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Association of initial assessment variables and mortality in severe pediatric traumatic brain injury

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ABSTRACT

Background Predictive scales have been used to prognosticate long-term outcomes of traumatic brain injury (TBI), but gaps remain in predicting mortality using initial trauma resuscitation data. We sought to evaluate the association of clinical variables collected during the initial resuscitation of intubated pediatric severe patients with TBI with in-hospital mortality.

Methods Intubated pediatric trauma patients <18 years with severe TBI (Glasgow coma scale (GCS) score ≤8) from January 2011 to December 2020 were included. Associations between initial trauma resuscitation variables (temperature, pulse, mean arterial blood pressure, GCS score, hemoglobin, international normalized ratio (INR), platelet count, oxygen saturation, end tidal carbon dioxide, blood glucose and pupillary response) and mortality were evaluated with multivariable logistic regression.

Results Among 314 patients, median age was 5.5 years (interquartile range (IQR): 2.2–12.8), GCS score was 3 (IQR: 3–6), Head Abbreviated Injury Score (hAIS) was 4 (IQR: 3-5), and most had a severe (25-49) Injury Severity Score (ISS) (48.7%, 153/314). Overall mortality was 26.8%. GCS score, hAIS, ISS, INR, platelet count, and blood glucose were associated with in-hospital mortality (all $p<0.05$). As age and GCS score increased, the odds of mortality decreased. Each 1-point increase in GCS score was associated with a 35% decrease in odds of mortality. As hAIS, INR, and blood glucose increased, the odds of mortality increased. With each 1.0 unit increase in INR, the odds of mortality increased by 1427%.

Conclusions Pediatric patients with severe TBI are at substantial risk for in-hospital mortality. Studies are needed to examine whether earlier interventions targeting specific parameters of INR and blood glucose impact mortality.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Although predictive scales have been developed for prognosticating long-term outcomes in patients with traumatic brain injury (TBI), there are no existing instruments that use initial trauma resuscitation data to predict in-hospital mortality. We sought to evaluate the association of clinical variables collected during initial resuscitation of intubated pediatric severe TBI patients with in-hospital mortality.

WHAT THIS STUDY ADDS

⇒ Among 314 pediatric patients intubated with severe TBI, Glasgow Coma Scale score, Head Abbreviated Injury Score, international normalized ratio (INR), platelet count, blood glucose and temperature were associated with in-hospital mortality (all $p<0.05$). The most significant predictors of in-hospital mortality were INR and blood glucose.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Integrating INR and blood glucose into algorithms that guide the initial trauma resuscitation in patients with pediatric trauma with severe TBI can help providers communicate in-hospital survival expectation and determine which patients would benefit from early escalation of care to pediatric hospitals with neurosurgical capabilities.

INTRODUCTION

Traumatic brain injury (TBI) remains the leading cause of disability and mortality in children, causing thousands of deaths each year.[1–5] Due to the devastating consequences associated with pediatric TBI, physicians and scientists have continued to study prediction tools to prognosticate patients' outcomes. These tools are helpful in providing guidance when counseling patients and their families on recovery expectations after TBI.

The Glasgow Outcomes Scale (GOS) was created as a global scale for functional outcomes following TBI using five categories (death, vegetative state, severe disability, moderate disability, and good recovery).[6] The Pediatric Overall Performance Category and Pediatric Cerebral Performance Category Scales, which quantify overall functional morbidity and cognitive impairment respectively, were created to describe short-term outcomes of pediatric patients with TBI in intensive care.[7] The Pediatric Glasgow Coma Scale is an instrument used to assess severity of TBI that was adapted from the original

GCS with modifications to motor and verbal components to improve the initial neurological assessment of preverbal children, and it has been found to accurately identify younger children needing acute intervention.[8] GCS has been combined with the Pupillary Response Score (0=0 non-reactive pupils, 1=1 non-reactive pupil, 2=both non-reactive pupils) to create the GCS-P.[9] In pediatric patients, a GCS-P score ≤2 was highly associated with death and an unfavorable functional outcome at discharge from the pediatric intensive care unit (PICU).[8]

Though these tools have proven useful, evidence supporting a reliable method to predict mortality in children during initial trauma resuscitation remains limited.[3] The objective of this study is to evaluate the association between clinical variables collected from intubated pediatric patients with severe TBI during initial assessment in the trauma bay and in-hospital mortality.

