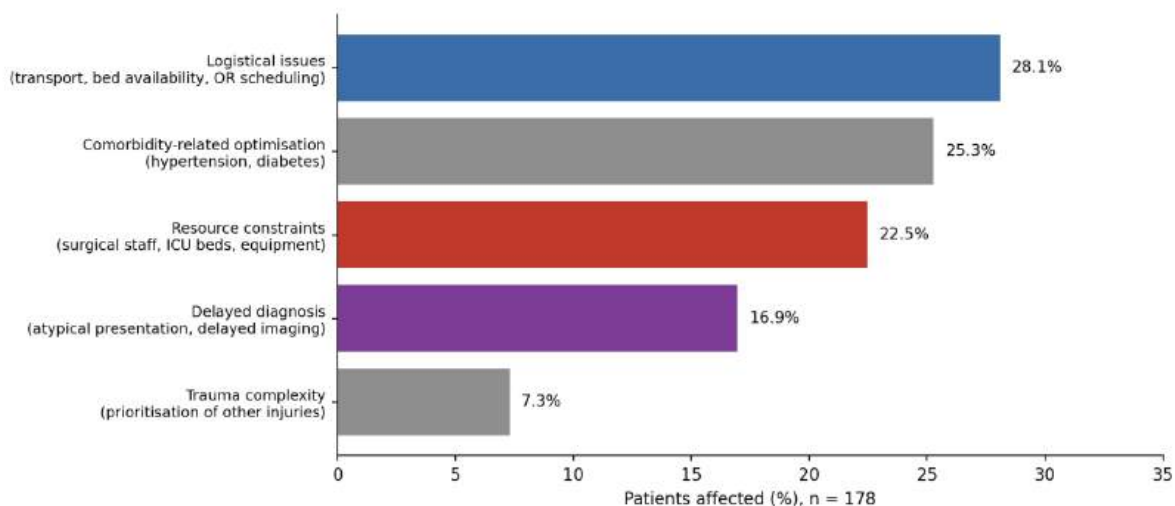


Figure 13. Reported causes of pre-surgical delay among 178 surgically treated EDH patients in Peshawar, Pakistan (proportion of patients affected). Facility- and human resource-related categories are highlighted.²⁶

Table 6. Facility- and human resource-related delay data reported by included studies, mapped to the three-delay framework

Study (setting)	Delay phase	Metric reported	Facility / human-resource factor implicated
Khan Z 2025 (Pakistan,	Delay	Logistics 28.1%; resource	Transport, bed

LMIC) ²⁶	2–3	constraints 22.5%; delayed imaging 16.9%	availability, theatre scheduling; surgical staff, ICU beds, equipment
Howlader 2021 (Bangladesh, LMIC) ⁹	Delay 2–3	3.1% operated $\leq$ 6 h; 30.6% > 24 h	Referral-dependent tertiary centre
Ayogu 2021 (Nigeria, LMIC) ³⁷	Delay 1–2	Median injury-to-presentation 15 h; 16.9% operated $\geq$ 4 days	Late presentation and referral
Mercea 2026 (South Africa, UMIC) ⁵¹	Delay 2–3	Injury-to-admission 8.5 h; admission-to-surgery 13 h	Limited neurosurgical centres serving public sector
Ndoubmé 2016/2018 (Cameroon, LMIC) ^{33,56}	Delay 1–3	Mean trauma-to-surgery 78 h; early surgery rarely performed	Limited access to emergency neurosurgery
Kandregula 2019 (India, LMIC) ³⁵	Delay 1–2	Median injury-to-diagnosis 14.7 h (children)	Transfer to tertiary centre
Rosyidi 2019 (Indonesia, UMIC) ⁸	Delay 2–3	Trauma–operation interval among outcome determinants	"Problems and challenges in the developing country"
Niryana 2017 (Indonesia, UMIC) ²⁵	Delay 2–3	35% operated $\geq$ 12 h; $\geq$ 12 h independent predictor	Referral to provincial tertiary centre
Tshiamala Ngalula 2025 (DR Congo, LIC) ⁵⁰	Delay 2–3	Time-to-surgery > 24 h associated with death	Resource constraints; CT availability
Marchesini 2026 (Italy, HIC) ⁷	Delay 2	Referred vs direct: trauma-to-surgery 5.2 vs 3.4 h; night vs day trauma-to-	Interhospital referral; out-of-hours arrival

		door 2.9 vs 1.2 h	
Gmeiner 2025 (Austria, HIC) ⁴⁹	Delay 2	Median time to surgery 4 h; mean distance 50 km; transfer not associated with outcome	Organised transfer system
Choi 2022 (Korea, HIC) ³⁹	Delay 3	Admission-to-CT longer in unfavourable group (33 vs 23.5 min)	In-hospital imaging workflow

Delay 1, recognition and decision to seek care; Delay 2, reaching a facility capable of surgery (transport and referral); Delay 3, receiving definitive evacuation after arrival (CT, neurosurgeon, theatre, ICU).

Pre-operative prognostic factors

Glasgow Coma Scale

Pre-operative GCS ≤ 8 was the most consistent predictor of poor outcome. In five studies (n = 353), it was associated with a nine-fold increase in the odds of death (OR 9.26, 95% CI 3.68–23.33; $I^2 = 0\%$; Peto OR 19.76, 95% CI 7.45–52.43), corresponding to pooled mortality of 25.1% (95% CI 13.8–41.2) in patients with GCS ≤ 8 versus 2.9% (95% CI 0.8–9.9) in those with GCS > 8 (Figure 15). In eight studies (n = 734), GCS ≤ 8 was associated with unfavourable outcome (OR 17.34, 95% CI 7.54–39.88; $I^2 = 59\%$), and excluding the cohort that included non-operated patients removed heterogeneity (OR 21.45, 95% CI 11.47–40.09; $I^2 = 3\%$). Unfavourable outcome occurred in 59.3% (95% CI 49.2–68.6) of comatose patients versus 6.6% (95% CI 3.1–13.5) of non-comatose patients. Leave-one-out estimates ranged from 14.14 to 21.46 (Figure 28). Multivariable analyses in Japan and Indonesia confirmed GCS as an independent predictor, while a German cohort was the only study to report no significant effect of admission GCS.^{7,25,32,33,36,37,40,43}

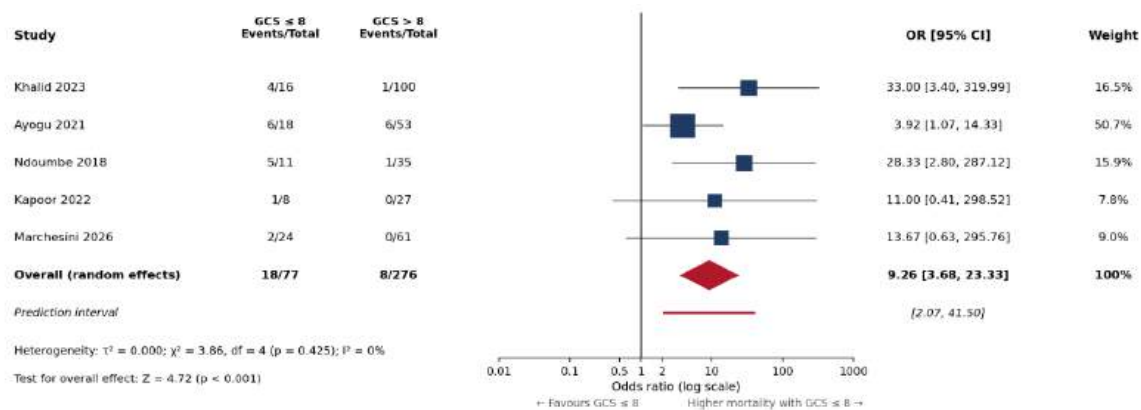


Figure 14. Forest plot of pre-operative GCS ≤ 8 versus GCS > 8 and mortality.^{33,43}

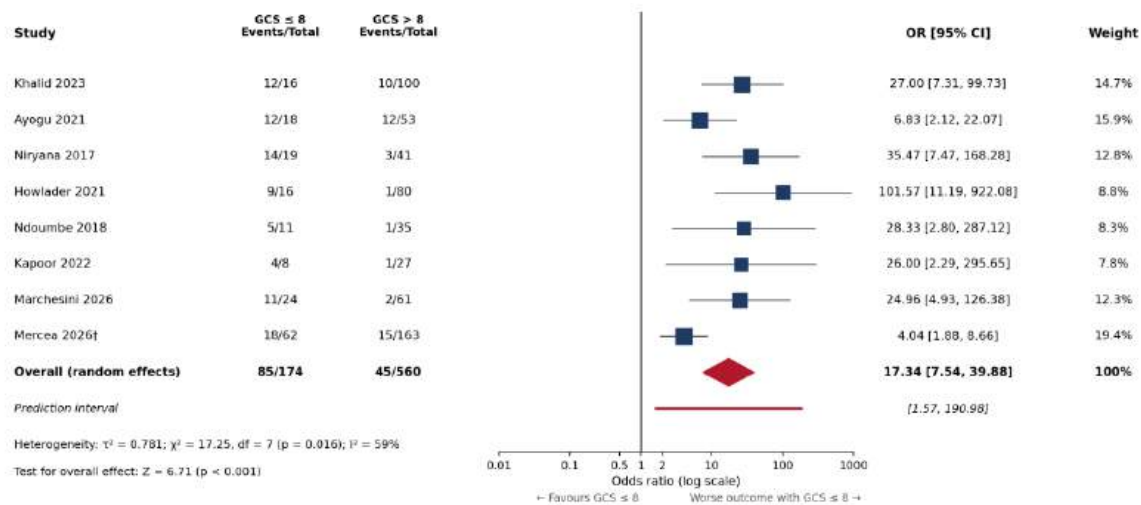


Figure 15. Forest plot of pre-operative GCS ≤ 8 versus GCS > 8 and unfavourable outcome.
†Mercea 2026 included 21.3% non-operated patients and used TBI severity categories.^{9,51}

