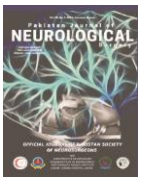

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Original Article (BRAIN)

The Efficacy of Surgery for Supra-Tentorial Gliomas in Preventing Seizures

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ABSTRACT

Objectives: The study examined the surgical outcome of supratentorial gliomas in terms of improvement in seizures in patients who presented to a tertiary care institution.

Material and Methods: A descriptive case series was conducted in Neurosurgery Department at Northwest General Hospital & Research, Peshawar. Patients (n = 95) with supratentorial gliomas with seizures between 18 – 70 years were included. Supratentorial gliomas were diagnosed by neuroimaging as MRI brain with contrast, diffusion-weighted, Fluid-attenuated inversion recovery, and magnetic resonance spectroscopy. The patient was observed for seizures postoperatively. Data was stratified for age and gender.

Results: The majority of patients (36.8%) were in 41 – 50 years. 55.78% of patients were males whereas 44.21% of patients were females. 42 (44.21%) involved the frontal lobe, 16 (16.84%) involved the parietal lobe, 26 (27.36%) involved the temporal lobe, and 11 (11.57%) patients involved the occipital lobe. According to Engel's classification, 53 patients were in class I, 16 in class II, 10 in class III, and 5 in class IV. 84 (88.42%) experienced post-op seizure reduction. An insignificant association was found with the seizure improvement (yes/no) with different age groups and gender.

Conclusion: The frontal lobe was the most prevalent location for supratentorial gliomas. After surgery, a large proportion of patients improved in terms of seizure management.

Keywords: Seizures, Supratentorial gliomas.

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INTRODUCTION

Gliomas are tumors that develop from glial cells, which are CNS supporting cells.[1] Glioma account for roughly 60% of the estimated 17,000 primary brain tumors identified each year.[2] The yearly incidence of cerebral gliomas is almost 3.7 per 100,000 male patients and 2.6 per 100,000 female patients. Cerebral gliomas are frequent in both

adults and children.[3] Seizures are the presenting ailment in 72 – 89 percent of glioma patients.[4-5] At the time of presentation, 3 – 30% of patients had mental status alterations. 7 Signs and symptoms of increased intracranial pressure, such as headache and vomiting, are present in 10 – 40% of patients.[6-8] In one trial, 56% of patients had no seizures after 6 months of follow-up.[9] In another trial, 52 percent of patients had seizure control after 6 months of follow-up.[10] If seizures are left untreated, they contribute significantly to patient morbidity and have a negative impact on quality of life. Tumor location and histology impact epilepsy risk. The etiology of tumor-related epilepsy is complex and may differ amongst tumor histologies. In addition to clinical factors such as preoperative seizure duration and type, as well as antiepileptic drug (AED) therapy, gross total resection is the best predictor of seizure independence. Epilepsy surgery may enhance seizure management. The newer AEDs (Levetiracetam, Topiramate, and Lacosamide) tend to be more tolerated than the earlier AEDs (phenobarbital, phenytoin, carbamazepine).[11-12]

The incidence of seizures varies greatly depending on the kind of tumor. Glioneuronal tumors, such as gangliogliomas and dysembryoplastic neuroepithelial tumors, are linked with persistent pharmacoresistant epilepsy.[13] They are more common in children and young adults, as well as in the temporal lobe. Another uncommon grade I gliomas that occur in children and young adults, such as supratentorial pilocytic astrocytomas, pleomorphic xanthoastrocytoma, and angiocentric gliomas, commonly induce seizures. Topiramate has been used as an adjunct in patients with low-grade tumors and active epilepsy who had poor seizure control despite using one AED. Only 8% of patients experienced good seizure control. Tiagabine was studied as an adjunct in ten individuals with LGG (low-grade glioma) and drug-resistant partial epilepsy.[14] However, it is still unknown if newer AEDs have any advantage in seizure prevention. When compared to multiple regimens, treating seizures with monotherapy provides a safer therapeutic window, greater compliance, and is more cost-efficient. However, if patients develop breakthrough seizures that are refractory to dosage increase and monotherapy switching, additional medications may be required. In one study of 99 patients, 54 individuals did not react to any AED medication. Despite adequate medical therapy, some studies indicate that up to 60–70% of people will continue to suffer.[15] Some findings show that AEDs should not be used frequently for seizure prevention in patients with brain tumors because they are ineffective and, in fact, cause damage through side events. Prophylactic medication is discouraged not just due to its dubious effectiveness in these individuals, but also because several AEDs are known to interact with cytotoxic chemotherapeutics and steroids. Furthermore, AEDs have negative effects that must be balanced against the possible advantage that the medicine has to provide.[16-17]

