Pediatric Neurosurgery

Research Article

Pediatr Neurosurg
DOI: 10.1159/000535023

Received: March 8, 2023
Accepted: October 30, 2023
Published online: November 3, 2023

Effectiveness and Safety of Epilepsy Surgery for Pediatric Patients with Intractable Epilepsy: A Clinical Retrospective Study from a Single-Center Experience

Müge Dolgun[a] Duygu Dölen[b] Emek Uyur Yalçın[c] İlyas Dolaş[b] Tuğrul Cem Ünal[b] Nermin Görkem Şirin[d] Ayfer Sakarya Güneş[e] Nerses Bebek[d] Aydın Aydoseli[b] Candan Gürses[f] Bülent Kara[e] Altay Sencer[b]

[a]Department of Neurosurgery, Haseki Training and Research Hospital, Istanbul, Turkey; [b]Department of Neurosurgery, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey; [c]Department of Pediatric Neurology, Zeynep Kamil Maternity and Children's Diseases Training and Research Hospital, Istanbul, Turkey; [d]Department of Neurology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey; [e]Division of Child Neurology, Department of Pediatrics, University of Kocaeli, Faculty of Medicine, Izmit, Turkey; [f]Department of Neurology, Koc University, Istanbul, Turkey

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

Keywords
Pediatric epilepsy · Drug-resistant epilepsy · Functional neurosurgery · Epilepsy surgery

Abstract

Introduction: Pediatric epilepsy surgery is an effective treatment modality for patients with drug-resistant epilepsy (DRE). Early pediatric surgery yields favorable results for DRE in terms of seizure control and neurophysiological outcome. In this study, pediatric patients were categorized based on their age (above 3 years old and below 3 years old) to demonstrate the effectiveness and safety of surgical procedures. ***Methods:*** In this retrospective, single-center study, 60 pediatric patients who underwent epilepsy surgery at Istanbul Faculty of Medicine between 2002 and 2018 were evaluated. Overall morbidity and mortality rates, as well as seizure outcomes of the patients, were assessed and compared based on two age groups: those aged 3 years old or younger and those older than 3 years old. The effectiveness of invasive monitoring was also evaluated in relation to pathological results. The postoperative seizure outcome rates were evaluated using Engel's classification, with an average follow-up period of 8.7 years. ***Results:*** Out of the total number of patients, 47 (78.4%) underwent resective surgery, while 13 (21.6%) had palliative surgery. Ten patients (16.6%) had invasive monitoring. Among all patients, 34 were classified as Engel I and II (56.6%), while 26 were classified as Engel III and IV (43.4%) postoperatively. 47% of patients who were under 3 years old, 60.4% of patients who were over 3 years old, and 50% of patients who underwent invasive monitoring had a favorable seizure outcome (Engel I–II). Postoperative morbidity and mortality rates were 35% ($n = 21$) and 1.6% ($n = 1$), respectively. ***Conclusion:*** Pediatric epilepsy surgery is an important treatment modality for preserving cognitive abilities and providing effective

karger@karger.com
www.karger.com/pne

Karger
OPEN ACCESS

© 2023 The Author(s).
Published by S. Karger AG, Basel

This article is licensed under the Creative Commons Attribution 4.0 International License (CC BY) (http://www.karger.com/Services/OpenAccessLicense). Usage, derivative works and distribution are permitted provided that proper credit is given to the author and the original publisher.

Correspondence to:
Müge Dolgun, mugedolgun@gmail.com

treatment for pediatric DRE. In our study, we claim that both invasive monitoring and epilepsy surgery lead to favorable seizure outcomes for all age groups. Further clinical studies should be conducted to provide more reliable data on the safety and effectiveness of the surgery, particularly in patients under the age of three.
© 2023 The Author(s).
Published by S. Karger AG, Basel

Introduction

Pediatric epilepsy patients constitute 25% of the global population with epilepsy. Epilepsy affects 3.2 to 5.5 per 1,000 children, and 20–30% of children with epilepsy develop medically intractable epilepsy despite aggressive medical treatment [1, 2]. The burden of epileptic seizures on children is significant due to the undesirable side effects of antiepileptic drugs, progressive cognitive decline, behavioral problems, and overall morbidity and mortality associated with the seizures. Epilepsy surgery is a safe and effective treatment method for patients with epilepsy.

With recent advances in identifying the epileptogenic zone (EZ), such as advanced imaging techniques and invasive monitoring using intracranial electrodes, as well as new technological developments in postoperative intensive care unit facilities, surgery has become a safe and effective treatment method with satisfactory results. Previous studies have shown that surgery has resulted in a favorable seizure outcome in 50–75% of patients, including the pediatric population [3–6].

In this study, we present the results of seizure outcomes, postoperative morbidity and mortality rates, and pathological findings in 60 patients who were under the age of 18. We aimed to determine the effectiveness and safety of epilepsy surgery in the pediatric population, with or without invasive monitoring. Additionally, we investigated whether there were differences in outcomes between young children (aged three and under) and older children (over 3 years old).

Materials and Methods

Between 2002 and 2018, 60 patients with drug-resistant epilepsy (DRE) (under the age of 18) who underwent epilepsy surgery at our department were retrospectively investigated. A decision to perform surgery was made by a multidisciplinary council comprising neurosurgeons, neurologists, child neurologists, neuroradiologists, and psychiatrists.

All patients had a routine neurological examination, as well as a high-resolution magnetic resonance imaging (MRI) using a specialized epilepsy protocol. In addition, interictal routine scalp electroencephalography (EEG) and video EEG monitoring were performed. For advanced evaluation, some patients underwent functional MRI, diffusion tensor imaging, cranial ictal single photon emission computed tomography, and interictal positron emission tomography. When these studies were inconclusive, invasive monitoring was performed to identify the epileptic focus and its relation to eloquent areas. Patients were followed up during their routine visits and have also been contacted via telephone for long-term follow-up.

Clinical features of patients, results of radiological examinations, pathological findings, complication rates, and overall seizure outcomes were retrospectively reviewed. We subdivided our patients based on their age at the time of surgery. The first group included patients older than 3 years, while the second group included patients aged 3 years and younger. The seizure outcomes, surgical approaches, as well as the mortality and morbidity rates were compared between the two groups of patients. Seizure prognosis was evaluated using the Engel Outcome Scale. Patients with Engel class I and II outcome scores are considered to have a favorable seizure outcome.

Statistical Analysis

Descriptive statistical methods (mean value, standard deviation, median, frequency, percentage, minimum, and maximum) were used to describe the basic features of the study data. The Pearson χ^2 test, Fisher's exact test, and Fisher-Freeman-Halton Exact test were used to compare seizure outcomes for different surgical interventions, histopathological findings, and localization of the EZ. A probability value (p value) of <0.05 was regarded as significant. Statistical analyses were conducted using NCSS (Number Cruncher Statistical System) 2007 (Kaysville, UT, USA).

