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EEG Monitoring and Antiepileptic Drugs in Children with Severe TBI

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Abstract

Introduction—Traumatic brain injury (TBI) causes substantial morbidity and mortality in U.S. children. Post-traumatic seizures (PTS) occur in 11–42% of children with severe TBI and are associated with unfavorable outcome. Electroencephalographic (EEG) monitoring may be used to detect PTS and anti-epileptic drugs (AEDs) may be used to treat PTS, but national rates of EEG and AED use are not known. The purpose of this study was to describe the frequency and timing of EEG and AED use in children hospitalized after severe TBI.

Methods—Retrospective cohort study of 2,165 children at 30 hospitals in a probabilistically linked dataset from the National Trauma Data Bank (NTDB) and the Pediatric Health Information Systems (PHIS) database, 2007–2010. We included children (age < 18 years old at admission) with linked NTDB and PHIS records, severe (Emergency Department [ED] Glasgow Coma Scale [GCS] < 8) TBI, hospital length of stay > 24 hours, and non-missing disposition. The primary outcomes were EEG and AED use.

Results—Overall, 31.8% of the cohort had EEG monitoring. Of those, 21.8% were monitored on the first hospital day. The median duration of EEG monitoring was 2.0 (IQR: 1.0, 4.0) days. AEDs were prescribed to 52.0% of the cohort, of whom 61.8% received an AED on the first hospital day. The median duration of AED use was 8.0 (IQR: 4.0, 17.0) days. EEG monitoring and AED use were more frequent in children with known risk factors for PTS. EEG monitoring and AED use were not related to hospital TBI volume.

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Conclusion—EEG use is relatively uncommon in children with severe TBI, but AEDs are frequently prescribed. EEG monitoring and AED use are more common in children with known risk factors for PTS.

Keywords

seizures; traumatic brain injury; electroencephalography; anticonvulsant; pediatric

Introduction

Pediatric traumatic brain injury (TBI) is a common cause of morbidity and mortality in the United States. Annually, children require nearly 500,000 emergency department visits⁽¹⁾ and 35,000 hospitalizations for TBI.⁽²⁾ Severe TBI causes more than 2,000 deaths annually.⁽²⁾ In addition, many survivors have significant cognitive, physical, and behavioral morbidities.⁽³⁾

Post-traumatic seizures (PTS) have been associated with unfavorable outcome in pediatric TBI.^(4, 5) Combined rates of clinical and subclinical PTS in children with moderate to severe TBI are estimated at 11–42%.^(5–7) Accurate estimates for rates of PTS are difficult to obtain because of variation in clinical practice⁽⁸⁾ in the use of EEG and the lack of multi-institutional data.

Electroencephalographic (EEG) monitoring may be used to detect PTS and anti-epileptic drugs (AEDs) may be used to prevent or treat PTS. Data on the use of EEG monitoring and AEDs in severe pediatric TBI are limited. A recent retrospective analysis of children with severe TBI at five regional pediatric trauma centers concluded that 79% received seizure prophylaxis with AEDs, 63% of those within 24 hours of injury.⁽⁹⁾ In a survey of 43 sites participating in a large observational cohort study, 90% of sites reported seizure prophylaxis with AEDs in children with severe TBI.⁽¹⁰⁾ The same survey also reported wide center variation in approach to EEG monitoring. Other aspects of the care of children with severe TBI are known to vary widely.^(11–14) The purpose of this study was to determine the frequency and timing of actual EEG and AED use during the acute hospitalization of children with severe TBI. To do so, we conducted a retrospective cohort study using a large, linked dataset representing 30 U.S. children's hospitals.⁽¹⁵⁾

Methods

Data Sources and Cohort Design

Two data sources provided information for this study, the National Trauma Data Bank (NTDB) and the Pediatric Health Information Systems (PHIS) database.

