[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

Original Article

Long-Term Surgical Outcomes and Predictors of Surgical Treatment in Temporal Lobe Epilepsy

Irem Yildirim, Asli Akyol Gurses, Esra Erkoc Ataoglu, Gokhan Kurt[1], Umit Ozgur Akdemir[2], Ali Yusuf Oner[3], Tugba Hirfanoglu[4], Lutfiye Ozlem Atay[2], Ayşe Serdaroglu[4], Erhan Bilir

Department of Neurology, Gazi University Faculty of Medicine, [1]Department of Neurosurgery, Gazi University Faculty of Medicine, [2]Department of Nuclear Medicine, Gazi University Faculty of Medicine, [3]Department of Radiology, Gazi University Faculty of Medicine, [4]Department of Pediatric Neurology, Gazi University Faculty of Medicine, Ankara, Turkey

Abstract

Background: Surgical treatment of epilepsy is a favored modality in the management of refractory temporal lobe epilepsy (TLE) and known to be quite effective. The aim of this study was to evaluate the long-term outcomes in surgical treatment of TLE and to identify prognostic factors influencing postoperative seizure remission. **Materials and Methods:** The patients who underwent anterior temporal lobectomy (ATL) with the diagnosis of refractory TLE in our center between the years of 2006 and 2020 were included. Preoperative workup process was carried out by a multidisciplinary team and consisted of neuropsychological examination, long-term electroencephalography, brain magnetic resonance imaging (MRI), and fluorodeoxyglucose positron emission tomography (FDG-PET) for each patient. Postoperative assessment of seizure control was repeated every year following surgery and categorized according to Engel's outcome classification. The predictive value of baseline demographic, clinical, laboratory, imaging, and histopathological parameters on postoperative seizure control was also evaluated. **Results:** One hundred and forty-three patients who underwent ATL with the diagnosis of TLE were included. According to Engel's classification, the seizure freedom rate was found to be 83.2% at the 2nd year, 81.3% at the 4th year, and 79.2% at the 10th year after surgery. In the univariate analysis, febrile seizure (FS) history, unilateral interictal epileptiform discharges (IEDs), hippocampal sclerosis (HS) on MRI, unilateral temporal hypometabolism (HM) on FDG-PET, and HS in histopathology were predictors of seizure control at the postoperative 2nd and 10th years. FS history, unilateral localization of IEDs, and unilateral FDG-PET findings of temporal HM were found to be the independent predictors of postoperative seizure control on multivariate analysis. **Conclusions:** In the current study, we revealed that epilepsy surgery provides effective seizure control and represents a beneficial therapeutic option in refractory TLE. Our results also suggested that FS history, unilateral IEDs, and unilateral FDG-PET findings of temporal HM were independent predictors of seizure remission in these patients.

Keywords: *Electroencephalography, refractory temporal lobe epilepsy, surgical treatment of epilepsy*

Submitted: 21-Oct-2021
Revised : 29-Oct-2021
Accepted : 31-Oct-2021
Published : 29-Dec-2021

Introduction

Temporal lobe epilepsy (TLE) is the most common localization-related epilepsy syndrome in adults. Previous reports have revealed that complete remission was achieved in only 8%–23% of TLE patients with antiepileptic drugs (AEDs) and surgical treatment was quite superior to medical therapy in these patients.[1-4] Refractory TLE has been the most common indication for epilepsy surgery,[5,6] and approximately 59%–82%

Access this article online

Quick Response Code:

Website: www.nsnjournal.org

DOI: 10.4103/nsn.nsn_200_21

Address for correspondence: Dr. Irem Yildirim, Department of Neurology, Gazi University Faculty of Medicine, Besevler, Ankara 06500, Turkiye.
E-mail: driremyildirim@yahoo.com.tr

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Yildirim I, Gurses AA, Ataoglu EE, Kurt G, Akdemir UO, Oner YA, *et al.* Long-term surgical outcomes and predictors of surgical treatment in temporal lobe epilepsy. Neurol Sci Neurophysiol 2021;38:209-18.

[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

of refractory TLE patients benefit from temporal lobe resection in terms of seizure remission.[7-11]

Surgery in TLE actually targets long-term seizure freedom. Postoperative seizure remission state is a quite dynamic process, and recurrence rate gradually decreases within years depending on many variables.[7,12] Although seizures mostly recur within the first 6 months after surgery, recurrences may occur until 2–5 years postoperatively.[9,13]

While the majority of studies on epilepsy surgery have focused on postoperative outcomes, which is now a quite well-known issue, the number of studies investigating the predictors of postoperative seizure control is limited and the results are contradictory. Clinical predictors that were reported in the previous studies included gender, age of disease onset, disease duration, febrile seizure (FS) history, presence of focal to bilateral tonic-clonic seizures (FBTCSs), presence of hippocampal sclerosis (HS) on pathology, side of surgery, extent of resection (total-subtotal), and unilateral localization of interictal epileptiform discharges (IEDs) on electroencephalography (EEG).[14-19]

The objectives of this study were long-term assessment of seizure control after surgery and identification of prognostic factors related to postoperative remission in patients with refractory TLE.

Materials and Methods

Patient selection and preoperative workup

This retrospective study was conducted in Gazi University Medical Faculty Epilepsy Center. Medical records of patients who underwent standard anterior temporal lobectomy (ATL) between the years of 2006 and 2020 with a diagnosis of refractory TLE were reviewed. Among 167 patients, 143 with a follow-up duration of 10 years or more were included in the study. All patients were aged over 17 years. The same standard preoperative evaluation protocol was performed in each patient. The study protocol was approved by the local ethics committee.