Pupillary status

Abnormal pupillary status (anisocoria, unilateral or bilateral unreactive pupils) was associated with unfavourable outcome in six studies ($n = 623$; OR 5.85, 95% CI 3.10–11.05; $I^2 = 41\%$), with unfavourable outcome in 59.4% of patients with abnormal pupils versus 17.6% with normal pupils. The estimate was stable after excluding the mixed-management cohort (OR 7.46, 95% CI 4.03–13.82; $I^2 = 13\%$) and after restriction to low/moderate risk-of-bias studies (OR 4.92, 95% CI 2.72–8.91). Two studies provided mortality data (OR 24.97, 95% CI 4.75–131.36). In the

Korean comatose cohort, bilateral unreactive pupils were an independent predictor of unfavourable outcome, yet 8 of 26 patients with bilateral unreactive pupils (31%) still achieved a favourable six-month outcome.^{7,25,36,39,43,51}

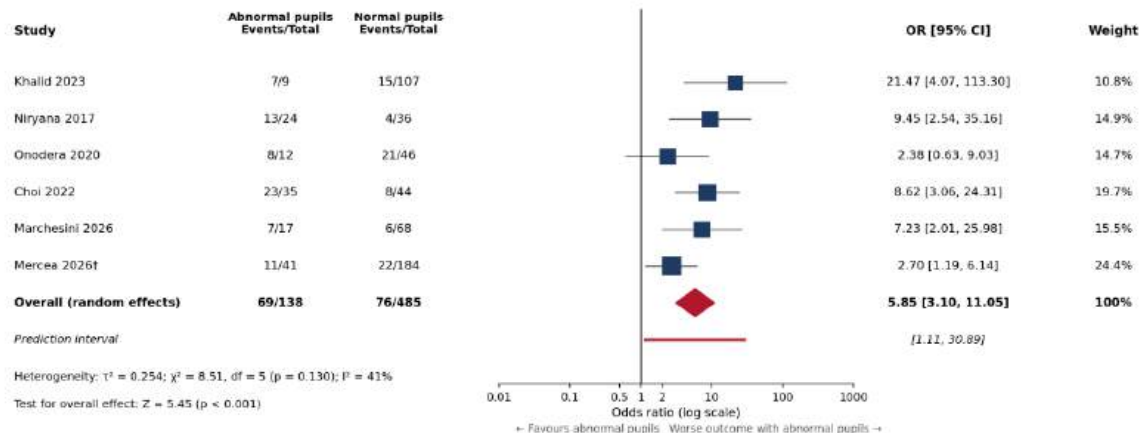


Figure 16. Forest plot of abnormal pupillary status and unfavourable outcome.^{36,39}

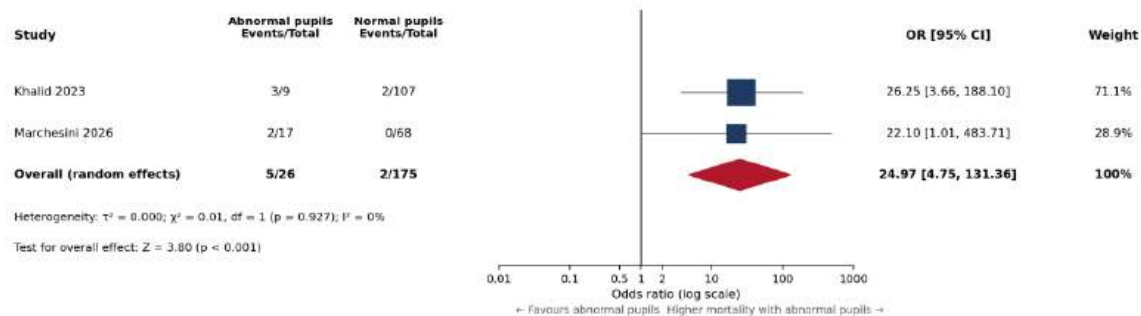


Figure 17. Forest plot of abnormal pupillary status and mortality (exploratory; $k = 2$).^{7,43}

Associated intracranial lesions, age and paediatric status

Associated intradural lesions (contusion, subdural hematoma or traumatic subarachnoid haemorrhage) tripled the odds of unfavourable outcome (OR 3.44, 95% CI 1.78–6.63; $I^2 = 0\%$; $k = 3$; Figure 19) and were associated with a borderline increase in mortality (OR 5.17, 95% CI 0.98–27.19; $p = 0.052$; $k = 3$). In the Austrian long-term cohort, all deaths occurred in patients with combined lesions (7/38 vs 0/32). Older age, defined by study-specific cut-offs of 40, 46 or 50 years, was associated with unfavourable outcome (OR 2.85, 95% CI 1.33–6.08; $I^2 = 0\%$; $k = 3$), consistent with independent age effects in Japanese (optimal cut-off < 55 years) and Korean multivariable

models. Paediatric status was not associated with mortality in pooled within-study comparisons (OR 0.65, 95% CI 0.11–3.82; $I^2 = 66\%$): a large Pakistani cohort showed markedly lower mortality in children (3.1% vs 14%), whereas another reported excess mortality in children younger than five years.^{5,7,25,36,39,43,52}

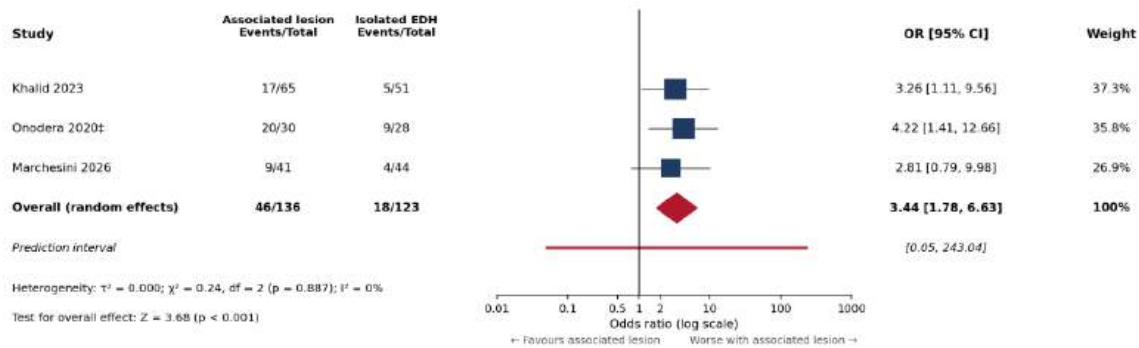


Figure 18. Forest plot of associated intracranial lesions and unfavourable outcome. ‡Onodera 2020: cerebral contusion used as the associated lesion.³⁶

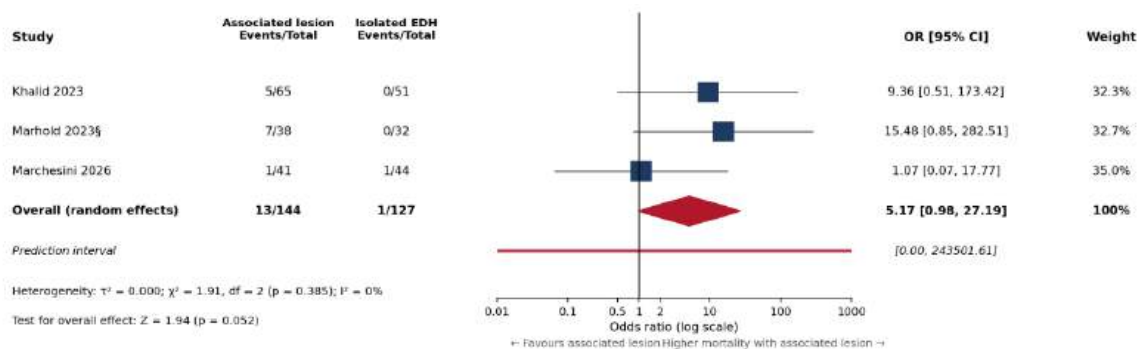


Figure 19. Forest plot of associated intracranial lesions and mortality. §Marhold 2023: deaths during long-term follow-up.⁵

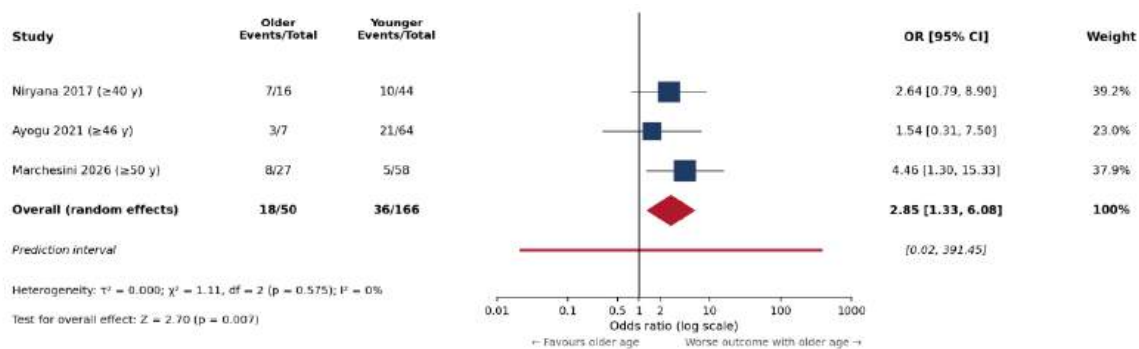


Figure 20. Forest plot of older age (study-specific thresholds) and unfavourable outcome.^{7,25,37}

