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## Seizure clustering during presurgical electroencephalographic monitoring in children

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### ABSTRACT

**Background:** Presurgical evaluation with antiseizure medication tapering in patients with refractory epilepsy places them at risk for seizure clustering or prolonged seizures. We looked at the occurrence of seizure clustering (3 or more seizures within 24 h) and prolonged seizures and the factors that influence seizure clustering and affect length of stay (LOS) in pediatric patients during presurgical monitoring.

**Methods:** We retrospectively reviewed the medical records of all consecutive admissions to the epilepsy monitoring unit (EMU) and included patients undergoing noninvasive presurgical evaluation. Data were extracted regarding demographics, seizure history, details of the EMU admission including occurrence of seizure clusters, prolonged seizures, status epilepticus, treatment, and LOS.

**Results:** Sixty-nine patients met our inclusion criteria. Seizure clustering during monitoring was observed in 33 patients (48%). Prolonged seizures lasting >5 min was observed in 14 (20%) patients including 2 with status epilepticus (3%). Seizure clusters necessitated rescue treatment in around 30%. History of seizure clustering at home was the only factor associated with the occurrence of seizure clustering during the EMU stay ( $p < 0.0001$ ). The LOS did not differ significantly between patients who had seizure clustering during monitoring versus those who did not ( $p = 0.369$ ).

**Conclusions:** Seizure clustering was common in children undergoing presurgical monitoring and seen especially in those with a history of seizure clustering at home. Occurrence of seizure clustering did not prolong the LOS but necessitated the use of rescue medications in about a third of the patients with seizure clusters due to multiple seizures.

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### 1. Introduction

Epilepsy affects approximately 0.5 to 1% of all children through the age of 16 years [1], and among this group, approximately 20% of children will have pharmaco-resistant epilepsy [2]. Surgical resection can be an effective treatment option for refractory epilepsy. Video electroencephalogram (EEG) monitoring in the epilepsy monitoring unit (EMU) and successful recording of seizures are essential steps in presurgical evaluation [3]. Tapering or withdrawal of antiseizure medications is often necessary to complete these recordings, though these medication adjustments may place patients at risk for seizure clustering or prolonged seizures [4,5]. The occurrence of seizure clusters and status epilepticus have been identified by some as quality indicators in adult EMUs [6]. Seizure clustering during these presurgical evaluations may contribute to longer inpatient stays in adults [7]. Additionally, seizure clustering can be associated with an increased risk for SE and exhibit a

cluster effect (whereby concordance of seizure localization is affected by length of interseizure interval within a cluster) [8]. The cluster effect can affect surgical decision making.

Defining seizure clustering can be challenging [9]. Seizure clustering can be defined for the purposes of identifying the cluster effect whereby seizures separated by shorter interseizure intervals are more likely to be concordant for localization than temporally isolated seizures. Seizure clustering can also be defined for the purposes of EMU safety to determine the threshold for rescue treatment, with the goal of preventing adverse events. A recent study defined seizure cluster by an interseizure interval of less than 4 h [10]. A cluster definition of three or more seizures within any 24-hour period of EMU monitoring has been commonly employed in the literature [4,5,11,12]. Currently there is no consensus for a definition of seizure clusters, either for the purpose of ensuring safety in the EMU monitoring or for identifying the cluster effect.

The prevalence of seizure clustering in the outpatient setting has been reported to be nearly 30% [13] and varied (depending upon the definition of clustering) from 18 to 61% for inpatient epilepsy

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monitoring [8]. A population-based study of the prevalence of acute repetitive seizures reported that about 3% of people with active epilepsy are affected by acute repetitive seizures (as defined by three or more focal or generalized seizure episodes over a 24-hour period) [14] with highest prevalence in the very young. Despite the increased prevalence of seizure clustering in the pediatric population, there is a paucity of information regarding seizure clustering in children admitted to the EMU.

We have previously reported the predictors of seizure occurrence in children undergoing presurgical monitoring [15] and found that 92% of the presurgical admissions had at least one seizure during a mean length of stay of 5.2 days, and home seizure frequency was the only predictor influencing occurrence of seizures while in the EMU.

In the current study, we examined the occurrence of seizure clustering in consecutive admissions for presurgical monitoring. We also assessed factors affecting seizure clustering and the influence of seizure clustering on the duration of hospital stay.

## 2. Methods

Patient eligibility and inclusion were previously described [15]. We retrospectively reviewed the medical records of all consecutive admissions to the EMU from October 2009 to May 2011 and included only patients undergoing noninvasive presurgical evaluation. If patients were admitted twice during the study period, only the first admission was considered. We included patients with electroclinical seizures and excluded those with no seizures or electrographic-only seizures. Patients with exclusively spasms/tonic spasms, head drops, and myoclonic seizures were excluded, as these seizure types tend to occur with high frequency (see flow sheet).

