ADDIS ABABA UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF SURGERY, NEUROSURGERY UNIT

A RETROSPECTIVE STUDY ON POSTOPERATIVE SEIZURE STATUS AMONG PATIENTS OPERATED FOR BRAIN TUMOR WITH SEIZURE IN THREE TEACHING HOSPITALS, CENTRAL ETHIOPIA

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List of Abbreviations

AAU - Addis Ababa University

AEDs – Anti-Epileptic Drugs

BTRE – Brain Tumor Related Epilepsy

CI- Confidence Interval

CNS- Central Nervous System

CT- computed Tomography

DNET - Dysembryoplastic Neuroepithelial tumor

ECoG- Electrocorticography

EEG- Electroencephalography

GG- Ganglioglioma

GTR - Gross Total Resection

HGG-High Grade Glioma

ILAE- International League Against Epilepsy

LGG- Low Grade Glioma

MCM- Myungsung Christian Medical Center

MRI- Magnetic Resonance Imaging

OR- Odd Ratio

TASH - Tikur Anbessa Specialized Hospital

STR- Sub-Total Resection

WHO- World Health Organization
ZMH- Zewditu Memorial Hospital

Abstract

Background: Seizure is one of common presentations of brain tumor. Surgical resection is useful in controlling seizures and in eradicating the symptoms associated with compression.

Objective: The aim of this research was to examine postoperative seizure status and factors significantly associated with postoperative seizure control following brain tumor surgery in patients with brain tumor and seizure.

Methods: Multicenter retrospective cross-sectional study was conducted among 97 patients with brain tumor and seizure who had undergone initial surgery at three selected teaching hospitals in central Ethiopia from January 1, 2015 to December 31, 2019. Assessment of postsurgical seizure status were described using Engel's classification of seizure: completely seizure free (Engel class I), and not seizure free (Engel classes II, III, IV). Demographic, seizure history, radiographic characteristics, histopathologic diagnosis, treatment, preoperative and postoperative antiepileptic drug use data were collected and analyzed for statistical association with postoperative seizure control using univariate and multivariate logistic regression analyses. P- Values of less than 0.05 and confidence level of 95% were considered to indicate statistical significance and strength of association respectively.

Results: Ninety seven patients (60 females, 37 males) were included, with a mean age of 41.7 years and a median seizure duration of 8 months. There were generalized tonic-clonic seizures in 52 patients (53.6%).The histopathology confirmed meningioma in 71.1% (n = 69) of patients, low grade glioma in 12.4% (n = 12), and high grade glioma in 11.3% (n = 11) of patients. Gross total resection was achieved in 80.4% (n = 78) of patients and subtotal resection in 19.6% (n = 19) of patients. During a median follow-up of 6 months (range 3 months to 3 years), 66% of patients were seizure free (Engel's Class I). Seizure freedom was predicted by gross total resection (adjusted OR 6.24, 95% CI: 1.79-21.71, P=0.004) and seizure duration ≤ 1 year before surgery (adjusted OR 3.60, 95% CI: 1.20-10.82, P=0.022) on multivariate analysis. Occurrence of postoperative weakness after surgery (adjusted OR 16.23, 95% CI: 2.57-103.09, P=0.003) and uncontrolled preoperative seizure (adjusted OR 4.69, 95% CI: 1.49-14.75, P=0.008) were found to be significant independent predictors associated with uncontrolled postoperative seizure status.

Conclusions: Sixty six percent of brain tumor patients in this study were seizure-free following surgery. Specific variables that were strongly associated with seizure-free outcome included gross total resection and seizure duration ≤ 1 year prior to surgery. These findings suggest that strict preoperative seizure control, early surgical intervention, and complete tumor resection increases the chance of postoperative seizure control.

1. Introduction

1.1. Background

Seizures are one of the most common brain tumor presentations. Depending on the type of tumor, the frequency of seizure in brain tumor patients varies from 30% to 100% (1,2). Seizures can happen either as an original symptom leading to tumor diagnosis (seen in approximately 30–50% of patients) or during the course of the illness (seen in 10–30% of patients) (2).

