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Authors

Pehlivan, Esra
Zempel, John
Coble, Janette
et al.

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Advanced Technology Clinic Provides Personalized Approach to Pediatric Epilepsy Surgery: Early Data and Future Directions

by Esra Pehlivan, MD, John Zempel, MD, PhD, Janette Coble, RN, Sara Graves, RN, Sean McEvoy, MD, Matt Smyth, MD, Kwee Liu Lin Thio, MD, Christina Gurnett, MD, PhD, Jarod Roland, MD, Réjean M. Guerriero, DO & Stuart R. Tomko, MD

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by Esra Pehlivan, MD, John Zempel, MD, PhD, Janette Coble, RN, Sara Graves, RN, Christina Gurnett, MD, PhD, Kwee Liu Lin Thio, MD, Réjean M. Guerriero, DO, (pictured), and Stuart R. Tomko, MDs, are all in the Division of Pediatric and Developmental Neurology, Department of Neurology. Washington University School of Medicine, St. Louis, Missouri.
Sean McEvoy, MD, Jarod Roland, MD, and Matt Smyth, MD, are in the Division of Pediatric Neurosurgery, Department of Neurology, Washington University School of Medicine, St. Louis, Missouri.
Matt Smyth, MD, is also in the Division of Pediatric Neurosurgery, Johns Hopkins All Children's Hospital, St. Petersburg, Florida.

Abstract

Objective: Postoperative improvement in seizures may impact quality of life. We examined the relationship between reduced seizure burden and quality of life in a surgical epilepsy clinic.

Methods: We reviewed data from all children who received epilepsy surgery at our center. Surgeries were classified as palliative or definitive based on the seizure outcome goals. We collected demographics, surgical data, Engel classification, and quality of life outcomes.

Results: Between 2016 and 2024, 282 patients underwent 338 surgeries. In the definitive surgery group, 66 patients (58%) attained an Engel 1 outcome at six months and 46 patients (58%) at 24 months. In the palliative surgery group, six patients (7%) attained an Engel 1 outcome at six months. At 12 months, 75% of patients who attained Engel 1 reported lower depression scores.

Conclusion: Improvement in seizure burden and quality of life outcomes following epilepsy surgery may be related. Further outcomes research is required.

Introduction

Epilepsy is the most prevalent long-term neurological condition in children, affecting up to 1% of the pediatric population.[1] Nearly a quarter of children with epilepsy become drug-resistant.[2,3] Children with drug-resistant epilepsy (DRE) have decreased life expectancy and reduced quality of life (QOL).[4] Surgical intervention is an option to eliminate or reduce seizures for children with medication-resistant epilepsy and increases life expectancy.[5-7] However, post-operative reduction in seizure burden may not always improve quality of life, indicating there may be multifactorial risk factors responsible for suboptimal outcomes.[8,9]

The documented rate of seizure control ranges from 41% to 76% following definitive surgery,[10-13] with the majority of studies referencing Engel classification.[14] Seizure-free rates decline over time following epilepsy surgery. A recent meta-analysis of 258 studies on temporal, extratemporal lobe resections, and hemispherotomies demonstrated a decline of seizure-free patients from 64.8% to 60.3% and 39.7% after one, five, and ten years of follow-up.[6]

