

# Surgical Results in Temporal Lobe Epilepsies Due to Structural Lesions

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## Abstract

**Objective:** Temporal lobe epilepsy (TLE) is the most common localization-related epilepsy syndrome in adults. The aim of this study was to determine the long-term efficacy of epilepsy surgery in patients with TLE with focal lesions and to evaluate the predictive factors for seizure-free status after surgery.

**Methods:** Among 109 patients aged more than 17 years, 26 cases with a postoperative follow-up period of at least 2 years and who underwent anterior temporal lobectomy and lesionectomy were included in the study. Each patient was evaluated with a detailed history, video-electroencephalography (EEG), neuroimaging, and postsurgical outcomes according to Engel classification to predict postsurgical seizure freedom.

**Results:** Patients with chronic TLE (n=26) associated with structural lesions were included in the study. According to Engel's classification, the seizure freedom rate was found to be 92.3% in the first year and 80.8% in the second year after surgery. At the postoperative 2<sup>nd</sup> year, demographic parameters, disease duration before surgery, mean age of patients, presence of focus to bilateral tonic-clonic seizure, EEG, video EEG monitoring, clinical lateralization, scanning results, surgical technique, and histopathological diagnosis did not demonstrate a significant difference between the seizure-free (Engel's class I) and non-seizure-free groups (Engel's class II, III, IV) (p>0.05).

**Conclusion:** Refractory epilepsy surgery for temporal lobe tumors often offers complete seizure freedom. Complete surgical excision of the epileptogenic region is of great importance for achieving seizure-freeness.

**Keywords:** Engel classification, epilepsy surgery, temporal lobe epilepsy

## INTRODUCTION

Temporal lobe epilepsy (TLE) is the most common localization-related epilepsy syndrome in adults. Previous reports have shown that only 8-23% of TLE patients achieve complete remission with antiepileptic drugs (AEDs) and that surgical treatment is highly superior to medical treatment in these patients.<sup>1,2</sup> Approximately 10-30% of TLE cases are associated with brain tumors, the majority of which are low-grade tumors.<sup>3</sup> The frequency and variety of epileptic seizures vary depending on the tumor localization and histopathological type. Accordingly, low-grade tumors are more epileptogenic than high-grade tumors. Among the most common causes of drug-resistant epilepsy are developmental brain lesions, particularly glioneuronal tumors, cortical developmental anomalies, and focal cortical dysplasias, and surgical treatment is recommended in these patients.<sup>3</sup> The main goal is to provide seizure control.<sup>4</sup>

The aim of this study was to determine the long-term efficacy of epilepsy surgery in patients with TLE with focal lesions and to evaluate predictive factors in terms of post-surgical seizure-free (SF) status.

## METHODS

Patients who were diagnosed with medically refractory TLE and underwent standard anterior temporal lobectomy (ATL) between 2010 and 2015 at the Gazi University Medical Faculty Epilepsy Center were retrospectively evaluated. Among 109 patients aged more than 17 years, 26 cases with a postoperative follow-up period of at least 2 years and who underwent ATL and lesionectomy were included in the study. The same examination protocols were applied to all patients before surgery. The present study was approved by the Institutional Ethical Board of the Gazi University Faculty of Medicine (decision no: 49, date: 25.01.2016) and performed in accordance with the ethical standards

laid down in the 1964 Declaration of Helsinki. In preoperative examinations, detailed clinical and medical history and physical and neurological examinations of the patients were performed first. Subsequently, all cases were monitored with scalp electrodes using a 32-channel electroencephalography (EEG), an international 10-20 electrode system, and anterior temporal electrodes. Patients were monitored until they had enough typical seizures. In EEG, interictal epileptiform discharges were accepted as unilateral if they were seen at a rate of 80% and above in one temporal lobe. Temporal lobe localization and right/left lateralization of the patients were determined by correlation with ictal clinical signs and ictal and interictal EEG. Magnetic resonance imaging (MRI) was performed using 1.5- or 3-T thin-sliced epilepsy protocols, including axial and sagittal T1-weighted, axial and coronal T2-weighted, oblique coronal fluid-attenuated inversion recovery perpendicular to the long axis of both hippocampi, and three-dimensional inversion recovery. All images were evaluated by experienced neuroradiologists.