The risk of seizure is affected by tumor type and location and amount of lesions. Seizures with glioneuronal tumors (70–80%) are most prevalent among all types of tumors, especially in patients with frontotemporal or insular lesions (3). Seizures are also prevalent in patients with glioma, with the largest epilepsy rates (60–75%) in patients with low-grade gliomas in surface cortical or insular areas. Approximately 20-50% of meningioma patients and 20-35% of brain metastasis patients also suffer from seizures (2). Also essential is the location of the tumor, for example, cortical tumors are associated with an increased risk of seizures. In addition, frontal, temporal and parietal tumors pose a greater risk of seizure than occipital tumors (4).

Tumor-related seizure, when uncontrolled, has a major effect on the quality of life of patients, causes intellectual deterioration and can result in significant morbidity (3–5). While AEDs may control seizures in some patients, most have systemic side effects that are unfavorable and often fail to totally control seizures, even at higher doses. Despite these clear effects on quality of life, seizure control continues extremely underappreciated in patients with brain tumors, with most neurooncological trials focused on recurrence and survival. Several studies have now recorded beneficial seizure outcomes after brain tumor resection, indicating that surgical variables may play a significant role in tumor-related seizure control. However, variables associated with seizure control stay incompletely understood owing to patient diversity and small sample size (6).

While oncological control is typically the main focus of brain tumor surgery, attaining seizure control is also a critical objective in patients with intractable epilepsy to enhance quality of life. This is particularly true for patients with low-grade tumors, who can survive for many years or decades. Approximately 60-90% are made seizure-free after tumor resection, with the most favorable seizure results seen in glioneuronal tumor patients (3).

Post-operative seizure control patterns are poorly understood (7,8). A better knowledge of treatment-response patterns for brain tumor related epilepsy is crucial for the implementation of rational treatment strategies, including timing of withdrawal of AED therapy and discussion of lifestyle problems such as fitness to drive (8).

Although there are many reports from around the globe about the postoperative seizure outcome of brain tumor-related seizure patients, very few African studies have been released on this topic. Most of these researches have shown comparatively excellent results in line with other non-African researches (9,10). So in this study, we aimed to evaluate seizure results and factors that are significantly associated with seizure control after brain tumor surgery in patients who initially had seizure in low-income set up.

1.2. Statement of the problem

Epilepsy is a major public health issue affecting over 50 million people worldwide, more than 80% of whom were living in developing countries (11). One of the highly affected regions is African countries, and it is estimated that ten million people live in Africa with epilepsy(12).

Similarly, Ethiopia is affected by epilepsy with a reported prevalence of 5.2/1000 population and 64 per 100,000 population annual incidence (13,14). Patients with epilepsy have poor health outcomes, including increased psychological distress, depression, anxiety, job restriction, more physical injuries such as fractures and burns, and increased risk of premature death with a mortality risk of 1.2-9.3 of all causes of death and a long-term fatality rate of 24% (15,16). In addition, epileptic seizures have devastating social consequences, leading to poor quality of life and stigmatizing, discriminating and excluding people with epilepsy from society (15,17). There are many recognized risk factors for epilepsy ranging from head injuries at birth to those at any age, to chromosomal / genetic syndromes, as well as multiple inborn metabolism errors, CNS tumors or infections, etc.(11).

Brain tumors, mostly low grade tumors, are associated with epilepsy in more than a half of cases (3,18) and are the second most common cause of focal intractable epilepsy in epilepsy surgery series (2,19). Brain tumor-related epilepsy is usually controlled unsatisfactorily by antiepileptic drugs, while excellent results can be achieved through surgery (20–24). Brain tumors represented 1-10% of structurally associated epilepsy in sub-Saharan Africa (25,26) is comparable to those observed in industrialized nations (27). More cases of epilepsy secondary to cerebral tumors are becoming evident with the introduction and installation of CT in some tertiary institutions in several sub-Saharan African countries. Although there are many retrospective studies conducted around the world on postoperative seizure control of patients with brain tumors associated epilepsy, there are few published studies from the African continent and there are no systematic Ethiopian studies published on postoperative seizure outcome after brain tumor resection.

