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Comparison of risk factors for pediatric convulsive status epilepticus when defined as seizures ≥5 min versus seizures ≥30 min

Iván Sánchez Fernández [a,b,*], Jacquelyn Klehm [a], Sookee An [a], Dinesh Jillella [a], Kush Kapur [a], Jacqueline Zelener [a], Alexander Rotenberg [a], Tobias Loddenkemper [a]

[a] Division of Epilepsy and Clinical Neurophysiology, Department of Neurology, Boston Children's Hospital, Harvard Medical School, 300 Longwood Avenue, Boston, MA 02115, USA
[b] Department of Child Neurology, Hospital Sant Joan de Déu, Universidad de Barcelona, Passeig Sant Joan de Déu s/n, 08950 Esplugues de Llobregat, Barcelona, Spain

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ABSTRACT

Purpose: To identify risk factors (RF) of pediatric convulsive status epilepticus (SE) and to determine whether defining SE as seizures ≥5 min (SE_5) or seizures ≥30 min (SE_{30}) would modify the risk factors identified.
Methods: Retrospective case–control study. We included patients 1 month to 21 years of age at the time of convulsive SE. We compared the characteristics of patients with SE (cases) versus those without SE (controls) using two different seizure duration thresholds: 5 min and 30 min.
Results: 1062 patients (54% males) were enrolled. The median (p_{25}–p_{75}) age at the episode was 6.4 (2.8–11.8) years. 444 (41.8%) patients had SE_5 and 149 (14%) patients had SE_{30}. On univariate analysis, risk factors for SE were not markedly different when considering a 5 or 30 min threshold. Compared to their respective controls patients with both SE_5 and SE_{30} were younger at the age of seizure onset and at the age of SE, were on more antiepileptic drugs (AEDs) at baseline, had a higher rate of changes in AEDs in the three months prior to the episode, were more likely to have developmental delay at baseline, and a higher mortality rate. A higher baseline seizure frequency, and a higher increase in seizure frequency prior to the index episode were seen only in SE_5.
Conclusion: This series identifies RF which predict convulsive SE in pediatric patients. These RF are similar when considering a 5 min or a 30 min threshold for the definition of SE.

1. Introduction

Status epilepticus (SE) is one of the most common neurologic emergencies in the pediatric population.[1–4] 17–23/100,000 children suffer from SE every year with an average mortality rate of 0–3%.[1,5–10] Additionally, a high proportion of patients with pediatric SE subsequently develop epilepsy and are left with severe cognitive deficits.[8]

Little is known about the factors that can identify individuals at a higher risk for SE. Further, there is almost no information on whether different SE definitions influence these factors. In adults, SE episodes are most frequently secondary to underlying diseases such as brain tumors or strokes or to irregular administration of antiepileptic drugs (AEDs), and these etiologies cannot be easily extrapolated to children (Table 1).[11,12] In pediatric patients, only a few series evaluated the risk factors (RF) for SE (Table 1).[13–15] In these studies, the following independent RF for pediatric SE were identified: "polypharmacy," "discontinuation of antiepileptic medication," "neuromotor retardation," and "generalized background abnormalities on EEG,"[14] "focal background EEG abnormalities," "partial seizures with secondary generalization," "history of first seizure as SE," and "generalized abnormalities on neuroimaging,"[15] "history of SE", "younger age at onset" and "structural/metabolic etiology".[13] However, these RF are not fully concordant among series and it is not known whether this reflects different inclusion criteria, such as seizure duration thresholds for defining SE. At present, SE is defined as "impending" SE if it lasts ≥5 min (SE_5)[16] or as "established" SE if it lasts ≥30 min (SE_{30}).[5] It is

Abbreviations: AED, antiepileptic drug(s); EEG, electroencephalogram; MRI, magnetic resonance imaging; RF, risk factor(s); SE, status epilepticus; SE_5, status epilepticus defined as seizures of 5 or more minutes; SE_{30}, status epilepticus defined as seizures of 30 or more minutes.

* Corresponding author at: Boston Children's Hospital, 300 Longwood Avenue, Fegan 9, 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).

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Table 1
Risk factors for convulsive status epilepticus.