Fluorodeoxyglucose/positron emission tomography (FDG-PET) was performed on all patients before surgery. PET images were acquired using the Discovery ST Camera (GE Medical Systems). Experienced nuclear medicine specialists evaluated the images with respect to the presence of regional hypometabolism, which is an expected abnormal finding in the epileptogenic zone. Psychiatric and neuropsychological evaluations were performed in all cases before surgery, and no psychiatric disorder with contraindications for surgery was found in any patient. Neuropsychological evaluation was given to all patients by a neuropsychologist in the form of a battery before surgery. All patients underwent a WADA test or functional MRI to obtain information about hemispheric lateralization of language and memory functions and make an opinion on possible postoperative deficits. The results of the pre-operative evaluation protocols were discussed in the multidisciplinary council, and if the clinical semiological findings, interictal and ictal EEG, neuroimaging, and neuropsychological examinations were compatible with each other and localized to a single focus, a surgical decision was made and the surgical technique was determined. The surgical procedure was performed by the same surgeon in all patients in the neurosurgery department of our hospital. The surgery was tailored and guided by the involvement of the hippocampus, mesial temporal structures, and tumor size. If the tumor involved the hippocampus and mesial temporal structures, ATL with amygdala hippocampectomy was performed; if not, only lesionectomy was performed. Patients with other mesial temporal lesions underwent lesion resection and removal of the mesial temporal structures and surrounding cortex. The World Health Organization (WHO) definition of primary brain neoplasms was used for pathological diagnosis.<sup>5</sup> In the postoperative period, the patients were examined by the same epileptology at the 2<sup>nd</sup> and 6<sup>th</sup> months, and then once a year, and were

evaluated in terms of seizure status and AED use. In accordance with the AED cut-off protocol of our clinic, the drug treatment of all patients was continued for 6 months after surgery, and at the end of the 6<sup>th</sup> month, the AEDs of the patients who were SF were gradually reduced to one drug. The second drug was also reduced, and it was planned to discontinue all drugs at the end of the second year. The Engel seizure classification was used in the evaluation of postoperative outcomes (class I: free of disabling seizures, class II: rare disabling seizures, class III: worthwhile improvement, class IV: no worthwhile improvement).<sup>6</sup> For the analysis, the SF group (Engel I) was compared with the group with seizures (Engel II, III, IV). The seizure state of the cases was followed up at 6 months, 1 and 2 years, and once a year thereafter. Finally, all factors of both presurgical workup and postsurgical outcomes were compared to predict the possibility of seizure freedom. The following data were matched to postsurgical Engel classifications to determine the predictive value of postsurgical seizure freedom: age at seizure onset, duration of epilepsy, etiology, seizure classification, interictal-ictal EEG findings, MRI, PET, age at surgery, type of surgery, and pathological results.

### Statistical Analysis

Statistical Package for Social Sciences (SPSS) version 21.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Descriptive statistics were expressed as mean, standard deviation, median, minimum, and maximum values. Pearson's chi-square test and Fisher's exact chi-square test were used in the analysis of categorical variables. Non-parametric tests (Mann-Whitney U test and Kruskal-Wallis test) were used in the analysis of continuous variables because the sample size was less than 30. The Spearman's correlation test was used to evaluate the relationship between two continuous variables. The statistical significance level was set as  $p < 0.05$ .

