



4-30-2024

Section: Neurosurgery

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How to Cite This Article

Mansour, Mohamed Hasan; Ibrahim, Alaa Rashad; and Negm, Sabry Elsayed Ali (2024) "Surgical Management of Extratemporal Epilepsy," *Al-Azhar International Medical Journal*: Vol. 5: Iss. 4, Article 7. DOI: <https://doi.org/10.58675/2682-339X.2351>

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Surgical Management of Extratemporal Epilepsy

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Abstract

Background: Surgery is a commonly established therapy option for pharmaco-resistant extratemporal epilepsies.

Aim and objectives: To evaluate the clinical outcome of different surgical procedures for patients admitted to Al-Azhar Hospitals with drug-resistant extratemporal epilepsy.

Patients and methods: We enrolled 15 patients with drug-resistant epilepsy in our prospective and retrospective study between June 20, 2022, and May 30, 2023. After their admission to the neurosurgery department at Al-Azhar University Hospitals, these patients underwent epilepsy surgery and underwent follow-up monitoring for six months.

Results: The majority of the patients under study were female, with a mean age of 11.5 ± 6.5 years, and 80% had a normal mentality. Eight cases (53.3%) presented generalized-onset seizures, three patients (20%) presented Jacksonian seizures, two patients (13.3%) presented focal seizures, one patient (6.7%) presented drop attacks, and one patient (6.7%) presented multiform presentations. Six patients (40%), 5 patients (33.3%), 1 patient (6.7%), and 3 patients (20%) underwent partial callosotomy, laminectomy, and combined technique. Four patients (26.7%) reported surgical complications. Eight cases (53.3%) achieved English class I. Three cases (20%) showed a rare, disabling seizure (Engle class II). One case (6.7%) achieved Engle class III, while three cases (20%) achieved Engle class IV (no improvement).

Conclusion: Despite several obstacles, surgical treatment can successfully treat extratemporal lobe epilepsies, yielding satisfactory epileptological findings with manageable morbidity.

Keywords: Extratemporal lobe epilepsy; Surgical treatment; Short-term outcome

1. Introduction

Epilepsy, one of the most prevalent neurological conditions, affects over 50 million people globally.¹ Roughly one-third of epileptic patients have seizures that are resistant to medication, which lowers life expectancy, lowers their quality of life, and has disastrous socioeconomic effects.^{2, 3}

Out of the total, around 70% of individuals receive a diagnosis of temporal lobe epilepsy (TLE), while the remaining 30% experience seizures characteristic of extratemporal lobe

epilepsy (ETLE). The ratio of temporal to extratemporal resections mostly shows changes in the ability of different parts of the brain to cause seizures. However, it also highlights the challenges faced in defining the epileptogenic zone in cases of extratemporal epileptogenesis.⁴

This study's goal is to evaluate the clinical outcomes of various surgical procedures performed on extratemporal epilepsy patients hospitalized at Al-Azhar Hospitals who are resistant to pharmacological treatment.

Accepted 13 April 2024.
Available online 30 April 2024

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<https://doi.org/10.58675/2682-339X.2351>

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2. Patients and methods

We conducted a study that looked both forward and backward in time, involving 15 patients diagnosed with drug-resistant epilepsy by a multidisciplinary team of epileptology experts. The study took place between June 2022 and May 2023. The neurosurgery department at Al-Azhar University Hospitals (Al-Hussien and Bab El-Shaeria) admitted the individuals above for epilepsy surgery. A 6-month post-operative follow-up was conducted.

We included all patients aged above two years and below 60 years who are not controlled on two antiepileptic drugs (drug-resistant) or cannot tolerate the side effects of antiepileptic drugs. We excluded individuals diagnosed with temporal lobe epilepsy and those with bad general conditions.

We subjected all patients involved in this study to a complete medical history and clinical examination (clearance of epilepsy semiology), brain imaging using MRI and EEG, preoperative investigation by full labs, ECG and echo in some cases, and post-operative clinical and radiological assessment.