As the first step of preoperative evaluation, detailed medical history was obtained from all patients and full physical and neurological examinations were completed. After clinical evaluation, all patients underwent long-term scalp EEG monitorization, using a 32-channel montage in the guidance of a 10–20 electrode system and together with anterior temporal electrodes. The patients were monitored until adequate number of typical seizures was observed. On EEG, the presence of IEDs at a rate of 80% or greater in only a single temporal lobe was accepted as unilateral. For localization (temporal or extratemporal) and lateralization (right or left) of seizures, both clinical signs and interictal-ictal EEG changes were taken into consideration.

Cranial magnetic resonance imaging (MRI) records of all patients were compatible with temporal lobe protocol, including included axial and sagittal T1-weighted, axial T2-weighted, oblique coronal fluid-attenuated inversion recovery perpendicular to the long axis of both hippocampi, and three-dimensional (3D) inversion recovery (IR) [Figure 1a and b]. The whole-brain volumetric series were acquired using a 3D IR technique. During the previous years, MRI had been performed via a 1.5T MR scanner (Ge Signa Excite, Milwaukee, USA). However, a 3T MR scanner (Magnetom Verio; Siemens, Erlangen, Germany) has been used for the last 9 years. The images were reviewed by expert neuroradiologists.

Brain fluorodeoxyglucose positron emission tomography (FDG-PET) was performed in all patients, and static brain PET images were acquired using a Discovery ST PET-computed tomography scanning system (GE Medical Systems, Milwaukee, WI, USA). Experienced nuclear medicine specialists evaluated the images with respect to the presence of regional hypometabolism (HM), which is an expected abnormal finding in the epileptogenic zone [Figure 2].

Psychiatric examination and neuropsychological tests were completed for all patients prior to surgery. None had a psychiatric disorder that would be a contraindication for surgery. Preoperative neuropsychological tests were applied by a neuropsychologist in the form of a standard battery. All patients underwent WADA test or functional MRI in order to obtain information about hemispheric

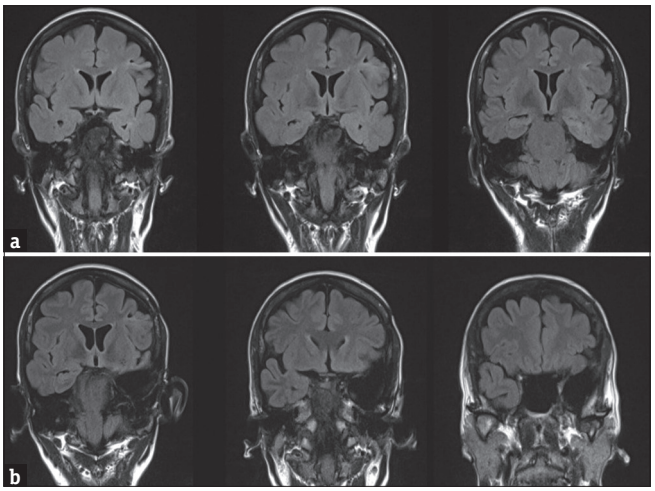


Figure 1: Brain magnetic resonance imaging of a 27-year-old male with 6-year history of focal impaired awareness seizures twice a week. The patient was diagnosed left temporal lobe epilepsy. (a) Preoperative images demonstrating increased T2 signal and atrophy on the left hippocampus which indicate left hippocampal sclerosis, (b) Postoperative images 2 months after surgery

[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

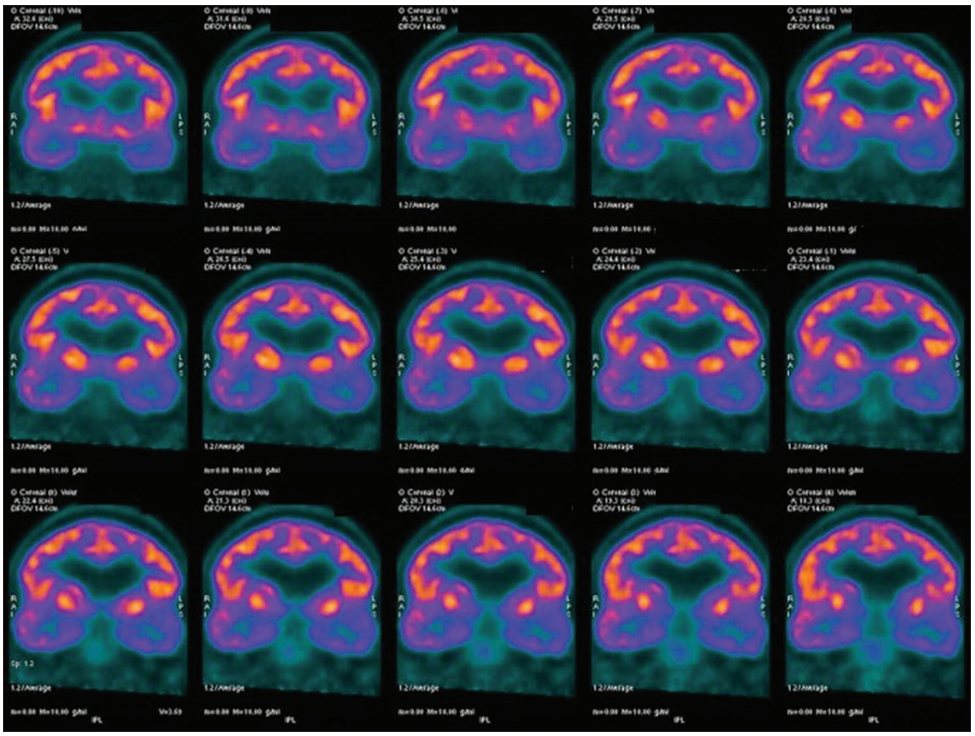


Figure 2: Brain fluorodeoxyglucose positron emission tomography images of the patient in Figure 1, demonstrating diffuse temporal hypometabolism on the left side

lateralization of language and memory functions and make an opinion about possible postoperative deficits.