METHODS

This study was performed at an American College of Surgeons-verified Level 1 Pediatric Trauma Center and was approved by the Institutional Review Board of Nationwide Children's Hospital. Pediatric trauma patients 0–18 years old arriving to our institution between January 2011 and December 2020 with severe TBI, defined as a GCS score ≤8, requiring intubation, and with a Head Abbreviated Injury Score (hAIS) of ≥1, were included. Patients were excluded if their presenting injury mechanism was asphyxiation. The association between clinical variables collected during initial trauma resuscitation (temperature, pulse, mean arterial blood pressure (MAP), GCS score, hemoglobin, international normalized ratio (INR), platelet count, oxygen saturation, end tidal carbon dioxide ($ETCO_2$), lactate, blood glucose, and pupillary response) and mortality was evaluated. Patients meeting inclusion criteria and with complete data available created the final cohort for analysis.

Statistical analyses

Descriptive statistics were performed to examine the demographic characteristics (sex, race, age, weight), clinical characteristics (traumatic mechanism (blunt or penetrating), transfer status), clinical variables collected during initial trauma resuscitation, and injury severity defined during initial trauma resuscitation (Injury Severity Score (ISS) with ISS categories (minor: 1–8, moderate: 9–15, serious: 16–24, severe: 25–49, critical: 50–74, maximum: 75) and abbreviated injury scores (AIS) with AIS regions (head AIS (hAIS), face AIS (fAIS), thorax AIS (tAIS), abdomen AIS (aAIS), extremity AIS (eAIS) and external AIS)) of the cohort. Data were summarized according to groups (survivors and mortalities) with median and interquartile range (IQR) and analyzed using the Wilcoxon rank sum test. Categorical variables, whenever dichotomous or nominal, were reported as frequencies and percentages and analyzed using χ^2 or Fisher's exact tests. Median days from hospital arrival to date of death were estimated for the subgroup of patients who experienced in-hospital mortality using survival analysis methods.

Patients with incomplete demographic, clinical, or mortality data were excluded from all analyses. First, univariable logistic regression was performed to evaluate the association of individual covariates with in-hospital mortality. Second, a stepwise logistic regression variable selection process was used to select the best model using Akaike information criteria (AIC).[10] This method iteratively adds and removes predictors to determine the subset of variables resulting in the best fit model, subsequently lowering prediction error. The preselected variables included were demographic characteristics (sex, race, age, weight) and clinical variables collected during initial trauma resuscitation (trauma mechanism, type of trauma (isolated head injury vs polytrauma), hospital transfer status, pupil response (normal vs abnormal), ISS, GCS score, hAIS, temperature, pulse, MAP, hemoglobin, INR, platelet count, oxygen saturation, $ETCO_2$, and blood glucose). In-hospital mortality was also evaluated. Hematocrit was not included due to high correlation with hemoglobin (correlation coefficient of 0.98). Lactate was excluded from the variable selection model due to apparent non-random missingness between survivors and those patients who experienced in-hospital mortality. A final multivariable logistic regression with the smallest AIC was then built to identify significant predictors of in-hospital mortality.

RESULTS

Demographics and clinical characteristics

Our cohort consisted of 314 patients with a median age of 5.5 years (IQR: 2.2–12.8 (table 1)). The majority were white (74.9%) and male (66.9%). Most patients experienced blunt traumatic injury (93.9%) and 6.1% experienced penetrating injury. The majority of the cohort was transferred from another institution (53.5%). Traumatic mechanism was associated with survival (p=0.005) with a higher proportion of patients with blunt injury surviving (96.5% vs 86.9%) and a higher proportion of patients with penetrating injury (13.1% vs 3.5%) dying. There was no difference between the groups in the proportion of patients undergoing a neurosurgical operation (31.7% among surviving patients vs 23.8% among patients who died; p=0.173). The most common operation performed was a craniectomy (59.1%) and the proportion of patients undergoing this procedure was higher among patients who died (85.0% vs 52.1%, p=0.008).