Results

Patient Characteristics

Out of 60 patients, 18 were female (30%) and 42 were male (70%). The mean age of the patients was 9.1 years, ranging from 4 months to 18 years. The mean follow-up time was found to be 8.7 years, ranging from 1 to 17 years. 17 patients were under the age of three, while 43 were older than 3 years. Demographic and clinical data are listed in Table 1.

The onset of epilepsy was 2.4 years on average ranging from early postnatal period to 14 years. Time elapsed prior to surgery was 6 years on average; however, there is not any statistically significant correlation found between the time elapsed prior to surgery and surgical outcome in either group.

Clinical and Histopathological Outcomes

In our series, specific epileptogenic foci were found in 33 patients (55%). However, in 27 patients (45%), neuroimaging tools were unable to reveal any distinct

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

Table 1. Clinical characteristics and demographic data of the patients

	Age		Total
	≤3 years	>3 years	
Patients, *n* (%)	17 (28.3)	43 (71.7)	60
Sex, *n* (%)			
Female	6 (10)	12 (20)	18 (30)
Male	11 (18.3)	31 (51.7)	42 (70)
Seizure frequency, *n* (%)			
Daily	17 (28.3)	38 (63.4)	55 (91.7)
Weekly	0	3 (5)	3 (5)
Monthly	0	2 (3.3)	2 (3.3)
Type of surgery, *n* (%)			
ATL, TL, SAH	8 (13.3)	15 (25)	23 (38.3)
ExTL[2]	5 (8.3)	13 (21.7)	18 (30)
VNS[3]	0	10 (16.6)	10 (16.6)
FSH[4]	3 (5)	1 (1.6)	4 (6.6)
Others[5]	1 (1.6)	4 (6.6)	5 (8.3)
Time to intervention, years	5.7	6.4	6
Mean follow-up, years	9.9	8.2	8.7

ATL, anterior temporal lobectomy; TL, temporal lesionectomy; SAH, selective amygdalohippocampectomy; AH, amygdalohippocampectomy; ExT, extratemporal lesionectomy; VNS, vagal nerve stimulation; FH, functional hemispherectomy; CC, corpus callosotomy; others, biopsy, excision of hypothalamic hamartoma.

epileptogenic lesion. As a result, 10 of these patients underwent invasive monitoring procedures prior to resection, while others received vagal nerve stimulation (VNS), functional hemispherectomy (FH), or corpus callosotomy (CC).

Among the patients who were under 3 years old (n = 17), 3 patients had FH, and 1 patient had a biopsy confirming a diagnosis of Rasmussen encephalitis. Remaining patients underwent temporal or extratemporal resective surgery.

Throughout the 43 patients who were older than 3 years, 1 patient had FH due to a diagnosis of Rasmussen encephalitis, 2 patients had CC, ten had VNS surgery, and the remaining patients underwent temporal or extratemporal resective surgery.

Most of the patients had epileptogenic foci in the temporal lobe (n = 23, 38.3%). Out of the 60 patients studied, 20 (33.3%) had extratemporal epileptogenic foci (mostly frontal lobe [n = 13, 72.2%]). Two of these patients had a hypothalamic hamartoma. In the group of infants (≤3 years old, n = 13), 8 patients had temporal loci (13.3%) and 5 patients (8.3%) had frontal loci as an epileptogenic region. In the children's group (>3 years old, n = 30), an equal number of 15 patients (25%) had temporal and extratemporal loci.

Among the 10 patients who had invasive monitoring prior to surgery, six had frontal foci (60%). The remaining patients had occipital (n = 2, 20%), parietal (n = 1, 10%), and temporal foci (n = 1, 10%). Two patients had frontal foci, and 1 patient had an occipital focus, all of whom were under the age of 3 (30%). The remaining patients were older (70%).

Among the patients who had resective surgery, the most common histopathological results were intracranial tumors, including glioneuronal tumors, low-grade glial tumors, and ependymomas. Cortical dysplasia (CD) was also a frequent finding, with an equal number of cases (n = 11). The diagnosis of mesial temporal sclerosis (MTS) is the second most common histopathological finding, with a total of 10 cases. Detailed histopathological entities are shown in Figure 1.

Intracranial Tumors

Out of the 11 cases of intracranial tumors studied, the most common pathology was found to be glioneuronal tumors. Glioneuronal tumors consist of dysembryoplastic neuroepithelial tumors (DNETs), gangliogliomas, and other types of glioneuronal tumors. In our study, 7 patients (11.6%) were diagnosed with glioneuronal tumors, of which four had DNET pathology (6.6%). Two patients (3.3%) were diagnosed with low-grade glioma, 1 patient (1.6%) had a hippocampal choroidal fissure cyst, and 1 patient (1.6%) had a cavernous hemangioma. Only three of them were under 3 years old (low-grade glioma, glioneuronal tumor).

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

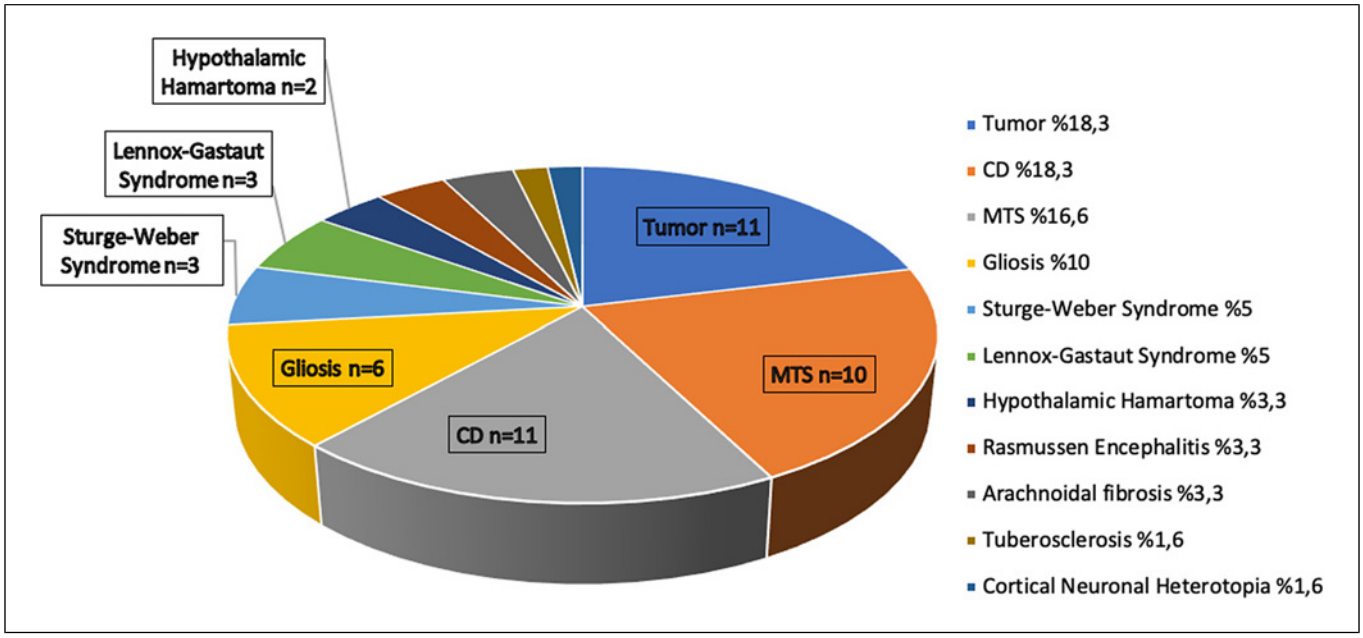


Fig. 1. Histopathological entities of patients.