NTDB—The NTDB contains standardized trauma registry data from more than 3 million admissions at 900 trauma centers in the United States.⁽¹⁶⁾ It contains injury and clinical variables necessary for studies of TBI, but does not contain detailed treatment information. The NTDB contains no protected health information (PHI). The NTDB has a continuous data quality improvement process.⁽¹⁶⁾

PHIS—PHIS is a benchmarking and quality improvement database containing inpatient data from 44 U.S. children's hospitals with more than 500,000 discharges per year.(17) PHIS contains administrative data, diagnoses, and procedures as well as detailed utilization information for pharmacy, imaging, laboratory, supply, nursing, and therapy services. These utilization data are coded using Clinical Transaction Classification (CTC) codes.(18) PHIS data are only available to approved researchers at member hospitals. PHIS data are subjected to 175 reliability and validity checks and are accepted into the database when classified errors occur in <2% of a hospital's quarterly data.(19) Systematic data quality monitoring includes bimonthly coding consensus meetings, coding consistency reviews, and quarterly data quality reports.(20)

Dataset Linkage—We used Markov chain Monte Carlo-augmented probabilistic linkage to link the records of injured children (< 18 years old at admission) in the NTDB and PHIS databases from 2007-2010. The linkage methodology has been reported in detail and is accurate for the study cohort: sensitivity 88%, positive predictive value 98%, and specificity 99.99%.(15)

From the linked dataset, we selected the patients with severe TBI (Emergency Department [ED] Glasgow Coma Scale [GCS] score = 8), hospital length of stay (LOS) ≥ 24 hours, and non-missing disposition.

Variable definitions

We coded the presence of PTS and other "medical" diagnoses (cardiac arrest, for example) using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes from the PHIS file. PTS was defined using a validated set of ICD-9-CM diagnosis codes: 345.x, 780.3, 780.33, or 780.39.(21) We have previously validated those codes for use in children with severe TBI.(22) In that validation study, they captured only new seizures and not children with pre-existing seizures or epilepsy. Importantly, those codes did not capture children who only had impact seizures.

For injury-related variables (injury mechanism, severity scores, and specific injury diagnoses including non-accidental trauma), we used ICD-9-CM diagnosis codes from the NTDB file. We calculated injury severity score (ISS) and maximum abbreviated injury scale (AIS) body region scores from ICD-9-CM diagnosis codes using ICDMAP-90 software.(23) We categorized injury mechanism using the external cause-of-injury matrix created by the CDC (with ICD-9-CM diagnosis code 995.5 added to the child abuse/assault category) and injury type using the Barell matrix.(24, 25)

The primary outcomes were EEG use and AED use. EEG was identified using any of ICD-9-CM procedure codes 89.14 or 89.19 or CTC code 515001. AEDs were identified using CTC codes 114016 (phenobarbital), 116001 (levetiracetam), 116015 (fosphenytoin), 116021 (phenytoin), and 116067 (valproic acid). We chose to evaluate these medications because in our clinical experience they are the most common AEDs given to children with TBI. Each ICD-9-CM and CTC code in PHIS has an accompanying day of service, where day 0 is the first day of the hospitalization. Day 0 ends at the first midnight of the hospital stay and may vary in length depending on the time of day when the patient is admitted to the

hospital. We assumed that EEG or AED use beginning on day 0 was more likely to be prophylactic than reactive to events. We tested that assumption by conducting a sensitivity analysis in which we expanded the definition of day 0 to encompass up to 28 hours for admissions occurring after 20:00.

We dichotomized age at 2 years based on several previous reports suggesting substantially higher seizure risk in children younger than 2 years of age.(6, 8, 26, 27)

Statistical Methods

In addition to standard summary statistics, we used four types of multivariable generalized estimating equations (GEE) models to determine the frequency and timing of EEG and AED use in children with severe TBI. These models were necessary to account for variation between hospitals in the use of EEG monitoring(8) and AEDs. In each case, the GEE models were clustered by hospital, assumed an exchangeable correlation structure, and produced robust standard errors. For binary outcomes (any EEG or AED use), the GEE models were logistic models. To test AED use over time, the GEE models assumed a log-linear relationship between AED use and time. For time to event outcomes (time to first EEG or AED use), the GEE models were multivariable Cox models. Model estimates will differ from the unadjusted results shown in Tables 1-2.