There is some evidence that treating the brain tumor with radiation and/or chemotherapy may improve seizure control.[18-19] Surprisingly, this advantage does not always correlate with changes in tumor burden on magnetic resonance imaging (MRI) or overall survival. 20 A meta-analysis of 24 studies looked at the effects of anticancer treatment with either radiation or chemotherapy on tumor-related epilepsy rates. While not all trials indicated a decrease in tumor burden or therapeutic benefits, all studies did report improved seizure outcomes following anticancer therapy.[20-21] Because surgery is the primary therapy for brain tumors, surgical procedures are used more frequently in tumor-related epilepsy than in any other kind of epilepsy. In the great majority of cases, surgical treatment is focused on the tumor rather than on alleviating epilepsy. If a correctable lesion is present in patients who have failed monotherapy with two first-line medicines, surgery may be

indicated.[22-23] Patients with brain tumors are often in this group and can benefit greatly from surgery. A well-planned strategy before tumor excision can give a window of opportunity to manage seizures in the same environment. This may not only cure or limit the course of their tumor, but it may also reduce or eliminate seizures. The goal of this study was to look at the surgical outcome of supratentorial gliomas in terms of seizure improvement in patients who came to a tertiary care facility.[20-25]

MATERIALS AND METHODS

Study Design & Setting

A descriptive study was conducted at the Department of Neuro Surgery Northwest General Hospital & Research, from 25 May 2020 to 25 November 2020.

Sample Size

The sample size of 95 was estimated by using a 95% confidence level with a 10% margin of error and taking an expected percentage of controlled seizures i.e., 56% in patients with supratentorial gliomas.[11]

Inclusion Criteria

Patients with supratentorial gliomas who had seizures ranged in age from 18 to 70 years old and were of both male and female gender.

Exclusion Criteria

Those cases were excluded who were Unfit for general anesthesia (GA). Patients who were unwilling to have surgery were eliminated. Patients whose condition was not diagnosed as glioma on histology were excluded. Patients with strong risk factors for metabolic acidosis (obesity > 160 kg, unstable ischemic heart disease) were also excluded.

Data Collection

Informed consent was obtained from each patient. Supratentorial gliomas were diagnosed by neuroimaging as MRI brain with contrast, diffusion-weighted, Fluid-attenuated inversion recovery (FLAIR), and magnetic resonance spectroscopy (MRS). Gliomas were confirmed on histopathology.

An operative microscope was used for the proper localization of the tumor. For tissue diagnosis, a biopsy was taken and preserved in 10% formalin and sent to the laboratory. All patients were kept in ICU for 24 hours and then shifted toward. Following surgery, the patient was monitored for seizures. Engel's categorization was used to assess seizure outcomes. All the data was collected through a pre-designed proforma. An examination by a skilled neurosurgeon was used to develop surgical planning. The patient was monitored post-operatively till he was discharged.

Data Analysis Procedure

The collected data was entered and analyzed in SPSS v 24.0. All the quantitative variables like age were presented as Mean ± S.D. Qualitative variables like gender and surgical outcome (improvement) were presented in the form of frequencies and percentages. Data was stratified for age and gender. Post-stratification was done with the Chi-square test.

RESULTS

Age Distribution

12 (12.6%) patients were recorded in the 18-30 years age group, 19 (20.1%) patients were recorded in the 31 – 40 years age group, 35 (36.8%) patients were recorded in 41 – 50 years age group, 21 (22.3%) patients were recorded in 51 – 60 years age group and 08(08.3%) patients were recorded in 61-70 years age group (**Table1**).

Table 1: Age Distribution (N = 95).

Age Group	Frequency	Percentages
18 – 30 Years	12	12.6%
31 – 40 Years	19	20.1%
41 – 50 Years	35	36.8%
51 – 60 Years	21	22.3%
61 – 70 Years	08	8.3%

Gender Distribution

53 (55.78%) patients were males whereas 42 (44.21%) patients were females.

