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Short communication

Acute postoperative seizures and long-term outcome following pediatric epilepsy surgery

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ABSTRACT

Purpose: Acute post-operative seizures (APOS) after epilepsy surgery, previously believed to be benign, are increasingly associated with poor long-term prognosis. Prior literature has focused primarily on adult temporal lobe epilepsy. This retrospective study aimed to identify the prevalence, prognostic significance and risk factors for APOS in pediatric epilepsy surgery at a single center.
Method: Retrospective chart review of all children aged 0–21 years undergoing resective surgery for epilepsy between 2009 and 2012 at a single center. APOS were defined as seizures within 30 days of resection. Surgical outcome was determined, using a minimum of 12 months postoperative follow-up for inclusion.
Results: APOS, defined as a seizure within 30 days of resection, were identified in 50/112 (44%) of patients. APOS were a significant predictor of poor postoperative seizure outcome (ILAE 4–6); only 26% of those with APOS had a good outcome (ILAE 1–3), compared to 76% without APOS. Timing of postoperative seizure was not correlated with outcome. Most (54%) with APOS and good outcome had continued seizures between 14-30 days postoperatively. Patients with APOS after temporal ($p = 0.05$) and extratemporal ($p < 0.001$) resections had a significantly worse prognosis. APOS after hemispherectomy were not associated with a worse prognosis ($p = 0.22$). Key risk factors for APOS include lack of ictal EEG lateralization to operated hemisphere/side of MRI abnormality.
Conclusion: This study shows an association between APOS and poor outcome in both temporal and extratemporal pediatric epilepsy surgery. Findings support the expansion of APOS duration to 30 days.

1. Introduction

Acute post-operative seizures (APOS) are seizures occurring shortly after resective epilepsy surgery. APOS have been conventionally defined as seizures occurring during the first postoperative week.[1] However, experience particularly with complex extratemporal epilepsy surgery in children suggests that APOS may continue up to the first month after surgery. This is reflected in the new ILAE outcome classification, which excludes seizures occurring during the first month after surgery since they may be related to the surgery itself and "do not predict long-term outcome".[2] Previous studies defined APOS as seizures occurring between 1 and 14 days postoperatively, typically only 1 week. The reported prevalence of APOS in pediatric studies ranged from 22% to 26%.[3–5]

There is considerable disagreement in the literature on whether APOS predict poor long-term seizure outcome. Although initially regarded as unimportant, several studies report a significant association with APOS and poor outcome.[3,4,6–8] Several risk factors for APOS, including younger age, invasive monitoring, postoperative interictal EEG abnormalities and incomplete MRI abnormality resection, were identified, predominantly in adults with temporal lobe epilepsy.[5,7] APOS with similar semiology to preoperative seizure was an important negative prognostic factor for adults with nonlesional temporal lobe epilepsy[8]; this has not been studied in children. There is very little pediatric literature investigating the impact of surgery location (temporal, extratemporal or hemispherectomy), risk factors for APOS and long-term prognosis. In a large single-center pediatric series, we sought to determine the risk factors for APOS and impact of APOS on long-term prognosis.

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2. Materials and methods

2.1. Patients and APOS definition

This study is a single-center retrospective chart review. Electronic medical records for children age 0–21 years undergoing resective surgery for epilepsy between 2009 and 2012 were reviewed. A minimum 12 months postoperative follow-up was required. For patients who had a re-operation due to poor initial outcome, long-term seizure outcome was assessed on the date of the second operation. Children undergoing re-operation with sufficient follow-up after second operation were analyzed for APOS again and therefore could be "counted twice" if both operations occurred during the study period. All follow-up visits were reviewed and date of first postoperative seizure was recorded. APOS were defined as seizure(s) occurring within 30 days after resection. Seizure semiology both pre-and-postoperatively was reviewed to determine similarity. Seizure semiology was considered similar if a) parents reported the seizures appeared similar or b) detailed pre-and-postoperative descriptions were available and were highly concordant.

