Turk Neurosurg 36(3):440-449, 2026
DOI: 10.5137/1019-5149.JTN.48548-25.4

Original Investigation
Stereotactic and Functional

Received: 31.01.2025
Accepted: 26.09.2025
Published Online: 22.05.2026

Long-Term Outcomes of Anterior Temporal Lobectomy in Adults with Temporal Lobe Epilepsy: A Comprehensive Analysis of a 20-Year, 168-Patient Cohort

Ozan HASIMOGLU[1], Tuba Ozge KARACOBAN[1], Taha HANOGLU[1], Nur Bahar GEYLAN[2], Demet KINAY[3], Gunay GUL[4], Ayten Ceyhan DIRICAN[4], Murat Mert ATMACA[5], Ozan BARUT[6], Omer Batu HERGUNSEL[7], Bekir TUGCU[1]

[1]Basaksehir Cam and Sakura City Hospital, Department of Neurosurgery, Istanbul, Türkiye
[2]Basaksehir Cam and Sakura City Hospital, Neurosurgery Nursing, Department of Neuropsychiatry, Istanbul, Türkiye
[3]University of Health Sciences Prof. Dr. Cemil Taşcıoğlu City Hospital, Department of Neurology, Istanbul, Türkiye
[4]University of Health Sciences Turkey, Bakırköy Prof. Dr. Mazhar Osman Mental Health and Neurology Training and Research Hospital, Department of Neurology, Istanbul, Türkiye
[5]Sultan 2. Abdul Hamıd Khan Educatıonal and Research Hospital, Department of Neurology, Istanbul, Türkiye
[6]Bingol State Hospital, Department of Neurosurgery, Bingol, Türkiye
[7]Sisli Hamidiye Etfal Training and Research Hospital, Department of Neurosurgery, Istanbul, Türkiye

Corresponding author: Ozan HASIMOGLU ✉ ozanhasim@hotmail.com

ABSTRACT

AIM: To evaluate the long-term clinical outcomes and histopathological classifications of anterior temporal lobectomy in adult patients with mesial temporal lobe epilepsy (TLE) associated with hippocampal sclerosis.

MATERIAL and METHODS: This was a retrospective study of 168 adult patients diagnosed with drug-resistant mesial temporal lobe epilepsy who underwent resection surgery and were histopathologically confirmed to have hippocampal sclerosis between 2006 and 2025. Preoperative evaluations included video-EEG, high-resolution brain Magnetic Resonance Imaging, neuropsychological tests, and PET-CT. Postoperative outcomes were assessed using the Engel classification. The impact of demographic characteristics, age at epilepsy onset, epilepsy duration, initial precipitating injury, family history, histopathological findings, and diagnostic evaluations on long-term seizure outcomes was evaluated using Kaplan-Meier and multivariate analyses.

RESULTS: Among the 168 patients included in the study, 95.2% achieved Engel Class I seizure freedom in the first year, with a long-term seizure freedom rate of 85.1%. The mean follow-up duration was 117.74 months. Histopathological evaluations revealed that HS-ILAE Type 1 was the most common histopathological classification, (73.8%). Longer preoperative epilepsy duration (p=0.009) and positive family history were risk factors for seizure recurrence (p=0.021). There was no significant association between histopathological classification and seizure control (p>0.05).

CONCLUSION: Anterior temporal lobectomy are effective surgical options for achieving high rates of seizure freedom in patients with mesial TLE associated with hippocampal sclerosis. Longer preoperative epilepsy duration and a positive family history were identified as negative prognostic factors for seizure recurrence. This study makes a significant contribution to the literature, with long-term outcomes of these procedures in a large cohort of adult patients with TLE.

KEYWORDS: Hippocampal sclerosis, Temporal lobe epilepsy, Anterior temporal lobectomy, Amygdalohippocampectomy, Engel classification, Histopathological classification, Outcome

Ozan HASIMOGLU : 0000-0003-1394-5188
Tuba Ozge KARACOBAN : 0009-0007-9219-3864
Taha HANOGLU : 0000-0001-5517-4735
Nur Bahar GEYLAN : 0009-0001-4548-1202
Demet KINAY : 0000-0001-6496-6080
Gunay GUL : 0000-0003-2485-1654
A. Ceyhan DIRICAN : 0000-0002-8658-1568
Murat Mert ATMACA : 0000-0003-2048-4930
Ozan BARUT : 0000-0001-6572-9589
Omer Batu HERGUNSEL : 0000-0003-3143-0575
Bekir TUGCU : 0000-0003-0385-0054

ABBREVIATIONS: EEG: Electroencephalography, **MRI:** Magnetic resonance imaging, **PET:** Positron emission tomography, **CT:** Computed tomography, **NPT:** Neuropsychological testing, **DRE:** Drug-resistant epilepsy, **TLE:** Temporal lobe epilepsy, **HS:** Hippocampal sclerosis, **ILAE:** International league against epilepsy, **FCD:** Focal cortical dysplasia, **SD:** Standard deviation, **SAH:** Subarachnoid hemorrhage, **WAIS:** Wechsler adult intelligence scale, **WMS:** Wechsler memory scale, **MRS:** Magnetic resonance spectroscopy

INTRODUCTION

Epilepsy is a common neurological disorder affecting approximately 1% of the global population, impacting millions of individuals worldwide (47). The quality of life of individuals with epilepsy is significantly compromised, not only by seizures but also by the profound social, economic, and psychological consequences of the condition. Despite being a treatable disorder, a substantial proportion of individuals with epilepsy lack access to appropriate treatment, a phenomenon referred to as the "treatment gap." This disparity is particularly pronounced in developing countries, where the treatment gap can reach as high as 75%. In the United States, approximately 1% of surgical candidates are able to access specialized epilepsy centers (35).

Approximately 20%-30% of epilepsy cases continue to experience seizures despite receiving antiepileptic treatment, including appropriate doses and durations (40). These patients are classified as having drug-resistant epilepsy (DRE), making them ideal candidates for epilepsy surgery. The management of DRE poses a significant challenge, and for this subset of patients, surgical intervention, particularly resective surgery, has emerged as an effective method for achieving seizure control.

Temporal lobe epilepsy (TLE) accounts for a substantial portion of DRE cases and is among the subgroups most responsive to surgical intervention. Notably, hippocampal sclerosis is identified as the primary histopathological cause in nearly 80% of TLE cases, often considered the hallmark of DRE (1,5,12). Characterized by neuronal loss and gliosis, predominantly in the CA1 and CA4 regions, hippocampal sclerosis remains a complex condition with pathophysiological mechanisms that are not yet fully elucidated (2,5). Various factors have been implicated in its development, including febrile convulsions, head trauma, central nervous system infections, and genetic predisposition (6,50).

