Standardizing ICU management of pediatric traumatic brain injury is associated with improved outcomes at discharge

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OBJECTIVE The goal of critical care in treating traumatic brain injury (TBI) is to reduce secondary brain injury by limiting cerebral ischemia and optimizing cerebral blood flow. The authors compared short-term outcomes as defined by discharge disposition and Glasgow Outcome Scale scores in children with TBI before and after the implementation of a protocol that standardized decision-making and interventions among neurosurgeons and pediatric intensivists.

METHODS The authors performed a retrospective pre- and postprotocol study of 128 pediatric patients with severe TBI, as defined by Glasgow Coma Scale (GCS) scores < 8, admitted to a tertiary care center pediatric critical care unit between April 1, 2008, and May 31, 2014. The preprotocol group included 99 patients, and the postprotocol group included 29 patients. The primary outcome of interest was discharge disposition before and after protocol implementation, which took place on April 1, 2013. Ordered logistic regression was used to assess outcomes while accounting for injury severity and clinical parameters. Favorable discharge disposition included discharge home. Unfavorable discharge disposition included discharge to an inpatient facility or death.

RESULTS Demographics were similar between the treatment periods, as was injury severity as assessed by GCS score (mean 5.43 preprotocol, mean 5.28 postprotocol; p = 0.67). The ordered logistic regression model demonstrated an odds ratio of 4.0 of increasingly favorable outcome in the postprotocol cohort (p = 0.007). Prior to protocol implementation, 63 patients (64%) had unfavorable discharge disposition and 36 patients (36%) had favorable discharge disposition. After protocol implementation, 9 patients (31%) had unfavorable disposition, while 20 patients (69%) had favorable disposition (p = 0.002). In the preprotocol group, 31 patients (31%) died while 6 patients (21%) died after protocol implementation (p = 0.04).

CONCLUSIONS Discharge disposition and mortality rates in pediatric patients with severe TBI improved after implementation of a standardized protocol among caregivers based on best-practice guidelines.

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KEY WORDS critical care; discharge; trauma; traumatic brain injury; protocol

TRAUMATIC brain injury (TBI) is a heterogeneous condition characterized by marked variability in etiology and treatment.4,5,10,26 There have been numerous studies on the treatment of TBI in the adult population,4,6,8,9,11,13,16,24,25,29 but less research has been performed on treating TBI in pediatric patients.2,5,18,21,23 ‘These patients’ still-maturing CNS responds differently to injury and the current treatments available, making it imperative to determine the best course of action to improve outcomes in this population.’5,16,18,22

The 2003 Brain Trauma Foundation guidelines,4 which were most recently updated in 2012,24 summarized practice standards for treatment of severe TBI in children. The overarching goal of critical care in treating TBI is to reduce secondary brain injury by limiting cerebral ischemia and optimizing cerebral blood flow.3 Despite these evidence-based guidelines, there is considerable variability in how different physicians and institutions treat severe TBI, and the strength of the evidence is low.10

A study by Pineda et al. in 2013 showed significant ben-
The prospectively maintained Vanderbilt University Medical Board approved the study protocol. Those who died in the emergency department were excluded from the study. The Vanderbilt institutional review board based on the examination by the neurosurgery team after resuscitation. This process helped to limit those patients classified as having an artificially low GCS score upon admission with an emphasis on maintaining CPP and ICP within strict parameters to reduce secondary brain injury by optimizing cerebral blood flow. The hierarchy algorithm to a single hyperosmolar therapy would decrease variation in care. The protocol used hypertonic saline, so this was used as a surrogate measure of adherence. There were no studies about the use of mannitol that met inclusion criteria.

