Original Article

Factors Predicting Outcomes in Surgically Treated Pediatric Traumatic Brain Injury

Abstract

Introduction: Traumatic brain injury (TBI) is a common presentation to the pediatric emergency department. Understanding factors that predict outcomes will be useful in clinical decision-making and prognostication. The objective of this study was to identify important clinical parameters predictive of outcomes in pediatric TBI patients who underwent surgery. **Materials and Methods:** This retrospective study included 43 pediatric TBI patients who underwent surgery from January 2011 to January 2017. Clinical parameters, including presenting signs and symptoms, mechanism of injury, intracranial pressure (ICP), need for inotropes, and computed tomography findings were collected. Outcomes were assessed using the Glasgow outcome score (GOS) based on the latest follow-up. Outcomes were divided into favorable (GOS 4–5) and unfavorable (GOS 1–3). **Results:** Surgery was performed in 43 patients. The mean age was 9.6 ± 4.9. The mean follow-up period was 31 weeks. Thirty (70%) patients had favorable outcome and 13 (30%) had unfavorable outcome. On univariate analysis, mechanism of injury, vomiting, Glasgow coma scale score, pupil size and reactivity, hypotension, inotropic use, need for blood transfusion, and raised ICP (all $P < 0.005$) were significantly associated with outcomes. On step-wise logistic regression, only raised ICP (odds ratio [OR] = 35.6, $P = 0.008$) and hypotension (OR = 26.1, $P = 0.01$) were found to be statistically significant. **Conclusion:** The present study suggests that the majority of pediatric TBI patients who required neurosurgical intervention have favorable outcomes. Closer attention should be paid to raised ICP and hypotension as they were strong predictors of unfavorable outcomes. These findings also help manage expectations of patients' family and clinicians.

Keywords: *Head injury, outcomes, pediatric population, traumatic brain injury*

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Introduction

Traumatic brain injury (TBI) is a significant cause of mortality and disability worldwide.[1] In the United States, approximately 600,000 pediatric patients are admitted to the Emergency Department due to TBI.[2] In Singapore, TBI is the leading cause of trauma among pediatric patients.[3] Pediatric TBI is a crippling condition which extends not only to oneself but also to the society. However, significant variations of clinical data and management strategies exist in the literature.[2]

Adult and pediatric TBI have different pathophysiology and outcomes.[4,5] An infant skull being less rigid with higher plasticity allows more movement in response to mechanical stress. In neonates, the cerebral white matter contains less myelin. These factors result in different absorption of forces in adults and pediatric patients.[4] Furthermore, neonates having a larger head to body ratio are more susceptible to head injury. This corroborates with many studies that reported worse outcomes following TBI in infants.[6-8] Moreover, Bruce *et al.* found cerebral edema twice more common in pediatric patients after TBI due to cerebral hyperemia.[5,9]

A review of the literature revealed multiple factors which were associated with poor outcomes in pediatric TBI. Age, Glasgow coma scale (GCS) scores, clinical features (vomiting, pupil size, etc.,), and injury mechanisms have been reported in various studies.[5,10-12] Radiological studies also attempted to examine the relationship between computed tomography (CT) findings and outcomes. The presence of subarachnoid hemorrhage (SAH), diffuse axonal injury, and brain swelling has been reported to predict poor outcomes in pediatric TBI.[13] However, the few studies

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that investigated predictive factors of TBI outcomes have revealed variable results. For instance, pupil size was only a significant predictor only in certain studies.[13] Postresuscitation GCS score was a significant predictor[14] in some studies but not in others.[15] The same issue applies for age, duration of loss of consciousness, the presence of hypothermia, and the presence of injury severity scores.[2,5,10] Much debate exists between clinicians regarding the priority of management of clinical parameters on presentation of a pediatric TBI.

Surgery for pediatric patients with TBI remains a controversial topic of discussion. Commonly practiced procedures such as intracranial pressure (ICP) monitoring have conflicting evidence of utility.[16] Although many clinicians still edge on the conservative side of management, there is growing evidence that decompressive surgery could improve outcomes of pediatric TBI patients.[5,17] Minimal data exist in the literature that identifies risk factors which predict outcomes in pediatric TBI patients who underwent surgery.

