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Original Article

Seizure Control Following Palliative Resective Surgery for Intractable Epilepsy—A Pilot Study

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ABSTRACT

BACKGROUND: Patients with intractable epilepsy who have bilateral epileptic foci may not qualify for curative epilepsy surgery. In some cases palliative resection may be undertaken with a goal to decrease seizure frequency and improve quality of life. Here we present data on the outcome of palliative epilepsy surgery in children. **METHODS:** We reviewed medical charts of children who underwent palliative resection for intractable epilepsy during the years 1999-2013 at Children's Hospital of Michigan. The palliative intent of resection was declared preoperatively. Outcome was assessed in terms of seizure reduction. **RESULTS:** There were 18 patients (11 males, median age of surgery was 3.5 years [range 0.5-16 years]). The median duration of follow-up after surgery was 12.5 months (range 6-60 months). Hemispherectomy was the most commonly performed palliative resection (nine patients), followed by lobectomy (six patients), multilobar resection (one patient), and tuberectomy (two patients). Reduction in seizure frequency was observed in 11 patients, with eight patients achieving seizure freedom on antiepileptic drugs and three with >50% reduction in seizure frequency. Transient improvement in seizure frequency occurred in two patients, whereas there was no benefit in five patients. **CONCLUSIONS:** Beneficial effects of epilepsy surgery may be realized in carefully selected situations wherein the most epileptogenic focus is resected to reduce seizure burden and improve quality of life.

Keywords: palliative resection, epilepsy surgery, intractable epilepsy, quality of life

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Introduction

Medically refractory epilepsy in children imposes a significant burden on children and their caregivers, with their quality of life (QOL) negatively impacted in a multitude of ways. Current studies indicate that reduction in the severity of seizures can have a positive effect on medical and social outcomes in this patient population.[1] Curative epilepsy surgery,[2] defined as surgery being performed with the intention of complete resection of the presumed epileptogenic zone, is a viable option in many children with intractable epilepsy resulting in overall seizure freedom between 60% and 80% of cases.[3,4] However, except for certain noteworthy exceptions such as tuberous sclerosis,[5] children with bilateral epileptic foci are often not considered to be appropriate candidates for resective surgery because the perceived risks of surgery outweigh potential benefits. Palliative surgical options are often considered in such children with the goal of minimizing the seizure burden. Common palliative procedures

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encompass multiple subpial transections, corpus callosotomy, and vagus nerve stimulation,[6,7] whereas "palliative resective surgery" has only recently been recognized as a promising approach. Palliative resective surgery, in which the "major" epileptogenic focus is removed, is performed to achieve dual treatment goals of a reduction in seizure frequency and/or severity and improve QOL. The extent of cortical resection is determined "case by case" after extensive discussion regarding the pros and cons of surgical resection of such areas. Previous studies by Ciliberto et al.[8] and Boshuisen et al.[9] have described positive outcomes in small series of children who underwent palliative hemispherectomy for intractable epilepsy. Yet, we still have limited experience with seizure control after palliative resective surgery in the pediatric age group. Here we report the seizure outcome of children who underwent palliative resective surgery at a level 4 epilepsy specialty center.[10]

Materials and Methods

Identification of patients and data collection

We performed a retrospective cohort study of all children who underwent resective surgery for intractable epilepsy between June 1993 and June 2013 at the comprehensive epilepsy center of Children's Hospital of Michigan in Detroit. We then selected those children who were considered preoperatively to be palliative surgical candidates in view of seizure semiology, bilateral ictal electroencephalographic (EEG) abnormalities, and imaging findings. Collection of data was approved by the Wayne State University Institutional Review Board.

The inclusion criteria were children between the ages of 0 and 18 years who (1) had intractable epilepsy defined as failure to respond to adequate trials of multiple, well-tolerated, appropriately chosen antiepileptic drugs (AEDs) to achieve seizure freedom[11]; (2) were revealed to have bilateral epileptic foci on ictal scalp video-EEG; (3) underwent a palliative cortical resection for epilepsy management including hemispherectomy, multilobar resection, lobectomy, and/or tuberectomy; and (4) had a minimum follow-up period of 6 months after the surgical procedure. The exclusion criteria were children who underwent corpus callosotomy or multiple subpial transections alone.