Protocol Implementation

The TBI protocol was implemented on April 1, 2013. Prior to 2013, no specific multidisciplinary protocols were used at the institution in the management of pediatric brain injury. Variation in the overall management paradigm for patients with severe TBI was common. The evidence-based protocol was developed by a multidisciplinary group composed of local experts from pediatric services, including neurosurgery, critical care medicine, trauma surgery, and emergency medicine. Source material that was reviewed included the 2003 Brain Trauma Foundation guidelines and the 2012 update and institutional protocols from St. Louis Children’s Hospital and Children’s of Alabama. The standardized clinical protocol was devised to guide medical therapy in a stepwise fashion, with an emphasis on maintaining CPP and ICP within strict parameters to reduce secondary brain injury by optimizing cerebral blood flow. The tiered approach to therapy focuses first on optimization of oxygen delivery and cerebral perfusion, secondly on CSF diversion, thirdly on maintenance of adequate sedation/analgesia, and finally on maximization of hyperosmolar therapy prior to progression to second-tier therapies, as defined by the 2012 Brain Trauma Foundation guidelines. Each intervention step is followed by immediate reevaluation to determine efficacy and need for further escalation. When developing the protocol, it was determined that simplifying the algorithm to a single hyperosmolar therapy would decrease variation in care. The protocol used hypertonic saline, so this was used as a surrogate measure of adherence. In addition, the 2012 Brain Trauma Foundation guidelines note Level II and III evidence for the use of hypertonic saline. There were no studies about the use of mannitol that met inclusion criteria.

Outcomes of Interest

The primary outcome was discharge disposition, categorized as discharge home, discharge to rehabilitation, or death. A single patient was transferred to another acute care facility per the family’s request. This patient was considered to have a “rehabilitation” discharge disposition to maintain the model with only 3 discharge categories.

Methods

For this retrospective cohort study, we used data from the prospectively maintained Vanderbilt University Medical Center pediatric trauma registry. We included patients less than 18 years of age presenting with TBI with a GCS score of less than 8 between April 1, 2008, and May 31, 2014. All patient electronic medical records with radiographic evidence of TBI were reviewed for this study, and the GCS score used for determination of enrollment was based on the examination by the neurosurgery team after resuscitation. This process helped to limit those patients classified as having an artificially low GCS score upon initial emergency department assessment secondary to sedating medications. Variables not maintained prospectively were extracted from the electronic medical record, including ICP monitoring and hyperosmolar therapy. Patients were followed for the length of their hospitalization. Those who died in the emergency department were excluded from the study. The Vanderbilt institutional review board approved the study protocol.

Chart review was used to extract parameters, including age, sex, race, GCS score after resuscitation, need for surgery, injury type and mechanism, discharge disposition, GCS score at discharge, pediatric intensive care unit (PICU) length of stay, total length of stay, use of hyperosmolar therapy, use of barbiturates, and ICP monitoring. Due to the complexity of each patient’s clinical narrative and associated multiplicity of variables generated, protocol adherence was challenging to assess. However, use of 3% hypertonic saline instead of mannitol was identified as a surrogate measure of adherence given the 2012 guidelines’ focus on 3% NaCl as treatment for elevated ICP and its consistent availability in the medical record. Any usage of mannitol was considered a protocol deviation. Strict usage of solely 3% NaCl for elevated ICP was considered consistent with protocol requirements. Due to the real-time and rapid nature of patient care, we found that compliance for cerebral perfusion pressure (CPP) was challenging to adequately categorize during patients’ hospitalization, and it was not clear whether these data were an accurate representation of the actual clinic course. Therefore, this parameter was not used as a surrogate measure of adherence.
Our secondary outcome was GOS score at discharge. We did not use the extended scale, because we did not believe that the retrospective nature of this analysis was sensitive enough to adequately reproduce the scale in a meaningful way.

**Statistical Analysis**

No trends in outcomes were detected in the 5 years of the preprotocol cohort; as such, this group was analyzed as a whole versus the postprotocol cohort. Study outcomes measured before and after TBI protocol implementation were compared. Mean age, GCS score, and length of stay between cohorts were compared using the Wilcoxon rank-sum test. Need for surgery, the various injury types and mechanisms, ICP monitor placement, barbiturate use, and hyperosmolar use were compared using the chi-square test and Fisher’s exact test where appropriate. Discharge disposition and GOS scores were compared using the Kruskal-Wallis test. Individual groups within discharge disposition were compared using the Wilcoxon rank-sum test.

