

Original Investigation

Stereotactic and Functional





Received: 15.02.2023 Accepted: 07.08.2024 Published Online: 24.02.2025

Analysis of Patients Undergoing Anterior Temporal Lobectomy for Drug-Resistant Mesial Temporal Lobe Epilepsy: A Retrospective Study

Tural AHMADOV1, Tugrul Cem UNAL1, Ilvas DOLAS1, Duvgu DOLEN1, Cafer Ikbal GULSEVER1, Duran SAHİN¹, Nermin Gorkem SIRIN INAN², Pulat Akin SABANCI¹, Yavuz ARAS¹, Nerses BEBEK², Altay SENCER1, Aydin AYDOSELI1

1stanbul University, Istanbul Faculty of Medicine, Department of Neurosurgery, Istanbul, Türkiye ²Istanbul University, Istanbul Faculty of Medicine, Department of Neurology, Istanbul, Türkiye

Corresponding author: Cafer Ikbal GULSEVER Image: cafer.gulsever@gmail.com

ABSTRACT

AIM: To analyze the epidemiologic, clinical, neuroradiological, and histopathological data of patients who have undergone anterior temporal lobectomy (ATL) for drug-resistant mesial temporal lobe epilepsy (MTLE).

MATERIAL and METHODS: The study included patients who were diagnosed with MTLE refractory to medical treatment, underwent anterior temporal lobectomy at our institution between 2010 and 2020 and had postoperative clinical follow-up data. The epidemiologic, clinical, neuroradiological, and histopathological data of the patients were collected.

RESULTS: Fourteen patients were male, and thirty were female. The mean age at seizure onset was 15.3 years. Video electroencephalographic monitoring (VEM), magnetic resonance imaging (MRI), and positron emission tomography (PET) revealed lateralization in 37, 36, and 31 patients, respectively. The cranial MRI and PET were inconclusive in eight patients in whom the diagnosis was verified via invasive monitoring. Thirty-six (81.8%) patients were seizure-free postoperatively. The number and dosage of antiepileptic drugs used were reduced in 35 (79.5%) and 26 (78.8%) patients, respectively. Only six patients developed complications (cerebrospinal fluid fistula, n = 3; central nervous system infection, n = 2; and epidural hematoma, n = 1).

CONCLUSION: Epilepsy is a significant cause of morbidity for patients, and surgery plays a vital role in treating mesial temporal sclerosis, an etiology of epilepsy. Patients can be diagnosed using various tests such as cranial MRI, electroencephalography, VEM, PET, single-photon emission computerized tomography, neuropsychological tests, and invasive monitoring at advanced epilepsy centers. Surgical treatment is highly effective and safe in these patients.

KEYWORDS: Anterior temporal lobectomy, Epilepsy surgery, Hippocampal sclerosis, Mesial temporal lobe epilepsy

ABBREVIATIONS: AED: Antiepileptic drug, ATL: Anterior temporal lobectomy, CNS: Central nervous system, CSF: Cerebrospinal fluid, CT: Computerized tomography, EEG: Electroencephalogram, FLAIR: Fluid-attenuated inversion recovery, HS: Hippocampal sclerosis, ILAE: International League Against Epilepsy, IR: Inversion recovery, MRI: Magnetic resonance imaging, MTLE: Mesial temporal lobe epilepsy, MTLE-HS: Mesial temporal lobe epilepsy with hippocampal sclerosis, MTS: Mesial temporal sclerosis, NPT: Neuropsychological testing, NTLE: Neocortical temporal lobe epilepsy, PET-CT: Positron emission tomography-computerized tomography, SAH: Selective amygdalohippocampectomy, SPECT: Single-photon emission computerized tomography, TLE: Temporal lobe epilepsy, VEM: Video electroencephalograph monitoring

Ilyas DOLAS

Tural AHMADOV (i): 0000-0002-2835-4623 Tugrul Cem UNAL (0): 0000-0001-6228-1379 : 0000-0002-3425-3220

: 0000-0002-6929-4401

Cafer Ikbal GULSEVER Duran SAHIN

Nermin Gorkem SIRIN INAN (: 0000-0001-8792-2929 Pulat Akin SABANCI

: 0000-0002-9246-1378 : 0000-0003-2703-5687

• : 0000-0002-0283-0927

Yavuz ARAS

: 0000-0001-8418-2291 Aydin AYDOSELI (D): 0000-0002-4695-8295



Duygu DOLEN

This work is licensed by "Creative Commons BY NC Attribution-NonCommercial-4.0 International (CC)".

INTRODUCTION

ccording to the classification of epilepsies, epileptic syndromes, and seizures published by the International League Against Epilepsy (ILAE) in 2022, mesial temporal lobe epilepsy (MTLE) with hippocampal sclerosis (MTLE-HS) is an etiology-specific epilepsy syndrome. Although MTLE is usually a focal epilepsy that occurs in adults, it can present in childhood. MTLE is the most common epileptic syndrome caused by the unique epileptogenicity of HS, which requires imaging confirmation (7,8,18). The prevalence of temporal lobe epilepsy (TLE) is 1.7 per 1000 people. However, the prevalence of MTLE-HS is 5.1-6.6 per 1000 people, which is much lower than its estimated annual incidence of 3.1-3.4 per 100000 people (1,11). Because surgical treatment is superior to medical treatment in patients with MTLE-HS, patients with MTLE should be recommended early surgery (25,30).

In this study, we aimed to retrospectively analyze the epidemiologic data, preoperative and postoperative clinical status. neuroradiological imaging results, antiepileptic drug (AED) requirements, and histopathological examination findings, as well as the effect of side of lesion on the resection volume and seizure-free outcome, in patients who underwent anterior temporal lobectomy (ATL) for drug-resistant MTLE.