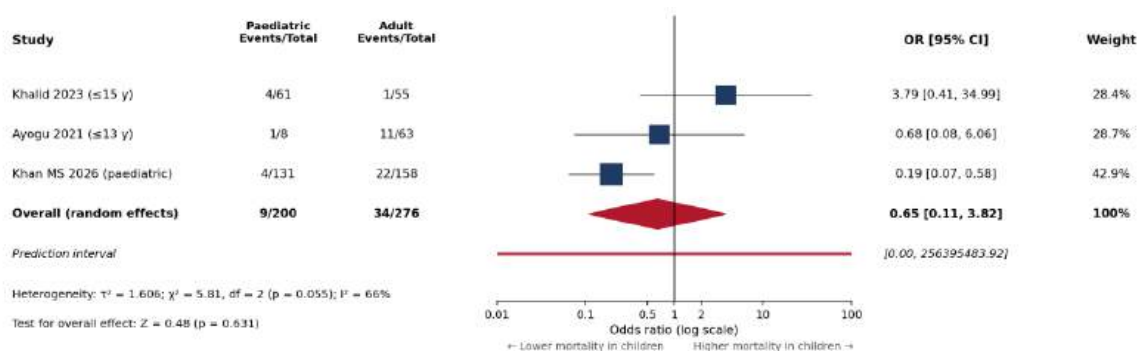


Figure 21. Forest plot of paediatric versus adult patients and mortality (within-study comparisons).^{37,43,52}

Radiological and other factors

Radiological markers of mass effect were reported as significant in several studies but could not be pooled because of heterogeneous definitions. Hematoma volume thresholds associated with poor outcome included > 30 mL (Indonesia; 38.2% vs 15.4% unfavourable), > 40 mL (Bangladesh), > 50 mL (Bangladesh; all patients with poor outcome) and < 60 mL as a marker of good outcome (Pakistan), with a paediatric-specific threshold of ≥ 33.5 mL predicting mortality (area under the curve 0.763). Midline shift ≥ 5 mm (Indonesia; 50.0% vs 11.8% unfavourable), effacement of the basal cisterns (Ethiopia, Bangladesh, Pakistan) and convex hematoma morphology in paediatric posterior fossa EDH were also associated with poor outcome. Other reported predictors included alcohol intoxication and Injury Severity Score, hypotension, low oxygen saturation, hemiparesis, hypertension and diabetes, coagulation-related laboratory abnormalities, and decompressive

craniectomy rather than osteoplastic craniotomy in comatose patients—an association likely confounded by more severe brain swelling.^{10,25,27,31,32,38,41,42,44,48,52}

Table 7. Direction of association for candidate prognostic factors across included studies (harvest table) and pooled estimates

Factor	Studies reporting a significant association with poor outcome	Studies reporting no significant / inverse association	Pooled estimate (this review)
Pre-operative GCS (low)	22 studies, including Onodera, Choi, Nirvana, Khalid, Ayogu, Howlader, Marchesini, Mercea, Kebede, Jabbar ^{7,9,25,36,37,39,43,44,48,51}	Gutowski 2018 ³²	Mortality OR 9.26; unfavourable OR 17.34
Abnormal pupils	14 studies, including Choi (independent), Khalid, Nirvana, Kebede, Das, Jabbar, Echara, Kandregula, Taha ^{10,25,35,39,41,43,44,48,53}	Onodera 2020 (p = 0.15) ³⁶	Unfavourable OR 5.85; mortality OR 24.97
Associated intracranial lesion	Gutowski, Marhold, Khalid, Onodera, Kandregula, Echara, Das, Ali, Khan MS ^{5,10,27,32,35,36,41,43,52}	Marchesini 2026 (p = 0.11) ⁷	Unfavourable OR 3.44
Hematoma volume	Ali, Das, Jabbar, Echara, Khan Z, Choi (univariate), Khan MS, Elsayed ^{10,26,27,34,39,41,44,52}	Onodera, Mercea, Nirvana (p = 0.052) ^{25,36,51}	Not pooled (heterogeneous thresholds)
Midline shift / basal cisterns	Gutowski, Nirvana, Jabbar, Kebede, Javed, Khan MS ^{25,31,32,44,48,52}	Onodera, Mercea ^{36,51}	Not pooled

Age (older)	Onodera, Choi, Rosyidi, Khan Z, Mercea (univariable) ^{8,26,36,39,51}	Ali, Das, Ayogu, Nirvana ^{10,25,27,37}	Unfavourable OR 2.85
Age (very young children)	Khalid (< 5 y), Javed (younger age) ^{31,43}	Khan MS (children lower mortality) ⁵²	Paediatric vs adult mortality OR 0.65 (n.s.)
Delayed surgery	Javed, Ali, Nirvana, Rosyidi, Echara, Khalid, Das, Ullah, Adalat, Elkholy, Khan Z, Tshiamala Ngalula, Khan MS (children) ^{8,10,25–27,31,41,43,45–47,50,52}	Onodera, Ayogu, Choi, Gmeiner, Mercea, Marchesini ^{7,36,37,39,49,51}	Unfavourable OR 6.17; mortality (6 h) OR 14.23
Interhospital transfer / referral	—	Gmeiner, Marchesini (longer delay but no worse outcome) ^{7,49}	Not pooled
Systemic and other factors	Alcohol, ISS (Gutowski); hypotension (Echara); SpO ₂ , hemiparesis (Kebede); HTN, DM (Khan Z); female sex (Khalid); D-dimer, haemoglobin (Onodera) ^{26,32,36,41,43,48}	Anticoagulants (Gutowski) ³²	Not pooled

n.s., not significant. Significance as reported by primary studies (univariable or multivariable). ISS, Injury Severity Score; HTN, hypertension; DM, diabetes mellitus; SpO₂, peripheral oxygen saturation.

Summary of meta-analyses, subgroup and sensitivity analyses

Table 8. Summary of all meta-analyses (random effects, DerSimonian–Laird)

Outcome / comparison	k	n	Pooled estimate (95% CI)	I ²	95% prediction interval

Mortality after evacuation	21	1,907	Proportion 7.5% (5.2–10.6)	74%	1.7–27.8%
Favourable outcome (GOS 4–5)	15	1,116	Proportion 78.9% (72.8–84.0)	79%	50.5–93.2%
Delayed vs early surgery → mortality (all thresholds)	5	387	OR 6.52 (0.95–44.88); MH 4.60 (1.98–10.68)	67%	0.01–4080
Delayed vs early surgery → mortality (6 h)	4	316	OR 14.23 (2.90–69.78); Peto 18.84 (7.00–50.72)	16%	—
Delayed vs early surgery → unfavourable outcome	6	447	OR 6.17 (1.27–29.94); MH 3.72 (2.38–5.82)	86%	0.03–1396
GCS ≤ 8 → mortality	5	353	OR 9.26 (3.68–23.33)	0%	—
GCS ≤ 8 → unfavourable outcome	8	734	OR 17.34 (7.54–39.88)	59%	1.57–191.0
Abnormal pupils → unfavourable outcome	6	623	OR 5.85 (3.10–11.05)	41%	1.11–30.89
Abnormal pupils → mortality	2	201	OR 24.97 (4.75–131.36)	0%	—
Associated lesion → unfavourable outcome	3	259	OR 3.44 (1.78–6.63)	0%	0.05–243
Associated lesion → mortality	3	271	OR 5.17 (0.98–27.19)	0%	—
Older age → unfavourable outcome	3	216	OR 2.85 (1.33–6.08)	0%	—
Paediatric vs adult → mortality	3	476	OR 0.65 (0.11–3.82)	66%	—

k, number of studies; *n*, number of patients; OR, odds ratio (exposed vs reference; OR > 1 indicates worse outcome with the exposure); MH, Mantel–Haenszel fixed-effect OR. Prediction intervals were not calculated (—) when *k* < 3 or not informative.

Table 9. Subgroup analyses, sensitivity analyses and meta-regression

Outcome	Analysis	Result (95% CI)
Mortality	Income setting: LMIC vs HIC	7.2% (5.0–10.2) vs 8.2% (3.1–20.0); $p = 0.81$
Mortality	Population: adult/mixed vs paediatric vs comatose-only	6.9% vs 4.2% vs 21.1%; $p = 0.036$
Mortality	All-comer adult/mixed cohorts: LMIC vs HIC	7.7% (5.3–10.9; $k = 13$) vs 3.7% (1.4–9.7; $k = 3$)
Mortality	Excluding comatose-only cohorts	6.6% (4.7–9.2); $k = 19$
Mortality	Low/moderate risk-of-bias studies only	5.6% (3.2–9.6); $k = 9$
Mortality	Full-text-extracted studies only	7.5% (5.0–11.0); $k = 14$
Mortality	Indonesian cohorts	9.0% (4.1–18.4); $k = 2$
Mortality	Meta-regression on % GCS ≤ 8	OR 1.20 per 10% (1.05–1.37); $p = 0.008$; $R^2 = 38\%$
Mortality	Meta-regression on publication year	Slope $-0.055/\text{year}$; $p = 0.35$; $R^2 = 0\%$
Favourable outcome	Excluding GOS-5-only definition	79.8% (73.5–84.9)
Favourable outcome	Low/moderate risk-of-bias studies only	71.6% (59.2–81.4); $k = 6$
Delay → unfavourable	LMIC studies only	OR 10.56 (1.81–61.58); $k = 5$
Delay → unfavourable	6-h threshold, LMIC only	OR 16.88 (2.08–136.88); $k = 3$
Delay → unfavourable	Low/moderate risk-of-bias only	OR 4.78 (0.06–387.3); $k = 2$ (conflicting)