To compare study outcomes before and after TBI protocol implementation while accounting for potential con-
founders, we used multivariate ordered logistic regression. Variables were determined a priori based on clinical significance and perceived importance. These variables were pre- and postprotocol status, GCS score after resuscitation, age, ICP monitor placement, and PICU length of stay. The number of parameters was limited to 5 to prevent overfitting the model. In the model, odds ratios (ORs) greater than 1 were associated with increasingly favorable discharge disposition. Ordered logistic regression was also used to predict discharge disposition based on GCS score after resuscitation across the spectrum of TBI severity and to create a plot comparing trends. Statistical significance was set a priori at \( p < 0.05 \), and the analysis was conducted using Stata statistical software (version 13, StataCorp).

Results

A total of 128 patients (preprotocol \( n = 99 \), postprotocol \( n = 29 \)) were included in the study. Table 1 shows demographics, injury severity, injury mechanism, length of stay, and ICP treatment parameters. Baseline demographics were not significantly different in the pre- and postprotocol groups. Injury severity as assessed by initial GCS was similar, with a mean of 5.43 in the preprotocol cohort versus 5.28 in the postprotocol group (\( p = 0.671 \)). Rates of patients requiring a neurosurgical operation were not significantly different (20% preprotocol vs 32% postprotocol; \( p = 0.648 \)). A significant difference existed in the number of patients presenting with subdural hemorrhage as the predominant radiographic finding (33% preprotocol vs 61% postprotocol; \( p = 0.009 \)). The injury mechanism was similar, except there was significantly more abusive head trauma in the postprotocol group (48% vs 20%, \( p = 0.003 \)) and a trend toward fewer motor vehicle collisions (35% vs 17%, \( p = 0.064 \)). Length of stay was not significantly different between the number of patients presenting with subdural hemorrhage as the predominant radiographic finding (33% preprotocol vs 61% postprotocol; \( p = 0.009 \)). The injury mechanism was similar, except there was significantly more abusive head trauma in the postprotocol group (48% vs 20%, \( p = 0.003 \)) and a trend toward fewer motor vehicle collisions (35% vs 17%, \( p = 0.064 \)). Length of stay was not significantly different between the pre- and postprotocol cohorts. Mean PICU length of stay and overall length of stay did not differ between cohorts (\( p = 0.986 \) and \( p = 0.871 \), respectively). Before protocol implementation, ICP monitors were placed in 46% of patients compared with 28% of patients after protocol implementation (\( p = 0.07 \)). Use of barbiturates was similar before and after protocol implementation (16% vs 21%; \( p = 0.68 \)).

Protocol Adherence

Protocol adherence was difficult to assess based on existing electronic medical records, but use of 3% hypertonic saline over mannitol was used as a surrogate measure. The protocol calls for preferential use of 3% hypertonic saline for treatment of elevated ICP. After protocol implementation, hypertonic saline was given to a greater percentage of patients (22% vs 41%, \( p = 0.04 \)) and mannitol was administered to a smaller percentage (48% vs 14%, \( p = 0.001 \)).

Short-Term Outcomes

Table 2 shows pre- and postprotocol outcomes. In unadjusted bivariate analysis, discharge disposition improved significantly after protocol implementation. Prior to protocol implementation, 63 patients (64%) had unfavorable discharge disposition (classified as death or inpatient facility placement) and 36 patients (36%) had favorable discharge disposition (classified as discharge home). After protocol implementation, 9 patients (31%) had unfavorable disposition while 20 patients (69%) had favorable disposition (\( p = 0.002 \)). The number of deaths was significantly decreased, as were overall unfavorable outcomes. In the preprotocol group, 31 patients (31%) died while 6 patients (21%) died after protocol implementation (\( p = 0.041 \)). GOS scores were generally improved after the protocol was initiated, but this difference was not statistically significant (\( p = 0.124 \)).

Regression Models

A proportional odds ordered logistic regression model of discharge disposition revealed that an improvement in outcomes was associated with being in the postprotocol implementation group and increasing GCS score (Table 3). Treatment in the postprotocol implementation group was associated with an OR of 4.046 (\( p = 0.007 \)) of increasingly favorable outcomes. GCS score was associated with an OR of 1.844 (\( p < 0.001 \)). ICP monitor placement itself was associated with worsening categorical outcome, with an OR of 0.206 (\( p < 0.001 \)). Increasing PICU length of stay was associated with increasingly favorable outcomes, but
the OR close to 1 reveals this association to be clinically immaterial. Age was not associated with outcome in the model. Given that GOS scores were not statistically significantly improved in the postprotocol group, an ordered logistic regression model did not reveal a significant positive relationship with postprotocol status.