The overall median GCS score was 3 (IQR: 3–6), hAIS was 4 (IQR: 3–5), and the most common ISS category was severe (48.7% (table 2)). Patients who survived had significantly lower hAIS scores (4 (IQR: 3–5) vs 5 (IQR: 4–5); p<0.0001) and tAIS scores (3 (IQR: 2–3) vs 3 (IQR: 3–4); p=0.008). Patients who survived also had a higher GCS score (3 (IQR: 3–6) vs 3 (IQR: 3–3); p<0.0001). Most patients experienced polytrauma (70.1%) as opposed to isolated head injury.

Table 1 Demographics of pediatric patients with severe traumatic brain injury

	Total (*n*=314)	Survived (*n*=230, 73.2%)	Died (*n*=84, 26.8%)	*P* value*
Sex				0.750
Male	210 (66.9)	155 (67.4)	55 (65.5)	
Female	104 (33.1)	75 (32.6)	29 (34.5)	
Race				0.494
White	224 (74.9)	172 (76.1)	52 (71.2)	
Asian	3 (1.0)	2 (0.9)	1 (1.4)	
Black	47 (15.7)	32 (14.2)	15 (20.5)	
Multiracial/other	25 (8.4)	20 (8.8)	5 (6.8)	
Age, years	5.5 (2.2–12.8)	6.5 (2.6–13.0)	4.3 (1.4–11.1)	**0.037**
Weight, kg (*n*=313)	21.0 (12.9–47.7)	23.7 (13.6–49.3)	18.0 (11.1–42.6)	0.064
Transfer from another hospital	168 (53.5)	130 (56.5)	38 (45.2)	0.076
Traumatic mechanism				**0.005**
Blunt	295 (93.9)	222 (96.5)	73 (86.9)	
Penetrating	19 (6.1)	8 (3.5)	11 (13.1)	
Neurosurgical operative intervention within 48 hours of injury†	93 (29.6)	73 (31.7)	20 (23.8)	0.173
Craniotomy	24 (25.8)	22 (30.1)	2 (10.0)	0.087
Craniectomy	55 (59.1)	38 (52.1)	17 (85.0)	**0.008**
Subdural hematoma evacuation	34 (36.6)	24 (32.9)	10 (50.0)	0.159
Epidural hematoma evacuation	12 (12.9)	10 (13.7)	2 (10.0)	1.00
External ventricular drain placement	18 (19.4)	14 (19.2)	4 (20.0)	1.00
Intracranial pressure monitor placement	33 (35.5)	28 (38.4)	5 (25.0)	0.305
Other neurosurgical procedure‡	21 (22.6)	16 (21.9)	5 (25.0)	0.768

Count (percentage) for categorical variables and median (first quartile, third quartile) for continuous variables reported.
*Wilcoxon rank sum test or χ^2 or Fisher's exact test. Bold indicates significance at $p<0.05$.
†Patients may have had multiple procedures performed during the index operation.
‡Other includes: scalp laceration debridement and/or repair (*n*=7), partial or complete lobectomy (*n*=6), halo traction brace placement (*n*=3), cortical artery cauterization (*n*=1), intracranial packing (*n*=1), open skull fracture repair (*n*=1), ventriculostomy (*n*=1), cervical spine instrumentation (*n*=1).

Table 3 presents the comparison of clinical variables between those alive at discharge and in-hospital mortalities. Temperature, MAP, hemoglobin, platelets, and $ETCO_2$ were all significantly lower in patients who experienced in-hospital mortality (all $p<0.0001$). INR, lactate, blood glucose, and the percentage of patients with abnormal pupil response were significantly higher in patients who experienced in-hospital mortality (all $p<0.05$). Over the 10-year study period, the incidence of mortality in pediatric patients with TBI in this cohort was 26.8% (84/314). Most in-hospital mortality occurred within the first 3 days of hospital admission (median: 1.9 days; IQR: 0.94–3.2 days (figure 1)); however, mortality occurred up to 23 days after hospital admission.