Mode of Patient Admission

32 (33.68%) patients were admitted with an emergency, whereas 63 (66.31%) were admitted from OPD **(Table 2)**.

Table 2: Mode of Admission (N = 95).

Mode of Admission	Frequency	Percentages
Emergency	32	33.68%
OPD	63	66.31%

Incidence of Supratentorial Glioma Location

As per frequencies and percentages of supratentorial glioma location, 42 (44.21) involved the frontal lobe, 16 (16.84%) involved the parietal lobe, and 26 (27.36%) involved the temporal lobe, and 11 (11.57%) patients involved occipital lobe **(Table 3)**.

Supratentorial Gliomas Seizure Improvement

As per postoperative frequencies and percentages for supratentorial gliomas seizure improvement according to Engel's classification, 53 patients in class I,16 in class II,10 in class III, and 05 in class IV **(Table4)**.

Seizure Improvement

As per frequencies and percentages for seizure improvement, 84 (88.42%) experienced post-op seizure reduction **(Table 5)**.

Table 3: Incidence of Supratentorial Gliomas Location (N = 95).

Location	Frequency	Percentages
Frontal Lobe	42	44.21%
Parietal Lobe	16	16.84%
Temporal Lobe	26	27.36%
Occipital Lobe	11	11.57%

Table 4: Postoperative For Supratentorial Gliomas Seizure Improvement According To Engel's Classification (N = 84).

Classes	Number of Patients	Percentages
I	53	63.09%
II	16	19.04%
III	10	11.90%
IV	05	5.95%

Table 5: Seizures Improvement (N = 95).

Seizures Improvement	Frequency	Percentages
Yes	84	88.42%
No	11	11.57%

Stratification of Seizure Improvement Concerning Age & Gender

Stratification of seizure improvement with regard to age, and gender is mentioned in **Tables 6-7**. An insignificant association was found with the seizure improvement (yes/no) with different age groups and gender.

Table 6: Stratification of Seizure Improvement with Respect to Age (N = 95).

Age	Seizure Improvement	Frequency	Percentage	P-Value
18 – 30 Years	Yes	10	10.52%	
	No	02	2.10%	
31 – 40 Years	Yes	17	17.89%	
	No	02	02.10%	
41 – 50 Years	Yes	31	32.63%	0.086
	No	04	04.21%	(Insignificant Result)
51 – 60 Years	Yes	19	20.00%	
	No	02	02.10%	
61 – 70 Years	Yes	07	07.36%	
	No	01	01.05%	

Table 7: Stratification of Seizure Improvement with Respect to Gender (N = 95).

Gender	Seizure Improvement	Frequency	Percentage	P-Value
Male	Yes	47	49.47%	0.603 (Insignificant Result)
	No	06	06.31%	
Female	Yes	37	38.94%	
	No	05	05.26%	

Radiography of Patients

A typical left frontonasal, precentral, low-grade glioma affecting the supplementary motor region may be seen in an axial and in sagittal MRI **(Figures 1A and 1B)**. A typical right, low-grade glioma affecting the insular lobe is viewed in axial RI and in a coronal MRI **(Figures 2A and 2B)**. An axial T1-weighted MRI scan revealed a frontal lobe lesion in the center of the brain **(Figure 3A)**. Edema surrounds a frontal lobe lesion in the center of this axial T2-weighted scan **(Figure 3B)**. Hydrocephalus is caused by an axial FLAIR sequence of a frontal lobe lesion squeezing the frontal ventricular horn **(Figure 3C)**.

