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Electrographic Status Epilepticus is Associated with Mortality and Worse Short-Term Outcome in Critically Ill Children

Alexis A. Topjian, MD, MSCE[1], **Ana M. Gutierrez-Colina, BA**[2], **Sarah M. Sanchez, BA**[2], **Robert A. Berg, MD**[1], **Stuart H. Friess, MD**[1], **Dennis J. Dlugos, MD, MSCE**[2,3], and **Nicholas S. Abend, MD**[2,3]

[1]Department of Anesthesia and Critical Care Medicine, Children's Hospital of Philadelphia and the University of Pennsylvania Perelman School of Medicine

[2]Division of Neurology, The Children's Hospital of Philadelphia

[3]Departments of Neurology and Pediatrics, The University of Pennsylvania Perelman School of Medicine

Abstract

Objectives—Electrographic seizures (ES) and electrographic status epilepticus (ESE) are common in critically ill children. We aimed to determine whether ES and ESE are associated with higher mortality or worse short-term neurologic outcome.

Design—Prospective observational study.

Setting—Pediatric intensive care unit of a tertiary children's hospital.

Patients—Non-neonatal children admitted to a pediatric intensive care unit (PICU) with acute encephalopathy underwent continuous electroencephalographic (cEEG) monitoring. EEGs were scored as (1) no seizures, (2) ES, or (3) ESE. Covariates included age, acute neurologic disorder category, prior neurodevelopmental status, sex, and EEG background category. Outcomes were mortality and worsening of Pediatric Cerebral Performance Category (PCPC) from pre-admission to PICU discharge. Chi-squared analysis, Fisher's exact test, and multivariable logistic regression were used to evaluate the associations between ES or ESE and mortality or short-term neurologic outcome, using odds ratios (OR) and 95% confidence intervals (95%CI).

Interventions—None

Main Results—Two hundred children underwent cEEG. Eighty-four (42%) had seizures which were categorized as ES in 41 (20.5%) and ESE in 43 (21.5%). Thirty-six subjects (18%) died and 88 subjects (44%) had PCPC worsening. In multivariable analysis ESE was associated with an increased risk of mortality (OR 5.1; 95%CI 1.4, 18, p=0.01) and PCPC worsening (OR 17.3; 95%CI 3.7, 80, p<0.001) while ES was not associated with an increased risk of mortality (OR 1.3; 95%CI 0.3, 5.1; p=0.74) or PCPC worsening (OR 1.2; 95%CI 0.4, 3.9; p=0.77).

Conclusions—ESE, but not ES, is associated with mortality and worse short-term neurologic outcome in critically ill children with acute encephalopathy.

Keywords

EEG Monitoring; Seizure; Status Epilepticus; Pediatric; Outcome; Non-Convulsive Seizure

Corresponding Author: Nicholas S Abend, MD, Division of Neurology, The Children's Hospital of Philadelphia, 3501 Civic Center Blvd, CTRC 10016, Philadelphia, PA 19104, abend@email.chop.edu, Phone: 215-590-1719, Fax: 215-590-1771.

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Introduction

Electrographic seizures (ES) and electrographic status epilepticus (ESE) denote electroencephalographic seizures with or without clinical signs of seizure activity. The majority of ES and ESE in critically ill children are not associated with any clinical signs of seizure activity (1) and are referred to as non-convulsive seizures (NCS) or non-convulsive status epilepticus (NCSE) in those able to exhibit motor features of seizures (ie. not receiving neuromuscular blockade). Studies of continuous EEG monitoring (cEEG) in pediatric intensive care units or emergency departments have reported ES and ESE in 7–47% of children with altered mental status or various types of acute structural or metabolic encephalopathy.(1–13)

In adults with traumatic brain injury, NCS are associated with detrimental changes in cerebral physiology and regional atrophy.(14, 15) Additionally, NCS and especially NCSE have been associated with worse outcome in critically ill adults and neonates.(16–20) Because the relationship between ES and outcome in critically ill non-neonatal children is unknown, we performed a prospective observational study of critically ill children with acute encephalopathy who underwent clinically indicated cEEG to determine whether ES or ESE were associated with higher mortality or worse short-term neurologic outcome.