We tested for differences in medians between two groups by estimating a median value for the whole sample and estimating the odds of a subject's data being less than the whole-sample median as a function of the group classifier. Fitting GEEs for these tests could be considered a generalization of a chi-squared test. We tested the relationship between hospital AED and EEG use and hospital TBI volume using standard linear regression.

Data analysis was conducted in R version 3.3.1 (28) supplemented by the *geepack*(29) and *survival*(30) packages. Statistical significance was set at the 0.05 level.

Regulatory Approvals

This study was approved by the university institutional review board and written permission was obtained from both the Children's Hospital Association (PHIS owner) and the American College of Surgeons (NTDB owner).

Results

Study Cohort

The cohort consisted of 2,110 children who were treated for severe TBI during 2007 - 2010. The mean age was 7.5 ± 5.5 years. The median hospital length of stay (LOS) was 8 days (range 1 - 286 days). Seizures were diagnosed in 535 (25.4%) of the cohort, including 238/492 (48.4%) of children under 24 months old and only 297/1,618 (18.4%) of those at least 24 months old, $P < 0.001$. We dichotomized age at twenty-four months based on other published work.(6, 8, 26, 27) Demographic data by receipt of EEG are shown in Table 1 and by receipt of AEDs in Table 2.

Intracranial Hemorrhages

Of the 732 patients with at least one form of intracranial hemorrhage (ICH), 505 (69.0%) had a subdural hemorrhage (SDH), 328 (44.8%) had a subarachnoid hemorrhage (SAH), and 102 (13.9%) had an epidural hemorrhage (EDH). 539 (73.6%) of those with at least one ICH had only one, 183 (25.0%) had two hemorrhages, and 10 (1.4%) had all three.

EEG Monitoring

Overall, 670/2,110 (31.8%) of our cohort had EEG monitoring. Annual EEG rates varied and ranged from 26.7% - 33.8% during 2007 - 2010 without a significant directional trend, $P = 0.643$. Of the patients who received EEG monitoring, 146/670 (21.8%) received it beginning on day 0 (annual rates increasing from 15.3% - 26.2%; $P = 0.020$ for trend). Overall, the median duration of monitoring was 2 days (range: 1 - 82 days).

EEG monitoring beginning on Hospital day 0—In those patients with EEG monitoring on day 0, the median duration of monitoring was 3 days (range: 1 - 82 days) compared to 2 days (range: 1 - 43 days) in those patients whose EEG monitoring began after day 0, $P < 0.001$.

Patients receiving EEG monitoring on day 0 had a median hospital LOS of 14 days (range: 1 - 118 days) and patients receiving their first EEG after day 0 had a median hospital LOS of 19 days (range: 1 - 286 days). Patients not monitored with EEG had a median LOS of 5 days (range: 1 - 196 days), $P = 0.025$.

EEG monitoring by Hospital Severe TBI Volume—EEG monitoring was not related to hospital severe TBI volume. The proportion of patients receiving any EEG was nearly constant over the range of volume, trend $P = 0.885$.

EEG monitoring by Injury Severity, Injury Mechanism, and Hemorrhage Type—Among patients with an initial GCS score of 3-5, 507/1,518 (33.4%) had an EEG compared to 163/592 (27.5%) of patients with an initial GCS score of 6-8, $P = 0.041$. Patients who had TBI from a motor vehicle crash (MVC), 223/901 (24.8%), or a fall, 79/312 (25.3%), were least likely to have EEG monitoring. In contrast, 159/281 (56.6%) of patients who suffered severe TBI as a result of abuse received EEG monitoring. The difference in rates of EEG monitoring between patients with different injury mechanisms is statistically significant, $P < 0.001$. Interestingly, only 46/159 (28.9%) of the patients with an abusive mechanism who were monitored with EEG received EEG monitoring on day 0.

