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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.

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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

different between the groups were entered into a univariate logistic regression model. Odds ratios and 95% confidence intervals (CI) were also calculated for each of these parameters. A p-value <0.05 was considered statistically significant. Approval for this study was granted by the Gazi University School of Medicine Ethical Committee (number: 78480).

3. Results

3.1. Demographics and etiology

The mean age of the 61 patients was 14.18 ± 3.8 years (range: 2–18 years; the youngest age of surgery was 2 years in our cohort) when the patients were admitted to the video-EEG monitoring unit for presurgical evaluation: 45.9% of the patients were girls, and 54.1% were boys. Of the patients, 45 (75%) had TLE, while 16 (25%) had extra-TLE. The patients with extra-TLE were significantly younger at the age of surgery (12.1 ± 4.1 years) than the patients with TLE (15.04 ± 3.5 years) ($p < 0.05$). The most important etiology and risk factor for TLE was febrile seizure (35.6%), while the most important etiology for extra-TLE was trauma–hypoxia or central nervous system (CNS) infections. The presence of daily seizures (62.5%) and the number of seizures due to lack of efficacy of AEDs (2.6 ± 0.9) were significantly higher in extra-TLE before the surgery ($p < 0.05$) (Table 1).

3.2. Presurgical workup

During presurgical workup, a total of 45 patients (61%) had focal seizures, while 16 (27.9%) had secondarily generalized seizures. Focal seizures were mostly seen in patients with TLE (75.6%), while generalized seizures were more frequent in patients with extra-TLE (37.5%). The predominant findings on EEG were significantly different between TLE (focal: 93.3%) and extra-TLE (hemispheric–multifocal: 56.3%) ($p < 0.05$). All the MRI findings were consistent with postsurgical histological findings. Hippocampal sclerosis was the most frequent lesion in TLE (57.8%), while FCD was the most frequent in extra-TLE (44%) ($p < 0.05$) (Table 2). The PET scan revealed that 31.1% of the patients (n: 14) had a hypometabolism restricted in the epileptogenic zone in TLE, while 37.5% of the patients had extended hypometabolism (n: 6) beyond the epileptogenic zone in extra-TLE. Almost 13% of the patients underwent WADA testing to identify the language-dominant hemisphere. Functional MRIs were performed mostly to find the dominant side for verbal memory in TLE (24.4%), while the fMRIs were performed to determine the dominant side for the motor cortex and the visual area in extra-TLE (~45%). Invasive recordings were also obtained from six patients. Four of them were in the group with TLE for the purposes of localizing Wernicke's area or the primary hearing center, while two of them were in the group with extra-TLE for the purposes of relating lesions and the primary motor and sensorial area. The epileptogenic zone was assessed in the temporal zone as expected in TLE, while it was assessed in the frontal (25%) or parietooccipital or multilobar zone (37.5%) in extra-TLE ($p < 0.001$) (Table 2).

3.3. Surgery and postsurgical outcome

After being presented with the recommendations based on comprehensive and multidisciplinary discussions in patient management conferences, two-thirds of the patients (n: 45) decided to undergo anterior temporal lobectomy (ATL) and amygdalohippocampectomy (AH) with a standard procedure, while one-third of the patients (n: 16) decided to undergo extended lesionectomy to remove as much of the epileptogenic zone as possible in extra-TLE, which was removed with the frontal lobe (n: 9, 14.7%) or the parietooccipital lobe (n: 7, 11.5%). Most patients underwent surgery of their dominant side in both TLE (62.2%) and extra-TLE (62.5%). The most frequent histopathological finding in TLE was hippocampal sclerosis (57.8%), while FCD was

Table 1
Demographics of the patients.