The results of standard workup process prior to surgery were reviewed in a multidisciplinary surgery conference. Decision to perform a surgical intervention was given and surgical technique was specified if there was consistency in the results of clinical, electrophysiological, neuroimaging, and neuropsychological examinations.

The same neurosurgeon performed anterior temporal lobectomies. During the standard surgical procedure, the neurosurgeon removed the medial structures, including hippocampus, parahippocampal gyrus, and amygdalar nucleus together with ATL. All patients underwent standard anterior temporal resection and also tumor resection was performed when required.

Follow-up visits with regard to seizure status and AED use were provided by the same epileptologist for all patients. During the first year after surgery; follow up visits were performed in the 2nd and 6th months. After the 6th month visit,, control examinations were repeated every year. In accordance with our AED discontinuation protocol, we recommended the same preoperative drug regimen to all patients during 6 months after surgery. At the end of the 6th month, gradual AED tapering was started which lasted approximately 1½ years. Two years after the surgery, patients were completely medication free.

Postoperative seizure outcome was categorized according to Engel's outcome classification (Class I: free of disabling seizures, Class II: rare disabling seizures, Class III: worthwhile improvement, and Class IV: no worthwhile improvement).[20] Baseline parameters were compared between seizure-free (Engel's Class I) and nonseizure-free (Engel's Class II, III, IV) groups. The seizure status of the groups was recorded at the 6th month following surgery and then at the 1st, 2nd, 3rd, 4th, and 10th years, respectively.

Data acquisition

Various preoperative parameters that may predict postoperative outcome were recorded for each patient. These parameters included age, gender, disease duration, seizure type (FBTCS±), lateralization of temporal lobe, FS history, type of surgery, ipsilateral occurrence of temporal IEDs, unilateral HS on brain MRI, and unilateral temporal HM on PET. Other recorded parameters were AED use after surgery and histopathology results of the surgical specimens.

Statistical analysis

Statistical analyses were performed using SPSS version 20.0 (SPSS, Inc., Chicago, Illinois, USA). Normally distributed continuous parameters were presented as mean ± standard deviation, and Student's *t*-test was applied for comparison between the groups. Categorical data were presented as percentages and compared using Chi-square test. In order to identify

[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

the potential predictors of favorable surgical outcome, a univariate logistic regression analysis was used. The variables with $P < 0.25$ were separately evaluated and further analyzed by a multivariable model. After applying a multivariate logistic regression analysis, independent predictors of surgical outcome were identified. Odds ratios, 95% confidence interval (CI), and the Wald statistics for each independent variable were also calculated for a seizure-free outcome at the 2nd and 10th years after the surgery. $P < 0.05$ was accepted as statistically significant.

Results

The demographic and clinical characteristics of the study group are given in Table 1. The mean age of the patients was 28.3 ± 7.8 (range, 17–55) years and the mean disease duration before surgery was 15.8 ± 15.0 (range, 1–46) years. Disease duration was shorter than 11 years in 36 (25.2%), between 11 and 20 years in 71 (49.7%), and longer than 20 years in 36 (25.2%) patients. The patients were followed up for 144.47 ± 14.52 (range, 120–168) months after surgery. ATL was performed in 131 (91.6%) and lesionectomy together with ATL was performed in 12 (8.4%) patients. The surgical side was left temporal lobe in 79 (55.2%) and right temporal lobe in 64 (44.8%) patients.

Histopathological findings of 143 patients were as follows: 119 (83.2%) – HS, 8 (5.5%) – cortical dysplasia (CD), 3 (2.1%) – arteriovenous malformation (AVM), 6 (4.2%) – tumor, 1 (0.7%) – tuberous sclerosis, 2 (1.4%) – meningioma, and 2 (1.4%) – gliosis.

The percentage of seizure-free patients in the postoperative follow-up visits is presented in Figure 3. The percentage of Engel's Class I patients was 95.8% at the 6th month, 89.5% at the 12th month, 83.2% at the 24th month, 82.1% at the 36th month, 81.3% at the 48th month, and 81.8% at the 60th month. At the 10th year of surgery, 79.2% of the patients were still meeting Engel's Class I criteria.

At the postoperative 2nd year, demographic parameters, disease duration before surgery, side of surgery, presence of FBTCS, type of surgery, or histopathological findings did not demonstrate a significant difference between the seizure-free (Engel's Class I) and nonseizure-free groups (Engel's Class II, III, IV) ($P > 0.05$). Frequencies of HS on MRI, unilateral temporal HM on PET, FS history, and unilateral temporal IEDs on EEG were significantly higher in the seizure-free group ($P = 0.004$, $P < 0.02$, $P < 0.037$, and $P < 0.001$, respectively).

At the 10th year follow-up, only frequencies of unilateral IEDs on EEG, HS on histopathological examination, and

Table 1: Demographical and clinical characteristics of the patients (n=143)

	n (%)
Age	28.3±7.8
Gender	
Female	84 (58.7)
Male	59 (41.3)
Mean duration of epilepsy (years)	
<11	36 (25.2)
11-20	71 (49.7)
>20	36 (25.2)
Febrile seizures	84 (58.7)
Side of resection	
Left	79 (55.2)
Right	64 (44.8)
Seizure	
FIAS + FBTCS	121 (84.6)
FIAS	22 (15.4)
EEG-ictal	
Left	79 (55.2)
Right	64 (44.8)
EEG-IEDs	
Bilateral	29 (20.3)
Unilateral	114 (79.7)
Surgery	
ATL	131 (91.6)
ATL + lesionectomy	12 (8.4)
MRI	
HS (−)	24 (16.8)
HS (+)	119 (83.2)
Pathological data	
HS (−)	22 (15.4)
HS (+)	121 (84.6)
FDG-PET	
Bilateral	26 (18.2)
Unilateral	117 (81.8)

FIAS: Focal impaired awareness seizure, FBTCS: Focal to bilateral tonic-clonic seizure, EEG: Electroencephalography, IEDs: Interictal epileptiform discharges, ATL: Anterior temporal lobectomy, MRI: Magnetic resonance imaging, HS: Hippocampal sclerosis, FDG-PET: Fluorodeoxyglucose positron emission tomography

FS history were found to be higher in the seizure-free group ($P = 0.030$, $P < 0.040$, and $P < 0.034$, respectively). No significant difference was observed between the two groups regarding other demographic and clinical parameters ($P > 0.05$).