Epilepsy surgery has emerged as an effective treatment modality for achieving seizure control, particularly in patients with drug-resistant TLE. Surgical procedures commonly employed in this patient population include anterior temporal lobectomy and selective amygdalohippocampectomy (16,38,39). Surgical intervention can achieve complete seizure freedom in 48% -84% of patients, depending on the duration of follow up (15,28,43,45).

The aim of this study was to evaluate the long-term clinical outcomes and histopathological classifications of anterior temporal lobectomy in adult patients with TLE caused by hippocampal sclerosis, with a follow up period spanning nearly two decades. Additionally, the study examined the impact of preoperative evaluation processes, the prognostic significance of histopathological classifications on surgical success, and the insights gained from surgical experience.

MATERIAL and METHODS

Patient Selection and Data Collection

This study was conducted with the approval of the Basaksehir Cam and Sakura City Hospital Ethics Committee under decision number 2025-67. This study includes adult patients diagnosed with drug-resistant mesial temporal lobe epilepsy who underwent resection surgery at Basaksehir Cam and Sakura City Hospital and Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatry, Neurology and Neurosurgery and were histopathologically confirmed to have hippocampal sclerosis between 2006 and 2025. A total of 179 patients who underwent anterior temporal lobectomy were initially included. Eight patients were excluded due to a lack of regular follow-up, and three patients were excluded due to death from non-epilepsy-related causes. The most recent status of all patients was verified through teleconferencing.

All patients underwent a comprehensive preoperative evaluation conducted by an experienced local epilepsy surgery council, comprising epileptologists, neurosurgeons, and neuropsychologists. DRE was defined as the persistence of seizures for ≥2 years despite the use of at least two antiepileptic drugs at tolerable doses and appropriate durations. Detailed medical histories were obtained from all patients, investigating potential risk factors for hippocampal sclerosis, such as trauma, febrile convulsions, family history, central nervous system malignancies, and infections.

The comprehensive preoperative evaluation included interictal electroencephalography (EEG), video-EEG monitoring with scalp electrodes, formal neuropsychological testing, and high-resolution magnetic resonance imaging (MRI) performed under an epilepsy protocol. Additional diagnostic modalities such as Wada testing, magnetic resonance spectroscopy, and positron emission tomography (PET), were employed in selected cases. Patients exhibiting a single seizure semiology, corroborated by clinical and electrophysiological recordings from video-EEG and other noninvasive tests, were considered suitable candidates for surgery, provided that these findings converged to lateralize the hypothesized epileptogenic zone. All patients underwent with high-resolution brain MRI using 1.5- or 3-Tesla devices, adhering to epilepsy-specific imaging protocols. The diagnosis of hippocampal sclerosis was confirmed through qualitative MRI assessments performed by the epilepsy surgery team. Hippocampal volume was assessed using T1-weighted sequences, while T2 and FLAIR sequences were examined for increased signal intensity. A standardized neuropsychological test battery was administered preopera-

tively and repeated one year after surgery. This included the Wechsler Adult Intelligence Scale intelligence test, Edinburgh Handedness Inventory, digit span memory test, verbal memory processing test, Wechsler Memory Scale (WMS) story learning test, WMS visual memory subtest, and frontal function assessments including the Wisconsin Card Sorting Test, Stroop test, and verbal fluency test. Furthermore, left hemisphere functions were evaluated through language assessments and visuospatial skills testing using the Benton Facial Recognition Test and Line Orientation Test. Postoperative follow-up evaluations were conducted in the first month, third month, sixth month, first year, and annually thereafter. During these follow-ups, epileptologists were primarily responsible for adjusting or discontinuing antiepileptic medications as necessary.

Histopathological classification was performed adhering to the criteria outlined in the 2013 International League Against Epilepsy (ILAE) Commission consensus report. To ensure consistency, specimens from patients diagnosed with hippocampal sclerosis before 2013 were retrospectively re-evaluated and classified based on these criteria. Hippocampal sclerosis with widespread neuronal loss and gliosis across all regions, with predominant involvement of the CA1 and CA4 segments, was classified as HS-ILAE Type 1. Cases exhibiting predominant neuronal loss in the CA1 region were classified as HS-ILAE Type 2, whereas those with predominant CA4 involvement were classified as HS-ILAE Type 3. Patients with coexisting focal cortical dysplasia were classified as FCD-3A, and cases showing reactive gliosis without accompanying neuronal loss were categorized as no-HS. Specimens that could not be excised en bloc during surgery were classified as fragmented-HS (4).

Postoperative evaluation was conducted using the Engel classification system (17), which categorizes patients into four distinct classes based on their seizure frequency. Specifically, Engel Class I indicates complete seizure freedom or the presence of only auras; Engel Class II indicates rare seizures, occurring only a few times per year; Engel Class III indicates a significant reduction in seizure frequency, despite the persistence of seizures; and Engel Class IV indicates seizures that are unchanged or worse following surgery. Seizures occurring within the first postoperative month were excluded from the analysis, as they may be attributed to the early recovery process or intraoperative exposure to blood products. Demographic and clinical variables, preoperative findings, histopathological classifications, and early postoperative outcomes were subjected to statistical analyses to identify prognostic factors predictive of surgical success. In this study, only patients classified as Engel Class I were considered seizure-free.

Statistical Analysis

Statistical analyses were performed using SPSS version 22, while Kaplan-Meier survival analysis was conducted using Python-based statistical libraries. Continuous variables were presented as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Chi-square tests were utilized to evaluate the associations between pathological classifications (ILAE) and clinical-demographic variables. Differences between continuous variables and ILAE pathological classifications were assessed using parametric methods for independent groups. Epilepsy duration was defined as the number of years from seizure onset to the time of surgery. Patients were divided into groups based on the epilepsy duration (0–10 years, 11–20 years, 21–30 years, and >30 years) to analyze its association with ILAE pathological classifications. Similarly, epilepsy onset age was categorized into four groups: <5 years, 5–12 years, 13–18 years, and >18 years. The association between onset age and ILAE classification was evaluated using the chi-square test. The normality of continuous variables was assessed using the Shapiro-Wilk test.

Seizure control probabilities over time were calculated using Kaplan–Meier survival analysis, and between-group differences were assessed for statistical significance using the log-rank test. The distribution of patients and seizure recurrence over time intervals was analyzed using categorical classifications, with results presented as percentages.

Additionally, the frequency of postoperative complications was analyzed, and their clinical management was described in detail. Multivariate analyses were performed to identify independent prognostic factors influencing surgical outcomes. A significance threshold of $p<0.05$ was applied for all statistical evaluations.

RESULTS

A total of 168 patients (58.9% female and 41.1% male; mean age: 31.1 years) were included in the study, with a mean postoperative follow-up duration of 117.74 months. The mean age at seizure onset was 13.6 years, and the mean epilepsy duration was 17.6 years. Regarding medical history, 47.6% of patients had a history of febrile convulsions, 25.6% reported head trauma, 8.9% had a history of central nervous system infections, 0.6% had central nervous system malignancies, and 17.9% had a family history of epilepsy.

