

Comparison of pediatric patients with status epilepticus lasting 5–29 min versus ≥ 30 min



Iván Sánchez Fernández^{a,b,*}, Martina Vendrame^{a,c,d,1}, Kush Kapur^a, Jacqueline Klehm^a, Serife Uysal^{a,e}, Mustafa Gedik^{a,f}, Sookee An^a, Dinesh Jillella^a, Jacqueline Zelener^a, Sana Syed^c, Vasu Gooty^a, Alexander Rotenberg^a, Tobias Loddenkemper^a

^a Division of Epilepsy and Clinical Neurophysiology, Department of Neurology, Boston Children's Hospital, Boston, MA, USA

^b Department of Child Neurology, Hospital Sant Joan de Déu, Universidad de Barcelona, Barcelona, Spain

^c Department of Neurology, Boston University School of Medicine, Boston, MA, USA

^d Department of Sleep Medicine, CGH Medical Center, Sterling, IL, USA

^e Department of Pediatrics, SUNY Downstate Medical Center, Brooklyn, NY, USA

^f Department of Internal Medicine, Carney Hospital, Dorchester, MA, USA

ARTICLE INFO

Article history:

Received 21 February 2014

Revised 12 May 2014

Accepted 23 May 2014

Available online 18 June 2014

Keywords:

EEG

Epidemiology

MRI

Pediatric

Status epilepticus

ABSTRACT

The most common thresholds for considering prolonged seizures as status epilepticus (SE) are 5 and 30 min. It is unknown whether these different thresholds (5 or 30 min) identify patient populations with different electroclinical characteristics. We compared the characteristics of patients with SE lasting 5–29 min (SE_{5-29}) with those with SE lasting ≥ 30 min ($SE_{\geq 30}$). Inclusion criteria were the following: 1) 1 month to 21 years of age at the time of SE, 2) convulsive seizures, and 3) seizure duration ≥ 5 min. Exclusion criteria were the following: 1) exclusively neonatal seizures, 2) psychogenic nonepileptic seizures, or 3) incomplete information about seizure duration. Four hundred forty-five patients (50.1% male) with a median (p_{25} – p_{75}) age at SE of 5.5 (2.8–10.5) years were enrolled. Status epilepticus lasted for 5–29 min in 296 (66.5%) of subjects and for ≥ 30 min in 149 (33.5%). Patients with $SE_{\geq 30}$ were younger than the patients with SE_{5-29} at the time of seizure onset (median: 1 versus 2.1 years, $p = 0.0007$). Status epilepticus as the first seizure presentation was more frequent in patients with $SE_{\geq 30}$ (24.2% versus 12.2%, $p = 0.002$). There was a tendency towards a higher rate of abnormalities in the magnetic resonance imaging at baseline in patients with $SE_{\geq 30}$ (70.5% versus 57.1%, $p = 0.061$). Differences were not detected in seizure frequency, seizure types, presence of developmental delay, and electroencephalogram abnormalities at baseline. In the pediatric population, SE thresholds of either 5 or 30 min identify groups of patients with very similar electroclinical characteristics, which may influence future definitions of pediatric SE.

© 2014 Elsevier Inc. All rights reserved.

1. Introduction

The classical definition of status epilepticus (SE) or “established” SE requires that seizures last for a minimum of 30 min [1]. This definition has been widely used in the literature. However, when seizures last longer than 5 min, they are unlikely to stop spontaneously both in adults and in children [2,3] and meet the definition of “impending” SE [4]. At present, both definitions of SE (with a threshold seizure duration of 5 and 30 min) coexist in the literature, but there is a striking lack of data comparing the characteristics of “impending” SE versus “established” SE [5]. A series of 226 patients (135 adults and 91 children) with prolonged seizures compared the characteristics of

“impending” and “established” SE [5]. However, in this study, the characteristics of the 91 pediatric patients were analyzed together with those of the 135 adult patients [5]. Therefore, there is the need to evaluate whether the different thresholds for SE duration (5 or 30 min) identify patient populations with different electroclinical characteristics.

This study aimed to address this gap in knowledge by describing and comparing the electroclinical characteristics of pediatric patients with a SE duration of 5–29 min (SE_{5-29}) to those with a SE duration of ≥ 30 min ($SE_{\geq 30}$).