We used logistic GEE models to estimate rates of EEG monitoring for patients with and without ICH. These models account for clustering by hospital and the eight different combinations in which SDH, EDH, and SAH may coexist. The estimated rate of EEG monitoring for patients with no ICH was 27.5% (95% CI: 23.5, 31.9). Given only one ICH, we estimated that patients with SDH alone were more likely to receive EEG monitoring [66.8% (95% CI: 63.3, 70.1)] than patients with EDH alone [28.0% (95% CI: 19.2, 39.0)] or SAH alone [30.5% (95% CI: 6.4, 73.8)], $P < 0.001$. We estimated the following EEG monitoring rates in patients with SDH and a second type of ICH: for SDH and SAH: 74.2%

(95% CI: 70.2, 77.8), SDH and EDH: 63.7% (95% CI: 42.7, 80.5), and SAH and EDH: 30.5% (95% CI: 6.4, 73.8). The estimated rate of EEG monitoring for patients with all three types of ICH was 53.0% (95% CI: 22.8, 81.2).

Time to EEG monitoring, by Seizure Risk Factors

Young age, abusive mechanism, and SDH are known to be associated with post traumatic seizures.(6, 26, 31–33) Figure 1a shows the number of days until the first EEG for all patients, by age, by abusive mechanism, and by the presence of SDH. The median time to EEG was 1 day (range: 0 - 210 days).

Using Cox proportional hazards models, we estimated that children at least 24 months of age received their first EEG later than children under 24 months of age, HR for < 24 months vs 24 months = 2.14 (95% CI: 1.68, 2.74). Patients with abuse/assault or with SDH tended to receive their first EEG earlier than patients without abuse/assault or without SDH Table 3. Children with all three risk factors - young age, abusive mechanism, and SDH - were very likely to receive EEG monitoring, 85/141 (60.3%). Of those, 22/85 (25.9%) received EEG monitoring on day 0.

Neuromuscular blockade and EEG—Some hospitals may use EEG monitoring in patients whose clinical neurologic exam is obscured by neuromuscular blockade (NMB). (10) Overall, 16.5% of all patients received NMB after day 0 (NMB use on day 0 is more likely be procedure-related and temporary). Those patients received a median of 2.0 (1.0, 3.0) days of NMB beyond day 0. Of the 4015 patient-days with NMB beyond day 0, only 27.7% had concurrent EEG monitoring (Figure 2).

Antiepileptic Drugs

Overall, 1,098/2,110 (52.0%) of the study cohort received any fosphenytoin, levetiracetam, phenobarbital, phenytoin, or valproic acid during the hospital stay. The proportion of patients receiving any AED during their acute hospitalization did not change during the study: Figure 3, monthly odds ratio 1.00 (0.99, 1.02). Levetiracetam use increased, monthly odds ratio 1.04 (1.02, 1.05), but fosphenytoin/phenytoin and phenobarbital use did not change in a statistically significant manner during the study: (fos)phenytoin monthly odds ratio 0.99 (0.97, 1.00) and phenobarbital monthly odds ratio 0.99 (0.98, 1.01). Valproic acid was only administered to 12/2,110 (0.6%) patients.

The median duration of AED use was 8 days (range: 1 - 154 days). Patients without a PTS diagnosis had a median duration of AED use of 7 days (range: 1 - 121 days) versus 11 days (range: 1 - 154 days) in those with a PTS diagnosis, $P < 0.001$. Of the patients who received an AED, 553/1,098 (50.4%) received any EEG monitoring.

AED use by Hospital Severe TBI Volume—The proportion of patients receiving any AED was not related to hospital severe TBI volume, $P = 0.486$.

AED use beginning on Hospital day 0—Of the patients who received AEDs, 679/1,098 (61.8%) received their first dose on day 0 of the hospitalization. Over time between 2007 and 2010, patients tended to begin AEDs sooner: 52.9% of patients in 2007

received their first dose of AED on day 0, 59.6% in 2008, 70.5% in 2009, and 60.1% in 2010, $P=0.055$. In patients who received AEDs on day 0, the median duration of AED use was 8 days (range: 1 - 154 days). In comparison, the median duration of AED use was 8 days (range: 1 - 121 days) in patients receiving their first AED after day 0.

