

ORIGINAL ARTICLE

Admission Glucose-to-Potassium Ratio and MOST-Based Mortality Risk Category in Severe Traumatic Brain Injury Undergoing Craniotomy: A Retrospective Observational Study

Purwoko¹, Sugeng Budi Santosa¹, Lichte Christian Purbono¹¹ Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia

ARTICLE INFO

Article history

Received: August 16, 2026
Revised: September 12, 2026
Accepted: September 29, 2026
Available online: October 4, 2026
Published: October 7, 2026

Keywords

Craniotomy
Glucose-to-potassium ratio
Mortality
Neuroanesthesia
Traumatic brain injury

DOI

<https://doi.org/10.37275/jacr.v7i2.977>

Corresponding author

Purwoko
purwoko@staff.uns.ac.id

ABSTRACT

Background. The admission glucose-to-potassium ratio (GKR) combines the hyperglycemic and hypokalemic arms of the post-traumatic stress response, but its relation to mortality-risk scores in surgically treated severe traumatic brain injury (TBI) is unexamined in Indonesia.

Objective. To relate admission GKR to the Mortality Score for TBI (MOST) risk category and to compare observed in-hospital mortality with published benchmarks.

Methods. Retrospective observational study of 95 adults (18–60 years; Glasgow Coma Scale ≤ 8) undergoing craniotomy at Dr. Moewardi Regional General Hospital, Surakarta (March–August 2024). GKR was admission glucose (mg/dL) divided by potassium (mmol/L); risk was graded with MOST. Analyses comprised Spearman correlation, Kruskal–Wallis tests, exact benchmark tests and a sensitivity analysis over all datasets consistent with the observed summaries.

Results. Median GKR rose from 26.94 (low risk, $n = 4$) to 35.21 (moderate, $n = 86$) and 55.67 (high, $n = 5$) and correlated with MOST ($\rho = 0.376$; 95% CI 0.189–0.537). Every high-risk GKR exceeded every low-risk value (exact $p = 0.016$). GKR was not demonstrably more strongly correlated than glucose ($\rho = 0.329$). Potassium declined linearly ($p = 0.018$; ANOVA $p = 0.059$, Kruskal–Wallis $p = 0.033$). In-hospital mortality was 4.2% (95% CI 1.6–10.3), below all five published benchmarks. The attainable area under the curve for high risk was 0.436–0.898; associations of death with MOST stratum, sex and pupils were not identified.

Conclusion. Admission GKR tracked the MOST risk category and separated the extreme strata, but its discrimination and superiority over glucose need patient-level validation against observed outcomes.

Access licence: Open access. This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence (CC BY-NC-SA 4.0), which permits non-commercial use, sharing, adaptation and reproduction in any medium, provided the original author and source are credited and derivative works are licensed under identical terms.

Copyright: © 2026 The Author(s). Published by HM Publisher in collaboration with CMHC Research Center. e-ISSN 2745-9497.

1. Introduction

Traumatic brain injury (TBI) remains a leading cause of death and acquired disability worldwide. The Global Burden of Disease 2021 analysis estimated 20.84 million incident and 37.93 million prevalent cases, with falls and road injuries as the main mechanisms.¹ Low- and middle-income countries carry a disproportionate share of severe injury, because road-traffic trauma among vulnerable road users predominates there and the route from injury to neurosurgical care is the longest. In the Global Neurotrauma Outcomes Study, 14-day mortality was 18% among 1,635 patients receiving emergency neurosurgery for TBI. Patients treated in medium-human-development settings had an adjusted odds ratio for death of 2.84 relative to very-high-development settings.² A meta-analysis of 33 cohorts put the mortality of severe TBI at 27.8%, rising to 38.0% in developing countries.³ Asian low-resource cohorts report in-hospital mortality in severe TBI between 12.2% and 68.9%,^{4,5} and 23.5% at discharge across all severities.⁶ Case-mix differs sharply. Median age

is 27 years in Indian registries but 55 years in European ones,⁷ and high-income severe-TBI populations have aged by more than a decade.⁸ In Indonesia, a North Maluku registry found that 91.8% of road-traffic TBI was motorcycle-related, with 9.3% mortality.⁹

Brain damage after trauma has two parts: a primary mechanical insult and a secondary cascade that evolves over hours to days. Systemic secondary insults are frequent. They matter. In a national intensive-care cohort of patients with TBI, hypotension, hyperglycemia and hypoxemia occurred in 49.8%, 29.2% and 50.3%, respectively.¹⁰ Across Asian trauma centers, an admission systolic pressure below 100 mmHg carried an adjusted odds ratio of 7.05 for 30-day mortality.¹¹ An intense neuroendocrine stress response sits at the center of this cascade. Catecholamine and cortisol surges drive glycogenolysis, gluconeogenesis and peripheral insulin resistance, and the result is stress hyperglycemia that is largely independent of pre-existing diabetes. A meta-analysis of 12 cohorts and 16,387 patients without diabetes found that stress-induced hyperglycemia doubled the risk of death (RR 2.00, 95% CI 1.72–2.33).¹² The stress-

hyperglycemia ratio keeps its prognostic value after adjustment.¹³ Pooled data show admission glucose 1.20 mmol/L higher in patients with unfavorable outcome,¹⁴ and the glucose–outcome relation is bell-shaped rather than monotonic.¹⁵ Potassium moves the other way. β_2 -adrenergic stimulation of the Na^+/K^+ -ATPase shifts potassium into cells, so hypokalemia affects 46–48% of patients after TBI.^{16,17} Some electrolyte derangement is present in almost every patient.¹⁸

Hyperglycemia and hypokalemia diverge as stress intensifies. Their quotient, blood glucose divided by serum potassium, has therefore been proposed as a single index of both arms of the response: the glucose-to-potassium ratio (GKR). Among 132 patients with severe TBI requiring surgery, a ratio above 42 identified death with 85.4% sensitivity and 51.1% specificity.¹⁹ In 4,357 patients with isolated moderate-to-severe TBI, the identically defined Stress Index had an optimal cut-off of 48.5, an area under the receiver-operating-characteristic curve (AUC) of 0.724 and an adjusted odds ratio of 1.94.²⁰ Similar thresholds appeared in 20,040 general trauma patients (42.7) and in Japanese adults and Brazilian children with severe TBI (50).^{21–23} Smaller operative series reported associations that were large but imprecise.^{24,25} In mild-to-moderate TBI, the ratio alone reached an AUC of 0.670. It improved discrimination when added to the Rotterdam computed-tomography score.²⁶ The marker has also been linked to mortality after aneurysmal subarachnoid and intracerebral hemorrhage, ischemic stroke and acute myocardial infarction,^{27–32} and to non-fatal outcomes such as early post-traumatic epilepsy and acute kidney injury.^{33–35} The evidence is not uniform. No association with mortality emerged after isolated blunt head trauma, GKR did not differ between patients with and without computed-tomography lesions in mild TBI, and no association with long-term outcome emerged after aneurysmal hemorrhage in a Peruvian cohort.^{36–38}

Outcome after severe TBI is conventionally estimated with the CRASH and IMPACT models. They discriminate similarly, but their calibration is inconsistently reported.³⁹ External validations in Thailand, Malaysia and Chinese surgical cohorts showed good discrimination with systematic over-prediction of risk.^{40–42} In an Indonesian surgical cohort managed by anesthesiologists, CRASH reached an AUC of 0.838 for 14-day mortality.⁴³ The Mortality Score for TBI (MOST) sums points for age, the eye, verbal and motor components of the Glasgow Coma Scale, and pupillary reactivity; derived in 259,404 patients from a United States trauma registry, it discriminated in-hospital mortality better than CRASH-Basic and IMPACT-Core (AUC 0.875, 0.837 and 0.821, respectively).⁴⁴ Its components are available at the bedside within minutes. Independent external validation is still missing. Blood-based protein biomarkers such as glial fibrillary acidic protein reach an AUC of about 0.81 for in-hospital mortality, yet they remain costly.⁴⁵ Composite hematological ratios have shown inconsistent value.⁴⁶ So attention stays on markers drawn from routine admission chemistry.

Indonesian evidence on admission chemistry in operative neurotrauma is limited and mixed. Among 90 surgically treated patients in Bandung, admission glucose

correlated with mortality overall but did not predict death within severe TBI.⁴⁷ Pediatric operative data from Surabaya showed markedly higher glucose among non-survivors.⁴⁸ Earlier biomarker work at Dr. Moewardi Regional General Hospital dealt with S100 β in mild injury.⁴⁹ No Indonesian study has related GKR to a contemporary mortality score. Small cohorts pose a second, methodological problem. Youden-optimal cut-offs estimated in samples of 100 recover the true optimum only 17% of the time and overstate sensitivity,⁵⁰ and models developed in small datasets are unstable at the level of individual risk.⁵¹ Here the extreme risk strata hold four and five patients. Separating what the observed data identify from what they cannot is therefore a substantive requirement, not a technicality.

The study had four objectives in adults undergoing craniotomy for severe TBI at a Central Java referral center. First, to describe admission glucose, potassium and GKR across MOST risk strata. Second, to quantify how strongly each marker correlates with MOST-based risk category and to test whether GKR correlates more strongly than glucose. Third, to compare observed in-hospital mortality with published benchmarks. Fourth, to bound the discrimination and covariate associations that these data cannot estimate directly. The working hypothesis was that GKR would rise monotonically across MOST strata.

2. Methods

2.1. Study design and reporting

The study was a single-center retrospective observational study, reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.⁵² Exposure was measured at hospital admission. The outcome was the MOST-based mortality-risk category assigned during the same admission.

2.2. Setting

Dr. Moewardi Regional General Hospital in Surakarta serves as the tertiary referral and teaching hospital of the Faculty of Medicine, Universitas Sebelas Maret. It receives neurotrauma referrals from across Central Java. The source population was patients with TBI treated in the emergency department and intensive care unit between 1 March and 31 August 2024. Medical records were reviewed in December 2025, after all index admissions had ended.

2.3. Participants and eligibility

Consecutive patients were eligible when four conditions were met. They were aged 18–60 years. They had a clinical diagnosis of severe TBI (Glasgow Coma Scale ≤ 8) and were scheduled for craniotomy, with random blood glucose and serum electrolytes, including potassium, measured on the first admission venous sample. Follow-up extended to at least seven days after admission. Exclusion criteria were significant extracranial multiple trauma, severe comorbidity such as diabetic nephropathy requiring hemodialysis, bilateral fixed dilated pupils on arrival, and refusal of consent by the next of kin. All eligible patients within the study window were included (total sampling) to limit selection bias (Figure 1).