1.3. Significance of the study

This study will try to assess the effects of surgical resection on the control of seizures in patients with seizure associated with brain tumors in a low income setup. It will also attempt to describe some of the variables that influence the seizure control after surgical resection. This in turn helps for the implementation of rational treatment strategies, including timing of withdrawal of AED therapy. It is the hope of researchers that the results of this study will fill some of the perceived gap in Sub-Saharan Africa's postoperative seizure control literature and might serve as a preliminary study to encourage future prospective studies in this area.

2. Literature Review

The incidence of brain tumors is around 4% (28) in patients with epilepsy. Depending on the type of tumor (4,28) the rate of epilepsy is 30% or more of patients with brain tumors. An epileptic seizure is the presenting clinical sign of a tumor for 30% to 50% of brain tumor patients; 10% to 30% will develop seizures later in the course of the illness (2).

In patients with primary brain tumors, the lifetime risk of epileptic seizures differs by age, tumor grade, location, and size. In high-grade brain tumors such as glioblastoma and primary CNS lymphoma, the incidence of preoperative seizure is smaller but greater in some lower-grade tumors. The likelihood of developing epilepsy varies from 10% in primary CNS lymphomas to 100% in dysembryoblastic neuroepithelial tumors (DENTs). In up to 90% of patients with low-grade gliomas, 20-50% of meningioma, and 30-45% of patients with high-grade glioma, epilepsy was reported. In patients with tumors situated in cortical regions as opposed to subcortical areas, seizures also happen more frequently, with a seizure frequency of 56% compared to 15% (3,4).

In the frontal and temporoinsular areas, preoperative seizure incidence is highest in gliomas. Sup ratentorial meningiomas, primarily convexity and parasagittal, and peritumoral edema were disco vered to be associated with the highest risk of seizures (2,3,29).

Pathogenesis of BTRE remains poorly understood, but it seems to be multifactorial. In order to promote epileptogenesis, local inflammation, hypoxic-ischemic injury, metabolic changes and disruption of blood-brain barrier (BBB) were suggested (4,19).

Seizure semiology represents primarily the location of the lesion and would manifest as focal-conscious, focal impaired-conscious, generalized tonic–clonic, or focal to bilateral tonic–clonic seizures (4,30). Overall, the form of seizure in brain tumors is defined as partial or localization-related epilepsy and differs between simple partial seizures in 23%-58%, complex partial seizures in 7%-31%, and generalized secondary seizures in 10%-68% (31). Thus, even patients with a generalized tonic-clonic seizure at presentation likely have a focal onset and can be classified as secondarily generalized tonic-clonic or focal seizures evolving to a bilateral, convulsive seizure.

There are currently no evidence-based guidelines for brain tumor related seizure management. The general management of brain tumor related seizure needs an interdisciplinary approach with considerations for antiepileptic drugs (AEDs), concurrent chemotherapy, radiotherapy, and surgical intervention. AEDs are frequently BTRE's first line treatment. Generally speaking, the selection of a particular AED is based mainly on the type of seizure and the factors of the individual patient. Pharmacoresistant seizure, adverse effects, and prospective drug interactions between AEDs and chemotherapy drugs, however, often complicate brain tumor seizure management (2,31,32).

On the other hand, brain tumor surgery is not only aimed at improving survival by reducing tumor burden, but also at gaining control of seizure. Multiple retrospective studies have shown the effectiveness of tumor resections with positive postoperative seizures control reported in many literatures (20,21,23,33). Overall, about 60–90% are rendered seizure-free, with most favorable seizure outcomes in patients with glioneuronal tumors (3,4,32).

Many authors (2,7,8,31,34) demonstrate improved control of brain tumor related seizures after surgery. In 53–87% of LGG patients and in about 60–80% of meningioma patients with seizure, seizure freedom after surgery was reported. Long-term seizure freedom was noted in up to 94% of cases in slow-growing glioneuronal tumors such as gangliogliomas and dysembryoplastic neuroepithelial tumors (DNETs). 77% of patients became seizure-free 1 year after surgery in HGG patients with preoperative seizures.

There are many factors that appear to influence postoperative seizure control patterns described in the literature. Early surgery, extent of tumor resection, type of tumor are important factors in achieving seizure freedom, especially for intra-axial tumors (8,35–37).