Delay → unfavourable	Leave-one-out range	OR 3.38 (omitting Adalat) to 10.56 (omitting Marchesini)
Delay → mortality	LMIC studies only	OR 9.56 (0.83–110.08); k = 4
GCS $\leq$ 8 → unfavourable	Excluding mixed-management cohort	OR 21.45 (11.47–40.09); I ² = 3%
GCS $\leq$ 8 → unfavourable	Low/moderate risk-of-bias only	OR 13.43 (2.88–62.51); k = 3
GCS $\leq$ 8 → mortality	Peto OR (sparse data)	19.76 (7.45–52.43)
Abnormal pupils → unfavourable	Excluding mixed-management cohort	OR 7.46 (4.03–13.82); I ² = 13%
Abnormal pupils → unfavourable	Low/moderate risk-of-bias only	OR 4.92 (2.72–8.91); k = 5

Across all sensitivity analyses, the direction and statistical significance of the associations for GCS $\leq$ 8 and abnormal pupils were preserved (Tables 10 and 11). The timing association was robust to sparse-data methods and to restriction to LMIC studies, but was not robust to restriction to low/moderate risk-of-bias studies, which left only two studies with opposite directions of effect. Leave-one-out analysis showed that no single study determined the significance of the GCS association, whereas the pooled timing estimate was fragile, losing statistical significance when any one of the four LMIC cohorts using 6- or 12-hour thresholds was omitted and remaining significant only when the Italian or Nigerian cohort was removed.^{7,25,46}

Small-study effects and publication bias

For pooled mortality, Egger's test (intercept -2.99 ; $p = 0.002$) and Begg's test ($p = 0.013$) indicated asymmetry, with small studies reporting higher mortality; however, these tests are known to be unreliable for single-arm proportions with low event rates, and the asymmetry is more plausibly explained by case-mix differences between small severe-injury cohorts and large all-

comer series than by selective publication. For favourable outcome ($p = 0.15$), delayed surgery ($p = 0.13$) and abnormal pupils ($p = 0.17$) no significant asymmetry was detected. For $GCS \leq 8$ and unfavourable outcome, Egger's test was significant ($p = 0.006$), suggesting that smaller studies may overstate the magnitude, although not the direction, of this association.^{21,54}

Table 10. Assessment of small-study effects

Analysis	k	Egger intercept (p)	Begg rank correlation	Interpretation
Mortality (proportion)	21	-2.99 ($p = 0.002$)	$\tau = -0.39$ ($p = 0.013$)	Asymmetry; likely case-mix driven
Favourable outcome (proportion)	15	2.94 ($p = 0.15$)	—	No significant asymmetry
Delay → unfavourable outcome	6	5.13 ($p = 0.13$)	—	Underpowered ($k < 10$)
$GCS \leq 8 \rightarrow$ unfavourable outcome	8	3.36 ($p = 0.006$)	—	Possible small-study inflation of magnitude
Abnormal pupils → unfavourable outcome	6	3.40 ($p = 0.17$)	—	Underpowered ($k < 10$)

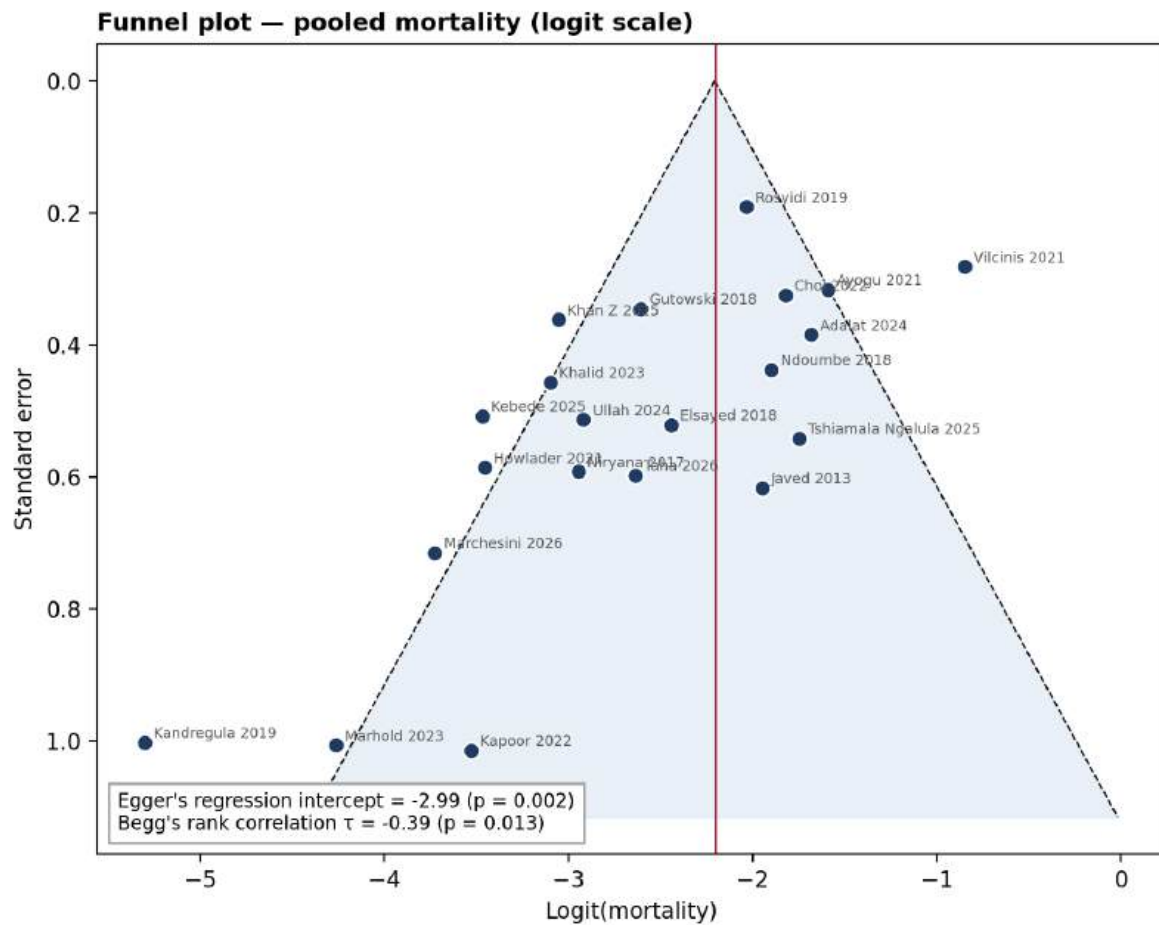


Figure 22. Funnel plot for pooled mortality (logit scale) with Egger's and Begg's tests.⁵⁴