MATERIAL and METHODS

This study is approved by institutional review board (29.12.2021 - 676248).

Preoperative Evaluation

The semiology, electroencephalography (EEG), video electroencephalograph monitoring (VEM), magnetic resonance (MR) imaging (MRI), and positron emission tomography-computerized tomography (PET-CT) data of each patient were collected. All patients were evaluated by a neurologist, radiologist, nuclear radiologist, psychologist, and neurosurgeon before a diagnosis of MTLE was made. The treatment modality was selected by this team of doctors.

Patient Selection

Patients who were diagnosed with TLE that were refractory to medical treatment had undergone ATL at Istanbul University, Istanbul Faculty of Medicine between 2010 and 2020, and postoperative clinical follow-up data were included in the study. The exclusion criteria were as follows: seizure semiology inconsistent with TLE, histopathological findings inconsistent with mesial temporal sclerosis (MTS), previous selective amygdalohippocampectomy (SAH), less than six months of regular follow-up, and irregular use of AEDs.

Neuroradiological Examination

Coronal T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences (3-mm thick slices) and inversion recovery (IR) T1-weighted sequence (1.7 / 0.2 mm gap) were obtained. When acquiring the coronal sequences, the hippocampus was localized in the T1-weighted sagittal sequence, and the slices were obtained perpendicular to the long axis of this structure. The cranial examination was completed upon acquisition of the axial whole-brain FLAIR, T1-weighted, and T2-weighted sequences (Figure 1). An experienced neuroradiologist reviewed the cranial MR images.

Calculation of Resection Volume

The mesial temporal region was localized in the coronal sections of the preoperative neuroradiological images using the MRI software (Extreme RIS & PACS 2017), and it was manually measured (mm²) in two dimensions. The obtained value was multiplied by the coronal slice thickness that covered the region, and the resultant value was the preoperative mesial temporal region volume. The same measurements and calculations were performed in the postoperative neuroradiological images. The two values were used to determine the percentage of resection. Anatomical landmarks (hippocampus, amygdala, and entorhinal cortex) were used to ensure consistency during measurements. The accuracy of the measurements was verified by a neuroradiologist.

Surgery

After the noninvasive and invasive preoperative examinations, a group of doctors, including a neurologist, neurosurgeon. and neuroradiologist, decided that surgical treatment was necessary. The senior author performed all the surgeries.

The hippocampus, choroid plexus of the temporal horn, choroidal fissure, and collateral eminence were used as landmarks during the surgery. The amygdala was approached at the anterosuperior part of the choroidal point. An ultrasonic aspirator was used to aid in the resection of the mesial temporal region. Between the amygdala and the hippocampal head, the uncus was identified mesially, and it was resected. The hippocampal head was resected subpially down to the tentorium. Thus, the entorhinal cortex and a part of the parahippocampal and fusiform gyri were resected. Subsequently, the hippocampal body was removed en bloc and sent for histopathological examination. The posterior limit of the resection was the hippocampal tail. Finally, the fimbria was aspirated along the choroidal fissure. After achieving hemostasis, the surgical site was closed in the standard fashion.

Histopathological Findings

The histopathological findings of the patients who underwent TLA were screened for segmental loss of pyramidal neurons in the hippocampus and the presence of fibrillary gliosis, which are consistent with an MTS diagnosis (26).

Postoperative Follow-Up

The patients were followed up at the outpatient clinic for at least one year after surgery. Their postoperative seizure outcomes were evaluated using the Engel classification (5). The AED requirements and dosage of each patient were reevaluated at each follow-up visit. Patients with less than one year of follow-up were excluded from the study.

Statistical Analysis

Descriptive statistics are presented as means and standard deviations, medians (minimum-maximum), or frequencies and percentages. The variables were assessed for normality

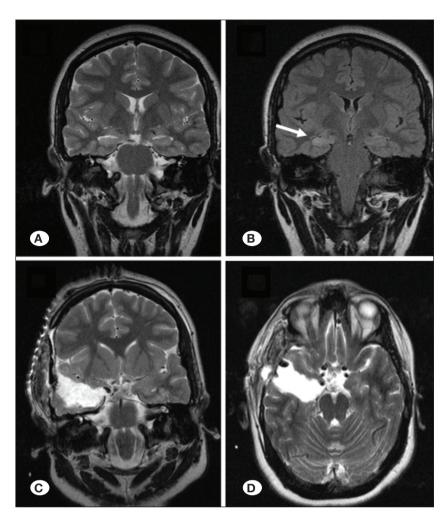


Figure 1: Preoperative coronal A) T2-weighted and B) FLAIR MR sections and postoperative coronal C) T2-weighted and D) axial MR sections of a patient with right-sided MTS. Right mesial temporal structures appear hyperintense in the FLAIR sequence due to sclerosis (arrow). FLAIR: Fluid-attenuated inversion recovery. MR: magnetic resonance, MTS: mesial temporal sclerosis.

of distribution using the Kolmogorov-Smirnov test. The quantitative independent variables were analyzed using the Mann-Whitney U test. The qualitative independent variables were analyzed using the chi-square test. Fisher's test was used when the conditions for chi-square test were not met. Data were analyzed using SPSS (version 28.0).