Methods

This was a prospective observational study of infants and children treated in the Pediatric Intensive Care Unit (PICU) of a single tertiary care referral hospital between July 2008 and January 2011 who underwent clinically indicated cEEG. During this time frame 7040 patients were admitted to the PICU. Neonates (< 1 month) were excluded. Informed written consent was obtained from the guardians of patients undergoing clinically indicated cEEG. This study was approved by the Children's Hospital of Philadelphia Institutional Review Board.

Clinical practice at our institution is to perform cEEG in patients with acute encephalopathy (with or without prior convulsions) to identify NCS-NCSE and/or to determine whether abnormal movements or vital sign fluctuations of unknown etiology are seizures. When critical care or neurology physicians identified patients meeting these criteria, cEEG was initiated urgently. EEG interpretation was performed by the neurophysiology service and patients were managed by the PICU and Neurology Consult services. Per clinical protocol, patients underwent cEEG for at least 24 hours when screening for ES, unless they were undergoing therapeutic hypothermia after cardiac arrest in which case they were monitored for 72 hours. Patients with ES during cEEG were monitored for approximately 24 hours after their last ES. Prophylactic anticonvulsants are not routinely administered for any condition, although patients with epilepsy continued to receive their standard antiepileptic drugs (AEDs). The PICU is separate from the Cardiac ICU so patients with cardiac arrest in the cardiac ICU or undergoing cardiac surgery were not included.

Our critical care and neurology services aim to terminate ES and ESE when identified. However, there is no formal institutional clinical pathway for ES management, so individualized patient management decisions are made by on-service physicians. Most physicians in our PICU administer a loading dose of phenobarbital, phenytoin/fosphenytoin, levetiracetam. Valproate is less commonly administered. If seizures persist then a second loading dose is administered. If seizures still persist, then another anticonvulsant is generally added.

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Long-term monitoring was performed using a Grass-Telefactor (West Warwick, RI) video-EEG system. Twenty-one gold-over-silver scalp surface electrodes were positioned according to the international 10–20 system and affixed with collodion adhesive. EEG data were acquired on a portable bedside computer networked to the hospital's EEG server.

Clinical and cEEG data were prospectively collected. Clinical data consisted of: age, sex, acute neurologic disorder category, prior neurodevelopmental status, medications (including benzodiazepine and muscle relaxant use), AED administration, AED efficacy, intubation status, cEEG indication, cEEG findings including seizure occurrence and characteristics, hospital and PICU admission and discharge dates, pre-admission Pediatric Cerebral Performance Category (PCPC), and PICU discharge disposition (including mortality and PCPC). The Pediatric Risk of Mortality Score (PRISM III score), a predictor of mortality, (21) was obtained from a PICU database. Patients were assigned to only one of the following acute neurologic disorder categories: (1) epilepsy with altered mental status following a seizure, (2) hypoxic ischemic encephalopathy, (3) encephalitis, (4) traumatic brain injury, (5) stroke, (6) sepsis, (7) posterior reversible leukoencephalopathy syndrome, (8) neurosurgical procedure, (9) provoked seizures (such as febrile seizures), or (10) systemic/metabolic disorders (such as electrolyte abnormalities or hepatic encephalopathy). A subject was determined to have a prior abnormal neurodevelopmental status if they had a baseline PCPC ≥2.