Overall, patients with intracranial tumors had an 81% seizure-free outcome rate (n = 10) (Engel I–II). One patient, who was under 3 years old and had a low-grade glioma located in the temporal lobe, had an Engel III outcome score during the long-term follow-up. One patient with temporal DNET required early revision surgery to achieve gross total excision of the tumor.

Cortical Dysplasia

Eleven patients were diagnosed with CD based on histopathological examination. Out of the 11 patients with CD, four were diagnosed with CD type I. Three of these patients had frontal CD type Ia, while one had CD type Ic with a temporal origin. All patients with CD type I pathology were under the age of 3, and three of them had an unfavorable seizure outcome (75%) despite undergoing surgical intervention (Engel III–IV). Among the 3 patients with a poor prognosis, two had a frontal origin. One of these patients had invasive monitoring prior to excision and had an Engel III outcome. The third patient had a temporal origin. The remaining patient with CD type Ia had an Engel I seizure outcome and also had invasive monitoring prior to surgery. The overall outcome of seizures was 63.6% (Engel I–II; n = 7).

Seven patients were diagnosed with type II CD; three had type IIa and four had type IIb. Out of 7 patients, two were under the age of three and had CD type IIb pathology. Two of the patients with CD type II pathology had temporal origin, while the other patients with type II CD had frontal and parietal origins (as shown in Fig. 2a, b). One patient with frontal CD type IIb, who had anterior temporal lobectomy (ATL) at the age of two, required ventriculoperitoneal shunt placement 1 year later during follow-up visits. The patient's condition was complicated by autism and had an Engel III seizure outcome, while the remaining patients had a favorable seizure outcome (Engel I–II) (n = 6, 85.7%).

Six patients were diagnosed with CD based on MRI scans and neurophysiological tests that were in agreement. In 4 patients with inconclusive results from noninvasive evaluations, invasive monitoring was conducted prior to surgery. Among these patients, three had a favorable seizure outcome (Engel I–II).

For patients with CD, the lesion was predominantly located in extratemporal regions. However, there was not any statistically significant difference found between the outcomes of temporal and extratemporal surgical procedures in relation to seizure control. Age predominance was also statistically insignificant when compared to the outcome of seizures (see Table 2).

Mesial Temporal Sclerosis

Ten patients with MTS had temporal resective surgeries. Four patients had ATL + amygdalohippocampectomy (AH) and 3 patients had selective amygdalohippocampectomy (SAH). The remaining patients

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

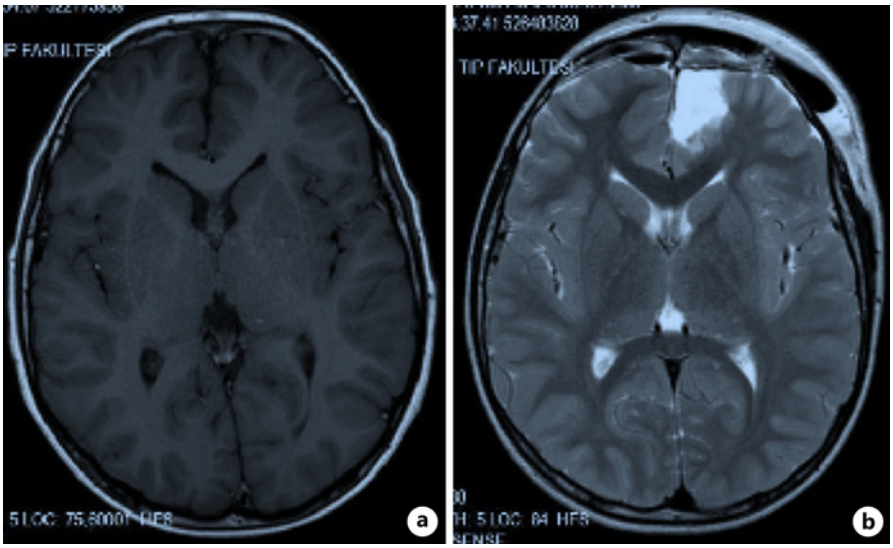


Fig. 2. a A left frontal lobe lesion just anterior to the cingulate gyrus is seen on preoperative MRI (T1-weighted FLAIR sequence) of a patient with CD type IIb. **b** The resection site of this lesion is seen on the postoperative MRI (T2-weighted sequence).

Table 2. CD patients compared according to age, type of surgery, and surgical outcome

		Surgical outcome, *n* (%)		*p* value
		Engel I–II	Engel III–IV	
Age	≤3 years	2 (33.4)	4 (66.6)	*0.076
	>3 years	4 (80)	1 (20.0)	
Type of surgery	Extratemporal	5 (62.5)	3 (37.5)	*0.500
	Temporal	1 (33.4)	2 (66.6)	

*Fisher's exact test.

had ATL procedure. Overall, 8 patients achieved successful seizure control postoperatively with an Engel I–II outcome score (80%), while the remaining 2 patients had an Engel III–IV seizure outcome.

All of the patients were over 3 years old, except for 1 patient who was 3 years old and had hypoxic ischemic encephalopathy and mesial temporal sclerosis. This patient underwent ATL with AH. Seizure control (Engel II) was achieved postoperatively for 1 year. However, 1 year after the surgery, seizures have become persistent, despite the use of three antiepileptic agents. After 5 years from ATL surgery, FH was decided to be the appropriate surgical choice for the patient. Following the FH procedure, seizures were under control with the appropriate antiepileptic drug regimen (Engel II).

Functional Hemispherectomy

Four patients diagnosed with Sturge-Weber syndrome and Rasmussen encephalitis had FH procedure, representing 6.6% of the total cases. Two individuals with Sturge-Weber syndrome had Engel I and II seizure outcomes (shown in Fig. 3). The third patient diagnosed with Rasmussen encephalitis had an Engel III outcome. The fourth patient, a two-year-old with Sturge-Weber syndrome, was lost due to diffuse cerebral edema during the early postoperative period.

Excision of Hypothalamic Hamartoma

Two patients who were over 3 years old (3.3%) were diagnosed with hypothalamic hamartoma and had partial resection of the hamartoma. One patient had an Engel II seizure outcome, while the other had an Engel III seizure outcome.