AED use by Injury Severity, Injury Mechanism, and Hemorrhage Type—Among patients with an initial GCS score of 3-5, 788/1,518 (51.9%) had an AED compared to 310/592 (52.4%) of patients with initial GCS score of 6-8, $P=0.690$. Cardiac arrest, which is often associated with severe injuries, occurred in 72/2,110 (3.4%) of the patients. 40/72 (55.6%) of those patients received AEDs, 19/40 (47.5%) of which were prescribed on day 0.

Children who suffered TBI as a result of abuse were more likely to receive AEDs, 199/281 (70.8%), than children with falls, 155/312 (49.7%), those injured in motor vehicle crashes, 406/901 (45.1%), or those with other causes of TBI, 338/616 (54.9%), ($P<0.001$ across groups).

Using logistic GEE models, we estimated that 45.2% (95% CI: 39.6, 50.8) of patients without an ICH received AEDs. Given only one ICH, we estimated that patients with SDH alone were more likely [69.3% (95% CI: 64.6, 73.6)] than those with SAH alone [57.2% (95% CI: 53.4, 61.0)] or EDH alone [50.9% (95% CI: 43.7, 58.2)] to receive AEDs, $P=0.002$. Given two ICHs, we estimated that AED use was common: for SDH and SAH, 71.3% (95% CI: 66.5, 75.6), SDH and EDH, 71.4% (95% CI: 58.4, 81.5), and SAH and EDH, 75.9% (95% CI: 48.8, 91.2). Of the patients with all three ICH types, we estimated that 47.7% (95% CI: 35.0, 60.7) received AEDs.

Time to AED use, by Seizure Risk Factors—Figure 1b show the number of days until the first AED for all patients, by age, by abusive injury mechanism, and by the presence of SDH. The median time to AED was 0 days (range: 0 - 58 days). Using a Cox model, age was not significantly associated with hazard of first AED use (Table 3). However, children with abuse/assault received AEDs sooner than those with other injury mechanisms, HR = 1.26 (95% CI: 1.08, 1.47). Similarly, those who had a SDH received their first AED earlier than patients without an SDH: HR = 1.37 (95% CI: 1.17, 1.61). Children with all three risk factors - young age, abusive mechanism, and SDH - were very likely to receive AEDs, 102/141 (72.3%). Of those, 54/102 (52.9%) received AEDs on day 0.

Sensitivity Analysis: Defining Day 0

As described in the Methods, PHIS defines day of service 0 as the day of admission from the time of admission until 23:59. Thus, a patient admitted at 23:45 has a day 0 only fifteen minutes long, whereas a patient admitted at 03:30 has a day 0 20.5 hours long. Therefore, the likelihood of receiving a treatment on day 0 versus day 1 depends on the admission time. Treatments are recorded by day of service and not by time. As a sensitivity analysis, we defined a modified day of service as follows: if the patient was admitted to the hospital before 20:00, then the reported days of service were unchanged. If the patient was admitted after 20:00, then we defined the modified day of service 0 to include the few hours in day 0 and all of the following day.

Using the standard day of service definition, 146/670 (21.8%) of patients who received an EEG did so on day 0. Based on our modified day of service, the percentage of EEGs on day 0 increased to 223/670 (33.3%). Using the standard day of service definition, 679/1,098 (61.8%) of patients who received an AED did so on day 0. Based on our modified day of service, the number of patients receiving AEDs on day 0 increased to 835/1,098 (76.0%).

Discussion

In a large cohort of children with severe TBI cared for at 30 U.S. children's hospitals, we found that fewer than one-third (31.8%), received EEG monitoring during their initial hospitalization. This finding was not related to hospital TBI volume, as some high-volume centers had low rates of EEG monitoring and some low-volume centers monitored frequently. This rate of monitoring is consistent with recently published results of a survey of site principal investigators from the Approaches and Decisions in Acute Pediatric TBI (ADAPT) study. That manuscript reported that 40% of North American and 42% of European centers state that they routinely provide EEG monitoring for children with severe TBI.(10) Children in our study with known risk factors for PTS(6, 26, 31–33) including young age, abusive injury mechanism, and SDH, were more likely to receive EEG monitoring. Young children and those who suffered child abuse tended to receive EEG monitoring earlier in the hospitalization. However, fewer than one-quarter (21.8%) of those who received EEG monitoring received it on the first day of the hospitalization, likely indicating that EEG use was predominantly reactive rather than prophylactic. EEG use that appears to be prophylactic (beginning on day 0) varied over the 4 years of our study between 15.3% - 26.2%.