The objective of this study was to identify pertinent clinical parameters and radiological factors that could predict outcomes in pediatric TBI patients who underwent surgery.

Materials and Methods

This Institutional Review Board approved study was conducted in the National University Hospital of Singapore. Pediatric patients aged 18 and under were retrospectively collected from June 2011 to January 2017. Inclusion criteria were any pediatric patient who suffered a TBI and was referred to the neurosurgical unit for any form of the neurosurgical procedure, including decompressive craniectomy, craniotomy, and external ventricular drain insertion. Pediatric TBI patients who did not undergo surgery, patients with preinjury neurological or psychiatric conditions, patients who had no follow-up after initial hospitalization and patients who did not survive before any surgery performed were excluded from the study.

Demographic data collected include age, gender, mechanism of injury, and type of hemorrhage. Patients were grouped into three groups based on their age as follows: 0–6 years, 7–12 years, and 13–18 years. Predictor variables collected for analysis include: GCS score, mechanism of injury, the presence of loss of consciousness, vomiting, palpable skull fracture, signs of basilar skull fracture, presence of a nonfrontal scalp hematoma, pupil size and reactivity, CT findings of type of hemorrhage, CT findings of severity of injury (midline shift, mass effect), presence of hypotension (age adjusted), ICP, need for blood transfusion, and use of inotrope prior or during surgery. Hypotension was defined as systolic blood pressure (SBP) <90 mmHg for patients over 10 years, SBP <70 + (2 × age in years) mmHg for patients aged 1–10 years old and SBP <70 mmHg for infants (1 month to 12 months). Mass effect was defined as the presence of effacement or

compression of basal cisterns with midline shift <0.5 cm. Midline shift is defined as a measured perpendicular distance >5 mm between the septum pellucidum and the midline. Table 1 summarizes all the predictor variables included for analysis. The verbal and motor component of the GCS scale was modified for pediatric patients below the age of 2 according to local institutional guidelines. For the verbal component, 5 describes an infant that coos and babbles. Four corresponds to an infant who is irritable and crying, 3 describes crying in response to pain, 2 moaning in response to pain, and 1 has no response. For the motor component: 6 describes an infant moving spontaneously and purposely, 5 corresponds to withdrawing in response to touch, 4 for withdrawing in response to pain, 3 for abnormal flexion, 2 for abnormal extension, and 1 for no response. The severity of TBI was categorized into mild (GCS 13–15), moderate (GCS 9–12), and severe (GCS ≤8). Raised ICP was defined as ICP >20 mmHg. At our center, The CODMAN ICP intraoperative monitor was used to measure ICP intraoperatively at the parenchymal level. The highest reading intraoperatively was chosen. All data were extracted from electronic medical records.

Outcomes were measured using the Glasgow outcome score (GOS). The GOS scale was modified for it to be applicable to pediatric patients based on Prasad's *et al*. report.[5] Good recovery (GOS 5) referred to patients who returned to age appropriate levels of functioning or returned to normal classes without special assistance. Moderate disability (GOS 4) referred to patients with reduced cognitive function from premorbid levels, neurological deficits affecting daily activities or patients who were enrolled in classes with special needs. Severe disability (GOS 3) referred to patients who were deficient in cognitive function or patients who were unable to carry out age-appropriate motor tasks. Vegetative state (GOS 2) referred to patients who required full dependence on daily activities. GOS 1 represented the death of the patient. Patients were divided into two groups based on their GOS scores. Patients with a GOS score of 1–3 represented the unfavorable outcome group while patients with a GOS score of 4–5 represented the favorable outcome group. Outcomes of the patients were taken at their latest follow-up appointment. The mean follow-up period was 31 weeks postdischarge. Neurological, psychological, and social assessments were reviewed by study investigators before awarding a GOS score to the patient.