2. Patients and methods

2.1. Study characteristics, design, and setting

This study was approved by the Institutional Review Board of Boston Children's Hospital, and, therefore, has been performed in accordance

* Corresponding author at: Division of Epilepsy and Clinical Neurophysiology, Fegan 9, Boston Children's Hospital, 300 Longwood Ave., Boston, MA 02115, USA. Tel.: +1 617 355 2443; fax: +1 617 730 0463.

E-mail address: ivan.fernandez@childrens.harvard.edu (I. Sánchez Fernández).

¹ Both are first authors of this manuscript.

with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. This was a retrospective descriptive cohort study of pediatric patients presenting with seizures of at least 5 min in duration at a tertiary referral pediatric hospital.

2.2. Participants

Charts of patients admitted to the hospital for seizures from January 1st, 2005 to December 31st, 2010 were screened. Patients were identified through two different word search mechanisms of our electronic medical records. The search terms “seizure”, “status epilepticus”, “convulsions”, and “epilepsy” were used in the reason for admission, discharge diagnoses, and body of the clinical documents. Inclusion criteria were the following: 1) 1 month to 21 years of age at the time of a SE episode, 2) convulsive seizures at onset of SE, and 3) seizure duration of at least 5 min. Exclusion criteria were the following: 1) exclusively neonatal seizures, 2) psychogenic nonepileptic seizures or seizures of unclear epileptic nature, and 3) SE with incomplete or unclear information about seizure duration.

If a patient presented with an episode of ≥ 30 min during the study period, that patient was considered to belong to the $SE_{\geq 30}$ group regardless of whether this patient had a seizure of 5 to 29 min at any other time during the study period. Both single continuous prolonged seizures and repetitive seizures without return to baseline were considered as SE as long as they met the threshold duration. Both focal and generalized seizures were considered SE as long as they met the threshold duration.

2.3. Clinical variables

Demographic and clinical variables included age at seizure onset, age at SE, seizure frequency, number of antiepileptic drugs, seizure semiology at baseline, and EEG and magnetic resonance imaging (MRI) results.

2.4. Assessments

The main exposure was duration of seizures stratifying by 5 or 30 min. Based on the two subgroups defined by these two seizure duration thresholds, the outcome measures, electroclinical characteristics, were compared in subjects with SE_{5-29} versus those with $SE_{\geq 30}$.

2.5. Statistical analysis

On univariate analysis, categorical variables were compared with Fisher's exact tests, and continuous variables were compared with Wilcoxon rank-sum tests. On multivariate analysis, the influence of seizure duration on death was evaluated controlling for potential confounders. All tests were performed at a “two-sided” significance level of 0.05. For all statistical analyses, STATA 12.0 (Stata Corp., College Station, TX, USA) was used.

3. Results

3.1. Demographic and clinical characteristics

Four hundred forty-five patients with a median age at SE of 5.5 years were included. Status epilepticus lasted for 5–29 min in 296 (66.5%) patients and for ≥ 30 min in 149 (33.5%). The specific duration of SE is presented in Fig. 1. Patients with $SE_{\geq 30}$ were younger at the time of seizure onset and at the time of the SE episode. After stratification by SE type (febrile versus nonfebrile SE), the differences in age at the first seizure persisted for the group with nonfebrile SE. In contrast, stratification by SE type showed that the differences at the age of the SE episode were reflecting the different distributions of febrile SE in the comparison groups. Additionally, patients with $SE_{\geq 30}$ more frequently presented SE as the first seizure presentation compared to patients with SE_{5-29} . After stratification by febrile versus nonfebrile SE, the predominance

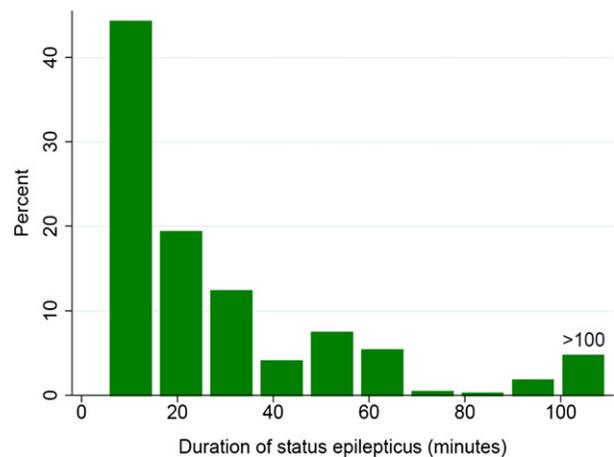


Fig. 1. Bar graph representing the percentage of cases within each seizure duration category. The last column includes all cases with seizure duration of more than 100 minutes.

of SE as the first seizure presentation for the $SE_{\geq 30}$ group remained marginally significant for the nonfebrile SE group. Etiologies were different between the two groups. Three hundred thirty-three patients had a prior diagnosis of epilepsy, 246 of whom were on treatment without a difference in duration 5–29 or ≥ 30 min between those treated and those not treated at baseline. Details are presented in Table 1.