	Setting	Study design	Risk factors (after correction for potential confounders)
Studies in adults			
Canouï-Poitrine et al.[11] *N* = 252	Consecutive elderly patients (≥70 y) managed at a geriatrics department in the period 2003–2005	Case–control retrospective Cases (status epilepticus) = 63 Controls (no seizure) = 189	Acute decompensation (cardiac, respiratory or hepatic) OR = 2.57 History of epilepsy OR = 3.93 Chronic cerebrovascular disease OR = 7.96 Non-vascular dementia OR = 4.16 Dysnatremia OR = 5.08
Maldonado et al.[12] *N* = 82	Patients managed in the outpatient clinics with epilepsy in the period 2003–2007	Case–control retrospective Cases (patients with epilepsy and status epilepticus): 41 Controls (patients with epilepsy without status epilepticus): 41	Irregular antiepileptic treatment OR = 2.9
Studies in children			
Karasalİhoĝlu et al.[14] *N* = 249	All children (1 mo–16 y) admitted to pediatric neurology unit with seizure(s) in the period 1994–2001	Case–control retrospective Cases = 83 Controls (seizures without status epilepticus) = 166	Polypharmacy (more than one antiepileptic drug) OR = 5.17 Discontinuation of antiepileptic medication OR = 4.04 Neuromotor retardation (delays in development that significantly challenged the child in at least two aspects: personal-social skills, fine motor skills, adaptive skills, language, gross motor skills) OR = 4.03 Generalized background abnormalities on EEG. OR = 2.48
Novak et al.[15] *N* = 132	All children with symptomatic epilepsy managed at a Child Neurology Clinic in the period 1991–1995	Case–control retrospective Cases (symptomatic epilepsy with episodes of status epilepticus) = 44 Controls (symptomatic epilepsy without episodes of status epilepticus during the study period) = 88	Focal background EEG abnormalities OR = 6.51 Partial seizures with secondary generalization OR = 4.61 First seizure as status epilepticus OR = 3.99 Generalized abnormalities on neuroimaging OR = 2.85
Berg et al.[13] *N* = 613	Children (1 mo–15 y) diagnosed with epilepsy during the period 1993–1997	Prospective cohort study	Previous status epilepticus RR: 4.49 Younger age at onset RR: 0.91 increase of risk per year Symptomatic etiology RR: 2.47

N: number of patients included in the study; mo: months; OR: odds ratio; RR: risk ratio; y: years.

still unknown whether different seizure duration thresholds for SE might have an impact on the identified risk factors leading to SE.

This study aims to address this gap in knowledge by describing the risk factors of pediatric patients with "established" and "impending" SE and to evaluate whether a seizure duration threshold of 5 or 30 min modifies the identified risk factors for SE. Our results may allow the comparison of studies with different seizure duration thresholds in previous literature and may inform the potential development of seizure duration thresholds in pediatric SE in the future.

2. Patients and methods

This was a retrospective case–control study of pediatric patients presenting with, at least one episode of seizures or SE. This study was approved by the Institutional Review Board of Boston Children's Hospital.

2.1. Patients

Patients were included if admitted to Boston Children's Hospital between January 1st 2005 and December 31st 2010 inclusive. Inclusion criteria were: (1) age from 1 month to 21 years at the time of the seizures or SE episode and (2) convulsive seizures at the beginning of SE. The exclusion criteria were: (1) neonatal seizures only, (2) psychogenic non-epileptic seizures or seizures of unclear epileptic nature, and (3) incomplete or unclear information about seizure duration.

2.2. Search process

The list of patients admitted to the hospital was screened for patients with seizures or SE. The search terms "seizure", "status epilepticus", "convulsions" and "epilepsy" were used in the reason for admission, discharge diagnoses, and in the body of the clinical documents. The clinical charts of potential study subjects were retrieved and reviewed in order to assess whether they met inclusion/exclusion criteria.

2.3. Variables

Demographic and clinical variables included age at seizure onset, age at the SE episode, baseline seizure frequency, baseline number of AEDs, and seizure semiology at baseline. Information on results of electroencephalogram (EEG) and the magnetic resonance imaging (MRI) were also reviewed and recorded. Data was obtained using an electronic data acquisition form. The duration of seizures was assessed by information present in the clinical charts.

2.4. Seizure duration

Seizure duration was collected from the available clinical information in the clinical charts. Documents reviewed included physicians' notes, nurses' notes, emergency department notes, and emergency medical services' sheets. Seizure duration was based on the numerical information present in the clinical charts and not on the definitions of status epilepticus of individual health-care providers.