Chang et al, evaluated 269 adult LGG patients with seizure retrospectively to determine the seizure features and the frequency of seizure control. They discovered seizure freedom rates of 67% for both 6 and 12 months. Poor control of seizures was more prevalent in patients with longer (> 1 year) history of seizures ($p < 0.001$), uncontrolled preoperative seizures, and simple partial seizures ($p= 0.004$) (38).

Another study was retrospectively done by You et al. on 508 patients with LGG from whom 69% had seizure. A seizure control (Engel class I) at 6 and 12 month was observed in 65.3 % and 62.5% respectively. The factors associated with postoperative seizure control were secondary generalized seizure type ($P = .003$), simple partial seizure type ($P = .001$), partial and generalized seizure type combination ($P = .037$), temporal lobe location ($P < .026$) with MRI edema ($P = .043$) and calcification ($P = .034$), resection extent ($P < .0001$) (39).

Englot et al. (6) performed a systematic review of seizure results in 773 patients from 20 research following surgical resection of low-grade brain tumors. The authors of the study found that 71% of patients were seizure-free (Engel Class I). Higher seizure freedom rates were achieved in patients with ≤ 1 year seizure duration (OR 1.85, 95% CI 1.22–2.79), GTR (OR 3.41, 95 % CI 2.36–4.93), and in patients whose seizure was preoperatively controlled by AEDs (OR 2.12, 95 % CI 1.33–38). There was no significant difference between temporal and extratemporal tumors or with the use of intraoperative electrocorticography (ECoG) in the epilepsy outcome.

In 2012 Southwell et al. has reported seizure freedom rate of 85% among ganglioglioma following surgery and in similar other study Chang et al. reported seizure freedomrate of 87%among DNETs after resection. They concluded that the most important predicting factor for seizure freedom was gross total resection (21,33).

Chow and others (1995) (3) conducted a retrospective study of 323 patients undergoing surgery for meningioma: 98 (30%) had seizure. Seizure freedom was observed postoperatively in 67% of individuals, and this result was more common in patients with less peritumoral edema. Another series reported by Lieu and Howng (2000) (40) also supports the relationship after meningioma resection between increased brain edema and persistent seizures.

In other studies like Chaichana et al. (2013) (34), Zheng et al. (2013) (41) and Wirsching et al. (42) the postoperative seizure freedom after resection of supratentorial meningioma were 90%, 63.9% and 59.1% respectively. Uncontrolled preoperative seizures ($P= 0.04$) and new postoperative neurologic deficit (OR= 4.327) were predicting factors associated with poor seizure control. The most striking finding was that the frequency of preoperative seizure, tumor location and extent of tumor removal were not significantly related with seizure outcome. This directly contradicted several other studies' results.

Additionally, 128 patients with supratentorial brain tumor and preoperative seizure were retrospectively analyzed by Sitthinamsuwan et al. (2017) (43) to assess seizure outcomes and factors that correlate with seizure control following surgery. After surgery, the seizure freedom rate was 78 % with complete postoperative follow-up of more than one year. Factors contributing to seizure-free outcome in univariate analysis were older age at seizure onset, preoperative seizure duration ≤ 15 months, preoperative seizure frequency ≤ 1 episode per month, absence of cortical involvement, presence of hydrocephalus, tumor of non-glial origin, tumor of meningeal origin, absence of postoperative seizure, gross total resection, and lower number and shorter duration of postoperative use of AEDs.

The prevalence of epilepsy in African ranges from 2.2 to 58 per 1000 population and constitutes the second or third reason for consultation and hospitalization (44). In Ethiopia, epilepsy is a huge problem, which affects about 5.2 per 1000 population with an estimation of about 0.5 % of patients with active epilepsy (with seizers in the past 1–2 years) (13,14). Brain injuries, neurodevelopmental problems, and genetic predispositions that cause epilepsy in developed settings certainly result in epilepsy in developing countries as well (45). In addition, unique causes for epilepsy in developing and tropical settings must be considered. In some tropical settings, parasitic infestations are a common cause of epilepsy (45). Brain tumors represented 1-10% of structurally associated epilepsy in sub-Saharan Africa (25,26) is comparable to those observed in industrialized nations (27).