In order to determine the potential predictors of postoperative outcomes, a univariate logistic regression analysis was performed, and the results are presented in Table 2. Presence of IEDs on EEG, FS history, unilateral HS on brain MRI, and presence of unilateral temporal HM on PET were predictors of postoperative seizure control at the 2nd year ($P < 0.001$, $P = 0.004$, $P < 0.001$, and $P < 0.001$, respectively).

[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

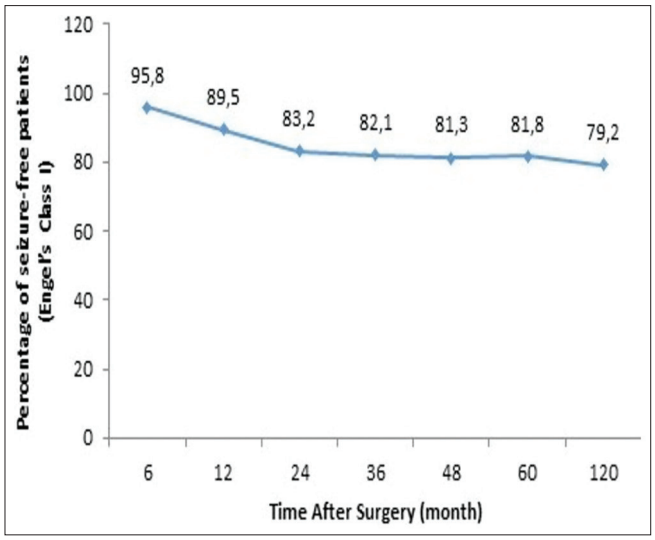


Figure 3: Rates of seizure-free patients (Engel's Class I) according to the postoperative follow-up periods

Another univariate logistic regression analysis was performed for the same parameters at the 10th year, and the results are presented in Table 3. Presence of unilateral temporal IEDs on EEG, FS history, HS in histopathological evaluation, and presence of unilateral temporal HM on PET were found to be predictors of postoperative seizure control ($P < 0.001$, $P < 0.001$, $P = 0.030$, and $P = 0.022$, respectively).

Predictors detected in the univariate analyses were further evaluated in a multivariate model, and the results of these multivariate logistic regression analyses are given in Table 4. Unilateral localization of temporal IEDs on EEG, FS history, and unilateral temporal HM on PET were found to be independent predictors of postoperative seizure control at the 2nd and 10th years.

Discussion

Epilepsy surgery ensures seizure remission in approximately 70% in refractory TLE patients.[21-23] In the current study, surgical outcomes were quite successful and 89.5% of the patients had no seizures at the 12th month following surgery. Seizure remission rates were 83.2% at the 24th month and 81.3% at the 48th month. At the 10th year following surgery, 79.2% of the patients were still meeting the criteria for Engel's Class I.

Despite the advances in epilepsy surgery within the last decade, detailed studies investigating the prognostic indicators of surgical outcome are still scarce. Therefore, we evaluated predictive clinical factors likely to affect postoperative seizure remission in TLE.

In our study, postoperative 2nd-year findings demonstrated that unilateral localization of interictal epileptiform activity, FS history, unilateral HS on brain MRI, and unilateral temporal HM on PET were predictive factors associated with good postoperative prognosis. At the postoperative 10th year, unilateral localization of interictal epileptiform activity, FS history, HS in histopathology, and unilateral temporal HM on PET were found to be the clinical predictors of favorable surgical outcome. However, the significance of unilateral HS on brain MRI and histopathology was disappeared in the multivariate analysis. Based on these findings, we demonstrated that unilateral temporal IEDs on EEG, FS history, and unilateral temporal HM on PET were independent predictors of postoperative seizure control.

In our study, FS history was found to have a significant prognostic effect on outcome. While some previous studies also reported a predictive value of FS on favorable surgical outcomes,[14,24,25] others did not come up with a similar result.[26,27] Prognostic effect of FS history on postoperative outcome might be based on its association with HS. In the light of translational studies indicating the sustained effects of FS on hippocampal excitability through influencing both expression of ion channels and GABAA receptor-mediated neurotransmission, it is possible to hypothesize that FS contributes to HS and epileptogenesis, as well.[28]

Cranial MRI has quite high sensitivity and specificity for detection of HS, and HS can be found in TLE patients at a rate of up to 90%.[29] Detection of HS on MRI was shown to be an important predictor of favorable surgical outcome in TLE.[17,30,31] In the previous series, HS was observed in 58%–72% of TLE patients, whereas MRI was reported to be normal in about 16%.[2,7,32] In the present study, HS was detected in 119 (83.2%) of the patients on cranial MRI. We noted that cranial MRI can predict good surgical outcome at the postoperative 2nd year; however, this effect disappeared when evaluated together with other variables using multivariate regression analysis. This might have resulted from the evaluation of MRI-positive patients together with MRI-negative ones. Although outcomes of patients with normal MRI are considered to be poor, recent studies have supported that this group has similar outcomes with patients who have HS if the results of PET, EEG, and other preoperative evaluations are consistent and if the lesion is localized to a single focus. The underlying pathophysiology in these cases has not been clarified yet; however, it is suggested to be a syndrome different from HS, which could be surgically treated.[32,33]