RESULTS

Patient Characteristics

The study included 44 patients. Fourteen patients were male, and thirty were female. The mean age at seizure onset was 15.3 years. Forty-two patients were right-handed, while two were left-handed. Approximately 25 patients (56.8%) developed febrile seizures during their childhood. Twenty-nine patients (66.0%) presented with focal seizures, and 95.5% of the patients required two or more antiepileptics. In eight patients, the results of the cranial MRI and PET-CT were inconclusive. and their diagnosis was verified using invasive monitoring (Table I). Video EEG, MRI, and PET-CT demonstrated lateralizing in 37, 36, and 31 patients, respectively (Table II).

Outcomes

Thirty-six (81.8%) patients were seizure-free after the surgery, exhibiting Engel 1a (seizure-free) status. Postoperatively, the number and dosage of AEDs required had reduced in 35 (79.5%) and 26 (78.8%) patients, respectively. Seven patients (15.9%) exhibited a resection volume of <80%. In two of these patients (28.5%), postoperative seizure-free status (Engel 1a) was not achieved. Both of these patients had left-sided MTS. In six of the remaining 37 patients with a resection volume of >80% (16.2%), Engel 1a seizure-free status was not achieved. Of the eight patients that underwent invasive monitoring, six (75%) were seizure-free (Engel 1a) postoperatively. However, among the 36 patients who did not require invasive monitoring, 30 (83.3%) were seizure-free (Engel 1a) postoperatively (p > 0.05). In two patients (4.5%) with persistent seizures after surgery, neuroradiological examinations revealed a resection volume of <70%. Thus, a second surgery was performed on these patients. The seizures stopped after the second surgery.

The overall mean resection volume was 86% (Table III). There was no significant difference in the outcome between patients with right-sided and left-sided MTS (p>0.05; Table IV). The

Table I: Preoperative Demographic and Clinical Data of the **Patients**

| Variable | Min-Max | Median | Mean ± SD | |
|--------------------------------|------------------------|-----------|-------------|--|
| Age (years) | 10.0-58.0 | 33.5 | 32.9 ± 9.8 | |
| First seizure age | 2.0-43.0 | 14.5 | 15.3 ± 10.3 | |
| Seizure duration (minutes) | 0.2-10.0 | 2.0 | 2.4 ± 1.9 | |
| Seizure frequency (in a month) | 1.0-20.0 | 4.0 | 4.9 ± 4.1 | |
| | | n (%) | | |
| Sex | | | | |
| Male Female | 14 (31.8) 30 (68.2) | | | |
| Dominant hand Right Left | 42 (95.5) 2 (4.5) | | | |
| Febrile Convulsion | | | | |
| Yes | | 25 (56.8) | | |
| No | 19 (43.2) | | | |
| Seizure type | | | | |
| Focal | | 29 (66.0) | | |
| GTC | 15 (34.0) | | | |
| AED number | | | | |
| 1 | | 2 (4.5) | | |
| II | 18 (40.9) | | | |
| III | 18 (40.9) | | | |
| IV | 6 (13.7) | | | |
| Invasive monitoring | | | | |
| No | | 36 (81.8) | | |
| Yes | | 8 (18.2) | | |

AED: Anti-epileptic drug, SD: Standard deviation, N: Number, GTC: Generalized tonic-clonic.

Table II: Distribution of the Patients' Clinical Characteristics in Relation to the VEM, MRI, and PET-CT Findings

| Modality | Consistency | n (%) |
|-----------------------|-------------|-----------|
| \ | (+) | 37 (84.1) |
| VEM side detection — | (-) | 7 (15.9) |
| MDI 'I I I I | (+) | 36 (81.8) |
| MRI side detection — | (-) | 8 (18.2) |
| | (+) | 31 (70.5) |
| PET-CT side detection | (-) | 11 (25.0) |
| _ | Not applied | 2 (4.5) |

MRI: Magnetic resonance imaging, PET-CT: Positron emission tomography-computerized tomography, VEM: Video electroencephalogram monitoring.

Table III: Postoperative Clinical Outcomes of the Study Patients

| 36 (81.8) 8 (18.2) 35 (79.5) 9 (20.5) 26 (59.1) 7 (15.9) 11 (25.0) |
|--|
| 35 (79.5) 9 (20.5) 26 (59.1) 7 (15.9) 11 (25.0) |
| 35 (79.5) 9 (20.5) 26 (59.1) 7 (15.9) 11 (25.0) |
| 9 (20.5) 26 (59.1) 7 (15.9) 11 (25.0) |
| 9 (20.5) 26 (59.1) 7 (15.9) 11 (25.0) |
| 26 (59.1) 7 (15.9) 11 (25.0) |
| 7 (15.9) 11 (25.0) |
| 7 (15.9) 11 (25.0) |
| 11 (25.0) |
| |
| |
| 00 (00 4) |
| 38 (86.4) |
| 6 (13.6) |
| 40 (07.7) |
| 43 (97.7) |
| 1 (2.3) |
| 20 (01 0) |
| 36 (81.8) |
| 5 (11.4) |
| 3 (6.8) |
| |
| |

Resection volume (%) 73.5-96.6 86.4 86.0 ± 5.7 Follow-up duration (year) 1.0-11.0 5.0 4.7 ± 2.7

AED: Anti-epileptic drug, MTS: Mesial temporal sclerosis, N: number.

postoperative resection volume rate was 84.5% in patients with right-sided MTS and 87.2% in those with left-sided MTS. In the postoperative period, 90% and 75% of the patients with right-sided and left-sided MTS, respectively, were seizurefree (Engel 1a status) (p=0.199) (Table V). No postoperative neurological deficits or mortality were observed.

Complications

Six (13.6%) patients developed postoperative complications. Three patients developed a cerebrospinal fluid (CSF) fistula, two developed a central nervous system (CNS) infection, and one developed an epidural hematoma. Among the three CSF fistulas, one resolved with acetazolamide administration, and two required a surgical repair. The patient with the epidural hematoma underwent an emergency surgery for hematoma evacuation. The two patients with a CNS infection were administered vancomycin and meropenem for two weeks.