Corpus Callosotomy

Two patients over the age of 3 years old (3.3%) had CC for polymorphic seizures without any apparent lesion and Lennox-Gastaut syndrome. The patient with polymorphic seizures had an Engel II outcome, while the patient with Lennox-Gastaut syndrome had a poor seizure outcome (Engel III).

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

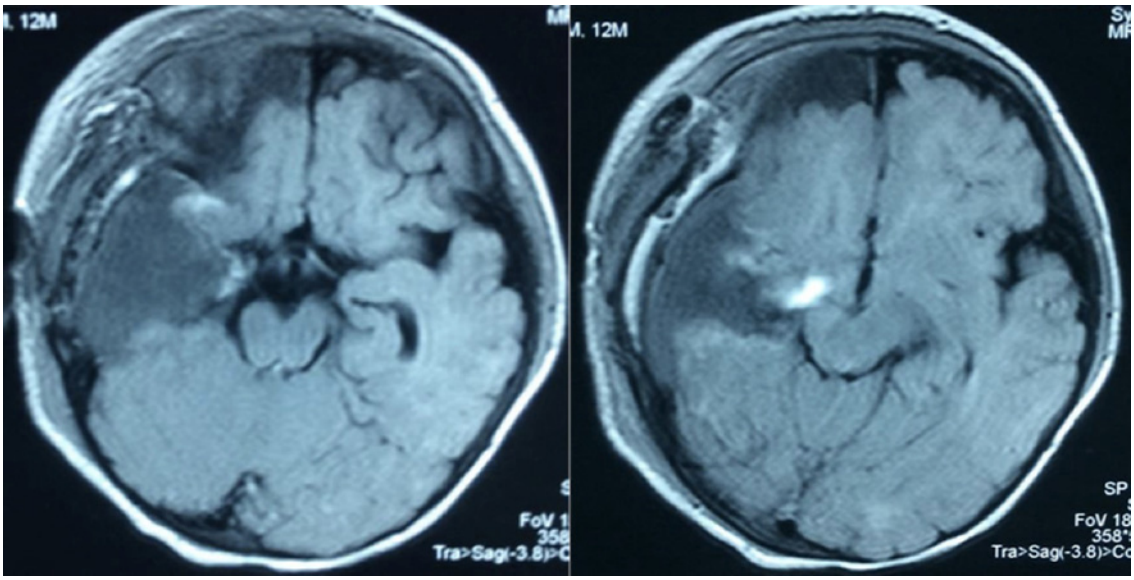


Fig. 3. Postoperative cranial MR images with axial T1-weighted FLAIR sequences of a patient diagnosed with Sturge-Weber syndrome who had FH.

Vagal Nerve Stimulation

Out of the 10 patients who had VNS procedure (16.6%), two had Lennox-Gastaut syndrome, one had tuberous sclerosis, while the remaining patients did not have any specific lesions related to a particular diagnosis. All of the patients were over 3 years old. Four patients (40%) had a favorable seizure outcome (Engel II).

Invasive Monitoring

Ten patients were operated for intracranial invasive monitoring procedures, representing 16.6% of the total sample. Six patients underwent frontal lesionectomy, two underwent occipital lesionectomy, 1 patient had parietal lesionectomy, and 1 patient had temporal lesionectomy following video EEG monitoring using subdural and/or depth electrodes (shown in Fig. 5). Seven patients had electrocorticography to define the motor cortex and establish the correlation between the EZ before undergoing resective surgery. Out of the total number of patients (n = 10), 50% (n = 5) had a favorable seizure outcome (Engel I–II), while the remaining patients had unfavorable outcomes (Engel III and IV).

Three patients who underwent invasive monitoring were under 3 years old. Following resection, two of them had CD type IIa, and one had gliosis as a pathological result. One patient with CD type IIa had an Engel I outcome, while the other 2 patients had Engel III and Engel IV outcomes.

Two patients (20%) had cerebrospinal fluid leakage following the insertion of the electrodes; however, the leakage ceased after the subsequent resection surgery and concomitant duraplasty. These patients were under 3 years of age and had also developed complications related to central nervous system (CNS) infection after undergoing a subsequent operation. However, they were successfully treated with antibiotics.

Among the patients who were over 3 years old, 1 patient developed a CNS infection after resection surgery, despite the absence of cerebrospinal fluid leakage. However, the infection was successfully controlled with antibiotics. There was not any other complications noted regarding the invasive monitoring procedure. However, one 12-year-old patient developed nosocomial pneumonia, and 3 patients aged 7, 9, and 11 years old experienced transient hemiparesis following the subsequent resection surgery. Patients with transient hemiparesis were diagnosed with DNET, CD type IIa, and West syndrome, respectively. Except for the patient with West syndrome (Engel IV), all of them had Engel I and II outcomes. No other complications related to the invasive monitoring procedure were noted.

Overall Surgical Outcome

47 patients had resective surgery, while 13 patients had palliative surgery (CC, VNS, biopsy). Detailed surgical approaches and their corresponding etiological entities are shown in Table 3.

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

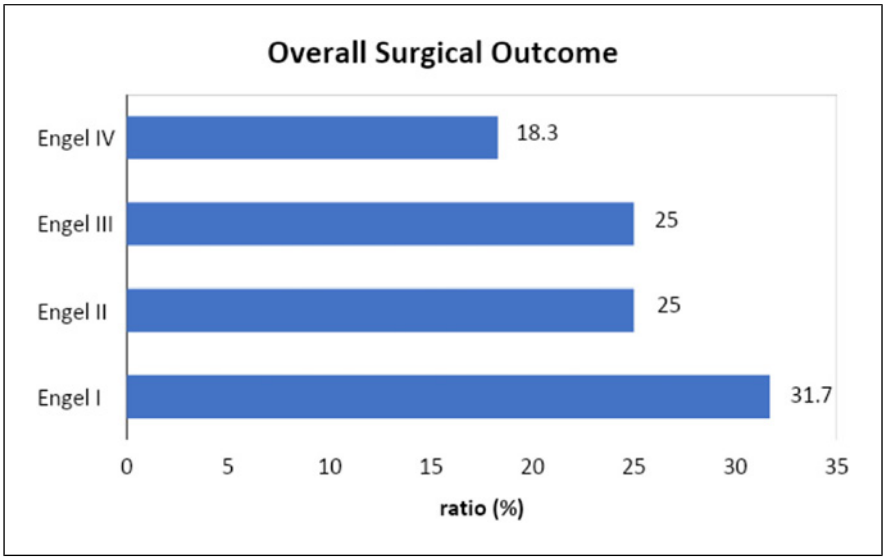


Fig. 4. Overall Engel outcome scores.

56.6% of the patients (n = 34) achieved Engel I and II seizure outcome scores, while 43.4% of the patients (n = 26) had Engel III and IV outcome scores postoperatively (shown in Fig. 4). Out of a total of 17 patients who were under 3 years old, 47% had a favorable seizure outcome (Engel I–II) (n = 8). On the other hand, out of a total of 43 patients who were over 3 years old (>3 years), 60.4% had Engel I and II seizure outcomes (n = 26). Although there appeared to be a difference in surgical outcome scores favoring older patients, there was no statistically significant difference in seizure outcome scores between the two patient groups (p = 0.345).