To ensure consistency and complete data, the cEEG tracings (including time-locked video) were reviewed and interpreted by one pediatric neurophysiologist (N.A.) using standardized terminology to: (1) define seizures, (2) distinguish between ES and ESE, (3) determine whether ES and ESE had any clinical correlate and (4) categorize EEG background. EEGs were scored as (1) no seizures, (2) ES, or (3) ESE. An ES was defined as an abnormal paroxysmal event that was different from the background lasting longer than ten seconds (or shorter if associated with a clinical change) with a temporal-spatial evolution in morphology, frequency, and amplitude, and with a plausible electrographic field. ESE was defined as either a single thirty minute ES or a series of recurrent independent ES totaling more than thirty minutes in any one hour period (50% seizure burden). Patients were scored as ESE if it occurred at any point during the recording. Periodic epileptiform discharges, defined as repetitive sharp transients either occurring in isolation or in repetitive runs (but without evolution into discrete ES), were not scored as seizures and per institutional practice were not managed with anticonvulsants. EEG background categories included (1) normal or sedated sleep, (2) slow and disorganized, (3) discontinuous or burst-suppression, and (4) attenuated and featureless. The EEG background category was derived from the predominant cEEG pattern over the first 12 hours. EEG background category was utilized as an overall marker of encephalopathy as these categories have been reported to have prognostic significance in children with hypoxic-ischemic encephalopathy.(22, 23)

Outcomes were classified using dichotomous variables: (1) mortality and (2) a worsening PCPC score from pre-admission to PICU discharge. The PCPC is a validated six point scale categorizing degrees of functional impairment. PCPC categories are 1 = normal, 2 = mild disability, 3 = moderate disability, 4 = severe disability, 5 = coma and vegetative state, and 6 = death.(24) The pre-admission PCPC was estimated based on information in the medical record provided by parents/guardians. The PCPC at PICU discharge was determined by the investigators.

Summary statistics are reported as medians and interquartile ranges [IQR] for continuous data and counts and proportions for categorical data. The association of each variable with mortality or neurologic outcome was examined using chi-square or Fisher's exact tests for categorical variables and Wilcoxon's rank-sum or Kruskal Wallis tests for continuous

variables. Chi-squared analysis and multivariable logistic regression were used to test the association between seizure category and outcomes. *A priori* covariates included in the model were age, acute neurologic disorder category, and EEG background category. Variables with $p < 0.2$ in univariable analysis were eligible for inclusion in the logistic regression model. In addition, if a covariate did not impact the association between the exposure and the outcome, it was not considered a confounder and was not included in the model. All statistics were performed on Stata 10.0 (College Station, TX).

Results

Two hundred encephalopathic children were enrolled; 50% (99/200) with preceding convulsions and 50% (101/200) without preceding convulsions. EEG monitoring was performed to define the etiology of abnormal movements or vital sign fluctuations in 14% (28/200). The median age was 3.7 [0.8,10] years. One-hundred and twelve subjects were male. The median length of stay in the PICU was 7 [3, 18] days. The median length of stay in the hospital was 13.5 [5.5, 32] days. The median cEEG duration was 2 [1, 3] days. The most common acute neurologic disorders were epilepsy with acute seizures and hypoxic-ischemic encephalopathy related to cardiac arrest or drowning (Table 1). One-hundred and forty-five (73%) subjects were intubated, and there was no difference in intubation frequency between subjects without seizures, with ES, or with ESE (p=0.19). One-hundred and fourteen (57%) subjects received benzodiazepines, and there was no difference in benzodiazepine use between subjects without seizures, with ES or ESE (p=0.09). Baseline PCPC scores ranged from 1 thru 5. The preadmission PCPC for 62% (n=124) was normal, 5% (n=10) had mild disability, 12% (n=23) had moderate disability, 21% (n=42) had severe disability, and 0.5% (n-=1) was vegetative.

One hundred sixteen subjects (58%) did not have seizures. ES occurred in 41 (20.5%) and ESE occurred in 43 (21.5%). Of those with ES or ESE, 63% (53/84) had only NCS while 37% (31/84) had some clinically evident seizures. During the EEG monitored period, 15% (30/200) received muscle relaxants. Of those who received muscle relaxants, 21 had no seizures and 9 had ES or ESE. Thus, only 17% (9/53) with exclusively NCS were receiving muscle relaxants.

Covariate distribution by seizure classification is found in Table 1. Age and EEG background category were associated with the presence of seizures while sex, PRISM score, acute neurologic disorder category, and prior neurodevelopmental status were not associated with the presence or absence of seizures.