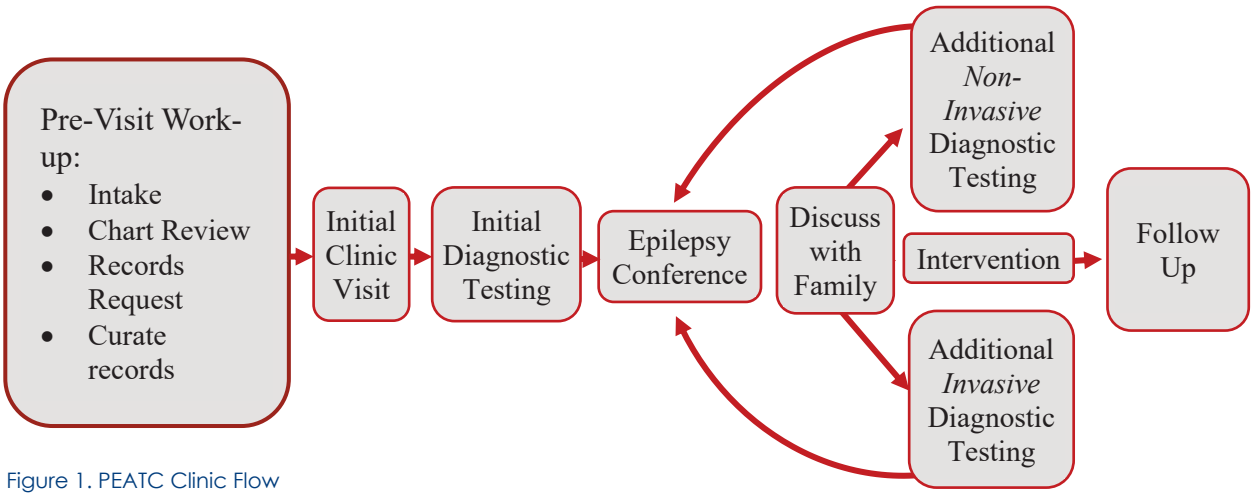

Figure 1. PEATC Clinic Flow

Previous studies have shown a correlation between a favorable seizure outcome and improved quality of life.[1,15,16] With improving diagnostic technologies and more refined, minimally invasive approaches to surgery, the number of patients eligible for surgery or device placement is increasing. In these patients, the goal of epilepsy surgery is "palliative" seizure reduction and improved quality of life. The relationship between decreased seizure burden and improved function and quality of life of individuals who have had surgery is less well defined.[17] In this report, we aimed to evaluate our seizure outcomes for patients undergoing definitive versus palliative surgeries and evaluate early data collected on postoperative functional and quality of life measures.

Methods

Data was collected for all patients evaluated in our Pediatric Epilepsy Advanced Technologies Clinic (PEATC) at the Washington University Pediatric Epilepsy Center at St. Louis Children's Hospital, St. Louis, Missouri. Patients are referred from the greater metropolitan region and surrounding states. The clinic workflow is summarized in Figure 1.

We collected demographic and clinical data in REDCap [18] for patients seen in PEATC from May 2019 to May 2024. This included age at referral, type of surgery, and postoperative outcomes scored by providers (Engel score), as well as a self-reported survey (QOLCE-16) by patients or families. The data was collected from surgery documentations between January 2016 and May 2019. We collected additional clinical data from EPIC, including age, sex, ethnicity, and PROMIS scores. QOL surveys were initiated in 2019, but there was a yearlong gap between 2019-2020 due to the COVID-19 pandemic.

Patients underwent individualized presurgical evaluation that may include scalp electroencephalography (EEG) with video telemetry, high-resolution magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), functional magnetic resonance imaging (fMRI), intracarotid amobarbital procedure (WADA), magnetoencephalography (MEG), high-density electroencephalography (EEG) recordings and neuropsychological evaluation. Patients were followed up as clinically indicated, but typically, occurring at approximately six, 12, and 24 months post-surgery.

Surgery was categorized into two groups: definitive and palliative. The definitive group included all procedures in which the primary goal was curative with an expectation for seizure freedom or freedom from primary seizure type, as would be the case for patients with tuberous sclerosis complex (TSC). The definitive procedures were lesionectomy, temporal and extratemporal resection, hemispherotomy, and disconnections. Surgery types were coded according to the operation note, not related to the pathology of the specimen or independent review of the MRI. Examples of lesionectomy included focal cortical dysplasia, tuberous sclerosis, and low-grade tumors. Temporal resection included mesial temporal and/or hippocampal sclerosis. Disconnections included frontal or posterior-quadrant disconnections.

The palliative group included procedures in which the primary goal was to decrease seizure burden or severity. The palliative procedures were vagus nerve stimulation (VNS), deep brain stimulation (DBS), and responsive neural stimulation (RNS), as well as corpus callosotomy. Radiofrequency ablation (RFA) was included as a separate category, given it was both a diagnostic and therapeutic procedure with anticipation for future definitive procedure as needed.