Predicted outcomes improved across the range of GCS scores based on an ordered logistic regression model. Figure 2 demonstrates a dramatic shift in the probability of discharge home in the postprotocol group, as well as a marked decline in the probability of death postprotocol. This remained consistent across the spectrum of GCS scores studied.

Discussion

Treatment in the postprotocol implementation group was associated with favorable discharge disposition and decreased mortality. Our ordered logistic regression model demonstrated improved discharge disposition in the postprotocol group with increasing GCS score, as one would expect with decreasing injury severity. In the model, the OR for postprotocol status can be interpreted as follows: in the postprotocol group, patients are 4 times as likely to be discharged home versus the combined disposition of rehabilitation or death, and patients are 4 times as likely to be discharged home or to rehabilitation versus suffer death during hospitalization. Prior to protocol implementation, the mortality rate for severe TBI was 31%, and the rate of discharge home was 36%. This mortality rate is consistent with that in large cohorts in the pediatric trauma literature.

After protocol implementation, the mortality rate dropped to 21%, and the rate of discharge home increased dramatically to 69%. This is a significant improvement and demonstrates the possibility of improving short-term outcomes by standardizing PICU care for pediatric patients with severe TBI.

Our results corroborate the findings of Pineda et al. and other groups that instituted standardized ICU care based on guidelines. Cuschieri et al. showed in 2012 that disease-focused implementation of standard operating procedures improves outcomes. Additionally, a 2014 study by Vavilala et al. demonstrated improvement in mortality and discharge GOS score with increasing adherence to clinical indicators derived from the 2012 Brain Trauma Foundation guidelines, including maintenance of CPP greater than 40 mm Hg and early start of nutrition. Our results build upon these findings, further reinforcing the evidence that guideline-based care can improve outcomes in pediatric patients with severe TBI.

Our primary outcome of interest was discharge disposition, which was significantly improved in the postprotocol cohort. With regard to discharge status, the neurosurgery, critical care, and trauma surgery teams worked with the physical therapists and case management teams to determine the optimal environment for discharge. There was no intentional influence by providers to have patients discharged home versus to rehabilitation. In addition, because cohorts were roughly similar, we anticipate that unmeasured factors such as family preference and availability of outpatient therapy services would look similar between cohorts, as well. One major benefit of using a 5-year preprotocol for comparison was that there was no generalized trend toward discharge disposition status noted prior to protocol implementation. There was a trend toward improvement in the secondary outcome GOS scores, but with 5 distinct categories and low overall sample size, this improvement did not reach the level of statistical significance. Discharge disposition is a better measure of overall well-being at discharge compared with GOS, which more narrowly represents neurological recovery. However, we chose to additionally analyze the GOS score because of its widespread use and focus on neurological outcome. We were unable to use the extended scale due to the retrospective nature of the analysis, which could not capture the finer variation in disability required of this scale.

The pre- and postprotocol cohorts were similar except the postprotocol group had a higher rate of abusive head trauma as well as a higher rate of subdural hemorrhage as the predominant radiographic finding. Studies have shown that mortality and outcomes are worse in children exposed to abusive head trauma, which could potentially lead to an underestimation of the overall improvement in outcomes seen in our postprotocol cohort. The finding that the rate of subdural hemorrhage in the postprotocol cohort was increased is significant given the association between subdural hemorrhage and more severe underly-

<table>
<thead>
<tr>
<th>TABLE 2. Pre- and postprotocol outcomes*</th>
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<tbody>
<tr>
<td>Variable</td>
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<tr>
<td>Discharge Disposition</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
<td>Rehabilitation</td>
</tr>
<tr>
<td>Home</td>
</tr>
<tr>
<td>Unfavorable (death/rehab)</td>
</tr>
<tr>
<td>Favorable (home)</td>
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<tr>
<td>GOS (score)</td>
</tr>
<tr>
<td>1 (death)</td>
</tr>
<tr>
<td>2 (vegetative)</td>
</tr>
<tr>
<td>3 (severe disability)</td>
</tr>
<tr>
<td>4 (moderate disability)</td>
</tr>
<tr>
<td>5 (good recovery)</td>
</tr>
<tr>
<td>Unfavorable (1–3)</td>
</tr>
<tr>
<td>Favorable (4–5)</td>
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</tbody>
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*All data shown as number (%) unless otherwise indicated.
† Difference between death and home.
‡ Difference among home, rehab, and death.
§ Difference among all GOS scores.