Eighteen percent (36/200) of subjects died, and mortality was attributable to progression to irreversible cessation of neurologic function (33%), withdrawal of technological support due to severe neurologic injury (47%), and withdrawal of technological support due to respiratory of cardiovascular disorders (20%). PCPC worsened in 44% (88/200) and did not improve in any subjects.

Univariable analyses of seizure category and outcomes are shown in Table 2. Seizure category was not associated with mortality on univariable analysis (p=0.064). There was no difference in mortality between subjects with only NCS and subjects who had some clinically evident seizures (23% versus 19%, p=0.7). Acute neurologic disorder category and EEG background category were associated with mortality. As expected, the PRISM score was associated with mortality. Seizure category, acute neurologic disorder category, and EEG background category were associated with PCPC worsening.

On multivariable analysis, ES were not associated with increased odds of mortality or worsened PCPC (Table 3). However, ESE was associated with an increased odds of

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mortality (OR 5.1; 95%CI 1.4, 18, p=0.01) and worsened PCPC (OR 17.3; 95%CI 3.7, 80, p<0.001). When excluding deceased subjects, ESE was still associated with an increased odds of worsened PCPC (OR 347; 95% CI, 11–10,694; p<0.001).

As noted in Table 3, several acute neurologic disorder categories were associated with mortality and worsened PCPC. More severely abnormal EEG backgrounds (discontinuous/burst-suppression or attenuated/featureless) were also associated with mortality and worsened PCPC. The more mild background abnormality (slow and disorganized) was not associated with mortality, but was associated with worsened PCPC (Table 3).

Of the 81 subjects who received anticonvulsants, the most commonly administered first anticonvulsants were levetiracetam in 38% (31/81), phenobarbital in 31% (25/81), and phenytoin-fosphenytoin in 27% (22/81), while only 4% (3/81) of subjects received valproate sodium. There was no difference in frequency of anticonvulsants administered based on seizure category (p=0.17). Standard clinical care involved aiming to terminate ES and ESE by sequentially administering anticonvulsants if seizures persisted. Forty seven percent (38/81) received one anticonvulsant, 23% (19/81) received two anticonvulsants, 9% (7/81) received three anticonvulsants, and 21% (17/81) received ≥4 anticonvulsants. Of those with ES 72% (28/39) had resolution of seizures after administration of one anticonvulsant. Of those with ESE 21% (9/42) had resolutions of seizures after administration of one anticonvulsant. One patient was treated with one anticonvulsant, continued to have seizures, but received no further medications.

Discussion

This prospective observational study of critically ill children who underwent cEEG showed that ESE was associated with increased mortality and a worsened PCPC at PICU discharge. ES were not associated with either increased mortality or worsened PCPC.

As cEEG has become more widely used in intensive care settings, it is clear that many critically ill patients experience ES and ESE, and that most ES have no discernible clinical correlate.(1, 12) NCS have been reported in critically ill adults, (15, 25, 26) children, (1–5, 7, 8, 10, 12, 13) and neonates.(27–29) A study of 570 critically ill patients identified seizures in 19% of the patients, of whom 92% had exclusively non-convulsive seizures. Age younger than 18 years was one of several risk factors for seizures.(25) ES are reported in 7–47% of critically ill children, with different yields partially dependent on cEEG indications. (1–5, 7, 8, 10–13) In a previous study addressing ES and ESE epidemiology that included the first 100 consecutive subjects described in this study, we reported that ES or ESE occurred in 46 subjects.(1) The cohort size has now doubled, and seizures are still common, occurring in 42% of 200 subjects. Despite the fact that ES are more common in critically ill children than adults, (1, 25) there has been little study of the neurodevelopmental impact of ES and ESE in non-neonatal children.

