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Characteristics and acute outcomes of ICU patients with initial presentation of seizure

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ABSTRACT

Purpose: Seizures are a common cause of presentation to the emergency department (ED) but vary widely in severity and prognostic significance, with some cases requiring ICU management. Most evidence regarding seizure outcomes in the ICU comes from patients exclusively with status epilepticus (SE) or with new seizures detected after ICU admission. To aid in determining early prognosis of ICU patients with and without SE, we performed an analysis of patients initially presenting with any type of seizure and requiring ICU management.

Method: Analysis of hospital records of 247 consecutive patients presenting to the ED initially with seizure and directly admitted to the ICU between January 2010 and June 2013. The primary outcome was composite in-hospital death or discharge to hospice, and the secondary outcome was recurrent ICU seizures.

Results: The primary outcome occurred in 7.7% of patients. Both early mechanical ventilation and an acute intracranial process on neuroimaging were associated with a poor outcome. About half of this cohort presented with SE. Although SE was associated with recurrent seizures in the ICU, the primary outcome was similar between patients presenting with and without SE. Patients with SE had greater rates of early intubation in the ED and were treated more aggressively with medication, whereas patients without SE had greater rates of first ever seizure, acute intracranial disease including intracranial hemorrhage, and neurosurgical intervention.

Conclusion: Patients presenting to the ED with and without SE requiring ICU admission may have similar acute outcomes, yet differ in risk factors and seizure etiologies.

1. Introduction

Seizures exist along a spectrum of severity, from benign febrile seizures to refractory status epilepticus (SE). ICU level of care is recommended for management of SE but may also be necessary after any seizure for hemodynamic monitoring and ventilatory support [1]. This commonly occurs in the context of airway protection or treatment using sedating medications with hypotensive side effects to terminate seizures. In these cases, intensive monitoring is necessary regardless of the underlying cause of seizures. When seizures are provoked by an acute intracranial process or a systemic condition such as sepsis, ICU management may be further indicated for treatment of the underlying condition [2].

Seizures represent 1% of visits to emergency departments (ED) in the United States and a small proportion of these cases will need immediate ICU management [3]. To date, most studies reporting ICU prognosis and outcomes after seizures have been limited to cohorts exclusively with SE or with seizures detected after ICU admission [4–8]. Risk factors to predict prognosis in patients that present to the ED with a single seizure of any cause and are admitted to the ICU have not been analyzed or stratified in detail; a descriptive analysis of this cohort of patients should provide valuable information to enlighten clinicians on this issue.

Here we report characteristics and acute outcomes for 247 consecutive patients presenting to a high-volume tertiary care center ED with witnessed seizure that either died in the ED or were directly admitted to the ICU. This represents a diverse group of the most high-risk patients with various seizure etiologies; about half of who present with SE.

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2. Methods

2.1. Patient selection

We queried the electronic ED database at Temple University Hospital for all records containing "seizure" in the differential diagnosis from January 2010 to June 2013. Hospital records for the given admission were then reviewed for inclusion and exclusion criteria. Inclusion criteria were age of 18 years or greater, witnessed seizure, direct transfer from the ED to the ICU or death in the ED, and a complete medical record. Exclusion criteria were seizures determined to be non-epileptic or uncertain seizure-like activity that was better explained by other conditions such as syncope, myoclonus, tremor, or altered mental status. Patients admitted to the neurological, medical, or cardiac ICU were included. Admission to the ICU was determined by the attending admitting physician.

2.2. Data collection

Hospital records were comprehensively reviewed, and all patients with the given inclusion and exclusion criteria were included in the analysis, although radiology and EEG studies were not performed on all patients. The primary outcome used for analysis was a composite outcome of in-hospital death or discharge to hospice, and the secondary outcome was ICU seizure recurrence. SE was defined as greater than five minutes of ictal activity or multiple seizures with incomplete recovery of consciousness, and included both convulsive and nonconvulsive subtypes. Patients presenting with multiple seizures by history or in the ED with return to baseline between episodes were grouped together with patients presenting with a single seizure. This study was carried out in accordance with policies approved for Human Subjects Research by the Temple University Institutional Review Board.

2.3. Statistical analysis

Univariate and multivariate logistic regression analysis were used to determine association of risk factors with the primary outcome. Welch's *t*-test was used for testing of continuous variables and Fisher's exact test for categorical variables in univariate analysis. Chi-squared goodness of fit test was used to compare seizure etiology frequencies between groups. A statistical threshold of 0.05 was used for all tests. All analyses were performed using the R statistical analysis package.