Table 2
Comparison of the demographic and clinical features of patients with and without SE using a cut-off value of 5 min or 30 min. Dichotomous variables are expressed as absolute number and percentage. Continuous variables are expressed as median with percentiles 25th and 75th [M (p_{25}–p_{75})], mean with standard deviation [x (SD)], and range.

Total		First comparison: threshold 5 min			Second comparison: threshold 30 min		
	Total	Seizures < 5 min N (%)	Seizures ≥ 5 min N (%)	Difference	Seizures < 30 min N (%)	Seizures ≥ 30 min N (%)	Difference
SE duration	1062 (100%)	618 (58.2%)	444 (41.8%)	N/A	913 (86%)	149 (14%)	N/A
Gender	Male 572 (53.9%) Female 490 (46.1%)	349 (56.5%) 269 (43.5%)	223 (50.2%) 221 (49.8%)	Fisher's exact test; $p = 0.046$	498 (54.6%) 415 (45.5%)	74 (49.7%) 75 (50.3%)	Fisher's exact test; $p = 0.288$
Age at the SE episode (years)	M (p_{25}–p_{75}): 6.4 (2.8–11.8) x (SD): 7.6 (5.6) Range: 0.08–20.8	7.1 (2.8–12.6) 7.9 (5.6) 0.08–20.5	5.5 (2.8–10.5) 7.1 (5.5) 0.08–20.8	Wilcoxon rank-sum test, $p = 0.0499$	6.8 (2.9–12.3) 7.7 (5.6) 0.08–20.5	4.2 (2.4–9.1) 6.4 (5.5) 0.08–20.8	Wilcoxon rank-sum test, $p = 0.0029$
Age at seizure onset (years)	M (p_{25}–p_{75}): 2.3 (0.5–6.2) x (SD): 4.1 (4.5) Range: 0–19.6	2.8 (0.8–7.3) 4.5 (4.7) 0–19.6	1.5 (0.4–5) 3.5 (4.2) 0–18.5	Wilcoxon rank-sum test, $p < 0.00005$	2.5 (0.6–6.7) 4.3 (4.6) 0–19.6	1 (0.3–3.6) 2.6 (3.6) 0–15.8	Wilcoxon rank-sum test, $p < 0.00005$
Baseline seizure frequency (seizures/month) if seizures prior to the index episode ($N = 767$)	M (p_{25}–p_{75}): 1.7 (0.05–30) x (SD): 103.5 (466.3) Range: 0–7200	1 (0–30) 102.6 (499.8) 0–7200	3 (0.1–30) 104.7 (419.4) 0–5500	Wilcoxon rank-sum test, $p = 0.0005$	1 (0.02–30) 97 (439) 0–7200	2.5 (0.2–30) 142.6 (605.6) 0–5500	Wilcoxon rank-sum test, $p = 0.1131$
Increase in seizure frequency if seizures prior to the index episode ($N = 767$)[a]	Yes 161 (21%) No 606 (79%)	64 (14.8%) 370 (85.3%)	97 (29.1%) 236 (70.9%)	Fisher's exact test; $p < 0.0005$	134 (20.4%) 523 (79.6%)	27 (24.6%) 83 (75.5%)	Fisher's exact test; $p = 0.314$
Baseline number of seizure types	None 657 (61.9%) One type 369 (34.8%) > one type 36 (3.4%)	384 (62.1%) 211 (34.1%) 23 (3.7%)	273 (61.5%) 158 (35.6%) 13 (2.9%)	Fisher's exact test; $p = 0.719$	558 (61.1%) 322 (35.3%) 33 (3.6%)	99 (66.4%) 47 (31.5%) 3 (2%)	Fisher's exact test; $p = 0.422$
Seizure semiology[b]	Positive 581 Negative 205 Aura 18 Gelastic 14	269 112 11 9	312 93 7 5	NA	475 173 17 14	106 32 1 0	NA
Likely etiology	F/I 280 (26.4%) Unknown 647 (60.9%) Other 135 (12.7%)	47 (7.6%) 508 (82.2%) 63 (10.2%)	233 (52.5%) 139 (31.3%) 72 (16.2%)	Fisher's exact test; $p < 0.0005$	183 (20%) 622 (68.1%) 108 (11.8%)	97 (65.1%) 25 (16.8%) 27 (18.1%)	Fisher's exact test; $p < 0.0005$
Mean number of baseline AED if seizures prior to the index episode ($N = 767$)	M (p_{25}–p_{75}): 1 (0–2) x (SD): 1.3 (1.3) Range: 0–12	1 (0–2) 1.1 (1.3) 0–12	1 (0–2) 1.6 (1.3) 0–6	Wilcoxon rank-sum test, $p < 0.00005$	1 (0–2) 1.3 (1.3) 0–12	2 (1–3) 1.8 (1.3) 0–5	Wilcoxon rank-sum test, $p = 0.0001$
Changes in AEDs in the three months prior to the event if seizures prior to the index episode ($N = 767$)	Yes 141 (18.4%) No 626 (81.6%)	32 (7.4%) 402 (92.6%)	109 (32.7%) 224 (67.3%)	Fisher's exact test; *$p < 0.0005$*	103 (15.7%) 554 (84.3%)	38 (34.6%) 72 (65.5%)	Fisher's exact test; *$p < 0.0005$*
Developmental delay	Yes 532 (50.1%) No 529 (49.9%)	276 (44.7%) 341 (55.3%)	256 (57.7%) 188 (42.3%)	Fisher's exact test; $p < 0.0005$	439 (48.1%) 473 (51.9%)	93 (62.4%) 56 (37.6%)	Fisher's exact test; *$p = 0.001$*

