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Research Paper

The Determiners of Temporal Lobe Epilepsy Surgery Outcome in a Developing Country

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ABSTRACT

Background: Epilepsy surgery has become a successful treatment option for patients with drug-resistant epilepsies.

Objectives: This study aimed to assess temporal lobe epilepsy (TLE) surgery outcome and its association with epilepsy duration, the presence of pre-surgical generalized tonic-clonic seizure (GTCS), and brain MRI findings.

Materials & Methods: This retrospective study was performed from 2016 to 2020 at Loghman-Hakim Hospital, Tehran, Iran. The patients' demographic data, epilepsy type, duration, frequency, brain image findings, the selected surgical approaches, and histopathological findings were collected. The post-operative seizure outcome was expressed one year according to the proposed International League Against Epilepsy (ILAE) classification system. The independent sample t-test, chi-square, and one-way analysis of variance were applied to analyze the differences between variables in terms of quantitative and categorical data.

Results: A total number of 69 TLE surgeries were enrolled in our study. No differences were found in the surgical outcome base on the ILAE classification system of patients with lesional vs non-lesional MRIs (P=0.834). In patients with mesial temporal sclerosis, no correlation was found between the surgical approaches including selective amygdalohippocampectomy, anterior temporal lobectomy, and post-operative seizure outcome (P=0.142). Seven patients (10.1%) developed post-operative functional seizures.

Conclusion: In our study, the epilepsy duration and the presence of GTCSs before surgery had no effect on the surgery outcome. In patients with mesial temporal sclerosis, amygdalohippocampectomy, and anterior temporal lobectomy did not confer different surgical outcomes. TLE patients with normal MRI showed similar surgical outcomes as lesional patients. A significantly high proportion of our patients developed functional seizures, postoperatively.

Keywords: Anterior temporal lobectomy, Epilepsy, Temporal lobe, Therapy

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Highlights

• In temporal lobe epilepsy surgery, there were no differences in surgical outcomes based on International League Against Epilepsy (ILAE) classification with lesional vs non-lesional MRIs in epilepsy patients.

• No correlation was observed between surgical approaches and seizure outcomes.

• Post-operative functional seizures occurred in 10.1% of epileptic patients.

Introduction

Temporal lobe epilepsy (TLE) is the most common form of localized-related epilepsy [1]. Hippocampal sclerosis (HS), also known as mesial temporal sclerosis (MTS), is the most common pathological substrate of TLE that accounts for up to 70% of patients with drug-resistant TLE [2, 3]. Over the recent decades, epilepsy surgery has become a successful treatment option for patients with drug-resistant epilepsies. Up to two-thirds of patients who underwent epilepsy surgery, had the chance of obtaining seizure freedom [2]. Randomized controlled trials have demonstrated improved quality of life after epilepsy surgery compared with medical management alone [2, 4-6].

A considerable variation exists in selecting the surgical methods in patients with drug-resistant TLE, especially MTS, with two major approaches including standard anterior temporal lobectomy (ATL) vs selective amygdalohippocampectomy (SAH). ATL is defined as removing 4-6 cm of the anterior temporal lobe, including the amygdala and hippocampus, whereas SAH preserves the temporal neocortex and underlying white matter, and offers the theoretical advantage of lower cognitive decline following the surgery. In recent years, it has been shown that epilepsy is a network disease rather than the involvement of a restricted epileptogenic lesion [7, 8]. According to the mentioned concept, more extensive resections should theoretically rend a higher rate of seizure freedom. Previous literature has reported discordant findings in terms of seizure freedom in various surgical approaches. Some meta-analyses reported that ATL could achieve a higher chance of seizure freedom [9, 10], whereas others indicated similar seizure outcomes between SAH and ATL in the treatment of temporal lobe epilepsy [11-13]. In selecting the surgical approach, the chance of obtaining seizure freedom must outweigh the better neuropsychological outcome [14-17].

Despite advances in structural and functional brain imaging techniques, a group of patients with TLE still have normal-appearing brain MRIs. Other modalities including MRI post-processing techniques, fluorodeoxyglucose positron emission tomography (FDG-PET), and single photon emission computer tomography have provided opportunities for these cases to benefit from epilepsy surgery. Although, the odds of seizure freedom after epilepsy surgery have been reported to be higher in the presence of a lesion on MRI [18].

In this study, we aimed to assess the epilepsy surgery outcome in patients with drug-resistant TLE. Moreover, the correlations between the post-surgical seizure outcome with the epilepsy duration, the presence of pre-surgical generalized tonic-clinic seizure (GTCS), and brain MRI findings were assessed.

