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The outcome of severe traumatic brain injury in Latin America

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Abstract

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Traumatic brain injury (TBI) disproportionately affects lower and middle income countries (LMIC). The factors influencing outcomes in LMIC have not been examined as rigorously as in higher-income countries (HIC). This study was conducted to examine clinical and demographic factors influencing TBI outcomes in Latin American LMIC. Data were prospectively collected during a randomized trial of intracranial pressure monitoring in severe TBI and a companion observational study. Participants were aged ≥ 13 years and admitted to study hospitals with GCS ≤ 8. The primary outcome was Glasgow Outcome Scale, Extended (GOS-E) at six months. Predictors were analyzed using a multivariable proportional odds model created by forward stepwise selection. 550 patients were identified. Six month outcomes were available for 88%, of whom 37% had died and 44% had achieved a GOS-E of 5–8. In multivariable proportional odds modeling, higher GCS motor (OR 1.41 per point, 95% CI 1.23–1.61) and epidural hematoma (OR 1.83, 95% CI 1.17–2.86) were significant predictors of higher GOS-E, whereas advanced age (OR 0.65 per 10 years, 95% CI 0.57–0.73) and cisternal effacement (P < .001) were associated with lower GOS-E. Notably, study site (P < .001) and race (P = .004) significantly predicted outcome, outweighing clinical variables such as hypotension and pupillary exam. Mortality from severe TBI is high in Latin American LMIC, although the rate of favorable recovery is similar to HIC. Demographic factors such as race and study site played an outsized role in predicting outcome; further research is required to understand these associations.

Keywords

Global health; Social determinants of health; Traumatic brain injury

Introduction

Traumatic brain injury (TBI) is a major public health problem worldwide, accounting for substantial morbidity and mortality. As many as 1.5 million people die annually from TBI,[1] and it is the leading cause of disability in young people.[2] The incidence of TBI varies considerably between nations, but in general the rate is thought to be higher in lower- and middle-income countries (LMIC).[3,4] This discrepancy is at least in part due to the lack of regulations aimed at injury prevention[5] and the higher frequency of risk factors in these nations; people in LMIC are more likely to be young, to live below the poverty line, and to reside in an area of conflict.[4,6,7]

While the pathophysiology is likely to be similar in high-income countries (HIC) and LMIC, there are important differences in demographics and injury mechanism that may influence outcome. For example, TBI patients in LMIC are younger, take longer to arrive at the hospital, and are more likely to have been involved in a motorcycle or pedestrian road traffic accident.[1,4,8] Once patients reach medical attention, the specific intracranial injuries identified on CT differ significantly, and there may be substantial differences in the care they receive compared to high-income countries.[8,9] Finally, the mortality rate appears to be higher in LMIC; secondary analyses of the Corticosteroid Randomization After Significant Head Injury (CRASH) trial demonstrated that patients in LMIC with severe TBI had higher mortality at two weeks and at six months.[8,10]

While differences between HIC and LMIC are important, there remain substantial social, cultural, and economic dissimilarities within these categories that may influence outcomes from TBI.[4] Latin America has a high proportion of LMIC, with approximately one-third of the overall population living at or under the poverty line.[11] The region also has a high incidence of TBI. Older estimates from the World Health Organization place the incidence of TBI due to road accidents alone at 163 per 100,000, the highest in the world.[1] With continued economic development and increased road traffic, the rate of TBI is likely to have risen since these estimates were published, and it will probably continue to rise as growth continues.[12] A better understanding of TBI in this region is therefore imperative.

The goal of this study is to better understand the long-term outcomes of severe traumatic brain injury in Latin America, and to identify factors associated with recovery. The analysis is based on the data collected during the BEST-TRIP study,[13] a multicenter randomized-controlled trial comparing the effectiveness of two treatment protocols for severe closed head injury – one based on intracranial pressure (ICP) monitoring, and one based on imaging and clinical examination (ICE) – and an observational study conducted in parallel.

Methods

The details of the study design, including patient enrollment and data collection, have been described previously.[13,14] In brief, patients were enrolled in the randomized trial through four hospitals in Bolivia and two hospitals in Ecuador. All six of these facilities featured intensive care units (ICU), 24-hour access to computed tomography (CT) scanners, and round-the-clock neurosurgical coverage. All patients arriving to the study hospitals were screened for traumatic brain injury.