The semiology, EEG, and MRI epilepsy protocols were the mainstays of the surgical decision. If these three studies are concordant, we proceed to surgery according to the indications mentioned below in the techniques; if they are not, we make another investigation, like an interictal PET scan, to specify the site of hypometabolism. Techniques used were corpus callosotomy, multiple subpial transactions, or resective (lesionectomy) surgery.

The Institutional Review Board of the Ethics Unit at the Faculty of Medicine, Al-Azhar University, approved the study and carried it out in accordance with the Helsinki Declarations.

2.1. STATISTICAL ANALYSIS

We analyzed the acquired data using the SPSS (Statistical Package for the Social Sciences) program version 25.0 (IBM Inc., Chicago, USA), Microsoft Office Excel 2016, and the MedCalc program software version 19.1.

We conducted descriptive statistics on numerical parametric data using the mean, SD (standard deviation), and the minimum and maximum values of the range. For numerical nonparametric data, we used the median and the first and third nonparametric ranges. We analyzed categorical data using numbers and percentages.

We subjected quantitative variables to inferential analyses using the independent t-test for cases involving a pair of separate groups with parametric data and the Mann-Whitney U test for cases involving two separate groups with nonparametric data. The qualitative data underwent inferential analyses using the Chi-

square test for independent groups. We set the significance level at a P value of less than 0.05 to determine statistical significance and considered values greater than or equal to 0.05 as non-significant. The p-value is a statistical metric that quantifies the likelihood that the observed results in a study may have happened just by chance.

3. Results

| STUDIED PATIENTS (N=15) | | | |
|-------------------------|---------------|----------------|-----|
| SEX | Male | 6 | 40% |
| | Female | 9 | 60% |
| AGE (YEARS) | Mean \pm SD | 11.5 \pm 5.6 | |
| | Min-Max | 5-27 | |
| MENTALITY | Normal | 12 | 80% |
| | Sub-normal | 3 | 20% |

Table 1. Characterization of age, gender, and cognitive state in all examined subjects.

The average age of all the patients included in the study was 11.5 ± 6.5 years. The youngest patient was 5 years old, while the oldest patient was 27 years old. The analyzed patients consisted of 6 men, accounting for 40% of the total, and 9 females, making up 60% of the total. Among the subjects under investigation, the mental state was within the normal range in 12 patients (80%) and below normal in 3 patients (20%).

| STUDIED PATIENTS (N=15) | | | |
|-------------------------|-----------------|---|-------|
| SEMIOLGY OF FITS | GTC fits | 8 | 53.3% |
| | Jacksonian fits | 3 | 20% |
| | Focal fits | 2 | 13.3% |
| | Drop attacks | 1 | 6.7% |
| | Multiform fits | 1 | 6.7% |

Table 2. Description of semiology of fits in all studied patients.

GTC fits were presented in 8 patients (53.3%), Jacksonian fits were presented in 3 patients (20%), focal fits were presented in 2 patients (13.3%), drop attack was presented in 1 patient (6.7%), and multiform presentation was presented in 1 patient (6.7%).

| STUDIED PATIENTS (N=15) | | | |
|-------------------------|-----------------|---|-------|
| EEG FINDINGS | Normal | 2 | 13.3% |
| | Frontal | 5 | 33.3% |
| | Fronto-temporal | 2 | 13.3% |
| | Occipital | 1 | 6.7% |
| | Multifocal | 1 | 6.7% |
| | Generalized | 4 | 26.7% |

Table 3. Description of EEG findings in all studied patients.

The distribution of the condition was as follows: frontal in 5 patients (33.3%), frontotemporal in two patients (13.3%), occipital in one patient (6.7%), multifocal in one patient (6.7%), and generalized in four patients (26.7%). In addition, the condition was found to be normal in two patients (13.3%).

| | | STUDIED PATIENTS (N=15) | |
|--------------|-----------------------|----------------------------|-------|
| MRI FINDINGS | Normal | 7 | 46.7% |
| | Frontal gliosis | 2 | 13.3% |
| | Cortical malformation | 1 | 6.7% |
| | Dysplasia | 1 | 6.7% |
| | intraaxial lesions | 4 | 26.6% |

Table 4. Description of MRI findings in all studied patients.