In the present study, a predominance of NCS persists, with 63% of subjects having no clinical seizures, and all subjects having at least some NCS. Only 17% with exclusively NCS were receiving muscle relaxants. These findings suggest that critically ill children may experience electromechanical uncoupling (electrical seizures without a clinical correlate) as described in critically ill neonates.(30)

Importantly, ESE was associated with increased mortality and worsened PCPC after controlling for age, acute neurologic disorder category, EEG background category, prior neurodevelopmental status and sex. The association between ESE and worse outcome in critically ill children is consistent with a study in critically ill adults indicating that the presence of NCSE, longer seizure durations, and delay to diagnosis were associated with

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increased mortality(16) and a neonatal study showing status epilepticus was associated with increased morbidity.(20)

ES were not associated with increased mortality or worse short-term outcome. These data suggest that a longer exposure to ES may be necessary before seizures independently impact outcome. Two studies in critically ill adults reported that ES are associated with worse outcome. However, seizures of varying durations were grouped together. One of these adult studies did not report the proportion of subjects with ES and ESE(17) while the other reported that 8 of the 14 critically ill adults with central nervous system infections and ES had ESE.(18) Similarly, in a study of neonates that showed an association between ES and morbidity and mortality, 43% of neonates with ES had ESE.(19) Had these studies separated subjects with ES and ESE, ES alone may not have been associated with worse outcome.

The association between ESE and worse outcome does not necessarily imply a causal relationship. Severe brain injury could result in ESE and worse outcome, without ESE causing worse outcome. However, even after controlling for the type of acute neurologic disorder and EEG background category, ESE was associated with worse outcome. In future studies, other measures might be considered, such as the degree and extent of abnormality on neuroimaging. Small studies in adults with traumatic brain injury have associated NCS with episodic increases in intracranial pressure and lactate/pyruvate ratios(14) and with later hippocampal atrophy ipsilateral to an acute NCS focus.(15) Additionally, adults with epilepsy experiencing NCSE have regional hyperperfusion concordant with the ES focus.(31) These changes could worsen brain injury and might explain the reported associations between acute seizures and worse outcome seen in our data and also in critically ill adults (16–18) and neonates.(19, 20)

As expected, certain acute neurologic disorder etiologies were also associated with mortality and worsened PCPC. Only sepsis was associated with mortality. The acute neurologic disorder categories hypoxic-ischemic encephalopathy, encephalitis, traumatic brain injury and systemic/metabolic were associated with worsened PCPC. Similarly, severely abnormal EEG background categories were associated with mortality and worsened PCPC. Severely abnormal EEG features have previously been associated with unfavorable outcome in critically ill children.(22, 23, 32–38)

A prior survey of adult and pediatric neurologists found that most respondents aim to terminate all ES and ESE but that there was substantial variability in specific anticonvulsant choices.(39) Survey responses may not reflect true clinical practice, and this observational study of clinical practice demonstrated that levetiracetam, phenobarbital and phenytoin are used with similar frequencies in critically ill children. Only one anticonvulsant had been administered when seizures terminated in 72% of children with ES and 21% of children with ESE. While this is only an observational study, since clinical practice was to administer sequential anticonvulsants if seizures persisted, this data at least hints that even a standard anticonvulsant may be effective in many children with ES and some children with ESE.

This study has several limitations. First, we measured only short-term outcome using a simple outcome assessment tool (PCPC), and this may not reflect long-term neurodevelopmental status. For example, patients with ES or ESE may have received anticonvulsant loads, and the relatively short-term residual sedating effects may have contributed to a worse PCPC at PICU discharge. Studies utilizing longer-term and more detailed neurodevelopmental outcome assessments are needed. Furthermore, the initial PCPCs were assessed retrospectively using data from medical records provided by the children’s parents/guardians while the final PCPCs were evaluated by the investigators. Second, cEEG was initiated when considered clinically indicated. Although physicians