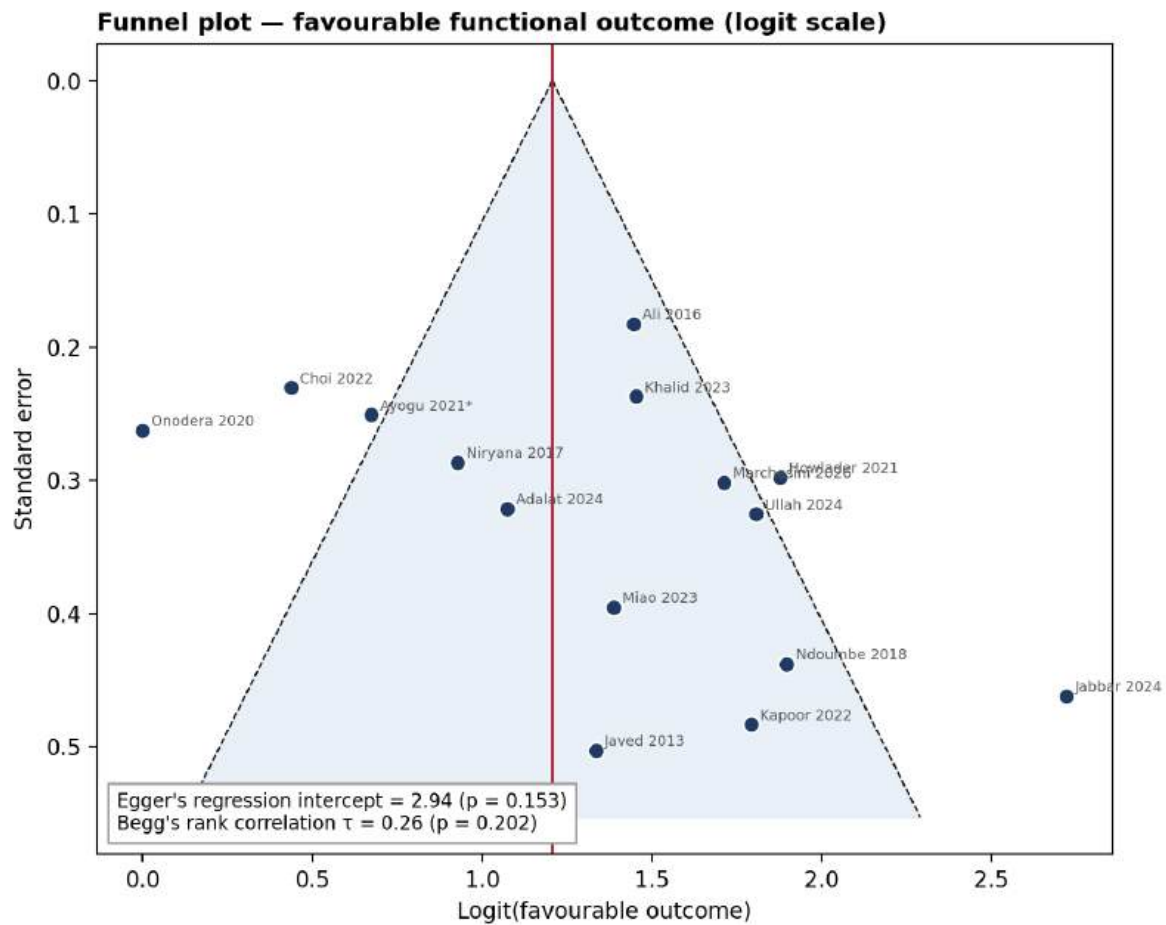


Figure 23. Funnel plot for favourable functional outcome (logit scale).⁵⁴

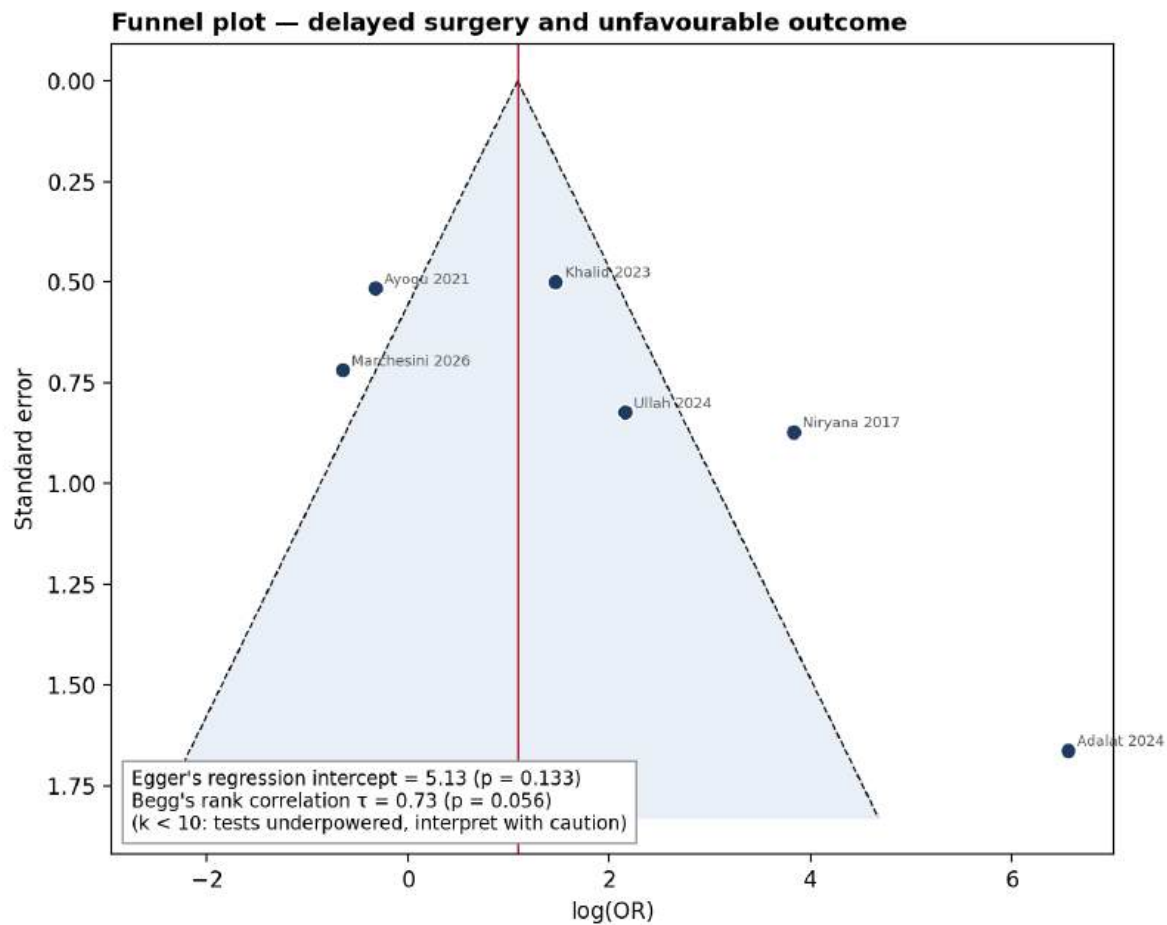


Figure 24. Funnel plot for delayed versus early surgery and unfavourable outcome (log OR).²¹

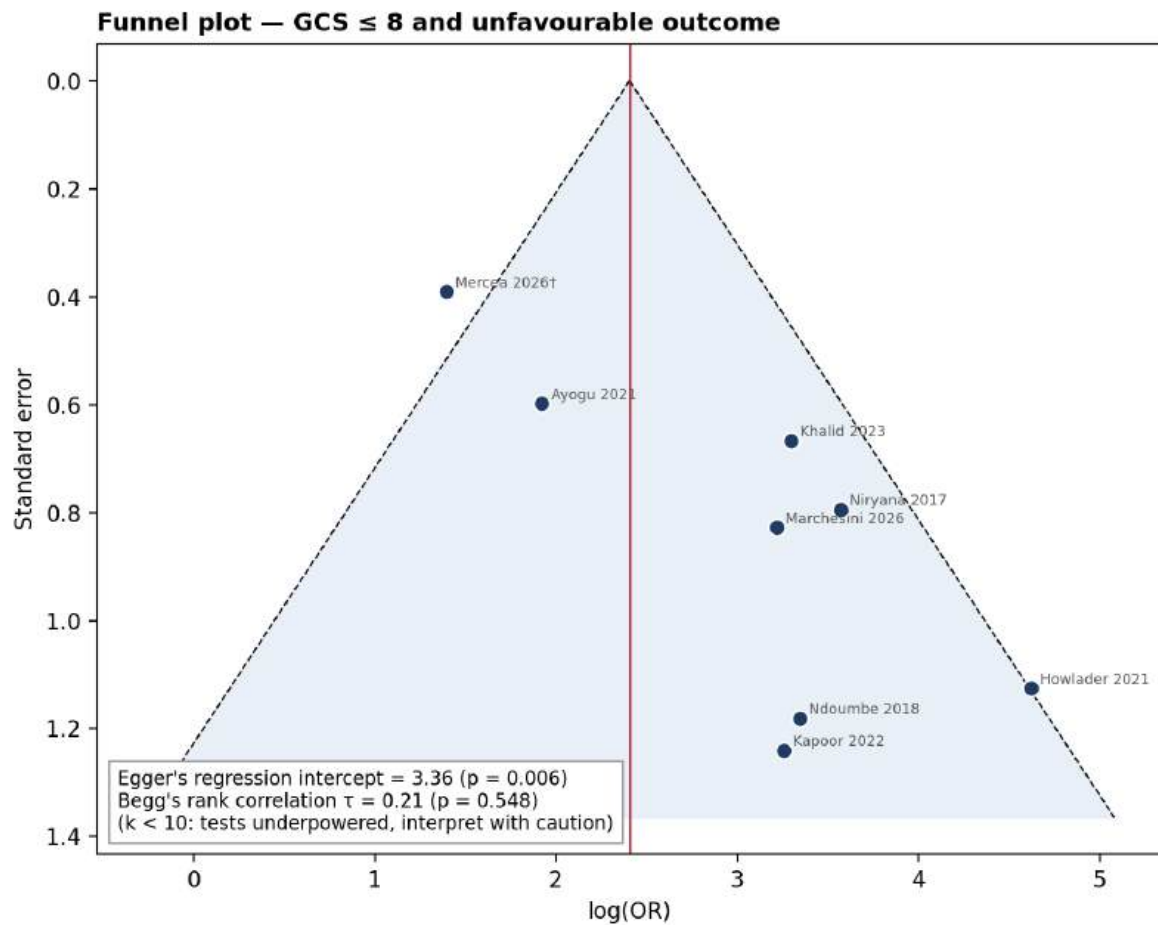


Figure 25. Funnel plot for GCS $\leq$ 8 and unfavourable outcome (log OR).²¹

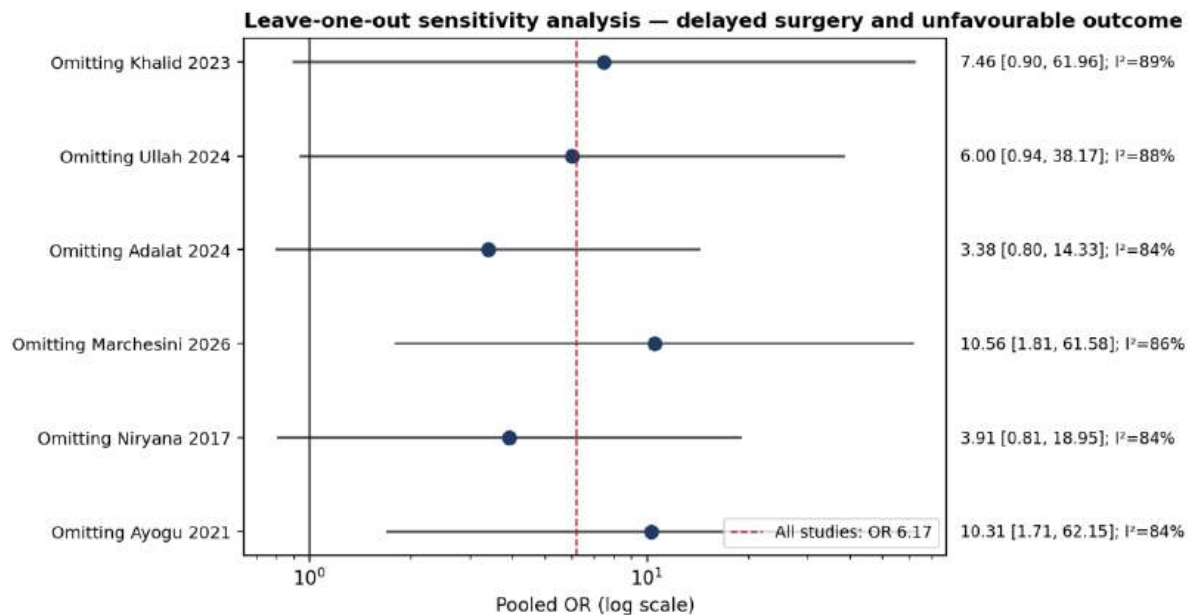


Figure 26. Leave-one-out sensitivity analysis for delayed surgery and unfavourable outcome.²¹