Statistical analysis was carried out using IBM SPSS 22.0 Armonk, New York, United States of America. Continuous variables were represented as mean ± standard deviation if normally distributed. For skewed distribution, data were presented as median and interquartile ranges. Chi-square, Fisher's exact, and paired *t*-test were used for univariate analysis. Binary logistic regression was used to examine variables that were significant on univariate analysis. A value of $P < 0.05$ was considered to be significant.

Results

A total of 43 pediatric patients were included in this study. Thirty-three were male and 10 were female. The mean age was 9.6 ± 4.9 years. 14 (33%) patients were aged 0–6 years, 15 (35%) patients were 7–12 years old, and 14 (32%) patients were 13–18 years old. Mean GCS score was 10.3 ± 4.3. Majority of the patients (17, 39.5%) presented with a mild GCS score of 13–15. The most common type of injury was an extradural hemorrhage (19, 44%), followed by a sub-dural hemorrhage (10, 23%), SAH (7, 16%), and intraparenchymal hemorrhage (4, 8%). 30 (70%) patients had favorable outcomes whereas 13 (30%) patients had unfavorable outcomes. The basic characteristics of the patients are summarized in Table 1.

Table 2 summarizes the factors that were analyzed for univariate analysis. On univariate analysis, the following factors were found to be significantly associated with outcomes following pediatric TBI: GCS scores ($P = 0.001$), mechanism of injury ($P = 0.043$), presence of vomiting ($P = 0.004$), pupil size >3 mm ($P = 0.001$), bilaterally nonreactive pupils ($P < 0.001$), use of inotropes ($P < 0.001$), presence of hypotension ($P < 0.001$), raised ICP ($P < 0.001$), and blood transfusion required during operation ($P = 0.007$).For the severity of TBI based on GCS scores, 15 patients had severe, 11 patients had moderate and 17 patients had mild TBI. Among the 15 patients with severe TBI, 9 (60%) had unfavorable outcomes. Among the 11 patients with moderate TBI, 4 (36.4%) had unfavorable outcomes. None of the 17 patients with mild TBI had unfavorable outcomes. Vomiting was seen in 13 patients. None of the patients who vomited had unfavorable outcomes. Nine patients had pupils >3 mm. Of these 9 patients, 7 (77.8%) had unfavorable outcomes. Two patients had unilaterally nonreactive pupils of which 1 had an unfavorable outcome. Nine patients had bilaterally nonreactive pupils. Seven of these 9 patients had unfavorable outcomes. Inotropes were used in 8 patients. 7 (87.5%) patients had unfavorable outcomes. Hypotension was recorded in 12 patients. 10 (83.3%) patients had unfavorable outcomes. ICP was raised intraoperatively in 17 patients. 12 (70.6%) had unfavorable outcomes. Six patients required blood transfusion intraoperatively. Five (83.3%) patients had unfavorable outcomes.

Factors that were statistically significant in univariate analysis were examined using a backward stepwise binary logistic regression. Table 3 shows the factors that were statistically significant after logistic regression. On multivariate analysis, only patients who had raised ICP (odds ratio [OR] = 35.6, $P = 0.008$, 95% confidence interval CI 2.6–493.5) and hypotension (OR = 26.1, $P = 0.010$, 95% CI 2.2–311.8) emerged to be statistically significant.

Table 1: Patient demographics and variables

Parameter	Value (%)
Gender	
Male	33 (76.7)
Female	10 (23.3)
Average age (years)	9.6±4.9
Age categories (years)	
0-6	14 (32.6)
7-12	15 (34.9)
13-18	14 (32.6)
Mechanism of injury	
Road traffic accident	20 (46.5)
Fall	23 (53.5)
GCS scores	
13-15	17 (39.5)
9-12	11 (25.6)
3-8	15 (34.9)
Type of injury	
Extradural hemorrhage	19 (44.2)
Subdural hemorrhage	10 (23.3)
Subarachnoid hemorrhage	7 (16.3)
GOS scores	
GOS 1	5 (11.6)
GOS 2	0
GOS 3	8 (18.6)
GOS 4	7 (16.3)
GOS 5	23 (53.4)
GOS scores	
Favorable (GOS 4-5)	30 (70)
Unfavorable (GOS 1-3)	13 (30)
Vomiting	
No	30 (69.8)
Yes	13 (30.2)
Pupil size (mm)	
<3	34 (79.1)
>3	9 (20.9)
Bilaterally nonreactive to light	
Nonreactive	9 (20.9)
Reactive	34 (79.1)
Hypotension	
No	31 (72.1)
Yes	12 (27.9)
Raised ICP	
No	26 (60.5)
Yes	17 (39.5)
Inotrope use	
No	35 (81.4)
Yes	8 (18.6)
Presence of polytrauma	
No	25 (58.1)
Yes	18 (41.9)
Blood transfusion required	
No	37 (86)
Yes	6 (14)
Unilaterally nonreactive to light	