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received extensive education regarding indications for cEEG, it is possible that not every patient who met cEEG criteria was monitored. It is likely that the more severely neurologically ill patients underwent cEEG while the less ill patients were missed. Studies with broader cEEG indications (10) have demonstrated a much lower incidence of NCS than studies focused on monitoring patients with neurologic illness, (1) indicating that less severely neurologically ill patients may have a lower NCS occurrence. If true, this would bias our results toward the null hypothesis, yet a difference in outcome was still demonstrated. Furthermore, variable durations of cEEG may impact whether seizures are identified. While cEEG for 24–48 hours identifies the majority of patients with ES, (1, 4, 10, 12, 13) it is possible that some patients scored as no-seizures actually did experience ES after cEEG was discontinued. This would bias our results toward the null hypothesis, yet a difference in outcome was still demonstrated. Third, we defined ES as lasting longer than ten seconds, unless there was a clinical correlate associated with briefer electrographic events. While this is consistent with prior studies,(1, 4, 5, 7, 11–13) it is not known whether brief evolving discharges impact outcome and warrant treatment.(40) Similarly, we defined ESE as a single seizure lasting longer than thirty minutes or recurrent seizures totaling more than thirty minutes in any one hour period (50% seizure burden). However, the optimal method for describing recurrent seizures has not been established and it remains unclear whether recurrent seizures have the same impact as a single prolonged seizure. Development of terminology to better define ES(41) and improved seizure burden quantification using continuous rather than categorical (ES or ESE) scoring would allow better assessment of seizure exposure. Fourth, patients with ES or ESE received benzodiazepines and anticonvulsants as determined by the consulting neurology service, with variability in peak AED dose administration, AED escalation, and time intervals for progression to a subsequent AED. The timing of seizure identification, management decisions and anticonvulsant efficacy may have impacted whether seizures remained as ES or developed into ESE. Future efficacy trials are needed to determine which AEDs and management approaches are optimal for ES and ESE management. Finally, our subject numbers were small and confidence intervals very large for some categories. Future studies with larger cohorts are needed.

Conclusions

ESE is associated with higher mortality and a worsened PCPC in critically ill children with acute encephalopathy. In contrast, ES are not associated with mortality or worsened PCPC. Further study is needed to determine whether earlier identification and termination of ESE is associated with improved neurodevelopmental outcome.

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Table 1

Patient characteristics by seizure category.

Variable	Total N	No Seizures N (%)	Electrographic Seizures N (%)	Electrographic Status Epilepticus N (%)	p-value
Total N=200	200	116 (58%)	41 (20.5%)	43 (21.5%)	
Age in Years Median [Interquartile Range]		4.3 [1, 11.7]	1.3 [0.4, 3.9]	5.4 [0.6, 10]	0.005
Sex	200				
Male	112	64 (57%)	21 (19%)	27 (24%)	0.54
Female	88	52 (59%)	20 (21%)	16 (18%)	
Pediatric Risk of Mortality (PRISM) III Score at 24 hours	154	12 [5,22]	8 [2,15]	8 [5,16]	0.16
Acute Neurologic Disorder Category					0.12
Epilepsy with altered mental status following a seizure	41	18 (44%)	13 (32%)	10 (24%)	
Hypoxic Ischemic Encephalopathy	50	32 (64%)	10 (20%)	8 (16%)	
Encephalitis	22	12 (55%)	2 (9%)	8 (36%)	
Traumatic Brain Injury	19	13 (68%)	1 (5%)	5 (26%)	
Stroke	13	5 (38%)	4 (31%)	4 (31%)	
Sepsis	8	6 (75%)	0 (0%)	2 (25%)	
Posterior Reversible Leukoencephalopathy Syndrome	4	1 (25%)	1 (25%)	2 (50%)	
Neurosurgical Procedure	12	7 (58%)	3 (25%)	2 (17%)	
Provoked Seizure	14	11 (79%)	1 (7%)	2 (14%)	
Systemic/Metabolic	17	11 (65%)	6 (35%)	0 (0%)	
Prior Normal Neurodevelopment	124	70 (57%)	25 (20%)	29 (23%)	0.7
EEG Background Category					<0.001
Normal or Sedated-Sleep	30	29 (97%)	1 (3%)	0 (0%)	
Slow and Disorganized	136	68 (50%)	35(26%)	33 (24%)	
Discontinuous or Burst-Suppression	23	9 (39%)	4 (17%)	10 (44%)	
Attenuated and Featureless	11	10 (91%)	1 (9%)	0 (0%)	
PICU Length of Stay (days)	200	6.5 [3,18]	9 [3,22]	7 [3,16]	0.54
Hospital Length of Stay (days)	200	12.5 [4.5, 33]	17 [7, 35]	16 [7,28]	0.28
Indication for EEG Monitoring	200				<0.001