Materials and Methods

In this retrospective study, all the consecutive patients with drug-resistant TLE, who underwent epilepsy surgery at Loghman-Hakim Hospital, Tehran, Iran, between 2016 to 2020, were included. The epilepsy type was determined by trained epileptologists, who clinically assessed the patients and reviewed their scalp video-EEG monitoring (V-EEG) findings, including interictal and ictal EEG findings and seizure semiology. The scalp V-EEG was captured according to the standard international 10-20 system. All the patients underwent 1.5-tesla structural brain MRI with standard epilepsy protocol. Patients with normal appearing brain MRI, according to an expert neuroradiologist report, underwent additional voxel-based morphometry (VBM) post-processing technique, as well as FDG-PET scan to help identify the epileptogenic lesion. Most of the patients underwent pre-surgical neuropsychological evaluation, but the results seemed unreliable to be reported.

For each patient, epilepsy duration, seizure types and frequency, the presence of GTCS one year before the surgery, brain MRI and PET scan findings, surgery method, outcomes and complications, and histopathological results were collected.

Patients with MTS on brain MRI, underwent ALT or SAH, mainly based on the neurosurgeon's preference. Patients with normal-appearing brain MRI, who had concordant scalp V-EEG and PET scan results, underwent ATL, according to the pre-surgical evaluation meeting decision. The surgical method for other lesions (including vascular malformations, gliosis, tumors, and malformations of cortical development) was based on the location, type, and extension of the lesion and involvement of the ipsilateral mesial temporal structures. These patients underwent one of the following three surgical approaches: (1) SAH plus lesionectomy, (2) pure lesionectomy sparing mesial structures, and (3) standard ATL (which obviously contained the epileptogenic lesion).

The surgical outcome was expressed in one of the following six categories, based on the proposed ILAE classification system [19]:

Class 1: Completely seizure free; no auras.

Class 2: Only auras; no other seizures.

Class 3: 1 to 3 seizure days per year; ±auras.

Class 4: 4 seizure days per year to 50% reduction of baseline seizure days; ±auras.

Class 5: Less than 50% reduction of baseline seizure days; ±auras.

Class 6: More than 100% increase of baseline seizure days; ±auras.

The patients were followed up regularly after surgery every 3-6 months and evaluated in terms of having auras, witnessed seizures, or any other complications. However, we reported outcomes after 1-year follow-up. Patients remained on their pre-surgical anti-seizure medications (ASMs) for at least one year after surgery. If patients did not experience any seizures for one-year post-operation and had normal follow-up routine scalp EEGs, the drugs were tapered off slowly to a sufficient dose of one ASM. After at least two years of seizure freedom, with normal follow-up scalp EEGs, the patients were offered to wean off ASMs, according to their social status and desire. Obviously, in the presence of any suspected seizures, appropriate management strategies were applied. A few patients reported suspected post-operative psychogenic seizures which were evaluated by detailed history and V-EEG.

Statistical analysis

The analysis was performed using SPSS software, version 22. The Kolmogorov-Smirnov test was used to assess the normal distribution of variables. The numeric and categorical variables were expressed as Mean±SD frequency and percentage, respectively. The independent sample t-test, Chi-square, and one-way ANOVA were applied to analyze the differences between variables in terms of quantitative and categorical data. A $P<0.05$ was considered statistically significant.

Results

According to Table 1, patients undergoing surgery had the following clinical characteristics. VBM post-processing technique was applied for 10 patients (14.5%) with normal brain MRI. Only in 3 patients (30%), VBM demonstrated a concordant lesion ipsilateral to the seizure-onset zone and PET hypometabolism. In the remaining 7 patients (70%), VBM did not show any abnormality or only displayed non-relevant findings. The histopathological results of a patient with concordant VBM findings were focal cortical dysplasia (FCD) in two patients and MTS in one.

In terms of the surgical method, out of 39 patients with MTS, 20 patients (51.2%) underwent SAH and 19 (48.7%) ALT. The surgical methods of the study population are shown in Table 2.

Unfortunately, one 47-year-old female developed left-side hemiparesis following right ATL surgery because of a right-side lenticulostriate artery ischemic stroke during the operation. She did not have any known vascular risk factors.

There was no significant correlation between the post-surgical seizure outcome and the epilepsy duration (P=0.842), age at epilepsy onset (P=0.548), the occurrence of GTCS within the year before the surgery (P=0.327), and post-op follow-up duration (P=0.706).