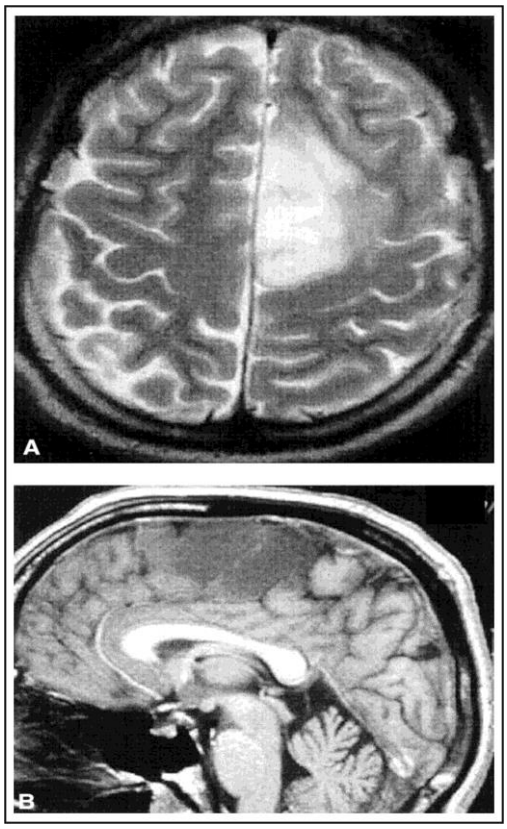


Figure 1(A): T2weighted axial magnetic resonance image (MRI) and Figure 2(B): A sagittal T1weighted MRI reveals a "typical" left frontonasal, precentral, low-grade glioma of the supplementary motor region.

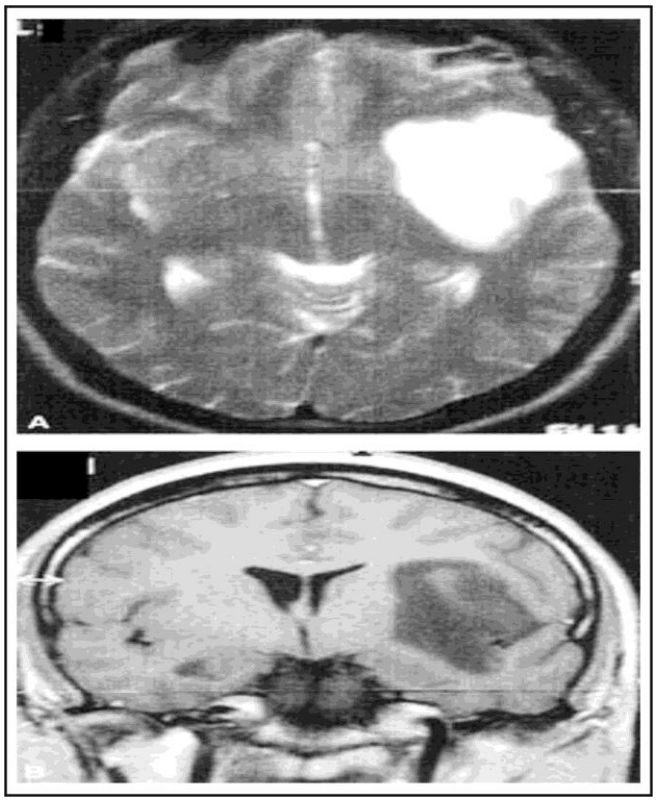
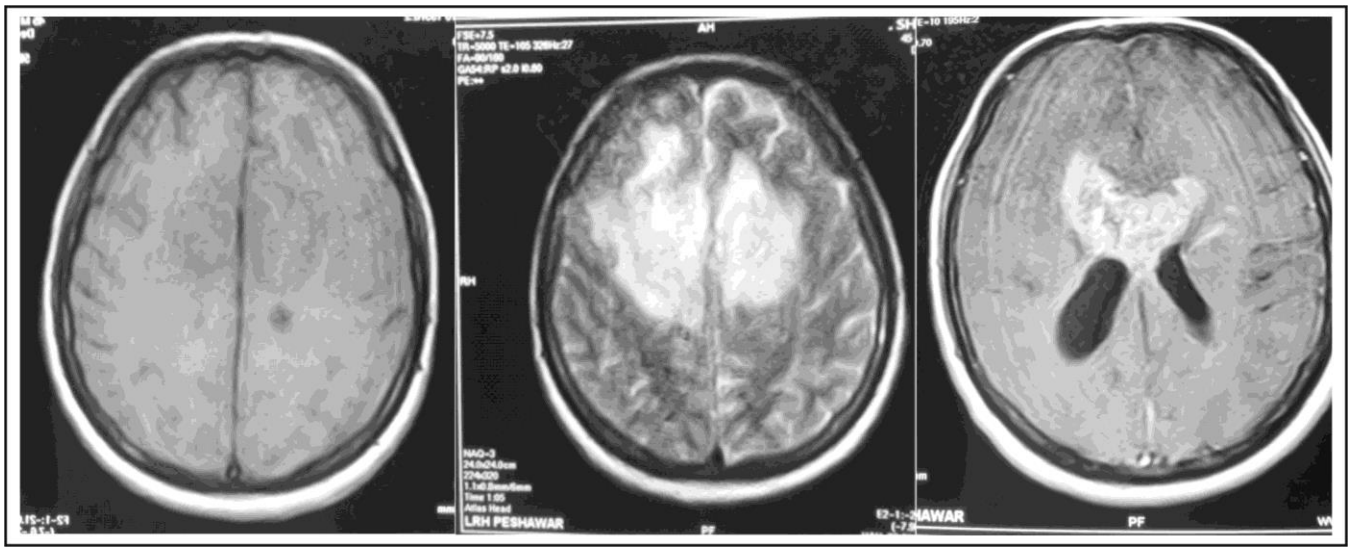


