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Factors Influencing Pediatric Recovery from Traumatic Brain Injury

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Abstract

Purpose: Many factors are linked to prolonged recovery from traumatic brain injury (TBI) in the pediatric population. This study investigated risk factors to aid anticipatory guidance and treatment strategies. **Methods:** A retrospective chart review was conducted utilizing 133 patients admitted to a pediatric trauma service at a Level 1 Pediatric Trauma Center. Results: No significant difference in recovery time was found based on acute injury severity as graded by initial Glasgow Coma Score (GCS) (GCS of 3-12 median recovery of 34 days vs GCS 13-15 median recovery of 34 days (p = 0.393)) and presence of intracranial hemorrhage (ICH) (ICH median recovery of 34 days vs no ICH median recovery of 30 days (p = 0.506)). Patients with post-concussive sleep disturbances (median recovery of 53.5 days (p = 0.002)) and comorbid mood disorders (anxiety and/or depression median recovery of 143 days (p = 0.009), ADHD median recovery of 45 days (p = 0.012) showed an increased median recovery length. The median recovery time severe of moderate initial injury (GCS of 3-12 median recovery of 34 days (p = 0.00244)) and mild initial injury (GCS 13-15 median recovery of 34 days (p<0.001)) was longer as compared to outpatient studies (17 days). **Conclusions:** This study verified that GCS and ICH upon admission are not correlated with recovery, whereas sleep disturbances and comorbid mood disorders are strong prognostic factors for prolonged recovery. A longer median recovery time, compared to outpatient studies, suggests that patients admitted to a pediatric trauma service are at risk for prolonged recovery.

Introduction

Traumatic brain injuries (TBIs) are a major source of morbidity and mortality, as TBIs contribute to approximately 30% of all injury-related deaths.[1] A number of different mechanisms can lead to TBIs: closed head injuries, blast-related injuries, and penetrating injuries.[2]

TBI severity is initially classified using a Glasgow Coma Score (GSC), which has a maximum score of 15 and assesses eye opening, verbal responses, and motor responses in patients. When scoring TBI severity, a mild TBI is classified as GCS 13-15, moderate as 9-12, and severe as 3-8.[1] TBIs are a heterogeneous group of injuries that cannot be differentiated necessarily by GCS alone because GCS scaling does not provide information about the specific patho-physiologic mechanisms responsible for neurological deficits.[3]

As such, hematomas (epidural, subdural, subarachnoid, intraparenchymal), contusions, and diffuse axonal injury all could present as severe TBIs based on the GCS classification. The terms “concussion” and “TBI” often are used interchangeably, though a concussion is a subset of TBI. Concussions are defined as low-velocity injuries that cause brain “shaking,” resulting in clinical symptoms not necessarily related to pathological injury.[4,5] For the purposes of this manuscript, we will use the term TBI except in referring to the title of a concussion clinic or citing a study that specifically refers to sports-related concussions.

The majority of pediatric patients tend to recover from a concussion within 7-10 days,[4,6] although recovery can be prolonged. Symptoms of minor TBI (mTBI) are often defined as physical, emotional, cognitive, and sleep. Studies have found that 11-17% of children with a mTBI remain symptomatic three months after injury.[7,8] Multiple factors have been found to influence pediat-ric mTBI recovery. Younger age,[9-11] female gender,[12-17] past medical history of TBI,[15,16,18] mood disorders,[11,14,15,19,20] and sleep disturbances[6,21-23] have all been associated with prolonged recovery time. Greater acute injury severity, as measured by initial symptom burden, loss of consciousness, and GCS < 15, also have been shown to be associated with more severe or longer-lasting symptoms.[16,19,24-28,32] Few studies have specifically looked at recovery time in children

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Table 1. Mechanism of Injury and Recovery Time

	Number of Patients	Median Recovery Time (Days)	P Value (vs. MVA)	P Value (vs. Fall)
Sport/Recreation	54 (41%)	33	0.962	0.0586
MVA*	44 (33%)	31	-	0.135
Fall	31 (23%)	39.5	0.135	-
Assault/Child Abuse	3 (2%)	31	-	-
Firearm	1 (1%)	143	-	-