Number of patients (n: 61)	TLE (n: 45, 75%)	Extra-TLE (n: 16, 25%)	p
Age — current (years): 14.18 ± 3.8 (range: 2–18 years)	14.9 ± 3.5	12.1 ± 4.1	0.007*
Seizure onset age (months): 83.6 ± 55.5	89.4 ± 55.6	67.3 ± 55.5	0.148*
Duration of epilepsy (years): 7 ± 4	7.2 ± 4.04	7.06 ± 4.3	0.934*
Age of surgery (years): 13.62 ± 3.8	15.04 ± 3.5	12.2 ± 4.1	0.009*
Gender			
Girl, 28 (45.9%)	25 (55.6)	3 (18.8)	0.011**
Boy, 33 (54.1%)	20 (44.4)	13 (81.3)	
Seizure frequency			
Daily (at least once a day)	10 (22.2%)	10 (62.5%)	0.003**
Persistent (at least once a week, not everyday)	28 (62.2%)	5 (31.3%)	
Rare (less than once a week)	7 (15.6%)	1 (6.3%)	
Number of AEDs	1.9 ± 0.7	2.6 ± 0.9	0.005**
Etiology and risk factors			
Febrile seizures	16 (35.6)	0	
Complex febrile seizures	3 (18.75)	0	
Before 1-year-old prolonged	2 (12.5)	0	
Trauma–hypoxia	10 (22.2)	3 (18.8)	0.539**
CNS infection	1 (2.2)	1 (6.3)	0.459**
Family history	3 (6.7)	2 (12.5)	0.394**
Comorbidity			
Intellectual disability	3 (6.7)	2 (12.5)	0.721**
Hemiparesis	–	1 (6.3)	

* Mann–Whitney U-test.
** Chi-square test.

Table 2
Pre- and postsurgical findings of the patients.

Number of patients (n: 61)	TLE (n: 45, 75%)	Extra-TLE (n: 16, 25%)	p*
Seizure classification			
Focal seizures	34 (76.6)	10 (62.5)	0.246
Secondarily generalized seizures (GS)	11 (24.4)	6 (37.5)	0.246
Only secondarily GS	7 (63.3)	4 (66.6)	
Both secondarily GS and focal seizures	4 (36.3)	2 (33.3)	
EEG findings			
Focal	42 (93.3)	7 (43.8)	0.000
Multilobar	3 (6.7)	6 (37.5)	0.007
Hemispheric ± secondarily generalized	–	3 (18.8)	–
MRI			
Hippocampal sclerosis	26 (57.8)	–	
Gliosis	6 (13.3)	2 (12.5)	0.652
FCD	4 (8.9)	7 (43.8)	0.005
Tumor	6 (13.3)	5 (31.3)	0.113
Vascular	3 (6.7)	2 (12.5)	0.394
Epileptogenic zone			
Temporal zone	41 (91.1)	–	
Frontal zone	–	4 (25)	
Parietooccipital zone	1 (2.2)	6 (37.5)	0.001
Multilobar–hemispheric-generalized	3 (6.7)	6 (37.5)	0.007
Pathology			
Hippocampal sclerosis	26 (57.8)	–	
Gliosis	6 (13.3)	2 (12.5)	0.652
FCD	4 (8.9)	7 (43.8)	0.005
Tumor	6 (13.3)	5 (31.3)	0.113
Vascular	3 (6.7)	2 (12.5)	0.394
Postsurgical Engel classification			
Class I — seizure-free	40 (88.9)	8 (50)	0.003
Continue having seizures	5 (11.1)	8 (50)	0.003
Class II	2 (4.4)	2 (12.5)	
Class III	1 (2.2)	4 (25)	
Class IV	2 (4.4)	2 (12.5)	
Postsurgical seizure severity score (LSSS)			
No seizures: The number of patients (score)	40 (0)	8 (0)	–
Continue having seizures: The number of patients (score)	5 (30.8 ± 8.7)	8 (28.5 ± 9.7)	0.591**
Minor seizures: The number of patients (%)	1 (20)	5 (62.5)	0.266
Major seizures: The number of patients (%)	4 (80)	3 (37.5)	

* Chi-square test.
** Mann–Whitney U-test.

the most frequent finding in extra-TLE (43.8%), which was consistent with the MRI findings prior to surgery ($p < 0.05$) (Table 2).

Engel classification was used to determine the postsurgical seizure status. Of the patients, 78.7% were seizure-free two years after the surgery ($p < 0.05$). In detail, 89% of the patients with TLE were seizure-free, which was significantly higher than those with extra-TLE (50%) ($p < 0.05$). A detailed subgroup classification is presented in Table 2. The severity of the seizures was assessed according to LSSS in five (11%) and eight (50%) patients in the groups with TLE and extra-TLE, respectively. There were no differences between TLE and extra-TLE in terms of seizure severity scores (LSSS) or minor–major seizure types (Table 2).