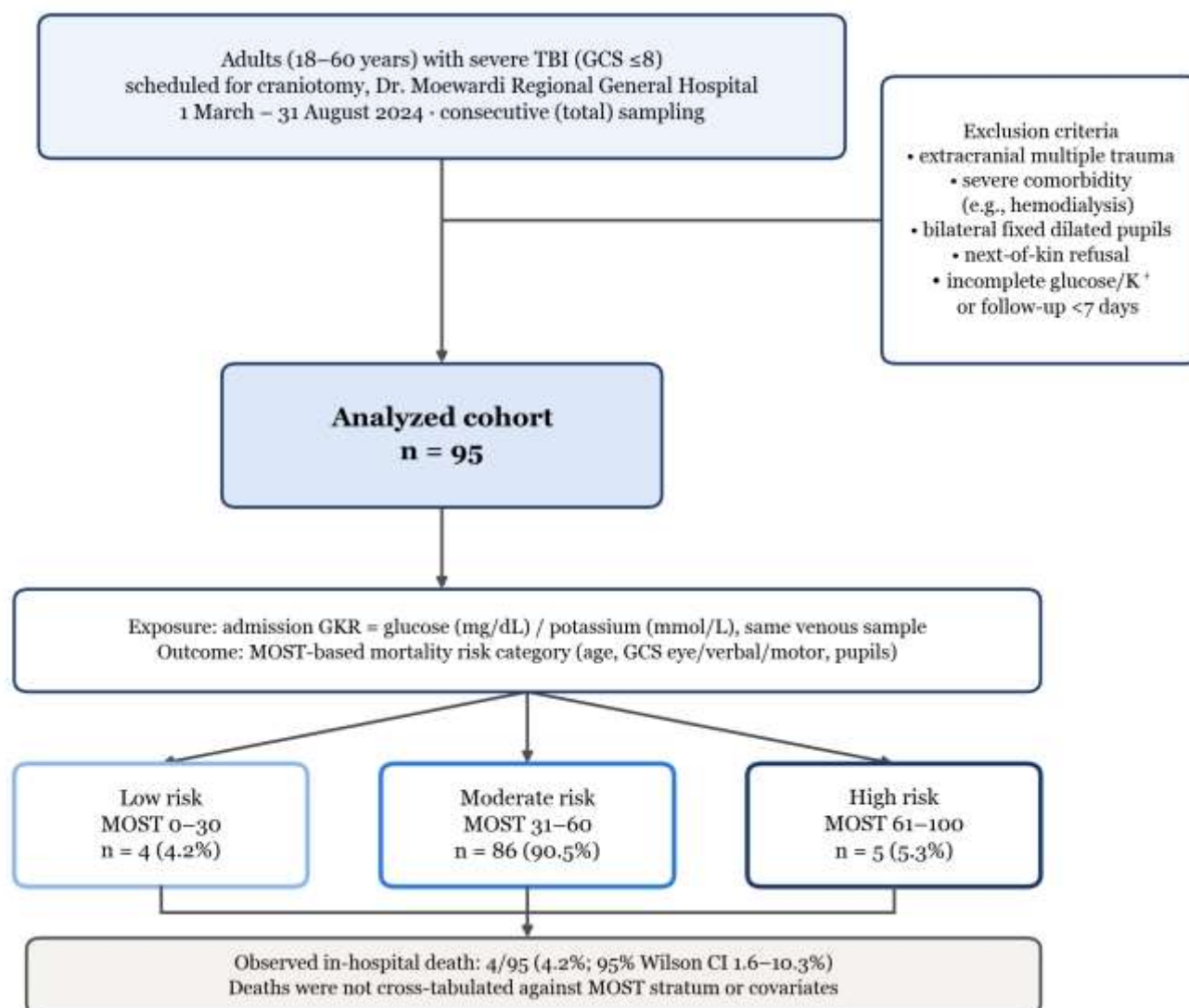


Figure 1. Study flow. Consecutive adults with severe traumatic brain injury scheduled for craniotomy at Dr. Moewardi Regional General Hospital (March–August 2024), the exclusion criteria applied, the analyzed cohort ($n = 95$) and its distribution across MOST mortality-risk strata.

2.4. Sample size

The protocol sample size was derived for a correlation of moderate magnitude, with a two-sided α of 0.05 and power of 0.80. It required 87 patients. The Fisher- z approximation for $\rho = 0.30$ gives 85. The achieved sample of 95 exceeded both figures. With 95 patients, the 95% confidence interval for a correlation of 0.376 has a half-width of approximately 0.17. The study was not powered for discrimination or multivariable analyses. These were addressed through the sensitivity analysis described below.

2.5. Variables and operational definitions

The exposure was GKR: random blood glucose (mg/dL) divided by serum potassium (mmol/L) from the same first venous sample. Using one sample avoided temporal mismatch between numerator and denominator. Published studies differ in glucose units, so the molar-scale ratio is given as the conventional value divided by 18.016. The outcome was the MOST score, computed from age, the eye, verbal and motor components of the Glasgow Coma Scale, and pupillary reactivity.⁴⁴ The investigators categorized it a priori as low (0–30), moderate (31–60) or high (61–100) mortality risk. Covariates abstracted from the records were sex, hemorrhage subtype, admission Glasgow Coma Scale, pupillary reactivity, sodium, arterial

pH, hemoglobin, leukocyte count, albumin, blood group and in-hospital survival status.

2.6. Data sources and measurement

Trained investigators abstracted variables onto a standardized case-report form and cross-checked them against the source records. Two assessors computed the MOST score independently. Complete admission glucose and potassium values were an inclusion criterion, so no exposure data were missing. No imputation was performed.

Perioperative management. All patients were managed under the institutional neuroanesthesia protocol, which aims to prevent secondary brain injury. Monitoring comprised electrocardiography, pulse oximetry, non-invasive arterial pressure (invasive where indicated), capnography, temperature and urine output. After preoxygenation with an inspired oxygen fraction of 1.0, rapid-sequence induction used fentanyl 2–3 $\mu\text{g/kg}$, propofol 1–2 mg/kg titrated to hemodynamic tolerance (or etomidate 0.3 mg/kg when unstable) and rocuronium 1.0–1.2 mg/kg. Manual in-line stabilization was applied. Anesthesia was maintained with sevoflurane below 1.0 minimum alveolar concentration and intermittent fentanyl, and a propofol infusion replaced the volatile agent when brain relaxation was inadequate. Ventilation

targeted normocapnia (PaCO₂ 35–40 mmHg) and PaO₂ above 60 mmHg. Brief moderate hyperventilation was reserved for acute intracranial hypertension. Systolic pressure was kept above 100–110 mmHg and cerebral perfusion pressure at 60–70 mmHg, using warmed, glucose-free isotonic fluids and norepinephrine when required. Signs of herniation were treated with mannitol 0.25–1.0 g/kg or hypertonic saline. Patients were transferred ventilated to the intensive care unit after surgery. The exposure was measured before induction, so these measures could not have influenced it. They do define the perioperative context to which the results apply.

2.7. Statistical analysis

Primary analysis. The primary analyses were performed in SPSS version 25.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test assessed distribution. Normally distributed variables are summarized as mean ± standard deviation and the rest as median (minimum–maximum). Spearman's ρ estimated the correlation of each marker with the MOST score, reported with Fisher- z 95% confidence intervals. The Kruskal–Wallis test compared the three risk strata, with $\varepsilon^2 = H/(n - 1)$ as the effect size.

Univariate estimates. Proportions are reported with 95% Wilson score intervals. An exact binomial test compared the sex distribution with parity, and the precision attained by each estimate is reported. Prevalence bounds for characteristics summarized only by median and range came from order statistics. The median of 95 values is the 48th ordered value. At least 48 patients therefore lie on each side of it. Observed in-hospital mortality was compared with five published benchmarks by exact binomial tests, with Holm correction for the five comparisons and Cohen's h as the effect size.

Parametric and comparative analyses. Potassium was the only normally distributed marker. One-way and Welch analysis of variance compared it across strata, and a linear trend contrast was computed exactly from the stratum means, standard deviations and sizes. Pairwise Hedges' g with 95% confidence intervals was added. The Meng–Rosenthal–Rubin test for correlated correlations asked whether GKR correlated more strongly with MOST than glucose or potassium did. That test needs the correlation between the two markers, which was not available. The p -value was therefore computed across the full range of that correlation, and the tipping value at which significance would be reached is reported.

Sensitivity analysis over datasets consistent with the observed summaries. Individual biomarker values were not cross-classified with survival status or covariates. Each biomarker was available as stratum-level order statistics (minimum, median and maximum for glucose and GKR) or as moments (mean and standard deviation for potassium). The categorical variables were available as marginal frequencies. Discrimination and covariate associations were therefore not estimated as point values. Instead, their attainable ranges were computed over the complete set of datasets consistent with every observed summary. These results are presented as a sensitivity analysis, not as observed associations. For glucose and GKR, exact mixed-integer linear programming gave the minimum and maximum of the Mann–Whitney U statistic (and hence the AUC) for each contrast between strata. It did the same for the Jonckheere–Terpstra trend statistic, and for sensitivity, specificity and the Youden index at every threshold.

For each pair of categorical variables, every contingency table compatible with the observed margins was enumerated. Each table yielded a conditional maximum-likelihood odds ratio, risk difference, Cramér's V and Fisher (or Freeman–Halton) exact p -value. For death across the three ordered MOST strata, the exact conditional Cochran–Armitage trend test was added. Multivariable associations were bounded with Firth-penalized logistic regression, which yields finite estimates under the separation that sparse events produce.⁵³ The models were fitted to 3,000 admissible patient-level configurations generated by independent permutation of each variable's labels, which preserves every margin. They were supplemented by 40 hill-climbing restarts of 400 label swaps towards each extreme coefficient (random seed 20261012). Penalized likelihood-ratio tests assessed significance. A measure whose attainable range included the null value was read as not identified by the data. A conclusion that held in every admissible dataset was read as robust.

Definition of the admissible set. For GKR, admissible datasets were all assignments of 4, 86 and 5 values to the low, moderate and high strata. Each assignment had to reproduce the stratum's minimum, maximum and median (for even-sized strata, the mean of the two central values), and the overall median of 35.14 as the 48th of 95 ordered values. Values were treated as continuous, with a minimum separation of 0.001 between distinct values, in keeping with reporting to two decimal places. Glucose values were restricted to integers in mg/dL, with tied pairs scored as one-half in U statistics. Potassium was excluded from rank-based bounds because only its moments were reported. Every optimization was solved to proven optimality. The bounds are exact for the stated constraints. They do not depend on distributional assumptions.

Plausible inter-marker correlation. For the comparison of correlations, plausible values of the unrecorded correlation between GKR and glucose were derived from the variance of a ratio on the logarithmic scale. Inputs were the pooled coefficient of variation of potassium (0.121), log-scale standard deviations of glucose between 0.12 and 0.25, and glucose–potassium correlations between 0 and –0.50.

Software and conventions. Derived analyses were performed in Python 3.14 with SciPy 1.18.1 (HiGHS solver for mixed-integer programming), statsmodels 0.15.0 and NumPy 2.4.4. All tests were two-sided with $\alpha = 0.05$, and p -values are reported to three decimal places. Holm correction was applied to the five benchmark comparisons. The remaining analyses were descriptive or sensitivity analyses and were not adjusted for multiplicity.

2.8. Ethics

Ethical approval for this study was granted by the CMHC Research Center Ethics Committee, Indonesia (Approval No. 2024/074). All patients lacked decision-making capacity at admission, so written informed consent was obtained from their next of kin. The study followed the Declaration of Helsinki. Records were de-identified before analysis.

3. Results

3.1. Participants and baseline characteristics

During the six-month study window, 95 consecutive adults with severe TBI undergoing craniotomy met the eligibility criteria and were analyzed (Figure 1). MOST classification

placed 4 patients (4.2%; 95% CI 1.6–10.3) in the low-risk stratum, 86 (90.5%; 83.0–94.9) in the moderate-risk stratum and 5 (5.3%; 2.3–11.7) in the high-risk stratum. The median MOST score was 44 (range 30–72). The minimum score was 30, so all four low-risk patients scored exactly at the upper boundary of their stratum.