Case note review

Demographic and clinical data of interest included age, sex, race, age at the time of seizure onset, and age at the time of surgery. Number of AEDs, underlying etiology, seizure semiology, seizure frequency, types of palliative resection, postoperative complications, and preoperative and postoperative neurological examinations were evident as well.

EEG measures of interest included interictal and ictal abnormalities on long-term scalp video-EEG recording. Review of the standard preoperative evaluation was performed in all patients.[12] Seizure semiology was noted as "generalized tonic-clonic seizures," "epileptic spasms," "focal seizures," and "status epilepticus."

Neuroimaging measures of interest included magnetic resonance imaging (MRI) and positron emission tomography (PET) of glucose metabolism. MRI was performed on 1.5-T or 3.0-T unit magnets with T_1-weighted sagittal spoiled gradient-recalled echo, axial fluid-attenuated inversion recovery images, coronal fluid-attenuated inversion recovery, diffusion-weighted images, and T_2-weighted axial and coronal sequences in all patients.[13] Interictal glucose metabolism PET scans were obtained in all patients, using the GE Discovery STE positron tomograph after intravenous administration of 18-fluoro-2-deoxyglucose.[14]

Assessment of surgical outcome

Surgical outcomes were assessed with respect to the following variables: (1) change in seizure frequency as defined by number of seizures per day and (2) number of AEDs that were used after the surgical procedure in a follow-up period ranging between 6 and 60 months. Surgical outcome was classified as "favorable" or "unfavorable" in the present study. A favorable outcome was defined as (1) complete seizure freedom on AEDs or (2) >50% reduction in seizure frequency. An unfavorable outcome was defined as <50% reduction of seizure frequency. We are fully aware that the large variance in the follow-up period is certainly a limitation of the present study; thus, we intended that the results be interpreted as preliminary data.

Statistical analysis

Descriptive statistics were calculated to describe the study group. Means and S.D. for normally distributed continuous variables, median and range for skewed continuous variables, and frequencies and percentages for categorical variables, are presented. The study group was then divided into subgroups based on different independent variables. Fisher's exact test was used to compare categorical variables between the subgroups and is valid for all sample sizes.[15] Wilcoxon signed ranks test was used to compare the total AEDs and the number of seizures before and after the surgery. Surgical outcomes were correlated with demographics, etiology, surgery type, and side of resection. Statistical Package for Social Sciences 21 (SPSS Inc, Chicago, IL) was used to conduct the statistical analysis. P value of ≤ 0.05 indicates a significant result.

Results

A total of 462 patient charts were reviewed spanning the interval from 1993 to 2013. Palliative surgery had been performed in 18 patients (3.9 %; see Table 1 for demographic data). The median and the range for follow-up period for this small cohort were 12.5 and 6-60 months, respectively. There was no significant association between demographic variables and seizure outcome after palliative resection.

Postoperative seizure control

Reduction in seizure frequency was observed in 11 of 18 patients (61.1%), with eight of 18 children (44%) achieving seizure freedom for the period of follow-up (International League Against Epilepsy [ILAE] class 1[16]; Patients 2, 4, 6, 8, 10, 13, 16, and 18 [in Table 2]) and three patients experiencing more than 50% reduction in seizure frequency (ILAE class 4; Patients 12, 14, and 17). Transient improvement in seizure frequency occurred in two patients (Patients 1 and 3) as they were seizure-free for a period of 6 months but experienced seizure recurrence later. These patients had a less than 50% decrease in their baseline seizure frequency, when the seizures recurred. Taken together, Patients 2, 4, 6, 8, 10, 12, 13, 14, 16, 17, and 18 were classified as having a "favorable outcome," while the remaining patients were classified as having an "unfavorable outcome."

No benefit was observed in five patients (Patients 1, 3, 9, 11, and 15), one of whom (Patient 15) had worsening of seizures (ILAE class 6). Long-term follow-up of these five children revealed that one of them (Patient 9) underwent implantation of a vagus nerve stimulator 4 years after surgery and that two others (Patients 11 and 15) were placed on a ketogenic diet 1 year after surgery. The median number of AEDs used preoperatively was 4 (2-7) and declined to 2.5 (1-4) postoperatively ($P = 0.007$).

Nature of surgery and relationship to postoperative seizure control

Hemispherectomy was the most commonly performed palliative surgical procedure (9/18, 50%), followed by single lobe resection (6/18, 33.3%), multilobar resection (1/18,