### RESULTS

A total of 26 patients with chronic TLE associated with structural lesions included in the study were analyzed. The mean age of the patients was  $32.31 \pm 7.72$  (range, 18-49) years, and the mean disease duration before surgery was  $17.38 \pm 8.34$  (range, 4-38) years. The demographic and clinical characteristics of the study group are presented in Table 1. The basic characteristics, seizure semiology, lesion characteristics, and postoperative findings of the patients were compared between the SF (Engel I) and non-SF (NSF) (Engel II, IV) groups. Regarding the risk factors present in patients, history of febrile convulsion (FC) was present in 38.5%, difficult birth, consanguineous marriage and family history of epilepsy was noted in 23.1%, infection history of the central nervous system (CNS) was found in 11.5%. The mean time they had with seizures was  $17.38 \pm 8.34$  years, and the median was 18 (4-38) years. Focal impaired awareness seizures were in all patients examined. Seizures in 69.2% of the patients were of the focus to bilateral tonic-clonic seizure (FBTCS) type. At the postoperative 2<sup>nd</sup> year, demographic parameters, disease duration before surgery, mean age of patients, presence of FBTCS, EEG, video EEG monitoring (VEM), and clinical lateralization did not demonstrate a significant difference between the SF (Engel's class I) and NSF groups (Engel's class II, III, IV) ( $p > 0.05$ ) (Table 1).

#### MAIN POINTS

- Resective surgery provides excellent results for intractable epilepsy.
- Surgery for refractory tumoral temporal lobe epilepsy offers complete seizure freedom. In majority, provided the complete epileptogenic zone is excised.
- Early successful surgical intervention will minimize adverse medical, behavioral, and psychosocial consequences of long-standing refractory epilepsy.

**Table 1.** Demographic and clinical characteristics in SF and NSF patients at the 2<sup>nd</sup> year after surgery for Engel's outcome

	SF group (n=21)	NSF group (n=5)	p
	n (%*)	n (%*)	
<b>Age (n=26) (32.31±7.72)</b>			
Mean±SD	31.38±7.01	36.20±10.16	0.308
Median (min-max)	31 (18-44)	36 (23-48)	
<b>Gender (n=26)</b>			
Female (n=14)	11 (52.4)	3 (60.0)	1.000 <sup>a</sup>
Male (n=12)	10 (47.6)	2 (40.0)	
<b>Lateralization (n=26)</b>			
Right (n=18)	14 (66.7)	4 (80.0)	1.000 <sup>a</sup>
Left (n=8)	7 (33.3)	1 (20.0)	
<b>Age of onset (year) (n=26) (14.92±7.50)</b>			
Mean±SD	14.43±6.84	17.00±10.56	0.900
Median (min-max)	16 (1-24)	15 (7-34)	
<b>Duration of epilepsy (year) (n=26) (17.38±8.34)</b>			
Mean±SD	16.95±7.19	19.20±13.10	0.659
Median (min-max)	18 (6-32)	21 (4-38)	
<b>Risk factors</b>			
Febrile seizure (n=10)	10 (47.6)	0	0.121 <sup>a</sup>
Trauma (n=6)	6 (28.6)	0	0.298 <sup>a</sup>
Dystocia (n=6)	6 (28.6)	0	0.298 <sup>a</sup>
Consanguineous marriage (n=6)	4 (19.0)	2 (40.0)	0.558 <sup>a</sup>
Family history (n=6)	5 (23.8)	1 (20.0)	0.998 <sup>a</sup>
CNS infection (n=3)	1 (4.8)	2 (40.0)	0.085 <sup>a</sup>
<b>FIAS</b>	21 (100)	5 (100)	
<b>FIAS frequency</b>			
1-10 seizure	6 (28.6)	2 (40.0)	0.628 <sup>a</sup>
11-30 seizure	15 (71.4)	3 (60.0)	
<b>FBTCS</b>	6 (28.6)	2 (40.0)	0.628 <sup>a</sup>
<b>FBTCS frequency</b>			
1-10 seizure	13 (86.7)	3 (100)	0.998 <sup>a</sup>
11-35 seizure	2 (13.3)	0	
<b>EEG</b>			
Left temporal	14 (66.7)	2 (40.0)	0.395
Right temporal	6 (28.6)	2 (40.0)	
Bitemporal	1 (4.8)	1 (20.0)	
<b>VEM IEDs</b>			
Left temporal	13 (61.9)	2 (40.0)	0.103
Right temporal	8 (38.1)	2 (40.0)	
Bitemporal	0	1 (20.0)	
<b>VEM ictal</b>			
Left temporal	13 (61.9)	2 (40.0)	0.103
Right temporal	8 (38.1)	2 (40.0)	
Bitemporal	0	1 (20.0)	
<b>Clinical lateralization</b>			
Left	11 (52.4)	2 (40.0)	0.877
Right	7 (33.3)	2 (40.0)	
Non-lateralized	3 (14.3)	1 (20.0)	