*MVA = Motor vehicle accident

Table 2. GCS and ICH

	Number of Patients			Median Recovery Time (Days)		
	GCS 3-12	GCS 13-15	GCS Unknown	GCS 3-12	GCS 13-15	GCS Unknown
GCS, n(%)	17 (13%)	99 (74%)	17 (13%)	34	32	0.393
	No ICH	ICH		No ICH	ICH	P Value
ICH,* n(%)	77 (58%)	55 (41%)		30	34	0.506

*ICH = Intercranial hemorrhage

presenting with mTBI to a pediatric trauma service, so the goal of this study was to examine factors that could influence recovery time in those patients.

Methods

Data Collection

A retrospective chart review was conducted on patients admitted for TBI to a pediatric trauma service at a Level 1 pediatric trauma center between January 1, 2014 and December 31, 2015. Patients within this 2-year time period were included in the study if they met the following inclusion criteria: aged 5-17, discharged to home, and a discharge diagnosis of TBI, concussion, intracranial hemorrhage (ICH), or mention of a TBI diagnosis in the patient's history and physical. The age range was chosen to analyze school-aged children. ICH included all hemorrhages — epidural, subdural, subarachnoid, intraparenchymal and contusion — identified on CT scan. Patients were excluded if they experienced an additional TBI before recovering from the initial injury. The selected patients were identified by filtering the trauma database for ICD 9 codes 850-854 (intracranial injury, excluding those with skull fracture). ICD 9 codes 800-804 also were checked to see if inclusion of skull fracture would increase the number of patients with TBIs, but none were found. Patients who had a TBI as well as an additional extracranial injury were not excluded. Stratification of the trauma data identified a total of 169 patients, of which 36 patients did not have a discharge diagnosis of TBI, concussion, or ICH and thus were excluded. Of the 133 patients who met the final inclusion criteria, 94 had definitive recovery time data available. Median recovery time was reported.

Using the information contained in the inpatient and outpatient electronic medical records, data was recorded regarding patient demographics, past medical history, mechanism of injury, injury presentation (GCS, ICH, presenting symptoms), inpatient treatment and length of stay, time missed from school, outpatient follow-up and treatment, longitudinal treatment and symptoms (sleep, mood, cognition, headache), and recovery time. Mechanism of injury was separated into sports/recreation, motor vehicle accident, fall-related injury, assault/child abuse, and firearm-related injury. Due to a lack of considerably depressed GCS scores, GCS was grouped into patients with severely or moderately depressed scores (GCS 3-12) and mildly depressed scores (GCS 13-15).

Recovery time was established as the length of time from the date of initial injury to date at which a provider note was written with one of the following: the patient was asymptomatic; follow up only as needed; or patient did not need to return for greater than six months. Recovery time was considered to be unknown if the patient did not attend a follow-up appointment or scheduled a follow-up appointment at another institution. The study was reviewed and approved by the Institutional Review Board (IRB).

Statistical analysis

Exploratory analyses were performed using R 3.4.1 (R Core Team),[29] including the computation of summary statistics and the creation of contingency tables. Boxplots were made to compare distributions of recovery time in groups defined by select categorical clinical variables.

Results were reviewed manually to select factors to be analyzed. Wilcoxon signed rank tests were applied

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Table 3. Past Medical History

	Number of Patients		Median Recovery Time		
	(-) PMH	(+) PMH	(-) PMH	(+) PMH	P Value
Anxiety and/or depression, n (%)	128 (96%)	5 (4%)	32	143	0.009
Autism, n (%)	128 (96%)	5 (4%)	33	38.5	0.691
ADHD, n (%)	116 (87%)	17 (13%)	32	45	0.0119
Learning disability, n (%)	132 (99%)	1 (1%)	33	13	0.162
Migraine, n (%)	126 (95%)	7 (5%)	33	37	0.772
Seizure disorder, n (%)	129 (97%)	4 (3%)	33	24.5	0.427
Previous TBI, n (%)	124 (93%)	9 (7%)	33	39	0.428