Table 1. Clinical characteristics of the study population (n=69)

Variables		No.(%)/Mean±SD
Gender	Male	35(50.7)
	Female	34(49.3)
	Age at the time of surgery (y)	30.79±12.65
	Epilepsy duration before surgery (y)	17±12.63
	The presence of GTCS within the year before surgery	20(29)
Scalp V-EEG result	Left TLE	38(55.1)
	Right TLE	31(44.9)
Brain MRI finding	Normal	10(14.5)
	MTS	39(56.5)
	Low-grade tumor	9(13)
	Vascular malformation	4(5.8)
	Focal cortical dysplasia	3(4.3)
	Gliosis/malacia	4(5.8)
Post-operation follow-up duration (months)		29.10±12.6

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TLE: temporal lobe epilepsy; V-EEG: video-electroencephalogram; MTS: mesial temporal sclerosis; GTCS: generalized tonic-clonic seizure.

No significant differences were found in the surgical outcome of patients with lesional (n=59) and non-lesional (n=10) brain MRI findings (P=0.834) (Table 3).

In addition, the two applied surgical approaches (SAH and ATL) rendered the same post-operative seizure outcome in patients with MTS (P=0.142) (Table 4).

Discussion

As found in this study, there was no difference between the surgery outcomes based on the proposed ILAE classification system and clinical features such as epilepsy duration, age at epilepsy onset, the occurrence of GTCS within the year before the surgery, and post-op follow-up duration patients. Also, no significant differences were observed in the surgical outcome of patients with lesional and non-lesional brain MRI findings and surgical approaches.

Our study did not show the effect of follow-up duration on the odds of remaining seizure-free, or postoperative. Some previous studies have implied that the probability of remaining seizure-free after surgery decreases over time. In a meta-analysis, it was demonstrated that seizure freedom at the 1-year follow-up ranged from 53% to 80%, whereas, the rate decreased to 52% and 58% at the 2- and 5-year follow-ups, respectively [20].

In the current study, the VBM post-processing technique did not appear to be significantly helpful in detecting occult epileptogenic lesions. VBM, a post-processing technique, is a fully automated computerized quantitative MRI analysis, developed to characterize differences in the cerebral gray matter and white matter. This technique may help detect some of occult epileptogenic lesions like FCD [21, 22]. According to the previous literature, PET-positive, MRI-negative TLE patients showed excellent surgical outcomes after ATL, very similar to patients with MTS, regardless of whether they undergo intracranial monitoring [23-25]. In our study, MRI-negative, PET-positive patients had the same post-surgical seizure outcome as lesional TLE patients, which is consistent with previous studies. In a systemic review and meta-analysis by José-Téllez-Zenteno et al. they compared the epilepsy surgery outcome in lesional vs non-lesion focal epilepsy cases. They concluded that the odds of post-surgical seizure freedom were two to three times higher in the presence of a lesion on histopathology or MRI [18]. In this review, they included patients with any epilepsy type, not just non-lesional TLE patients with concordant scalp V-EEG and PET scan findings.

Table 2. Results of surgery in the studied patients (n=69)

Variables		No.(%)
Surgery outcome	Completely seizure free; no auras	47(68.1)
	Only auras; no other seizures	1(1.4)
	1 to 3 seizure days per year; ±auras	12(17.4)
	4 seizure days per year to 50% reduction of baseline seizure days; ± auras	9(13)
Surgery type	SAH	26(37.7)
	ATL	29(42)
	Pure lesionectomy (sparing mesial temporal structures)	12(17.4)
	SAH+lesionectomy	2(2.9)
Surgical complication	Headache	5(7.2)
	Functional seizures	7(10.1)
	Hemiparesis	1(1.4)
Histopathology	MTS	35(50.7)
	Low-grade tumor	6(8.7)
	Vascular malformation	4(5.8)
	Focal cortical dysplasia	7(10.1)
	Gliosis	13(18.8)
	MTS+vascular malformation	1(1.4)
	Gliosis+vascular malformation	2(2.9)

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MTS: mesial temporal sclerosis; ATL: anterior temporal lobectomy; SAH: selective amygdalohippocampectomy.

Table 3. Surgery outcome in patients with lesional vs non-lesional brain MRIs

Brain MRI	Completely Seizure Free; No Auras	Only Auras; No Other Seizures	1-3 Seizure Days Per Year; ±Auras	4 Seizure Days Per Year to 50% Reduction of Baseline Seizure Days; ±Auras	P
Lesional	39	1	11	8	0.834
Non-Lesional	8	0	1	1	

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Table 4. Correlation between the surgical approach and post-operative seizure outcome in patients with MTS

Surgical Approach	Completely Seizure Free; No Auras	Only Auras; No Other Seizures	1-3 Seizure Days per Year; ±Auras	4 Seizure Days per Year to 50% Reduction of Baseline Seizure Days; ±Auras	P
SAH	10	1	5	4	0.142
ATL	16	0	2	1	-

ATL: anterior temporal lobectomy; SAH: selective amygdalohippocampectomy. CJNS

Multiple studies have shown that the presence of GTCS attacks before surgery will significantly reduce the chance of post-operative seizure freedom [26-31]. This finding was explained by the theory that the occurrence of GTCS may reflect more widespread epileptogenic network involvement as confirmed by a functional MRI study [32]. We did not find a similar finding in our study, which could be due to the lack of reliability of our data collection method regarding the presence of GTCS in patients. In our study, the history of GTCS was obtained from the patients and their relatives based on their recalls. The patients' impaired consciousness during GTCS attacks, occurring unwitnessed seizures, or misinterpretation of seizure types by family members may have resulted in our unreliable data.