3.2. Electroencephalographic findings

An EEG was performed prior to SE in 252 patients, with the baseline being abnormal in 218 (86.5%). The most frequent EEG abnormalities were generalized, and the most frequent types of abnormalities were spikes and nonepileptiform abnormalities such as slowing or asymmetries. There was no difference between patients with SE_{5-29} and patients with $SE_{\geq 30}$. Details are presented in Table 2.

3.3. MRI findings

An MRI was performed in 227 patients prior to the SE episode, being abnormal in 140 (61.7%). Among the abnormalities found in the MRI, most were bilateral, the most frequent localization was in the temporal lobe, and this site was observed to be more common in patients with SE_{5-29} than in patients with $SE_{\geq 30}$. The most frequent type of MRI abnormality was volume loss. Details are presented in Table 3.

3.4. Outcomes

Patients were followed up for a median of 3.7 years after SE. Twenty-one patients (4.7%) died, with a median time of 3.1 years from SE until death, and most of these deaths were unrelated to epilepsy (Table 4). Using logistic regression considering death as the primary outcome and duration of SE as the predictor and controlling for duration of follow-up, every additional minute of SE duration increased the odds ratio of dying by 0.005 (Online Table 1). When controlling for both duration of follow-up and age, this association persisted and also showed an increase of 0.005 in the odds of dying per minute of SE duration (Online Table 2). When controlling for duration of follow-up, age, and etiology, this association persisted and showed an increase of 0.004 in the odds of dying per minute of SE duration (Online Table 3). The increase in mortality with increasing duration of SE does not appear to be secondary to an outlier effect as shown by the progressive increase in the proportion of mortality across all SE durations (Fig. 2 and Table 5).

Table 1
Demographic and clinical features.