ADHD = Attention-Deficit/Hyperactivity Disorder, PMH = Past Medical History, TBI = Traumatic Brain Injury

to compare recovery times to fixed reference values identified in previous studies, whereas Wilcoxon rank sum tests were used to compare recover times between two groups of patients defined by categorical variables of interest. All tests were performed at the α = 0,05 level, and a Bonferroni adjustment was used to account for multiple testing. Correlation-based analysis was not appropriate in this study because analysis was not conducted involving two quantitative variables

Results

The average age of patients in this study was 10.8 years. Sixty-three percent of patients were male (n = 84) and had a median recovery time of 32.5 days, whereas females had a median recovery time of 34.0 days. Recovery times were not significantly different between the genders (p = 0.373). The median recovery time for all patients was 33.0 days.

Table 1 shows mechanism of injury and median recovery time. Forty-one percent of patients suffered from a sports/recreation-related injury (n = 54), 33% of patients were involved in a motor vehicle accident (n = 44), and 23% of patients were involved in a fall-related injury (n = 31). A comparison of mechanism of injury and recovery time showed recovery was not significantly different between sport-related, motor vehicle accidents, and fall-related injuries. Not enough assault or firearm victims were included in this study to be studied.

Initial GCS and ICH were not associated with median recovery time (Table 2). Thirteen percent of patients (n = 17) presented with a significantly or moderately depressed GCS 3-12 and had a median recovery rate of 34.0 days, whereas 74% of patients (n = 99) presented with a mildly depressed GCS 13-15 and had a median recovery time of 32.0 days (p = 0.393). Patients with no ICH had a median recovery of 30.0 days, whereas those with ICH had a median recovery of 34.0 days (p = 0.506).

Past medical history also was analyzed as a factor that could affect median recovery time (Table 3). Four percent of patients (n = 5) had a positive PMH of anxiety and/or depression, which was associated with a longer median recovery time (143.0 days) compared to a negative PMH of anxiety and/or depression (32.0 days) (p = 0.009). Patients with ADHD also had a longer recovery time (45.0 days) than patients without (32.0 days) (p = 0.012). Patients with autism, learning disabilities, migraines, or previous TBI each had longer median recovery times than the patients with negative PMHs, but none of these comparisons reached statistical significance.

Longitudinal complications of TBI were analyzed in relationship to median recovery time (Table 4). Thirteen percent of patients (n = 17) complained of sleep disturbances (difficulty falling asleep, staying asleep, or both) at one of their follow-up appointments and had a median recovery time of 53.5 days that was significantly longer than patients without a sleep disturbance (p = 0.002). Seventeen percent of patients with cognitive complications, such as difficulty concentrating, impaired memory, or slower processing speed, had a longer recovery than patients with no change from baseline (p = 0.035). However, using Bonferroni correction, P must be less than 0.0085 to be significant. Therefore, the increased recovery time with cognitive longitudinal complications is no longer significant. Symptoms of mood, headache, balance, and dizziness also showed increased median recovery times but these were not statistically different from the overall median recovery of 33.0 days.

Patients in the current study were admitted to an inpatient, pediatric trauma service. In contrast, most of the previous literature involves patients who are seen in an outpatient setting. Thomas et al. (2018) attempted to determine a precise pediatric recovery rate for those seen in outpatient clinics.[16] Patients aged 10-17 (n=1733) with sports-related concussions presented to seven concussion clinics and were found to have a median recovery of 17 days. Our

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Table 4. Longitudinal Symptoms Following TBI

	Number of Patients			Median Recovery Time (Days)		
	No Change	Symptomatic	Unknown	No Change	Symptomatic	No Change vs. Symptomatic P Value
Sleep	102 (77%)	17 (13%)	14 (11%)	32	53.5	0.002
Mood	101 (76%)	18 (14%)	14 (11%)	32	41	0.226
Cognition	97 (73%)	22 (17%)	14 (11%)	32	46	0.036
Headache	72 (54%)	47 (35.3%)	14 (11%)	32	36	0.198
Balance	112 (84%)	7 (5%)	14 (11%)	32.5	53	0.124
Dizziness	102 (77%)	17 (13%)	14 (11%)	32	43	0.099

inpatient study consisted of patients with significantly longer recovery times (33 days). Both patients with a severely or moderately depressed GCS 3-12 had a longer median recovery time than 17 days (34 days, p = 0.002) as did patients with a mildly depressed GCS 13-15 (32 days, p ≤ 0.0001) (Figure 1).