Death	23 (2.2%)	2 (0.3%)	21 (4.7%)	Fisher's exact test; $p < 0.0005$	14 (1.5%)	9 (6%)	Fisher's exact test; $p = 0.002$
Abnormal EEG prior to SE ($N = 516$)	Abnormal 429 (83.1%) Normal 87 (16.9%)	211 (79.9%) 53 (20.1%)	218 (86.5%) 34 (13.5%)	Fisher's exact test; $p = 0.059$	353 (81.7%) 79 (18.3%)	76 (90.5%) 8 (9.5%)	Fisher's exact test; $p = 0.056$
Focal vs. generalized EEG abnormality ($N = 426$)	Focal 152 (35.7%) Gener 274 (64.3%)	62 (29.7%) 147 (70.3%)	90 (41.5%) 127 (58.5%)	Fisher's exact test; $p = 0.012$	121 (34.6%) 229 (65.4%)	31 (40.8%) 45 (59.2%)	Fisher's exact test; $p = 0.355$
Type of abnormality on EEG[b]	Normal 87 Spikes 374 Seizures 139 NEA 250	53 181 55 111	34 193 84 139	NA	79 306 114 203	8 68 25 47	NA
Abnormal MRI prior to SE ($N = 446$)	Abnormal 266 (59.6%) Normal 180 (40.4%)	126 (57.5%) 93 (42.5%)	140 (61.7%) 87 (38.3%)	Fisher's exact test; $p = 0.386$	211 (57.3%) 157 (42.7%)	55 (70.5%) 23 (29.5%)	Fisher's exact test; $p = 0.032$
Lateralization of MRI abnormality	Left 76 (17%) Right 57 (12.8%) Bilateral 97 (21.7%) Midline 217 (48.6%)	40 (18.2%) 32 (14.6%) 36 (16.4%) 112 (50.9%)	36 (15.9%) 25 (11%) 61 (26.9%) 105 (46.3%)	Fisher's exact test; $p = 0.053$	62 (16.8%) 45 (12.2%) 74 (20.1%) 188 (51%)	14 (18%) 12 (15.4%) 23 (29.5%) 29 (37.2%)	Fisher's exact test; $p = 0.115$
Localization of MRI abnormality	Temporal 149 Extratemporal 60 Periventricular 100	81 35 50	68 25 50	NA	118 57 85	31 3 15	NA
MRI findings[b]	Vascular 53 Volume loss 105 Malformation 46 Myelination defect 36	31 59 24 22	22 45 22 14	NA	45 92 41 32	8 13 5 4	NA

AED: antiepileptic drugs; F/I: febrile/infectious; gener: generalized; M: median; min: minutes; NEA: non-epileptiform abnormalities; SD: standard deviation; SE: status epilepticus; *x*: mean.

[a] At least double from baseline during the two weeks before SE.

[b] Numbers do not sum up to the total as some patients belonged into several categories.

2.5. Etiology

Etiology was determined based on all available clinical information from the clinical charts. This included physicians' notes, neuroimaging reports and other laboratory results. Febrile/infectious etiology includes both febrile seizures and seizures secondary to other infections (meningitis, sepsis, etc.).