Home seizure frequency was categorized as follows: baseline seizure-frequency was considered low if patients had up to one seizure per month; medium if up to one seizure per week; and high if more than one seizure per week. Magnetic resonance images (MRIs) were classified as abnormal if they showed structural abnormalities that are commonly reported in children with epilepsy. Nonspecific MRI abnormalities included volume loss, thin corpus callosum, gliosis, and type I Chiari malformation.

We defined a cluster as three or more seizures within any 24-hour period; either focal seizures with impaired awareness or generalized tonic-clonic seizures [4,5,11,12]. A prolonged seizure was present if a seizure lasted more than 5 min. Status epilepticus (SE) was defined as a single seizure lasting  $\geq 30$  min or repeated seizures over 30 min without recovery of full consciousness.

The following data were extracted from the charts: age of seizure onset, duration of epilepsy, and personal history of seizure clustering or prolonged seizures including SE and MRI results. When a history of clustering or prolonged seizure was not explicitly stated, it was categorized as unknown. Details of the EMU course for each subject were collected including the following: reduction or discontinuation of anti-seizure medications, length of stay, number of electroclinical seizures recorded during the EMU admission, results of ictal single-photon emission computed tomography (SPECT), and the presence of seizure clustering and/or prolonged seizures/SE during monitoring. The presence of seizure clustering was ascertained from the patient records during hospitalization and confirmed on the EMU report. Time, date, seizure type, and need for intravenous medication were obtained from the medical records/EMU reports for all patients.

### 2.1. Medication withdrawal and seizure management in EMU

For patients who had multiple daily seizures at home, antiseizure medications were not tapered upon admission. Tapering was generally performed in the remainder of patients as follows: a 50% reduction in dosage on day 1, followed by tapering and complete discontinuation by day 2 or day 3. Sleep deprivation was performed in some patients to aid seizure capturing. In the setting of medication wean, we have a

treatment protocol to administer IV lorazepam in the event of  $\geq 2$  seizures in 1 h or  $\geq 3$  seizures in 4 h, or a single generalized tonic-clonic seizure lasting  $>5$  min. This study was approved by the Institutional Review Board at Boston Children's Hospital.

## 3. Statistical analysis

Descriptive statistics, including median and interquartile ranges (IQR) of continuous variables and frequencies of categorical variables are reported for the entire sample in Table 1. The primary outcome variable of seizure clustering was defined as a binary variable in terms of absence or presence of seizure clusters. The differences in the medians (or the ranks) for the continuous variables in the clustering and nonclustering groups were determined using the Wilcoxon rank-sum test. Similarly, the chi-square tests (or Fisher's exact test with any cell count  $<5$ ) were employed to test the associations between the categorical predictors and the primary outcome variable. Statistical analysis was performed using SAS, version 9.3 (SAS Inc., Cary, NC) and IBM SPSS Statistics, version 20 (IBM Corporation, Armonk, NY). The multiple comparison adjustment was performed using a conservative Bonferroni correction.

## 4. Results

Sixty nine patients (41% females) were eligible for analysis (see Fig. 1). Demographic and descriptive characteristics of the subjects are provided in Table 1. History of seizure clustering at home was reported by 33 patients (48%) and 25 (40%) reported a history of having had prolonged seizures.

### 4.1. Video EEG monitoring

Antiseizure medications were reduced in 91% of patients. A total of 755 seizures were recorded (median number of seizures per patient = 6; IQR: 3–13) during monitoring. Ictal SPECT was obtained in 58 patients (84%). Of the 11 patients without ictal SPECT, 5 patients had seizure clustering while the remainder did not (Table 2).

**Table 1**  
Demographic and clinical features (n = 69).

Characteristic	Total
Age	
Median (IQR)	12.00 (8.50)
Sex	
Male	41 (59.4%)
Seizure frequency	
low	11 (15.9%)
medium	22 (31.9%)
high	36 (52.2%)
Duration of epilepsy (years)	
Median (IQR)	5.50 (7.50)
Age of onset of seizures (years)	
Median (IQR)	4.00 (8.33)
History of seizure clusters at home	
Yes	32 (46.4%)
No	36 (52.2%)
Unknown	1 (1.4%)
History of prolonged seizure	
Yes	25 (36.2%)
No	37 (53.6%)
Unknown	7 (10.1%)
MRI	
Normal	18 (26.1%)
Abnormal	41 (59.4%)
Nonspecific	10 (14.5%)
Med reduction	
Yes	63 (91.3%)
No	6 (8.7%)
Time to first seizure in EMU (days)	
Median (IQR)	2.00 (2.00)

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