In terms of laterality, 45.8% of patients (n=77) underwent surgery on the right side and 54.2% (n=91) underwent surgery on the left side. Preoperative MRI examinations were conducted for all patients, revealing right hippocampal sclerosis in 44% (n=74), left hippocampal sclerosis in 52.4% (n=88), normal findings in 3% (n=5), and bilateral findings in 0.6% (n=1). Video-EEG monitoring was also performed on all patients, demonstrating epileptic activity in the right hemisphere in 45.2% (n=76), in the left hemisphere in 54.2% (n=91), and bilaterally in 0.6% (n=1). Neuropsychological tests (NPT) were conducted on 165 patients revealing right-sided dysfunction in 35.2% (n=58), left-sided dysfunction in 40.6% (n=67), normal findings in 6% (n=10), and bilateral dysfunction in 18.2% (n=30). Interictal PET was performed on 96 patients, revealing hypometabolism in the right mesial temporal region in 40.6%, the left mesial temporal region in 55.2%, and normal findings in 4.2%. The concordance rate between MRI and Video-EEG lateralization was 94.64% (n=159). Among these, 64.29% of patients (n=108) showed concordance between MRI, Video-EEG, and NPT lateralization, while 33.33% (n=56) exhibit-

ed concordance across MRI, Video-EEG, NPT, and PET findings (Table I). Postoperative complications occurred in 4.76% of patients. One patient required a second surgery the day after the initial operation to remove a retained surgical pad; one patient developed a subcutaneous infection that was successfully treated with wound debridement and antibiotic therapy; one patient underwent epidural hematoma drainage on the evening of surgery and recovered without sequelae. Other complications included otorrhea caused by surgical trauma to the external auditory canal, which resolved with medical treatment, and a subarachnoid hemorrhage (SAH) that healed without sequelae under clinical observation. Additionally, one patient developed foot drop of unknown etiology, which improved with physiotherapy, and another patient experienced carbamazepine-induced hyponatremia that resolved with medical treatment and medication change. Lastly, one patient underwent surgery two weeks postoperatively due to a suspected intracranial abscess caused by a cystic lesion; however, no abscess was found, and the patient was placed under follow-up.

Prognostic Variables

At the 1-year follow-up, 95.2% of patients were classified as Engel Class I, indicating complete seizure freedom or the presence of auras. Additionally, 1.8% of patients were classified as Engel Class II, 1.2% as Engel Class III, and 1.8% as Engel Class IV. In the long-term follow-up, 85.1% of patients maintained their Engel Class I status, while 10.7% were classified as Engel Class II, 3.6% as Engel Class III, and 0.6% as Engel Class IV (Figure 1). No statistically significant relation-

Table I: Clinical and Demographic Summary

Characteristic	Value
Age (Mean ± SD) (years)	31.1 ± 9.2
Gender; M, F (%)	41.1, 58.9
Epilepsy Onset Age (Mean ± SD) (years)	13.6 ± 9
Epilepsy Duration (Mean ± SD) (years)	17.6 ± 9.9
Follow-Up Duration (Mean ± SD) (months)	117.74 ± 64.99
Febrile Seizures (n)	80
Trauma (n)	43
Infection (n)	15
Malignancy (n)	1
Family History (n)	30
MTS Side [R; L (%)]	45.8; 54.2
MR Lateralization [(R; L; N; B (%)]	44.0; 52.4; 3.0; 0.6
Video EEG Lateralization [R; L; B (%)]	45.2; 54.2; 0.6
PET Lateralization [R; L; N (%)]	40.6; 55.2; 4.2
NPT Lateralization [R; L; N; B (%)]	35.2; 40.6; 6; 18.2

R: *Right,* ***L:*** *Left,* ***B:*** *Bilateral,* ***N:*** *Normal,* ***SD:*** *Standard deviation,* ***EEG:*** *Electroencephalography,* ***MRI:*** *Magnetic resonance imaging,* ***PET:*** *Positron emission tomography,* ***NPT:*** *Neuropsychological testing,* ***M:*** *male,* ***F:*** *female.*

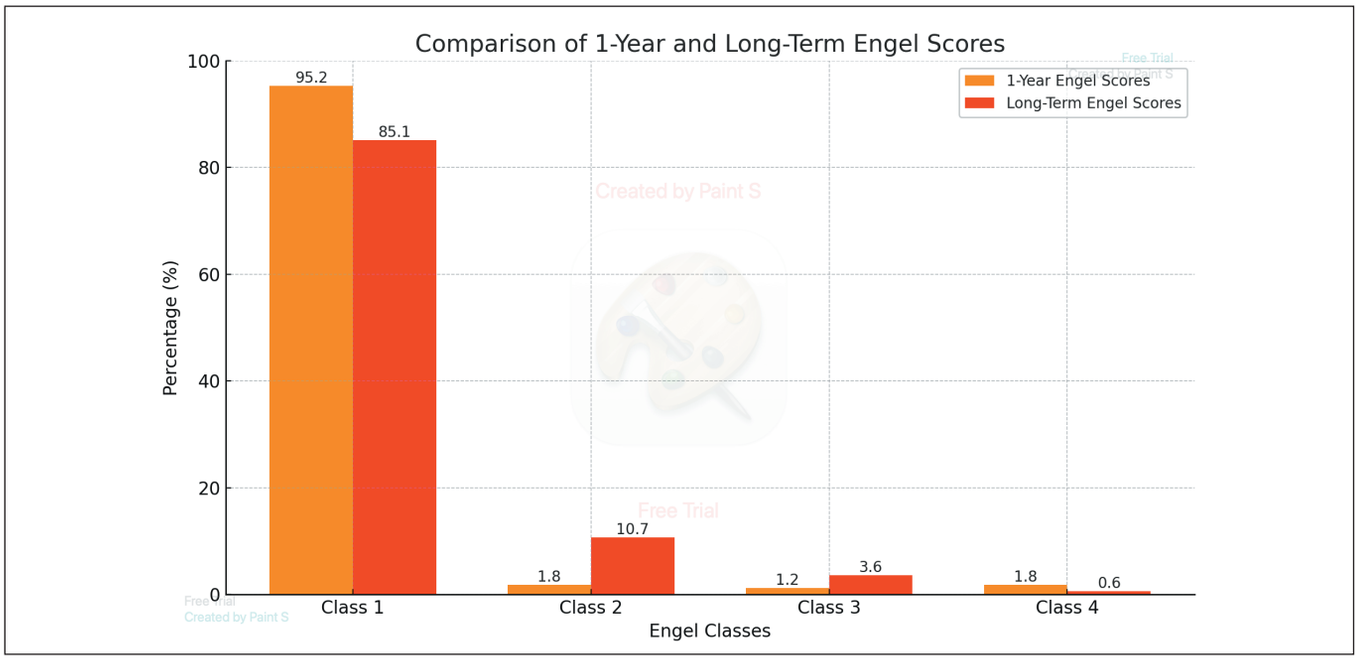

Figure 1: This figure illustrates the distribution of Engel scores at the 1-year follow-up and the long-term follow-up. The scores are categorized to evaluate seizure outcomes over time, providing a visual comparison of the immediate and sustained effects of the intervention. The chart highlights the proportion of patients achieving favorable seizure control (Engel Class I) and those with less optimal outcomes (Engel Classes II-IV) in both time frames.

ship was found between early or long-term Engel scores and any of the demographic or clinical variables analyzed.