2.2. Classification of presurgical testing and surgery type

Resection locations were determined based on operative reports. All surgeries were performed by a single neurosurgeon (FM), after multimodality presurgical evaluation as previously described.[9] Hemispherectomy was performed using a peri-insular functional hemispherotomy technique. Surgery locations were defined as either (1) *hemispherectomy*, (2) *temporal* resection only, (3) *extratemporal* single lobar resection only or (4) *multilobar* resections which could include temporal lobe. MRI was defined as either normal (which also included MRIs with only nonspecific findings); lesional unilateral (including neoplasm, focal cortical dysplasia, stroke, trauma or encephalitis); or lesional bilateral (including tuberous sclerosis complex (TSC). Ictal EEG was defined as lateralizing to left or right or bilateral (including both multifocal bilateral independent ictal onset and bilateral/diffuse ictal onset). EEG was classified as either concordant (ictal EEG lateralized to operated hemisphere) or discordant (ictal EEG either contralateral to operated hemisphere, bilateral independent or nonlateralizing). MRI/EEG concordance was defined as presence of a unilateral MRI lesion concordant with lateralized ictal EEG and operated hemisphere. A head computed tomography (CT) scan was routinely ordered 2 h postoperatively to evaluate for acute neurosurgical complications. Brain MRI and anticonvulsant levels were not routinely ordered. Long-term outcome was determined using ILAE classification 1–6 scale.[2]

2.3. Statistics

Descriptive statistics were performed using Microsoft Excel (Microsoft Corp., Redmond, WA). ILAE outcome was dichotomized as good for ILAE 1–3 (up to 3 seizure days/yr) and bad for ILAE 4–6 (between >3 seizure days/yr and >100% increase in seizure days). Using SAS (SAS Institute, Cary, NC), Fisher exact test was performed for categorical variables. Logistic regression was performed to analyze the relationship between time to first postoperative seizure and outcome as well as relationship between APOS, postoperative seizure semiology (similar or different to preoperative) and outcome.

3. Results

3.1. Patients and hospital course

One hundred five patients met initial inclusion criteria; one was lost to follow-up. Therefore 104 patients were included; 8 had two operations during the study period, for a total of 112 cases. APOS were observed in 50 (44%) patients. The mean age at surgery in both children with APOS and without APOS was 9.9 years (SD 6). There were no significant differences in proportion of hemispherectomy, temporal, extratemporal or multilobar surgeries (Table 1, Fisher exact). The most common etiology was focal cortical dysplasia ($n = 62$). Other etiologies included TSC ($n = 13$), stroke ($n = 6$), infectious encephalitis ($n = 6$), tumor ($n = 5$), Rasmussen encephalitis ($n = 4$), mesial temporal sclerosis without dual pathology ($n = 4$), hemimegalencephaly ($n = 3$), trauma ($n = 2$), hypoxic–ischemic encephalopathy ($n = 2$) and five other single causes. Serious acute adverse effects to surgery were seen in 9 patients. Six had a wound infection, two had venous infarctions with transient deficits and one had postoperative hematoma requiring re-operation. Of these, only two had APOS; both were the cases with venous infarctions and good long-term outcome was achieved.

3.2. APOS and long-term outcome

Mean length of follow-up was 26 months (SD 11), with a minimum postoperative follow-up of 12 months. In all, 42 (37%) had a class I outcome and 60 (54%) had up to 3 seizure days/yr (ILAE 1–3). Twenty-one were ILAE 4, 26 were ILAE 5, and 6 were ILAE 6. APOS were significantly associated with a higher rate of poor long-term seizure outcome (26% v. 76%, $p < 0.001$, Fisher exact). Of the 13 with APOS and good outcome, 10 had APOS onset <7 days postoperatively, compared to only three with good outcome when APOS onset was >7 days ($p = 0.104$, Fisher exact). However, seizures continued >14 days postoperatively in 7/13 (54%) with eventual good outcome. APOS with a similar postoperative semiology were associated with lower odds of good outcome; 56/77 patients with either no APOS or APOS with different semiology had good outcome, compared to 4/35 with a similar semiology APOS ($p < 0.001$, Fisher exact). However, using logistic regression to model the probability of a poor outcome, no significant difference was observed between APOS and APOS with similar semiology. Thirty patients were seizure free for duration of follow-up. In those with postoperative seizures ($n = 82$), the relationship between timing of first postoperative seizure and outcome was not significant using a logistic regression model, producing an odds ratio approximately equal to 1.0 (Fig. 1).

Table 1
Patient characteristics by the presence/absence of acute postoperative seizure (APOS).

	Mean age (yrs) at surgery	Hemispherectomy	Temporal	Extra-temporal	Multilobar	MRI lesion	Etiology FCD	ILAE 1–3 (good outcome)
No APOS ($n = 62$)	9.9 (SD 6.2)	20 (33)	10 (16)	16 (26)	16 (26)	48 (77)	35 (56)	47 (76)
APOS ($n = 50$)	9.9 (SD 6)	9 (18)	7 (14)	22 (44)	12 (24)	30 (60)	25 (50)	13 (26)*

FCD = focal cortical dysplasia; ILAE = International League Against Epilepsy seizure outcome classification.
* $p < 0.001$, Fisher exact.