DISCUSSION

The mean age of the patients included in this study was 32.9 \pm 9.8 years (range, 10–58). Of the 44 patients included in the study, 30 (68.2%) were female and 14 (31.8%) were male. Twenty patients (45%) were diagnosed with left-sided MTS,

Table IV: Comparative Analysis of the Preoperative Sociodemographic and Clinical Data Between Patients with Right- and Left-Sided MTS

| W - 11 | | Right side | | Left side | | | |
|--------------------------------|--------|------------------|--------|------------------|--------|-----------------------|--|
| Variable | | Mean ± SD, n (%) | Median | Mean ± SD, n (%) | Median | p-value | |
| Age (years) | | 34.8 ± 6.9 | 34.0 | 31.4 ± 11.6 | 33.0 | 0.232 ^t | |
| Sex | Male | 7 (35.0) | | 7 (29.2) | | - 0.070¥² | |
| | Female | 13 (65.0) | | 17 (70.8) | | - 0.679 ^{x²} | |
| First seizure age | | 15.2 ± 9.1 | 16.0 | 15.5 ± 11.5 | 14.0 | 0.832 ^m | |
| Seziure duration (minutes) | | 2.5 ± 1.8 | 2.0 | 2.3 ± 2.0 | 2.0 | 0.402 ^m | |
| Seizure frequency (in a month) | | 4.6 ± 4.1 | 4.0 | 5.2 ± 4.2 | 4.0 | 0.324 ^m | |
| Febrile convulsions | Yes | 10 (50.0) | | 15 (62.5) | | 0. 40 EY2 | |
| | No | 10 (50.0) | | 9 (37.5) | | - 0.405 ^{x²} | |
| Seizure type | Focal | 12 (60.0) | | 17 (70.9) | | 0.004Y2 | |
| | GTC | 8 (40.0) | | 7 (29.1) | | - 0.331 ^{x²} | |
| AED number | I | 1 (5.0) | | 1 (4.2) | | | |
| | II | 7 (35.0) | | 11 (45.8) | | 0 001Y2 | |
| | III | 8 (40.0) | | 10 (41.7) | | - 0.261 ^{X²} | |
| | IV | 4 (20.0) | | 2 (8.3) | | _ | |

^m Mann-whitney u test / x² Ki-kare test(Fischer test)

MTS: Mesial temporal sclerosis, AED: Anti-epileptic drug, GTC: Generalized tonic-clonic, N: Number, SD: Standard deviation.

Table V: Comparative Analysis of the Postoperative Examination Results Between Patients with Right- and Left-Sided MTS

| | | Right side n (%) | Left side n (%) | p-value |
|-------------------------------|-------------|------------------|-----------------|---------------------|
| Pathology consistent with MTS | | 19 (95.0) | 24 (100.0) | 1.000 |
| Postoperative seizure | Yes | 18 (90) | 18 (75.0) | |
| | No | 2 (10) | 6 (25.0) | 0.199 ^{X²} |
| Postoperative AED number | Decreased | 17 (85.0) | 18 (75.0) | 0 410 ^{X2} |
| | Not changed | 3 (15.0) | 6 (25.0) | 0.413 ^{x²} |
| Postoperative AED dose | Decreased | 14 (70.0) | 12 (50.0) | |
| | Not changed | 2 (10.0) | 5 (20.8) | 0.235 ^{X²} |
| | Stopped | 4 (20.0) | 7 (29.2) | |
| Complication | Yes | 17 (85.0) | 21 (87.5) | O 40EY2 |
| | No | 3 (15.0) | 3 (12.5) | 0.495 ^{x²} |
| Engel's score | 1a | 18 (90.0) | 18 (75.0) | |
| | 1b | 1 (5.0) | 4 (16.7) | 0.199 ^{X²} |
| | 1c | 1 (5.0) | 2 (8.3) | |

MTS: Mesial temporal sclerosis, AED: Anti-epileptic drug, MTS: Mesial temporal sclerosis.

while 24 (55%) were diagnosed with right-sided MTS. In a study of 83 patients with MTS, 42 were female and 41 were male. Furthermore, the mean patient age was 38 ± 11.2 years, 41 patients (49%) had right-sided MTS, 35 patients (42%) had left-sided MTS, and seven patients (8%) had bilateral MTS (12). In our study, the mean age at seizure onset was 15.3 \pm 10.3 years (range, 2-43), and the mean follow-up duration was 4.7 ± 2.7 years (range, 1–11).

One of the important factors affecting surgical success is the presence of a pathology co-existing with MTS, such as neoplasia, developmental abnormalities, and vascular pathologies in the temporal lobe. This is called dual pathology (14). A detailed and accurate histopathological examination of the hippocampus requires en bloc resection, which is not always surgically feasible. The histopathological examination usually reveals segmental loss of pyramidal neurons and the presence of fibrillary gliosis. Because hippocampal specimens were not resected en bloc in our study, the histopathology reports could not be prepared according to the ILAE classification. In a study investigating the histopathological results of 216 patients with TLE, 71.8% of the patients exhibited HS, 51 patients had non-neoplastic focal lesions.

13 patients had a co-existing tumor and non-neoplastic lesion, and 75 patients had a tumor (28). In our study, only one patient (2.2%) had a dual pathology (ganglioglioma and MTS). Guvenc and Kizmazoglu reported a dual pathology in four of their 18 patients with MTS. Two of these patients had an astrocytoma, one had a ganglioglioma, and one had an encephalomalacia (10).