All of the possible risk factors including history, etiologies, presurgical evaluation, surgical procedures, and postsurgical results were analyzed based on outcome in terms of any differences to predict being seizure-free or continuing to have seizures. Older age at surgery, infrequent/rare seizures, focal EEG findings, a temporal epileptogenic zone or TLE, focal seizures, and hippocampal sclerosis predicted favorable outcome for seizure freedom after surgery ($p < 0.05$) (Table 3). However, frequent seizures before the surgery, a frontal or multilobar epileptogenic zone, generalized seizures, extra-TLE with frontal lobe surgery, and the presence of FCD were found to predict unfavorable effects for seizure freedom ($p < 0.05$) (Table 3). There was no difference between seizure freedom or continuing to have seizures and duration of epilepsy, number of AEDs, etiologies, comorbidities, and developmental tumor.

4. Discussion

Epilepsy surgery is an effective treatment for intractable seizures in the pediatric age group as much as in the adult group [3,6,19]. However, limited data have been reported regarding postsurgical outcomes in different age groups of children who underwent focal lesionectomy [3,6,19]. Therefore, in the current study, we evaluated postsurgical outcomes by investigating two aspects: (1) comparing outcomes in patients with TLE and those with extra-TLE and (2) assessing the possible predictive factors to determine any relationships for postsurgical seizure freedom. There is no published study, to our knowledge, that investigates those two important points at the same time in children and adolescents.

Table 3
Predictive factors for postsurgical seizure freedom.

Variables	95% confidence interval		Exp (B)	p^*
	Lower limit	Upper limit		
Age of surgery	0.674	0.940	0.796	0.007
Seizure onset age	0.976	1.000	0.988	0.057
Epilepsy duration	0.820	1.119	0.958	0.588
Seizure frequency				
Rare seizure (less than once a week)	0.034	0.513	0.132	0.003
Frequent seizure (daily or weekly)	1.769	42.468	8.667	0.008
Surgery — the subgroup of the patients				
TLE	0.032	0.483	0.125	0.003
Extra-TLE	2.072	30.884	8.0	0.003
Frontal lobe	2.60	63.58	12.857	0.013
Parietooccipital lobe	0.267	9.166	1.264	0.620
Seizure classification				
Focal seizures	0.62	0.823	0.0226	0.024
Secondarily generalized seizures	1.216	16.169	4.433	0.024
EEG findings				
Focal	0.042	0.666	0.167	0.011
Multilobar	0.447	9.874	2.100	0.348
Hemispheric ± generalized	0.628	1.692	1.031	0.905
Epileptogenic zone				
Temporal zone	0.018	0.342	0.079	0.001
Temporal lobe				
Frontal zone	1.326	149.910	14.10	0.028
Parietooccipital zone	0.267	9.166	1.264	0.620
Multilobar–secondarily generalized zone	1.511	31.287	6.875	0.013
Histopathological findings				
HS	0.036	0.909	0.182	0.038
FCD	1.071	17.870	4.375	0.040
Tumor	1.488	4.193	0.788	0.780

* Univariate logistic regression.

Even if there is no clear consensus for the minimum duration of follow-up after surgery to assess long-term prognosis [3,6,19], the general tendency is that at least two years of follow-up is enough to determine the postsurgical seizure outcome [3,6,19]. The available studies have shown that almost 70–80% of children were in class I (seizure-free) at the end of the second year after surgery in different settings [6,10,11,19]. These findings are similar to the results of our current study, in which we confirmed that 78.6% of our patients were seizure-free at the end of the second year after surgery. Therefore, predictions about timing for the seizure condition may be important for prognosis notification.