Furthermore, temporal surgeries yielded better surgical outcomes in both groups. In the infant group, four out of eight patients (50%) who had temporal surgery had a favorable surgical outcome. In the children's group, thirteen out of 15 patients (86.6%) achieved Engel I–II outcome after temporal surgery. However, among the group of infants who had extratemporal surgery, a success rate of 40% was observed (n = 2). In the children's group, the success rate with extratemporal surgery was 46.1%.

33 patients were followed for a period of 9 years, with the duration of follow-up ranging from 1 to 9 years. Ten patients were under 3 years old, whereas 23 patients were over 3 years old at the time of intervention. At the last follow-up, 18 patients had an Engel I–II outcome (54%), of which 4 were under the age of 3 and 14 were older than 3 years old.

27 patients, including seven who were under 3 years old, were followed up for a period of 10–17 years. Among these patients, a total of 16 patients (59%) had a favorable outcome at the end of the follow-up period, as determined by Engel classification I and II. There was not any statistically significant difference found between the two groups of patients with different follow-up times.

Mortality and Morbidity

The overall complication rate was 35% (n = 21). Complications included CNS infection, nosocomial pneumonia, postoperative transient paresis, cerebrospinal fluid fistula, postoperative epidural hematoma, hydrocephalus, subdural effusion, and diffuse cerebral edema.

Infectious Complications

The most common complication was CNS infection which was observed in 9 patients (15%). However, the infections were resolved following an appropriate antibiotherapy regimen. The rate of CSF infection complications was found to be 23.5% (n = 4) for patients under 3 years old, while patients over 3 years old had a complication rate of 11.6% (n = 5).

In total, 10% of the patients developed nosocomial pneumonia (n = 6). Four of these patients (80%) were under the age of 3 and had both CD and arachnoidal fibrosis. All the patients recovered without any complications after receiving the appropriate antibiotic treatment.

Surgical Complications

Four patients (6.6%) diagnosed with CD type IIa, DNET, West syndrome, and Sturge-Weber syndrome had postoperative transient hemiparesis, which gradually

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

Table 3. Total number of patients according to etiological entity and type of surgery

Surgery and etiology	*ATL*, SAH, Lesionectomy	*FSH*	*VNS*	*CC*	Excision of hamartoma	Biopsy
Intracranial tumor	11					
MTS	10					
CD						
Type I	4					
Type II	7					
Hypothalamic hamartoma					2	
Sturge-Weber syndrome		3				
Lennox-Gastaut syndrome			2	1		
Landau-Kleffner syndrome	1					
Rasmussen encephalitis		1				1

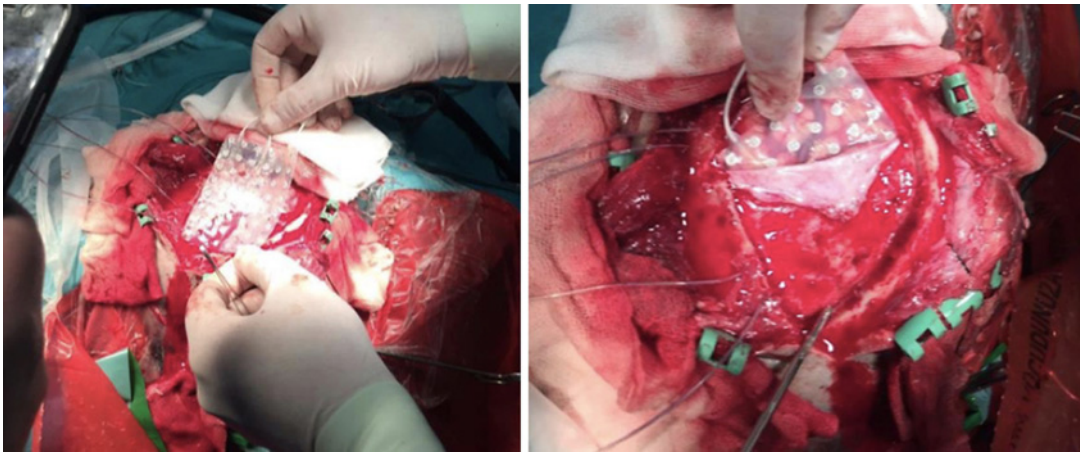


Fig. 5. Intraoperative images showing the implantation of subdural grids following a pterional craniotomy.

improved during the early postoperative stage. Three of them had invasive monitoring followed by surgery. The remaining patient who is 1 year old of age with Sturge-Weber syndrome had FH. There was not any statistically significant difference found in the complication rates among the different surgical procedures.

Four patients (6.6%) had cerebrospinal fluid leakage. Three of these patients recovered successfully following subsequent operations, while 1 patient had spontaneous resolution. All of the patients were under 3 years old.

Out of the 17 patients who were under 3 years old, 11 patients (64.7%) experienced complications related to surgery. These complications included nosocomial pneumonia (n = 4), postoperative transient paresis (n = 2), cerebrospinal fluid fistula (n = 4), and diffuse cerebral edema (n = 1).

Among the patients who were over 3 years old (n = 43), 11 patients (25.5%) experienced postoperative complications. These complications included nosocomial pneumonia (n = 2), postoperative transient paresis (n = 3), CSF infection (n = 5), anterograde amnesia following hypothalamic hamartoma excision (n = 1), and postoperative epidural hematoma evacuation following SAH procedure (n = 1).

Two patients had reoperations due to the recurrence of preexisting intracranial tumoral pathology such as anaplastic ependymoma (in a 3-year-old) and oligodendroglioma (in a 7-month-old). Both patients achieved an Engel I outcome. One 12-year-old patient with DNET pathology located in the temporal region had a residual

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

tumor in the early postoperative period following the initial surgery. Therefore, 1 week later, the patient underwent a reoperation to remove the residual temporal tumor, which resulted with total excision and an Engel I outcome.

Four patients with CD (type Ia and IIb), MTS, and arachnoidal fibrosis underwent ventriculoperitoneal or subduroperitoneal shunting due to postoperative hydrocephalus or subdural effusion. Three patients with CD were aged 1 and 2 years, while 1 patient with MTS who had ATL was 8 years old at the time of intervention.

A postoperative epidural hematoma occurred in a 13-year-old patient following a SAH procedure, which necessitated surgical decompression. The patient achieved an Engel I seizure outcome.

The reoperation rates did not show a statistically significant difference between the two age groups (>3 years vs. ≤3 years) ($p > 0.05$). The overall mortality rate was 1.6% ($n = 1$). A two-year-old patient with Sturge-Weber syndrome, who had FH, had early postoperative mortality due to diffuse cerebral infarction.