Investigations used to detect the epileptogenic focus include VEM, interictal and ictal EEG (Figures 2 and 3), cranial MRI, ictal single-photon emission computerized tomography (SPECT), neuropsychological testing (NPT), functional MRI, and invasive monitoring. In a study comparing preoperative test results with postoperative seizure outcomes reported that ictal EEG better localized the epileptogenic focus than interictal EEG (success rate, 88.9% vs. 80.9%) (24). Failure of EEG to localize the epileptogenic focus is associated with a poor prognosis (6). All patients underwent VEM in our study, and lateralization was observed in 37 (84.1%) patients. However, seven patients had bilateral electrophysiological findings (Figure 2). However, no study patient was operated solely on the basis of interictal EEG results.

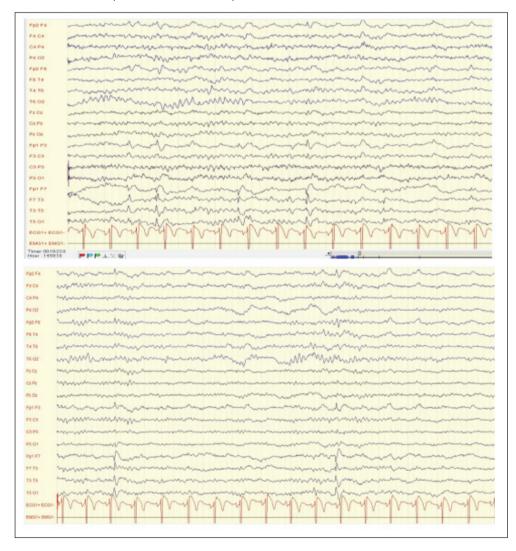
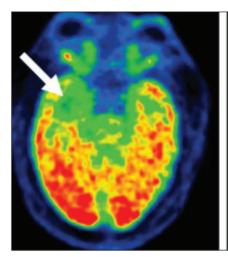


Figure 2: Interictal EEG demonstrating phase coincidence at the F7-T3 electrode position in the left frontotemporal region. EEG: Electroencephalogram.



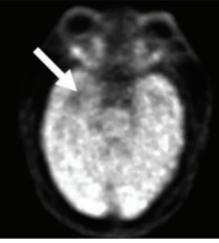


Figure 3: FDG-PET/CT is demonstrating hypometabolism in the right mesial (arrow) temporal structures in patients with rightsided MTS.

FDG: Fluorodeoxyglucose, PET/CT: Positron emission tomography-computerized tomography, MTS: Mesial temporal sclerosis.

Hypometabolism on PET-CT is a vital sign of an epileptogenic focus. In the study by So, hypometabolism was detected in 70% of the patients with TLE and lateralizing hypometabolism was observed in 56% of patients with TLE. However, 9% of the patients with extratemporal epilepsy did not exhibit lateralizing signs on MRI. In the same study, PET-CT was superfluous in patients with lateralized EEG and MRI findings (22). PET-CT is reportedly complementary to MRI in improving surgical outcomes. In another study, the lateralization rate on MRI and PET-CT was 94.5% and 83.4%, respectively. Furthermore, they found that lateralization on interictal PET-CT could be identified in 95%, 69%, and 84% of the patients with MR-positive, MR-borderline, and MR-negative lateralization, respectively (10). In our study, PET-CT was performed in 42 patients, and right-sided and left-sided hypometabolic regions were identified in 17 and 14 patients, respectively. Thus, PET-CT revealed lateralizing signs in 70.5% of our patients. Furthermore, bilateral hypometabolism was observed in five patients. In 6 patients, the PET-CT results were normal. Two patients did not undergo PET-CT (Figure 3).

Demonstration of HS and atrophy on cranial MRI, VEM results, and seizure semiology are essential for determining the need for surgery. In a meta-analysis by Tellez-Zenteno et al., postoperative seizure-free rates were lower (45%) in patients with TLE in whom MRI yielded no findings than in those in whom MRI yielded positive rates (23). In our study, MRI revealed lateralizing signs in 36 (81.8%) patients. Of the remaining eight patients (18.2%), five had no definitive MRI findings and three exhibited bilateral involvement.

The use of three examinations (VEM, MRI, PET-CT) individually or together for localizing the epileptic focus is essential to achieve a seizure-free outcome postoperatively. In the study by Uysal et al., 85.7% of the 29 patients in whom epileptogenic focus was localized via the three examinations exhibited a seizure-free status (Engel class 1) at 24 months after surgery (24). However, in our study, all the 31 patients who underwent all three examinations were seizure-free (Engel class 1) at the 12-month postoperative follow-up.

In a study of 47 patients, the epileptogenic focus was better defined and the postoperative seizure status was better in patients who were preoperatively evaluated using invasive monitoring (15). Therefore, invasive monitoring was performed in patients whose VEM, PET-CT, and MR examinations were not consistent with lateralization. In our study, invasive monitoring was used in eight patients (Figure 4). Both temporal and basal temporal depth and grid electrodes were placed. In two of the three patients whose results indicated right-sided MTS, a six-contact depth electrode was placed bilaterally. In the third patient, a five-contact depth electrode and subdural strips were placed bilaterally. Among the five patients whose results revealed left-sided MTS, 12- and 8-contact depth electrodes were placed bilaterally in one patient and 6- and 5-contact depth electrodes were placed bilaterally in three patients. In the fifth patient, a 5-contact depth electrode was placed bilaterally via the foramen ovale. The decision for surgery was made in consultation with epileptologists. During the postoperative follow-up of the patients in whom invasive monitoring was used, six were classified as Engel 1a and two as Engel 1c. This demonstrates that 75% of patients who underwent invasive monitoring exhibited a seizure-free status (Engel 1a). However, 83.3% of the patients who did not undergo invasive monitoring exhibited a seizure-free status. This difference was not statistically significant.