2.6. SE definition

Once the study population was defined (patients with seizures of any duration), two different comparisons were performed changing the threshold, but not the study population. The first comparison was between patients with seizure duration of more or less than 5 min. The second comparison was between patients with seizure duration of more or less than 30 min. Therefore, two different definitions of SE were used in the same population: "impending" SE (SE_5) and "established" (SE_{30}). The characteristics of the same patient population were compared in two different ways: comparison of the characteristics of patients with SE_5 with their respective controls (patients with seizures less than 5 min duration) and comparison of the characteristics of patients with SE_{30} with their respective controls (patients with seizures less than 30 min duration). Each patient was classified according to the longest seizure duration during the study period, so that if a patient presented with an episode of $\geq$30 min during the study period that patient was considered to belong to the SE_{30} group regardless of whether this patient had a seizure of 5–29 min at any other time during the study period. Clusters of convulsive seizures each lasting less than 5 min but recurring without return to consciousness were considered equivalent to continuous seizures. Non-convulsive SE, specifically electrographic seizures without a convulsive correlate, were not analyzed in this study as we only included episodes with convulsive onset.

2.7. Statistical analysis

The characteristics of patients with SE_5 and SE_{30} were compared to those of their respective controls. In univariate analysis, categorical variables were compared with Fisher's exact tests and continuous variables were compared with Wilcoxon rank-sum tests. A multivariable logistic regression was performed with the variables that were considered clinically relevant. Since this is a descriptive study with no specific hypothesis being tested, no attempt was made to correct for multiple comparisons. For descriptive data, we analyzed the non-missing data only. For logistic regression, we also performed a complete case analysis approach. All tests were performed at a "two-sided" significance level of 0.05. STATA 12.0 (Stata Corp, College Station, TX, USA) was used for all statistical analyses.

3. Results

3.1. Demographic and clinical characteristics

1062 pediatric patients were enrolled in the study. When considering the 5 min seizure duration threshold, 444 (41.8%) patients had SE_5 while 618 (58.2%) did not. When considering the 30 min seizure duration threshold, 149 (14%) patients had SE_{30} while 913 (86%) did not. The main demographic and clinical characteristics are summarized in Table 2.

3.2. Electroencephalographic findings

An EEG was performed prior to the index episode in 516 patients, being abnormal in 429 (83.1%) of them. EEG abnormalities were more frequently generalized spikes and non-epileptiform abnormalities such as slowing or asymmetries (Table 2).

3.3. MRI findings

An MRI was performed prior to the episode in 446 patients and was abnormal in 266 (59.6%). Among the abnormal MRIs, findings were most frequently bilateral localized to the temporal lobe. The most frequent type of MRI abnormality was neocortical or hippocampal volume loss (Table 2).

3.4. Potential RF for SE

On univariate analysis, risk factors for SE were not markedly different when considering a 5 min versus a 30 min cut-off. In both comparisons, patients with SE were younger at the age of seizure onset (median 1.5 versus 2.8 years for SE_5, $p < 0.00005$; and 1 versus 2.5 years for SE_{30}, $p < 0.00005$) and at the age of SE (median 5.5 versus 7.1 years for SE_5, $p = 0.0499$, and 4.2 versus 6.8 years for SE_{30}, $p = 0.0029$), were on more AEDs at baseline (median 1 versus 1 for SE_5, $p < 0.00005$ and 2 versus 1 for SE_{30}, $p = 0.0001$), had a higher rate of changes in AEDs in the three months prior to the episode (33% versus 7% for SE_5, $p < 0.0005$; and 35% versus 16% for SE_{30}, $p < 0.0005$), were more likely to have developmental delay at baseline (58% versus 45% for SE_5, $p < 0.0005$; and 62% versus 48% for SE_{30}, $p = 0.001$). Patients with SE had a higher baseline seizure frequency (3 versus 1 seizures per month for SE_5, $p = 0.0005$; and 2.5 versus 1 seizures per month for SE_{30}, $p = 0.1131$), and a higher increase in seizure frequency prior to the index episode (29% versus 15% for SE_5, $p < 0.0005$; and 25% versus 20% for SE_{30}, $p = 0.314$) although this difference only reached statistical significance when using the 5 min seizure duration threshold.

3.5. Mortality

On univariate analysis, patients with SE had a higher mortality rate within the study period (4.7% versus 0.3% for SE_5, $p < 0.0005$; and 6% versus 1.5% for SE_{30}, $p = 0.002$).