A total of 26 patients (15.5%) experienced seizure recurrence or incomplete seizure control (Engel Classes II-IV). The average time to seizure recurrence after surgery was 27.9 months. Notably, 11.3% of patients who were seizure-free during the first year postoperatively experienced recurrence afterward (Figure 2). The relationship between age and seizure recurrence was evaluated using logistic regression analysis, which showed no statistically significant effect of age (p=0.061). Additionally, no significant association was observed between sex and seizure recurrence (p=0.221).

Analysis of the relationship between epilepsy onset age and seizure recurrence revealed no significant difference between early- and late-onset (p=0.717). However, analysis of epilepsy duration revealed a significant association between seizure recurrence and preoperative epilepsy duration (p=0.009). Patients with a longer duration of DRE before surgery had

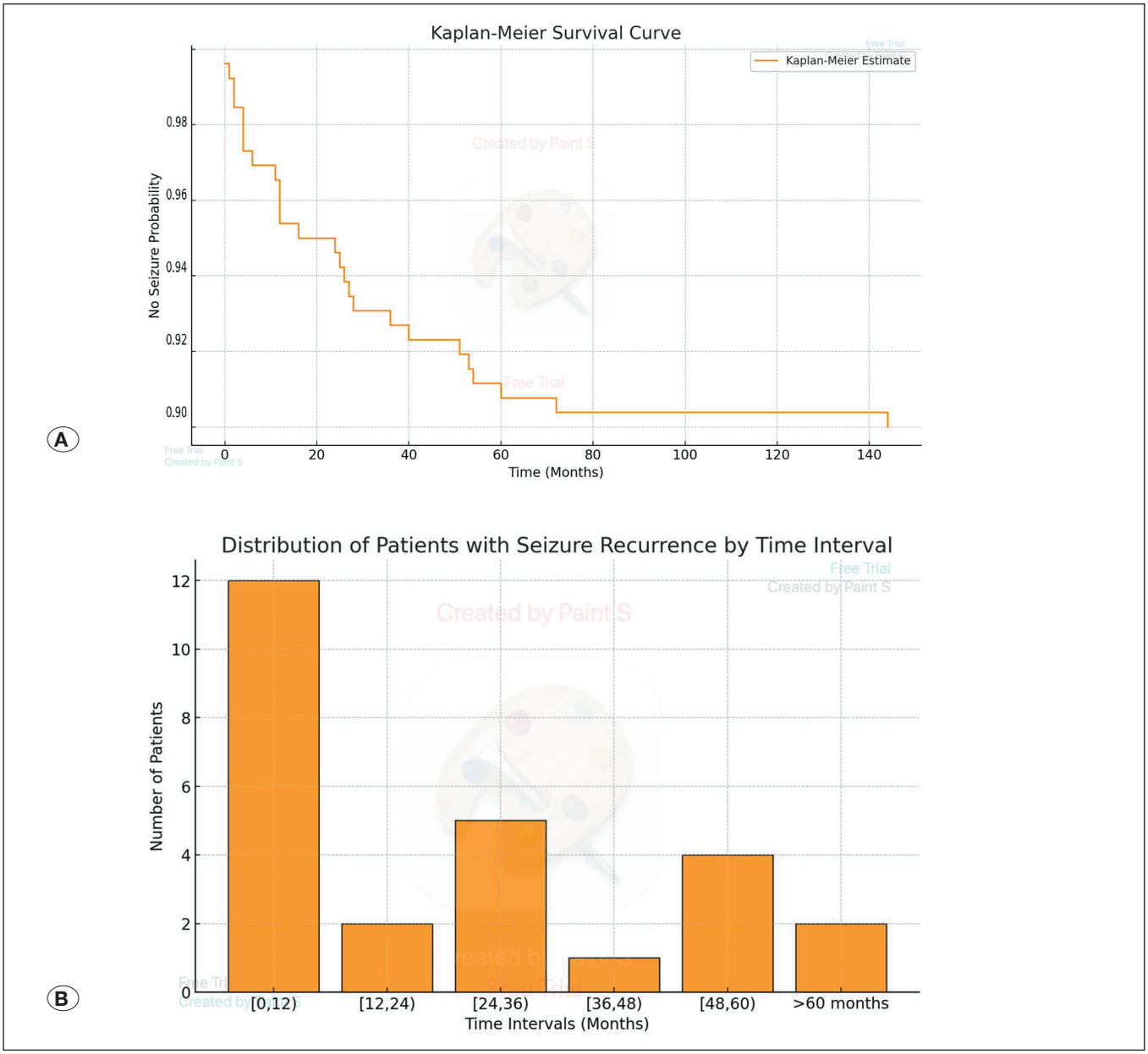

Figure 2: This composite figure combines two graphical representations related to seizure outcomes and patient follow-up. **A)** Kaplan-Meier Curve: This panel illustrates the seizure-free probability over time following surgical intervention. The x-axis represents the months since surgery, and the y-axis indicates the probability of remaining seizure-free. The stepwise declines in the curve reflect the occurrence of seizure recurrence events, providing a temporal overview of long-term seizure control among patients. **B)** Patient Distribution by Time Intervals: This panel displays the percentage distribution of patients across follow-up intervals. The x-axis categorizes patients into time intervals (in months), while the y-axis shows the proportion of the total patient population.

significantly lower postoperative seizure freedom rates. There was no significant association between a history of febrile convulsions, infections, trauma, or malignancy and seizure recurrence. However, family history was a significant risk factor for seizure recurrence (p=0.021). Concordance between MRI, video-EEG, PET, and NPT lateralization findings regarding hippocampal sclerosis showed no significant association with seizure recurrence (p=0.327). Concordance between these diagnostic modalities did not appear to influence postoperative seizure control outcomes.