Patients were included if they were admitted to the study hospital within 24 hours of injury, were 13 years of age or older, and had a composite Glasgow Coma Score (GCS) of 3 through 8 on presentation (or GCS motor component of 1 through 5 if the patient was intubated). Patients presenting with TBI and a GCS greater than 8 were also enrolled if they declined to a GCS of 8 or lower within 48 hours of injury. Patients with bilateral fixed and dilated pupils who also had a GCS of 3 and those with injuries that were deemed unsurvivable were excluded. Additional exclusion criteria were as follows: penetrating head injuries, lack of consent for any reason, pregnancy, incarceration, no beds available in the ICU, lack of available equipment for ICP monitoring, significant pre-existing neurological injury, and premorbid conditions with a life expectancy of less than one year. Subjects meeting these criteria were then randomly assigned to one of two treatment arms. In the ICP group, an intraparenchymal ICP monitor was placed (Integra Life Sciences, Plainsboro, NJ) and patients were managed in accordance with the guidelines for severe traumatic brain injury[15] to maintain an ICP of less than or equal to 20 mmHg. In the ICE group, the patient was followed with serial CT scans and clinical examinations; signs of intracranial hypertension on physical examination or imaging were treated with a stepwise protocol.[13,14]

In parallel with the randomized trial, patients at additional sites in Argentina, Brazil, and Colombia were prospectively enrolled in a separate observational study using the same enrollment criteria. These patients were treated with “usual care” at the enrolling center; two

of these hospitals were located in relatively affluent settings and routinely employed ICP monitoring, whereas the others were in substantially lower resource settings and rarely measured ICP. Some patients admitted to the randomized trial sites were enrolled in the observational study when ICU beds or equipment for ICP monitoring were not available. Thus, the observational cohort does not necessarily include patients who were managed less optimally or less aggressively than those in the randomized trial.

Demographic and clinical information was collected at all study centers, although details regarding the patient's course prior to arrival at the study hospital were frequently difficult to clarify. Patient race was classified as white, indigenous, or other, with the latter category including those who were African American or black, pacific islanders, of unknown race, or of another race. Individuals of mixed racial background were categorized separately. All injuries were recorded using the abbreviated injury scale (AIS), which allowed generation of body region AIS scores and cumulative injury severity scores (ISS) for all body regions outside the head (non-head ISS). A trained reviewer evaluated CT scans for the presence or absence of skull fractures, epidural hematomas, subdural hematomas, subarachnoid hemorrhage, cerebral contusions, intraparenchymal hemorrhage, intraventricular hemorrhage, compression or effacement of the basal cisterns, and midline shift greater than or equal to 5 mm. CT scans were also graded according to the Marshall classification.[16]

The primary outcome measure was the Glasgow Outcome Scale, Extended (GOS-E) at six months, which was assessed by a trained examiner. In-hospital mortality and discharge Glasgow Outcome Scale (GOS) were also recorded. Because there was no difference in outcome between the ICP and ICE study arms,[13] they were combined for the purposes of outcome analysis. Similarly, because the randomized study and observational study had identical inclusion criteria, these two populations were merged. GCS motor component scores were imputed from composite GCS when missing. Univariate comparisons of outcomes across groups were performed using the Mann-Whitney U test, the Kruskal-Wallis test, and the Spearman rank-order correlation, as appropriate. Proportional odds modeling was used to assess the odds of more favorable outcome associated with each variable.

To identify the variables most significantly associated with outcome, a multivariable proportional odds model was created using forward stepwise regression. All demographic and clinical variables presented in Tables 1 & 2 were considered for inclusion in the model with the exception of non-head ISS, which was excluded out of concern for erroneous miscoding of missing values as zero in many cases. In the case of the pupillary exam variable, the large proportion of patients with missing data were categorized as "unknown" to prevent the exclusion of these patients from the modeling process. Study site (ie, the treating hospital participating in the study) and the study through which the patient was enrolled (randomized trial vs. observational study) were also included. Variables derived from ICP monitoring were not included because these data were obtained in less than half of the cohort. Every model in the forward selection process was built using pairwise deletion, and interaction terms were not examined. Statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, North Carolina) and SPSS version 19 (IBM Corporation, Armonk, New York) for Windows.