Contd...

Table 1: Contd...	
Parameter	**Value (%)**
Nonreactive	2 (4.7)
Reactive	41 (95.3)
Loss of consciousness	
No	11 (25.6)
Yes	32 (74.4)
Altered level of consciousness	
No	30 (69.8)
Yes	13 (30.2)
Palpable skull fracture	
No	38 (88.4)
Yes	5 (11.6)
Signs of base of skull fracture	
Present	2 (4.7)
Absent	41 (95.3)
Nonfrontal scalp hematoma	
No	32 (74.4)
Yes	11 (25.6)
CT IPH	
No	39 (90.7)
Yes	4 (9.3)
CT EDH	
No	24 (55.8)
Yes	19 (44.2)
CT SDH	
No	33 (76.7)
Yes	10 (23.3)
CT SAH	
No	36 (83.7)
Yes	7 (16.3)
CT mass effect	
No	30 (69.8)
Yes	13 (30.2)
Midline shift >5 mm	
No	6 (14)
Yes	37 (86)
CT fracture	
No	17 (39.5)
Yes	26 (60.5)

GCS - Glasgow Coma Scale; GOS - Glasgow outcome score; ICP - Intracranial pressure; CT - Computer tomography; IPH - Intraparenchymal hemorrhage; EDH - Extradural hemorrhage; SDH - Subdural hemorrhage; SAH - Subarachnoid hemorrhage

Discussion

This study examined the relationship between different clinical parameters and the outcomes of pediatric TBI patients who required surgery. In our cohort of 43 patients who underwent surgery, it was found that raised ICP and hypotension were significant independent predictors of unfavorable outcomes. Although multiple predictor variables have been reported in the literature, there is no agreement as to which variable is most predictive of outcome. The aim of this study was to find out pertinent clinical parameters that would predict outcomes after TBI in a defined group of pediatric patients. Ultimately, this would improve the focus of management in pediatric TBI patients undergoing surgery.

Despite TBI being a common cause of mortality and morbidity, clinical management of pediatric patients is not as well established as adults. Many authors have reported different results over the past 20 years. An important point of discussion would be the use of GCS scores in predicting outcomes due to its extensive use in daily clinical practice. Initially, GCS was thought to be a significant predictor of outcome in pediatric TBI patients.[18] Subsequently, there have been two sides to the story regarding the value of GCS scores in predicting severity.[14,15,19] We believe this is due to a few reasons. First, different authors reported GCS scores at different stages of clinical assessment. Ducrocq *et al.* reported that initial GCS score at presentation was a significant predictor of unfavorable outcome.[20] However, Massagli *et al.* reported that GCS recorded only at 24 and 72 h were significant predictors of outcome.[18] Furthermore, the sample population in different studies varied in terms of sample size, age, and patient characteristics. Some studies included patients with only moderate-to-severe GCS scores[18,21] while others included all patients regardless of their GCS score.[5] The different range of GCS scores coupled with the different target age groups and sample size could have well affected statistical significance. In this study, different pediatric age groups were well represented at each age category had approximately one-third of the sample population. Furthermore, our sample population was specific to those who underwent surgery following TBI. Our results showed that GCS scores were significantly associated with outcomes only on univariate analysis ($P = 0.001$). This is in line with authors who reported the limited use of GCS scores to predict outcomes of pediatric TBI patients.[19]