Prediction of in-hospital mortality

The stepwise variable selection resulted in a final model, which included age, weight, temperature, platelet count, INR, GCS score, blood glucose, hAIS, and traumatic mechanism (table 4). In the multivariable regression model, age, platelet count, and GCS score were inversely associated with mortality (all $p<0.05$). With each 1-year age increase and each 1-point increase in GCS score, there was an associated 25% (95% CI 10% to 38%) and

Table 2 Injury severity of pediatric patients with severe traumatic brain injury

	Total (*n*=314)	Survived (*n*=230, 73.2%)	Died (*n*=84, 26.8%)	*P* value*
Glasgow Coma Score‡ (*n*=313)	3 (3-6)	3 (3-6)	3 (3-3)	**<0.0001**
Abbreviated Injury Scale				
Head	4 (3-5)	4 (3-5)	5 (4-5)	**<0.0001**
Face (*n*=106)	2 (1-2)	2 (1-2)	1.5 (1-2)	0.792
Thorax (*n*=89)	3 (2-3)	3 (2-3)	3 (3-4)	**0.008**
Abdomen (*n*=39)	3 (2-4)	3 (2-4)	2 (2-3)	**0.019**
Extremity (*n*=99)	2 (2-3)	2 (2-3)	2 (2-3)	0.244
External (*n*=250)	1 (1-1)	1 (1-1)	1 (1-1)	0.541
Injury Severity Score†				**<0.0001**
Minor (1–8)	3 (1.0)	3 (1.3)	0 (0)	
Moderate (9–15)	61 (19.4)	56 (24.3)	5 (6.0)	
Serious (16–24)	86 (27.4)	78 (33.9)	8 (9.5)	
Severe (25–49)	153 (48.7)	87 (37.8)	66 (78.6)	
Critical (50–74)	7 (2.2)	4 (1.7)	3 (3.6)	
Maximum (75)	4 (1.3)	2 (0.9)	2 (2.4)	
Trauma type				0.152
Isolated head injury	94 (29.9)	74 (32.2)	20 (23.8)	
Polytrauma	220 (70.1)	156 (67.8)	64 (76.2)	

Count (percentage) for categorical variables and median (first quartile, third quartile) for continuous variables reported.
*Wilcoxon rank sum test or χ^2 or Fisher's exact test. Bold indicates significance at $p<0.05$. All patients presented with a Glasgow Coma Scale score ≤8.
†Cochrane-Armitage test for trend.
‡All patients presented with a Glasgow Coma Scale score ≤8.

35% (95% CI 8% to 55%) decreased odds of mortality, respectively.

As weight, INR, blood glucose, and hAIS increased, the odds of mortality increased. With each 1 kilogram increase in weight and 1-unit increase in hAIS, the odds of mortality increase by 5% (95% CI 1% to 9%) and 432% (4.32-fold (95% CI 214% to 872%)), respectively. With each 1.0 unit increase in INR or 10 mg/mL increase in glucose, the odds of mortality increased by 1427% (14.27-fold (95% CI 379% to 5378%)) and 1% (95% CI 0% to 2%), respectively. When considering INR among patients with blunt injury, for example, by holding all other variables in the multivariable regression model constant, an INR of >2.3 would be associated with a greater than 50% chance of mortality and an INR of >3.1 would be associated with a 90% chance of mortality (figure 2).

DISCUSSION

Pediatric patients with severe TBI remain at substantial risk for mortality, which is demonstrated by the 26.8% incidence of in-hospital mortality within our cohort. This is similar to mortality incidences reported in previous pediatric studies (16%–28%).[11–14] Though predictive scales, models, and algorithms have been implemented to prognosticate acute and long-term outcomes, less attention has been given to using data from the initial resuscitation to predict mortality risk. Therefore, our study analyzed pediatric patients who were intubated with severe TBI with an aim to identify associations between clinical variables collected during trauma assessment and in-hospital mortality. Initial INR, platelet count, and blood glucose were significantly associated with in-hospital mortality. An INR greater than 2.3 was associated with at least a 50% chance of mortality among blunt trauma patients, which is consistent with prior literature demonstrating an association between elevated INR and in-hospital mortality in children with abusive head trauma.[15] Coagulopathy following TBI is well described in the literature and may be due to the release of tissue factor.[16] Increasing GCS score was associated with decreased odds of mortality.