Results

A total of 550 patients were enrolled between September 2008 and October of 2011 across the nine study centers. The six RCT sites screened 528 patients and enrolled 324, and the observational sites identified and enrolled 226 individuals. Overall, 484 (88%) were followed for six months or until death. 156 (28%) died during the index hospitalization.

Demographics and clinical data are presented in Table 1. In general, patients were young, with 69% under 40 years of age. Patients over 40 were more likely to die as an inpatient; those over 40 who survived were more likely to have worse functional outcomes than younger survivors. Males made up the majority, accounting for 87% of the sample. The most common racial background was mixed, followed by white and then indigenous; outcome varied significantly by race, with patients of mixed background faring worse than other categories. Most patients had between 4 and 12 years of education, with more highly educated individuals experiencing significantly higher survival and better functional outcomes. Road traffic accidents were by far the most common cause of injury, totaling 76% of all patients for whom this information was available; most of these accidents involved motorcycles.

Fifty-three percent of patients arrived to the study center within 3 hours of injury (Table 1), and the majority of these patients were brought directly from the field. The admission GCS did not vary significantly with time to the study center ($P = 0.76$, Spearman correlation, data not shown), and there was no overall relationship between prehospital time and GOS-E.

As expected in a severe TBI population, the head AIS scores were high, with a mean of 4.3. 258 (47%) had a head AIS of 5. The mean non-head ISS was 5.4, suggesting that most patients had relatively mild extracranial injuries. However, this variable may have been erroneously miscoded in some cases, as patients with no extracranial injuries (non-head ISS of 0) tended to fare worse than those with mild polytrauma (non-head ISS 1–3). Caution is therefore warranted when interpreting the relationship between ISS and outcome.

Thirty-five percent of patients were admitted to the hospital with a GCS greater than 8 and subsequently declined. GCS Motor on hospital arrival correlated significantly with outcome (Table 1). Bilateral reactive pupils were seen in 47%, while unilateral and bilateral fixed and dilated pupils were seen in 9% and 16%, respectively. The admission pupillary exam was not recorded in 28%. On admission to the study center, 12% were hypotensive, defined as a systolic blood pressure less than 90 mmHg; hypotension was not associated with outcome.

Intracranial pathology diagnosed by CT scan was strongly associated with outcome (Table 2). Sixty-three percent of patients presented with a diffuse injury pattern, with Marshall Grade III being the most common. Hospital mortality rose and functional outcome declined with increasing Marshall Grade. Two components of the Marshall Classification scheme, midline shift and cistern effacement, independently correlated with outcome. There were 177 subjects with mass lesions that required craniotomy and 19 with non-evacuated mass lesions; this latter group had high in-hospital mortality and low rates of functional recovery. Patients with a subdural hematoma, an intracerebral hematoma or contusion, and/or intraventricular hemorrhage had higher rates of inpatient mortality and long-term disability,

while those with an epidural hematoma had more favorable outcomes. Traumatic subarachnoid hemorrhage and skull fractures were both common, but neither was associated with outcome.

In patients who underwent ICP monitoring, there was a strong correlation between elevated intracranial pressure and both hospital mortality and long-term outcome (Table 3). Forty-nine percent of patients with an initial ICP greater than or equal to 20 mmHg died prior to discharge and only 38% made a favorable recovery. Similar findings were seen for low cerebral perfusion pressure (CPP), defined as mean arterial pressure minus the ICP.

Of the 394 who survived hospitalization, 6-month GOS-E was available for 328 (83%). 107 (32%) of these patients made functional improvements after discharge, with an increase in GOS between the discharge evaluation and long-term follow up (Table 4). 148 (45%) did not change and 73 (22%) declined, including 26 (8%) who died by follow up.