Histopathological Evaluation

Histopathological classification of hippocampal sclerosis revealed that the majority of patients were categorized as HS-ILAE Type 1 (73.8%), followed by HS-ILAE Type 2 (17.3%) and Fragmented-HS (7.1%). HS-ILAE Type 3 (1.8%) was the least common classification. This classification was based on the criteria outlined in the ILAE report. Dual pathology was most frequently observed as FCD-3A, occurring in 3.57% of patients. Additionally, three patients (1.79%) were diagnosed with ganglioglioma, and one patient (0.60%) had low-grade astrocytoma in the neocortical resection specimen alongside hippocampal sclerosis. Analysis of HS-ILAE classifications by age group revealed that HS-ILAE Type 1 was the most prevalent classification across all age groups. Notably, no significant relationship was found between age groups and ILAE classifications (p=0.843). Similarly, sex showed no signification association with ILAE classifications (p=0.071). Additionally, the relationship between epilepsy onset age and ILAE classifications was not statistically significant (p=0.435). However, epilepsy duration showed a significant association with HS-ILAE classifications (p=0.044), with HS-ILAE Type 1 being more commonly observed in patients with longer epilepsy duration. An analysis of the relationship between the side of mesial temporal sclerosis (MTS) and ILAE classifications revealed a borderline significant association (p=0.054). Notably, HS-ILAE Type 1 was more frequently observed in patients with left-sided MTS, while HS-ILAE Type 2 was more common in right-sided MTS. No significant associations were identified between initial precipitating injuries (e.g., febrile seizures, trauma, infections, malignancies, or family history) and ILAE pathological classifications (p>0.05). Furthermore, ILAE pathological classifications showed no significant association with postoperative seizure freedom (p=0.166) (Table II).

DISCUSSION

This study evaluated the long-term clinical outcomes and histopathological classifications of anterior temporal lobectomy in patients with TLE caused by hippocampal sclerosis. With a follow-up period of approximately 20 years and a large cohort of 168 patients, our study provides a robust and comprehensive dataset that surpasses similar studies in the literature. All surgeries were performed by the same surgical team, ensuring a homogenous patient group. This study offers an extensive evaluation of long-term follow-up results, epilepsy-related factors, surgical nuances, and histopathological findings.

In our study, 95.1% of patients achieved Engel Class I seizure freedom (complete seizure freedom) at the 1-year follow-up, and this rate was maintained at 85.2% in the long-term follow-up. In a meta-analysis of randomized controlled trials by Lee et al., the average rate of complete seizure freedom following surgery for adult TLE was 72.4% (29). Studies conducted independently of surgical technique have reported that patients undergoing surgery for hippocampal sclerosis-associated TLE, a more homogenous subgroup, achieved seizure freedom rates of 86-90% during the first two years of follow-up (13,33,37,44,45). However, these rates decline to 62-83% in follow-ups exceeding five years (13,24,32,51). Our results exceed the rates reported in previous studies. The superior seizure control rates in our study may be attributed to several factors. A meta-analysis by McIntosh et al. revealed worse outcomes in series that included cases without radiological or histopathological lesions (33). In our cohort, all patients had histopathological confirmation of hippocampal sclerosis, and

Table II: Clinical and Demographic Characteristics by ILAE Pathology Types

	HS-ILAE Type 1	HS-ILAE Type 2	HS-ILAE Type 3	Fragmented-HS
Age (Mean, SD) (years)	31.05 (9.63)	30.93 (8.06)	34.33 (9.87)	31.92 (8.36)
Gender; F, M (%)	60.0; 40.0	69.0; 30.0	0.0; 100.0	42.0; 58.0
Epilepsy Onset Age (Mean, SD) (years)	12.76 (8.50)	17.24 (9.99)	11.67 (8.08)	13.42 (9.95)
Epilepsy Duration (Mean, SD) (years)	18.31 (9.91)	13.69 (9.52)	22.67 (17.24)	18.42 (7.45)
Febrile (%)	51.61	34.48	66.67	33.33
Trauma (%)	28.23	20.69	0.00	16.67
Infection (%)	8.06	6.90	0.00	25.00
Malignancy (%)	0.81	0.00	0.00	0.00
Family History (%)	17.74	20.69	33.33	8.33
MTS Side L; R (%)	57; 43	34; 66	100; 0	58; 42

***R:** Right, **L:** Left, **SD:** Standard Deviation, **HS-ILAE:** International League Against Epilepsy classification system for hippocampal sclerosis.*

97% had corresponding findings on MRI. Additionally, all cases in our series exhibited focal semiological and electrophysiological findings pointing to the hypothesized epileptogenic side. In the study by Siegel et al., focal epileptiform activity concordant with MRI-detected lesions was a predictor of favorable prognosis (41). Although not statistically significant, the large proportion of patients in our series with concordant radiological, electrophysiological, and neuropsychological findings suggesting the same epileptogenic focus likely contributed to the favorable outcomes. Similar concordance-related findings have been linked to good seizure control in previous studies (16,22). Lastly, increasing surgical experience appears to play a critical role in improving outcomes. In our earlier series with less experience, Engel Class I seizure freedom rates were 84% at 1 year and 68.8% at 5 years (49). Over the past 15 years, advances in patient selection and surgical expertise have likely contributed to the improved outcomes observed. Although anterior temporal lobectomy are well-established procedures, attaining consistent and safe surgical outcomes necessitates navigating an adequate learning curve (20,42). Mastery of anatomical knowledge, refined subpial dissection techniques, and precise resection boundaries significantly enhance surgical success with growing experience. Consistent with this, previous studies have demonstrated that total or extended resections can effectively achieve better seizure control, highlighting the importance of surgical precision and expertise in optimizing patient outcomes (10,18,53).

Studies have consistently shown that the majority of seizure recurrences occur within the first two years after surgery (7,27,45). For instance, Yoon et al. reported that 17% of patients who were seizure-free in the first year experienced recurrence within five years, and 30% experienced recurrence within ten years. Similarly, another study found a 14% recurrence rate within the first five years (33,52). In the present study, 15.5% of patients who achieved seizure freedom in the first year experienced seizure recurrence, with an average time to recurrence of 27.9 months. After the fifth year, the seizure recurrence rate significantly declined (Figure 2), aligning with the trends observed in the literature. Of note, all patients who experienced seizure recurrence after the first year were classified as Engel Class II or III, implying that their seizure frequency remained significantly reduced compared to the preoperative period (Figure 1).

In our series, the risk factors for seizure recurrence included a longer preoperative epilepsy duration and a family history of epilepsy. There is no clear consensus on the relationship between epilepsy duration and seizure recurrence in the literature. While some studies have reported a similar association, others have found no significant relationship (14,17,19,28). Prolonged epilepsy duration may promote the development of secondary epileptic foci, thereby increasing the risk of recurrence (26). Long-standing epilepsy has been shown to cause structural changes, such as bilateral hippocampal volume reduction and altered glucose metabolism (29). potentially triggering ipsilateral or contralateral epileptogenesis (25). However, no previous studies have established a clear link between a family history of epilepsy and seizure recurrence. This may be related to the genetic basis of familial epilepsy. Further research incorporating genetic evaluations is required to address this question. There is a consensus that age, epilepsy onset age, sex, and the side of resection do not significantly influence surgical outcomes (31,34,48,53). In our series, we observed no significant relationship between initial precipitating injuries (including febrile convulsions, central nervous system infections, malignancies, and head trauma) and surgical outcomes. This finding appears consistent with the existing literature (28). However, some studies have reported an association between prolonged febrile convulsions and favorable outcomes (33,48).