| | | Total, N (%) | 5–29 min, N (%) | ≥30 min, N (%) | Difference |
|---|--|----------------|-----------------|----------------|-------------------------------|
| SE duration | | 445 (100%) | 296 (66.5%) | 149 (33.5%) | N/A |
| Gender | Male | 223 (50.1%) | 149 (50.3%) | 74 (49.7%) | FE; <i>p</i> = 0.92 |
| | Female | 222 (49.9%) | 147 (49.7%) | 75 (50.3%) | |
| Age at the episode of SE (years) | Median (<i>p</i> ₂₅ – <i>p</i> ₇₅) | 5.5 (2.8–10.5) | 6.3 (3–11.3) | 4.2 (2.4–9.1) | WRS; <i>p</i> = 0.0147 |
| | Mean (SD) | 7.1 (5.5) | 7.5 (5.5) | 6.4 (5.5) | |
| | Range | 0.08–20.8 | 0.08–20.3 | 0.08–20.8 | |
| | | | | | |
| <i>Stratification of age at the episode of SE by the presence or absence of febrile SE</i> | | | | | |
| Age at the episode of SE (years) in patients without febrile SE | Median (<i>p</i> ₂₅ – <i>p</i> ₇₅) | 7.4 (3.4–12.8) | 7.7 (3.6–12.8) | 6.8 (2.9–12.4) | WRS; <i>p</i> = 0.3275 |
| | Mean (SD) | 8.2 (5.6) | 8.4 (5.5) | 7.9 (5.9) | |
| | Range | 0.08–20.8 | 0.08–20.3 | 0.08–20.8 | |
| Age at the episode of SE (years) in patients with febrile SE | Median (<i>p</i> ₂₅ – <i>p</i> ₇₅) | 3 (1.3–4.3) | 3 (1.6–4.8) | 3 (1.2–4.1) | WRS; <i>p</i> = 0.5069 |
| | Mean (SD) | 3 (1.7) | 3.1 (1.7) | 2.8 (1.7) | |
| | Range | 0.5–6 | 0.5–5.9 | 0.5–6 | |
| Age at seizure onset (years) | Median (<i>p</i> ₂₅ – <i>p</i> ₇₅) | 1.5 (0.4–5) | 2.1 (0.5–5.9) | 1 (0.3–3.6) | WRS; <i>p</i> = 0.0007 |
| | Mean (SD) | 3.5 (4.2) | 3.9 (4.5) | 2.6 (3.6) | |
| | Range | 0–18.5 | 0–18.5 | 0–15.8 | |
| <i>Stratification of age at seizure onset by the presence or absence of febrile SE</i> | | | | | |
| Age at seizure onset (years) in patients without febrile SE | Median (<i>p</i> ₂₅ – <i>p</i> ₇₅) | 1.9 (0.5–6.3) | 2.4 (0.5–6.9) | 1 (0.25–4.6) | WRS; <i>p</i> = 0.0019 |
| | Mean (SD) | 3.9 (4.6) | 4.3 (4.7) | 3 (4.1) | |
| | Range | 0–18.5 | 0–18.5 | 0–15.8 | |
| Age at the episode of SE (years) in patients with febrile SE | Median (<i>p</i> ₂₅ – <i>p</i> ₇₅) | 1 (0.5–3.1) | 1 (0.5–3.1) | 1 (0.5–3) | WRS; <i>p</i> = 0.6763 |
| | Mean (SD) | 1.7 (1.7) | 1.8 (1.7) | 1.7 (1.7) | |
| | Range | 0.5–5.8 | 0.5–5.8 | 0.5–5.8 | |
| SE was first seizure presentation | Yes | 72 (16.2%) | 36 (12.2%) | 36 (24.2%) | FE; <i>p</i> = 0.002 |
| | No | 373 (83.8%) | 260 (87.8%) | 113 (75.8%) | |
| <i>Stratification of SE was first seizure presentation by the presence or absence of febrile SE</i> | | | | | |
| SE was first seizure presentation in patients without febrile SE | Yes | 44 (12.6%) | 25 (10.2%) | 19 (18.3%) | FE; <i>p</i> = 0.051 |
| | No | 306 (87.4%) | 221 (89.8%) | 85 (81.7%) | |
| SE was first seizure presentation in patients with febrile SE | Yes | 28 (29.5%) | 11 (22%) | 17 (37.8%) | FE; <i>p</i> = 0.116 |
| | No | 67 (70.5%) | 39 (78%) | 28 (62.2%) | |
| Baseline seizure frequency (seizures/month) if seizures prior to SE (N = 333) | Median (<i>p</i> ₂₅ – <i>p</i> ₇₅) | 3 (0.1–30) | 3 (0.1–45) | 2.5 (0.2–30) | WRS; <i>p</i> = 0.8618 |
| | Mean (SD) | 104.7 (419.4) | 86 (286.2) | 142.6 (605.6) | |
| | Range | 0–5500 | 0–3300 | 0–5500 | |
| Increase in seizure frequency if seizures prior to SE (N = 333) ^a | Yes | 97 (29.1%) | 70 (31.4%) | 27 (24.6%) | FE; <i>p</i> = 0.203 |
| | No | 236 (70.9%) | 153 (68.6%) | 83 (75.5%) | |
| Baseline number of seizure types | No data available | 112 (25.2%) | 74 (25%) | 38 (25.5%) | FE; <i>p</i> = 0.408 |
| | One type | 158 (35.5%) | 111 (37.5%) | 47 (31.5%) | |
| | More than one type | 175 (39.3%) | 111 (37.5%) | 64 (43%) | |
| Seizure semiology at baseline ^b | No data available | 112 | 74 | 38 | N/A |
| | Positive | 312 | 206 | 106 | |
| | Negative | 93 | 61 | 32 | |
| | Aura | 7 | 6 | 1 | |
| | Gelastic | 5 | 5 | 0 | |
| Likely etiology of SE | Febrile/infectious | 233 (52.4%) | 136 (46%) | 97 (65.1%) | FE; <i>p</i> < 0.0005 |
| | Unknown | 140 (31.5%) | 115 (38.9%) | 25 (16.8%) | |
| | Other etiologies | 72 (16.2%) | 45 (15.2%) | 27 (18.1%) | |
| Prior epilepsy | Yes | 333 (74.8%) | 223 (75.3%) | 110 (73.8%) | FE; <i>p</i> = 0.73 |
| | No | 112 (25.2%) | 73 (24.7%) | 39 (26.2%) | |
| Treatment for epilepsy if epilepsy prior to SE (N = 333) | Yes | 246 (73.9%) | 159 (71.3%) | 87 (79.1%) | FE; <i>p</i> = 0.145 |
| | No | 87 (26.1%) | 64 (28.7%) | 23 (20.9%) | |
| Mean number of baseline AED if epilepsy prior to SE (N = 333) | Median (<i>p</i> ₂₅ – <i>p</i> ₇₅) | 1 (0–2) | 1 (0–2) | 2 (1–3) | WRS; <i>p</i> = 0.0548 |
| | Mean (SD) | 1.6 (1.3) | 1.5 (1.3) | 1.8 (1.3) | |
| | Range | 0–6 | 0–6 | 0–5 | |
| Changes in AEDs in the three months prior to the event if epilepsy prior to SE (N = 333) | Yes | 109 (32.7%) | 71 (31.8%) | 38 (34.6%) | FE; <i>p</i> = 0.622 |
| | No | 224 (67.3%) | 152 (68.2%) | 72 (65.4%) | |
| Developmental delay | Yes | 256 (57.5%) | 163 (55.1%) | 93 (62.4%) | FE; <i>p</i> = 0.155 |
| | No | 189 (42.5%) | 133 (44.9%) | 56 (37.6%) | |