A multivariable model was built with a forward stepwise selection process to identify the variables most strongly associated with worse functional status at six months (Table 5). As in the univariate analysis, advanced age, lower GCS motor, cisternal effacement were strong predictors of lower GOS-E, and the presence of an epidural hematoma was associated with higher GOS-E. Notably, patient race and the study site at which the patient received care were also strongly related to outcome. Enrollment in the observational versus randomized studies did not influence outcome in this analysis.

Discussion

While clinical outcomes after TBI have been the subject of numerous publications, the majority of these studies have focused on clinical outcomes in high-resource settings such as Europe and North America.[17] Although the pathophysiology is likely to be similar, discrepancies in clinical outcomes may exist due to differences in clinical care and socio-cultural factors.[10]

Here we describe the outcomes of 550 patients with severe TBI from lower- and middle-income countries in Latin America. Overall, this cohort consisted of severely injured patients, with at least one fixed pupil in 40% of the patients for whom this information was available. Highlighting the severity of these injuries, over a quarter died before hospital discharge and mortality reached 37% by 6 month follow up.

As others have shown in HIC, clinical factors such as the pupillary exam, GCS motor, and intracranial pathology were strongly associated with functional outcome in our univariate analyses. Our multivariable model showed that the GCS motor exam, the presence or absence of an epidural hematoma, and the degree of cisternal effacement were the clinical variables most strongly associated with outcome. In general, these findings mirror those from large trials in HIC.[8,16]

However, we did not find an effect of an abnormal pupillary exam or hypotension, which have been repeatedly shown to associate with poor outcome in HIC.[8,18–24] These discrepancies may be related to the large proportion of patients with an unknown pupillary

exam and to the lack of reliable information regarding prehospital blood pressure. Because the majority of these patients did not reach the study center for hours after their injury, those with uncorrected hemodynamic instability may not have survived to reach care, whereas those with treated hypotension may have been more likely to survive. Such a “survivor bias” could also explain why patients whose presentations were delayed by several hours did not fare any worse than those who arrived early; the sickest of these patients may have died before arriving at the hospital.

Notably, demographic factors such as age, race, education, and study site had very strong associations with GOS-E. Nearly half of patients of mixed racial backgrounds died, compared to less than a quarter of white patients; similarly, favorable outcomes were seen in only one-third of mixed-race patients, whereas over half of white patients achieved a favorable outcome. In our study population, “mixed race” typically describes individuals whose forebears were a mixture of indigenous and white. The majority of patients with 13 or more years of education recovered to a favorable outcome, compared to only 22% of patients with less than three years. In the multivariable model generated by forward-stepwise selection, age, race, and study site were found to be powerful predictors of outcome, outweighing many clinical variables.

The importance of demographic factors in driving patient outcome is not entirely novel. Race and education were seen to independently associate with outcome in IMPACT-TBI, and investigators also identified significant outcome variability between centers when accounting for clinical factors.[25,26] However, the outsized role that these variables appear to play in predicting outcome has not been described previously.

Socioeconomic status and cultural differences between study site may underlie these associations. As in high-income settings, race and socioeconomic status are inextricably linked in many Latin American countries, with whites earning significantly greater wages than nonwhites.[27] While the ICU-level care received by all patients was similar as prescribed by the treatment protocols of the trial, the interventions received after the patient left the ICU may have depended heavily on family resources. Indeed, there is significant variability among the countries represented in the trial with regard to public support for rehabilitative services and disability-related care, in part due to widely varying economic conditions.[27,28] Older estimates suggest a minority of people with disabilities receive public rehabilitative services, and that the proportion may be as small as 1% among disabled individuals living in more rural settings.[29] The out of pocket cost for these services would be prohibitive for many, thus limiting the benefit of post-injury rehab to the patients with greater family resources.

Furthermore, the socio-cultural implications of surviving injury with severe disability vary considerably across cultures and countries. At some of the study sites, the concept of withdrawal of care for patients unlikely to make a meaningful recovery is foreign both to providers and to families; at others, families were willing to allow loved ones to pass if the prognosis was not favorable. Because cultural conditions are also likely to vary considerably by race, it is not surprising that outcomes were so dependent these two variables.