Another focus of our study was to investigate the etiological and prognostic implications of the histopathological hippocampal sclerosis classification proposed by the ILAE in 2013 (4). Given the relatively recent introduction of this classification system, long-term follow-up studies incorporating this framework are scarce in the literature. The re-evaluation and reclassification of previously collected surgical specimens according to the ILAE criteria enabled us to conduct these assessments. Consistent with existing literature, HS-ILAE Type 1 was the most common histopathological subtype identified in our cohort (21,23,46). Our study found no significant association between histopathological subtypes and factors such as age, sex, or initial precipitating injury. This finding aligns with some previous studies (9,21). However, other studies have identified associations between specific events, such as early-onset febrile seizures, and histopathological subtypes (36). In patients with a longer epilepsy duration, HS-ILAE Type 1 was more frequently observed. This finding remains controversial. Na et al. attributed this association to the vulnerability of the CA1 subfield (36). Prolonged epilepsy is expected to cause widespread neuronal loss across all Cornu Ammonis regions, a finding supported by some studies but refuted by others (8). Finally, our study found no significant association between histopathological subtypes and surgical outcomes. This topic remains contentious, with most studies failing to detect a strong correlation between subtypes and outcomes. However, some studies suggest that Type 1 may be associated with better seizure control (3,11,21,36). More robust studies with homogenous datasets are required to validate these findings.

Limitations

Some limitations of this study should be considered while interpreting the findings. First, its retrospective design inherently introduces methodological constraints in data collection and evaluation. Additionally, the relationship between seizure types, genetics, and surgical outcomes was not explored. Moreover, psychiatric and cognitive outcomes were beyond the scope of this research.

Furthermore, electrophysiological evaluations were limited to non-invasive methods, and only cases that did not require invasive electrophysiology were included, focusing on safer patients. This approach reduced the opportunity to evaluate outcomes in more complex cases. Although no patients in our series underwent invasive EEG evaluations, such cases are not uncommon among drug-resistant epilepsy populations. The lack of detailed presentation of electrophysiological findings

also restricted the ability to investigate potential correlations between surgical outcomes and electrophysiological data.

Despite these limitations, our study offers valuable insights due to its extended long-term follow-up, sizable cohort, and comprehensive evaluation processes. Future studies addressing these limitations can yield more robust findings.

CONCLUSION

This study comprehensively evaluated long-term clinical outcomes and histopathological classifications of anterior temporal lobectomy in adult patients with TLE caused by hippocampal sclerosis. With an extended follow-up period of nearly 20 years and a large, homogenous cohort of 168 patients, our study provides a significant reference in the field of epilepsy surgery. A notable strength of our research is its multifaceted approach to assessing DRE in adult patients, offering a broad perspective from preoperative evaluations to postoperative outcomes. The study also presents an in-depth analysis of the relationship between histopathological classifications and clinical outcomes. The high seizure freedom rates observed during long-term follow-up (85.1%) and the detailed analysis of prognostic factors underscore the efficacy of surgical intervention.

In conclusion, our study highlights the importance of evaluating the impact of histopathological classifications on clinical outcomes and conducting multidimensional assessments of surgical success. These findings significantly contribute to informed patient selection and the development of tailored surgical strategies in epilepsy surgery. Future studies with more homogeneous datasets are necessary to validate these findings and further refine the understanding of the complex relationships between histopathological classifications, clinical outcomes, and surgical success.

Declarations

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: The authors declare no competing interests.

AUTHORSHIP CONTRIBUTION

Study conception and design: OH, TOK, TH
Data collection: NBG, OB, MMA, TOK, TH
Analysis and interpretation of results: OH, TOK, TH, NBH, OBH
Draft manuscript preparation: DK, GG, ACD, BT
Critical revision of the article: OBH, BT
Other (study supervision, fundings, materials, etc...): BT
All authors (OH, TOK, NBG, OB, MMA, TH, OBH, DK, GG, ACD, BT) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Blair RDG: Temporal lobe epilepsy semiology. Epilepsy Res Treat 2012:751510, 2012. https://doi.org/10.1155/2012/751510
2. Blümcke I, Coras R, Miyata H, Ozkara C: Defining clinico-neuropathological subtypes of mesial temporal lobe epilepsy with hippocampal sclerosis. Brain Pathol 22:402-411, 2012. https://doi.org/10.1111/j.1750-3639.2012.00583.x
3. Blümcke I, Pauli E, Clusmann H, Schramm J, Becker A, Elger C, Merschhemke M, Meencke HJ, Lehmann T, von Deimling A, Scheiwe C, Zentner J, Volk B, Romstock J, Stefan H, Hildebrandt M: A new clinico-pathological classification system for mesial temporal sclerosis. Acta Neuropathol 113:235-244, 2007. https://doi.org/10.1007/s00401-006-0187-0
4. Blümcke I, Thom M, Aronica E, Armstrong DD, Bartolomei F, Bernasconi A, Bernasconi N, Bien CG, Cendes F, Coras R, Cross JH, Jacques TS, Kahane P, Mathern GW, Miyata H, Moshe SL, Oz B, Ozkara C, Perucca E, Sisodiya S, Wiebe S, Spreafico R: International consensus classification of hippocampal sclerosis in temporal lobe epilepsy: A Task Force report from the ILAE commission on diagnostic methods. Epilepsia 54:1315-1329, 2013. https://doi.org/10.1111/epi.12220
5. Blümcke I, Thom M, Wiestler OD: Ammon's horn sclerosis: A maldevelopmental disorder associated with temporal lobe epilepsy. Brain Pathol 12:199-211, 2002. https://doi.org/10.1111/j.1750-3639.2002.tb00436.x
6. Cendes F, Sakamoto AC, Spreafico R, Bingaman W, Becker AJ: Epilepsies associated with hippocampal sclerosis. Acta Neuropathol 128:21-37, 2014. https://doi.org/10.1007/s00401-014-1292-0
7. Chen H, Modur PN, Barot N, Van Ness PC, Agostini MA, Ding K, Gupta P, Hays R, Mickey B: Predictors of postoperative seizure recurrence: A longitudinal study of temporal and extratemporal resections. Epilepsy Res Treat 2016:7982494, 2016. https://doi.org/10.1155/2016/7982494
8. Davies KG, Hermann BP, Dohan FC Jr, Foley KT, Bush AJ, Wyler AR: Relationship of hippocampal sclerosis to duration and age of onset of epilepsy, and childhood febrile seizures in temporal lobectomy patients. Epilepsy Res 24:119-126, 1996. https://doi.org/10.1016/0920-1211(96)00008-3
9. de Lanerolle NC, Kim JH, Williamson A, Spencer SS, Zaveri HP, Eid T, Spencer DD: A retrospective analysis of hippocampal pathology in human temporal lobe epilepsy: Evidence for distinctive patient subcategories. Epilepsia 44:677-687, 2003. https://doi.org/10.1046/j.1528-1157.2003.32701.x
10. de Tisi J, Bell GS, Peacock JL, McEvoy AW, Harkness WF, Sander JW, Duncan JS: The long-term outcome of adult epilepsy surgery, patterns of seizure remission, and relapse: A cohort study. Lancet 378:1388-1395, 2011. https://doi.org/10.1016/S0140-6736(11)60890-8
11. Deleo F, Garbelli R, Milesi G, Gozzo F, Bramerio M, Villani F, Cardinale F, Tringali G, Spreafico R, Tassi L: Short- and long-term surgical outcomes of temporal lobe epilepsy associated with hippocampal sclerosis: Relationships with neuropathology. Epilepsia 57:306-315, 2016. https://doi.org/10.1111/epi.13277