There are few publications/studies from Africa on the postoperative seizure outcome in patients with seizure and brain tumor. Mustafa et al. (10) from Egypt, prospectively assessed 54 patients with drug-resistant brain tumor related seizure to determine seizure result after treatment with resection of the epileptogenic cortex around the tumor by lesionectomy as recognized by intraoperative ECoG. According to Engel's seizure result scale, the author discovered that 77.8% (n= 42) of patients had excellent seizure control (classes I and II) and that 90.7% (n= 49) of patients had more than 75% decrease in seizures (class I –III) with average 40-month follow-up (range 6-72 months). Worthwhile seizure control was linked to gross total resection, which compares positively with other studies that showed that the extent of resection significantly predicts seizure freedom following surgery.

In order to determine predictive variables for postoperative seizure control, Morsy et al.(2019) (9), prospectively assessed 20 patients with seizure and meningioma. They discovered that there was excellent seizure control in 8 (40%) patients. Postoperative complications (P= 0.0194) were factors substantially associated with poor seizure control. The relationship between tumor side, tumor size, peritumoral edema, and tumor location and seizure control was not statistically significant.

3. Objective

3.1. General objective:

To assess postoperative seizure status and associated factors among brain tumors patients with seizure

3.2. Specific objective:

To determine magnitude of seizure status after surgical resection among brain tumors patients with seizure

To identify factors affecting postoperative seizure status after surgical resection among brain tumors patients with seizure

4. Methodology

4.1. Study setting and design

A hospital based multi-center retrospective cross-sectional study on postoperative seizure status among patients with brain tumor related seizure who underwent brain tumors surgery was done.

The study was conducted at three institutions, Tikur Anbessa Specialized Hospital (TASH), Zewditu Memorial Hospital (ZMH) and Myungsung Christian Medical Center (MCM), that provided a comprehensive specialized neurosurgical care in Addis Ababa, the capital city of Ethiopia. Tikur Anbessa Specialized Hospital which is the largest public tertiary referral teaching hospital in the country. Its neurosurgical unit, the first in the country, is currently run by nine consultants involved in providing care to a spectrum of neurosurgical conditions. The unit currently has 6 operating tables per week and around 30 elective neurosurgical procedures are performed in a typical month. This center also serves around 600 outpatient visits per month. Zewditu Memorial Hospital (ZMH) is one of public hospital with affiliations to the neurosurgical unit of TASH. On the other hand, Myungsung Christian Medical Center (MCM) is a privately owned teaching center with affiliations to the neurosurgical unit of TASH. This center also accepts referrals from different parts of the country.

4.2. Study period

The study was conducted from April 1, 2020 to August 20, 2020

4.3. Source and study population

Source population

All neurosurgical patients who underwent surgery for brain tumor in three selected hospital in Ethiopia.

Study population

All neurosurgical patients who underwent surgery for brain tumor in three selected hospital in Ethiopia from January 1, 2015 to December 31, 2019 with a minimum follow up period of 3 months post-surgery were reviewed retrospectively.

4.3.1. Inclusion criteria

All adult patients who had undergone surgical resection of brain tumors with preoperative seizure at the previously mentioned hospitals in the stated study period and those who had sufficient information in the medical record, including at least a tumor pathology report, an operative report, and imaging report were included in the study.

4.3.2. Exclusion criteria

Patients with missing medical records

Patients who did not have follow-up for at least 3 months postoperatively

Patients for whom only biopsy was done

Patients who did not have preoperative seizure

Patients who underwent previous brain surgery

Patients with multiple brain lesions

Patients with infratentorial lesions

Patients with sellar/suprasellar lesion and pituitary hormone abnormality

4.3.3. Sampling method

All patients fulfilling the inclusion criteria during the study period were enrolled in the study by using convenience sampling.

4.4. Study variables

1. Independent variables:-age, sex, tumor location, tumor pathology, seizure type, seizure duration, extent of resection, radiologic characteristics, and postoperative surgical complications. Seizures were classified as focal aware (simple partial), focal impaired awareness (complex partial), generalized, and focal to bilateral seizure (secondary generalized), as recommended by the International League Against Epilepsy (46).