Prehospital care of injured patients is an important aspect of trauma care, and implementation of trauma systems incorporating timely emergency transport are thought to have improved outcomes in patients with head injury.[30–32] One study directly comparing TBI care in the United States and India found that patients in India were far less likely to be transported by ambulance and far more likely to arrive to the hospital in a delayed fashion, which may have contributed to the tendency for worse outcomes in that group.[33] However, we did not observe an effect of transport time in our cohort; the rate of mortality and long-term functional outcomes did not differ between patients who arrived within one hour and after ten hours. This finding may in part be due to stabilization of patients at referring facilities prior to arrival at the study center, but most studies of trauma triage have suggested that patients directly transported to trauma centers fare better.[34] More likely, the data are influenced by a survivor bias; those who were healthy enough to survive the long transport survived and were enrolled in the study, whereas those who were more severely injured may have succumbed to their injuries prior to reaching the hospital or enrolling in the study.

Patients in our cohort had a higher rate of mortality than has been reported in HIC, but the proportion of patients achieving functional outcomes is not substantially different. For example, several multi-national studies of severe TBI conducted in HIC and published since 2000 found mortality rates ranging from 24–30%, markedly lower than the 38% we observed.[10,35,36] In these studies, favorable outcomes, defined as moderate disability or better, were seen in 43–54% of patients; 44% of our patients achieved this outcome. Survival differences between HIC and LMIC are not entirely surprising given the significant discrepancies in available resources between these settings. Indeed, subset analysis of the MRC CRASH randomized controlled trial revealed that the odds of poor outcome were substantially higher in LMIC compared to HIC, even when adjusting for patient characteristics.[10] Furthermore, predictive models generated in HIC tend to underestimate mortality and unfavorable outcomes when applied to data generated in LMIC, suggesting that unmeasured confounders in these countries influence patient outcomes. Notably, the mortality rate we observed is more in line with older studies from HIC, in which mortality rates as high as 36–40% were seen.[37–39]

The study is subject to several limitations. The GOS-E is a reliable instrument for measuring functional recovery after brain injury in HIC, but to our knowledge it has not been validated in LMIC.[40] This is an important limitation, as social and cultural factors defining “satisfactory” recovery may vary considerably between HIC and LMIC, and also from one LMIC to another; an outcome that constitutes moderate disability in one society or cultural setting may be considered severe disability in another. Further, the classifications of race were specified by the funding agency, which was located in the United States, and the composition of the “mixed race” group may have varied considerably by country; therefore, the categorization of race used in this study may not be ethnologically correct. It is also important to note that patient care and data collection were conducted in specialized centers with intensive care units, round-the-clock neurosurgical coverage, and 24-hour access to CT scanners, which may not be typical of hospital capabilities in LMIC. Furthermore, the majority of patients received care based on one of two specified protocols that utilized ICP monitoring or routine imaging and clinical examination, and it is not clear to what extent these care pathways are utilized in LMIC. Differences in patient populations and care

delivery between the observational study sites and centers participating in the randomized trial may also contribute to some of the findings of this study. Broader generalization of these results should therefore be undertaken with caution.

While patients with severe TBI in Latin American LMIC have a high rate of mortality, comparable to that reported in North America and Europe in the 1980s and 1990s, the rate of favorable outcomes is similar to modern studies from HIC. Clinical characteristics predicting recovery are similar to those from HIC, and demographics appear to significantly influence outcome. Further research will be required to elucidate the means by which socio-cultural factors influence patient recovery from severe TBI.

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Abbreviations

AIS	abbreviated injury scale
CRASH	corticosteroid randomization after significant head injury
CT	computed tomography
GCS	Glasgow coma scale
GOS	Glasgow outcome scale
GOS-E	Glasgow outcome scale, extended
HIC	high-income countries
ICE	imaging & clinical examination
ICP	intracranial pressure
ICU	intensive care unit
ISS	injury severity score
LMIC	lower- and middle-income countries
TBI	traumatic brain injury

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Highlights

- TBI outcomes in lower and middle income countries are poorly understood.
- In Latin America, 37% of patients with TBI died; 44% achieved favorable outcomes.
- Study site and patient race were significantly associated with functional outcome.
- Socio-cultural factors strongly influence recovery from traumatic brain injury.