Although 3T MRI has been shown to enhance the detection of subtle lesions at a rate of 20%–48% in comparison to 1–1.5T MRI, another neuroimaging method is required in patients reported to have normal

[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

Table 2: Univariate analysis of variables at the 2nd year after surgery for Engel's I outcome

	Nonseizure-free group (*n*=4), *n* (%)	Seizure-free group (Engel's Class I) (*n*=119), *n* (%)	*P*	OR (95% CI)
Age	28.3±6.7	27.7±8.0	0.736	0.990 (0.931-1.051)
Gender				
Female	17 (70.8)	67 (56.3)	-	1.000[a]
Male	7 (29.2)	52 (43.6)	0.538	1.368 (0.503-3.726)
Side of operation				
Left	15 (62.5)	64 (53.7)	-	1.000[a]
Right	9 (37.5)	55 (46.3)	0.715	1.200 (0.451-3.193)
Seizure				
FIAS + FBTCS	20 (83.4)	101 (84.8)	-	1.000[a]
FIAS	4 (16.6)	18 (15.2)	1.000	0.933 (0.242-3.605)
EEG-ictal				
Left	15 (62.5)	64 (53.7)	-	1.000[a]
Right	9 (37.5)	55 (46.3)	0.715	1.200 (0.451-3.193)
EEG-IEDs				
Bilateral	19 (79.1)	10 (8.5)	-	1.000[a]
Unilateral	5 (20.8)	109 (91.5)	<0.001	29.000 (8.301-101.310)
Surgery				
ATL	22 (91.6)	109 (95.6)	-	1.000[a]
ATL + lesionectomy	2 (8.4)	10 (8.4)	0.675	0.791 (0.155-4.038)
Duration of epilepsy (years)				
<11	6 (25.0)	35 (29.4)	-	1.000[a]
11-20	9 (37.5)	70 (58.8)	0.356	1.746 (0.535-5.703)
>20	9 (37.5)	14 (11.7)	0.333	0.540 (0.155-1.880)
MRI				
HS (−)	10 (41.6)	14 (11.7)	-	1.000[a]
HS (+)	14 (58.3)	105 (88.2)	0.004	5.333 (1.789-15.900)
Pathological data				
HS (−)	5 (20.0)	19 (16.0)	-	1.000[a]
HS (+)	19 (80.0)	100 (84.0)	0.470	1.813 (0.519-6.332)
Febrile seizures	-	84 (70.9)	<0.001	1.000[a]
FDG-PET				
Bilateral	22 (91.6)	4 (3.4)	-	1.000[a]
Unilateral	2 (8.4)	115 (96.6)	<0.001	35.833 (8.160-157.365)

[a]Reference category. OR: Odds ratio, CI: Confidence interval, FIAS: Focal impaired awareness seizure, FBTCS: Focal to bilateral tonic-clonic seizure, EEG: Electroencephalography, IEDs: Interictal epileptiform discharges, ATL: Anterior temporal lobectomy, MRI: Magnetic resonance imaging, HS: Hippocampal sclerosis, FDG-PET: Fluorodeoxyglucose positron emission tomography

MRI.[34,35] Therefore, many epilepsy clinics routinely use FDG-PET for preoperative evaluation. FDG-PET localizes the epileptogenic focus with 85%–90% accuracy in TLE patients. In MRI-negative patients, regional HM on FDG-PET is observed at a rate of 60%–82%.[36-38] A large meta-analysis found that the predictive value of ipsilateral HM was 86% for good surgical outcomes, whereas it was 71%–80% in the group with normal MRI.[39] In many series including a previous research of our group, the surgical outcomes of MRI-negative patients were comparable to the patients with HS.[33,36-40] Ipsilateral HM on FDG-PET shows a high correlation with the onset of ictal EEG in cases undergoing intracranial monitoring.[39,41] Based on this, the need for intracranial monitoring can be reduced in cases with normal MRI, when all other findings are consistent. In addition, the need for preoperative invasive EEG monitoring, its cost and complication risks as well, can also be decreased. In our series, while MRI-negative patients underwent invasive EEG monitoring initially, the surgery decision was made without invasive monitoring in the recent years, in the case of consistent ictal electrophysiological findings on scalp EEG, HM on FDG-PET, and neuropsychological tests.

In line with the numerous previous reports, our results revealed that unilateral IEDs were significant independent predictors of the 2nd- and 10th-year outcomes.[12,42,43] On the other hand, there are some studies which do not support this finding.[44,45] In the case of clear localization

[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

Table 3: Univariate analysis of variables at the 10th year after surgery for Engel's I outcome

	Nonseizure-free group (*n*=29), *n* (%)	Seizure-free group (Engel's Class I) (*n*=114), *n* (%)	*P*	OR (95% CI)
Age	26.5±6.3	28.4±8.4	0.612	1.035 (0.910-1.177)
Gender				
Female	20 (68.9)	64 (56.1)	-	1.000[a]
Male	9 (31.0)	50 (43.8)	0.654	2.333 (0.362-15.053)
Side of operation				
Left	10 (34.4)	69 (60.5)	-	1.000[a]
Right	19 (65.5)	45 (39.5)	0.672	0.583 (0.090-3.763)
Seizure				
FIAS + FBTCS	24 (82.7)	101 (88.5)	-	1.000[a]
FIAS	5 (17.3)	13 (11.5)	1.000	0.652 (0.056-7.642)
EEG-ictal				
Left	10 (34.4)	69 (60.5)	-	1.000[a]
Right	19 (65.5)	45 (39.5)	0.672	0.583 (0.090-3.763)
EEG-IEDs				
Bilateral	29 (100.0)	13 (11.5)	-	1.000[a]
Unilateral	-	101 (88.5)	<0.001	-
Surgery				
ATL	20 (68.9)	111 (97.3)	-	1.000[a]
ATL + lesionectomy	9 (31.0)	3 (2.7)	0.853	0.744 (0.355-3.001)
Duration of epilepsy (years)				
<11	9 (31.0)	32 (28.0)	-	1.000[a]
11-20	13 (44.8)	65 (57.1)	0.347	2.833 (0.324-24.808)
>20	7 (24.2)	17 (14.9)	0.571	0.500 (0.045-5.514)
MRI				
HS (−)	10 (34.4)	14 (12.3)	-	1.000[a]
HS (+)	19 (11.8)	100 (87.7)	0.150	6.000 (0.647-55.661)
Pathological data				
HS (−)	20 (68.9)	2 (17.5)	-	1.000[a]
HS (+)	9 (31.1)	112 (98.2)	0.030	-
Febrile seizures	-	84 (70.5)	<0.001	0.003
FDG-PET				
Bilateral	15 (51.7)	-	-	1.000[a]
Unilateral	14 (48.2)	114 (100.0)	0.022	-