Age at surgery and duration of epilepsy are the most important factors for postsurgical seizure control and the improvement of quality of life [1,3,5–7,10,19]. There are controversial and various results regarding the appropriate age for surgery. The majority of these studies reported that a younger age of onset and a longer duration of epilepsy were important factors for poorer surgical outcome [6,19,20]. Similarly, we found that the seizure onset age was somewhat younger in those still having seizures after surgery [6,7,19–24]. These results led us to infer that the connections of the immature brain may be more expansive than previously thought, which would result in difficulty in limiting the epileptogenic zone [6,7,19–22]. In support of those findings, we also found that the patients of older age at surgery may have a chance to be seizure-free. This may also be the result of many of our patients having HS, and therefore, the surgical limits could be better assessed [7]. As another aspect, it should be kept in mind that earlier surgery should be considered in some specific conditions such as hemispherectomy due to large hemispheric malformation to help plasticity [6,10,19,23]. However, it is still difficult to clearly indicate the margins of the resection and the recovery ability in the young brain after surgery [6,7,19–24].

Jayalakshmi and Spencer reported that the most common type of surgery was temporal resection (88.9%) in adolescents and extratemporal resection (60.6%) in preschool and school ages [7,25]. We found that a younger seizure onset age and age at surgery were seen in the group with extra-TLE than were found in the group with TLE, which is consistent with previous findings. A meta-analysis that included 36 studies revealed that those with an epilepsy duration of less than seven years had better outcomes in TLE than in extra-TLE, and the duration of epilepsy apparently was longer in those with extra-TLE [10]. The most important issue is deciding the margins of the resection, which may affect later postsurgical neurological deficits, cognitive status, seizure freedom, and quality of life [1,3,5–7,9]. Therefore, a comprehensive evaluation before surgery would help to predict the long-term outcome [3,5,9,19]. Video-EEG monitoring is assumed to be the most important step in detecting the epileptogenic zone [6,9,12,26]. Both scalp and invasive studies have shown that unilateral focal lesion, temporal lobe localization, and focal EEG findings have favorable outcomes [1,9]. On the other hand, it has been reported that having extra-TLE, difficult localization, bilateral or no MRI findings, and overlapping with the eloquent cortex may be related to unfavorable results for seizure outcome [9,11,19,20,27]. In concordance with those studies, we detected better seizure control in the group with TLE (89%) versus the group with extra-TLE (50%). As shown in some previous studies [9,20–22], Kumar et al. also reported that both children and adults had better seizure control after temporal resection than frontal resections, especially in those with normal neuroimaging prior to the surgery [22]. Overall, we confirmed that both a multilobar epileptogenic zone and frontal lobe localization were the most important factors for unfavorable prognosis after surgery. On the other hand, since all of our cases were in the group with lesional epilepsy, patients with no lesions may have less favorable results due to limitations in the surgery width [9–12,20–22,28]. Related to this, Englot et al. investigated pediatric patients with TLE by dividing them into

groups with and without lesions and found that 76% of patients with TLE have a good outcome, with 81% in the group with lesions having good outcomes compared with 75% in the group without lesions [11].

Recently, there has been some effort to develop a scoring system that includes the most important factors for postsurgical status [2,5]. Those scores depend on a calculation system that includes seizure type, frequency, epilepsy duration, EEG and MRI findings, and localization, which may facilitate the understanding and prediction of more reliable outcomes [2]. According to the scores, a single semiology at seizure onset [10,21] and focal seizures without evolution to secondarily generalized seizures in both TLE and extra-TLE had better outcomes in pediatric cases [10,11,21,22]. In accordance with those findings, we demonstrated that focal seizures with focal EEG findings in TLE had the best outcomes, in contrast to secondarily generalized seizures before the surgery. Additionally, it has previously been shown that secondarily generalized seizures with multilobar EEG findings were prominent and gave poorer outcomes in patients with extra-TLE [28]. With this in mind, focal seizures may have more promising results when combined with EEG results [10,11,28]. Consistent with the results of the current study, focal background slowing and localized or multifocal–bilateral ictal and interictal EEG findings were shown to play an important role in outcome, especially in nonlesional cases [10,21,22,28]. As another factor for scoring, frequent seizures were strongly associated with the persistence of postsurgical seizures in both TLE and extra-TLE in some studies [10,11] as was also shown by our study.