AED use occurred more frequently than EEG monitoring: 52.0% of patients. This result is very similar to a recent study that reported AED use in half of children with moderate to severe TBI.(6) Another recently published retrospective study of data from five centers reported an even higher rate of seizure prophylaxis, 79%.(9) Many (61.8%) of the children who received AEDs in our study received them on day 0 of the hospitalization, likely indicating prophylactic use. Similar to EEG monitoring, children with known risk factors for PTS were particularly likely to receive AEDs, as both child abuse and SDH were associated with AED use earlier in the hospitalization.

Interestingly, the rate of observed AED use in our study (52.0%) was much lower than the rate of stated AED prophylaxis reported by site principal investigators in the ADAPT study (90%).(10) This lack of congruence between stated and actual clinical practice could be related to within-center variation, as a minority of ADAPT sites stated that they have standardized clinical pathways for the administration of AEDs in severe TBI.(10) Alternatively, the survey may not have captured the level of detail needed to explore this question. It will be important to compare the results of the ADAPT survey(10), this study, and the ADAPT observational data when they are available.

Two small retrospective studies evaluating seizure prevalence in pediatric patients with abusive head trauma described rates of EEG use between 50% and 64%(34, 35). We found less EEG use in our study, likely because those studies only included patients with abusive

mechanism, a known risk factor for PTS. Goldstein et al. also reported EEG monitoring being initiated a median of 2 days after admission, similar to our finding that EEG monitoring appears to be predominantly reactive rather than prophylactic in children with severe TBI.

More widespread use of EEG monitoring in children with severe TBI may result in increased detection of PTS. Two prospective studies evaluating the use of continuous EEG after TBI have supported this hypothesis. Those studies reported rates of PTS between 30 and 42% (5, 36), including a substantial proportion of patients with only subclinical seizures. In those two studies, PTS diagnosis rates increased by 1.5 to two-fold with the institution of routine continuous EEG monitoring in children with severe TBI. Recently published guidelines from the American Clinical Neurophysiology Society recommend routine EEG monitoring in children with severe TBI. (37)

The first edition of the severe TBI guidelines did not recommend prophylactic AED use. (38) The second edition, published in 2012, contains a level III recommendation for prophylactic AED use and does not comment on whether EEG is necessary. (39) Our data were collected in the time period between the two editions of the guidelines. Other recent work reports rates of prophylactic AED use in adults with severe TBI of 15% (40) and in children with severe TBI of 50%. (6) The rate of presumed prophylactic AED use in our cohort was similar to the latter study.

Only half of the children who received AEDs ever received EEG monitoring. This finding could warrant further investigation. There is emerging evidence that AEDs could be harmful to brain development. (41, 42) Routine EEG monitoring might detect the presence or absence of PTS earlier, enabling targeted treatment of PTS and reducing need for prophylactic AEDs. The potential benefit of this concept is yet to be determined. Future studies should test the effect of both seizures and AEDs on long-term patient outcomes.