AED: antiepileptic drugs, FE: Fisher's exact test, N/A: not applicable, SD: standard deviation, SE: status epilepticus, and WRS: Wilcoxon rank-sum test.

^a At least double from baseline during the two weeks before SE.^b Numbers do not sum up to the total as some patients belong to several categories.

4. Discussion

We compared the characteristics of pediatric patients with SE_{5–29} with the characteristics of those who experienced SE_{≥30}. The characteristics of pediatric patients with SE were similar regardless of the time threshold (5 versus 30 min) used for its definition. Patients with SE_{≥30} were younger at the onset of epilepsy. Status epilepticus as the first seizure was more frequent in patients with SE_{≥30}. The odds of dying increased with every minute of SE duration.

An increase in mortality with longer duration of SE was previously noted in the literature. One series showed that pediatric mortality was 0% for SE lasting 10 to 29 min and 4% for SE_{≥30}, although this difference did not reach statistical significance due to the low number of events in each group [5]. Our series had enough statistical power to show that each minute increase of SE duration led to a higher odds ratio of death by 0.005, a small but significant increase possibly suggesting a continuous rather than a discrete cut-off value for the risk of dying. Longer SE duration likely reflects a more severe underlying SE cause [6,7],

Table 2
EEG features.

| | | Total, N (%) | 5–29 min, N (%) | ≥30 min, N (%) | Difference |
|--|-------------------------------|--------------|-----------------|----------------|------------------|
| Abnormal EEG prior to SE (N = 252) | Abnormal | 218 (86.5%) | 142 (84.5%) | 76 (90.5%) | FE; $p = 0.242$ |
| | Normal | 34 (13.5%) | 26 (15.5%) | 8 (9.5%) | |
| Focal vs generalized EEG abnormality (N = 217) | Focal | 90 (41.5%) | 59 (41.8%) | 31 (40.8%) | FE; $p > 0.9999$ |
| | Generalized | 127 (58.5%) | 82 (58.2%) | 45 (59.2%) | |
| Type of abnormality on EEG ^a | Normal | 34 | 26 | 8 | N/A |
| | Spikes | 193 | 125 | 68 | |
| | Seizures | 84 | 59 | 25 | |
| | Nonepileptiform abnormalities | 139 | 92 | 47 | |

EEG: electroencephalogram, FE: Fisher's exact test, N/A: not applicable, and SE: status epilepticus.

^a Numbers do not sum up to the total as some patients belong to several categories.

although when controlling for etiology in three large groups (febrile/infectious, others, unknown), differences in mortality persisted.

The traditional definition of SE (seizure activity ≥ 30 min) is not operationally used in clinical practice because of the realization that seizures are more difficult to treat the longer they last [8–12]. In addition, seizures that last ≥ 5 min are likely to persist without medical intervention both in adults [2] and in children [3]. Thus, seizures ≥ 5 min of duration are often considered as “impending” SE and treated aggressively. A concern that may arise when treating patients with seizure duration of ≥ 5 min equally aggressive as patients with seizure duration of ≥ 30 min is whether the patients identified by one and the other thresholds represent the same or equivalent population of patients. Our study suggests that these patient populations are comparable.