<table>
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<th>TABLE 3. Ordered logistic regression</th>
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<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Group (pre- vs postprotocol)</td>
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<tr>
<td>GCS score</td>
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<tr>
<td>Age (yrs)</td>
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<tr>
<td>ICP monitor placement</td>
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<td>PICU length of stay (days)</td>
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Cl = confidence interval.
Interestingly, there was a trend toward fewer ICP guideline recommendations for the treatment of elevated hypertonic saline and decreased use of mannitol per protocol, although we noted significantly increased use of sedating medication for rapid neurological assessment and receive serial examinations over the earliest portions of their hospital course, which may show improvement beyond the need for ICP monitoring. It may be that the attention to a protocol (i.e., the Hawthorne effect) may be at play here, but the overall goal of improved care is achieved. Whether the effect is sustained in this cohort in follow-up assessments or in future patients is a source of ongoing study and remains to be seen. Our intent was to determine how a multidisciplinary approach with commitment from various groups to care for these challenging patients impacted care. As evidenced by our results, we believe this did improve outcomes. Those who did not require a monitor were still treated under the protocol with goals to maintain adequate mean arterial pressure, normonatremia, adequate hematocrit, sufficient sedation and analgesia, appropriate oxygenation, and glucose control. In addition, the initial neurosurgical examination was used to guide treatment of patients rather than presenting examinations in the emergency department, which can often be clouded by patient sedation.

Additionally, our study did not show significant differences in length of stay despite the improvement in outcomes. ICP monitoring–focused care may be associated with longer PICU stays and overall increased length of stay,6,13 but this did not hold true based on the results in this study. Although costs were not measured in this study, length of stay has been validated as a surrogate measure for cost.19 The results of this study could thus imply that outcomes were improved without increasing costs, a significant benefit in a cost-conscious environment.11,28 However, it is premature to draw conclusions in this regard, because complexity and intensity of therapy may be increased with protocol-based care, as demonstrated in a study by Palmer et al.20 This could ultimately increase overall costs despite similar lengths of stay. However, improving outcomes in pediatric patients would be justified even if costs were increased.

There were some limitations to the study, including the retrospective portion of the design, small sample size, and single-center involvement. However, our study attempted to account for these limitations by analyzing outcomes over several years to increase sample size and ensuring our ordered logistic regression model was not overfit with excessive parameters. Ultimately, we were able to demonstrate that short-term outcomes in pediatric patients with severe TBI were improved after a standardized protocol was implemented among caregivers. Further studies are needed that include multiple pediatric critical care centers and assess long-term outcomes.
Conclusions
Discharge disposition and mortality rates in pediatric patients with severe TBI improved after implementation among caregivers of a standardized protocol based on best-practice guidelines. This improvement occurred despite a higher rate of abusive head trauma in the postprotocol group. Those patients ultimately undergoing ICP monitor placement had worse outcomes as a subgroup. Length of stay was not increased in the postprotocol cohort.

Acknowledgments
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References

Disclosure
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: O’Lynnger, Shannon, Lamb, Wellons. Acquisition of data: O’Lynnger, Greeno. Analysis and interpretation of data: all authors. Drafting the article: O’Lynnger, Shannon, Le, Wellons. Critically revising the article: O’Lynnger, Shannon, Le, Wellons. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: O’Lynnger. Statistical analysis: O’Lynnger, Shannon. Administrative/technical/material support: Greeno. Study supervision: Chung, Lamb, Wellons.

Supplemental Information
Previous Presentation
Portions of this work were presented in poster form at the AANS/CNS Section on Pediatric Neurosurgery, Amelia Island, Florida, December 3, 2014.

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