There was frontal gliosis in 2 patients (13.3%), cortical mal formation in 1 patient (6.7%), dysplasia in 1 patient (6.7%), right frontal intraaxial SOL in 2 patients (13.3%), right occipital intraaxial SOL in 2 patients (13.3%) while it was normal in 7 patients (46.7%).

| | | STUDIED PATIENTS (N=15) | |
|-----------|---------------------|----------------------------|-------|
| TECHNIQUE | Partial Callosotomy | 6 | 40% |
| | Lesionectomy | 5 | 33.3% |
| | MST | 1 | 6.7% |
| | Combined technique | 3 | 20% |

Table 5. Comprehensive analysis of the procedure in all patients under study.

Partial Callosotomy was applied in 6 patients (40%), Lesionectomy was applied in 5 patients (33.3%), MST was applied in 1 patient (6.7%), and combined technique was applied in 3 patients (20%) (Lesionectomy + partial Callosotomy in 1 patient and MST + partial Callosotomy in 2 patients).

| | | STUDIED PATIENTS (N=15) | |
|----------------------------------|--------------------|----------------------------|-------|
| SEIZURE OUTCOME NEUROPSYCHIATRIC | The same | 10 | 66.7% |
| | Increase alertness | 5 | 33.3% |
| COMPLICATIONS | No | 11 | 73.3% |
| | Yes | 4 | 26.7% |

Table 6. Description of surgical complications and Seizure outcome neuropsychiatric in all studied patients.

It was the same in 10 patients (66.7%), and there was an increase in alertness in 5 patients (33.3%). Regarding surgical complications in all studied patients, surgical complications were recorded in 4 patients (26.7%) of the studied patients. 1 patient

showed 1-month disconnection, 1 patient showed 3 months of disconnection, 1 patient showed CSF leak, and 1 patient showed mutism then chest infection and death from COVID.

| | | STUDIED PATIENTS (N=15) | |
|-------------------------|------|----------------------------|-------|
| SEIZURE OUTCOME ENGLSES | IA | 6 | 40% |
| | IB | 2 | 13.3% |
| | IIA | 2 | 13.3% |
| | IIB | 1 | 6.7% |
| | IIIA | 1 | 6.7% |
| | IVB | 2 | 13.3% |
| | IVC | 1 | 6.7% |

Table 7. Description of Seizure outcome engles in all studied patients.

It was IA in six patients (40%), IB in two patients (13.3%), IIA in two patients (13.3%), IIB in one patient (6.7%), IIIA in one patient (6.7%), IVB in two patients (13.3%) and IVC in one patient (6.7%).

4. Discussion

In contrast to our results, it was noted that male predominance was common in most studies done on patients with DRE, and there was, in general, male predominance in epilepsy.⁵

As regards the semiology of seizure in all studied patients, generalized onset seizures were the most common type of seizure in 8 cases (53.3%), Jacksonian seizures were presented in 3 patients (20%), focal seizures were presented in 2 patients (13.3%), drop attacks were presented in 1 patient (6.7%), and multiform presentations were presented in 1 patient (6.7%). On repeated EEG, generalized epileptogenic activity was predominant. To this day, we depend on surface EEG due to the lack of other advanced measures like stereotactic EEG.

In the study of Tan et al.⁶, Focal epilepsy was the predominant kind observed in 24 instances, accounting for 73% of the total. Out of the total sample, eight individuals (24%) were diagnosed with Lennox Gastaut syndrome (LGS), and two individuals (6%) were diagnosed with West Syndrome (WS), characterized by both widespread and localized epileptogenic activity.