Following surgery, the patient's primary epileptologist was asked to provide Engel classification at six, 12, and 24 months. The Engel epilepsy surgery outcome scale is extensively used to categorize results after surgical intervention for medically resistant epilepsy. Engel class 1 refers patients who are free of disabling seizures, with 1A considered to have complete seizure freedom. Class 2 is classified as rare disabling seizures. Class 3 represents worthwhile improvement in seizures and Class 4 is described as no appreciable change in seizures. For analyses we considered Engel 1 and 2 as favorable outcome. Engel outcome at 12 months was chosen for group comparisons due to the longer outcome than six months and relatively few responses at 24 months.

Depression and cognitive function scores were evaluated using the patient-reported outcomes measurement information system (PROMIS), a measurement system that evaluates physical, mental, and social health, well-being, life satisfaction, as well as sensory, motor, and cognitive function[19]. The quality of life in childhood epilepsy questionnaire (QOLCE-16) was utilized to assess overall QOL.[20] For QOL and cognitive function, increasing scores suggest improvement while for depression a decrease implies improvement. Patients were sent these surveys to fill out. Subsequent surveys were requested periodically during follow-ups. Due to the small number of QOL metrics, all surgical resections were considered one group for statistical analysis.

Basic statistics were completed, including summary statistics and Chi-square to evaluate for group difference. A p-value of less than or equal to 0.05 was deemed as statistically significant. Statistics were done with Stata version 16 (College Station, TX: StataCorp LLC).

Table 1. Patient demographics

	N= 282 (%)
Sex	
• Female	129 (46)
• Male	153 (54)
Race	
• White	239 (85)
• African/American	26 (9)
• Asian	5 (2)
• Hispanic	10 (3)
• American Indian	1 (0.4)
• Pacific Islander	1 (0.4)

Results

Between May 2019 and May 2024, PEACT received referrals for surgical evaluation from 534 patients, with 209 being selected for surgery. Seventy-three patients underwent epilepsy surgery between January 2016 and May 2019. Between January 2016 and May 2024, a total of 338 surgeries were performed on 282 patients, with the number of procedures per patient varying from one to four. Patient demographics, including sex and self-identified race are reported in Table 1. Patient age ranged from three months to 28 years at the time of referral. Surgery types are summarized in Table 2.

Of the 338 surgeries, 200 were palliative, 130 were definitive, and eight RFA. For neuromodulation, most received VNS therapy 133 (39%), while DBS and RNS were performed on 10 (0.02%) and four (0.01%) patients, respectively. Corpus callosotomy was performed on 53 (16%) patients. Among the definitive surgery group, lesionectomy was the most performed, accounting for 54 cases (16%). This was followed by extratemporal lobe resection, 24 cases (7%) and temporal lobe resection, 22 cases (6.5%). Laser interstitial thermal therapy (LITT) was used in 59 procedures (17%). Eight (2%) radiofrequency ablation was performed.

Engel score was reported for 204 procedures at six months, 179 procedures at 12 months, and 121 procedures at 24 months combined with definitive and palliative procedures. A favorable clinical outcome

Table 2. Surgical intervention and favorable seizure outcome during follow up

	N= 338 (%)	6 mo	12 mo	24 mo
Palliative				
Corpus callosotomy	53 (16)	8 (15)	8 (15)	6 (11)
Neuromodulation	147 (43)			
VNS	133 (39)	7 (5)	7 (5)	3 (2)
DBS	10 (3)	1 (10)	5 (50)	5 (50)
RNS	4 (1)	0	1 (25)	1 (25)
Definitive				
Lesionectomy	54 (16)	29 (54)	25 (46)	20 (37)
Extratemporal resection	24 (7)	21 (87)	14 (58)	13 (54)
Temporal resection	22 (7)	12 (54)	11 (50)	7 (32)
Hemispherotomy	20 (6)	15 (75)	12 (60)	11 (55)
Disconnection	10 (3)	5 (50)	5 (50)	5 (50)
RFA	8	3 (38)		

VNS vagal nerve stimulation, DBS deep brain stimulation, RNS responsive neurostimulation, RFA radiofrequency ablation

(Engel class 1 or 2) was observed in 79 patients (69%) with 66 (58%) patients being seizure-free at six-month follow-up in the definitive surgery group. Engel 1 scores were in 55 (55%) and 46 (58%) patients at 12 and 24-month follow-up, respectively. As anticipated, there was a significant difference in Engel classification between patients in definitive versus palliative surgery groups. The definitive surgery group had an Engel score of 1.9 (SD 1.13), while the palliative surgery group was 3.1 (0.09), ($p < 0.005$) at 12-month follow-up. Engel scores are summarized in Table 3.