Baseline characteristics are given in Table 1. Median age was 52 years (range 32–60), and no patient was younger than 32 years. Women made up 52 of 95 patients (54.7%; 95% CI 44.7–64.4), a proportion that did not differ from parity (exact binomial $p = 0.412$). Subdural hematoma was the most frequent lesion (33.7%; 25.0–43.7). Epidural

hematoma and traumatic subarachnoid hemorrhage followed at 29.5% each (21.2–39.3), and combined lesions accounted for 7.4% (3.6–14.4). The median admission Glasgow Coma Scale was 7 (range 3–8), and 88 patients (92.6%; 85.6–96.4) had bilaterally reactive pupils. Order-statistic bounds showed that at least 48 patients (50.5%) had an arterial pH of 7.25 or lower, an albumin of 3.3 g/dL or lower and a Glasgow Coma Scale of 7 or lower. Every patient had a leukocyte count of at least $11.0 \times 10^3/\mu\text{L}$. Hyponatremia ($<135 \text{ mmol/L}$) affected between 1 and 47 patients. Blood groups O, A, B and AB accounted for 30.5%, 28.4%, 28.4% and 12.6% of patients, respectively.

Table 1. Baseline characteristics of the cohort ($n = 95$).

Characteristic	Value	95% CI or order-statistic bound
Age, years — median (range)	52 (32–60)	—
Female sex, n (%)	52 (54.7)	44.7–64.4
Male sex, n (%)	43 (45.3)	35.6–55.3
Subdural hematoma, n (%)	32 (33.7)	25.0–43.7
Epidural hematoma, n (%)	28 (29.5)	21.2–39.3
Subarachnoid hemorrhage, n (%)	28 (29.5)	21.2–39.3
Combined lesions, n (%)	7 (7.4)	3.6–14.4
Glasgow Coma Scale — median (range)	7 (3–8)	≥ 48 patients ($\geq 50.5\%$) with GCS ≤ 7
Pupils reactive bilaterally, n (%)	88 (92.6)	85.6–96.4
Sodium, mmol/L — median (range)	135 (110–145)	Hyponatremia (<135) in 1–47 patients
Arterial pH — median (range)	7.25 (7.14–7.36)	≥ 48 patients ($\geq 50.5\%$) with pH ≤ 7.25
Hemoglobin, g/dL — median (range)	12.7 (11.0–13.8)	—
Leukocytes, $\times 10^3/\mu\text{L}$ — median (range)	13.3 (11.0–16.5)	All 95 patients ≥ 11.0
Albumin, g/dL — median (range)	3.3 (2.7–3.8)	≥ 48 patients ($\geq 50.5\%$) with albumin ≤ 3.3
Blood group O / A / B / AB, n (%)	29 (30.5) / 27 (28.4) / 27 (28.4) / 12 (12.6)	22.2–40.4 / 20.3–38.2 / 20.3–38.2 / 7.4–20.8
MOST score — median (range)	44 (30–72)	—
MOST low / moderate / high risk, n (%)	4 (4.2) / 86 (90.5) / 5 (5.3)	1.6–10.3 / 83.0–94.9 / 2.3–11.7
In-hospital death, n (%)	4 (4.2)	1.6–10.3

Notes: Proportions with 95% Wilson score intervals. Order-statistic bounds use the fact that the median of 95 values is the 48th ordered value. GCS, Glasgow Coma Scale; MOST, Mortality Score for Traumatic Brain Injury.

3.2. Observed mortality against published benchmarks

Four patients died in hospital (4.2%; 95% Wilson CI 1.6–10.3). As shown in Table 2 and Figure 2, this proportion was significantly lower than each of five published benchmarks after Holm correction. The benchmarks were 18.0% after emergency neurosurgery in the Global Neurotrauma Outcomes Study (17.1 deaths expected; $p < 0.001$; Cohen's $h = -0.46$), 23.5% at discharge in an eastern Indian cohort ($p < 0.001$; $h = -0.60$), 22.3% after

craniotomy in older adults ($p < 0.001$; $h = -0.57$), 12.2% in severe TBI in Peshawar (Holm $p = 0.024$; $h = -0.30$) and 10.6% in moderate-to-severe TBI in Taiwan (Holm $p = 0.044$; $h = -0.25$). At $\alpha = 0.05$, the highest benchmark mortality compatible with the observed count was 10.4% (Clopper–Pearson upper limit). The benchmarks differed in outcome horizon (14-day, in-hospital or at discharge) and in case-mix. The comparison is therefore indicative, not a matched contrast.

Table 2. Observed in-hospital mortality (4/95, 4.2%) compared with published benchmark cohorts.

Benchmark cohort	Mortality, %	Expected deaths	Exact p	Holm p	Cohen's h
Emergency neurosurgery for TBI, 57 countries ^a	18.0	17.1	<0.001	<0.001	–0.46
Severe TBI, Peshawar, Pakistan ^a	12.2	11.6	0.012	0.024	–0.30
TBI, mortality at discharge, Patna, India ^a	23.5	22.3	<0.001	<0.001	–0.60
Isolated moderate–severe TBI, Taiwan ^a	10.6	10.1	0.044	0.044	–0.25
Craniotomy in adults ≥ 65 years, India ^a	22.3	21.2	<0.001	<0.001	–0.57

Notes: Observed 4/95 (4.2%; 95% Wilson CI 1.6–10.3; Clopper–Pearson 1.2–10.4). Exact two-sided binomial tests of the observed count against each benchmark proportion; Holm correction across the five comparisons. Highest benchmark compatible with the observed count at $\alpha = 0.05$: 10.4%.

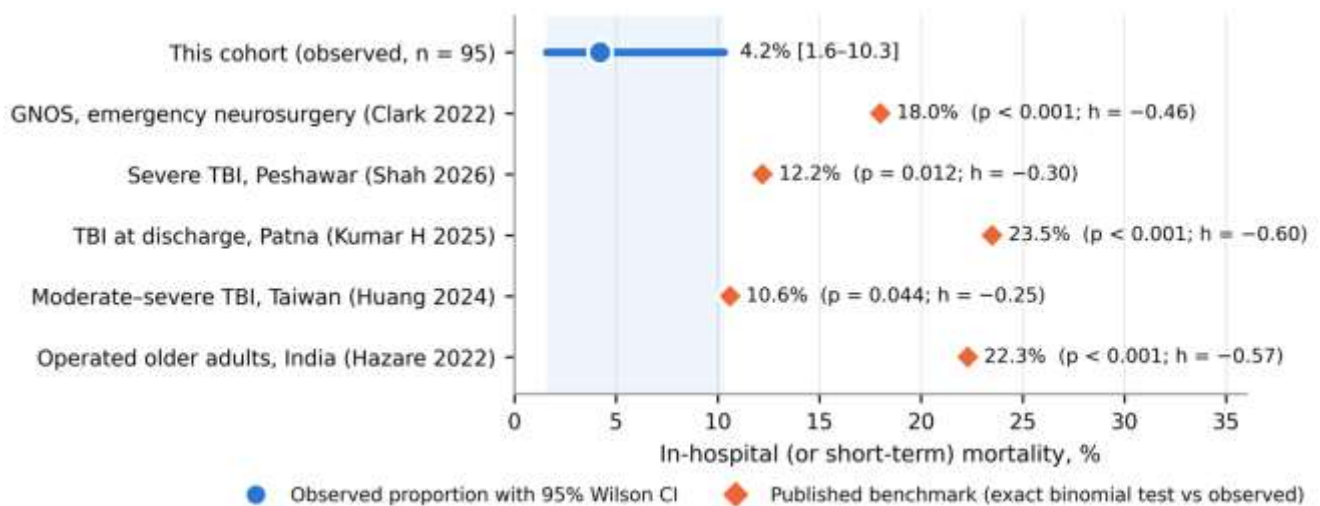


Figure 2. Observed in-hospital mortality (4.2%; 95% Wilson CI 1.6–10.3) compared with five published benchmark cohorts. Diamonds show benchmark mortality; p-values are exact binomial tests of the observed count against each benchmark (all remained significant after Holm correction), and h is Cohen's h.

3.3. Admission biomarkers across MOST strata

Table 3 and Figure 3 show the distribution of the three admission markers across MOST strata. Median glucose increased from 102 mg/dL (range 100–123) in the low-risk stratum to 127 mg/dL (100–200) in the moderate-risk and 167 mg/dL (125–200) in the high-risk stratum. Mean potassium fell from 4.05 ± 0.35 to 3.65 ± 0.44 and 3.34 ± 0.44 mmol/L. The overall median GKR was 35.14 (range 23.18–64.14). Stratum medians rose monotonically from 26.94 (23.18–28.60) to 35.21 (23.26–56.36) and 55.67 (31.25–64.14), corresponding to 1.50, 1.95 and 3.09 on the molar scale. Between-stratum differences were significant

for GKR ($H = 17.24$, $p < 0.001$; $\varepsilon^2 = 0.183$), glucose ($H = 14.12$, $p < 0.001$; $\varepsilon^2 = 0.150$) and potassium ($H = 6.80$, $p = 0.033$; $\varepsilon^2 = 0.072$).

The highest low-risk value lay below the lowest high-risk value for both GKR (28.60 versus 31.25) and glucose (123 versus 125 mg/dL). All 20 low-high pairs were therefore concordant in every dataset consistent with the observations (Mann-Whitney $U = 20$; $AUC = 1.00$; exact $p = 0.016$ for each marker). That p-value is the smallest two-sided value attainable with four and five patients. The extreme strata therefore did not overlap, however the unobserved values were distributed within the strata.

Table 3. Admission biomarkers across MOST mortality-risk strata.

Marker	Low risk (n = 4)	Moderate risk (n = 86)	High risk (n = 5)	Spearman ρ [95% CI]	p (ρ)	H	p (H)	ε^2	Low vs high U; exact p
Glucose, mg/dL — median (range)	102 (100–123)	127 (100–200)	167 (125–200)	+0.329 [0.137 to 0.498]	0.001	14.12	<0.001	0.150	20; 0.016
Potassium, mmol/L — mean $\pm$ SD	4.05 ± 0.35	3.65 ± 0.44	3.34 ± 0.44	-0.243 [-0.424 to -0.044]	0.018	6.80	0.033	0.072	—
GKR — median (range)	26.94 (23.18–28.60)	35.21 (23.26–56.36)	55.67 (31.25–64.14)	+0.376 [0.189 to 0.537]	<0.001	17.24	<0.001	0.183	20; 0.016
GKR, molar scale — median	1.50	1.95	3.09	—	—	—	—	—	—

Notes: p with the continuous MOST score, 95% CI by Fisher z transformation. H, Kruskal–Wallis statistic ($df = 2$); $\varepsilon^2 = H/(n - 1)$. U = 20 is the maximum attainable value (complete separation), giving an exact two-sided Mann–Whitney p in every dataset consistent with the summaries. GKR, glucose-to-potassium ratio, mg/dL per mmol/L; molar scale = GKR/18.016. Overall median GKR 35.14 (23.18–64.14). p (ρ), p-value of the Spearman correlation; p (H), p-value of the Kruskal–Wallis test.