\*Column percentage; SD: Standard deviation; <sup>a</sup>Fisher's exact test.

CNS: Central nervous system, FIAS: Focal impaired awareness seizure, FBTCS: Focal to bilateral tonic-clonic seizure, EEG: Electroencephalography, VEM: Video EEG monitoring, IEDs: Interictal epileptiform discharges, SF: Seizure-free, NSF: Non-SF, min-max: Minimum-maximum

According to the Engel classification of the cases at the 6<sup>th</sup> month, 1<sup>st</sup>, and 2<sup>nd</sup> years after the operation, at the 6<sup>th</sup> month follow-up, 96.2% of the patients were Engel's class I and 3.8% were Engel's class II. In the first year of follow-up, 92.3% of the patients were Engel's class I and 7.7% were Engel's class II. In the second-year follow-up, 80.8% of the patients were Engel's class I and 19.2% were Engel's class II. There were no patients with Engel's class III and IV in the 6<sup>th</sup> month, 1<sup>st</sup>, and 2<sup>nd</sup> year follow-ups (Table 2).

Preoperative MRI, interictal EEG, and long-term VEM studies were performed on all 26 patients included in the study, and FDG-PET (84.6%) was performed on all patients except 4 patients. PET is not performed in these patients because VEM, EEG, and MRI results can best localize the epileptogenic focus and do not require additional examination. Considering the MRI appearances of the patients, one patient's MRI result was normal. Mesial temporal sclerosis (MTS) was found in 42.3% (n=11) of the patients, tumors were present in 30.8% (n=8), vascular lesions were seen in 15.4% (n=4), and developmental anomalies were found in 7.7% (n=2). No statistically significant difference was found between the patients with and without seizures in the second postoperative year in terms of lateralization and pathological appearance on MRI (p=0.632, p=0.775, respectively) (Table 3). In terms of surgical approach, 50.0% of patients underwent ATL and amygdalohippocampectomy (AH), 38.5% underwent ATL + lesionectomy and AH, 11.5% underwent lesionectomy + AH. When we evaluated the postoperative pathology results, low-grade tumor was found in 42.3% of the patients, cortical dysplasia in 38.5%, cavernous hemangioma in 11.5%, and high-grade tumor in 7.7%. No statistically significant difference was found between the patients with and without seizures in the second postoperative year in terms of the type of surgery and pathology results (p=0.774 p=1.00, respectively) (Table 3).

## DISCUSSION

In this study, after a 2-year follow-up of lesional TLE patients, the SF rate was 92.3% in the first year and 80.8% in the second year. This is consistent with the results of previous studies on the positive outcome of surgery in lesional epilepsy.<sup>7,8</sup>

Although there are various opinions about the adequate postoperative follow-up time to determine the prognosis, the general trend is that at least two years of follow-up is sufficient to determine the outcome of the seizure after surgery.<sup>9</sup> For example, Panda et al.<sup>10</sup> observed that 79% of the patients were completely SF at a mean follow-up of 4 years. In the study by Ravat et al.,<sup>11</sup> 85.29% of the patients were SF (Engel's class I) in a mean follow-up of 62 months.