Stereo electroencephalography (sEEG) was performed in 55 (47%) of the 118 resective procedures. There was no statistically significant difference between Engel scores for patients who did (mean 2.21, SD 1.14) or did not undergo sEEG (mean 1.84, SD 1.51) ($p = 0.23$). For resective procedures there was no statistically significant difference in Engel score at 12 months between the use of LITT (mean 2.29, SD 1.12) versus open surgery (mean 1.87, SD 1.14), ($p = 0.17$).

Pilot data was collected on patient reported QOL using PROMIS and QOLCE-16 questionnaires. The QOLCE-16 was completed by 39 patients at baseline and 22, 28, and 18 patients at six, 12, and 24 months, respectively. Some patients who had multiple surgeries completed multiple questionnaires for each surgery. The PROMIS was completed by 62 patients at baseline and 43, 49, and 32 patients at six, 12, and 24 months, respectively. QOL, depression, and cognitive function were analyzed as post-operative changes from baseline (increase, decrease, or no change) at six and 12 months due to the few observations with both baseline and 24-month results.

At the 12-month follow-up, depression and Engel scores were available for 18 patients, and QOL and Engel scores for 12 patients. Three out of the four patients with Engel 1 reported a decrease in their depression scores, while one patient reported no change, as their score remained within normal limits. Two of three patients (66%) with Engel 1 reported mild decrease in quality of life. Of the patients who reported a change in QOL, there was not a significant difference in Engel score between increase or decrease QOL (p=0.66). There was also not a significant difference in Engel score between those reporting an increase or decrease in depression (p=0.1), though there was a trend toward higher Engel scores in patients reporting an increase in depression.

Discussion

The Pediatric Epilepsy Advanced Technologies Clinic (PEATC) was created for concierge service to streamline the patient experience and personalize the medical and presurgical workup for pediatric patients with medically intractable epilepsy. A randomized controlled trial of epilepsy surgery in 116 children, found that patients who underwent epilepsy surgery were more likely to be seizure free (77%) than patients that received medical therapy alone (4%).[5] In our cohort, 71% of patients who underwent definitive

Table 3. Engel scores following definitive and palliative surgery

Engel Score	6 months	12 months	24 months
Definitive Surgery, N (%)	N=113	N=99	N=79
1	66 (58)	55 (56)	46 (58)
2	13 (11)	12 (12)	10 (13)
3	19 (16)	19 (19)	12 (15)
4	15 (13)	13 (13)	11 (14)
Palliative Surgery, N (%)	N=88	N=80	N=42
1	6 (7)	6 (8)	2 (5)
2	10 (11)	6 (8)	8 (19)
3	49 (56)	42 (52)	19 (45)
4	23 (26)	26 (32)	13 (31)

surgery attained Engel class 1 or 2 outcome, with these rates persisting to two-year follow-up. As anticipated, seizure outcomes following palliative surgery were less favorable, with 16% having rare or free of disabling seizures at six months with similar rates persisting to two-year follow-up (See Tables 2 and 3). These findings align with previously published surgical outcomes.[6,10-13]

The assessment and interpretation of seizure outcomes demonstrate substantial variability across the country and quality of life outcomes are frequently overlooked.[21] With early data, we sought to better understand whether measures of quality of life and depression improved with variable rates of seizure freedom. There has been increasing emphasis placed on quality-of-life factors in epilepsy management with an association between favorable seizure outcome and improved QOL.[15,16,22,23] Our initial data, deployed on a subset of the population, supports aspects of these findings with greater than half of the patients in the definitive surgery group reporting a decrease in depressive symptoms and 18% in the palliative group. Conversely, 66% of the patients with Engel score 1 reported decreased QOL at 12 months. This finding suggests that seizure control alone does not provide a comprehensive picture of QOL. Patients may have challenges while transitioning from a state of illness to normalcy, and experience frustration if improvements are not fulfilled promptly.[24] In our early data, we also did not find a relationship between cognitive and depression scores and seizure outcome, although these observations are limited by a small sample size.