Figure 2(A): An axial, T2-weighted magnetic resonance image (MRI) and **Figure 2 (B):** a coronal, T1-weighted MRI shows a "typical" right, low-grade glioma involving the insular lobe. (images used with patients' permission).

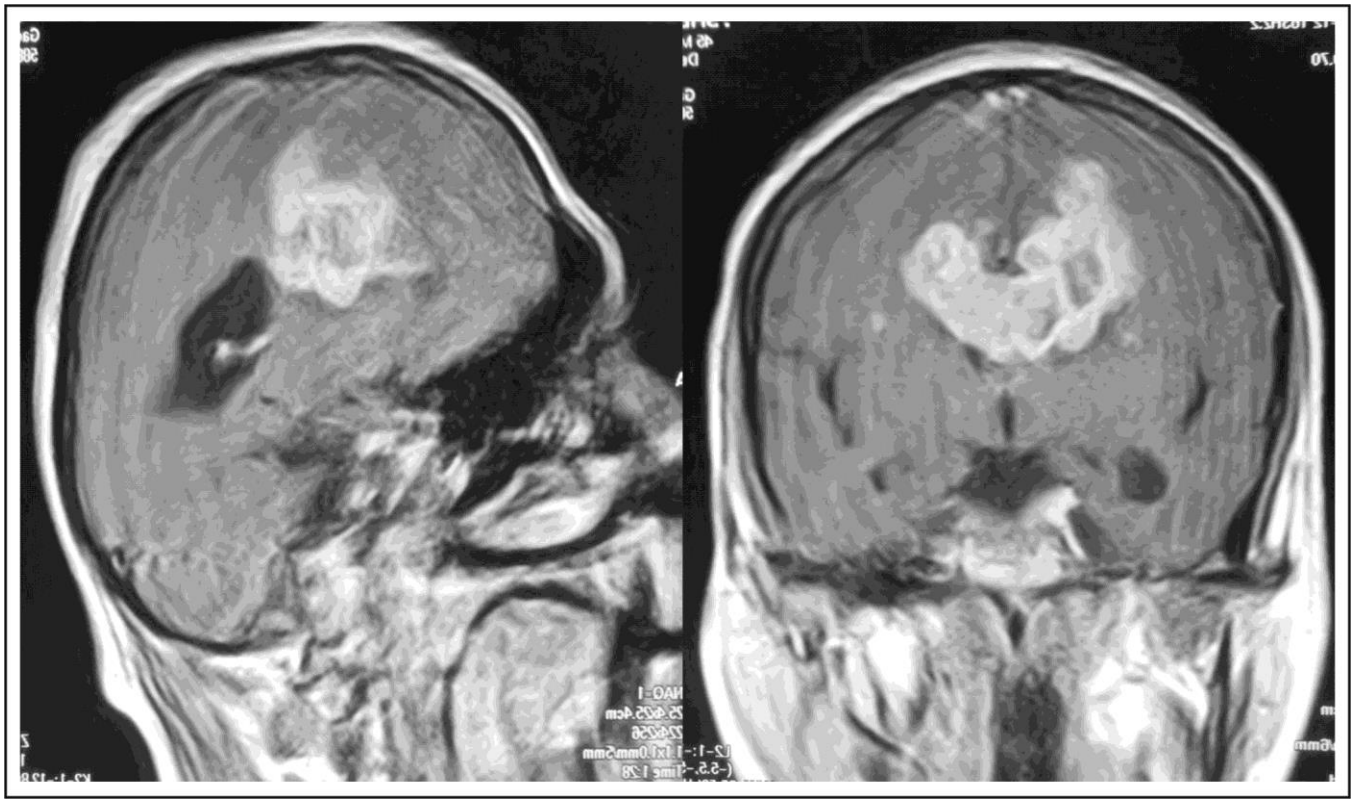
DISCUSSION

With seizure being the most prevalent presenting sign and a favorable prognostic factor for patients with gliomas, this research will be done to determine the improvement of seizures following surgery in patients with supratentorial gliomas. We did this study to better understand the impact of surgery on seizure alleviation, as seizures are more typically linked with primary brain tumors than with cerebral metastasis. 18 Seizures have been proven in many studies to have an impact on the quality of life of patients suffering from supratentorial gliomas. Tumor-related seizures appear clinically as simple or complex partial seizures with or without subsequent generalization, and in more than half of patients, despite maximal pharmacological therapy, are resistant to anti-epileptic medicines. Frontal, temporal, and parietal lobe tumors are more typically linked with seizures than occipital lesions. Severe epilepsy is more common in tumors involving the temporal lobe and insular cortex. Our patients had frontal lobe tumors, accounting for 44.21 percent of the total. We



(A) (B) (C)

Figure 3(A): Axial T1-weighted sequence showing frontal lobe lesion in the center.
Figure 3(B): Axial T2-weighted sequence showing frontal lobe lesion in the center with surrounding edema.
Figure 3(C): Axial FLAIR sequence showing frontal lobe lesion in center compressing frontal ventricular horn causing hydrocephalus. (Images used with patients' permission).



(D) (E)

Figure 3(D): Sagittal sequence showing frontal lobe lesion. **Figure 3 (E):** Coronal cuts showing lesion in center compressing the ventricular system, irregular in shape, equal on both sides. (images used with patients' permission).

examined the incidence of post-operative seizures was examined using the Engels Classification, with 63 percent of patients falling into class1 (53 out of 84 patients). There was no significant variation in seizure control depending on age or gender.

In another study, the seizure result was 53% in Engel's class. It was higher in patients who had a whole tumor removal as opposed to a partial removal [26]. These surgeons performed gross total removal on 51 (53.68 percent) of the patients, which is close to the findings of Kahlenberg et al.[27] performed gross entire removal on 56 percent of the patients. Chang et al.[28] revealed 67 percent seizure-free (Engel class I) following supratentorial surgery for gliomas. However, because there is more heterogeneity in seizure outcomes following glioma surgery, the findings are comparable to those of previous research. In our study, the frontal and temporal lobes were implicated in 42 percent and 26 percent of cases, respectively, followed by the parietal and occipital lobes. Our findings are comparable to those of previous studies performed throughout the world, which found frontal lobe involvement in 50% of patients and temporal lobe involvement in 26% of patients. Tumors positioned close or emerging from the cerebral cortex have a higher frequency of seizures than tumors found in deeper areas of the brain.[26,28]