The same problem with GCS scores is encountered for other factors that have been reported in the literature. A review of the literature showed that common predictor variables investigated include: age, injury severity scores, mechanism of injury, pupil size, vomiting, loss of consciousness, the base of skull fracture, CT findings, blood pressure, and ICP.[5,11,21,22] Prasad *et al.* and Wells *et al.* reported that age at injury was not a good predictor of outcomes in pediatric TBI patients.[5,23] However, Prigatano *et al.* found that age was the strongest predictor of post-TBI performance in neuropsychological tests in school going children.[24] Similarly, pupil size was only found to be a significant predictor in certain studies.[5,25] Kamal *et al.* reported that GCS score, brain CT findings, and hypotension were significant predictors of outcome on univariate analysis in the pediatric population younger than 12 years old.[26] In a French trauma center with 585 patients of mean age 7 years, Ducrocq *et al.* reported that initial hypotension, GCS and injury severity score were significant predictor

Table 2: Factors analyzed on univariate analysis			
Variables	**Favorable (GOS 4-5)**	**Unfavorable (GOS 1-3)**	***P***
GCS categories			
Mild	17	0	0.001
Moderate	7	4	
Severe	6	9	
Vomiting			
No	17	13	0.004
Yes	13	0	
Pupil size (mm)			
<3	28	6	0.001
>3	2	7	
Bilateral nonreactive pupils			
Nonreactive	1	8	<0.001
Reactive	29	5	
Hypotension			
No	28	3	<0.001
Yes	2	10	
Raised ICP			
No	25	1	<0.001
Yes	5	12	
Inotrope use			
No	29	6	<0.001
Yes	1	7	
Presence of polytrauma			
No	24	1	<0.001
Yes	6	12	
Blood transfusion required			
No	29	8	0.007
Yes	1	5	
Mechanism of injury			
RTA	13	10	0.043
Fall	17	3	
Age			
0-6	8	6	0.455
7-12	9	3	
13-18	13	4	
Unilateral nonreactive pupils			
Nonreactive	29	12	0.518
Reactive	1	1	
Loss of consciousness			
No	25	7	0.061
Yes	5	6	
Altered level of consciousness			
No	22	8	0.485
Yes	8	5	
Palpable skull fracture			
No	27	11	0.630
Yes	3	2	

Contd...

Table 2: Contd...			
Variables	**Favorable (GOS 4-5)**	**Unfavorable (GOS 1-3)**	***P***
Signs of base of skull fracture			
No	28	13	0.340
Yes	2	0	
Nonfrontal scalp hematoma			
No	22	10	0.804
Yes	8	3	
CT IPH			
No	29	10	0.075
Yes	1	3	
CT EDH			
No	14	10	0.098
Yes	16	3	
CT SDH			
No	24	9	0.458
Yes	6	4	
CT SAH			
No	27	9	0.172
Yes	3	4	
CT mass effect			
No	19	11	0.279
Yes	11	2	
Midline shift >5 mm			
No	5	1	0.649
Yes	25	12	
CT fracture			
No	13	4	0.513
Yes	17	9	

GCS - Glasgow Coma Scale; GOS - Glasgow outcome score; ICP - Intracranial pressure; CT - Computer tomography; RTA - Road traffic accident; IPH - Intraparenchymal hemorrhage; EDH - Extradural hemorrhage; SDH - Subdural hemorrhage; SAH - Subarachnoid hemorrhage

variables on multivariate analysis.[20] Results from this study on univariate analysis were not entirely different from those published. We found that only bilaterally nonreactive pupils were significantly associated with unfavorable outcomes. The presence of unilaterally nonreactive pupils was not a significant factor. Furthermore, the use of inotrope and patients requiring blood transfusion are variables that have not been reported before. It is to the best of our knowledge that the present study included the most number of predictor variables for analysis. Essentially, in the few studies that investigated predictor variables of outcome in pediatric TBI, no consensus has been reached by authors. This presents as a clinical problem as doctors are unaware of important clinical parameters to pay close attention to when managing pediatric TBI patients. Although all clinical parameters should be monitored, there are some that require closer attention.