4.1. Strengths and weaknesses

Although interrater reliability in recognizing SE is usually good [13], clinical features were interpreted by different medical teams introducing information bias and leaving room for misclassification. We overcame this potential challenge by classifying SE based on objective seizure durations in the clinical charts and not based on different interpretations of the definitions of SE by the individual medical teams. The potential for information bias in retrospective data collection was overcome by collecting information with a standardized data collection instrument.

One of the main factors predicting SE duration is timely and appropriate treatment of SE [9,10], and it is likely that the duration of SE was influenced by the timing of treatment administration. Because of the retrospective nature of the present study, this information was not available, and it was not possible to control for it. In ongoing prospective studies, we are collecting information of timing of antiepileptic drug

administration. Differences between groups reached statistical significance but were of moderate clinical relevance like the age at seizure onset or the age of SE episode. As a descriptive, hypothesis-generating study, we did not find it necessary to correct for multiple comparisons, and some of these differences could have arisen by chance. Considering the sample size of our study and the relatively minor differences between the groups, our results suggest that the patient populations captured are similar regardless of the use of a 5- or 30-minute threshold.

Results need to be interpreted in the clinical context of data acquisition. This is a study of patients admitted to a tertiary referral hospital. Although patients admitted to the emergency department and discharged without inpatient admission were also included in the study, there is likely a certain degree of selection bias in the study population. A patient with chronic epilepsy and frequent seizures may not go to the hospital even when a seizure is prolonged. This limitation is inherent to a hospital-based study and could only be overcome by performing a study that includes patients who are not cared for in the hospital during most of their episodes. On the other hand, a hospital-based study provides a large number of patients and is less resource intensive.

Some SE_{5–29} patients may have had episodes of longer duration before or after the study period, but both sets of patients may have averaged out based on our numbers, and they likely also represent a minor proportion of the patients given the long study period. We had no information on the occurrence of seizures or their duration before or after the study period. Having a prolonged seizure is a risk factor for having another prolonged seizure and is also an indication for having rescue medications at home. We did not have information on the proportion of patients with rescue medication at home or the proportion of patients who used rescue medication during the episode. We have provided information on the proportion of patients in whom the index episode was

Table 3
MRI features.

| | | Total, N (%) | 5–29 min, N (%) | ≥30 min, N (%) | Difference |
|--|--------------------|--------------|-----------------|----------------|-------------------------------------|
| Abnormal MRI prior to SE (N = 227) | Abnormal | 140 (61.7%) | 85 (57.1%) | 55 (70.5%) | Fisher's exact test; $p = 0.061$ |
| | Normal | 87 (38.3%) | 64 (43%) | 23 (29.5%) | |
| Lateralization of MRI abnormality (N = 227) | Left | 36 (15.9%) | 22 (14.8%) | 14 (18%) | FE; $p = 0.181$ |
| | Right | 25 (11%) | 13 (8.7%) | 12 (15.4%) | |
| | Bilateral | 61 (26.9%) | 38 (25.5%) | 23 (29.5%) | |
| | None | 105 (46.3%) | 76 (51%) | 29 (37.2%) | |
| Localization of MRI abnormality ^a | Temporal | 68 (29.3%) | 37 (23.1%) | 31 (43.1%) | FE; $p = 0.007$ |
| | Extratemporal | 25 (10.8%) | 22 (13.8%) | 3 (4.2%) | |
| | Periventricular | 50 (21.6%) | 35 (21.9%) | 15 (20.8%) | |
| | Normal | 89 (38.4%) | 66 (41.3%) | 23 (31.9%) | |
| MRI findings ^a | Vascular | 22 | 14 | 8 | N/A |
| | Volume loss | 46 | 33 | 13 | |
| | Malformation | 22 | 17 | 5 | |
| | Myelination defect | 14 | 10 | 4 | |
| | Normal | 104 | 78 | 26 | |

FE: Fisher's exact test, MRI: magnetic resonance imaging, N/A: not applicable, and SE: status epilepticus.

^a Numbers do not sum up to the total as some patients belong to several categories.