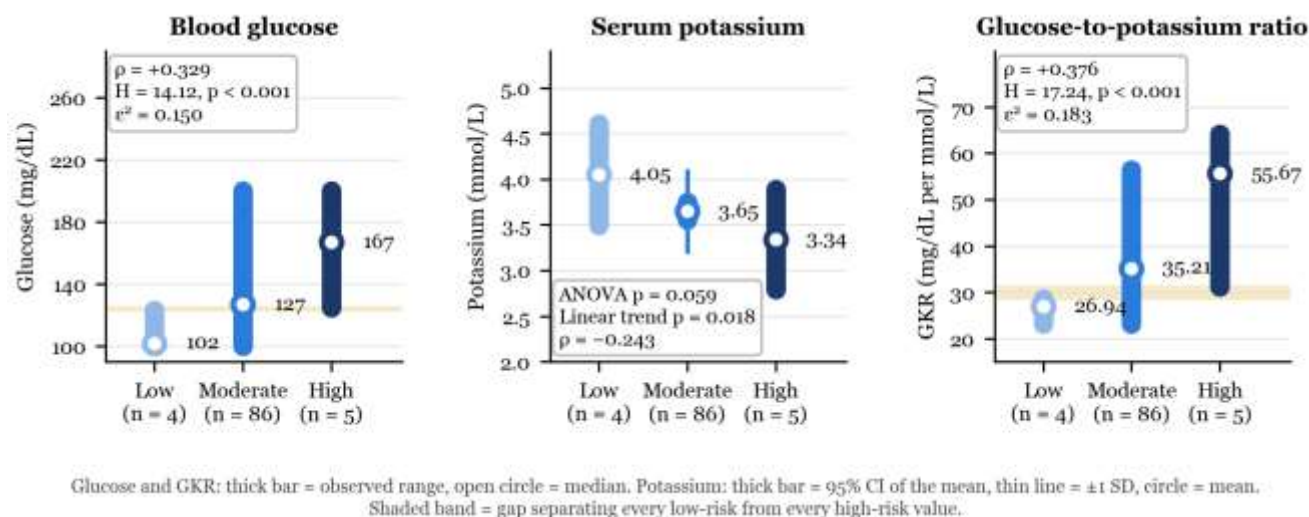


Figure 3. Admission blood glucose, serum potassium and glucose-to-potassium ratio (GKR) across MOST mortality-risk strata. For glucose and GKR, thick bars show the observed range and open circles the median; for potassium, thick bars show the 95% CI of the mean, thin lines ± 1 SD and circles the mean. The shaded band marks the gap separating every low-risk from every high-risk value. ρ , Spearman correlation with the MOST score; H , Kruskal–Wallis statistic; $\epsilon^2 = H/(n-1)$.

3.4. Correlation with MOST-based risk category and comparison between markers

GKR correlated positively with MOST-based risk category ($\rho = 0.376$; 95% CI 0.189–0.537; $p < 0.001$), as did glucose ($\rho = 0.329$; 0.137–0.498; $p = 0.001$). Potassium correlated inversely ($\rho = -0.243$; -0.424 to -0.044 ; $p = 0.018$), as shown in Table 3 and Figure 4. The difference between the GKR and glucose correlations was not significant at any plausible value of their mutual correlation (Table 4; Supplementary Table S2). It was $z = 0.77$ ($p = 0.443$) at $r = 0.80$, $z = 1.08$ ($p = 0.280$) at $r = 0.90$ and $z = 1.53$ ($p = 0.127$) at $r = 0.95$. Significance was reached only if the two markers correlated at 0.97 or above. Against potassium, the stronger correlation of GKR became significant only if the absolute correlation between GKR and potassium were at least 0.77 ($z = 1.36$, $p = 0.174$ at 0.50).

Under the log-scale approximation, plausible correlations between GKR and glucose ranged from 0.705 to 0.948. Across that range, the difference between the GKR and glucose correlations stayed non-significant ($p = 0.135$ to 0.526; Supplementary Table S2).

Potassium was also analyzed parametrically (Table 4). It did not differ across strata in one-way analysis of variance ($F(2, 92) = 2.93$, $p = 0.059$; $\eta^2 = 0.060$) or Welch analysis ($F(2, 5.2) = 3.39$, $p = 0.115$), whereas the Kruskal–Wallis test was significant ($H = 6.80$, $p = 0.033$; Table 3). The linear trend contrast was significant ($t(92) = -2.42$, $p = 0.018$). Among pairwise contrasts, only high versus low risk reached significance (Hedges' $g = -1.56$; 95% CI -3.06 to -0.06 ; $p = 0.031$). High versus moderate ($g = -0.70$; -1.61 to 0.21) and low versus moderate ($g = 0.91$; -0.10 to 1.92) did not.

Table 4. Comparative strength of the correlations and parametric analysis of potassium.

Analysis	Statistic	p	Effect size [95% CI]
A. GKR vs glucose correlation (ρ 0.376 vs 0.329), by assumed $r(\text{GKR, glucose})$			
$r = 0.80$	$z = 0.77$	0.443	$\Delta\rho = 0.047$
$r = 0.90$	$z = 1.08$	0.280	$\Delta\rho = 0.047$
$r = 0.95$	$z = 1.53$	0.127	$\Delta\rho = 0.047$
Tipping value for $p < 0.05$	$r \geq 0.97$	—	—
B. GKR vs potassium correlation (ρ 0.376 vs 0.243), by assumed $r(\text{GKR, K})$			
$ r = 0.30$	$z = 1.16$	0.247	$\Delta \rho = 0.133$
$ r = 0.50$	$z = 1.36$	0.174	$\Delta \rho = 0.133$
$ r = 0.70$	$z = 1.75$	0.081	$\Delta \rho = 0.133$
Tipping value for $p < 0.05$	$ r \geq 0.77$	—	—
C. Potassium across MOST strata (from reported mean $\pm$ SD)			
One-way ANOVA	$F(2, 92) = 2.93$	0.059	$\eta^2 = 0.060$; $\omega^2 = 0.039$
Welch ANOVA	$F(2, 5.2) = 3.39$	0.115	—
Linear trend contrast ($-1, 0, +1$)	$t(92) = -2.42$	0.018	—
High vs moderate (Welch t)	$t = -1.53$	0.193	$g = -0.70$ [-1.61 to 0.21]
Low vs moderate (Welch t)	$t = 2.21$	0.103	$g = 0.91$ [-0.10 to 1.92]
High vs low (Welch t)	$t = -2.70$	0.031	$g = -1.56$ [-3.06 to -0.06]

Notes: Panels A–B: Meng–Rosenthal–Rubin test for correlated correlations ($n = 95$); the correlation between GKR and its component was not available, so the test is shown across its plausible range. Panel C: computed exactly from stratum sizes, means and SDs; g , Hedges' g . ANOVA, analysis of variance.

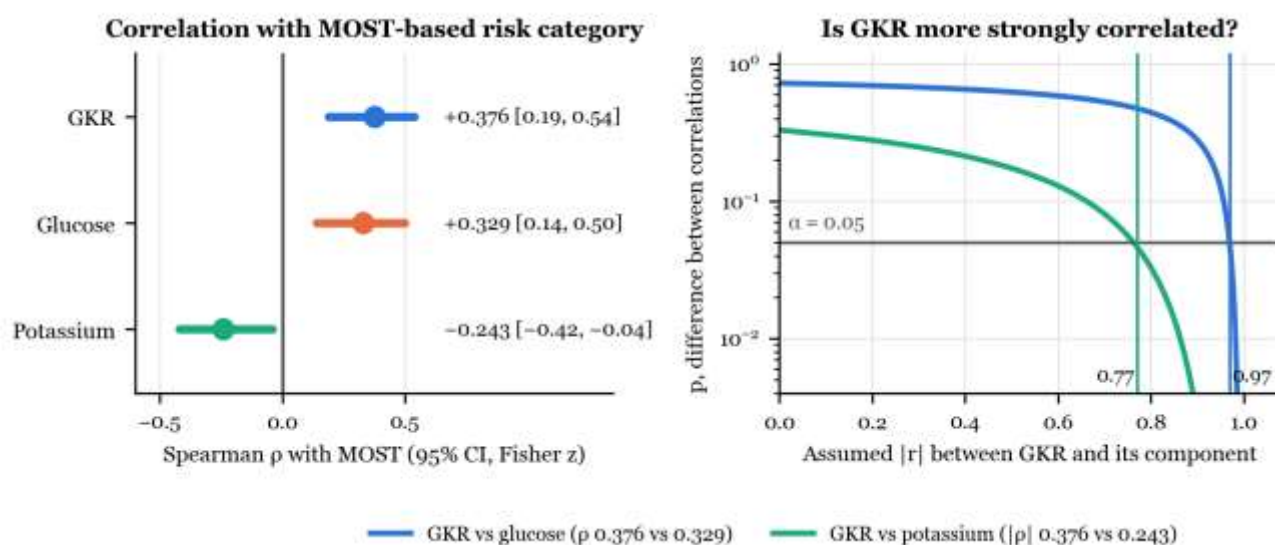


Figure 4. Left: correlation of each marker with the MOST score (Spearman ρ with Fisher-z 95% CI). Right: p-value of the Meng-Rosenthal-Rubin test comparing the GKR correlation with that of glucose or potassium, as a function of the unrecorded correlation between GKR and its component; vertical lines mark the tipping values (0.97 and 0.77) at which the difference would reach significance.

3.5. Sensitivity analysis: attainable discrimination

Across all datasets consistent with the stratum summaries (Table 5, Figure 5), the attainable AUC of GKR for the high-risk stratum ranged from 0.436 to 0.898 against all other patients and from 0.409 to 0.893 against the moderate stratum. The corresponding ranges for glucose were 0.389–0.898 and 0.360–0.893. Both ranges span 0.5, so the summaries do not identify discrimination of high risk. Contrasts against the low stratum stayed above 0.5 in every admissible dataset. For the moderate and high strata combined, the range was 0.654–0.992 for GKR and 0.587–0.992 for glucose.

The Jonckheere-Terpstra statistic for an ordered increase in GKR (expected value under the null 397, SD 78.80) ranged from 496 ($z = 1.26$, $p = 0.209$) to 745 ($z = 4.42$, $p < 0.001$). For glucose it ranged from 452.5 ($z = 0.70$, $p = 0.481$) to 745. The direction of the trend was positive in every admissible dataset, while its significance rests on the observed Kruskal-Wallis and Spearman statistics. At every GKR threshold between 31.25 and 55.67, including the published values of 42.0, 42.7, 48.5 and 50.0, attainable sensitivity for high risk was 60–80% and specificity 53.3–98.9% (Figure 6; Supplementary Table S4). The maximum attainable Youden index at any threshold was 0.789 for both markers.

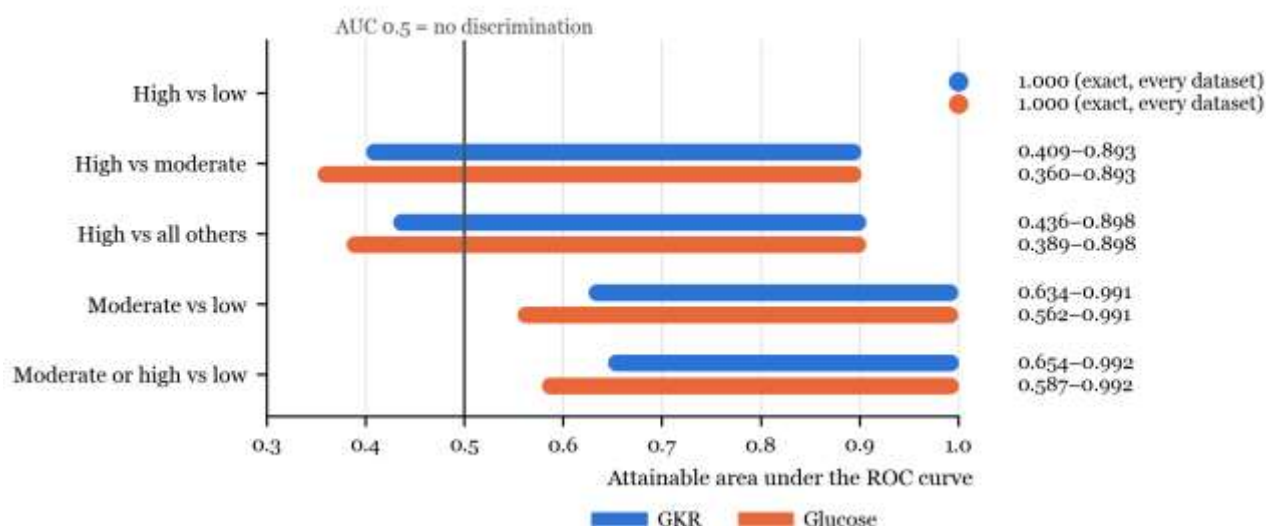


Figure 5. Attainable areas under the ROC curve (AUC) for GKR and glucose over all datasets consistent with the observed stratum summaries (sensitivity analysis). Contrasts of the high-risk stratum span 0.5 except against the low-risk stratum, where separation is complete in every admissible dataset.