2. Dependent Variable:-seizure status at final follow up by using the Engel classification of seizures (class I: seizure-free; class II: rare seizures; class III: meaningful seizures improvement; and class IV: no seizure improvement or worsening) (47).

4.5. Operational definitions

1. Epilepsy is defined, according to criteria of the International League Against Epilepsy (ILAE), as a single seizure with a probability of 60% for a second seizure within 10 years. (If there is any epileptiform discharge on EEG, or a potential epileptogenic structure on brain imaging, the probability of recurrent epileptic seizure exceeds 60%) (48).
2. Neurological deficit is deficits attributable to a focal cerebral lesion but not headache or seizures (42).
3. Perilesional edema is defined as hypo-density on CT scans or as T2 hyper-intensity on MRI scans (42).
4. Extent of resection is designated as gross total or subtotal resection as recorded from postoperative imaging or as determined by the surgeon’s intraoperative impressions (39,42).

5. Gross-total resection is defined based on the lack of residual tumor intraoperatively and/or absence of contrast enhancement on postoperative CT or MRI scans (6,49).
6. Postoperative surgical complications are defined as any infarction, edema, intracranial hematoma, CNS infection or new postoperative neurologic deficit, and recraniotomy for hematoma, abscess or brain swelling (42).
7. Early postoperative seizure defined as those appearing within the first week after surgery (41,42).
8. New postoperative neurological deficits are defined as neurological deficits or deterioration of neurological function first appearing during postoperative period due to surgical injury (cerebral or vascular) or cerebral edema (41).
9. The Engel Epilepsy Surgery Outcome Scale has four class depending seizure occurrence and frequency after surgery for refractory epilepsy (See Annex IV)
10. Preoperative seizure control is defined as the complete absence of seizures in the 1 month before surgery with the use of AEDs, as previously published (34).
11. Preoperative uncontrolled seizure is more than one seizure in the month before surgery while being on treatment with a therapeutic level of AEDs (34).
12. Postoperative seizure freedom is defined based on patient self-reporting, without confirmatory electrophysiological testing (6).

4.6. Data collection and analysis

The data was collected from patients' medical records and in person/telephone interviews using a standardized questionnaire prepared by the principal investigator. The collected data was then cleaned and coded. The statistical analyses was performed using SPSS for Windows software (version 25.0; IBM SPSS, Armonk, NY, USA).

Participants' socio-demographic characteristics, seizure history, radiographic characteristics, histopathologic diagnosis, treatment, preoperative and postoperative antiepileptic drug use data were analyzed using the relevant descriptive statistics. For outcome analyses, Engel classification of seizure was dichotomized as class I (completely seizure free or controlled seizure) versus class (es) II–IV (not seizure free or uncontrolled seizure). Univariate analyses were carried out using the Fisher exact test, Pearson chi-square test, as well as exact chi-square test when appropriate for categorical variables, and the Mann–Whitney U-test for continuous nonparametric data. Multivariate analyses were performed by entering variables with a p value < 0.25 from previous univariate analyses into a backward stepwise logistic regression. Strength of association was evaluated using adjusted odds ratio (AOR) and 95% confidence interval (95% CI). A *p*-value of less than 0.05 was considered statistically significant.

4.6. Ethical consideration

The study was conducted in accordance with the ethical principles stated in applicable guidelines on good clinical practice, whichever represents the greater protection of the individual. Ethical clearance was obtained from the Institutional review board (IRB) of AAU, medical faculty and respective hospitals.

5. Result

5.1. Socio-demographic characteristics of the study Participants

Among 146 cases of brain tumor patients with seizure who were considered for the study, 97 cases fulfilling the inclusion criteria were included in the study. Out of these 97 patients, 60 (61.9%) were female and 37 (38.1%) were male. The youngest patient was 14 years old, whereas the oldest patient was 76 years old, with a mean age of 41.7 years and median age of 39 years (SD = 13.5 years). Overall, 81.5% of patients were age of 30 years or greater. The details of sociodemographic characteristics of the study participants are presented in Table 1.