Discussion

DRE is one of the major debilitating childhood diseases, which creates a significant socioeconomic burden. Even in developed countries, DRE patients may have difficulties reaching proper evaluation and care at an experienced epilepsy center. With advancements in evaluation and management techniques, as well as a better understanding of diseases, patients are more frequently referred to epilepsy surgery. In our study, we retrospectively reviewed pediatric patients who underwent epilepsy surgery during the early stages of the field, as well as during a more recent era characterized by advanced technology, invasive monitoring, and sophisticated microsurgical techniques. We investigated the etiology, complications, and surgical outcomes in different age groups, dividing the pediatric population into two groups: patients under 3 years of age and those over 3 years of age. This division was made because complications may be more common in younger children [7].

Early referral to surgery has been proven to be effective in achieving a seizure-free outcome, as reported in previous literature [8]. In our study, we found that patients' referral to surgical intervention has been delayed for various reasons, such as low socioeconomic status or inadequate referral to experienced epilepsy centers. This delay may be due to inadequate appreciation of epilepsy surgery as a safe and effective treatment method.

The location of epileptogenic foci is another crucial aspect of epilepsy surgery. In our series, we investigated 60 patients. Of these, 23 patients had temporal lesionectomy, and 20 patients had extratemporal epilepsy surgery. This finding is inconsistent with current literature, which reports that extratemporal EZ is more prevalent in the pediatric population [9]. We assume that our results were impacted by the limited number of patients, which was due to a lack of referrals at that time.

According to Cascino's 2004 study, the outcomes of extratemporal resections are less satisfactory compared to resections in the temporal region [10]. In 2020, Widjaja et al. [11] conducted a meta-analysis that included hemispheric surgery, temporal surgery, and extratemporal surgery. They concluded that the lowest degree of seizure freedom was achieved with extratemporal surgery (60.2%). In our study, we observed that 73% of patients with temporal lobe seizures and 50% of patients with extratemporal lobe seizures achieved a seizure-free outcome. Our findings align with the current literature as mentioned earlier.

It has been reported that the most common cause of pediatric epilepsy patients who undergo surgery is focal CD. The second most common cause is intracranial tumors [12]. Even though more patients with CD would be expected than intracranial tumors, the same number of cases were noted ($n = 11$). The reason for this could be the reason of prompt referral to surgical centers after being diagnosed with tumoral pathologies, unlike CD patients. Especially in the early years of our study, only 3 patients with CD were referred between 2002 and 2011, while the rest of the CD patients ($n = 8$) were operated between 2011 and 2018.

There is a dominance of DNET pathology compared to low-grade glioma and other pathologies in our series. Patients with intracranial tumoral pathologies had an excellent outcome with 80% of seizure relief regardless of their age. This leads to better results when compared to complicated cases such as CD, in which it is often difficult to determine the extent of the epileptogenic region. Hence, patients with intracranial tumors in this group typically achieve satisfactory results, as previously stated in the literature [11]. In 2020, Widjaja et al. [11] conducted a systematic review of outcomes for pediatric epilepsy surgery. The study found that patients with tumoral pathologies had higher rates of seizure freedom (79.8%) compared to those with other etiologies. Especially for non-lesional epilepsy surgery, the success rate was found to be lower when compared to lesional epilepsy surgery.

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

Among CD patients, 63.6% (n = 7) have achieved seizure control, which may be attributed to the underlying pathology. Patients with CD type I were found to have inferior seizure control compared to those with CD type II. Krsek et al. conducted a retrospective review of 40 pediatric patients with histopathologically confirmed CD type I and II. The study found that the seizure freedom rate was 21% for CD type I patients, while it was 75% for CD type II patients [13, 14]. Our cases with lower rates of seizure freedom are mostly associated with CD type I pathology, which is consistent with current literature.

MTS is another significant cause of DRE. Even though it is not as prevalent as it is in adults, MTS is still the third leading cause of DRE, following CD and intracranial tumors [12]. There have been different approaches suggested over the years for cases of MTS, such as ATL or SAH. Some studies suggest that SAH may be preferable to ATL, as it has been claimed that SAH produces better neurophysiological results [15]. In our study, there were not enough patients to conduct such an evaluation. However, the overall seizure-free outcome rate for patients with MTS was 80%, which is similar to the study conducted by Wjdaja et al. [11]. In their study, they reported a seizure-free outcome rate of 79.8% for patients with intracranial tumors and 77.9% for patients with MTS.

In addition to common cerebral pathologies such as tumors, CD, and MTS, there are specific hemispheric brain disorders that may cause pediatric DRE, such as Sturge-Weber syndrome and Rasmussen encephalitis. Hemispherectomy procedures have been reported to be effective in controlling seizures, especially in younger children (<5 years of age) with Sturge-Weber syndrome and Rasmussen encephalitis. Bourgeois et al. [16] presented a seizure control rate of 70% in 27 patients with Sturge-Weber syndrome who had hemispherectomy. Bellamkonda et al. also stated that, after 5 years of follow-up, 47.6% of the patients (n = 41) with Rasmussen encephalitis who underwent hemispherectomy achieved seizure freedom [17]. As these cohorts included cases of both anatomical hemispherectomy and FH, overall hemispherectomy procedure appears to be an important treatment option for these patients during long-term follow-up. Furthermore, no statistically significant difference was found between the anatomical hemispherectomy procedure and the FH procedure in terms of seizure control [18]. In our series, FH was the preferred technique. However, due to the small sample size (n = 4), we cannot make any definitive conclusions about these findings.

Early surgery is recommended for these patients, as studies have shown that delaying surgery can lead to significant deterioration in cognition and neurological development [18, 19]. In our series, 75% of the patients were under the age of 3, and two-thirds of them had an Engel II outcome score, which supports early surgical intervention.

Invasive monitoring is an essential component of epilepsy surgery [20]. In 2018, Goldstein et al. [21] reported an Engel I outcome rate of 53% in 25 patients who had SEEG implantation after a mean follow-up of 3 years. In our series, we observed a success rate of 50% in terms of seizure outcomes.

Complication rates of approximately 1–3% have been reported with invasive monitoring [22, 23]. The most common complication of invasive monitoring is known to be CNS infections [24]. However, complication rates as high as 6–25% have also been reported with subdural electrode implantations [21]. These complications tend to occur mostly due to the craniotomy that was performed to insert the subdural grid for investigation of EZ and/or electrocorticography concerns [25]. In our study, we also observed a 20% rate of CNS infection, which was a consequence of cerebrospinal fluid leakage and occurred regardless of age.

For patients who are not suitable candidates for resective epilepsy surgery, VNS has been recommended as a treatment option to reduce the frequency of seizures [26]. In 2009, Zamponi et al. [27] demonstrated that in a study of 100 patients ranging in age from 0.64 to 51.04 years, those under the age of 12 had a better seizure outcome (50%) compared to the rest of the group. More favorable results have been reported in the literature. For instance, Arhan et al. [28] reported a seizure-free outcome rate of 61.6% in 2010. However, financial constraints and restrictions on social security may limit the use of VNS in certain countries. These issues may be the cause of our limited number of cases. Over a period of 16 years, 10 patients had VNS implantation and were followed up in the long term. The seizure-free outcome rate for these patients was 40%. We may speculate that for patients with DRE who are not eligible for surgical resection, VNS remains a significant treatment option to reduce the frequency of debilitating seizures.