Perhaps another reason for the dissimilarity in predictor variables is the measure of outcome in pediatric patients

Variables	B	SE	df	Significant	Exp (B)	95% CI for EXP (B)	
						Lower	Upper
Hypotension	3.262	1.265	1	0.010	26.108	2.186	311.769
Raised ICP	3.572	1.342	1	0.008	35.588	2.567	493.452

Table 3: Factors significant on multivariate analysis

ICP - Intracranial pressure; SE - Standard error; CI - Confidence interval

post-TBI. Authors reported different follow-up periods as well as different outcome measures. Anderson *et al.* utilized intellectual measures such as verbal and nonverbal skills, attention and processing speed to examine outcome 5 years postinjury in preschool pediatric TBI patients.[27] Prigatano *et al.* measured outcome based on performance cerebral functioning tests.[24] A recent study by Hale *et al.* measured outcome by the presence of postdischarge seizures.[28] The GOS scale is the most commonly used measure of outcome in the literature.[20,21] However, it has been reported that the GOS scale underestimates the impact of brain injury in young children[5] as it was developed for use in adults.[29] In 1981, the GOS scale was modified to the GOS-Extended (GOS-E)[30] and a pediatric revision, GOS-E Peds was created and validated by Beers *et al.*[31] However, to the best of our knowledge, very few studies reported the use of GOS-E Peds to measure outcomes.[32] The GOS-E Peds has a maximum score of 8 which is more time consuming to conduct than the original GOS scale. In this study, we used a GOS scale modified by Prasad *et al.* for pediatric patients.[5] Although further validation is required, the modifications appeared to have increased the sensitivity of GOS in pediatric TBI outcomes.[5] The study shows that the majority of the patients had favorable outcomes (70%) after undergoing a neurosurgical procedure. This result is similar to most of the data published in the literature.[5,13,20,33]

Several authors have used stepwise logistic regression to identify variables most predictive of outcome.[5,18,20,21] We adopted the same method for our study. The results from the present study found that raised ICP and hypotension were variables most predictive of outcomes. This is similar to the findings of a French trauma center reported by Ducrocq *et al.* on multivariate analysis.[20] White *et al.* also reported that supra-normal blood pressures and mannitol administration were associated with improved outcomes on multivariate analysis.[21] However, both studies only focused on pediatric patients with GCS ≤8. This present study included all patients regardless of GCS scores that underwent any form of neurosurgical procedure. Reduced blood pressure would result in a decrease in cerebral perfusion leading to ischemic brain damage. This increases secondary brain damage which worsens outcome. Furthermore, raised ICP would cause a decrease in cerebral perfusion pressure which has been reported by Carter *et al.*[34] to be an accurate cause of the unfavorable outcome in pediatric TBI patients. Our results show that priority must be given to manage these two clinical parameters in a pediatric TBI patient. Further work needs

to be done to accurately identify blood pressure and ICP targets which are more precise in preventing unfavorable outcomes.

There were several limitations in this study. Being a retrospective review in a single-center neurosurgical unit, the sample size was smaller compared to multicenter studies. Larger sample size and multi-center studies should be undertaken to validate the current findings. However, our targeted sample population is the first of its kind which will be beneficial to neurosurgeons. Since our study only included patients who underwent surgery, the results might not apply to pediatric TBI patients managed conservatively. Third, it is also important to recognize that the GOS scale measures neurological and psychiatric disorders.[35] Other outcome measures such as quality of life, education level, and social function were not clearly defined in the GOS scale.

Conclusion

This study is the first of its kind to quantify that raised ICP and hypotension were variables most predictive of unfavorable outcomes in a targeted population of pediatric TBI patients who underwent neurosurgery. Our results also suggest that the majority of pediatric TBI patients who required surgery have favorable outcomes. Neurosurgeons should play closer attention to ICP and blood pressure when managing pediatric TBI patients.

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Conflicts of interest

There are no conflicts of interest.

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