12. Duarte JTC, Jardim AP, Comper SM, De Marchi LR, Gaça LB, Garcia MTFC, Sandim GB, Assunção-Leme IB, Carrete Jr H, Centeno RS: The impact of epilepsy duration in a series of patients with mesial temporal lobe epilepsy due to unilateral hippocampal sclerosis. Epilepsy Research 147:51-57, 2018. https://doi.org/10.1016/j.eplepsyres.2018.08.009
13. Dupont S, Tanguy ML, Clemenceau S, Adam C, Hazemann P, Baulac M: Long-term prognosis and psychosocial outcomes after surgery for MTLE. Epilepsia 47:2115-2124, 2006. https://doi.org/10.1111/j.1528-1167.2006.00852.x
14. Elsharkawy AE, Alabbasi AH, Pannek H, Oppel F, Schulz R, Hoppe M, Hamad AP, Nayel M, Issa A, Ebner A: Long-term outcome after temporal lobe epilepsy surgery in 434 consecutive adult patients. J Neurosurg 110:1135-1146, 2009. https://doi.org/10.3171/2008.6.JNS17613
15. Engel J Jr, McDermott MP, Wiebe S, Langfitt JT, Stern JM, Dewar S, Sperling MR, Gardiner I, Erba G, Fried I, Jacobs M, Vinters HV, Mintzer S, Kieburtz K, Early Randomized Surgical Epilepsy Trial Study G: Early surgical therapy for drug-resistant temporal lobe epilepsy: A randomized trial. JAMA 307:922-930, 2012. https://doi.org/10.1001/jama.2012.220
16. Engel J Jr, Wiebe S, French J, Sperling M, Williamson P, Spencer D, Gumnit R, Zahn C, Westbrook E, Enos B, Quality Standards Subcommittee of the American Academy of N, American Epilepsy S, American Association of Neurological S: Practice parameter: Temporal lobe and localized neocortical resections for epilepsy: Report of the quality standards subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons. Neurology 60:538-547, 2003. https://doi.org/10.1212/01.wnl.0000055086.35806.2d
17. Engel Jr J, Van Ness P, Rasmussen T, Ojemann L: Outcome with respect to epileptic seizures. In: Engel J Jr (ed), Surgical Treatment of the Epilepsies, 2nd ed. New York: Raven Press, 1993
18. Englot DJ, Berger MS, Barbaro NM, Chang EF: Predictors of seizure freedom after resection of supratentorial low-grade gliomas. A review. J Neurosurg 115:240-244, 2011. https://doi.org/10.3171/2011.3.JNS1153
19. Englot DJ, Breshears JD, Sun PP, Chang EF, Auguste KI: Seizure outcomes after resective surgery for extra–temporal lobe epilepsy in pediatric patients: A systematic review. J Neurosurg Pediatr 12:126-133, 2013. https://doi.org/10.3171/2013.5.PEDS1336
20. Falconer MA, Meyer A, Hill D, Mitchell W, Pond DA: Treatment of temporal-lobe epilepsy by temporal lobectomy; a survey of findings and results. Lancet 268:827-835, 1955. https://doi.org/10.1016/s0140-6736(55)90421-9
21. Gales JM, Jehi L, Nowacki A, Prayson RA: The role of histopathologic subtype in the setting of hippocampal sclerosis-associated mesial temporal lobe epilepsy. Hum Pathol 63:79-88, 2017. https://doi.org/10.1016/j.humpath.2017.02.013
22. Harkness W: Temporal lobe resections. Childs Nerv Syst 22:936-944, 2006. https://doi.org/10.1007/s00381-006-0140-5
23. Hasimoglu O, Barut O, Kapar MO, Hergunsel OB, Kinay D, Gul G, Dirican AC, Bilgic B, Tugcu B: Relation between ilae hippocampal sclerosis classification and clinical findings in temporal lobe epilepsy. Turk Neurosurg 31:404-411, 2021. https://doi.org/10.5137/1019-5149.JTN.32026-20.1
24. Hemb M, Palmini A, Paglioli E, Paglioli EB, Costa da Costa J, Azambuja N, Portuguez M, Viuniski V, Booij L, Nunes ML: An 18-year follow-up of seizure outcome after surgery for temporal lobe epilepsy and hippocampal sclerosis. J Neurol Neurosurg Psychiatry 84:800-805, 2013. https://doi.org/10.1136/jnnp-2012-304038
25. Hennessy MJ, Elwes RD, Binnie CD, Polkey CE: Failed surgery for epilepsy. A study of persistence and recurrence of seizures following temporal resection. Brain 123 Pt 12:2445-2466, 2000. https://doi.org/10.1093/brain/123.12.2445
26. Janszky J, Janszky I, Schulz R, Hoppe M, Behne F, Pannek HW, Ebner A: Temporal lobe epilepsy with hippocampal sclerosis: Predictors for long-term surgical outcome. Brain 128:395-404, 2005. https://doi.org/10.1093/brain/awh358
27. Jeha LE, Najm IM, Bingaman WE, Khandwala F, Widdess-Walsh P, Morris HH, Dinner DS, Nair D, Foldvary-Schaeffer N, Prayson RA, Comair Y, O'Brien R, Bulacio J, Gupta A, Luders HO: Predictors of outcome after temporal lobectomy for the treatment of intractable epilepsy. Neurology 66:1938-1940, 2006. https://doi.org/10.1212/01.wnl.0000219810.71010.9b
28. Jobst BC, Cascino GD: Resective epilepsy surgery for drug-resistant focal epilepsy: A review. JAMA 313:285-293, 2015. https://doi.org/10.1001/jama.2014.17426
29. Jokeit H, Ebner A, Arnold S, Schuller M, Antke C, Huang Y, Steinmetz H, Seitz RJ, Witte OW: Bilateral reductions of hippocampal volume, glucose metabolism, and wada hemispheric memory performance are related to the duration of mesial temporal lobe epilepsy. J Neurol 246:926-933, 1999. https://doi.org/10.1007/s004150050484
30. Lee AT, Burke JF, Chunduru P, Molinaro AM, Knowlton R, Chang EF: A historical cohort of temporal lobe surgery for medically refractory epilepsy: A systematic review and meta-analysis to guide future nonrandomized controlled trial studies. J Neurosurg 133:71-78, 2020. https://doi.org/10.3171/2019.4.JNS183235
31. Lerner JT, Salamon N, Hauptman JS, Velasco TR, Hemb M, Wu JY, Sankar R, Donald Shields W, Engel J, Jr., Fried I, Cepeda C, Andre VM, Levine MS, Miyata H, Yong WH, Vinters HV, Mathern GW: Assessment and surgical outcomes for mild type I and severe type II cortical dysplasia: A critical review and the UCLA experience. Epilepsia 50:1310-1335, 2009. https://doi.org/10.1111/j.1528-1167.2008.01998.x
32. Mathon B, Bedos Ulvin L, Adam C, Baulac M, Dupont S, Navarro V, Cornu P, Clemenceau S: Surgical treatment for mesial temporal lobe epilepsy associated with hippocampal sclerosis. Rev Neurol (Paris) 171:315-325, 2015. https://doi.org/10.1016/j.neurol.2015.01.561
33. 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 127:2018-2030, 2004. https://doi.org/10.1093/brain/awh221