[a]Reference category and means that odds ratio is 1.000 for that categorical variable. OR: Odds ratio, CI: Confidence interval, FIAS: Focal impaired awareness seizure, FBTCS: Focal to bilateral tonic-clonic seizure, EEG: Electroencephalography, IEDs: Interictal epileptiform discharges, ATL: Anterior temporal lobectomy, MRI: Magnetic resonance imaging, HS: Hippocampal sclerosis, FDG-PET: Fluorodeoxyglucose positron emission tomography

Table 4: Multivariate logistic regression analysis for postoperative Engel's I outcome at the 2nd and 10th years

	OR	95% CI (lower limit–upper limit)	Wald	*P*
Second year				
HS in MRI	1.422	0.189-10.716	0.117	0.733
Unilateral IEDs	24.691	2.027-300.715	6.321	0.012
Febrile seizures	8.810	1.031-75.270	3.952	0.047
FDG-PET- Unilateral	33.098	3.526-310.720	9.380	0.002
Tenth year				
HS in histopathology	7.784	0.556-108.933	2.323	0.127
Unilateral IEDs	223.857	6.030-8311.049	8.610	0.003
Febrile seizures	24.516	1.779-337.925	5.713	0.017
FDG-PET-unilateral	24.691	2.027-300.715	6.321	0.012

OR: Odds ratio, CI: Confidence interval, IED: Interictal epileptiform discharges, HS: Hippocampal sclerosis, MRI: Magnetic resonance imaging, FDG-PET: Fluorodeoxyglucose positron emission tomography

[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

of unilateral IEDs on the surgical side, they serve as good predictors of favorable postoperative outcome. However, widespread IEDs may indicate the probability of diffuse irritative zone and thus poor postoperative prognosis. In a prospective study, seizures were reported to decrease by more than 90% in patients who had IEDs localized in the operated temporal lobe, whereas the rate of seizure freedom was found to be 54% if the IEDs were less lateralized.[46]

Many recent studies have reported that surgical success in TLE regarding seizure remission depends on histopathological and MRI findings. HS was the most frequently encountered histopathology in patients with refractory TLE. However, in addition to HD, CD, tumor, and vascular abnormalities, hippocampal specimens that include normal neurons which progress with reactive gliosis were also encountered.[47] Together with predominating HS cases, our study also included a number of patients with other pathologies such as tumor, CD, AVM, and nonspecific gliosis.

It was shown that postoperative prognosis was quite good in cases with mesial TLE associated with HS.[43-46] Compared to other pathologies, the seizure recurrence rate was lower in patients with HS. The rate of seizure remission was reported to be 85% at the 1st year and 74% after 5 years.[46] Similar to previous literature, our results demonstrated a seizure remission rate of 79.4% at the end of 10-year follow-up. In a previous study, the seizure remission rate was lower in patients with CD compared to patients with HS, tumor, or vascular lesions.[48] In a recent series of pediatric TLE patients, resection of temporal MRI abnormalities other than HS was found to be associated with better long-term outcome.[49]

In our study, the effect of HS on postoperative outcome was significant at the 10th year, however, this effect was disappeared in the multivariate analysis. Failure of histopathology in predicting postoperative prognosis can be explained by high number of HS and tumor cases having good prognosis, together with CD and AVM cases. As a result, more precise interpretation of the effects of histopathology on outcome would be possible when the patients having HS alone are compared with similar number of patients having other pathologies.

FBTCSs in TLE indicate rapid spread of seizures. In the current study, we observed that FBTCS had no effect on surgical outcome, in line with the previous reports.[44,50] On the other hand, some studies have suggested that the presence and frequency of FBTCS have a predictive value for negative surgical outcomes.[14,16,17] In a previous study, seizure freedom in patients without FBTCS was found to be 2.2 times higher than the ones with FBTCS at the 5th year following surgery.[50] Taken together, FBTCS in TLE is associated with higher grade of HS, more than one irritative zone, larger hypometabolic area on PET, and thus, a diffuse epileptogenic zone. Therefore, it might be plausible to expect a poorer surgical outcome in patients with FBTCS.

The present study has some limitations due to its retrospective design; however, this applies to all other studies on surgical outcomes. It is quite difficult to perform a prospective study on epilepsy surgery due to personal decisions that stand for randomization. Nevertheless, the present study included a quite large number of patients and good follow-up duration as compared to other studies regarding this subject.