Whereas in the study of Kim et al.⁷, The most prevalent form of seizure observed was complex partial seizure with focal onset, accounting for 97 instances.

In analyzing the history of the patients in our study, the type of seizures was of focal onset at first, then changed over the years and became generalized. The predominance of generalized seizures in our study may be due to the delay in the referral from a neurologist. The cause of this delay is the practice of trialing a large number of antiepileptic drugs (AEDs), reaching 6 drugs in

some cases, before referring the patient for further intervention. This may lead to some brain encephalopathy, causing generalized epileptic discharge.

Our study utilized neuronavigation for both surgical approach planning and delineating the resection area. Functional MRI and intraoperative electrophysiological mapping and monitoring aid in the removal of tissue in regions associated with speech, motor function, and the insula. Specifically, subdural electrodes that are surgically inserted to identify the epileptogenic zone can be utilized to restrict regions of heightened functionality. When the epileptogenic zone overlaps with highly functioning areas, iEEG is essential and cannot be readily replaced by fMRI.

The EEG findings in all studied patients were frontal in five patients (33.3%), Frontotemporal in two patients (13.3%), occipital in one patient (6.7%), multifocal in one patient (6.7%), and generalized in four patients (26.7%). In comparison, it was normal in two patients (13.3%). The MRI findings in all studied patients were frontal gliosis in two patients (13.3%), cortical malformation in one patient (6.7%), dysplasia in one patient (6.7%), right frontal intraracial SOL in two patients (13.3%), right occipital intraracial SOL in two patients (13.3%). In comparison, it was normal in seven patients (46.7%).

Regarding the technique in all studied patients, partial Callosotomy was applied in six patients (40%), Lesionectomy was applied in five patients (33.3%), MST was applied in one patient (6.7%), and combined technique was applied in other patients (20%) (Lesionectomy + partial Callosotomy in one patient and MST + partial Callosotomy in 2 patients).

In the study of Delev et al.⁸, The majority of surgeries conducted for extratemporal epilepsies were frontal resections, which comprised 48% of all operations. The parietal occipital and insular resections accounted for 24% of the procedures.

The study found that the extended laminectomy, which involves removing the epileptogenic zone, was the most often performed procedure in 66% of the patients. It is worth mentioning that in their study, multilobectomies made up 28% of all extratemporal surgeries, specifically targeting the parieto-occipital area. In other studies, extratemporal resections involving a single lobe have been reported to range from 12% to 22%.

The study emphasized the importance of carefully considering the removal of highly vascularized areas and epileptogenic zones surrounding regions with high functionality. In these cases, surgery should be conducted in a subpial manner, which involves removing the

gyri while keeping the pial banks intact. This approach aims to preserve all arteries and major veins. Based on their expertise, it has been observed that the primary motor cortex can be surgically removed up to a distance of 3.0 cm beyond the Sylvian fissure without causing harm to the motor hand area.

This is especially accurate as these resections are solely accompanied by a temporary facial weakness, which entirely heals within a few days. Suppose the epileptogenic zone in the frontal lobe extends to the insula. In that case, it is possible to surgically remove this area using a frontal approach by carefully dissecting between the basal ganglia and the Sylvian arteries. Alternatively, the Transylvanian, or specifically on the non-dominant side, the transcortical route through the frontal opercula, can be employed for the treatment of insular epilepsies.⁹

A comprehensive and precise understanding of problems is crucial for providing guidance to those considering surgery and devising methods to prevent these risks. Nevertheless, it is challenging to make a direct comparison of the complication rates due to variations in surgical procedures, pathologies, and patient groups (children/adults) included in the different studies. Furthermore, several of the identified hazards (such as quadrantanopia, cognitive impairments, and psychiatric illnesses) are assessed to be partly unavoidable consequences and partly complications.