In our study, two patients (4.5%) continued to experience seizures after the first surgery. Neuroradiological examination of these patients exhibited a resection volume < 70%. Following a second surgery, the seizures stopped after surgery. In one prospective study of 70 patients, patients with complete hippocampal resection reported higher postoperative seizurefree rates than those who underwent conservative resection (60% vs. 38% at one year) (29). Wieser and Yasargil were the first to describe SAH to reduce lateral temporal damage (27). However, several surgeons still prefer ATL, as they believe that it removes more hippocampal tissue volumetrically and contribute to a better seizure-free outcome. Sagher et al. demonstrated that ATL allowed for a near-total resection of the amygdala (99.5%), whereas the extent of resection in SAH was 93.7%. Furthermore, the hippocampal resection rate

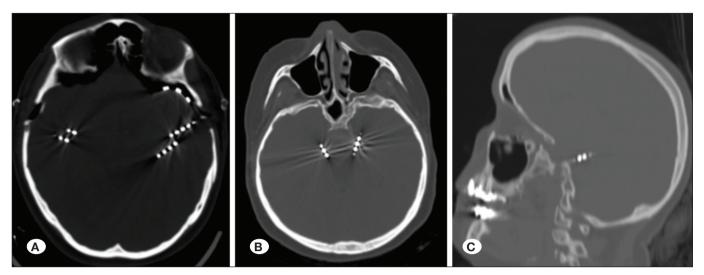


Figure 4: Neuroradiological images of patients who underwent invasive monitoring. A) CT image showing a strip and grid electrodes bilaterally on the axial section. Depth electrodes implanted bilaterally via the foramen ovale can be observed on the axial (B) and sagittal (C) sections.

was higher in those who underwent ATL than in those who underwent SAH (95.8% vs 89.2%; p<0.0001). Despite this, there was no significant difference in the seizure-free rates at the 2-year clinical follow-up (19). In our study, the mean hippocampus resection rate was 85.8%, and 81.8% of these patients were seizure-free postoperatively (Engel 1a). In our study, the resection volume was <80% in seven (15.9%) patients. Two of these patients (28.5%) exhibited Engel 1b seizure outcome. Both these patients had left-sided MTS, and the remaining five had right-sided MTS. In our study, resection volume was >80% in 37 (84%) patients. In six of these patients (16.2%), seizure-free status (Engel 1a) was not achieved. This indicates that a more volumetric resection is required to achieve a seizure-free, especially in patients with left-sided MTS.

The difference between SAH and ATL is the resection of the anterolateral temporal neocortex. Piao et al. demonstrated that among 73 patients with HS, 70 had a dual pathology, including focal cortical dysplasia, encephalomalacia, or tumors (17). However, the incidence of dual pathologies was lesser in other studies, ranging from 15% to 30% (14,17,20). Lesions outside mesial temporal structures are not always detected on MRI. Therefore, patients might exhibit poor seizure outcomes after SAH (16). Furthermore, according to a meta-analysis, SAH does not have a better intellectual outcome than ATL, and it reduces the odds of being seizure-free (12). These differences in the results can be explained by some neurophysiological studies. Fountas et al. demonstrated altered metabolism on proton MR spectroscopy in the ipsilateral temporal pole in patients with HS. These changes were associated with histopathological changes (9). In another study, depth electrodes used to record temporopolar cortex and mesiotemporal structures revealed that the temporal pole was involved in the onset of a seizure before or with HS in 48% of the patients (4). Therefore, ATL is preferred over SAH in our institution. The technique allows a more volumetric resection, is safe, and exhibits better seizure outcomes.

In our study, 20 (45.4%) patients had right-sided MTS, while 24 (54.6%) had left-sided MTS. There was no significant difference in the age, sex, age at first seizure, seizure frequency, febrile seizure history, seizure type, and number of AEDs used between the right- and left-sided MTS. Furthermore, there was no significant difference in pathology detection via VEM. MRI, PET-CT, and invasive monitoring between the right- and left-sided MTS groups. The postoperative number of AEDs used, dosage reduction, and complication rates were similar between the right- and left-sided MTS groups. Furthermore, although the rate of postoperative Engel 1a classification was 90% in right-sided MTS and 75% in left-sided MTS. the difference was not statistically significant (p=0.199). The mean resection volume was also not significantly different between the right- and left-sided MTS groups (84.5% vs. 87.2%; p=0.122). Kumlien et al. demonstrated that there is no difference in outcomes on the basis side of MTS (13). In the study by Schramm et al., Engel class 1 was achieved in 74% and 72.8% of the patients in the 2.5 cm (volume: 72.8%) and 3.5 cm (volume: 83.4%) mesial temporal resection groups, respectively, at the 1-year follow-up. Because this difference was not significant, they concluded that instead of maximal volume resection, adequate volume resection could lead to good seizure outcomes (21). In the study by Bonilha et al., the outcomes were better when medial temporal lobe structures. such as the entorhinal cortex, were resected in addition to the hippocampus (2). To the best of our knowledge, no study in literature has compared the resection volume of the mesial temporal structures on the basis of side of MTS and seizure outcome. Thus, further studies with larger patient samples are required.