Table 4
Outcomes.

| | | Total, N (%) | 5–29 min, N (%) | ≥30 min, N (%) | Difference |
|--|--|---------------|-----------------|----------------|------------------------|
| Duration of seizures | Median (p ₂₅ –p ₇₅) | 15 (7–30) | 10 (5–15) | 45 (30–60) | N/A |
| | Mean (SD) | 30.9 (61.2) | 10.5 (5.7) | 71.3 (93.2) | |
| | Range | 2–720 | 2–27 | 30–720 | |
| Death | No | 424 (95.3%) | 284 (96%) | 140 (94%) | FE; <i>p</i> = 0.352 |
| | Yes | 21 (4.7%) | 12 (4.1%) | 9 (6%) | |
| Cause of death | Epilepsy related | 2 (20%) | 1 (16.7%) | 1 (25%) | FE; <i>p</i> > 0.9999 |
| | Nonepilepsy related | 8 (80%) | 5 (83.3%) | 3 (75%) | |
| Duration from SE index episode until death (in years) | Median (p ₂₅ –p ₇₅) | 3.1 (2.1–4.9) | 2.5 (1.9–4.9) | 4 (2.8–5.4) | WRS; <i>p</i> = 0.2568 |
| | Mean (SD) | 3.6 (1.6) | 3.3 (1.7) | 4.1 (1.6) | |
| | Range | 1.4–6 | 1.4–5.8 | 2.6–6 | |
| Duration of follow-up from SE index episode (in years) | Median (p ₂₅ –p ₇₅) | 3.7 (1.3–5.5) | 3.7 (1.4–5.5) | 3.6 (1.3–5.4) | WRS; <i>p</i> = 0.9076 |
| | Mean (SD) | 3.5 (2.4) | 3.5 (2.4) | 3.5 (2.4) | |
| | Range | 0–14.6 | 0–14.6 | 0.04–7.9 | |
| | Sum | 1563.2 | 1047.4 | 515.7 | |
| Rate of death (in deaths/year of follow-up) | | 0.0134 | 0.0115 | 0.0175 | N/A |

FE: Fisher's exact test, N/A: not applicable, SE: status epilepticus, and WRS: Wilcoxon rank-sum test.

the first seizure, the proportion of patients with a prior diagnosis of epilepsy, and the proportion of patients with a diagnosis of epilepsy on chronic treatment. Since this is a retrospective study, there were certain data that were missing in some of the categories. For example, not all patients with prior seizures had data available on seizure frequency. Therefore, results ultimately need to be interpreted in the setting of partially missing data and information bias, inherent to all similar studies.

A major strength of this study is the large patient numbers, allowing us to establish the correlation between seizure duration and odds ratio of death.

4.2. Outlook

Starting from the end date of this retrospective data collection, in 2011, we are developing a larger prospective data series at several centers within the pediatric Status Epilepticus Research Group (pSERG; www.pserg.org) to evaluate the differences between patients with SE_{5–29} and SE_{≥30} and the association of duration of SE with death in more detail. In addition, the time of administration of antiepileptic drugs is being systematically collected to control for that relevant confounding factor.

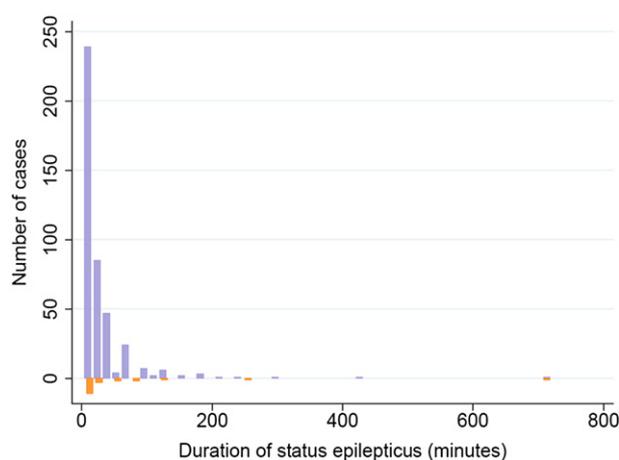


Fig. 2. Histogram of the seizure duration comparing patients who survived (lavender, positive values in the y axis) and those who died (orange, negative values in the y axis).

4.3. Conclusions

Most baseline characteristics of pediatric patients with SE are similar regardless of the threshold duration defines SE. These similarities may facilitate comparisons of prior studies with different SE duration thresholds and may influence future definitions of SE. Seizures present earlier in patients with “established” SE than in patients with “impending” SE. Longer duration of SE correlates with higher odds of subsequent death.

Acknowledgments

This study was supported by a Career Development Fellowship Award from Harvard Medical School and Boston Children's Hospital (TL) and by a grant from the Program for Quality and Safety at Boston Children's Hospital (TL).

Iván Sánchez Fernández is funded by a grant for the study of epileptic encephalopathies from “Fundacion Alfonso Martín Escudero” and the HHV6 Foundation.