In 2016, Jenny et al. [29] showed that patients who are under 3 years old have better surgical outcome yet similar morbidity rates when compared to the children and adolescent group (>3 years). According to their study, epileptogenic loci in the developing brains of infants are typically more restricted, making them more amenable to adequate resection compared to those in older children. In our study, we found that children over 3 years old had a more favorable seizure outcome (60.5%). This may be due

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

to differences in the underlying causes of the seizures among the patients. For example, the majority of intracranial tumor cases consisted of children and adolescents, with the exception of 3 patients who were infants at the time of intervention.

Between 2002 and 2010, 7 patients under the age of three underwent surgery, while from 2010 to 2018, the number increased to ten. This indicates a growing number of cases of small children being referred to for epilepsy surgery. This observation indicates that the referral of patients for epilepsy surgery, especially of small children, is a gradual process. Because of that reason, there was a limited number of cases in each subgroup of patients with various surgical approach. The statistical significance remained to appear as insufficient; however, our clinical experience indicates that performing surgery for DRE patients is a safe and effective treatment, even during the early stages of a department's practice. Our results provide well-grounded data for this specific field of pediatric neurosurgery and thus contribute to the literature as to demonstrate the effectiveness and safety of epilepsy surgery for younger population.

The average morbidity rate for pediatric epilepsy surgery was reviewed by Hader et al. in 2013 [30]. Complications were classified as minor and major. Minor complications included CSF infections, CSF leakage, transient hemiparesis, and pneumonia. Major complications included permanent hemiparesis, hydrocephalus, and drainage for postoperative intracerebral hematoma. For pediatric patients, the rate of minor complications was found to be 11.2%, while the rate of major complications was 5.1% [30]. In our study, the overall morbidity rate was noted to be 35%, which exceeded the expected rate. This may be because of the reason that Hader et al. included 543 pediatric patients instead of 60 patients as it was in our study group. Second, in 2015, Kumar et al. [31] conducted a study that included a group of 25 infants who had epilepsy surgery. The authors reported a complication rate of 36%, which is similar to our own findings.

In the literature, mortality rates in pediatric epilepsy surgery tend to range from 1 to 2%, as reported by Kwon in 2019 [12]. Our study correlates these results with a mortality rate of 1.6% (n = 1). Since there was only 1 patient who was 2 years old with mortality due to diffuse cerebral edema following a FH operation for Sturge-Weber syndrome, we claim that specific syndromes in the younger population need a meticulous management during the perioperative period.

Our study presents a cohort from a single center performing epilepsy surgery over a period of 15 years to demonstrate the differences in etiology and effectiveness of the surgery in pediatric epilepsy patients. As a comprehensive perioperative process is necessary for younger children, we emphasize that morbidity and mortality rates may vary from those of older children, as demonstrated in our study. Therefore, we think that evaluation criteria may be different regarding the age of the patient.

Our department has been practicing epilepsy surgery for over 20 years, which has resulted in considerable experience in the evolution of epilepsy surgery in a developing country. With the advent of technological developments and socioeconomic improvements, the referral of patients with DRE has remarkably increased since the early years of our practice. The improvement of archiving technology has also had a significant impact on creating a cohort and analyzing the associated data. It is of utmost importance to establish a team of specialized neurologists, neuroradiologists, and neurosurgeons for epilepsy surgery to make appropriate perioperative decisions. We assert that favorable outcomes can be attained by conducting a thorough perioperative investigation and utilizing appropriate archiving techniques.

Pediatric patients with DRE are well selected and thoroughly evaluated patients in order to be referred to epilepsy surgery programs. The number of patients being referred to surgery and the documentation of these patients are quite limited because of the rarity of the pathology. Hence, the contribution to the literature can be achieved by each cohort presented by experienced departments explaining the possible morbidity and mortality rates regarding different aspects of the patients, in our case, the age difference (>3 and 3> years of age). Therefore, we would like to encourage other departments to publish their results as they progress in this field of surgery.

In our study, albeit a limited number of patients, our results indicate sufficient seizure control with acceptable complication rates in the pediatric population. Even though there was not any statistically significant difference found to demonstrate the safety and the effectiveness of the surgery between the two different groups of patients, our trends which were correlated well with the current literature indicate that safe and effective surgical outcomes can be achieved for both groups of patients.

The limitation of our study is its small sample size and retrospective design. As the number of cases increases, statistical significance also improves. Therefore, studies with a similar number of patients are expected to yield similar results. However, this study represents a single-center experience spanning 16 years, highlighting the

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

epidemiological differences among pediatric patients with DRE during a long-term follow-up period. The study emphasizes the significance and efficacy of pediatric epilepsy surgery for patients with intractable seizures, while also discussing the potential complications for different age groups, along with the feasibility of building an epilepsy surgery program.

Conclusion

Epilepsy surgery is often necessary for infants and children with DRE to prevent developmental delays and achieve a seizure-free state. The risk of surgical morbidity or mortality remains a major concern for neurosurgeons worldwide, particularly when operating on infants. In our study comparing infants and older children, we may conclude that the surgical complications for the infant population can be challenging when compared to the older population based on our overall clinical experience. Therefore, a thorough preoperative assessment is necessary to determine the optimal treatment approach for the patient, and appropriate perioperative precautions should be implemented to prevent potential complications. This study is encouraging other departments to be assertive in starting an epilepsy surgery program from the beginning since we demonstrated the feasibility and effectiveness of building an epilepsy surgery program with a growing number of patients. Further studies with a larger number of patients are needed in order to demonstrate the presence of a statistically significant difference regarding the efficacy and safety of epilepsy surgery.

Statement of Ethics

Ethical approval for our study was obtained from the Clinical Research Ethics Committee at Istanbul University (154357-1129). Written informed consent was obtained from each patient and their parents in accordance with the principles outlined in the World Medical Association Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding was obtained during the process of this study.

Author Contributions

Altay Sencer, Aydın Aydoseli, Bülent Kara, Candan Gürses, and Müge Dolgun contributed to the design and baseline of the study. Nermin Görkem Şirin, Emek Uyur Yalçın, Ayfer Sakarya Güneş, and, Nerses Bebek contributed in revising the manuscript. Müge Dolgun, Duygu Dölen, Ilyas Dolaş, and Tuğrul Cem Ünal contributed to data collection, analysis, and drafting of the manuscript.

Data Availability Statement

All of the analyzed data have been included in the study, and the collected database of our study was declared to the research data repository Zenodo (https://doi.org/10.5281/zenodo.7503984). Further inquiries may be directed to the corresponding author.