Postsurgical seizure freedom can depend on the etiology and pathological findings [3,10,11]. While the most frequent lesion is HS (33%) in adult TLE series [6,9,19], FCD, trauma, and vascular malformations were also frequently seen in children [19,21,23,25]. In our current study, we found that the most frequent histopathological finding in TLE was HS (57.8%), which was much higher than previously reported in pediatric case series (13–36%) [9,19]. In addition, we found that HS had a favorable outcome as reported by previous studies [7,25]. Even if the underlying pathogenesis of mesial temporal lobe sclerosis is not clear, the most responsible reasons are thought to be damage to the amygdala and hippocampus which are the most vulnerable structures to injury (such as prolonged febrile seizures) in early childhood [23,29]. After a latent period, because of derangement in the balance between glutamatergic and GABAergic synaptic transmission, both affected and preserved neurons can gain epileptogenic features; this process may be irreversible. Therefore, early surgical intervention should be considered as soon as possible in patients with this specific condition [23,29].

The most prevalent etiology of neocortical epilepsies is FCD in the pediatric age group [6,19]. Therefore, intractable epilepsy is more frequently seen in this group, because of the nature of this unique condition [6]. In our current study, the most frequent histopathological finding was FCD in extra-TLE, and this had a negative association with seizure freedom, which is in accordance with the results of the study by Jayakar et al. [4]. Mühlebner et al. showed that seizure onset age, epilepsy duration, and age of surgery (2.9, 4.8, and 8.0 years, respectively) were lower in those with FCD [27]. Consistent with those results, we found that the age of surgery for FCD was much lower than that of the other etiologies. Therefore, it can be said that earlier surgical interventions should become increasingly more common in those with FCD [4,6,27]. However, there are many controversial results regarding the postsurgical outcome of FCD: the completely seizure-free group constitutes about 55–80% of the patients [4,6,7,19,24]. Some predisposing factors that may also affect the favorable results of FCD include surgery at a younger age, unilobar involvement, focal EEG findings, total resection, and FCD type II [4,6,19,24,27,30,31].

In general, developmental tumors have a more favorable outcome than FCD [3,7,10,19]. Nagarajan et al. reported a higher likelihood of seizure freedom (89%) in children with tumors after surgery [3]. We found that 18.75% of our patients with tumors were in Class I, which is a lower rate than in the literature. The low rate in our study could be due to the fact that most of these tumors were located outside the temporal lobe, which is known to have poorer outcomes. On the other hand, the results can change depending on whether the patient has a total or subtotal resection [4,6,23]. Overall, subtypes of tumors, such as ganglioglioma with temporal location were reported to have a longer duration of seizure freedom [4,6,32]. Therefore, our cohort with tumors localized in the temporal lobe and with total resection had the best results for seizure control after surgery. When considering the high possibility of favorable results in patients with this specific etiology, the early scheduling of surgery is very important in preventing side effects of multiple AEDs and for the protection of cognitive and motor functions [3,10,11]. Related to those arguments, Ramantani et al. found that 62% of patients with tumor can stop using AEDs and that 76% of these patients are seizure-free after surgery [23]. On the other hand, higher presurgical cognitive function was related to shorter epilepsy duration [6,23]. Therefore, one can assume that cognitive functions may deteriorate with time in those with glioneuronal tumor-related refractory epilepsies [6,23].

5. Conclusion

Resective surgery is one of the most effective treatment options in children with pharmacoresistant epilepsy. The factors with a favorable outcome include focal seizure semiologies, focal EEG findings, temporal lobe localization, and hippocampal sclerosis, while younger age of seizure onset, frequent seizures before surgery, generalized seizures, a multilobar epileptogenic zone, frontal lobe localization, and FCD showed a poorer outcome for seizure freedom. We suggest that our study provides an important contribution to evaluate postsurgical outcomes by investigating the possible risk factors and etiologies in comparing TLE and extra-TLE at the same time in children with lesional epilepsy. To our knowledge, this is the first comprehensive investigation from the region of Turkey. With respect to limitations, the current study does not include children younger than two years old and the changes in quality of life after surgery. These points may also present a valuable assessment for postsurgical outcome. Overall, well-developed and dedicated multidisciplinary centers are needed in order to develop a reliable scoring system that also includes quality of life, which can predict satisfactory results prior to epilepsy surgery in children with epilepsy. As supportive and advanced techniques are developed, better assessment of the margins of the resection will become possible prior to the surgery.

Conflict of interest

There is no conflict of interest between the authors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.yebeh.2016.07.039.

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