**Table 2.** Postoperative sixth month, first and second year surgical results

(n=26)	Seizure-free group (Engel's class I)	Non-seizure-free group
	n (%)	n (%)
<b>Sixth month</b>	25 (96.2)	1 (3.8)
<b>First year</b>	24 (92.3)	2 (7.7)
<b>Second year</b>	<b>21 (80.8)</b>	<b>5 (19.2)</b>
*: percentage		

**Table 3.** Distribution of radiological imaging, type of operation and pathology results of patients at the 2<sup>nd</sup> year after surgery for Engel's outcome

	Seizure-free group (n=21)	Non-seizure-free group (n=5)	p
	n (%*)	n (%*)	
<b>MRI lateralization</b>			
Left	12 (57.1)	2 (40.0)	0.632
Right	8 (38.1)	3 (60.0)	
Normal	1 (4.8)	0	
<b>MRI</b>			
Mesial temporal sclerosis	9 (42.8)	2 (40.0)	0.775
Tumor	7 (33.3)	1 (20.0)	
Vascular lesion	3 (14.3)	1 (20.0)	
Developmental anomaly	1 (4.8)	1 (20.0)	
Normal	1 (4.8)	0	
<b>Operation type</b>			
ATL + AH	11 (52.4)	2 (40.0)	0.774
ATL+ lesionectomy + AH	8 (38.1)	2 (40.0)	
Lesionectomy + AH	2 (9.5)	1 (20.0)	
<b>Pathology result</b>			
Tumor	11 (57.9)	2 (50.0)	1.000 <sup>a</sup>
Cortical dysplasia	8 (42.1)	2 (50.0)	

\*Column percentage, <sup>a</sup>Fisher's exact test.  
MRI: Magnetic resonance imaging, ATL: Anterior temporal lobectomy, AH: Amygdalohippocampectomy

Age and duration of epilepsy during surgery are undoubtedly one of the most important factors in terms of patient quality of life. In this study, we found that the mean age and duration of epilepsy of the patients were not effective on surgical outcomes. Most studies reported that a younger age of onset and long epilepsy duration were associated with poor surgical outcomes.<sup>12,13</sup> It has been shown that there is a delay in the referral of patients with focal epilepsy to epilepsy centers, and similar to our study, the average time from the onset of epilepsy to surgery is 20 years.<sup>14</sup> The long delay before surgery may be due to the anxiety of complications such as possible post-operative disability and cognitive deficits, delayed referral of possible candidates, and long waiting lists in specialized hospitals.<sup>15</sup> Considering the studies evaluating prognostic factors for surgical results, no clear feature was specified in predicting the outcome. When the relationship between FC and MTS is investigated, there is a strong relationship between these two conditions, although there is no definite evidence that FC is a risk factor for MTS. In addition to studies showing that FC has a positive predictive value on surgical outcome,<sup>16,17</sup> many studies did not show any independent effect of this factor on surgical outcome despite high SF rates,<sup>8,18</sup> consistent with our study. Similarly, we could not find a relationship between other factors such as perinatal complications, developmental delay, FCs, family history of seizures, history of head trauma and CNS infection, and seizure-freeness after surgery.

The most common appearance in the MRI of the patients was MTS, and the second most common was tumor. MRI results of one patient were normal. No statistically significant difference was found between patients with and without seizures in the second postoperative year in terms of lateralization and pathological appearance on MRI. While MRI can detect 80% of patients with

MTS, it has 100% diagnostic value in lesions consistent with the mass. In studies using MRI techniques, it has been reported that an accurate diagnosis can be made at a rate of 80-90% when the findings are compared with the pathological findings.<sup>19</sup> Hippocampal sclerosis (HS) is the most common pathology detected on MRI in patients with drug-resistant TLE. Other pathological MRI findings include tumors, vascular malformations, malformations of cortical development, and evidence of distant trauma, post-infection, or ischemic injury. However, approximately 30% of patients with electroclinical evidence of drug-resistant TLE have normal MRI scans on visual inspection (MRI-negative TLE). This causes an inherent difficulty in identifying the epileptogenic site in these patients. However, with advanced localization techniques, these cases are usually suitable for surgical resection.<sup>20</sup> In the study, there was no significant relationship between MRI results (in order of frequency, MTS, tumor, vascular lesion, developmental anomaly, normal appearance) and second-year SF rates. Hu et al.<sup>21</sup> reported that there was no significant relationship between MRI results and Engel classification.