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Table 1

Demographic and clinical characteristics

		6-month GOS-E				Proportional Odds	
	Total	**Inpatient Death**	**Later Death**	**2–4**	**5–8**	**Odds Ratio**	**95% CI**
Total	550	156	28	92	215		
Age			P < .001 *			P < .001	
< 25	210	45 (24%)	5 (3%)	25 (14%)	109 (59%)	[1.00]	
26–39	171	43 (29%)	5 (3%)	26 (17%)	76 (51%)	0.72	(0.49, 1.06)
≥ 40	168	67 (43%)	18 (12%)	41 (26%)	30 (19%)	0.24	(0.16, 0.36)
Gender			P = .30 †			P = .30	
Male	476	131 (31%)	24 (6%)	78 (18%)	190 (45%)	[1.00]	
Female	74	25 (37%)	4 (6%)	14 (21%)	25 (37%)	0.79	(0.49, 1.25)
Race			P < .001 ‡			P < .001	
White	137	26 (20%)	4 (3%)	27 (21%)	72 (56%)	[1.00]	
Mixed	326	115 (41%)	19 (7%)	53 (19%)	96 (34%)	0.35	(0.24, 0.51)
Indigenous	59	12 (21%)	3 (5%)	7 (13%)	34 (61%)	0.81	(0.46, 1.41)
Other/Unk	28	3 (13%)	2 (9%)	5 (22%)	13 (57%)	0.79	(0.36, 1.74)
Education			P < .001 ‡			P < .001	
0 years	4	2 (50%)	1 (25%)	0 (0%)	1 (25%)	0.16	(0.02, 1.52)
1–3 years	55	16 (33%)	8 (16%)	14 (29%)	11 (22%)	0.44	(0.23, 0.86)
4–6 years	122	42 (40%)	7 (7%)	18 (17%)	39 (37%)	0.54	(0.32, 0.93)
7–9 years	131	31 (26%)	3 (3%)	25 (21%)	60 (50%)	1.20	(0.72, 2.00)
10–12 years	133	36 (29%)	3 (2%)	20 (16%)	66 (53%)	1.10	(0.66, 1.82)
≥13 years	79	21 (28%)	2 (3%)	13 (18%)	38 (51%)	[1.00]	
Cause			P = .006 ‡			P = .003	
Car	70	19 (29%)	6 (9%)	13 (20%)	28 (42%)	[1.00]	
Motorcycle	224	55 (28%)	5 (3%)	31 (16%)	106 (54%)	1.50	(0.91, 2.48)
Bicycle/Ped	29	35 (31%)	7 (6%)	33 (29%)	37 (33%)	0.80	(0.46, 1.39)
Fall	75	31 (46%)	7 (10%)	6 (9%)	23 (34%)	0.62	(0.34, 1.16)
Other/Unk	25	16 (33%)	3 (6%)	9 (18%)	21 (43%)	1.08	(0.56, 2.09)