Similar to adult studies (43), we found increasing levetiracetam use over the study period. Providers may be more likely to use levetiracetam because it has few drug-drug interactions, does not require frequent drug concentration monitoring, and has shown neuroprotective effects in a recent pre-clinical study. (44) A single-center randomized trial comparing PTS prophylaxis with levetiracetam versus phenytoin in adults with TBI found no difference in seizure incidence. (45)

Strengths of our study include generalizability, as this is the first pediatric investigation of EEG and AED use to include 30 centers and 4 years of data. Limitations to our study not mentioned previously include those inherent to the retrospective observational design. Diagnostic and therapeutic interventions were determined by procedure codes and billing data. Because the presence of procedure codes and billing data is a binary phenomenon, timing of seizure occurrence was not available, and we were unable to determine definitively if the decision to use EEG or AEDs was prophylactic or reactive. We made the assumption that EEG or AED use occurring on the first calendar day of service in the PHIS database was likely to be prophylactic. A sensitivity analysis suggested that that assumption was reasonable. Expanding the criteria for prophylactic use to include the second calendar of day

of service if admission occurred in the late evening increased our estimates, but did not change our overall conclusions about EEG and AED use. Overall, however, further prospective investigation is needed to determine how best to use AED's in children with severe TBI. Finally, information about the dose of AEDs, timing of seizure occurrence, and the exact duration (in hours) of EEG is not available in our dataset.

Conclusions

This analysis of a large, multi-institutional cohort demonstrates relatively lower EEG use compared to AED use in children with severe TBI. Use of EEG monitoring and AEDs is more common in children with known risk factors for PTS.

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Figure 1a. Time to first Electroencephalogram (EEG)

Number of days to first EEG overall, by age < 2 years, by abuse, and by subdural hemorrhage (SDH).

Figure 1b. Time to first Antiepileptic Drug (AED)

Number of days to first AED overall, by age < 2 years, by abuse, and by subdural hemorrhage (SDH).

Figure 2. Concurrent use of EEG monitoring and Neuromuscular Blockade
 EEG = Electroencephalographic; NMB = neuromuscular blockade

Figure 3. Antiepileptic Drug (AED) use over time

Proportion of patients who received any AED or a specific AED during their hospital stay. The shaded ribbon is a 95% confidence interval.

Table 1**Patient and Injury Characteristics by EEG Monitoring**

	All: n = 2,110	No EEG: 1,440 (68.2%)	EEG: 670 (31.8%)
Age, years			
mean $\pm$ sd	7.5 $\pm$ 5.5	8.1 $\pm$ 5.2	6.0 $\pm$ 5.8
Males			
n (%)	1,315 (63)	903 (63)	412 (62)
Admission Year			
2007: n (%)	318 (15)	233 (16)	85 (13)
2008: n (%)	665 (32)	455 (32)	210 (31)
2009: n (%)	568 (27)	376 (26)	192 (29)
2010: n (%)	559 (26)	376 (26)	183 (27)
Injury Mechanism			
Abuse/Assault: n (%)	281 (13)	122 (8)	159 (24)
Fall: n (%)	312 (15)	233 (16)	79 (12)
MV: n (%)	901 (43)	678 (47)	223 (33)
Other: n (%)	616 (29)	407 (28)	209 (31)
Hemorrhage Type (all without skull fracture)			
EDH: n (%)	102 (5)	83 (6)	19 (3)
SAH: n (%)	328 (16)	190 (13)	138 (21)
SDH: n (%)	505 (24)	274 (19)	231 (34)
Mechanism/Hemorrhage Combination			
No Abuse/Assault, No SDH: n (%)	1,503 (71)	1,120 (78)	383 (57)
Abuse/Assault, No SDH: n (%)	102 (5)	46 (3)	56 (8)
No Abuse/Assault, SDH: n (%)	326 (15)	198 (14)	128 (19)
Abuse/Assault and SDH: n (%)	179 (8)	76 (5)	103 (15)
Cardiac Arrest			
n (%)	72 (3)	36 (2)	36 (5)
ISS			
< 15: n (%)	362 (17)	279 (19)	83 (12)
15: n (%)	1,748 (83)	1,161 (81)	587 (88)
GCS			
3-5: n (%)	1,518 (72)	1,011 (70)	507 (76)
6-8: n (%)	592 (28)	429 (30)	163 (24)
Seizures			
n (%)	535 (25)	211 (15)	324 (48)
Hospital LOS (days)			
median (IQR)	8.0 (3.0, 20.0)	5.0 (3.0, 13.0)	18.0 (8.0, 32.0)

EEG = electroencephalographic. EDH = epidural hematoma. SAH = subarachnoid hemorrhage. SDH = subdural hemorrhage. ICD ISS = Injury Severity Score, derived using ICDMAP-90 software. ED GCS = Emergency Department Glasgow Coma Scale score. LOS = length of stay. IQR = interquartile range. n (%) unless noted.