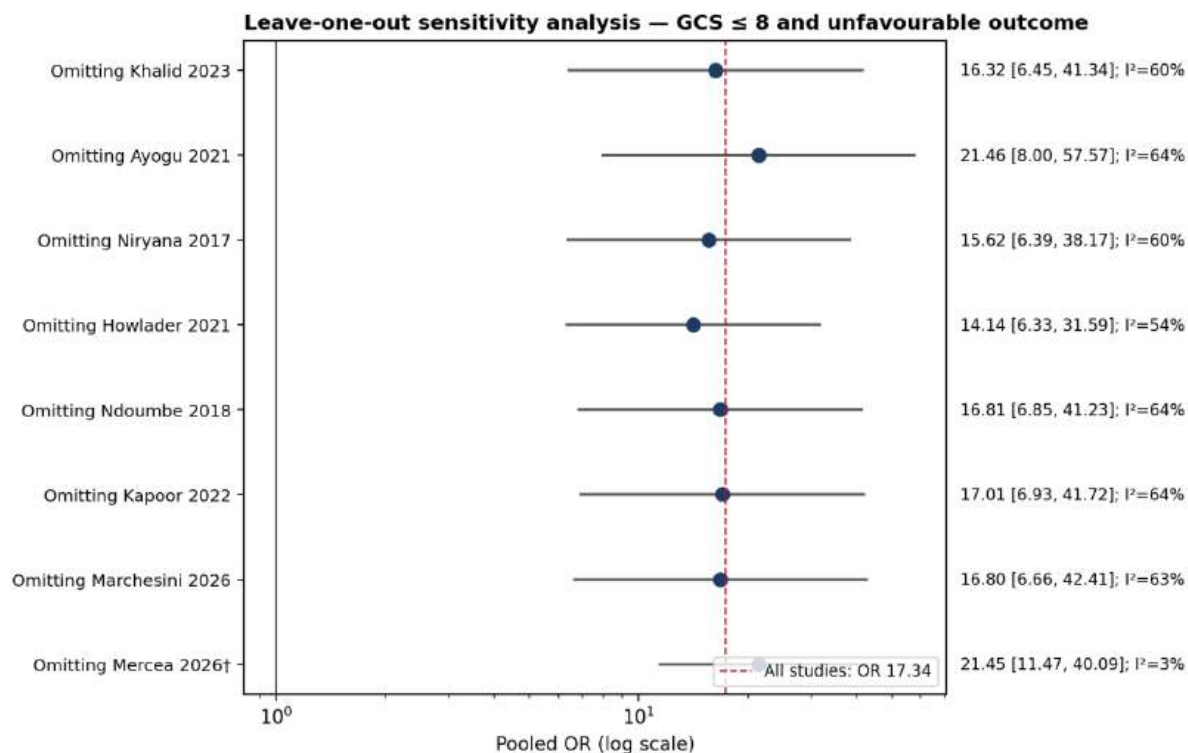


Figure 27. Leave-one-out sensitivity analysis for GCS $\leq$ 8 and unfavourable outcome.²¹

Certainty of evidence

Using GRADE for prognosis, certainty was moderate for the associations of GCS ≤ 8 and abnormal pupillary status with poor outcome, low for pooled mortality, favourable outcome, associated intracranial lesions and older age, and very low for the association between delayed surgery and outcome and for paediatric status. The principal reasons for rating down were risk of bias in the confounding domain, unexplained inconsistency and imprecision; the GCS and pupillary associations were rated up for large magnitude of effect.^{21,54,55}

Table 11. GRADE summary of findings for prognosis

Outcome / factor	Studies (patients)	Estimate (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade	Certainty
Mortality after evacuation (event rate)	21 (1,907)	7.5% (5.2–10.6)	Serious (–1)	Serious (–1)	Not serious	Not serious	Undetected*	—	Low
Favourable outcome (event rate)	15 (1,116)	78.9% (72.8–84.0)	Serious (–1)	Serious (–1)	Not serious	Not serious	Undetected	—	Low
Delayed surgery → unfavourable outcome	6 (447)	OR 6.17 (1.27–29.94)	Serious (–1)	Serious (–1)	Not serious	Serious (–1)	Undetected	—	Very low
Delayed surgery (> 6 h) → mortality	4 (316)	OR 14.23 (2.90–69.78)	Serious (–1)	Not serious	Not serious	Serious (–1)	Undetected	Large effect (+1)	Low
GCS ≤ 8 →	5	OR 9.26	Serious	Not serious	Not serious	Not serious	Undetected	Large	Mod

mortality	(353)	(3.68– 23.33)	us (–1)	serio us	serio us	serio us	tecte d	e effec t (+1)	erate
GCS ≤ 8 → unfavourable outcome	8 (734)	OR 17.34 (7.54– 39.88)	Serio us (–1)	Not serio us	Not serio us	Not serio us	Susp ected (–1)	Larg e effec t (+1)	Mod erate
Abnormal pupils → unfavourable outcome	6 (623)	OR 5.85 (3.10– 11.05)	Serio us (–1)	Not serio us	Not serio us	Not serio us	Unde tecte d	Larg e effec t (+1)	Mod erate
Associated lesion → unfavourable outcome	3 (259)	OR 3.44 (1.78– 6.63)	Serio us (–1)	Not serio us	Not serio us	Serio us (–1)	Unde tecte d	—	Low
Older age → unfavourable outcome	3 (216)	OR 2.85 (1.33– 6.08)	Serio us (–1)	Not serio us	Serio us (–1) †	Not serio us	Unde tecte d	—	Low
Paediatric vs adult → mortality	3 (476)	OR 0.65 (0.11– 3.82)	Serio us (–1)	Serio us (–1)	Not serio us	Serio us (–1)	Unde tecte d	—	Ver y low

Starting certainty: high (observational prognostic evidence). *Funnel asymmetry judged attributable to case mix. †Heterogeneous age thresholds.

DISCUSSION

Principal findings

This systematic review of 31 studies and 3,368 patients, three-quarters of them from LMICs, yields five principal findings. First, contemporary surgical evacuation of acute EDH is associated with a pooled mortality of 7.5% and favourable recovery in almost four of five patients, but the 95% prediction interval (1.7–27.8%) shows that centre-level mortality varies more than four-fold. Second, the neurological state at the time of surgery dominates prognosis: $GCS \leq 8$ increased the odds of death nine-fold and of unfavourable outcome seventeen-fold, and abnormal pupils increased the odds of unfavourable outcome almost six-fold. Third, case mix—the proportion of comatose patients—explained 38% of between-study variance in mortality. Fourth, delayed evacuation was associated with substantially worse outcomes in LMIC cohorts, where delays commonly exceed 12–24 hours, but not in high-income cohorts where triage ensures that the sickest patients are operated first. Fifth, the delays in LMICs are largely structural, arising from logistics, referral and shortages of staff, intensive care beds and equipment.^{7,26,39,51}

Contemporary mortality and functional outcome

The pooled mortality of 7.5% is close to the operative mortality of 8.3% reported in the global EDH meta-analysis by Rahimi and colleagues, which drew on 49 studies and adjusted for small-study effects. Our estimate falls to 6.6% when cohorts restricted to comatose patients are excluded, and to 3.7% in all-comer cohorts from high-income settings, approaching the near-zero mortality reported from organised European trauma systems. That the Verona group, which first proposed the “zero mortality” goal, still recorded 2.4% in-hospital mortality four decades later is instructive: the residual deaths occur in patients who deteriorate before or during referral, and the goal remains a property of the whole system rather than of the operating theatre.^{4,5,7,32}

The meta-regression finding that mortality rises by approximately 20% in odds for each 10-percentage-point increase in the proportion of comatose patients reframes much of the apparent variation between centres and countries. A Korean national registry restricted to $GCS \leq 8$ recorded 13.9% mortality and a Lithuanian series of deeply comatose patients (GCS 3–5) 30%, while large Pakistani and Ethiopian series dominated by patients with mild injury recorded 3–5%. Comparisons

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of crude mortality between hospitals or countries without adjustment for admission GCS are therefore misleading; benchmarking of neurotrauma services in Indonesia should use severity-stratified or risk-adjusted indicators.^{26,38,39,43,48}