3.6. Multivariate analysis

On multivariate analysis, the etiology (or MRI abnormality) and AEDs at baseline were the main predictors of the presence or absence of SE (Tables 3 and 4).

4. Discussion

We compared the characteristics of pediatric patients with SE and identified the following potential RF for SE: a younger age at seizure onset and at the time of the episode, being on more AEDs at baseline, a higher rate of changes in AEDs in the months preceding

Table 3
Multivariate regression model for the probability of having SE_5.

	Odds ratio	95% confidence interval	*p*-Value
Intercept	0.1813	0.0671–0.4897	NA
Gender	0.8259	0.5124–1.3314	0.432
Age at SE	0.9741	0.9310–1.019	0.255
Etiology	2.298	1.4869–3.5515	<0.0005
Developmental delay	1.186	0.7020–2.004	0.524
Number of AED at baseline	1.2799	1.0252–1.5979	0.029
AED changes	7.2645	3.6957–14.2798	<0.0005
Abnormal EEG	0.8578	0.4299–1.7117	0.663
Abnormal MRI	1.3028	0.7869–2.1569	0.304

AED: antiepileptic drugs; EEG: electroencephalogram; MRI: magnetic resonance imaging; SE: status epilepticus.

Table 4
Multivariate regression model for the probability of having SE_{30}.

	Odds ratio	95% confidence interval	*p*-Value
Intercept	0.0297	0.0065–0.136	NA
Gender	0.8785	0.4631–1.667	0.692
Age at SE	0.9597	0.9002–1.023	0.208
Etiology	1.5761	0.9200–2.7000	0.098
Developmental delay	1.6429	0.7317–3.6889	0.229
Number of AED at baseline	1.0292	0.7766–1.364	0.841
AED changes	3.0428	1.5076–6.1413	0.002
Abnormal EEG	1.0221	0.3542–2.9488	0.968
Abnormal MRI	3.2600	1.4779–7.1909	0.003

AED: antiepileptic drugs; EEG: electroencephalogram; MRI: magnetic resonance imaging; SE: status epilepticus.

the episode, and the presence of developmental delay at baseline. Risk factors did not differ markedly when comparing the different seizure duration thresholds for definition of SE at 5 and 30 min.

4.1. The concept of RF for SE

Reliable RFs that identify patients at higher risk for SE are essential for management, and counseling in patients with SE. Surprisingly, few studies have compared patients with SE to patients without SE in order to identify RFs[11–15] (Tables 1 and 5). Most RF identified in adults are related to medical co-morbidities that are much less common in children; therefore these identified RF cannot easily be applied to pediatric populations.[11,12]

4.2. RF for SE in children

As shown in Table 5, some pediatric RFs are more consistently reported than others. "Polypharmacy," "discontinuation/inconsistency of antiepileptic treatment," "developmental retardation,"[14] and "younger age at onset"[13] were reported in some series but did not present as RF in others.[14,15] The present series found more AEDs at baseline and changes in AEDs during the three months prior to the event as being a RF for SE. "Abnormal EEG,"[14,15] "history of SE as the first seizure presentation,"[15] and "presence of previous episodes of SE"[13] were identified as RFs for SE in other series. As previously reported,[13,15,17,18] the present series found that patients with a known etiology and underlying structural brain lesion had a higher risk for SE, although the group of patients with abnormal MRI is heterogeneous. The longer duration of seizures in SE may therefore also reflect a more severe underlying etiology in patients with SE compared to patients without SE.

4.3. SE definitions

The classical definition of status epilepticus (SE) or "established" SE requires that seizures (continuous or intermittent without return to baseline mental status) last for a minimum of 30 min.[5] However, seizures that last longer than 5 min are unlikely to stop spontaneously[19,20] and meet the definition of "impending" SE.[16] At present both definitions of SE ("impending" and "established") coexist in the literature but there is a striking lack of data evaluating whether RF are similar for "impending" or "established" SE.[21] Our study shows that RF for SE are similar regardless of the seizure duration threshold used for SE definition: SE_5 or SE_{30}. We compared different variables that define the main demographic and clinical characteristics of the study population. In these comparisons, the results were unaffected by the threshold considered: 5 or 30 min. Seizure frequency at baseline and increased seizure frequency prior to the index episode were higher in the SE episode regardless of the seizure duration threshold, adding to the robustness of our results, although they only reached statistical significance in the SE_5 group.