Table 2**Patient and Injury Characteristics by Antiepileptic Drug Use**

	All: n = 2,110	No AED: 1,012 (48.0%)	AED: 1,098 (52.0%)
Age, years			
mean $\pm$ sd	7.5 $\pm$ 5.5	8.0 $\pm$ 5.2	7.0 $\pm$ 5.7
Males			
n (%)	1,315 (63)	626 (62)	689 (63)
Admission Year			
2007: n (%)	318 (15)	180 (18)	138 (13)
2008: n (%)	665 (32)	291 (29)	374 (34)
2009: n (%)	568 (27)	270 (27)	298 (27)
2010: n (%)	559 (26)	271 (27)	288 (26)
Injury Mechanism			
Abuse/Assault: n (%)	281 (13)	82 (8)	199 (18)
Fall: n (%)	312 (15)	157 (16)	155 (14)
MV: n (%)	901 (43)	495 (49)	406 (37)
Other: n (%)	616 (29)	278 (27)	338 (31)
Hemorrhage Type (all without skull fracture)			
EDH: n (%)	102 (5)	50 (5)	52 (5)
SAH: n (%)	328 (16)	128 (13)	200 (18)
SDH: n (%)	505 (24)	169 (17)	336 (31)
Mechanism/Hemorrhage Combination			
No Abuse/Assault, No SDH: n (%)	1,503 (71)	810 (80)	693 (63)
Abuse/Assault, No SDH: n (%)	102 (5)	33 (3)	69 (6)
No Abuse/Assault, SDH: n (%)	326 (15)	120 (12)	206 (19)
Abuse/Assault and SDH: n (%)	179 (8)	49 (5)	130 (12)
Cardiac Arrest			
n (%)	72 (3)	32 (3)	40 (4)
ISS			
< 15: n (%)	362 (17)	199 (20)	163 (15)
15: n (%)	1,748 (83)	813 (80)	935 (85)
GCS			
3-5: n (%)	1,518 (72)	730 (72)	788 (72)
6-8: n (%)	592 (28)	282 (28)	310 (28)
Seizures			
n (%)	535 (25)	71 (7)	464 (42)
Hospital LOS (days)			
median (IQR)	8.0 (3.0, 20.0)	5.0 (2.0, 12.0)	13.0 (5.0, 27.0)

AED = antiepileptic drug. EDH = epidural hematoma. SAH = subarachnoid hemorrhage. SDH = subdural hemorrhage. ICD ISS = Injury Severity Score, derived using ICDMAP-90 software. ED GCS = Emergency Department Glasgow Coma Scale score. LOS = length of stay. IQR = interquartile range. n (%) unless noted.

Table 3

Time to EEG or AED by PTS Risk Factors

	HR of EEG	HR of AED
Age		
Age ≥ 2	Reference	Reference
Age < 2 yr	2.14 (95% CI: 1.68, 2.74)	1.27 (95% CI: 1.03, 1.57)
Abuse/Assault		
No Abuse/Assault	Reference	Reference
Abuse/Assault	1.47 (95% CI: 1.18, 1.84)	1.26 (95% CI: 1.08, 1.47)
Subdural Hemorrhage		
No Subdural Hemorrhage	Reference	Reference
Subdural Hemorrhage	1.21 (95% CI: 0.99, 1.49)	1.37 (95% CI: 1.17, 1.61)

EEG = electroencephalographic. AED = antiepileptic drug. PTS = post-traumatic seizures. HR = hazard ratio. A hazard ratio greater than 1 indicates that the patients are expected to receive either the EEG or AED before the reference level. On average, patients who present with abuse/assault or with SDH will receive AEDs and EEGs before patients who present without abuse/assault or without SDH. Children under two years of age tend to receive EEGs before children over two years of age.