Functional recovery after EDH evacuation is remarkably good even after severe injury. Six-month favourable recovery was achieved by 60.8% of comatose Korean patients, and long-term follow-up in Austria demonstrated continued improvement after discharge, with good recovery rising from 36% at discharge to 69% at a mean of more than six years. Outcomes measured at 48 hours or at discharge, as in most LMIC studies, therefore underestimate eventual recovery and may contribute to therapeutic nihilism in comatose patients. A meta-analysis of patients with bilateral fixed dilated pupils found favourable outcome in 54.3% of those with EDH versus 6.6% of those with acute subdural hematoma, and a Spanish multicentre registry of patients with GCS 3 and bilateral dilated pupils identified an evacuated mass lesion as a protective factor. Similarly, an Indian cohort of patients with GCS 3–4 found that surgery was associated with favourable outcome, particularly in patients with EDH and in those operated within 6 hours.^{5,17,39,63,77}

Children fared at least as well as adults. Pooled paediatric mortality was 4.2%, one large Indian series recorded a single death among 201 children, and a meta-analysis of paediatric posterior fossa EDH reported good functional outcome in 93.7% and mortality of 0.57% after surgery. The within-study comparison did not show a statistically significant mortality advantage for children because of heterogeneity: a Pakistani cohort showed much lower paediatric mortality (3.1% vs 14%), whereas another found excess mortality in children younger than five years, a group in whom small circulating blood volume, delayed recognition and a thin, deformable skull may allow rapid decompensation.^{18,35,41,43,52}

Timing of evacuation: interpreting a heterogeneous signal

The biological rationale for early evacuation of EDH is strong. An arterial EDH expands until intracranial compliance is exhausted; beyond the inflection point of the pressure–volume curve, small increments in volume produce steep rises in intracranial pressure, uncal herniation and brainstem compression. Because the brain beneath an isolated EDH is often initially intact, the interval between the onset of herniation and decompression largely determines whether the injury is

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reversible. In our analysis, delays beyond study-specific thresholds in LMIC cohorts were associated with an approximately ten-fold increase in the odds of unfavourable outcome, and delays beyond 6 hours with a fourteen-fold increase in the odds of death, and patient-level analyses from Peshawar found a 16% increase in the odds of adverse outcome for each additional hour of delay. An Egyptian group, comparing patients with large hematomas whose baseline characteristics were similar, also found higher mortality and worse recovery with surgery after 6 hours.^{26,43,45–47}

The opposite pattern in high-income cohorts does not refute the benefit of speed; it reflects confounding by indication and survivor bias. In Verona, patients operated within 6 hours had a higher rate of unfavourable outcome than those operated later, because urgent cases with neurological deterioration were taken directly to theatre (median trauma-to-surgery 3.8 vs 9.8 hours for urgent vs deferred cases). In South Africa, patients with unfavourable outcome were operated about 16 hours sooner than those with favourable outcome, an association that disappeared after adjustment for severity. Identical patterns have been described for acute subdural hematoma, for severe TBI in a Japanese national data bank, and for Swedish patients transferred from primary hospitals, in whom delayed surgery after accurate triage was not harmful. Patients who are stable enough to wait—those with small, slowly expanding or venous hematomas and preserved consciousness—have a good prognosis regardless of timing, whereas patients who deteriorate are operated on immediately.^{7,14,51,67,78}

Studies that partially overcome this confounding support a time-dependent benefit. In a single-centre cohort of isolated severe TBI, evacuation within 200 minutes of arrival was independently associated with survival (adjusted OR 7.41). In combat casualties, craniectomy within 5.33 hours of injury was associated with lower post-operative mortality after adjustment for immortal-time bias (adjusted hazard ratio 0.28). A meta-analysis of traumatic intracranial hematomas found lower mortality with evacuation within 4 hours, although a contemporary level-1 trauma system reported median injury-to-operation times of nearly 5 hours and no improvement over 13 years. Taken together, these data suggest that the relevant clinical question is not whether a fixed time threshold is crossed, but whether neurological deterioration occurs during the wait—

which is precisely the risk that is magnified when patients must be referred over long distances without monitoring.^{15,16,79,80}

The 6-hour threshold used in most included studies should therefore be regarded as a pragmatic system benchmark rather than a biological deadline. For comatose patients with anisocoria, the relevant interval is minutes rather than hours: in a level-1 trauma centre the median time from emergency department arrival to skin incision for immediately life-threatening cases was still 131 minutes, with substantial contributions from CT-to-theatre transfer and theatre preparation. Guidelines of the Neurosurgical Society of Australasia, as summarised in an accompanying commentary, advise that general surgeons seek neurosurgical advice and proceed with emergency surgery when the predicted delay to a neurosurgical centre exceeds 2 hours, and an analysis of neurotrauma workforce needs in LMICs proposed that patients should be within 4 hours of a neurosurgical facility.^{2,81–83}

Facility- and human resource-related causes of delay

The time-to-care metrics extracted in this review show that delay in LMICs is not a matter of minutes at the operating-theatre door but of many hours along the referral chain. Median intervals of 15 hours to presentation in Abuja, 32 hours from injury to surgery in South Africa and a mean of 78 hours in Yaoundé contrast with medians of 4–5 hours in Austria and Italy. In Dhaka, only 3% of patients were operated within 6 hours. In Ethiopia, a prospective series excluded from our quantitative synthesis reported that more than half of EDH patients arrived more than 24 hours after injury. These intervals are long enough for many patients with expanding hematomas to deteriorate or die before reaching surgery; such patients are not captured in hospital-based series, so that the true cost of delay is likely underestimated.^{9,37,49,51,56,68}

The only included study that measured causes of delay found that logistical problems (transport, bed availability and theatre scheduling) and resource constraints (surgical staff, intensive care beds and equipment) together affected half of all patients and were independently associated with adverse outcome. This mirrors the systematic review of 18 LMICs, in which the lack of in-house CT (35%), limited theatre space (28%) and the absence of in-house neurosurgeons and neurosurgical facilities (28% each) were the dominant in-hospital causes of delay, and poor referral

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systems, long travel distances and inadequate emergency medical services were the dominant pre-hospital causes. In Kampala, the interval from CT to surgery reached 24 hours for severe TBI and 96 hours for mild TBI, and post-arrival delays were associated with mortality; in the Ugandan neurosurgical registry, failure to receive indicated surgery and hospital arrival more than 4 hours after injury predicted death.^{11,12,26,84}

Similar bottlenecks have been documented across Africa, South Asia and Latin America. In Tanzania, 95% of severely injured TBI patients who needed a CT scan did not receive one, and only 19.9% of patients with severe TBI at the national neurosurgical institute underwent surgery, with an observed two-week mortality 24% higher than predicted. In Cape Town, median door-to-neurosurgery times were 20 hours for severe TBI and 28 hours for moderate TBI, driven by interfacility transfer for after-hours CT and neurosurgical services. In India, a “third delay” of more than 60 minutes after arrival was independently associated with early mortality, and in Ecuador arrival at a trauma unit more than 5 hours after injury tripled mortality. In a regional referral hospital in Sri Lanka, 72% of TBI patients were referred from peripheral facilities without neurosurgical support, and delayed CT reporting prolonged the time to neurosurgical management. A multinational cohort from Ghana, Pakistan, Rwanda and South Africa found that 57% of injured patients took more than one hour to reach definitive care and that a prior encounter at another health facility was the strongest predictor of delay (OR 8.44). Conversely, a Peshawar study found no independent association between distance or pre-hospital delay and mortality after adjustment for severity, emphasising again that crude time metrics must be interpreted together with case mix.^{85–92}

These facility gaps reflect a profound mismatch between workforce and need. An estimated 23,300 additional neurosurgeons are required worldwide, and a minimum of one neurotrauma surgeon per approximately 212,000 people has been proposed for LMICs. In East Asia and the Pacific, only about 30% of the population lives within 2 hours of a city offering neurosurgical care, and in low- and lower-middle-income countries 75.6% of paediatric patients must travel more than 2 hours for emergency neurosurgical care. The Global Neurotrauma Outcomes Study found that resource disparities across Human Development Index strata were greatest in pre-hospital and

rehabilitation care rather than within operating theatres, and that participants most often identified pre-hospital improvement as the intervention with the greatest potential impact.^{1–3,24,93,94}

The Indonesian context

Indonesia combines a large neurotrauma burden, dominated by road traffic injury in young adults (73.9% of the Surabaya EDH cohort; mean age 27 years), with an archipelagic geography in which neurosurgeons and CT scanners remain scarce in rural regions. The two included Indonesian cohorts illustrate the consequences. At Dr. Soetomo General Hospital in Surabaya, 27% of 268 operated EDH patients were comatose on admission, 29% had anisocoria and 11.6% died after surgery; the authors identified the trauma–operation interval among the main determinants of outcome and explicitly framed their findings as problems and challenges of a developing country. At Sanglah Hospital in Denpasar, 35% of patients were operated 12 hours or more after injury, and this delay was, together with $GCS \leq 8$, one of only two independent predictors of unfavourable outcome. At Dr. Sardjito General Hospital in Yogyakarta, craniotomy performed more than 17 hours after injury was independently associated with poor GOSE in a mixed TBI cohort (OR 7.94), and at Dr. Soetomo, 83.8% of patients operated with critical GCS died.^{8,25,61,62}

A recent Indonesian scoping review of delayed management of massive epidural hematomas identified geographical constraints, the lack of organised emergency transport, and the scarcity of neurosurgical specialists and CT scanners in rural regions as the primary barriers to timely care. For regency-level hospitals such as the authors' institution, where a patient with an expanding EDH may require transfer to a provincial referral centre, these barriers translate into precisely the multi-hour, unmonitored delays that our analysis associates with poor outcome. Strengthening the regional referral network—clear transfer criteria, pre-transfer resuscitation, direct communication with the receiving neurosurgeon and teleradiology for CT review—is therefore a priority with direct relevance to EDH survival.^{8,11,13}