Conclusions

Many predictors for surgical outcomes in TLE have been determined to date. In the current study, we revealed that unilateral temporal IEDs on EEG, FS history, and unilateral temporal HM on FDG-PET were independent predictors of postoperative seizure control. Our findings can be useful in selection of appropriate refractory TLE patients for surgical treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Semah F, Picot MC, Adam C, Broglin D, Arzimanoglou A, Bazin B, *et al.* Is the underlying cause of epilepsy a major prognostic factor for recurrence? Neurology 1998;51:1256-62.
2. Wiebe S, Blume WT, Girvin JP, Eliasziw M; Effectiveness and Efficiency of Surgery for Temporal Lobe Epilepsy Study Group. A randomized, controlled trial of surgery for temporal-lobe epilepsy. N Engl J Med 2001;345:311-8.
3. Kumlien E, Doss RC, Gates JR. Treatment outcome in patients with mesial temporal sclerosis. Seizure 2002;11:413-7.
4. Schmidt D, Stavem K. Long-term seizure outcome of surgery versus no surgery for drug-resistant partial epilepsy: A review of controlled studies. Epilepsia 2009;50:1301-9.
5. Spencer S, Huh L. Outcomes of epilepsy surgery in adults and children. Lancet Neurol 2008;7:525-37.

[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

6. Engel J Jr., Wiebe S, French J, Sperling M, Williamson P, Spencer D, *et al.* Practice parameter: Temporal lobe and localized neocortical resections for epilepsy. Epilepsia 2003;44:741-51.
7. Berkovic SF, McIntosh AM, Kalnins RM, Jackson GD, Fabinyi GC, Brazenor GA, *et al.* Preoperative MRI predicts outcome of temporal lobectomy: An actuarial analysis. Neurology 1995;45:1358-63.
8. Luyken C, Blümcke I, Fimmers R, Urbach H, Elger CE, Wiestler OD, *et al.* The spectrum of long-term epilepsy-associated tumors: Long-term seizure and tumor outcome and neurosurgical aspects. Epilepsia 2003;44:822-30.
9. Asztely F, Ekstedt G, Rydenhag B, Malmgren K. Long term follow-up of the first 70 operated adults in the goteborg epilepsy surgery series with respect to seizures, psychosocial outcome and use of antiepileptic drugs. J Neurol Neurosurg Psychiatry 2007;78:605-9.
10. Picot MC, Jaussent A, Kahane P, Crespel A, Gélisse P, Hirsch E, *et al.* Medicoeconomic assessment of epilepsy surgery in adults with medically intractable partial epilepsy. Three-year outcomes from a multicenter French cohort. Neurochirurgie 2008;54:484-98.
11. Cohen-Gadol AA, Wilhelmi BG, Collignon F, White JB, Britton JW, Cambier DM, *et al.* Long-term outcome of epilepsy surgery among 399 patients with nonlesional seizure foci including mesial temporal lobe sclerosis. J Neurosurg 2006;104:513-24.
12. Salanova V, Andermann F, Rasmussen T, Olivier A, Quesney L. The running down phenomenon in temporal lobe epilepsy. Brain 1996;119:989-96.
13. Jeha LE, Najm IM, Bingaman WE, Khandwala F, Widdess-Walsh P, Morris HH, *et al.* Predictors of outcome after temporal lobectomy for the treatment of intractable epilepsy. Neurology 2006;66:1938-40.
14. Hennessy MJ, Elwes RD, Rabe-Hesketh S, Binnie CD, Polkey CE. Prognostic factors in the surgical treatment of medically intractable epilepsy associated with mesial temporal sclerosis. Acta Neurol Scand 2001;103:344-50.
15. Hardy SG, Miller JW, Holmes MD, Born DE, Ojemann GA, Dodrill CB, *et al.* Factors predicting outcome of surgery for intractable epilepsy with pathologically verified mesial temporal sclerosis. Epilepsia 2003;44:565-8.
16. Janszky J, Janszky I, Schulz R, Hoppe M, Behne F, Pannek HW, *et al.* Temporal lobe epilepsy with hippocampal sclerosis: Predictors for long-term surgical outcome. Brain 2005;128:395-404.
17. McIntosh AM, Kalnins RM, Mitchell LA, Fabinyi GC, Briellmann RS, Berkovic SF. Temporal lobectomy: Long-term seizure outcome, late recurrence and risks for seizure recurrence. Brain 2004;127:2018-30.
18. Salanova V, Markand O, Worth R. Temporal lobe epilepsy: Analysis of failures and the role of reoperation. Acta Neurol Scand 2005;111:126-33.
19. Wieshmann UC, Larkin D, Varma T, Eldridge P. Predictors of outcome after temporal lobectomy for refractory temporal lobe epilepsy. Acta Neurol Scand 2008;118:306-12.
20. Engel J, Van Ness P, Rasmussen T, Ojemann LM. Outcome with respect to epileptic seizures. In: Engel J, editor. Surgical Treatment of Epilepsies. 2nd ed. New York: Raven Press; 1993. p. 609-21.
21. Engel J Jr. Surgery for seizures. N Engl J Med 1996;334:647-52.
22. McIntosh AM, Wilson SJ, Berkovic SF. Seizure outcome after temporal lobectomy: Current research practice and findings. Epilepsia 2001;42:1288-307.
23. Téllez-Zenteno JF, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: A systematic review and meta-analysis. Brain 2005;128:1188-98.
24. Salanova V, Markand ON, Worth R. Clinical characteristics and predictive factors in 98 patients with complex partial seizures treated with temporal resection. Arch Neurol 1994;51:1008-13.
25. Elsharkawy AE, Alabbasi AH, Pannek H, Oppel F, Schulz R, Hoppe M, *et al.* Long-term outcome after temporal lobe epilepsy surgery in 434 consecutive adult patients. J Neurosurg 2009;110:1135-46.
26. Tezer FI, Akalan N, Oguz KK, Karabulut E, Dericioglu N, Ciger A, *et al.* Predictive factors for postoperative outcome in temporal lobe epilepsy according to two different classifications. Seizure 2008;17:549-60.
27. Burneo JG, Black L, Martin R, Devinsky O, Pacia S, Faught E, *et al.* Race/ethnicity, sex, and socioeconomic status as predictors of outcome after surgery for temporal lobe epilepsy. Arch Neurol 2006;63:1106-10.
28. Swijsen A, Avila A, Brône B, Janssen D, Hoogland G, Rigo JM. Experimental early-life febrile seizures induce changes in GABA(A)R-mediated neurotransmission in the dentate gyrus. Epilepsia 2012;53:1968-77.
29. Kuzniecky RI, Bilir E, Gilliam F, Faught E, Palmer C, Morawetz R, *et al.* Multimodality MRI in mesial temporal sclerosis: Relative sensitivity and specificity. Neurology 1997;49:774-8.
30. Spencer SS, Berg AT, Vickrey BG, Sperling MR, Bazil CW, Shinnar S, *et al.* Predicting long-term seizure outcome after resective epilepsy surgery: The multicenter study. Neurology 2005;65:912-8.
31. Gilliam F, Bowling S, Bilir E, Thomas J, Faught E, Morawetz R, *et al.* Association of combined MRI, interictal EEG, and ictal EEG results with outcome and pathology after temporal lobectomy. Epilepsia 1997;38:1315-20.
32. LoPinto-Khoury C, Sperling MR, Skidmore C, Nei M, Evans J, Sharan A, *et al.* Surgical outcome in PET-positive, MRI-negative patients with temporal lobe epilepsy. Epilepsia 2012;53:342-8.
33. Carne RP, O'Brien TJ, Kilpatrick CJ, MacGregor LR, Hicks RJ, Murphy MA, *et al.* MRI-negative PET-positive temporal lobe epilepsy: A distinct surgically remediable syndrome. Brain 2004;127:2276-85.
34. Phal PM, Usmanov A, Nesbit GM, Anderson JC, Spencer D, Wang P, *et al.* Qualitative comparison of 3-T and 1.5-T MRI in the evaluation of epilepsy. AJR Am J Roentgenol 2008;191:890-5.
35. Schmitz BL, Aschoff AJ, Hoffmann MH, Grön G. Advantages and pitfalls in 3T MR brain imaging: A pictorial review. AJNR Am J Neuroradiol 2005;26:2229-37.
36. Casse R, Rowe CC, Newton M, Berlangieri SU, Scott AM. Positron emission tomography and epilepsy. Mol Imaging Biol 2002;4:338-51.
37. Gok B, Jallo G, Hayeri R, Wahl R, Aygun N. The evaluation of FDG-PET imaging for epileptogenic focus localization in patients with MRI positive and MRI negative temporal lobe epilepsy. Neuroradiology 2013;55:541-50.
38. Henry TR, Van Heertum RL. Positron emission tomography and single photon emission computed tomography in epilepsy care. Semin Nucl Med 2003;33:88-104.
39. Willmann O, Wennberg R, May T, Woermann FG, Pohlmann-Eden B. The contribution of 18F-FDG PET in preoperative epilepsy surgery evaluation for patients with temporal lobe epilepsy a meta-analysis. Seizure 2007;16:509-20.
40. Capraz IY, Kurt G, Akdemir Ö, Hirfanoglu T, Oner Y, Sengezer T,