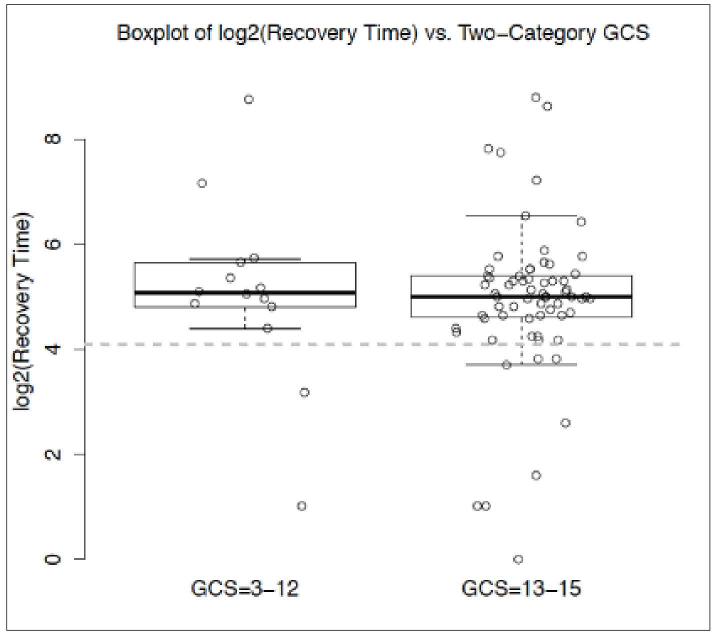

Figure 1. Comparison of severely and mildly depressed GCS to 17-day recovery time

Discussion

Multiple factors previously have been shown to influence recovery from a TBI.[9-28,32] In this retrospective chart review study, we found that patients with post-concussive sleep disturbances and comorbid mood disorders showed an increased median recovery length. Moreover, the overall median recovery time for patients admitted to the trauma service was longer compared to outpatient studies. These results may inform clinicians regarding patients who may experience longer recovery times.

The relationship between gender and TBI recovery time has been well documented. Prior studies have demonstrated that females have a prolonged recovery time compared to males.[13-16] The current study did not show the same association. The cause of the lack of a difference is unclear. This is an interesting finding that could be related to the particular patient population because most other studies show prolonged female recovery in outpatient, sports-related concussions, but more research should be conducted to further explore this question.

This study showed a significantly longer median recovery time than Thomas et. al found in its outpatient study.[16] This longer median recovery time could suggest that patients admitted to a pediatric trauma service are at risk for prolonged recovery. However, it should be noted that these studies cannot be directly compared, as Thomas et. al, focused on sports-related concussions, which is a only subset of the mTBI patients included in this study.

The GCS is a common assessment tool utilized after head injury. Whereas some studies suggest that its initial severity, as defined by degree of symptoms, can predict TBI recovery,[16,19,24-28,32] the current study found no association between initial GCS score and recovery time. This could have been due to GCS not being a good predictor of prolonged recovery with less severe TBI.[32,33] Another consideration is that all patients included in this study improved to the point they could be discharged home. Therefore, patients with a low initial GCS who had a more severe initial presentation and might have been at risk for a longer recovery could have been excluded from this study because they were instead discharged to a rehabilitation setting.

The relationship between GCS and intracranial hemorrhage (ICH) is unclear, as some studies suggest an inverse relationship while others suggest no correlation.[34,35] However, ICH can be used to assess injury severity, as it can lead to worse, potentially life-threatening, patient outcomes and is thought to be an important criteria in classifying TBI by pathology.[33] ICH has been shown to be associated with prolonged recovery from increased cognitive symptoms and functional impairment.[36-38] In this study, the presence of ICH was not a factor in recovery time. One possible explanation is that the presence of

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ICH was not a prognostic factor because the lesions were too small to prolong recovery. Another explanation is that while ICH may be associated with increased initial symptom burden, it may not overly prolong recovery. One study found that patients with intracranial pathology have worse quality of life at three months, but the adverse consequences resolved before one year.[36] Collectively, the data suggest that the use of either the GCS or presence of ICH is equivocal for predicting recovery after TBI. Although GCS and ICH were not shown to be associated with recovery time in our study, the prolonged recovery time of patients in this study compared to prior studies may reflect more severe injury that prompted an inpatient admission for these patients.

