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Outcomes of resective surgery in children and adolescents with focal lesional epilepsy: The experience of a tertiary epilepsy center

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ABSTRACT

Objective: This study aimed to investigate the efficacy of resective surgery in children with focal lesional epilepsy by evaluating the predictive value of pre- and postsurgical factors in terms of seizure freedom.
Methods: This study included 61 children aged between 2 and 18 years who were admitted to the pediatric video-EEG unit for presurgical workup. Each patient was evaluated with a detailed history, video-EEG, neuroimaging, and postsurgical outcomes according to Engel classification to predict postsurgical seizure freedom. All the possible factors including history, etiology, presurgical evaluation, surgical procedures, and postsurgical results were analyzed for their predictive value for postoperative seizure freedom.
Results: Of the 61 patients, 75% were diagnosed as having temporal lobe epilepsy (TLE), and 25% were diagnosed with extra-TLE. Two years after the surgery, 78.6% were seizure-free, of which 89% had TLE, and 50% had extra-TLE ($p < 0.05$). Patients were more likely to have a favorable outcome for seizure freedom if they had rare seizure frequency, focal EEG findings, and focal seizures; had a temporal epileptogenic zone; or had TLE and hippocampal sclerosis. On the other hand, patients were more likely to have unfavorable results for seizure freedom if they had younger age of seizure onset, frequent seizures before the surgery, a frontal or multilobar epileptogenic zone, secondarily generalized seizures, extra-TLE with frontal lobe surgery, or focal cortical dysplasia.
Significance: Resective surgery is one of the most effective treatment methods in children with intractable epilepsy. A history of young age of seizure onset, frequent seizures before surgery, secondarily generalized seizures, a multilobar epileptogenic zone, frontal lobe surgery, and focal cortical dysplasia (FCD) are the most important predictive factors indicating that a patient would continue having seizures after surgery. On the other hand, focal seizure semiologies, temporal lobe localization, and hippocampal sclerosis indicate that a patient would have better results in terms of seizure freedom.

1. Introduction

Epilepsy is one of the most common chronic neurological disorders [1]. Despite many effective therapies, about 20–30% of patients still continue having refractory seizures, which are substantially related to morbidity [1–3]. Beyond antiepileptic drug (AED) therapy, epilepsy surgery as a promising and successful treatment method seems to be an increasing trend [4]. The surgical approach should not be thought of as a younger-age version of adult treatment for children. Because there is a large diversity in history, clinical presentation, etiology, response to AEDs, localization of the lesions or epileptogenic zone, and type of lesions, the timing and type of surgery should be unique for every patient [1,4–7]. Even if young brains are more vulnerable to external stimuli, the capacity for plasticity is much higher than that of adults, especially in specific conditions like hemispheric malformations [1,4–6]. Therefore, the primary goal of epilepsy surgery should not be to only remove the epileptic foci but also to provide further improvement for plasticity by performing surgery as soon as possible for facilitating transfer of the functions to the normal side without worsening the existing deficits [7].

While the most common epilepsy type is temporal lobe epilepsy (TLE) in adults, extra-TLE with an etiology of focal cortical dysplasia (FCD) and developmental tumors is frequently seen in children [5,8]. Some data were reported for predictive factors of postsurgical seizure freedom in children [1,3–7,9–12]. However, there are no separate data about specific age groups like neonates, preschool and school age, or adolescents [1,4–6,9]. Recently, some efforts for scoring systems were developed as promising approaches to predict expectation of postsurgical status [7]. However, those approaches are limited by different criteria

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including seizure type, frequency, epilepsy duration, EEG and MRI findings, localization, and quality of life [2,5]. Furthermore, more questions are arising regarding either the importance of a clear focality or lesions on MRI or having refractory seizures before the surgery; the possibility of seizure freedom after surgery is encountered increasingly when deciding to undergo epilepsy surgery [1,3–7,9–12].

The purpose of this study was to determine the long-term efficacy of epilepsy surgery by comparing TLE and extra-TLE and also to evaluate the predictive factors in terms of postsurgical freedom (Engel classification) in children and adolescents with focal lesional epilepsies.

2. Materials and methods

2.1. Patients and demographics

Nine hundred and twenty-eight consecutive children were admitted to Gazi University School of Medicine, Division of Pediatric Epilepsy-Video-EEG Monitoring Unit between 1998 and 2013 for the purposes of presurgical workup and clinical seizure definition or to differentiate epileptic and nonepileptic paroxysmal events and were evaluated retrospectively. After comprehensive evaluation, a total of 172 patients underwent either focal resective surgery (n: 61, 35.4%), vagus nerve stimulation (VNS) (n: 101, 58.7%), hemispherotomy (n: 5, 2.9%), or corpus callosotomy (n: 3, 1.7%). After excluding those surgeries for disconnection and VNS, a total of 61 children (35.4%) were included in our study. To predict postsurgical outcome, detailed history; prenatal, natal, and postnatal characteristics; etiology; risk factors; number of AEDs; and physical and neurological examination were evaluated from the chart reviews.