Some previous studies considered the shorter presurgical epilepsy duration as a factor associated with more favorable postoperative seizure outcomes. In a recent systemic review and meta-analysis, patients with shorter epilepsy duration were more likely to become seizure-free postoperatively [33]. In our study, the epilepsy duration did not show any significant effect on the post-surgical seizure outcome. Some previous studies are in favor of our results [26, 30] and others against it [33, 34], which could be due to the difference in the study population.

An interesting finding in our study was the development of functional seizures in approximately 10% of our patients following epilepsy surgery, which was significantly higher than what was previously reported. In a study by Asadi-Pooya et al. 3.9% of their patients developed PNES after epilepsy surgery, which was associated with a lower intelligence quotient (IQ) and a history of pre-surgical psychiatric disorders [35]. Similarly, in another study, among TLE patients who underwent epilepsy surgery and were followed up for 4 years, 3.2% reported episodes of psychogenic seizures [36]. This discrepancy in results could be due to the different socioeconomic situations. The two previous studies were conducted in a developed country, which has a significantly higher socioeconomic situation than ours. Moreover, a higher amount of pre-surgical psychiatric co-morbidities may result in this difference.

In our study, all the patients benefited from epilepsy surgery and experienced at least more than a 50% reduction in their seizure frequency, and 68% became seizure-free. The possible causes of TLE surgery failure include insufficient resection of the epileptogenic mesial temporal structures, relapse on the contralateral mesial temporal lobe, remaining lateral neocortical temporal epileptogenic area, dual pathology, extratemporal epilepsy mimicking TLE (pseudo-temporal epilepsy), or multi-lobar epileptogenic zone (temporal plus epilepsy) [37]. We did not investigate the causes of epilepsy surgery failure in our patients.

In our study, 68% of the patients showed sustained seizure freedom in their postsurgical follow-up, which is in the range of what was previously reported [24, 28, 38, 39]. Moreover, among patients with MTS, those who underwent ATL had a higher percentage of remaining seizure-free compared to SAH. Although, the statistical analysis did not show any significant differences between the two surgical methods. There is a large diversity in selecting surgical approaches in patients with drug-resistant TLE, especially MTS. In a review by Josephson et al. the seizure outcome between standard ATL and SAH was compared. They implied that standard ATL confers a higher chance of achieving seizure freedom compared to SAH. Although, they concluded that, improved seizure outcomes must outweigh the potential neuropsychological impact of each procedure [10]. Some other studies indicated that SAH appears to have a similar seizure outcome, with a better cognitive consequence, compared to ATL [40-46]. Furthermore, some literature implied no significant differences in the postoperative seizure outcome, as well as verbal memory function between SAH and ATL, after one year of post-op follow-up [11, 13].

We had some limitations in our study. The patients' pre-surgical seizure frequency was collected based on the patients' and their relatives' recalls, not a reliable seizure diary. Additionally, we did not have access to a standard neuropsychiatric evaluation to assess the cognitive effects of surgery. Our financial restrictions and lack of instrumental accessibility prevented us to perform invasive EEG monitoring in selected patients.

Conclusion

This study is a report of 1-year follow-up results of TLE surgery in a tertiary epilepsy center in a developing country. We showed that, in patients with MTS, the neocortical temporal lobe resection did not offer a significantly higher rate of seizure freedom. This finding is promising in financially low-resource areas. A unique finding in our study was a high rate of postoperative functional seizures, which may be due to patients' lower socioeconomic conditions and psychiatric co-morbidities.

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Ethical Considerations

Compliance with ethical guidelines

All study procedures followed the ethical guidelines of the Declaration of Helsinki 2013. Ethical approval was obtained by the ethics committee of the Shahid Beheshti University of Medical Sciences, Tehran, Iran (Code: IR.SBMU.MSP.REC.1399. 641).

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Authors' contributions

Study concept and design: Marjan Asadollahi and Mohammad Samadian; Data analysis and interpretation: Leila Simani and Marjan Asadollahi; Manuscript preparation: Marjan Asadollahi, Leila Simani, Mohammad Samadian; Data collection: Zeinab Hashemi.

Conflict of interest

The authors declared no conflict of interest.

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