This analysis supports previous studies that demonstrate an association between premorbid psychiatric conditions and prolonged recovery time following TBI, though our sample size for these conditions was quite low (n=5). Each patient with anxiety or depression, however, had a longer recovery time than the overall median recovery time of 33.0 days (34, 49, 143, 434, and 435 days). One potential confounding factor could be the linkage between anxiety, depression, and poor sleep quality. In general, anxiety and depression are associated with poor sleep quality.[30] After TBI, post-concussive depression has been shown to predict the presence of insomnia.[31] The relationship between poor sleep, anxiety and depression, however, does not explain the risk of prolonged recovery in patients with anxiety or depression who do not have noticeable sleep difficulties.[11,14,15,19,20] Along with anxiety and depression, ADHD also was found to increase recovery time (n = 17). All patients in this group had a longer recovery time than the overall median recovery time of 32.0 days. These findings support the need for proper psychiatric screening of patients presenting with TBI.

Patients with sleep disturbance had a prolonged recovery as compared to patients without. Current literature shows that sleep disturbance, such as increased sleep need, daytime sleepiness, or insomnia aggravate other sequelae of TBI and significantly prolong recovery from TBI.[6,21,22] Sleep disturbance has been found to be associated with a three- to fourfold increase in pediatric recovery time and may not present immediately after injury.[6,23] Thus, it is important not only to identify these patients on initial evaluation, but to educate patients to be aware of the possibility of sleep disturbances and the need to follow up in a concussion clinic if these symptoms arise.

Limitations

Several potential limitations should be noted. The data may not represent patient populations from different regions of the world. Only 79% of patients (n = 133) met all of the inclusion criteria for this study and this high exclusion rate could have prevented certain statistical comparisons from becoming significant. Twenty-nine percent of patients (n = 39) had unknown recovery times, either due to follow up out of network or because they did not attend scheduled follow-up visits. Recovery was measured as the length of time from the initial injury to the last day of follow-up. Recovery time also could have been overestimated in this study if a large number of patients with unknown follow up did not return because they were already asymptomatic. This value also could have been overestimated by patients' last visit occurring after full recovery, as well as delayed recovery from other traumatic injuries, such as skull fracture. In contrast, recovery could have been underestimated by patients having activity restrictions or mild to moderate symptoms on the last day of follow up. When calculating recovery time, we attempted to differentiate recovery due to TBI from other inju-ries. When looking at follow-up notes, patients were only considered recovering if symptoms were noted to be due to TBI and not extracranial injuries. This is an imperfect solution and extracranial injuries still influenced recovery time.

GCS was obtained from a variety of sources such as outside hospitals or the EMS, arrival at our institution may have been obtained at different times post injury, and categorical values were not obtained. To overcome this obstacle in the future, a uniform time point should be chosen to obtain GCS, such as presentation in the emergency department. The location of ICH was recorded, but the volume of hematoma or presence of midline shift was not. It is possible that the patients in this study who were ICH positive had small hemorrhages not significant enough to delay recovery. Because not all patients underwent imaging, it is also possible that patients with undiagnosed ICH were included in this study. Finally, this was a retrospective chart review and not all data were available for each patient. Whereas all of the trauma providers were experts in TBI, it is possible that each medical discipline (pediatrics, etc.) does not each equally address specific information that was recorded in this study. In particular, past medical history such as behavioral health disorders, most likely was underdiagnosed.

Conclusion

This study found that GCS score and ICH upon admission are not prognostic factors for TBI recovery, whereas sleep and behavioral health are associated with prolonged TBI recovery. Patients admitted to a pediatric trauma service may be at risk for prolonged recovery. Therefore, these centers need to assess for sleep and be-havioral health disorders prior to discharge and provide anticipatory guidance for follow up. A well-designed prospective study should be conducted to confirm our findings and provide additional guidelines.

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