A study of 207 individuals with tumor-related epilepsy found that 82 percent of them were seizure-free after surgery. A short duration of seizures before surgery and a single seizure focus enhances seizure freedom results.[29] A comprehensive assessment of the literature, which included 773 individuals with tumor-related epilepsy described in 20 series, found that

roughly 71% of patients will attain seizure independence after surgery. This success was observed to be substantially higher among individuals who received gross complete excision of the tumor as opposed to subtotal resection.[23-24] In a limited study of 36 patients with mesial temporal lobe tumors with seizures, the majority of whom were resistant to AEDs, older patients, big tumor size, and penetration beyond the mesial temporal lobe were linked to poor outcomes. Interestingly, they discovered that individuals with a mesial temporal lobe tumor had persistent epilepsy, while those with a short duration of episodes had a more aggressive condition. Epileptic individuals with DNETs (dysembryoplastic neuroepithelial tumors) or gangliogliomas are frequently ideal surgical candidates since their epilepsy is extremely resistant to medicinal treatment. Tumors associated with long-term intractable epilepsy, such as those in the mesial temporal lobe or insula, as well as childhood lesions such as glioneuronal tumors, should be given special consideration for early surgical intervention, not only for their reported superior treatment efficacy but also for improving quality of life and patient satisfaction. Surprisingly, the extent of surgical resection may be related to the degree of cancer. Seizure independence was observed in these individuals, as well as those with a variety of different tumor types studied in previous investigations. Other factors that were found to predict postoperative seizure freedom are the time until surgery, localization of foci, concordant MRI and EEG findings, and lack of secondary generalization.[22-24] Although, current evidence supports the use of AEDs in the treatment of tumor-related epilepsy, however, use of a newer AED as monotherapy should be the first step in treatment. If this treatment is unsuccessful, a second monotherapy may be tried. Subsequent seizure control attempts may involve the use of a mix of first and second-line medicines. If medicinal care fails to provide more seizure relief, surgical surgery may be required. The duration of surgery, localization of foci, concordant MRI and EEG results, and absence of subsequent generalization are all factors linked with postoperative seizure independence.