4.4. Strengths and weaknesses

Findings need to be interpreted in the setting of data acquisition as retrospective data collection can be subject to information bias. Duration of seizures is recorded heterogeneously in the clinical charts and sometimes information was not available, which accounts for missing data in the "variable" duration of seizures. Duration of seizures may have been both under- and over-estimated as information is dependent on the accuracy of seizure duration data in the clinical charts. A standardized data collection instrument was used to overcome potential heterogeneity in data collection from available information. In addition, information was collected from all available sources within the clinical charts (physicians' notes, nurses' notes, and emergency medical services' notes) to minimize the potential for information bias and the potential of under- and over-estimation of seizure duration. Inaccurate data can be found in the clinical charts, but this limitation is minimized when collecting information from different sources, which allows for identification of observation and documentation errors.

Patients admitted to a reference pediatric hospital are an inherently biased population with more severe conditions. This limitation is common in tertiary reference hospital studies. However, only reference hospital studies allow for the collection of large patient populations. Some degree of selection bias is expected in this study as seizures lasting more than 30 min are more likely to be cared for in a hospital than shorter seizures. We did not intend to capture all patients with seizures of short duration, but to compare groups with the same characteristics except for the duration of seizures.

Table 5
Risk factors of pediatric convulsive status epilepticus.

	Drugs	DR	EEG	Status epilepticus	Trigger/predisposition	Types of seizures	Age
KarasalİhoĞlu et al.[14] *N* = 249	PP OR = 5.2 D OR = 4	OR = 4	OR = 2.5				
Novak et al.[15] *N* = 132			OR = 6.5	FSE OR = 4	MRI OR = 2.85	PSSG OR = 4.61	
Berg et al.[13] *N* = 613				HS RR = 4.5	SE RR = 2.5		YA RR = 0.9 per year
Present study, *N* = 1062	PP CD	DR					YA

CD: changes in AEDs in the three months prior to the episode; D: discontinuation/inconsistency of antiepileptic treatment; DR: developmental retardation; EEG: abnormal EEG; FSE: first seizure as status epilepticus; HS: history of status epilepticus; MRI: other abnormal magnetic resonance imaging; *N*: number of patients included in the study; OR: odds ratio; PP: polypharmacy; PSSG: history of partial seizures with secondary generalization; RR: rate ratio; YA: younger age at onset.

Clinical features were interpreted and recorded in the clinical charts by different medical teams for each patient posing the potential for variability and confounding of results. However, inter-rater reliability in recognizing SE in an acute setting is good with a concordance reported in the literature of 60–81%.[22] In addition, we retrospectively classified patients as having or not having SE based on objective features from the clinical charts (i.e. duration) and not on different interpretations or definitions of SE by the different medical teams.

Our study did not evaluate EEG findings or neuroimaging findings with the level of detail which can be found elsewhere.[9,23] A major factor in SE duration is the timely and appropriate administration of AEDs. Unfortunately, we did not have enough information on that aspect to perform a formal analysis of these relevant factors. The Pediatric Status Epilepticus Research Group (pSERG) is developing a prospective approach to describe the timing of SE treatment and its impact on management and outcome.[24]

Our results support the hypothesis that defining SE as seizures lasting either 5 or 30 min does not change most of the characteristics of the population defined as having SE. This may influence future categorizations of SE as seizures lasting for at least 5 min. Further, our study may facilitate comparisons of prior studies that defined SE with different thresholds of 5 or 30 min duration. The current findings suggest that these populations were roughly comparable.

Our findings apply to convulsive SE. Non-convulsive SE is usually different from convulsive SE in terms of etiology and clinical features. We preferred to focus only on convulsive SE to have a more homogeneous study population.

A major strength of this study is the large patient population that allowed us to identify RFs that may have gone unnoticed in previous smaller series. In addition, the large number in this series allowed the comparison of RFs for the most frequent seizure duration thresholds of SE used in the pediatric literature: 5 and 30 min.

4.5. Conclusions

This study of pediatric patients identified several RFs that predicted SE: younger age, developmental delay at baseline, more AEDs at baseline and a higher rate of changes in AEDs prior to the episode. These risk factors were similar when considering SE with a seizure duration threshold of 5 min versus 30 min.

Conflicts of interest statement

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None of the authors has any conflict of interest to disclose.

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