Many factors compromise QOL, including psychosocial and cognitive outcomes with ongoing work needed to refine these patient-reported questionnaires and surveys. Common assessments of QOL rely on more generic or disease-oriented questionnaires reporting a mean score of QOL for a group that lacks insights into individual factors.[25] There is also the issue of differences that are statistically significant versus those with a meaningful clinical effect size. By addressing the minimum clinically important change (MCIC), investigators may be able to quantify the change in QOL that an individual patient deems significant.[26,27] When applied to medical and surgical epilepsy groups in adults, patients achieving MCIC was not always the same across different QOL questionnaires.[25] Using QOL assessment tools, including MCIC, in pediatric populations is confounded by the difficulty of standardizing assessments across age, developmental level, and self- versus parent-reported measurements. More investigation is needed to determine QOL measures more customized for the pediatric epilepsy surgery population.[28]

Nursing has a profound impact on the care of surgical patients. Early patient information and

education is one of the most critical components of ensuring a positive outcome.[29]

The Pediatric Epilepsy Advanced Technologies Clinic provides a patient centric structure to personalize the approach to epilepsy surgery work-up and tailored management. We have a fully dedicated nurse navigator who directs appropriate referrals and assists with triage, scheduling, record retrieval and review, as well as preparing a summary for providers prior to the patient's visit. Additionally, this individual tracks and coordinates post-op testing and follow up visits and serves as a liaison between the PEATC team, referring neurologist, and child's family, as well as providing patient and family counseling throughout the process.

The recent growth in minimally invasive methods of monitoring, including stereoencephalography (sEEG), have opened the door for patients previously not felt to be surgical candidates. In our cohort there was no significant difference in seizure outcomes among the patients who underwent sEEG and those who did not. A meta-analysis that reviewed the outcomes of 3511 epilepsy surgeries revealed that intracranial monitoring was associated with an unfavorable prognosis.[30] This is likely related to patient selection with increasing numbers of patients, who previously were not resective candidates, but are now more amenable to palliative or staged approaches with less invasive treatment options, including radiofrequency ablation (RFA) and laser ablation. RFA delivers a radiofrequency via single electrodes to heat surrounding tissue and create a focal lesion. RFA has been used for interrupting epilepsy networks, lesioning the seizure onset zone near eloquent areas, and has been used as a treatment predictor of future surgical intervention.[31-33] These less invasive methods of evaluation and treatment also relieve patient and family anxiety and may facilitate earlier referral for surgical evaluation; and earlier epilepsy surgery leads to improvements in QOL and neurocognitive outcomes.[34]

There are several limitations of this pilot study. This is a retrospective study that relied on clinically gathered data. There was incomplete follow-up data that limits the interpretation of the quality-of-life measures collected and underscores the importance of more consistent collection of this data. The PEATC population is heterogenous with a mix of ages, developmental levels, and types of epilepsy. This makes extrapolating meaningful averages or generalizable conclusions challenging. Additionally, we used patient and family reported questionnaires for QOL. Such inquiries can be confounded by many factors not related to epilepsy surgery, including other medical conditions, psychosocial factors, and timing of the responses. We also did not ensure all outcomes and questionnaires were consistently reported at all time points, limiting the sample size and interpretation. Furthermore, the limited sample size in QOL outcomes was likely exacerbated by the interruption in data collection caused by the COVID-19 pandemic.

Future directions for the PEATC team will lean into the strengths of this program and improve on the limitations. We will utilize our nurse coordinator to strengthen our relationships with local neurologists and primary providers to improve coordinated care and provide educational opportunities for patients, families and healthcare providers. We will continue to refine our minimally invasive approach to monitoring and surgery and build-out our palliative surgical options with newer techniques including reactive and deep brain neurostimulation. Finally, we need to continue to work with patients and their families to identify the outcome measures that are the most meaningful to them.

Conclusion

Patients receiving diagnostic work-up and epilepsy surgery through a personalized pediatric epilepsy clinic had rare to no disabling seizures (Engel 1 or 2) over 70% of the time in the definitive seizure group and at least a worthwhile improvement in seizures (Engel 3 or better) in the palliative group 69% of the time at two-year follow-up. Quality of life measures and assessment of depression were less clear with increases and decreases in these scores independent of seizure outcomes. Future epilepsy surgery studies, particularly in the setting of more refined and minimally invasive diagnostic and surgical approaches, need improved assessments of patient-focused outcomes.

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