Conflict of interest

Tobias Loddenkemper serves on the Laboratory Accreditation Board for Long-term (Epilepsy and ICU) Monitoring (ABRET), serves as a member of the American Clinical Neurophysiology Council (ACNS), serves on the American Board of Clinical Neurophysiology, serves as an Associate Editor of *Seizure*, performs video EEG long-term monitoring, EEGs, and other electrophysiological studies at Boston Children's Hospital and bills for these procedures, receives support from the HHV6 foundation NIH/NINDS and PCORI by the Payer Provider Quality Initiative, receives funding from the American Epilepsy Society, the

Table 5
Proportion of deaths by seizure duration.

| Seizure duration in minutes | Patients in each category | Deaths in each category | Proportion of deaths in each age category |
|-----------------------------|---------------------------|-------------------------|---|
| 5 | 82 | 2 | 0.0244 |
| >5–10 | 115 | 5 | 0.0435 |
| >10–20 | 86 | 5 | 0.0581 |
| >20–30 | 55 | 2 | 0.0364 |
| >30–40 | 18 | 0 | 0 |
| >40–50 | 33 | 0 | 0 |
| >50–60 | 24 | 2 | 0.0833 |
| >60–70 | 2 | 0 | 0 |
| >70–80 | 1 | 1 | 1 |
| >80–90 | 8 | 1 | 0.125 |
| >90–100 | 0 | 0 | Not applicable |
| >100 | 21 | 3 | 0.1429 |

Epilepsy Foundation of America, the Epilepsy Therapy Project, the Pediatric Epilepsy Research Foundation, CURE, and the Danny Did Foundation, and received investigator initiated research support from Eisai Inc. and Lundbeck LLC.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.yebeh.2014.05.018>.

References

- [1] DeLorenzo RJ, Hauser WA, Towne AR, Boggs JG, Pellock JM, Penberthy L, et al. A prospective, population-based epidemiologic study of status epilepticus in Richmond, Virginia. *Neurology* 1996;46:1029–35.
- [2] Jenssen S, Gracely EJ, Sperling MR. How long do most seizures last? A systematic comparison of seizures recorded in the epilepsy monitoring unit. *Epilepsia* 2006;47:1499–503.
- [3] Shinnar S, Berg AT, Moshe SL, Shinnar R. How long do new-onset seizures in children last? *Ann Neurol* 2001;49:659–64.
- [4] Brophy GM, Bell R, Claassen J, Alldredge B, Bleck TP, Glauser T, et al. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care* 2012;17:3–23.
- [5] DeLorenzo RJ, Garnett LK, Towne AR, Waterhouse EJ, Boggs JG, Morton L, et al. Comparison of status epilepticus with prolonged seizure episodes lasting from 10 to 29 minutes. *Epilepsia* 1999;40:164–9.
- [6] Berg AT, Shinnar S, Testa FM, Levy SR, Frobish D, Smith SN, et al. Status epilepticus after the initial diagnosis of epilepsy in children. *Neurology* 2004;63:1027–34.
- [7] Raspall-Chaure M, Chin RF, Neville BG, Scott RC. Outcome of paediatric convulsive status epilepticus: a systematic review. *Lancet Neurol* 2006;5:769–79.
- [8] Alldredge BK, Wall DB, Ferriero DM. Effect of prehospital treatment on the outcome of status epilepticus in children. *Pediatr Neurol* 1995;12:213–6.
- [9] Chin RF, Neville BG, Peckham C, Wade A, Bedford H, Scott RC. Treatment of community-onset, childhood convulsive status epilepticus: a prospective, population-based study. *Lancet Neurol* 2008;7:696–703.
- [10] Eriksson K, Metsaranta P, Huhtala H, Auvinen A, Kuusela AL, Koivikko M. Treatment delay and the risk of prolonged status epilepticus. *Neurology* 2005;65:1316–8.
- [11] Goodkin HP, Yeh JL, Kapur J. Status epilepticus increases the intracellular accumulation of GABA_A receptors. *J Neurosci* 2005;25:5511–20.
- [12] Naylor DE, Liu H, Wasterlain CG. Trafficking of GABA_A receptors, loss of inhibition, and a mechanism for pharmacoresistance in status epilepticus. *J Neurosci* 2005;25:7724–33.
- [13] Shinnar S, Hesdorffer DC, Nordli Jr DR, Pellock JM, O'Dell C, Lewis DV, et al. Phenomenology of prolonged febrile seizures: results of the FEBSTAT study. *Neurology* 2008;71:170–6.