			6-month GOS-E			Proportional Odds	
	Total	Inpatient Death	Later Death	2–4	5–8	Odds Ratio	95% CI
Time to study hospital			P = .98 *			P = .32	
< 1 hour	132	38 (31%)	5 (4%)	22 (18%)	57 (47%)	[1.00]	
1–3 hours	160	46 (31%)	7 (5%)	33 (22%)	63 (42%)	1.00	(0.65, 1.53)
3–6 hours	101	34 (40%)	8 (9%)	13 (15%)	30 (35%)	0.59	(0.36, 0.98)
6–10 hours	75	12 (20%)	5 (8%)	12 (20%)	31 (52%)	1.19	(0.68, 2.06)
≥ 10 hours	81	26 (35%)	3 (4%)	12 (16%)	33 (45%)	0.93	(0.56, 1.56)
GCS Motor			P < .001 *			P < .001	
1	57	23 (46%)	0 (0%)	11 (22%)	16 (32%)	0.50	(0.28, 0.87)
2	71	34 (53%)	5 (8%)	14 (22%)	11 (17%)	0.23	(0.13, 0.39)
3	62	22 (39%)	7 (12%)	15 (26%)	13 (23%)	0.32	(0.19, 0.56)
4	98	21 (23%)	5 (5%)	15 (16%)	51 (55%)	1.02	(0.66, 1.57)
5 or 6	250	54 (25%)	10 (5%)	33 (15%)	120 (55%)	[1.00]	
Fixed Pupils			P < .001 *			P = .003	
Neither	260	62 (27%)	8 (3%)	42 (18%)	121 (52%)	[1.00]	
One	48	16 (37%)	3 (7%)	8 (19%)	16 (37%)	0.66	(0.37, 1.18)
Both	87	36 (44%)	7 (9%)	17 (21%)	21 (26%)	0.40	(0.25, 0.64)
Unknown	155	42 (31%)	8 (6%)	25 (19%)	57 (43%)	0.76	(0.52, 1.11)
AIS Head			P < .001 *			P < .001	
1–3	116	25 (25%)	5 (5%)	21 (21%)	51 (50%)	[1.00]	
4	171	35 (23%)	5 (3%)	28 (18%)	86 (56%)	1.31	(0.84, 2.04)
5	258	96 (41%)	17 (7%)	43 (18%)	77 (33%)	0.53	(0.35, 0.81)
ISS Non-Head			P = .62 *			P < .001	
0	192	67 (39%)	7 (4%)	32 (19%)	65 (38%)	1.92	(1.05, 3.49)
1–3	173	38 (25%)	8 (5%)	31 (20%)	78 (50%)	4.01	(2.09, 7.70)
4–15	125	26 (23%)	8 (7%)	23 (20%)	56 (50%)	2.53	(1.39, 4.60)
≥16	55	25 (50%)	4 (8%)	6 (12%)	15 (30%)	[1.00]	
Hypotension			P = .21 †			P = 0.23	
Absent	458	130 (32%)	25 (6%)	66 (16%)	189 (46%)	[1.00]	
Present	66	21 (36%)	2 (3%)	17 (29%)	18 (31%)	0.74	(0.45, 1.22)

GOS-E, Glasgow outcome scale extended; CI, confidence interval; GCS, Glasgow coma scale; AIS, abbreviated injury scale; ISS, injury severity score. Odds ratios listed are for more favorable outcomes.

* Spearman

† Mann-Whitney U

‡ Kruskal Wallis.

Table 2

Intracranial pathology and outcome.

			6-month GOS-E			Proportional Odds	
	Total	**Inpatient Death**	**Later Death**	**2–4**	**1**	**Odds Ratio**	**95% CI**
Marshall Grade			P = .001‡			P = .001	
DI Type 1&2	111	15 (15%)	6 (6%)	21 (21%)	56 (57%)	1.82	(1.16, 2.85)
DI Type 3	207	62 (34%)	8 (4%)	33 (18%)	79 (43%)	1.11	(0.76, 1.62)
DI Type 4	32	16 (55%)	1 (3%)	2 (7%)	10 (34%)	0.64	(0.31, 1.33)
EVM	177	50 (31%)	12 (7%)	35 (22%)	64 (40%)	[1.00]	
NEVM	19	13 (72%)	1 (6%)	0 (0%)	4 (22%)	0.23	(0.08, 0.67)
Cisterns			P < .001 *			P < .001	
Normal	118	17 (16%)	7 (7%)	22 (21%)	60 (57%)	[1.00]	
Compressed	269	75 (31%)	10 (4%)	44 (18%)	111 (46%)	0.73	(0.49, 1.10)
Absent	159	64 (45%)	11 (8%)	25 (18%)	42 (30%)	0.34	(0.21, 0.53)
Midline Shift			P = .011 †			P = .014	
< 5mm	357	89 (28%)	16 (5%)	61 (19%)	150 (47%)	[1.00]	
≥ 5mm	188	67 (39%)	11 (6%)	30 (17%)	64 (37%)	0.64	(0.46, 0.90)
Epidural			P = 0.002 †			P = .002	
Absent	434	134 (34%)	24 (6%)	76 (19%)	161 (41%)	[1.00]	
Present	99	20 (23%)	3 (3%)	13 (15%)	50 (58%)	1.97	(1.30, 3.00)
Subdural			P = .023 †			P = .028	
Absent	350	94 (30%)	17 (5%)	55 (17%)	149 (47%)	[1.00]	
Present	181	61 (37%)	10 (6%)	32 (19%)	62 (38%)	0.67	(0.48, 0.95)
Contusion			P = .045 †			P = .039	
Absent	295	74 (28%)	15 (6%)	45 (17%)	128 (49%)	[1.00]	
Present	237	81 (37%)	12 (6%)	42 (19%)	83 (38%)	0.72	(0.52, 0.99)
Traumatic SAH			P = .28 †			P = .26	
Absent	209	55 (29%)	11 (6%)	31 (17%)	90 (48%)	[1.00]	
Present	324	100 (34%)	16 (5%)	57 (19%)	121 (41%)	0.84	(0.60, 1.16)
Traumatic IVH			P = .002 †			P = .003	