2.2. Presurgical workup

Video-EEG monitoring was recorded by either a Telefactor Beehive system (Telefactor, Philadelphia, PA) or a Nihon-Kohden EEG system (Tokyo, Japan). All patients were connected with 32-channel scalp electrodes, which were placed according to the International 10–20 System. If needed, invasive electrode grids or strips were also placed around the lesion for mapping and to determine extension limits of surgery in specific settings. The video and EEG records were synchronized with a closed circuit system. The duration of the video-EEG recording ranged from 1 to 7 days depending on the number and quality of the seizures. The AEDs were gradually tapered so that seizures could be obtained. Trained EEG technicians and nurses examined the patients until they regained consciousness after the seizures and to determine the level of consciousness or motor responses.

Seizures were classified as focal or generalized seizures (may or may not have secondarily generalized) according to International League Against Epilepsy (ILAE) 2010 criteria [13].

Interictal EEG findings were classified as interictal epileptiform abnormalities including localized, generalized, or nonlocalizable spike or sharp waves and also nonepileptiform changes like asymmetry or slowing. Ictal EEG was described as localized, generalized, or nonlocalizable rhythmic activities, electrodecrements, or suppression. The interictal and ictal EEG findings were combined for the final classification of EEG as focal, multifocal, or hemispheric ± secondarily generalized EEG findings for each patient.

Magnetic resonance imaging (MRI) was performed with 1.5- or 3-Tesla thin-sliced epilepsy protocols, including axial and sagittal T1-weighted, axial and coronal T2-weighted, oblique coronal fluid-attenuated inversion recovery (FLAIR) perpendicular to the long axis of both hippocampi, and 3-dimensional inversion recovery.

Fludeoxyglucose-positron emission tomography (FDG-PET) standard brain images were evaluated to detect hypometabolic regions of the brain. The PET images were reconstructed with the Fourier rebinning–ordered subsets expectation maximization (FORE–OSEM) iterative reconstruction method. Imaging was performed with the Discovery ST (GE Medical Systems, Milwaukee, WI, USA) PET–CT camera system. Statistical parametric mapping (SPM) analysis was performed in patients with specific conditions.

With regard to additional functional tests, WADA (intracarotid methohexital injection test) or fMRI (functional MRI) was performed before the surgery. The WADA test was applied to clarify the dominant hemisphere for language lateralization [4,14]. Functional MRI was performed to detect the proximity of lesions to the eloquent cortex, including memory–language, motor, and visual cortex.

Invasive electrodes with grid or strip electrodes were placed if the patients needed them for extensive evaluation of language–memory, motor, sensorial, and visual areas.

The decision of the final ‘epileptogenic zone’ was mainly assessed by the clinical seizure types, ictal and interictal EEGs, MRI, and additional supplementary tests including functional PET and fMRI [14,15]. Epileptogenic zones were classified as temporal, frontal, parietooccipital, or multilobar–hemispheric-generalized [15,16]. In addition, the patients were divided into two groups: temporal lobe or extra-temporal lobe epilepsy (extra-TLE) to compare historical, clinical, presurgical, and postsurgical findings.

2.3. Postsurgical outcomes and predictive factors

The duration of postsurgical follow-up was between 2 and 15 years. Two years after their surgery, some patients continued to follow up with us, while some of them were followed up in their local hospitals. We checked their status either by calling their physicians or their families. Therefore, we included the 2-year follow-up to avoid the debatable data. Overall, the state of postoperative seizure status was assessed by Engel seizure classification [17] at least 2 full years after surgery. The patients were grouped as follows: Class I — seizure-free, Class II — rare disabling seizures, Class III — worthwhile improvement, and Class IV — no worthwhile improvement. For statistical purposes, the patients were divided into two main groups: the seizure-free group (Engel I) and those with continuing seizures (Engel II, III, IV) [17].

Revised Liverpool seizure severity score (LSSS) was also applied to assess the severity of the seizures [18]. The scale contains 12 items arranged as a Likert scale for ictal/postictal states. If the patient had not had any seizure for the previous 4 weeks, the subject did not do an evaluation with the LSSS. Scoring was between 0 and 100, with an increasing score indicating increasing severity of the seizures. The seizures could also be divided into ‘minor’ and ‘major’ types according to the presence of generalized seizures or their effects on patients independent from the ILAE seizure classification [18].

Finally, all factors of both the presurgical workup and postsurgical outcomes were compared to predict the possibility of seizure freedom. The following data were matched to postsurgical Engel classifications to determine the predictive value of postsurgical seizure freedom: age of seizure onset, duration of epilepsy, number of AEDs, etiology, seizure classification, interictal–ictal EEG findings, MRI, PET, fMRI, invasive recording, the final presence of TLE or extra-TLE, age at surgery, side and type of surgery, and results of pathology.

2.4. Statistical analysis

Statistical analysis was performed with Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 16.0 for Windows. Data were expressed as means ± standard deviations, evaluated using Mann–Whitney U-test for continuous variables, and expressed as numbers and percentages for categorical variables. Categorical data were evaluated by Pearson's chi-square or Fisher's exact test. A p-value <0.05 was considered statistically significant. After the data were analyzed based on outcome (seizure-free or continuing to have seizures) by chi-square or Mann–Whitney U-test, the factors significantly