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Variable	Total N	No Seizures N (%)	Electrographic Seizures N (%)	Electrographic Status Epilepticus N (%)	p-value
Acute encephalopathy with prior convulsion	99	43 (43%)	27 (27%)	31 (31%)	
Acute encephalopathy without prior convulsion	100	73 (73%)	14 (14%)	12 (12%)	
Abnormal movements or vital sign fluctuations	200				0.313
Yes	172	97 (57%)	35 (20%)	40 (23%)	
No	28	19 (68%)	6 (21%)	3 (11%)	

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Table 2

Patient characteristics by mortality outcome and Pediatric Cerebral Performance Category (PCPC) outcome.

Outcome Measure	Total N	Died N (%) N=36	Survived N (%) N=164	p-value	Worsened PCPC N (%) N=88	Unchanged PCPC N (%) N=112	p-value
Age (years) Median [Interquartile Range]	200	5.8 [1, 11.5]	3.4 [0.7, 9.7]	0.28	4.7 [0.6, 10]	3.7 [1, 9.9]	0.77
Sex	200						
Male	112	15 (13%)	97 (87%)	0.06	49 (44%)	63 (56%)	0.9
Female	88	21 (24%)	67 (76%)		39 (44%)	49 (56%)	
Pediatric Risk of Mortality (PRISM) III Score at 24 hours	154	23[12,29]	8 [3,16]	<.001	10 [5,21]	8 [3,18]	0.16
Seizure Category				0.064			<.001
No Seizures	116	18 (16%)	98 (84%)		42 (36%)	74 (64%)	
ElectrographicSeizures	41	5 (12%)	36 (88%)		14 (44%)	27 (66%)	
ElectrographicStatus Epilepticus	43	13 (30)	30 (70%)		32 (74%)	11 (26%)	
Acute Neurologic Disorder Category				0.004			<.001
Epilepsy with altered mental status following a seizure	41	2 (5%)	39 (9%)		4 (10%)	37 (90%)	
Hypoxic Ischemic Encephalopathy	50	18 (36%)	32(64%)		31 (62%)	19 (38%)	
Encephalitis	22	6 (27%)	16 (73%)		18 (82%)	4 (18%)	
Traumatic Brain Injury	19	2 (11%)	17 (89%)		15 (79%)	4 (21%)	
Stroke	13	1 (8%)	12 (92%)		6 (46%)	7 (54%)	
Sepsis	8	3 (37.5%)	5 (62.5%)		3 (37.5%)	5 (62.5%)	
Posterior Reversible Leukoencephalopathy Syndrome	4	0 (0%)	4 (100%)		2 (50%)	2 (50%)	
Neurosurgical Procedure	12	2 (17%)	10 (83%)		4 (33%)	8 (67%)	
Provoked Seizure	14	1 (7%)	13 (93%)		1 (7%)	13 (93%)	
Systemic/Metabolic	17	1 (6%)	16 (94%)		4 (24%)	13 (76%)	
Prior Neurodevelopment				0.16			<.001
Abnormal	76	10 (13%)	66 (87%)		13 (17%)	63 (83%)	
Normal	124	26 (21%)	98 (79%)		75 (60%)	45 (40%)	
EEG Background Category				<.001			<.001
Normal or Sedated-Sleep	30	1 (3%)	29 (97%)		5 (17%)	25 (83%)	
Slow and Disorganized	136	16 (12%)	120 (88%)		56 (41%)	80 (59%)	