3. Results

Query of the ED database returned 8174 records from January 2010 through June 2013 containing the search term "seizure," of which 344 were directly admitted to the ICU. After exclusion of records with seizure-like activity that was unwitnessed or better explained by other conditions, 247 records were included for analysis. Patient demographics and admission characteristics are shown in Table 1.

The primary outcome of in-hospital death ($n = 10$) or discharge to hospice ($n = 9$) occurred in 7.7% of this cohort. Causes of death included septic shock ($n = 3$), cocaine-associated intracranial hemorrhage ($n = 2$), cardiac death ($n = 2$), ruptured cerebral aneurysm ($n = 1$), acute ischemic stroke ($n = 1$), and ethylene glycol ingestion ($n = 1$). Both the presence of an acute intracranial process on head CT or brain MRI (OR 4.89, 95%CI 1.58–16.8, $p = 0.002$) and intubation in the ED (OR 3.38, 95%CI 1.10–12.4, $p = 0.029$) were significantly associated with the primary outcome in univariate analysis (Table 1). Multivariate analysis to assess association of status epilepticus, third-line antiepileptic medication (midazolam, phenobarbital, and propofol), early intubation, and acute neuroimaging with the primary outcome was also performed. Early intubation (OR 6.44, 95%CI 1.88–26.6, $p = 0.005$) and acute intracranial disease (OR 5.78, 95%CI 1.97–18.6, $p = 0.002$) were again associated with poor outcome, and no significant effect was observed for SE (OR 0.64, 95%CI 0.20–2.08, $p = 0.458$) or third-line medication in the ED (OR 0.67, 95%CI 0.16–2.35, $p = 0.545$) or ICU (OR 2.47, 95%CI 0.47–10.5, $p = 0.238$). Two patients died in the ED before transfer to the ICU, and exclusion of these cases produced no significant change in the results of primary outcome analysis (data not shown).

SE occurred in 51.8% of this cohort, nearly always at presentation to the ED, yet interestingly was not associated with the primary outcome in univariate or multivariate analysis (Table 1). Comparison between patients with and without SE revealed different baseline and admission characteristics (Table 2). Patients with SE presented with lower Glasgow Coma Scale (GCS) scores in the ED (median 6 vs. 13, $p < 0.0001$) and had higher rates of intubation in the ED (60.2 vs. 33.6%, $p < 0.0001$) than patients

Table 1
Patient demographics and admission characteristics.

	Total ($n = 247$)	Discharge to home or rehab ($n = 228$)	Death or discharge to hospice ($n = 19$)	*p*
Age (years)	52.1 (18–91)	51.9 (18–91)	54.9 (38–88)	0.3800
Female (%)	36.4	36.4	36.8	1.0000
History of epilepsy (%)	47.8	47.8	47.4	1.0000
History of stroke (%)	31.2	30.3	42.1	0.3076
Active alcohol abuse (%)	26.3	27.6	10.5	0.1719
Presenting GCS (median)	9 (3–15)	9 (3–15)	10 (3–15)	1.0000
Status epilepticus (%)	51.8	52.2	47.4	0.8122
Intubated in ED (%)	47.4	45.2	73.7	0.0290
Duration of mechanical ventilation (days)	1.8 (0–23)	1.6 (0–23)	3.8 (0–22)	0.0964
ICU length of stay (days)	4.6 (0–47)	4.6 (1–47)	5.3 (0–26)	0.6117
Total AEDs (mean)	2.7	2.7	2.6	0.7918
Third-line AED in ED (%)	26.3	26.8	21.1	0.7876
Third-line AED in ICU (%)	15.4	15.4	15.8	1.0000
Recurring ICU seizures (%)	13.0	13.2	10.5	1.0000
Neurosurgical intervention (%)	4.5	4.4	5.3	0.5948
Acute intracranial process on CT/MRI (%)[a]	29.8	27.1	64.7	0.0021
Intracranial hemorrhage (%)[a]	14.5	13.3	29.4	0.0796
Epileptiform EEG (%)[b]	43.0	42.3	55.6	0.5008

[a] Reported as percent of patients with imaging study during admission: $n = 242$, $n = 225$, $n = 17$ respectively.
[b] Reported as percent of patients with EEG during admission: $n = 165$, $n = 156$, $n = 9$ respectively.