References

1 Camfield P, Camfield C. Incidence, prevalence and aetiology of seizures and epilepsy in children. Epileptic Disord. 2015;17(2):117–23.
2 Berg AT, Shinnar S, Levy SR, Testa FM, Smith-Rapaport S, Beckerman B. Early development of intractable epilepsy in children: a prospective study. Neurology. 2001;56(11):1445–52.
3 Ramey WL, Martirosyan NL, Lieu CM, Hasham HA, Lemole GM Jr, Weinand ME. Current management and surgical outcomes of medically intractable epilepsy. Clin Neurol Neurosurg. 2013;115(12):2411–8.
4 Duchowny MS. Surgery for intractable epilepsy: issues and outcome. Pediatrics. 1989;84(5):886–94.
5 Perry MS, Duchowny M. Surgical management of intractable childhood epilepsy: curative and palliative procedures. Semin Pediatr Neurol. 2011;18(3):195–202.
6 Guan J, Karsy M, Ducis K, Bollo RJ. Surgical strategies for pediatric epilepsy. Transl Pediatr. 2016;5(2):55–66.
7 Iwasaki M, Iijima K, Kawashima T, Tachimori H, Takayama Y, Kimura Y, et al. Epilepsy surgery in children under 3 years of age: surgical and developmental outcomes. J Neurosurg Pediatr. 2021;28(4):395–403.
8 Helmstaedter C, Beeres K, Elger CE, Kuczaty S, Schramm J, Hoppe C. Cognitive outcome of pediatric epilepsy surgery across ages and different types of surgeries: a monocentric 1-year follow-up study in 306 patients of school age. Seizure. 2020;77:86–92.
9 Gadgil N, LoPresti MA, Muir M, Treiber JM, Prablek M, Karas PJ, et al. An update on pediatric surgical epilepsy: Part I. Surg Neurol Int. 2019;10:257.
10 Cascino GD. Surgical treatment for extratemporal epilepsy. Curr Treat Options Neurol. 2004;6(3):257–62.
11 Widjaja E, Jain P, Demoe L, Guttmann A, Tomlinson G, Sander B. Seizure outcome of pediatric epilepsy surgery: systematic review and meta-analyses. Neurology. 2020;94(7):311–21.
12 Kwon HE, Kim HD. Recent aspects of pediatric epilepsy surgery. J Epilepsy Res. 2019;9(2):87–92.
13 Choi SA, Kim KJ. Focal cortical dysplasia in pediatric epilepsy. Ann Child Neurol. 2019;27(4):93–104.
14 Krsek P, Pieper T, Karlmeier A, Hildebrandt M, Kolodziejczyk D, Winkler P, et al. Different presurgical characteristics and seizure outcomes in children with focal cortical dysplasia type I or II. Epilepsia. 2009;50(1):125–37.

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024

15 Schramm J. Temporal lobe epilepsy surgery and the quest for optimal extent of resection: a review. Epilepsia. 2008;49(8):1296–307.
16 Bourgeois M, Crimmins DW, de Oliveira RS, Arzimanoglou A, Garnett M, Roujeau T, et al. Surgical treatment of epilepsy in Sturge-Weber syndrome in children. J Neurosurg. 2007;106(1 Suppl l):20–8.
17 Bellamkonda N, Phillips HW, Chen JS, Tucker AM, Maniquis C, Mathern GW, et al. Epilepsy surgery for Rasmussen encephalitis: the UCLA experience. J Neurosurg Pediatr. 2020;26(4):389–97.
18 Bien CG, Granata T, Antozzi C, Cross JH, Dulac O, Kurthen M, et al. Pathogenesis, diagnosis and treatment of Rasmussen encephalitis: a European consensus statement. Brain. 2005;128(Pt 3):454–71.
19 Devlin AM, Cross JH, Harkness W, Chong WK, Harding B, Vargha-Khadem F, et al. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. Brain. 2003;126(Pt 3):556–66.
20 Barba C, Cross JH, Braun K, Cossu M, Klotz KA, De Masi S, et al. Trends in pediatric epilepsy surgery in Europe between 2008 and 2015: country-center-and age-specific variation. Epilepsia. 2020;61(2):216–27.
21 Goldstein HE, Youngerman BE, Shao B, Akman CI, Mandel AM, McBrian DK, et al. Safety and efficacy of stereo-electroencephalography in pediatric focal epilepsy: a single-center experience. J Neurosurg Pediatr. 2018;22(4):444–52.
22 Bourdillon P, Ryvlin P, Isnard J, Montavont A, Catenoix H, Mauguière F, et al. Stereotactic electroencephalography is a safe procedure, including for insular implantations. World Neurosurg. 2017;99:353–61.
23 Mullin JP, Shriver M, Alomar S, Najm I, Bulacio J, Chauvel P, et al. Is SEEG safe? A systematic review and meta-analysis of stereo-electroencephalography-related complications. Epilepsia. 2016;57(3):386–401.
24 Tanriverdi T, Ajlan A, Poulin N, Olivier A. Morbidity in epilepsy surgery: an experience based on 2,449 epilepsy surgery procedures from a single institution. J Neurosurg. 2009;110(6):1111–23.
25 Lesko R, Benova B, Jezdik P, Liby P, Jahodova A, Kudr M, et al. The clinical utility of intraoperative electrocorticography in pediatric epilepsy surgical strategy and planning. J Neurosurg Pediatr. 2020;26(5):533–42.
26 Tsai JD, Fan PC, Lee WT, Hung PL, Hung KL, Wang HS, et al. Vagus nerve stimulation in pediatric patients with failed epilepsy surgery. Acta Neurol Belg. 2021;121(5):1305–9.
27 Zamponi N, Cesaroni E, Petrelli C, Passanonti C, Trignani R, Rychlicki F. Vagal nerve stimulation in intractable epilepsy: clinical experience on 100 patients and review of the literature. J Pediatr Sci. 2009;1:e17.
28 Arhan E, Serdaroglu A, Kurt G, Bilir E, Durdağ E, Erdem A, et al. The efficacy of vagal nerve stimulation in children with pharmacoresistant epilepsy: practical experience at a Turkish tertiary referral center. Eur J Paediatr Neurol. 2010;14(4):334–9.
29 Jenny B, Smoll N, El Hassani Y, Momjian S, Pollo C, Korff CM, et al. Pediatric epilepsy surgery: could age be a predictor of outcomes? J Neurosurg Pediatr. 2016;18(2):235–41.
30 Hader WJ, Tellez-Zenteno J, Metcalfe A, Hernandez-Ronquillo L, Wiebe S, Kwon CS, et al. Complications of epilepsy surgery: a systematic review of focal surgical resections and invasive EEG monitoring. Epilepsia. 2013;54(5):840–7.
31 Kumar RM, Koh S, Knupp K, Handler MH, O'Neill BR. Surgery for infants with catastrophic epilepsy: an analysis of complications and efficacy. Childs Nerv Syst. 2015;31(9):1479–91.

Downloaded from http://karger.com/pne/article-pdf/doi/10.1159/000535023/4050784/000535023.pdf by Koç University user on 13 February 2024