A meta-analysis of 16 studies reported 19 deaths among the 2382 patients who underwent ATL. Furthermore, 458 complications were reported. The most common complications were psychiatric disorders (7%), visual field disorders (6%), and cognitive disorders (5%). The less frequent complications included hemiparesis/hemiplegia (3%), dysphasia (3%), infection (3%), hemorrhage (2%), cranial nerve symptoms (especially trochlear nerve involvement) (3%), hydrocephalus and CSF-related complications (2%), extra-axial fluid collections (2%) and medical complications (2%) (3). In our study, three patients developed a CSF fistula, two developed a CNS infection, and one developed an epidural hematoma.

Limitations

Our study's small sample size precluded us from obtaining statistically significant results in comparative analyses and conducting subgroup analyses. Furthermore, the lack of a comparison group, patients who were conservatively managed or patients who underwent a different surgery, limits our ability to attribute the seizure-free to ATL alone. The cranial MRIs used for calculating hippocampal volume were performed in different years and differed in quality and slice thickness. Moreover, in some patients, not all the tests could be performed. Furthermore, routine preoperative and postoperative psychiatric and cognition testing were not conducted.

CONCLUSION

Epilepsy is a significant cause of morbidity in patients, and surgery plays a vital role in treating MTS, which is an etiology of epilepsy. Epileptic foci can be localized using various tests, such as cranial MRI, EEG, VEM, PET-CT, SPECT, NPT, and invasive monitoring, that are performed at advanced epilepsy centers. Furthermore, the diagnosis involves the combined efforts of the Neurology, Radiology, Nuclear Medicine, Psychology, and Neurosurgery units. Surgical treatment is highly effective in patients with MTSE, especially those with drug-resistant epilepsy.

Declarations

Funding: No financial support was received for this research.

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: TA, CIG, DS

Data collection: TA, CIG, DS

Analysis and interpretation of results: TCU, ID, DD, NGSI

Draft manuscript preparation: TA, CIG, DS

Critical revision of the article: NGSI, PAS, YA, AS, AA

Other (study supervision, fundings, materials, etc...): PAS, YA, NB,

AS, AA

All authors (TA, TCU, ID, DD, CIG, DS, NGSI, PAS, YA, NB, AS, AA) reviewed the results and approved the final version of the manuscript.

■ REFERENCES

- 1. Asadi-Pooya AA, Stewart GR, Abrams DJ, Sharan A: Prevalence and incidence of drug-resistant mesial temporal lobe epilepsy in the United States. World Neurosurg 99:662-666, 2017. https://doi.org/10.1016/j.wneu.2016.12.074
- 2. Bonilha L, Yasuda CL, Rorden C, Li LM, Tedeschi H, de Oliveira E, Cendes F: Does resection of the medial temporal lobe improve the outcome of temporal lobe epilepsy surgery? Epilepsia 48:571-578, 2007. https://doi.org/10.1111/j.1528-1167.2006.00958.x
- 3. Brotis AG, Giannis T, Kapsalaki E, Dardiotis E, Fountas KN: Complications after anterior temporal lobectomy for medically intractable epilepsy: A systematic review and meta-analysis. Stereotact Funct Neurosurg 97:69-82, 2019. https://doi. ora/10.1159/000500136
- 4. Chabardès S, Kahane P, Minotti L, Tassi L, Grand S, Hoffmann D, Benabid AL: The temporopolar cortex plays a pivotal role in temporal lobe seizures. Brain 128:1818-1831, 2005. https:// doi.org/10.1093/brain/awh512
- 5. Durnford AJ, Rodgers W, Kirkham FJ, Mullee MA, Whitney A, Prevett M, Kinton L, Harris M, Gray WP: Very good interrater reliability of Engel and ILAE epilepsy surgery outcome classifications in a series of 76 patients. Seizure 20:809-812, 2011. https://doi.org/10.1016/j.seizure.2011.08.004
- Dworetzky BA, Reinsberger C: The role of the interictal EEG in selecting candidates for resective epilepsy surgery. Epilepsy Behav 20:167-171, 2011. https://doi.org/10.1016/j. yebeh.2010.08.025
- 7. Engel J: Mesial temporal lobe epilepsy: What have we learned? Neuroscientist 7:340-352, 2001. https://doi. org/10.1177/107385840100700410
- 8. Engel J, Pedley TA, Aicardi J: Epilepsy: A comprehensive textbook, Lippincott Williams & Wilkins, 2008
- Fountas KN, Tsougos I, Gotsis ED, Giannakodimos S, Smith JR, Kapsalaki EZ: Temporal pole proton preoperative magnetic resonance spectroscopy in patients undergoing surgery for mesial temporal sclerosis. Neurosurg Focus 32:E3. 2012. https://doi.org/10.3171/2012.1.FOCUS11327
- 10. Guvenc G, Kizmazoglu C: The effect of neocortical pathology on lateralization and seizure outcome in lobectomy materials in surgically treated hippocampal sclerosis patients. Dokuz Eylül Univ Tıp Fak Derg, 33:69-81, 2019
- 11. Hauser WA, Kurland LT: The epidemiology of epilepsy in Rochester, Minnesota, 1935 through 1967. Epilepsia 16:1-66, 1975. https://doi.org/10.1111/j.1528-1157.1975.tb04721.x
- 12. Hu WH, Zhang C, Zhang K, Meng FG, Chen N, Zhang JG: Selective amygdalohippocampectomy versus anterior temporal lobectomy in the management of mesial temporal lobe epilepsy: A meta-analysis of comparative studies. J Neurosurg 119:1089-1097, 2013. https://doi.org/10.3171/2013.8. JNS121854
- 13. Kumlien E, Doss RC, Gates JR: Treatment outcome in patients with mesial temporal sclerosis. Seizure 11:413-417, 2002. https://doi.org/10.1053/seiz.2001.0614