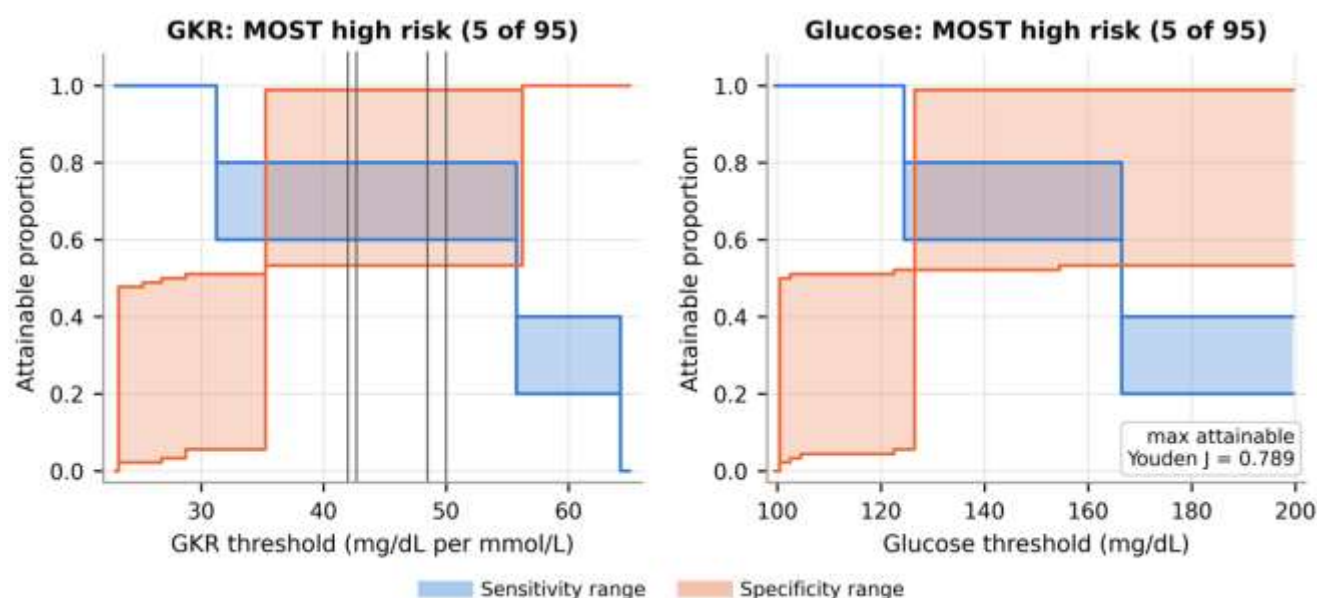


Figure 6. Attainable sensitivity and specificity for MOST high risk across thresholds of GKR (left) and glucose (right) over all datasets consistent with the observed summaries (sensitivity analysis). Vertical lines mark published GKR thresholds (42.0, 42.7, 48.5 and 50.0); the maximum attainable Youden index is 0.789 for both markers.

3.6. Sensitivity analysis: categorical and multivariable associations

Table 5 and Figure 7 summarise associations between categorical variables. Fifteen allocations of the four deaths across the three MOST strata were compatible with the observed margins (Supplementary Table S3). The exact Cochran–Armitage test was significant in eight of them: four in the expected positive direction and four in the inverse direction. For death and high MOST risk, attainable odds ratios ranged from 0 to infinity, and three of five admissible tables were significant. The corresponding counts were one of five for death and male sex, three of five for death and pupils that were not bilaterally reactive, one of six for high MOST risk and male sex, and four of six for high MOST risk and abnormal pupils. Death was

significantly associated with hemorrhage subtype in 12 of 35 admissible tables (34.3%), and high MOST risk in 25 of 56 (44.6%).

In Firth-penalized models fitted to 3,000 admissible datasets, the median odds ratio of death for high MOST risk was 1.73 (2.5th–97.5th percentile 0.73–15.39). It reached significance in 1.2% of datasets. Hill-climbing drove the attainable odds ratio of every predictor from below 0.01 to above 10^5 . No predictor of death or of high MOST risk reached significance in more than 6.2% of admissible datasets (Supplementary Table S5). With 1.0 and 1.7 events per variable, these models show that the data cannot identify multivariable associations. They do not provide effect estimates.

Table 5. Sensitivity analysis: attainable ranges over all datasets consistent with the observed summaries.

Quantity	Attainable range	Admissible datasets with $p < 0.05$	Interpretation
A. Discrimination of MOST strata (exact mixed-integer programming)			
AUC, GKR, high vs all others	0.436–0.898	—	Not identified
AUC, GKR, high vs moderate	0.409–0.893	—	Not identified
AUC, GKR, moderate or high vs low	0.654–0.992	—	Robust (>0.5 in every dataset)
AUC, glucose, high vs all others	0.389–0.898	—	Not identified
AUC, glucose, moderate or high vs low	0.587–0.992	—	Robust (>0.5 in every dataset)
AUC, GKR and glucose, high vs low	1.000 (exact)	—	Robust (complete separation)
Jonckheere–Terpstra, GKR	496–745 (z 1.26 to 4.42)	—	Direction robust; significance not identified
Jonckheere–Terpstra, glucose	452.5–745 (z 0.70 to 4.42)	—	Direction robust; significance not identified
Sensitivity at GKR 42.0, 42.7, 48.5 or 50.0	60–80%	—	At least one high-risk patient below threshold
Specificity at the same thresholds	53.3–98.9%	—	Not identified
Maximum Youden index, any threshold	0.789 (GKR and glucose)	—	Upper bound
B. Categorical associations (complete enumeration of tables)			
Death × MOST stratum (exact trend test)	p 0.000–1.000	8/15 (4 positive, 4 inverse)	Not identified
Death × MOST high risk	OR 0.00 to ∞; RD −0.044 to +0.800	3/5	Not identified

Quantity	Attainable range	Admissible datasets with $p < 0.05$	Interpretation
Death × male sex	OR 0.00 to ∞ ; RD -0.077 to +0.093	1/5	Not identified
Death × pupils not bilaterally reactive	OR 0.00 to ∞ ; RD -0.045 to +0.571	3/5	Not identified
Death × hemorrhage subtype	Freeman–Halton p 0.000–1.000	12/35	Not identified
MOST high × male sex	OR 0.00 to ∞ ; RD -0.096 to +0.116	1/6	Not identified
MOST high × pupils not bilaterally reactive	OR 0.00 to ∞ ; RD -0.057 to +0.714	4/6	Not identified
MOST high × hemorrhage subtype	Freeman–Halton p 0.000–1.000	25/56	Not identified
C. Multivariable bounds (Firth-penalized logistic regression, 3,000 admissible datasets)			
Death: MOST high risk	median OR 1.73 [0.73–15.39]; attainable <0.01 to $>10^3$	1.2%	Not identified
Death: male sex	median OR 1.15 [0.12–10.11]; attainable <0.01 to $>10^3$	4.3%	Not identified
Death: pupils not bilaterally reactive	median OR 1.31 [0.62–14.11]; attainable <0.01 to $>10^3$	3.5%	Not identified
Death: subdural hematoma	median OR 0.90 [0.18–5.37]; attainable <0.01 to $>10^3$	1.5%	Not identified
MOST high: male sex	median OR 0.90 [0.10–4.52]; attainable <0.01 to $>10^3$	6.2%	Not identified
MOST high: pupils not bilaterally reactive	median OR 1.08 [0.63–9.96]; attainable <0.01 to $>10^3$	3.0%	Not identified
MOST high: subdural hematoma	median OR 1.27 [0.15–6.20]; attainable <0.01 to $>10^3$	3.9%	Not identified

Notes: Sensitivity analysis over all datasets reproducing every observed stratum minimum, median and maximum (GKR, glucose) or every observed margin (categorical variables); these ranges are not observed estimates. Conditional maximum-likelihood odds ratios (OR; 0 or ∞ when a cell is empty); RD, risk difference. In panel C, hill-climbing extremes exceeded 10^3 for every predictor; percentages are the share of admissible datasets with penalized likelihood-ratio $p < 0.05$.

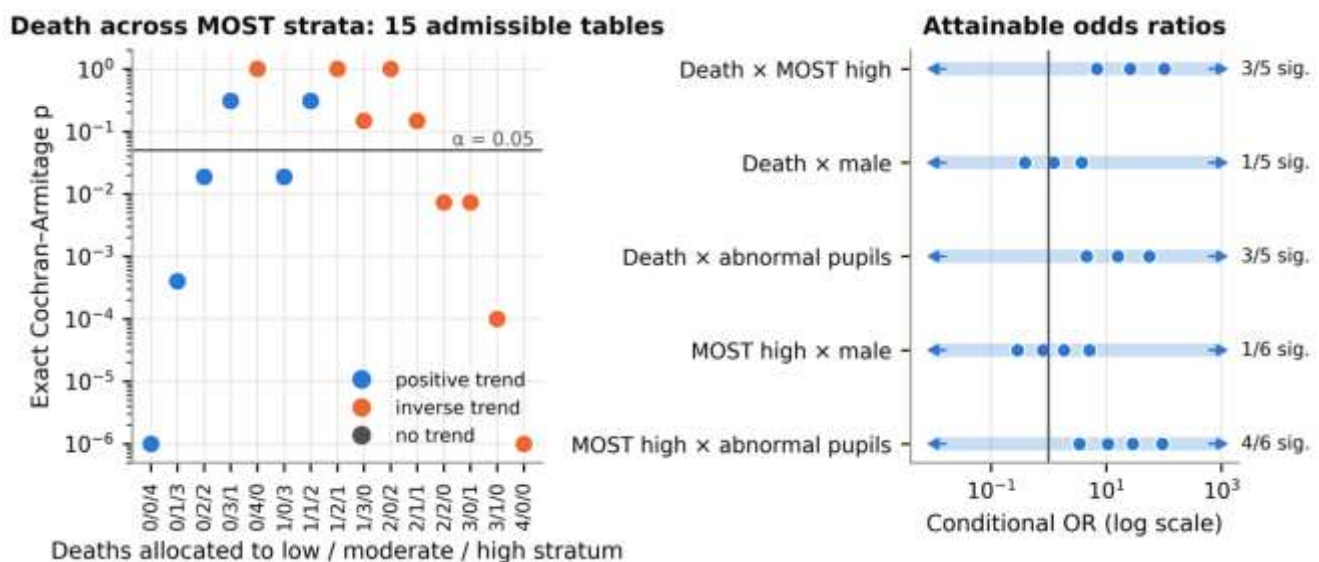


Figure 7. Categorical associations over all contingency tables consistent with the observed margins (sensitivity analysis). Left: exact Cochran–Armitage p -values for the 15 admissible allocations of the four deaths across the low, moderate and high MOST strata. Right: attainable conditional odds ratios, with the number of admissible tables reaching $p < 0.05$.