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Outcome Measure	Total N	Died N (%) N=36	Survived N (%) N=164	p-value	Worsened PCPC N (%) N=88	Unchanged PCPC N (%) N=112	p-value
Discontinuous or Burst Suppression	23	12 (52%)	11 (48%)		19 (83%)	4 (17%)	
Attenuated and Featureless	11	7 (64%)	4 (36%)		8 (73%)	3 (27%)	
PICU Length of Stay (days)	200	7 [4,21.5]	7 [3,15.5]	0.2	9.5 [5,22.5]	4 [2,13]	<0.001
Hospital Length of Stay (days)	200	8 [4, 31.5]	14.5 [7, 33]	0.029	18.5 [9.5, 44.5]	10 [4,27.5]	0.0015
Indication for EEG Monitoring	200			0.003			0.2
Acute encephalopathy with prior convulsion	99	10 (10%)	91 (90%)		40 (40%)	61 (60%)	
Acute encephalopathy without prior convulsion	101	26 (26%)	73 (74%)		48 (48%)	51 (52%)	
Abnormal movements or vital sign fluctuations	200			0.03			.08
Yes	**28**	1 (4%)	27 (96%)		8 (29%)	20 (71%)	
No	172	35 (20%)	137 (80%)		80 (47%)	92 (53%)	

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Table 3

Adjusted outcomes for seizures categories.

Variable	Mortality OR (95% CI)	p-value	Worsened PCPC OR (95% CI)	p-value
Seizure Category				
No Seizures	Ref	Ref	Ref	Ref
Electrographic Seizures	1.3 (0.3, 5.1)	0.74	1.2 (0.4, 3.9)	0.77
Electrographic Status Epilepticus	5.1 (1.4, 18)	0.01	17.3 (3.7, 80)	<0.001
Age	1 (0.9, 1)	0.8	1 (0.99, 1.01)	0.61
Sex				
Male	ref	ref	Ref	Ref
Female	2.5 (0.9, 6.6)	.06	1.7 (0.7, 4)	0.24
Acute Neurologic Disorder Category				
Epilepsy with altered mental status following a seizure	Ref	Ref	Ref	Ref
Hypoxic Ischemic Encephalopathy	3.6 (0.5,26)	0.2	12 (2, 72)	0.006
Encephalitis	3.3 (0.43, 25)	0.3	40 (5.2, 304)	<0.001
Traumatic Brain Injury	0.9 (0.08, 11)	0.9	25 (3.1,197)	0.002
Stroke	0.8 (0.05, 12)	0.85	4.7 (0.5, 430)	0.16
Sepsis	10.6 (0.8, 137)	0.07	6.6 (0.5, 88)	0.15
Posterior Reversible Leukoencephalopathy Syndrome	-	-	2.5 (0.14, 43)	0.5
Neurosurgical Procedure	2 (0.2, 22)	0.56	4.6 (0.6, 33)	0.13
Provoked Seizure	2.2 (0.12, 38)	0.6	0.4 (0.03, 6)	0.5
Systemic/Metabolic	1.5 (0.1, 21)	0.77	7.4 (0.95, 52)	0.06
Prior Neurodevelopment				
Abnormal	Ref	Ref	Ref	Ref
Normal	2.2 (0.74, 6.6)	0.16	10.5 (3.6, 31)	<0.001
EEG Background Category				
Normal or Sedated-Sleep	Ref	Ref	Ref	ref
Slow and Disorganized	4.2 (0.4, 40)	0.2	4.3 (1.08, 17)	0.04
Discontinuous or Burst-Suppression	18 (1.5, 207)	0.02	15.8 (2.3, 107)	0.005

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Variable	Mortality OR (95% CI)	p-value	Worsened PCPC OR (95% CI)	p-value
Attenuated and Featureless	41 (2.7, 617)	0.007	28 (3, 244)	0.003
Indication for EEG Monitoring				
Acute encephalopathy without prior convulsion	Ref	Ref	Ref	Ref
Acute encephalopathy with prior convulsion	0.3 (0.1, 1)	0.05	0.8 (0.27, 2.2)	0.63

CI: Confidence Interval; OR: Odds ratio; Pediatric Cerebral Performance Category: PCPC; Ref: reference group

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