- 14. Lévesque MF, Nakasato N, Vinters HV, Babb TL: Surgical treatment of limbic epilepsy associated with extrahippocampal lesions: the problem of dual pathology. J Neurosurg 75:364-370, 1991. https://doi.org/10.3171/jns.1991.75.3.0364
- 15. Mail Gurkan Z, Sirin NG, Kara B, Gul G, Sengul Eren F, Tekin Guveli B, Velioglu S, Sabanci A, Aydoseli A, Aras Y, Bebek N, Baykan B, Sencer A, Canbolat AT, Gokyigit A, Aydogan Culha U, Gurses C: Surgical treatment in refractory epilepsy: Seizure outcome results based on invasive eeg monitorization. Turk Neurosurg 32:143-148, 2021. https://doi.org/10.5137/1019-5149.JTN.32796-20.2
- 16. Mühlebner A, Coras R, Kobow K, Feucht M, Czech T, Stefan H, Weigel D, Buchfelder M, Holthausen H, Pieper T, Kudernatsch M, Blümcke I: Neuropathologic measurements in focal cortical dysplasias: validation of the ILAE 2011 classification system and diagnostic implications for MRI. Acta Neuropathol 123: 259-272, 2012. https://doi.org/10.1007/s00401-011-0920-1
- 17. Piao YS, Lu DH, Chen L, Liu J, Wang W, Liu L, Yu T, Wang YP, Li YJ: Neuropathological findings in intractable epilepsy: 435 Chinese cases. Brain Pathol 20:902-908, 2010. https:// doi.org/10.1111/j.1750-3639.2010.00386.x
- 18. Riney K, Bogacz A, Somerville E, Hirsch E, Nabbout R, Scheffer IE, Zuberi SM, Alsaadi T, Jain S, French J, Specchio N, Trinka E, Wiebe S, Auvin S, Cabral-Lim L, Naidoo A, Perucca E, Moshé SL, Wirrell EC, Tinuper P: International League Against Epilepsy classification and definition of epilepsy syndromes with onset at a variable age: Position statement by the ILAE Task Force on Nosology and Definitions. Epilepsia 63:1443-1474, 2022. https://doi.org/10.1111/epi.17240
- 19. Sagher O, Thawani JP, Etame AB, Gomez-Hassan DM: Seizure outcomes and mesial resection volumes following selective amygdalohippocampectomy and temporal lobectomy. Neurosurg Focus 32:E8, 2012. https://doi. org/10.3171/2011.12.FOCUS11342
- 20. Salanova V, Markand O, Worth R: Temporal lobe epilepsy: Analysis of patients with dual pathology. Acta Neurol Scand 109:126-131, 2004. https://doi.org/10.1034/j.1600-0404.2003.00183.x
- 21. Schramm J, Lehmann TN, Zentner J, Mueller CA, Scorzin J, Fimmers R, Meencke HJ, Schulze-Bonhage A, Elger CE: Randomized controlled trial of 2.5-cm versus 3.5-cm mesial temporal resection in temporal lobe epilepsy-Part 1: Intentto-treat analysis. Acta Neurochir 153:209-219, 2011. https:// doi.org/10.1007/s00701-010-0900-6

- 22. So EL: Role of neuroimaging in the management of seizure disorders. Mayo Clin Proc 77:1251-1264, 2002. https://doi. org/10.4065/77.11.1251
- 23. Téllez-Zenteno JF, Ronquillo LH, Moien-Afshari F, Wiebe S: Surgical outcomes in lesional and non-lesional epilepsy: A systematic review and meta-analysis. Epilepsy Res 89:2-6, 2010
- 24. Uysal Al, Eroglu E, Erdogan E, Gokcil Z: Clinical spectrum, seizure outcomes, correlation of neuroradiology and neuropathology in surgically treated epileptic patients. Arch Epilepsy 19:63-70, 2013. https://doi.org/10.5505/epilepsi.2013.25733
- 25. 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 temporallobe epilepsy. N Engl J Med 345:311-318, 2001. https://doi. org/10.1056/NEJM200108023450501
- 26. Wieser HG; ILAE Commission on Neurosurgery of Epilepsy: ILAE commission report. Mesial temporal lobe epilepsy with hippocampal sclerosis. Epilepsia 45:695-714, 2004. https:// doi.org/10.1111/j.0013-9580.2004.09004.x
- 27. Wieser HG, Yasarqil MG: Selective amvadalohippocampectomy as a surgical treatment of mesiobasal limbic epilepsy. Surg Neurol 17:445-457, 1982. https://doi.org/10.1016/s0090-3019(82)80016-5
- 28. Wolf HK. Campos MG. Zentner J. Hufnagel A. Schramm J. Elger CE. Wiestler OD: Surgical pathology of temporal lobe epilepsy. Experience with 216 cases. J Neuropathol Exp Neurol 52:499-506, 1993. https://doi.org/10.1097/00005072-199309000-00008
- 29. Wyler AR, Hermann BP, Somes G: Extent of medial temporal resection on outcome from anterior temporal lobectomy: A randomized prospective study. Neurosurgery 37:982-990, 1995. https://doi.org/10.1227/00006123-199511000-00019
- 30. Yasuda CL, Tedeschi H, Oliveira ELP, Ribas GC, Costa ALC, Cardoso TAMO, Montenegro MA, Guerreiro CAM, Guerreiro MM, Li LM, Cendes F: Comparison of short-term outcome between surgical and clinical treatment in temporal lobe epilepsy: A prospective study. Seizure 15:35-40, 2006. https:// doi.org/10.1016/j.seizure.2005.10.005