4. Discussion

4.1. Principal findings

In 95 adults undergoing craniotomy for severe TBI at Dr. Moewardi Regional General Hospital, admission GKR rose monotonically across MOST risk strata. It correlated weakly to moderately with MOST-based risk category. For GKR and for glucose alone, the highest low-risk value lay below the lowest high-risk value, which holds for every dataset compatible with the observations (four versus five patients). Three further findings qualify this signal. GKR was not demonstrably more strongly correlated with risk than glucose. Potassium declined linearly, yet the parametric omnibus test was non-significant. Observed in-hospital mortality, at 4.2%, was lower than in comparable surgical and severe-TBI cohorts. The sensitivity analysis showed that the stratum-level data cannot identify the

discrimination of GKR for high risk or its operating characteristics at published thresholds. They also cannot identify any association of death with MOST stratum, sex, pupils or lesion type.

4.2. Comparison with the published literature

The gradient observed here lies within the range reported for the ratio when glucose is expressed in mg/dL. Among 4,357 patients with isolated moderate-to-severe TBI, the Stress Index averaged 61.7 in non-survivors and 44.1 in survivors, with an optimal threshold of 48.5.²⁰ These values bracket the high-risk (55.67) and moderate-risk (35.21) medians of the present cohort. Thresholds of 42 in operated severe TBI, 42.7 in general trauma and 50 in Japanese adults and Brazilian children,^{19,21–23} and an upper-quartile boundary of 47.2 after aneurysmal subarachnoid hemorrhage,²⁷ all fall between our moderate and high medians. The convergence is notable. The cohorts differed in age, mechanism, lesion type and outcome definition, and

the present outcome was a score rather than death, yet thresholds derived for different outcomes appear to cluster between the low 40s and 50 on the mg/dL scale. Our high-risk stratum sat in the region where published cohorts observed excess mortality.

Harmonizing units sharpens the comparison. It also exposes gaps. Dividing by 18.016, the published mg/dL thresholds of 42.0, 42.7, 48.5 and 50 correspond to molar ratios of 2.33, 2.37, 2.69 and 2.78. Conversely, the molar inflection points reported after subarachnoid hemorrhage (2.3) and the mild-to-moderate TBI cut-off (2.286) correspond to 41.4 and 41.2 on the mg/dL scale.^{26,28} The inflection for early post-traumatic epilepsy (2.835) and the decision-tree threshold in grade V aneurysmal hemorrhage (3.2) correspond to 51.1 and 57.7.^{29,33} On either scale, the published thresholds cluster between our moderate-risk median (1.95 molar; 35.21 conventional) and high-risk median (3.09; 55.67). A unit-explicit threshold therefore appears transportable between centers, but only if each report states whether glucose was expressed in mg/dL or mmol/L, which several GKR studies omit. Many do not.

The central rationale for the ratio is that it outperforms its components, and the present data did not support this. The correlation with MOST was 0.376 for GKR and 0.329 for glucose. According to the Meng–Rosenthal–Rubin test, the difference could reach significance only if the two markers were almost collinear ($r \geq 0.97$). GKR is mathematically coupled to glucose through its numerator, so a high correlation between them is expected; a correlation near unity would also mean that the ratio adds little beyond glucose. Published evidence on incremental value is sparse. In mild-to-moderate TBI, the ratio alone reached an AUC of only 0.670 and gained most of its value in combination with imaging.²⁶ In an Indonesian operative cohort, glucose correlated with mortality ($r = 0.524$) yet failed to predict death within severe TBI.⁴⁷ Showing that the ratio improves on glucose will require paired comparisons of discrimination, such as the DeLong test for correlated AUCs, on patient-level data with observed outcomes.

The potassium findings deserve separate attention, because the denominator is the less studied half of the ratio. Potassium was normally distributed, so the parametric analysis is the matched method. It showed an ordered decline (linear trend $p = 0.018$) without a significant parametric omnibus difference (ANOVA $p = 0.059$; Kruskal–Wallis $p = 0.033$). Only the contrast between the extreme strata reached significance, and its confidence interval was wide. This pattern fits a craniotomy cohort in which hypokalemia was common (48.1%) yet potassium itself was not prognostic,¹⁷ and multicenter data showing in-hospital hypokalemia in 46.55% of patients with TBI.¹⁶ In a large retrospective cohort, by contrast, hyperkalemia carried the strongest adjusted association with death (OR 4.86).¹⁸ The potassium–outcome relation may therefore be U-shaped. Such a denominator would weaken a ratio that assumes potassium falls monotonically with severity, and it could explain part of the non-linear GKR curves reported in hemorrhagic stroke and in TBI-associated kidney injury.^{28,34}

4.3. Interpretation and possible mechanisms

Observed in-hospital mortality of 4.2% was lower than every benchmark examined. These included 18% after emergency neurosurgery worldwide,² 22.3% after craniotomy in older adults⁵⁴ and 23.5% at discharge in an eastern Indian cohort.⁶ The highest benchmark compatible with the data was 10.4%. The eligibility criteria plausibly

explain much of this gap. Exclusions matter. Excluding patients with bilateral fixed dilated pupils removes the subgroup with the worst prognosis; in one series, 30-day mortality after decompressive craniectomy reached 78.7% in such patients.⁵⁵ Excluding significant extracranial trauma and patients older than 60 years removes further high-risk groups. MOST high risk in this cohort therefore describes relative position within a selected surgical population, not absolute mortality.

A further mechanism is built into the design. Follow-up to at least seven days after admission was required, which excludes patients who died within the first week, when deaths after severe TBI are most frequent. Such deaths would be missing from the numerator, and their admission biochemistry, plausibly the most deranged, would be missing from the exposure distribution. This survivorship constraint biases observed mortality downwards. It would also be expected to compress the upper tail of GKR, so the observed gradient may be conservative rather than inflated. The data describe patients who survived long enough to complete a week of care, and early prognostic markers may be less informative in that population than in the full emergency cohort.

Using MOST as the outcome has advantages and costs. Its components are recorded for every patient, and they are less vulnerable than death itself to the short follow-up of a retrospective record review. In its derivation cohort, it outperformed CRASH-Basic and IMPACT-Core.⁴⁴ The score was nevertheless derived in a United States registry. The 0–30, 31–60 and 61–100 bands used here were defined by the investigators, not taken from the derivation study. Prognostic models transported to Asian and surgical populations have repeatedly over-predicted risk despite good discrimination.^{39–42} Placing 90.5% of patients in the moderate band also limits resolution. Most importantly, the premise that MOST stratum tracks observed death in this cohort could not be verified. Of the 15 allocations of the four deaths compatible with the data, the trend was significant in the expected direction in four and in the inverse direction in another four. An association between GKR and a score that partly encodes age and neurological status is therefore one step removed from an association with mortality.

Two further properties of MOST bear on interpretation. The score is a sum of points, not a probability, so a MOST value of 61 does not denote a 61% risk of death. Conversion to predicted mortality requires the published look-up table. It has not been calibrated in an Indonesian or surgical population. MOST also shares age and pupillary reactivity with the factors that determine operative risk. Pupils that were not bilaterally reactive affected only seven patients, so the high-risk stratum is probably driven largely by the Glasgow Coma Scale components and age. Part of the correlation between GKR and MOST may therefore reflect the known association between stress hyperglycemia and depth of coma, not a mortality-specific signal.

The sensitivity analysis turns these constraints into ranges that a clinician can read directly. An attainable AUC between 0.436 and 0.898 means that the stratum summaries are compatible with near-excellent discrimination of the high-risk stratum and with none at all. An attainable sensitivity of 60–80% at the literature thresholds means that at least one of the five high-risk patients necessarily fell below each of them. These ranges are not a weakness of the method. They simply state what four and five patients at the extremes can support. They

agree with methodological evidence that data-driven cut-offs from samples of about 100 recover the true optimum only 17% of the time and overstate sensitivity,⁵⁰ that small-sample prediction models are unstable at the individual level,⁵¹ and that penalized estimation is needed simply to obtain finite estimates when events are this sparse.⁵³ A single AUC or cut-off from such data would convey a precision that the cohort does not possess.

Biologically, the behavior of the ratio fits the integrated neuroendocrine and ionic response to severe brain injury (Figure 8). Sympathoadrenal activation drives hyperglycemia through glycogenolysis and gluconeogenesis, while β_2 -adrenergic stimulation of the Na^+/K^+ -ATPase drives potassium into cells. Cortisol and inflammatory cytokines add peripheral insulin resistance.

Hyperglycemia may aggravate the injured brain through anaerobic glycolysis, lactate accumulation and oxidative stress, which links the marker to secondary injury and not merely to severity. Three observations indicate that GKR should be treated as a marker of stress intensity and not as a therapeutic target: the bell-shaped glucose–outcome relation,¹⁵ the absence of a survival benefit from intensive glycemic control (RR 0.99),⁵⁶ and the imprecision of the hyperglycemia–mortality association in small low-resource cohorts.⁵⁷ The potassium limb carries a parallel caution. Hypokalemia that reflects transcellular shift rather than depletion may reverse as catecholamine levels fall. An elevated ratio should therefore prompt measured, not reflexive, potassium replacement, particularly after osmotherapy.

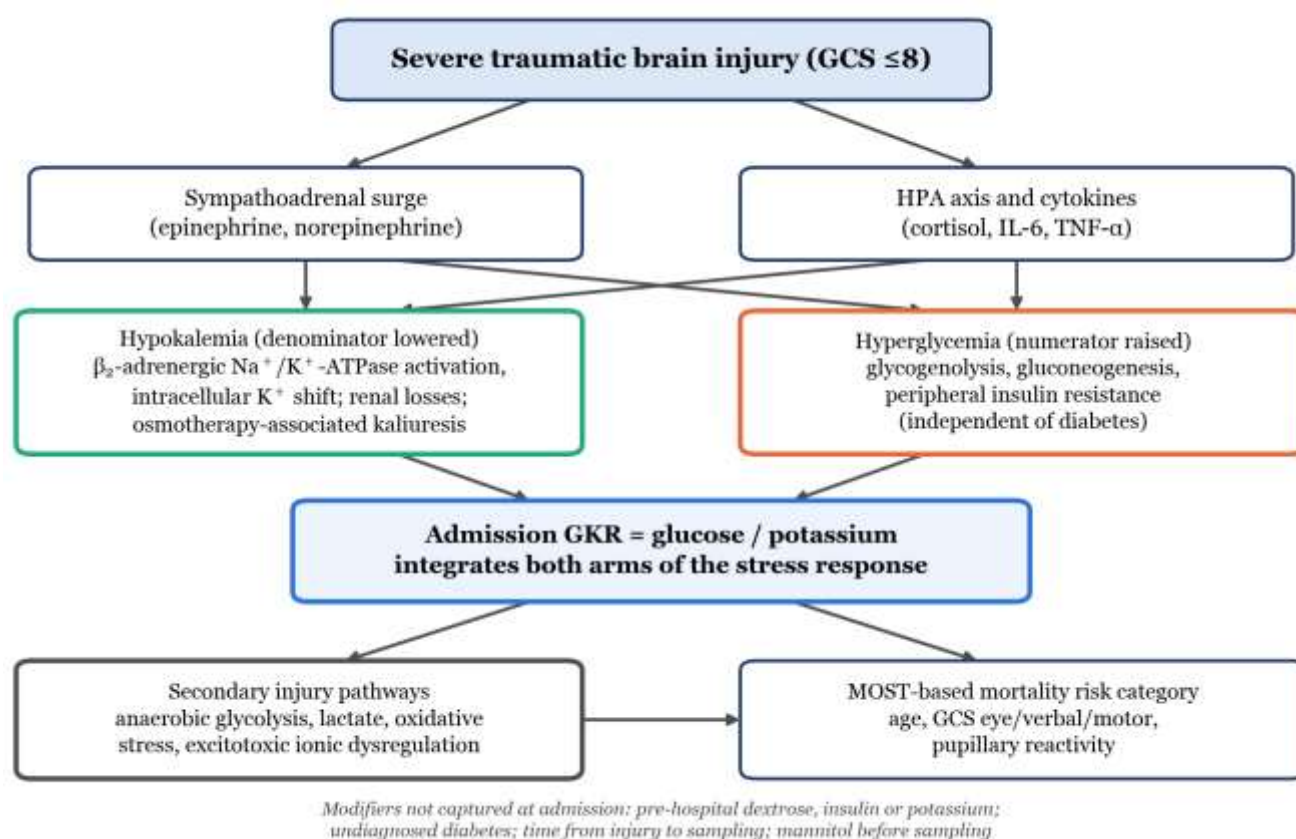


Figure 8. Proposed mechanism linking severe traumatic brain injury to an elevated admission glucose-to-potassium ratio and to MOST-based mortality risk category, with modifiers not captured at admission.