Bridging the gap when a neurosurgeon is not available

Where transfer to a neurosurgeon cannot be achieved within a safe interval, emergency cranial decompression by a non-neurosurgeon is an evidence-supported option. A systematic review of 14 studies (1,988 operations) found that general surgeons in rural, military and humanitarian

settings most commonly performed burr-hole decompression or craniectomy for head trauma, with heterogeneous mortality. A 2025 scoping review of 20 studies concluded that emergency decompression by non-neurosurgeons may be lifesaving for patients without timely access to a neurosurgical centre and that mortality was consistently lower for EDH than for subdural hematoma. In the Swedish national trauma registry, patients operated on by general surgeons at local hospitals had a slightly higher mortality but the same rate of favourable outcome as those operated by neurosurgeons at university hospitals, and in Darwin, where retrieval distances exceed 2,600 km, generalist surgeons achieved acceptable outcomes, with poor outcome associated with remote injury location and injury-to-operation intervals longer than 24 hours.^{23,83,95,96}

The technique matters. In regional Queensland, rurally performed burr holes were never effective, whereas larger craniotomies were frequently efficacious in producing clinical or radiological improvement, and 6 of 17 transferred patients required re-operation at the neurosurgical centre. In Cambodia, a structured training programme in emergency cranial neurosurgery raised the capacity of a regional hospital from zero to acceptable levels, with favourable three-month outcome in 93% of patients with acute EDH. In Tanzania, burr-hole surgery as definitive treatment for acute extra-axial hematomas achieved good outcome in 75.6% of patients. These experiences support a credentialed model in which selected general surgeons at regional hospitals are trained in damage-control craniotomy, supported by teleradiology and real-time neurosurgical advice, and audited against defined outcomes.^{24,64,65,97}

Table 12. Practical implications of the evidence for hospitals without on-site neurosurgery (synthesised by the authors)

Phase	Evidence-based target	Practical action for regional / district hospitals
Pre-hospital (Delay 1)	Early recognition of lucid interval and deterioration; GCS and pupil-based triage	Community and primary-care education; GCS/pupil monitoring protocol; direct transport of head-injured patients to CT-capable

		facilities
Diagnosis (Delay 2–3)	CT within the first hour; immediate neurosurgical review	24-hour CT availability; teleradiology link with the referral neurosurgeon; standardised CT reporting of volume, midline shift and cisterns
Referral (Delay 2)	Total injury-to-evacuation interval as short as possible; avoid unmonitored deterioration en route	"Call-before-transfer" hotline; pre-agreed transfer criteria; escorted transfer with airway control; osmotherapy as a bridge
Definitive care (Delay 3)	Evacuation of EDH > 30 mL or with deterioration/anisocoria without delay	"Brain code" pathway with reserved theatre, anaesthetist, blood products; administrative and financial clearance deferred until after surgery
When transfer is not feasible within 2–4 h	Damage-control decompression by trained non-neurosurgeon	Credentialing and simulation training of general surgeons in emergency craniotomy; cranial access kit; tele-neurosurgical supervision; follow-up transfer
Quality improvement	Severity-adjusted benchmarking	Local EDH/TBI registry recording injury-to-door, door-to-CT, CT-to-incision intervals, admission GCS, pupils and GOS at 3–6 months

Recommendations integrate findings of this review with evidence from health-system and non-neurosurgeon surgery studies; they are intended to inform local protocols rather than replace national guidelines.

Prognostic factors in clinical decision-making

Pre-operative GCS emerged as the strongest and most consistent predictor, in agreement with a Polish cohort in which each one-point decrease in GCS almost doubled the risk of in-hospital death among patients operated for EDH or subdural hematoma, and with a 2026 analysis in which higher admission GCS was the strongest independent predictor of favourable three-month outcome, with EDH itself conferring better outcomes than subdural hematoma. Absolute risks derived from our analysis—about 3% mortality and 7% unfavourable outcome with $GCS > 8$ versus 25% and 59% with $GCS \leq 8$ —provide practical anchors for counselling families. Importantly, the absolute risks for comatose patients still leave four in ten with a favourable outcome, a finding that argues strongly against withholding surgery on the basis of low GCS alone.^{39,57,58,63}

Pupillary abnormalities reflect herniation and therefore index both severity and the time that has elapsed since decompensation. Their association with outcome was strong and stable, but the Korean finding that almost one-third of patients with bilateral unreactive pupils achieved favourable recovery, together with meta-analytic evidence of 54% favourable outcome in EDH with bilateral fixed dilated pupils, indicates that fixed pupils caused by an extra-axial mass lesion should prompt immediate decompression rather than palliation. Associated intradural lesions mark diffuse or contusional brain injury that is not reversed by evacuation of the EDH; the Austrian long-term series and its accompanying meta-analysis of six studies showed substantially lower mortality and unfavourable outcome in isolated than in combined EDH. Older age reflects reduced physiological reserve and more frequent associated lesions, although the population of the included studies was young (most mean ages 25–40 years).^{5,17,36,39}

Hematoma volume, midline shift and effacement of the basal cisterns were frequently associated with outcome but could not be pooled because of inconsistent thresholds. These variables are more useful for deciding whether and how urgently to operate than for prognosis after evacuation, since they are also the indications for surgery. Their role in identifying which patients can safely be observed is illustrated by an Egyptian study of initially non-operated EDH, in which 30% progressed and required surgery, with temporal location, coagulopathy and early CT after trauma predicting progression.^{25,44,52,72}

Comparison with previous systematic reviews

Our pooled mortality agrees with the global estimate of operative EDH mortality, and our finding of better outcomes for isolated EDH is consistent with the meta-analysis of six studies by Marhold and colleagues (risk ratio for mortality 0.22 for isolated vs combined EDH). Our timing results differ from the null findings of the 2026 subdural hematoma meta-analysis, but the explanation offered by its authors—confounding by indication in contemporary cohorts—is the same mechanism we identify in high-income EDH cohorts. A Spanish-language systematic review of 19 LMIC studies concluded that EDH outcomes are strongly influenced by timely access to surgery and neuroimaging, and reported operative rates of only 42% in low-income countries, which is in line with our observation that facility-related delay is the dominant modifiable risk in these settings.^{4,5,14,19}

Strengths

The strengths of this review include a focus on surgically treated acute EDH, integration of outcome, timing, prognostic factor and health-system evidence, verification of every bibliographic record against Crossref, explicit detection of a suspected duplicate dataset and overlapping cohorts, prognosis-specific risk-of-bias and certainty assessment, sparse-data and leave-one-out sensitivity analyses, translation of relative effects into absolute risks, and a meta-regression that quantifies the contribution of case mix to heterogeneity. The evidence base, dominated by LMIC cohorts, is directly applicable to Indonesian regional practice.^{20–22}

Implications for research

Future studies should be prospective and registry-based, record the complete time course (injury, first contact, CT, arrival at the neurosurgical facility, skin incision), stratify or adjust timing analyses for admission GCS and pupillary status, use time-dependent methods to address immortal-time bias, measure GOSE at three and six months, and capture the reasons for delay at each phase. Multicentre Indonesian data linking regency hospitals with their referral centres, including patients who die before transfer, would allow the true population-level cost of delay to be estimated and the effects of interventions such as teleradiology or credentialed non-neurosurgeon craniotomy to be evaluated with stepped-wedge or interrupted time-series designs.^{13,79,94}

CONCLUSION AND RECOMMENDATIONS

Conclusion

Surgical evacuation of acute EDH achieves a pooled mortality of 7.5% and favourable recovery in 79% of patients, confirming EDH as one of the most treatable lesions in neurotrauma. Outcome is determined principally by the neurological condition at the time of surgery: pre-operative GCS ≤ 8 , abnormal pupillary status, associated intracranial lesions and older age are robust predictors of death and disability, with moderate certainty for GCS and pupils. Delayed evacuation is associated with markedly worse outcomes in LMIC settings, where injury-to-surgery intervals commonly exceed 12–24 hours because of transport, referral, imaging, staffing, intensive care and theatre constraints; in high-income systems with effective triage, the time–outcome association is obscured by confounding by indication. The hypotheses that delay (H1) and adverse pre-operative clinical status (H2) are associated with poor outcome are therefore supported, the former with low to very low certainty, and the hypothesis that income-setting differences reflect case mix and access (H3) is partially supported by the meta-regression and time-metric data.^{4,8,25,26}

Recommendations

For clinicians in regional hospitals. Patients with acute EDH should be managed as a time-critical emergency in which the objective is to evacuate the hematoma before neurological deterioration; GCS and pupils should be monitored at short intervals, and comatose patients with anisocoria should be treated as candidates for immediate decompression rather than palliation. Families should be counselled using severity-stratified absolute risks rather than overall averages.

For hospital managers. A “brain code” pathway that guarantees CT, theatre, anaesthesia, blood and intensive care access, with administrative and financial procedures deferred until after surgery, should be established; injury-to-door, door-to-CT and CT-to-incision intervals should be audited routinely.^{17,26,81}

For health-system planners and professional bodies in Indonesia. Regional neurotrauma networks with explicit transfer criteria, a direct consultation line and teleradiology between regency hospitals and provincial neurosurgical centres should be developed, alongside continued expansion and redistribution of the neurosurgical workforce. Where safe transfer within 2–4 hours is not

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feasible, a credentialed programme training selected general surgeons in damage-control craniotomy, supported by tele-neurosurgical supervision, should be considered. **For researchers.** Prospective multicentre registries with complete time stamps, severity adjustment and three- to six-month GOSE are needed to quantify the true cost of delay and to evaluate system-level interventions.^{2,13,23,24,95}

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