For patients with medically refractory epilepsy, surgery is widely seen as a potential therapy option. Numerous studies published in the last 20 years have reported seizure freedom for at least one year in 53 – 84 percent of patients after anteromesial temporal lobe resections for mesial temporal lobe sclerosis, 66 – 100% of patients with dual pathology, 36 – 76% of patients with localized neocortical epilepsy, and 43 – 79% of patients after hemispherectomies. Non-respective surgical reported rates of seizure independence have been less remarkable; nevertheless, the benefit is more obvious when described in terms of significant seizure reductions 30. Bjørnæs et al.[31] looked at potential predictors of seizure control in a group of children and adults with low IQs who had resective surgery for intractable focal epilepsy and looked at outcomes in terms of seizures and neuropsychological functioning. They looked at the psychosocial outcomes of adult patients. In individuals with intractable focal epilepsy and low IQ, resective surgery resulted in a good seizure outcome if therapy was initiated reasonably soon after the onset of epilepsy. There were no negative impacts on cognitive or psychosocial functioning.[3]

The resections had the lowest long-term seizure-free rates of any resective, but they were also the most diverse (up to 80%). Poorer and more diverse results might be explained by a variety of factors. Poorer results might be attributed to the difficulty to resect the whole epileptogenic region due to its closeness to the functionally essential brain. In addition, the epileptogenic zone in the frontal lobe may be larger, and seizure propagation may be particularly rapid and broad. Heterogeneity is most likely explained by differences in outcome evaluation, different etiologies, whether the

epileptogenic zone and surgical resection involve only the frontal lobe or surrounding tissues as well, and resection size. These difficulties demand careful consideration in a future study.[32]

CONCLUSION AND RECOMMENDATION

The frontal lobe was the most prevalent location for supratentorial gliomas. After surgery, a large proportion of patients improved in terms of seizure management. To minimize post-operative problems such as newly formed neurology or paralysis, safe surgical dissection and excision of the tumor are required. The neurosurgeon will be able to pinpoint the exact position of the lesion thanks to pre-operative surgical planning and incision labeling. Because tumors are more likely to produce epilepsy if they are located in the supratentorial compartment of the brain, the location of the tumor increases the risk of epilepsy. Supratentorial glioma surgical result in terms of improvement in Seizures during the six-month follow-up period involving the frontal, temporal, and parietal lobes had a higher risk of seizures than lesions in other lobes of the brain. Although we found no clear data to support this hypothesis, medications plus surgery may have worked synergistically to eventually achieve complete seizure control. Although tumor placement in the temporal lobe appears to be related to a better prognosis, no conclusions can be reached about the efficacy of extended cortical and/or mesial temporal resection in unresectable lesions at this time.

Limitations

Our study has limitations in that it is a single-center trial, and there was also operating surgeon bias. In order to adopt and promote our findings, further multi-center studies will be needed in the future to validate the findings.

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Additional Information

Disclosures: Authors report no conflict of interest.
Ethical Review Board Approval: The study was conformed to the ethical review board requirements.
Human Subjects: Consent was obtained by all patients/participants in this study.
Conflicts of Interest:
In compliance with the ICMJE uniform disclosure form, all authors declare the following:
Financial Relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.
Other Relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Muhammad Tariq, Faiqa Filza	1. Study design and methodology.
2.	Muhammad Farooq, Muhammad Tariq	2. Paper writing, referencing, and data calculations.
3.	Irfan Jan, Mustafa Qazi	3. Data collection and calculations.
4.	Mushtaq Ahmad Mian, Khial Jalal	4. Analysis of data and interpretation of results etc.
5.	Muhammad Tariq, Adnan Munir	5. Literature review and manuscript writing.
6.	Adnan Munir, Muhammad Farooq	6. Analysis of data and quality insurer.