4.4. Implications for practice

For anesthesiologists and intensivists, the practical message is modest but useful. GKR is available within minutes of arrival from tests already ordered for every patient with severe TBI, at no incremental cost. In this cohort the extreme risk strata did not overlap. A high admission ratio can therefore reasonably prompt heightened vigilance for secondary insults. The inference rests on nine patients. Suitable measures include early invasive arterial monitoring, strict maintenance of cerebral perfusion pressure, and avoidance of hypotension and hypoxemia. These insults are frequent,¹⁰ and systolic hypotension is strongly associated with death.¹¹ The measures are standard in severe TBI and are not specific to a high ratio. The ratio should not be used to triage patients away from surgery or intensive care. Until its discrimination against observed outcomes is established, it should supplement, not replace, the clinical examination,

imaging and established prognostic models. Its value relative to glucose alone remains to be demonstrated.

These findings belong in the context of neurotrauma care in Indonesia and the wider region. Road-traffic injury dominated by motorcycles drives the Indonesian burden,⁹ referral distances are long and access to neuromonitoring is uneven. Admission chemistry is attractive in this setting because it needs no additional infrastructure. Local prognostic work has so far examined CRASH in surgical patients⁴³ and glucose in operative cohorts, with mixed results in severe injury.^{47,48} Elsewhere in Southeast and South Asia, prognostic models discriminate well but over-predict,^{40,41} and severe-TBI mortality varies widely with resources and surgical access.^{4–6} A regional validation of GKR alongside MOST and CRASH, with shared definitions and units, would be more informative than further single-center studies.

Several incidental findings merit comment. First, age. The cohort was older (median 52 years, none younger than 32) than South Asian registry populations with a median

age of 27,⁷ and closer to the aging profile of high-income cohorts.⁸ Referral patterns or the upper age limit of 60 may explain this. Women formed a slight majority, which departs from the male predominance usually seen in neurotrauma series and may partly reflect the older age profile. Biochemically, at least half of the patients were acidemic (pH ≤ 7.25) and hypoalbuminemic. All had a leukocyte count of at least $11.0 \times 10^3/\mu\text{L}$, and hyponatremia may have affected up to 47 patients. This burden of systemic derangement matches the near-universal electrolyte disturbance reported after TBI.¹⁸ Traumatic subarachnoid hemorrhage accounted for 29.5% of lesions. GKR has been linked to outcome after spontaneous subarachnoid hemorrhage,^{27,28} so lesion-specific analyses are a natural next step.

4.5. Strengths

The study has several strengths. It addressed a clearly defined surgical population with severe TBI, used consecutive sampling, computed the ratio from a single admission sample and related it to a recently derived TBI-specific score. Every reported estimate is either computed from the observed data or presented as an attainable range over all datasets consistent with them, so no result depends on assumptions about unobserved joint distributions. The analysis also tested, rather than assumed, the superiority of the ratio over its components, and it benchmarked mortality against published cohorts.

4.6. Limitations

The limitations are substantial. The design was retrospective and single-center. Individual biomarker values were not cross-classified with survival status or covariates. Discrimination, calibration and adjusted associations could therefore be bounded but not estimated, and the correlation between GKR and glucose needed for a direct superiority test was unavailable. The outcome was a score rather than observed death, and its bands were study-defined and uncalibrated in this population. With four deaths and five high-risk patients, every analysis of the extreme strata is imprecise. Single admission values cannot capture the dynamic course of glucose and potassium during resuscitation and surgery. Pre-hospital fluids, insulin or potassium administration, undiagnosed diabetes and time from injury to sampling were not recorded. Finally, the eligibility criteria excluded the patients at highest risk, which limits generalizability to the full spectrum of severe TBI.

4.7. Recommendations for future research

Future work should proceed in three steps. First, patient-level data from this and comparable Indonesian centers should be pooled. The pooled data would estimate the AUC of GKR, glucose and potassium against observed in-hospital death, compare them with the DeLong test, and assess the calibration of MOST. Second, a prospective multicenter cohort should record serial GKR at admission, after resuscitation and on the first postoperative day, because longitudinal values have outperformed single measurements after aneurysmal hemorrhage.⁵⁹ Third, the ratio should be tested for incremental value over MOST or CRASH, not in isolation.

These studies can be sized now. Estimating an AUC of 0.75 with a 95% confidence interval half-width of 0.075 needs about 579 patients with 58 deaths at 10% mortality, or 397 patients with 60 deaths at 15%. A half-width of 0.05 requires about 1,300 and 892 patients, respectively. A

multivariable model with five candidate predictors at 10 to 20 events per variable requires 50 to 100 deaths, that is, 334 to 667 patients at 15% mortality. Recruitment on this scale is realistic only through a consortium of Indonesian referral hospitals working to a shared protocol that records glucose units, sampling time, pre-hospital treatment, MOST components and outcome at discharge and six months.

5. Conclusion

In adults undergoing craniotomy for severe TBI at an Indonesian referral center, admission GKR rose monotonically across MOST risk strata, correlated with MOST-based risk category ($p = 0.376$; 95% CI 0.189–0.537) and the low- and high-risk strata did not overlap (exact $p = 0.016$, the smallest value attainable with four and five patients). It was not demonstrably more informative than glucose. The data could not identify its discrimination of high risk (attainable AUC 0.436–0.898) or link MOST stratum to observed death. Observed mortality (4.2%) was well below published benchmarks, as expected in a selected surgical population. GKR costs nothing and may reasonably heighten perioperative vigilance. It should not guide triage, however, until patient-level validation against observed outcomes, with direct comparison to glucose and calibration of MOST, has been completed in multicenter Indonesian cohorts. The immediate priority is a pooled patient-level analysis across Indonesian referral hospitals. It should state glucose units explicitly and test GKR against observed death, against glucose alone and alongside MOST.

6. Declarations

Ethical approval and consent to participate. This study received ethical approval from the CMHC Research center Ethics Committee, Indonesia (Approval No. 2024/074). Written informed consent was obtained from the patients' next of kin. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication. Not applicable; the article contains no identifiable individual data.

Availability of data and materials. The aggregate data underlying this article are reported in the article and its supplementary material. The analysis code for the derived and sensitivity analyses is available from the corresponding author on reasonable request.

Artificial intelligence (AI) use statement. The authors declare that no generative artificial intelligence tools were used in the design, analysis, or writing of this manuscript.

Author contribution statement. P.: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing. S.B.S.: Investigation, Data curation, Writing – review & editing. L.C.P.: Supervision, Validation, Writing – review & editing. All authors read and approved the final manuscript.

Funding statement. This study received no specific funding.

Conflict of interest (competing interests) statement. The authors declare no competing interests.

Acknowledgements. The authors thank the medical-record staff of Dr. Moewardi Regional General Hospital for their assistance with record retrieval.