As in our study, other attempts have been made to predict survival of pediatric TBI on initial presentation. However, much of the focus is on the use of CT imaging, the gold standard for diagnosing intracranial injuries among children.[17] The CT Rotterdam score has been found to be significantly related to TBI outcome and is often used as a predictor of mortality.[18–21] The score is assigned based on CT evaluation of the basal cistern, midline shift, an epidural mass lesion, and intraventricular hemorrhage or subarachnoid hemorrhage. Talari et

Table 3 Clinical variables collected in the trauma bay and assessed in pediatric patients with severe traumatic brain injury

	Total (*n*=314)	Survived (*n*=230, 73.2%)	Died (*n*=84, 26.8%)	*P* value*
Temperature (*n*=313; degrees Fahrenheit)	97.2 (96.0–98.2)	97.6 (96.5–98.4)	95.1 (92.3–97.5)	**<0.0001**
Pulse (*n*=314; beats per minute)	120 (98–140)	120 (99–140)	120 (96–140)	0.609
Mean arterial pressure (*n*=314; mmHg)	84.0 (72.7–98.0)	86.0 (76.0–99.0)	75.4 (58.0–95.0)	**<0.0001**
International normalized ratio (*n*=304)	1.2 (1.1–1.5)	1.2 (1.1–1.3)	1.8 (1.5–2.6)	**<0.0001**
Hematocrit (*n*=305; %)	32.1 (28.0–36.8)	32.5 (29.4–37.0)	28.2 (24.1–34.7)	**<0.0001**
Hemoglobin (*n*=305; g/L)	108 (92–125)	111 (100–126)	92 (81–115)	**<0.0001**
Platelet count (*n*=304; x10^9/L)	)245 (188–325)	264 (214–344)	179 (121–251)	**<0.0001**
Oxygen saturation (*n*=314; %)	100 (99–100)	100 (100–100)	100 (94–100)	**<0.0001**
End tidal carbon dioxide (*n*=304; mm Hg)	35 (29–41)	37 (32–42)	29 (21–36)	**<0.0001**
Lactate (*n*=137; mmol/L)	2.6 (1.4–5.1)	1.8 (.9–3.0)	4.8 (2.6–6.8)	**<0.0001**
Blood glucose (*n*=295; mg/dL)	165 (131–227)	145 (126–189)	248 (180–290)	**<0.0001**
Pupillary response (*n*=301)				**0.015**
Normal	161 (53.5)	129 (57.6)	32 (41.6)	
Abnormal	140 (46.5)	95 (42.4)	45 (58.4)	

Count (percentage) for categorical variables and median (first quartile, third quartile) for continuous variables reported.
*Wilcoxon rank sum test or χ^2 or Fisher's exact test. Bold indicates significance at $p<0.05$.

al. demonstrated that each 1-point increase in Rotterdam score was associated with a 10.5-times increase in mortality rate. They also identified that scores ≥3 were associated with a mortality rate of 65.5%, compared with scores <3, which were associated with a mortality rate of 0.6%.[18] More recently, Dornbos III et al. published a retrospective study validating the Surgical Intervention for Traumatic Injury Scale in pediatric patients. This scale is based on both radiographic and clinical findings defined by neurosurgical guidelines and expert clinical experience. It was also created to rapidly identify patients with TBI at the highest risk for mortality, though it is specifically used to determine those who would likely need emergent decompression. Results demonstrated that a score threshold of 2 (sensitivity of 96.4%, specificity of 86.9%) was indicative of needing emergent surgery.[1 2] While our study did not aim to determine which patients would be most likely to require emergent decompression, there was a notably higher rate of emergent craniectomies among patients who died, consistent with their overall clinical picture of critical illness.

There are also a limited number of reports within the literature linking laboratory values to acute and long-term outcomes of severe TBI, though with varying results.[22–24] For example, in a large cohort of 1129 pediatric patients with TBI, an initial hematocrit ≤30% or a platelet count of greater than 400 000 on presentation was associated with an increased likelihood of abusive head trauma in children <5 years old.[23] Another study demonstrated that children with severe TBI who experienced a physiologic death compared with children undergoing withdrawal of life-sustaining devices had higher partial thromboplastin time (PTT) and lower albumin levels on admission.[14] Results from the IMPACT study (2007) used 6-month GOS as an endpoint and demonstrated that prothrombin time (PT) and glucose were strong predictors of outcomes, while hemoglobin and platelets were also predictors but to a lesser extent.[24] Podolsky-Gondim et al. demonstrated that abnormal PT, fibrinogen, and platelet count were associated with worse GOS outcomes at 1 and 6 months and found PT and PTT to be associated with mortality risk.[25] Most recently, Fu et al. studied 213 children with moderate to severe TBI at their tertiary pediatric hospital and found that admission lactate levels and GCS score were independent risk factors for in-hospital mortality, while glucose, hemoglobin, and hypotension were not significantly associated. Elevated lactate was also associated with a greater number of ventilator days,