In our study, surgical complications were recorded in 4 patients (26.7%) of the studied patients. One patient showed one-month disconnection, one patient showed 3 months of disconnection, one patient showed CSF leak, and one patient showed disconnection and chest infection, then death from COVID. The surgical morbidity of the operations done in our study was transient and minor if compared to the benefit of the surgery. The intraoperative mapping and EEG help us a lot while working around eloquent areas to avoid complications related to motor deficits.

We perform anterior callosotomy to prevent disconnection syndrome. Anterior corpus callosotomy is an effective treatment for controlling seizures in individuals with generalized tonic-clonic and multiform seizures that involve bilateral discharges. This approach is cost-effective and does not necessitate any specialized resources. It is significant in countries with limited resources.

Disconnection syndrome typically arises as a complication of complete callosotomy, and so it is only employed in circumstances that require more extensive division of the corpus callosum.¹⁰

In the study of Hosoyama et al.¹¹, zero fatalities resulted from surgical procedures. During their last follow-up, nearly all of the 85

patients reported that their morbidities did not significantly impair their everyday activities.

In the study of Kim et al.⁷, there was no postoperative mortality. In extratemporal resection, the commonest complication was hemiparesis, which was transient in most cases. Three patients suffering dysphasia. Complications were minor following corpus callosotomy.

Regarding their summary, Hader et al.¹² 16.0% of the cases experienced transitory morbidity due to surgical and neurological problems, whereas 6.2% experienced chronic morbidity. The incidence of complications was greater in extratemporal resections compared to temporal resections, with a perioperative mortality rate of 1.2% in extratemporal cases. The incidence of long-term complications resulting from extratemporal treatments ranges from 3% to 43% in various studies.¹³⁻¹⁵

The Seizure outcome neuropsychiatric in all studied patients was the same in 10 patients (66.7%), and there was increased alertness in 5 patients (33.3%); 3 of them were patients who underwent partial callosotomy.

In pediatric patients, we depended on parents' observation and questionnaires to assess cognitive outcomes; however, further tests in the future need to be done. Based on our study findings, Helmstaedter et al.¹⁶ found that all functions, except for verbal memory, figural memory, and IQ, showed considerable improvement compared to pre-surgery assessments.

As regards seizure freedom in our study, Engle class I was achieved by 8 cases (53.3%) (become seizure-free). Three cases (20%) showed rare disabling seizures (Engle class II). Engle class III was achieved by 1 case (6.7%), while Engle class IV was achieved by 3 cases (20%) (no improvement).

Multiple datasets regarding seizure outcomes following extratemporal resections can be found in the literature. McIntosh et al.¹⁷ The study found that 40.7% of patients experienced seizure freedom initially, but this percentage decreased to 14.7% five years after the surgery. Contentiously, Hanáková et al.¹⁸, D'Argenzio et al.¹⁹, and Elsharkawy et al.²⁰ Engel I rates have remained pretty consistent over the years, with roughly 50% in both adults and children.

Based on the previous discussion and the opinions of experts in relevant fields, surgical treatment of extratemporal lobe epilepsies is effective. It yields favorable epileptological outcomes with an acceptable level of complications. The subset of younger patients who have obvious lesions located far from the eloquent cortex and can be entirely removed through surgery have the highest likelihood of

achieving long-term seizure control.

Although the results of this study reflect an improvement in patients with

extratemporal lobe epilepsies by surgical treatment, yet there were some limitations. Firstly, this study is a cohort study conducted at a single center, and the authors' techniques and experiences limit the technical results. Secondly, a small number of cases were studied due to limited resources and limited referral specialists. Additional research examining the long-term management of seizures and their impact on cognitive and social functioning would also be beneficial. In future investigations, it is important to clearly establish the main objectives, such as assessing the impact of surgical therapy on quality of life and social integration. This will enable the collection of data that is supported by more robust evidence.

5. Conclusion

Despite facing multiple obstacles, surgical intervention for extratemporal lobe epilepsies is highly effective and yields favorable epileptological outcomes with an acceptable level of morbidity..

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

Funding

No Funds : Yes

Conflicts of interest

There are no conflicts of interest.

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