Postoperative seizure-freeness may be due to etiology and pathological findings.<sup>9</sup> When patients are evaluated in terms of pathology results, the most common causes according to the WHO classification are grade 1-2 tumors and cortical dysplasia. In a histopathological series of approximately 10,000 brain tissue samples obtained during epilepsy surgery, HS (36.4%) was the most common histopathological diagnosis. Brain tumors were the second most common histopathological diagnosis, occurring in 23.6% of the samples, and ganglioglioma was the most common (10.4%). Dysembryoplastic neuroepithelial tumors were the second most common tumor type (5.9%). The most common location of these tumors was the temporal lobe. One year after surgery, 68.4% of patients with tumors (79.9% of children and 63.5% of adults) were SF.<sup>14</sup>

Although we found a significant relationship between pathology results and SF rates in our study, the underlying pathology causing seizures affects surgical results. de Tisi et al.<sup>22</sup> and Bien et al.<sup>23</sup> showed in their studies that the resection of benign tumors and HS is associated with good surgical outcome. In another study, Mehvari Habibabadi et al.<sup>24</sup> reported that they could not find a significant relationship between pathology results and Engel classification. In a large, multicenter, cohort study of 9147 patients undergoing epilepsy surgery in 18 European countries, the proportion of patients with Engel class 1 was 68% 2 years after surgery, compared with 78% of patients with low-grade epilepsy-related neuroepithelial tumors. It has been emphasized that the histopathological diagnosis is an important and independent determinant of the outcome.<sup>15</sup>

Three types of surgical strategies were applied to the patients in this study. Half of the patients underwent ATL + AH, approximately 40% underwent ATL + lesionectomy + AH, and the rest underwent lesionectomy + AH. When these surgical procedures and postoperative SF rates were compared, no significant relationship was found. Several studies have reported satisfactory seizure control in lesional mTLEs, particularly in tumors, when the lesion is completely resected, although the extent of resection is more limited than that in conventional ATL.<sup>25,26</sup> It has been reported that this method is advantageous in terms of various complications that may occur with conventional ATL.<sup>27</sup> In addition, there are

studies in the literature that support better seizure outcome with anterior mesiotemporal resection compared with lesionectomy in temporal neoplastic lesion.<sup>28,29</sup> In a recent study by Raiyani et al.,<sup>30</sup> it was argued that for lesions located in the mesial temporal lobe, anteromesial temporal resection and lesionectomy provide a better seizure outcome than lesionectomy alone. As can be seen, there is no consensus in the literature on surgical procedures for epilepsy. In the clinic where the study was conducted, surgical treatment is decided with a multidisciplinary approach, considering many factors such as the location of the lesion, MRI, comorbid conditions of the patient, and socio-cultural status.

### Study Limitations

The main limitation of our study is the small sample size because we only included patients with lesional TLE. Another limitation is that our patients were limited to a short follow-up period. Simultaneously, the fact that the choice of surgical procedures mainly reflects our surgical strategy at that time can be considered among the limitations.

### CONCLUSION

Surgery for refractory epilepsy in temporal lobe tumors often offers complete seizure freedom. Complete surgical excision of the epileptogenic region is of great importance for achieving seizure-freeness. Early successful surgical intervention will minimize the adverse medical, behavioral, and psychosocial consequences of long-standing refractory epilepsy.

### Ethics

**Ethics Committee Approval:** The study was approved by Institutional Ethical Board of Gazi University Faculty of Medicine (decision no: 49, date: 25.01.2016).

**Informed Consent:** Informed consent was obtained from all participants.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: T.G.D., İ.Y., G.K., Concept: M T.G.D., İ.Y., E.B., Design: T.G.D., İ.Y., E.B., G.K., Data Collection or Processing: T.G.D., G.K., Analysis or Interpretation: T.G.D., İ.Y., E.B., Literature Search: T.G.D., Writing: T.G.D.

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