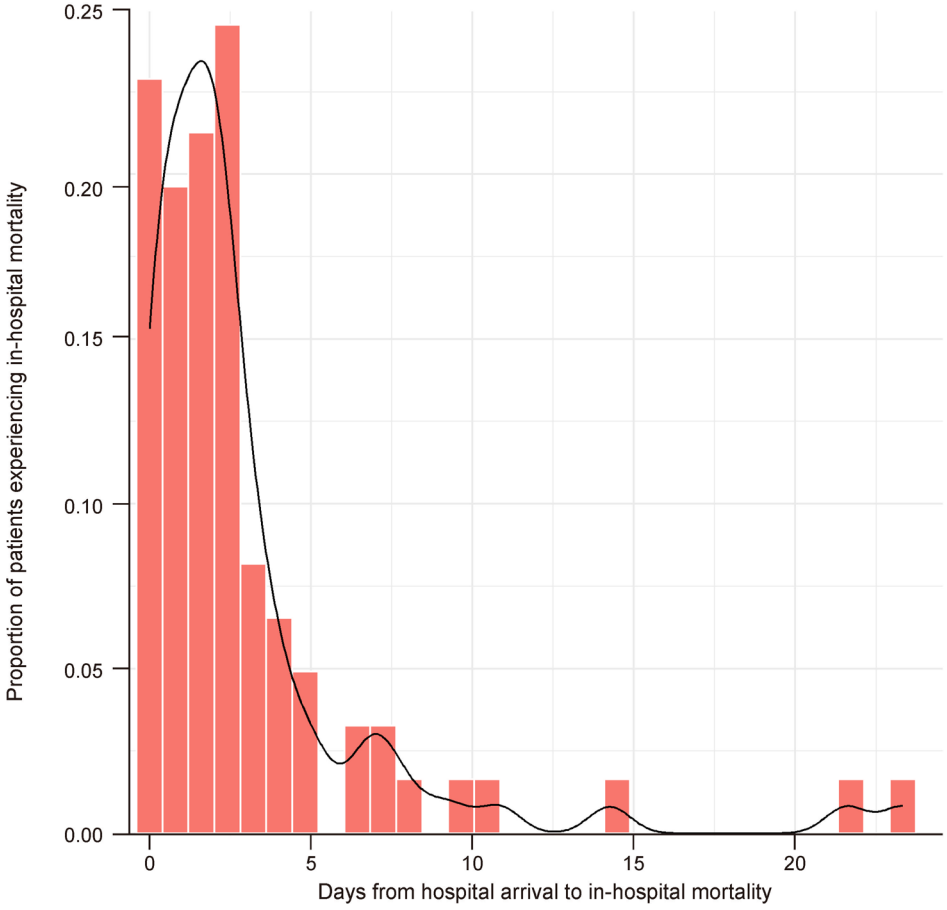

Figure 1 Histogram frequency plot with overlaid density curve demonstrating days to in-hospital mortality among pediatric patients with severe traumatic brain injury.

ICU days, and hospital days.[22] Of note, procalcitonin levels have also been studied in adult TBI patients, and results do not support their utility in predicting in-hospital mortality.[26] In our study, INR and blood glucose were significantly associated with in-hospital mortality, causing 14.3-fold higher odds of mortality with each 1.0 unit increase in INR and a 1% increase in odds with each increase in blood glucose by 10 mg/dL.