7. References

- Zhong H, Feng Y, Shen J, et al. Global Burden of Traumatic Brain Injury in 204 Countries and Territories From 1990 to 2021. *Am J Prev Med*. 2025;68(4):754–763. doi:10.1016/j.amepre.2025.01.001
- Clark D, Ioannides A, Adeleye AO, et al. Casemix, management, and mortality of patients receiving emergency neurosurgery for traumatic brain injury in the Global Neurotrauma Outcomes Study: a prospective observational cohort study. *Lancet Neurol*. 2022;21(5):438–449. doi:10.1016/S1474-4422(22)00037-0
- Liu MW, Ma ZQ, Liao RL, et al. Incidence and mortality related risk factors in patients with severe traumatic brain injury: A meta-analysis. *Exp Ther Med*. 2025;29(4):84. doi:10.3892/etm.2025.12834
- Shah SS, Khan MN, Khan MS, et al. Impact of Geographic Distance and Prehospital Delay on Mortality and Functional Outcomes in Severe Traumatic Brain Injury in a Low-Resource Setting. *Acute Med Surg*. 2026;13(1):e70131. doi:10.1002/ams2.70131
- Kumar K, Motwani S, Abdul Rahim K, et al. Outcomes of Moderate-to-Severe Traumatic Brain Injury in a Low-Resource Setting. *JAMA Netw Open*. 2026;9(8):e2628403. doi:10.1001/jamanetworkopen.2026.28403
- Kumar H, Kumar A, Sridhar R, et al. Traumatic brain injury outcomes and mortality predictors in Eastern India: An observational study. *SAGE Open Med*. 2025;13:20503121251399149. doi:10.1177/20503121251399149
- Gupta D, Singh RD, Vreeburg RJ, et al. Disparities in casemix, acute interventions, discharge destinations and mortality of patients with traumatic brain injury between Europe and India. *J Glob Health*. 2024;14:04227. doi:10.7189/jogh.14.04227
- Giner J, Mesa Galán L, Yus Teruel S, et al. Traumatic brain injury in the new millennium: new population and new management. *Neurologia (Engl Ed)*. 2022;37(5):383–389. doi:10.1016/j.nrleng.2019.03.024
- Nugroho AW, Masrika N. The epidemiology of motorcycle-related acute traumatic brain injury: The NOMADEN study. *Surg Neurol Int*. 2025;16:27. doi:10.25259/SNI.929.2024
- Chaplain X, Huet O, Rowan KM, et al. Hospital mortality, withdrawal of life-sustaining therapy decisions and early secondary brain insults for critically ill traumatic brain injury patients in England, Wales and Northern Ireland (2009–2024): an observational cohort study. *Lancet Reg Health Eur*. 2025;61:101538. doi:10.1016/j.lanepe.2025.101538
- Chen JM, Su YC, Cheng CY, et al. Association Between Admission Systolic Blood Pressure and Outcomes in Patients with Isolated Traumatic Brain Injury: A Cross-National Multicenter Cohort Study. *J Neurotrauma*. 2024;41(23–24):2590–2601. doi:10.1089/neu.2023.0392
- Cui S, Xu D, Xiong H, et al. Stress-induced hyperglycemia and mortality in patients with traumatic brain injury without preexisting diabetes: A meta-analysis. *Biomol Biomed*. 2025;25(2):291–303. doi:10.17305/bb.2024.10865
- He X, Zheng C, Zhang X, et al. Association between stress hyperglycemia ratio and mortality of traumatic brain injury patients based on MIMIC-IV and eICU databases. *BMC Neurol*. 2026;26(1):69. doi:10.1186/s12883-025-04602-w
- Ilderdar Y, Arraji M, Wachami NA, et al. Predictors of outcomes 3 to 12 months after traumatic brain injury: a systematic review and meta-analysis. *Osong Public Health Res Perspect*. 2024;15(1):3–17. doi:10.24171/j.phrp.2023.0288
- Yuan T, He H, Liu Y, et al. Association between blood glucose levels and Glasgow Outcome Score in patients with traumatic brain injury: secondary analysis of a randomized trial. *Trials*. 2022;23(1):38. doi:10.1186/s13063-022-06005-5
- Zhou Z, Huang C, Fu P, et al. Prediction of in-hospital hypokalemia using machine learning and first hospitalization day records in patients with traumatic brain injury. *CNS Neurosci Ther*. 2023;29(1):181–191. doi:10.1111/cns.13993
- Wang GH, Yan Y, Shen HP, et al. The Clinical Characteristics of Electrolyte Disturbance in Patients with Moderate and Severe Traumatic Brain Injury Who Underwent Craniotomy and Its Influence on Prognosis. *J Korean Neurosurg Soc*. 2023;66(3):332–339. doi:10.3340/jkns.2022.0078
- Mekodathil A, El-Menyar A, Chughtai T, et al. Initial serum electrolyte imbalances and mortality in patients with traumatic brain injury: a retrospective study. *World J Emerg Med*. 2025;16(4):331–339. doi:10.5847/wjem.j.1920-8642.2025.064
- Tsuchiya R, Ooigawa H, Kimura T, et al. Study of certain easily available biochemical markers in prognostication in severe traumatic brain injury requiring surgery. *Surg Neurol Int*. 2023;14:410. doi:10.25259/SNI.544.2023
- Huang CY, Rau CS, Huang CY, et al. The Stress Index as a Predictor of Mortality in Patients with Isolated Moderate to Severe Traumatic Brain Injury. *Diagnostics (Basel)*. 2024;14(12):1244. doi:10.3390/diagnostics14121244
- Kuo PJ, Huang CY, Hsu SY, et al. Evaluating the prognostic value of the stress index in trauma patients. *Heliyon*. 2024;10(17):e36884. doi:10.1016/j.heliyon.2024.e36884
- Shibata A, Matano F, Saito N, et al. Serum Glucose-To-Potassium Ratio as a Prognostic Predictor for Severe Traumatic Brain Injury. *J Nippon Med Sch*. 2021;88(4):342–346. doi:10.1272/jnms.JNMS.2021_88-506
- de Oliveira LD, Melo JRT, Chaves CVA, et al. Performance of the glucose-potassium ratio as a biomarker of mortality in children with severe traumatic brain injury. *Neurochirurgie*. 2026;72(3):101812. doi:10.1016/j.neuchi.2026.101812
- Marini JJ, Sein ME. The Role of the Glucose Potassium Ratio in the Management of Traumatic Brain Injury. *Korean J Neurotrauma*. 2023;19(1):82–89. doi:10.13004/kjnt.2023.19.e11
- Zhou H, Tang Y, Li Y, et al. Serum glucose-potassium ratio predicts prognosis of traumatic brain injury in patients undergoing emergency craniotomy: A retrospective study. *Asian J Surg*. 2023;46(7):2958–2959. doi:10.1016/j.asjsur.2023.02.034
- Wang J, Hong C, Feng Q, et al. Glucose-potassium ratio: a prognostic biomarker enhancing outcome prediction in mild-to-moderate traumatic brain injury. *Front Neurol*. 2025;16:1577390. doi:10.3389/fneur.2025.1577390
- Jung HM, Paik JH, Kim SY, et al. Association of Plasma Glucose to Potassium Ratio and Mortality After Aneurysmal Subarachnoid Hemorrhage. *Front Neurol*. 2021;12:661689. doi:10.3389/fneur.2021.661689
- Guo Y, Yang Y, Zhu J, et al. The U shape relationship between glucose and potassium ratio and mortality in patients with subarachnoid hemorrhage in the US population. *Sci Rep*. 2025;15(1):27084. doi:10.1038/s41598-025-11630-6
- Yamada S, Nishida T, Takenaka T, et al. Outcome prediction in aneurysmal subarachnoid hemorrhage with world federation of neurological societies grade V (OPAS-V). *Acta Neurochir (Wien)*. 2025;167(1):200. doi:10.1007/s00701-025-06611-7
- Liu J, Luo F, Guo Y, et al. Association between serum glucose potassium ratio and mortality in critically ill patients with intracerebral hemorrhage. *Sci Rep*. 2024;14(1):27391. doi:10.1038/s41598-024-78230-8
- Lu Y, Ma X, Zhou X, et al. The association between serum glucose to potassium ratio on admission and short-term mortality in ischemic stroke patients. *Sci Rep*. 2022;12(1):8233. doi:10.1038/s41598-022-12393-0
- Pan W, Ji TF, Yang J, et al. The ratio of serum glucose to potassium is associated with poor prognosis in patients with severe acute myocardial infarction. *Sci Rep*. 2025;15(1):28846. doi:10.1038/s41598-025-14002-2
- Wang J, Wu S, Chen J, et al. Glucose-to-potassium ratio as a predictor for early post-traumatic epilepsy: a retrospective cohort study. *Front Neurol*. 2025;16:1555328. doi:10.3389/fneur.2025.1555328
- Wang H, Dao Q, Li X, et al. Glucose-to-potassium ratio has a non-linear J-shaped association with acute kidney injury risk in traumatic brain injury. *Sci Rep*. 2026;16(1):26829. doi:10.1038/s41598-026-57082-4
- Chen Y, Li S, Zhang C, et al. Association between serum glucose/potassium ratio and acute kidney injury in patients with traumatic brain injury: based on MIMIC-IV database. *J Glob Health*. 2026;16:04108. doi:10.7189/jogh.16.04108
- Unal A, Dogan A. Comparison of glucose/potassium ratio and revised trauma score in predicting mortality in patients with isolated blunt head trauma. *Sci Rep*. 2025;15(1):33463. doi:10.1038/s41598-025-08604-z
- Lampros M, Vlachodimitropoulou L, Voulgaris S, et al. Correlation of Routine Admission Inflammatory Biomarkers with Individual Traumatic Brain Lesion Types in Mild Traumatic Brain Injury. *Biomedicines*. 2026;14(2):365. doi:10.3390/biomedicines14020365
- Cruzalegui-Bazán C, Durán-Pecho A, Botello-Gonzales D, et al. Association of serum glucose/potassium index levels with poor long-term prognosis in patients with Aneurysmal Subarachnoid Hemorrhage. *Clin Neurol Neurosurg*. 2024;247:108609. doi:10.1016/j.clineuro.2024.108609
- Dijkland SA, Foks KA, Polinder S, et al. Prognosis in Moderate and Severe Traumatic Brain Injury: A Systematic Review of Contemporary Models and Validation Studies. *J Neurotrauma*. 2020;37(1):1–13. doi:10.1089/neu.2019.6401
- Tienprattarn W, Phinyo P, Yuksen C, et al. Domain validation of the CRASH prognostic model for predicting 14-day mortality among patients with traumatic brain injury with intracranial hemorrhage in a Thai emergency department. *Int J Emerg Med*. 2025;18(1):202. doi:10.1186/s12245-025-01008-w
- Abdullah JM, Idris Z, Ghani AR, et al. Prediction of outcomes in traumatic brain injury: The IMPACT and CRASH prognostic models in a single neurosurgical center, Malaysia. *J Neurosurg Sci*. 2023;67(3):367–373. doi:10.23736/S0390-5616.21.05249-8
- Chen L, Xu H, He J, et al. Performance of the IMPACT and Helsinki models for predicting 6-month outcomes in a cohort of patients with traumatic brain injury undergoing cranial surgery. *Front Neurol*. 2022;13:1031865. doi:10.3389/fneur.2022.1031865
- Halimi RA, Fuadi I, Alby D. The Use of Corticosteroid Randomisation after Significant Head Injury (CRASH) Prognostic Model as Mortality Predictor of Traumatic Brain Injury Patients Underwent Surgery in Low-Middle Income Countries. *Anesthesiol Res Pract*. 2024;2024:5241605. doi:10.1155/2024/5241605
- Karabacak M, Jagtiani P, Dams-O'Connor K, et al. The MOST (Mortality Score for TBI): A novel prediction model beyond CRASH-Basic and IMPACT-Core for isolated traumatic brain injury. *Injury*. 2025;56(1):111956. doi:10.1016/j.injury.2024.111956
- Mondello S, Amrein K, Czeiter E, et al. Prognostic Value of Blood-Based Protein Biomarkers in Traumatic Brain Injury: A Living Systematic Review and Meta-Analysis. *J Neurotrauma*. 2025;42(15–16):1256–1286. doi:10.1089/neu.2024.0620
- Mishra RK, Galwankar S, Gerber J, et al. Neutrophil-lymphocyte ratio as a predictor of outcome following traumatic brain injury: Systematic review and meta-analysis. *J Neurosci Rural Pract*. 2022;13:618–635. doi:10.25259/jnpr-2022-4-21
- Hartanto AS, Faried A. Blood Glucose as a Prognostic Predictor of Traumatic Brain Injury in Patients That Underwent Surgical

- Intervention. Korean J Neurotrauma. 2026;22(1):14-23. doi:10.13004/kjnt.2026.22.e2
48. Parenrengi MA, Suryaningtyas W, Destiansyah RA. Hyperglycemia as a predictor of outcome in paediatric severe traumatic brain injury patients underwent surgery: a single center experience from Eastern Indonesia from 2017-2022. Wiad Lek. 2023;76(6):1342-1346. doi:10.36740/WLek202306103
 49. Wijanarko F, Alifianto U, Setyono H, et al. S100 β protein levels as a parameter to assess the clinical development of adult patients with mild traumatic brain injury in Dr. Moewardi Public Hospital, Surakarta. Surg Neurol Int. 2021;12:342. doi:10.25259/SNI_294_2021
 50. Levis B, Bhandari PM, Neupane D, et al. Data-Driven Cutoff Selection for the Patient Health Questionnaire-9 Depression Screening Tool. JAMA Netw Open. 2024;7(11):e2429630. doi:10.1001/jamanetworkopen.2024.29630
 51. Riley RD, Collins GS. Stability of clinical prediction models developed using statistical or machine learning methods. Biom J. 2023;65(8):e2200302. doi:10.1002/bimj.202200302
 52. von Elm E, Altman DG, Egger M, et al. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453-7. doi:10.1016/S0140-6736(07)61602-X
 53. Heinze G, Schemper M. A solution to the problem of separation in logistic regression. Stat Med. 2002;21(16):2409-2419. doi:10.1002/sim.1047
 54. Hazare P, Shukla D, Bhat D, et al. Prediction of Surgical Outcome for Acute Traumatic Brain Injury in Older Adults. Neurol India. 2022;70(3):1112-1118. doi:10.4103/0028-3886.349603
 55. Tang Z, Yang R, Zhang J, et al. Outcomes of Traumatic Brain-Injured Patients With Glasgow Coma Scale < 5 and Bilateral Dilated Pupils Undergoing Decompressive Craniectomy. Front Neurol. 2021;12:656369. doi:10.3389/fneur.2021.656369
 56. Garcia-Ballesteras E, Villafañe J, Nuñez-Baez K, et al. A systematic review and meta-analysis on glycemic control in traumatic brain injury. Clin Neurol Neurosurg. 2024;245:108504. doi:10.1016/j.clineuro.2024.108504
 57. Matovu P, Kirya M, Galukande M, et al. Hyperglycemia in severe traumatic brain injury patients and its association with thirty-day mortality: a prospective observational cohort study in Uganda. PeerJ. 2021;9:e10589. doi:10.7717/peerj.10589
 58. Lebiedzińska A, Kędziora J, Woźniak J, et al. Metabolic Chaos After Aneurysmal Subarachnoid Haemorrhage: Longitudinal Glucose-Potassium Ratio Dynamics and Clinical Outcomes. Biomedicines. 2026;14(6):1402. doi:10.3390/biomedicines14061402