		6-month GOS-E			Proportional Odds	
	Total	**Inpatient Death**	**Later Death**	**2–4**	**1**	**Odds Ratio**	**95% CI**
Absent	495	142 (32%)	20 (4%)	79 (18%)	206 (46%)	[1.00]	
Present	36	12 (38%)	7 (22%)	8 (25%)	5 (16%)	0.34	(0.17, 0.69)
Skull Fracture			P = .44[†]			P = .47	
Absent	304	84 (30%)	15 (5%)	52 (19%)	128 (46%)	[1.00]	
Present	226	70 (35%)	12 (6%)	36 (18%)	83 (41%)	0.88	(0.63, 1.22)

[*] Spearman

[†] Mann-Whitney U.

GOS-E, Glasgow outcome scale extended; CI, confidence interval; DI, diffuse injury; EVM, evacuated mass lesion; NEVM, non-evacuated mass lesion; SAH, subarachnoid hemorrhage; IVH, intraventricular hemorrhage. Odds ratios listed are for more favorable outcomes.

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Table 3

Intracranial pressure and outcome.

			6-month GOS-E			Proportional Odds	
	Total	**Inpatient Death**	**Later Death**	**2–4**	**5–8**	**Odds Ratio**	**95% CI**
Initial ICP			P < .001 *			P < .001	
< 20mmHg	125	16 (14%)	9 (8%)	24 (21%)	63 (56%)	[1.00]	
≥ 20 mmHg	76	34 (49%)	3 (4%)	6 (9%)	26 (38%)	0.35	(0.20, 0.61)
Initial CPP			P = .006 *			P = .005	
> 60 mmHg	128	20 (18%)	9 (8%)	20 (18%)	64 (57%)	[1.00]	
≤ 60 mmHg	73	30 (44%)	3 (4%)	10 (15%)	25 (37%)	0.45	(0.26, 0.78)

* Mann Whitney U.

GOS-E, Glasgow outcome scale extended; CI, confidence interval; ICP, intracranial pressure; CPP, cerebral perfusion pressure. Odds ratios listed are for more favorable outcomes.

Table 4

Discharge GOS vs. 6 month GOS-E. Shaded area corresponds to decline after discharge.

	Discharge GOS				
6 Month GOS-E	**1**	**2**	**3**	**4**	**5**
1	156	14	9	2	1
2	-	7	3		1
3–4	-	4	49	22	4
5–6	-	3	15	28	17
7–8	-	2	25	58	64

GOS-E, Glasgow outcome scale extended; GOS, Glasgow outcome scale

Table 5

Multivariable proportional odds model produced by forward stepwise regression

	Odds Ratio	95% CI	P Value
Age (per 10 years)	0.65	0.57, 0.73	< .001
GCS motor (per point)	1.41	1.23, 1.61	< .001
Cisterns			< .001
Normal	[1.00]		
Compressed	0.65	0.42, 1.01	
Absent	0.25	0.15, 0.44	
Epidural hematoma	1.83	1.17, 2.86	.008
Race			.004
White	[1.00]		
Mixed	0.36	0.19, 0.70	
Indigenous	0.66	0.29, 1.48	
Other/Unknown	0.96	0.36, 2.56	
Study site	*See footnote* *		< .001

CI, confidence interval; GCS, Glasgow coma scale.

* Odds ratios for individual study sites ranged from 0.15 to 1.48. Odds ratios listed are for more favorable outcomes.