34. McIntosh AM, Wilson SJ, Berkovic SF: Seizure outcome after temporal lobectomy: Current research practice and findings. Epilepsia 42:1288-1307, 2001. https://doi.org/10.1046/j.1528-1157.2001.02001.x
35. Meyer AC, Dua T, Ma J, Saxena S, Birbeck G: Global disparities in the epilepsy treatment gap: A systematic review. Bull World Health Organ 88:260-266, 2010. https://doi.org/10.2471/BLT.09.064147
36. Na M, Ge H, Shi C, Shen H, Wang Y, Pu S, Liu L, Wang H, Xie C, Zhu M, Wang J, Shi C, Lin Z: Long-term seizure outcome for international consensus classification of hippocampal sclerosis: A survival analysis. Seizure 25:141-146, 2015. https://doi.org/10.1016/j.seizure.2014.10.006
37. Nayel MH, Awad IA, Luders H: Extent of mesiobasal resection determines outcome after temporal lobectomy for intractable complex partial seizures. Neurosurgery 29:55-60; discussion 60-51, 1991. https://doi.org/10.1097/00006123-199107000-00009
38. Noachtar S, Borggraefe I: Epilepsy surgery: A critical review. Epilepsy Behav 15:66-72, 2009. https://doi.org/10.1016/j.yebeh.2009.02.028
39. Ryvlin P, Cross JH, Rheims S: Epilepsy surgery in children and adults. Lancet Neurol 13:1114-1126, 2014. https://doi.org/10.1016/S1474-4422(14)70156-5
40. Schuele SU, Luders HO: Intractable epilepsy: Management and therapeutic alternatives. Lancet Neurol 7:514-524, 2008. https://doi.org/10.1016/S1474-4422(08)70108-X
41. Siegel AM, Cascino GD, Meyer FB, McClelland RL, So EL, Marsh WR, Scheithauer BW, Sharbrough FW: Resective reoperation for failed epilepsy surgery: Seizure outcome in 64 patients. Neurology 63:2298-2302, 2004. https://doi.org/10.1212/01.wnl.0000147476.86575.a7
42. Spencer DD, Spencer SS, Mattson RH, Williamson PD, Novelly RA: Access to the posterior medial temporal lobe structures in the surgical treatment of temporal lobe epilepsy. Neurosurgery 15:667-671, 1984. https://doi.org/10.1227/00006123-198411000-00005
43. Spencer S, Huh L: Outcomes of epilepsy surgery in adults and children. Lancet Neurol 7:525-537, 2008. https://doi.org/10.1016/S1474-4422(08)70109-1
44. Tanriverdi T, Dudley RW, Hasan A, Al Jishi A, Al Hinai Q, Poulin N, Colnat-Coulbois S, Olivier A: Memory outcome after temporal lobe epilepsy surgery: Corticoamygdalohippocampectomy versus selective amygdalohippocampectomy. J Neurosurg 113:1164-1175, 2010. https://doi.org/10.3171/2009.10.JNS09677
45. Tellez-Zenteno JF, Dhar R, Wiebe S: Long-term seizure outcomes following epilepsy surgery: A systematic review and meta-analysis. Brain 128:1188-1198, 2005. https://doi.org/10.1093/brain/awh449
46. Thom M, Liagkouras I, Elliot KJ, Martinian L, Harkness W, McEvoy A, Caboclo LO, Sisodiya SM: Reliability of patterns of hippocampal sclerosis as predictors of postsurgical outcome. Epilepsia 51:1801-1808, 2010. https://doi.org/10.1111/j.1528-1167.2010.02681.x
47. Tian N, Boring M, Kobau R, Zack MM, Croft JB: Active epilepsy and seizure control in adults - United States, 2013 and 2015. MMWR Morb Mortal Wkly Rep 67:437-442, 2018. https://doi.org/10.15585/mmwr.mm6715a1
48. Tonini C, Beghi E, Berg AT, Bogliun G, Giordano L, Newton RW, Tetto A, Vitelli E, Vitezic D, Wiebe S: Predictors of epilepsy surgery outcome: A meta-analysis. Epilepsy Res 62:75-87, 2004. https://doi.org/10.1016/j.eplepsyres.2004.08.006
49. Tugcu B, Gungor A, Akpinar A, Kinay D, Kuscu DY, Gul G, Kayrak N, Keskinkilic C, Akdemir H, Emel E: Outcome of surgical treatment of hippocampal sclerosis from relatively new epilepsy surgery center. J Neurosurg Sci 60:159-168, 2016.
50. Walker MC: Hippocampal sclerosis: Causes and prevention. Seminars in Neurology, vol 35. Thieme Medical Publishers, 2015:193-200
51. Wieser HG, Ortega M, Friedman A, Yonekawa Y: Long-term seizure outcomes following amygdalohippocampectomy. J Neurosurg 98:751-763, 2003. https://doi.org/10.3171/jns.2003.98.4.0751
52. Yoon HH, Kwon H, Mattson R, Spencer D, Spencer S: Long-term seizure outcome in patients initially seizure-free after resective epilepsy surgery. Neurology 61:445-450, 2003. https://doi.org/10.1212/01.wnl.0000081226.51886.5b
53. Zhang J, Liu W, Chen H, Xia H, Zhou Z, Mei S, Liu Q, Li Y: Identification of common predictors of surgical outcomes for epilepsy surgery. Neuropsychiatr Dis Treat 9:1673-1682, 2013. https://doi.org/10.2147/NDT.S53802