Studies utilizing physical exam findings to predict outcomes of severe TBI have demonstrated more consistency. There is substantial evidence that GCS score is a significant predictor of mortality.[13 18 19 22 25 27–29] Studies

Table 4 Multivariable logistic regression estimates and odds ratios for in-hospital mortality among pediatric patients with severe traumatic brain injury

Variable	Odds ratio	95% CI	*P* value
Age, years	0.75	0.62 to 0.90	**0.002**
Weight, kilograms	1.05	1.01 to 1.09	**0.022**
Temperature, degrees Fahrenheit	0.87	0.74 to 1.04	0.126
Platelet count, x10^9/L	1.00	0.99 to 1.00	**0.035**
International normalized ratio	14.27	3.79 to 53.78	<0.0001
Glasgow Coma Scale	0.65	0.45 to 0.92	**0.017**
Blood glucose, mg/dL	1.01	1.00 to 1.02	**0.005**
Head Abbreviated Injury Score	4.32	2.14 to 8.72	<0.0001
Traumatic mechanism			0.169
Blunt	reference	--	
Penetrating	3.39	0.60 to 19.31	

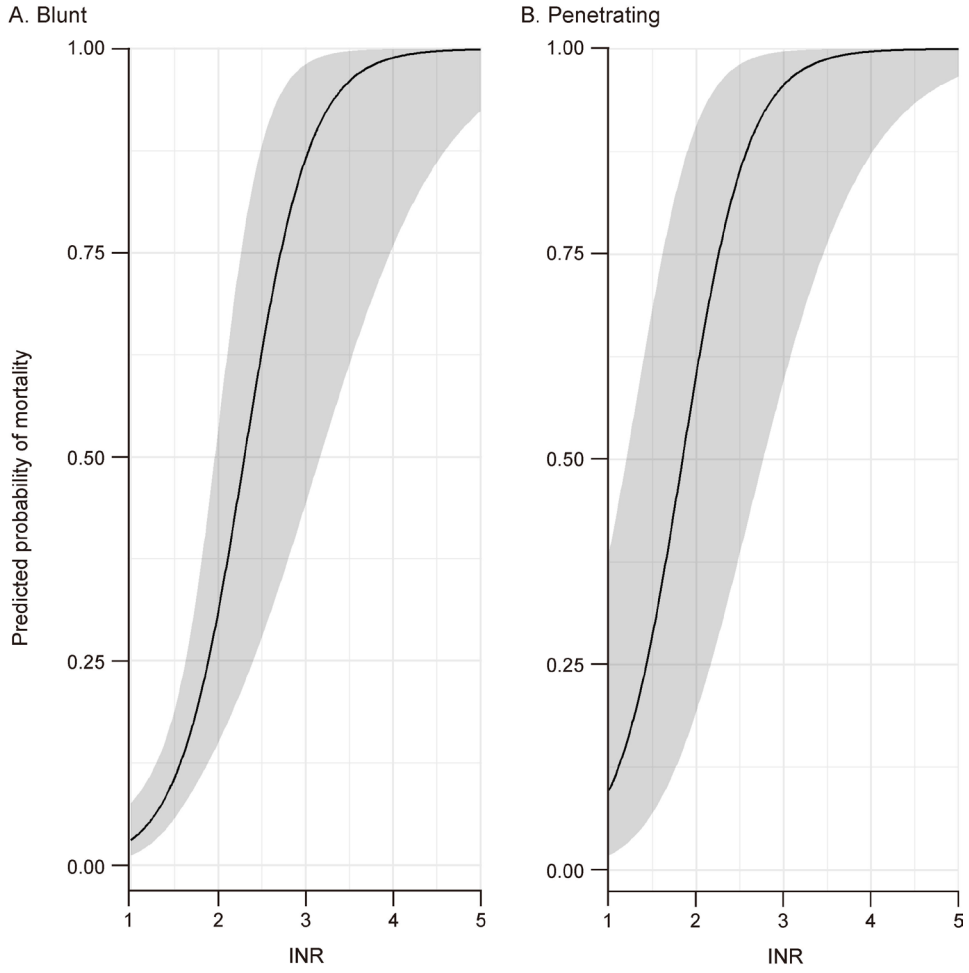

Figure 2 Predicted probability of in-hospital mortality for pediatric patients with severe traumatic brain injury based on international normalized ratio (INR) values for (A) blunt trauma and (B) penetrating trauma.