[Downloaded free from http://www.nsnjournal.org on Saturday, April 30, 2022, IP: 31.143.67.112]

et al. Surgical outcome in patients with MRI-negative, PET-positive temporal lobe epilepsy. Seizure 2015;29:63-8.

41. Delbeke D, Lawrence SK, Abou-Khalil BW, Blumenkopf B, Kessler RM. Postsurgical outcome of patients with uncontrolled complex partial seizures and temporal lobe hypometabolism on 18FDG-positron emission tomography. Invest Radiol 1996;31:261-6.
42. Chung MY, Walczak TS, Lewis DV, Dawson DV, Radtke R. Temporal lobectomy and independent bitemporal interictal activity: What degree of lateralization is sufficient? Epilepsia 1991;32:195-201.
43. Radhakrishnan K, So EL, Silbert PL, Jack CR Jr., Cascino GD, Sharbrough FW, *et al.* Predictors of outcome of anterior temporal lobectomy for intractable epilepsy: A multivariate study. Neurology 1998;51:465-71.
44. Aull-Watschinger S, Pataraia E, Czech T, Baumgartner C. Outcome predictors for surgical treatment of temporal lobe epilepsy with hippocampal sclerosis. Epilepsia 2008;49:1308-16.
45. Jeong SW, Lee SK, Kim KK, Kim H, Kim JY, Chung CK. Prognostic factors in anterior temporal lobe resections for mesial temporal lobe epilepsy: Multivariate analysis. Epilepsia 1999;40:1735-9.
46. Paglioli E, Palmini A, Paglioli E, da Costa JC, Portuguez M, Martinez JV, *et al.* Survival analysis of the surgical outcome of temporal lobe epilepsy due to hippocampal sclerosis. Epilepsia 2004;45:1383-91.
47. Blümcke I, Thom M, Aronica E, Armstrong DD, Bartolomei F, Bernasconi A. International consensus classification of hippocampal sclerosis in temporal lobe epilepsy: A task force report from the ILAE commission on diagnostic methods. Epilepsia 2013;54:1315-29.
48. Chung CK, Lee SK, Kim KJ. Surgical outcome of epilepsy caused by cortical dysplasia. Epilepsia 2005;46 Suppl 1:25-9.
49. Barba C, Cossu M, Guerrini R, Di Gennaro G, Villani F, De Palma L, *et al.* Temporal lobe epilepsy surgery in children and adults: A multicenter study. Epilepsia 2021;62:128-42.
50. Kilpatrick C, Cook M, Matkovic Z, O'Brien T, Kaye A, Murphy M. Seizure frequency and duration of epilepsy are not risk factors for postoperative seizure outcome in patients with hippocampal sclerosis. Epilepsia 1999;40:899-903.