have reported a 0.37-times to a 0.68-times decreased mortality rate with each 1-point increase in GCS score, which is similar to the 0.68-times decrease demonstrated in our study.[18 22] The IMPACT study has also identified the GCS motor score and pupillary response as being the most powerful predictors of GOS, with GCS eye and verbal scores also being strong predictors.[24] In a study by Fulkerson et al., 67 pediatric patients with a GCS score of 3 or 4 were evaluated for survival to discharge as well as long-term outcomes by GOS. They found that the highest correlation with survival in these patients was pupillary reaction, with a survival probability of 23% if one or both eyes was abnormal on examination, compared with a survival probability of 87% if reflexes in both eyes were normal. The second-strongest predictor of mortality was hypothermia, defined as <36°C. Patients with an absent pupillary reflex and hypothermia were predicted to have a 14% chance of survival, while patients with absent reflexes and no hypothermia had a 56% chance of survival.[30] Pupillary response and temperature were not found to be a significant predictor for mortality among our patients. This may be due to the relationship between hypothermia and poor pupillary response with the other indicators of critical illness among our patients. Though prophylactic hypothermia in pediatric TBI is of great interest as a potential treatment, it remains controversial and has not been proven to demonstrate a benefit in mortality and long-term outcomes among our patients or in other studies.[31–33]

Although our findings identify a correlation between INR, platelet count, and blood glucose values collected during initial trauma resuscitation and mortality in pediatric patients with severe TBI, it is important to recognize that these clinical variables often do not act in isolation. Some pathologies and clinical circumstances confound patients' hypo/hyperglycemia and coagulopathy. For example, liver failure, renal disease, diabetes, ongoing hemorrhage, prolonged transport time, and/or systemic anticoagulation may contribute to abnormal INR, platelet count, and blood glucose values in patients presenting with severe TBI. Therefore, if we are to target specific parameters of these values, management should also consider their interrelatedness and the correction of underlying, compounding clinical pathology. While findings from this study identify INR and blood glucose as having the most direct correlation with mortality in pediatric patients with severe TBI, further studies are needed to examine the value of targeting specific parameters

of these variables, which may contribute to the creation of potential standardized algorithms targeting parameters that improve survival. Algorithms can help guide trauma teams during the high-acuity resuscitation of critically ill pediatric patients with severe TBI, particularly in hospitals that do not routinely manage this pathology or patient population. Studies identifying parameters of patient age, weight, and GCS score, that are more likely to be associated with mortality, could be factored into these algorithms to guide providers in communicating survival expectations to caregivers and in escalating care to pediatric hospitals with neurosurgical capabilities. These data also provide insight into targeted intervention methods such as improving coagulopathy and abnormal glucose levels prior to presentation to the trauma center to perhaps improve outcomes.

Limitations

As in any retrospective cohort study, there were limitations related to the retrospective nature of the study. We did not have control over missing data, misclassified data, or data granularity. Additionally, in-hospital mortality was the outcome measured. Its binary nature did not account for other clinical outcomes or quality of life measures, which are also relevant when evaluating pediatric TBI patients. Furthermore, mortality outcomes after discharge from the index hospitalization are unknown and unaccounted for. Survival may be over-represented in this cohort due to the possibility that patients may have experienced a mortality secondary to their TBI after discharge.

Additionally, patient-specific comorbidities were not captured and could act as confounders that were not controlled for in our analyses. However, ISS, hAIS, and GCS score were utilized to control for injury severity among patients, specifically GCS score and hAIS to account for head injury severity and ISS to account for patients presenting with multiple regions of injury. While GCS score can be rapidly calculated and used to assess acute changes in neurologic status, we recognize that the clinical utility of hAIS may be limited during the initial triage of the patient since it is typically calculated during admission. However, hAIS has been shown in previous studies to better reflect in-hospital mortality than GCS score, so remains an important factor in prognostication following a patient's initial resuscitation.[34]

Finally, we evaluated intubated patients with severe TBI and did not have the granular data available to identify sedatives or neuromuscular blocking agents given prior to the patient's arrival. This could limit the accuracy of some of the neurological assessments of some patients, creating misclassification bias; however, the GCS is a well-recognized neurological assessment tool and was determined by an experienced Emergency Department or Trauma Surgery physician.[18]

Ultimately, INR and blood glucose values collected during initial trauma resuscitation in pediatric trauma patients intubated with severe TBI were associated with higher odds of in-hospital mortality. Further studies are needed to examine whether earlier interventions targeting specific parameters of these clinical variables impact mortality.

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