Table 1: Socio-demographic characteristics, of study participants in three selected hospitals, from January 1, 2015 to December 31, 2019 (n=97)

Sociodemographic variable		Postoperative seizure status: Total (n=97)	Seizure free (Engel class I) (n=64)	Not seizure free (Engel class II-IV) (n=33)
Sex	Male, n (%)	37 (38.1)	24(37.5)	13(39.4)
	Female, n (%)	60 (61.9)	40(62.5)	20(60.6)
Age in years, mean ± SD			42.8±13.9	39.9±12.6
Age in years	≤18, n (%)	2 (2.1)	1 (1.6)	1 (3)
	19-29, n (%)	16 (16.4)	9 (14.1)	7 (21.2)
	30-39, n (%)	31 (32)	20 (31.3)	11 (33.3)
	≥40, n (%)	48 (49.5)	34 (53.1)	14 (42.4)

5.2. Preoperative Findings of Study Participants

The median seizure duration was 8 months (range 1 month to 16 years). The most common type of seizure was generalized tonic-clonic seizures (53.6%), followed by secondary generalized (23.7%), simple partial (15.5%), and complex partial seizures (7.2%). The seizures frequency was classified into 4 categories: weekly (≥ 1 seizure per week), monthly (≥ 1 seizure per month), yearly (≥ 1 seizure per year), and one seizure ever (only one seizure episode). Forty three patients (44.3%) had monthly seizures, 32 patients (33%) had yearly seizures, 12 patients (12.4%) had one seizure ever, and 10 patients (10.3%) had weekly seizures. At the time of the surgery sixty three patients (64.9%) were taking AEDs with median duration of AEDs of 4 month (range 10 days to 7years). Overall, 43 patients (44.3%) had a history of controlled seizures and 54 patients (55.7%) had seizures that were not controlled preoperatively.

At presentation, about 85 % of patients had headache and about 46% had associated neurologic deficit. The details about patterns of clinical presentation are described in Table 2.

Table 2: Preoperative seizure characteristics and associated sign and symptoms of study participants in three selected hospitals, from January 1, 2015 to December 31, 2019 (n=97)

	Postoperative seizure status		
Preoperative clinical variables	Total (n=97)	Seizure free (Engel class I) (n=64)	Not seizure free (Engel class II-IV) (n=33)
Preoperative seizure duration			
≤ 1year, n (%)	65 (67.0)	48 (75)	17 (51.5)
> 1year, n (%)	32 (33.0)	16 (50)	16 (50)
Seizure type			
Simple partial, n (%)	15 (15.5)	9 (14.1)	6 (18.2)
Complex partial, n (%)	7 (7.2)	2 (3.1)	5 (15.2)
Primary generalized, n (%)	52 (53.6)	39 (60.9)	13 (39.4)
Secondary generalized, n (%)	23 (23.7)	14 (21.9)	9 (27.3)
Seizure frequency			
1 seizure ever, n (%)	12 (12.2)	8 (12.5)	4 (12.1)
≥1/year, n (%)	32 (33.0)	26 (40.6)	6 (18.2)
≥1/month, n (%)	43 (44.3)	25 (34.1)	18 (54.5)
≥1/week, n (%)	10 (10.3)	5 (7.8)	5 (15.2)
Preoperative AEDs use			
Yes, n (%)	63 (64.9	42 (65.6)	21 (63.6)
No, n (%)	34 (35.1)	22 (34.4)	12 (36.4)
Seizure in 1 month before surgery (uncontrolled seizure)			
Yes, n (%)	54 (55.7)	29 (45.3)	25 (75.8)
No, n (%)	43 (44.3)	35(54.7)	8(24.2)
Associated sign and symptoms			
Headache, n (%)	82 (84.5)	55 (85.9)	27 (88.8)
Neurologic deficit, overall, n (%)	45 (46.4)	28 (43.8)	17 (51.5)
Motor weakness, n (%)	30 (30.9)	18 (28.1)	12 (36.4)
Language disturbance, n (%)	6 (6.2)	5 (7.8)	1 (3.0)
Visual deficit, n (%)	16 (16.5)	13(20.1)	3(9.1)
Cranial nerve deficit, n (%)	2 (2.1)	1 (1.6)	1 (3.0)

With regards to imaging (CT/MRI) characteristics, the extra-axial lesion (meningioma) were present in sixty-six patients (68%) with most common location being convexity (23.7%) followed by sphenoid wing/clinoidal (18.6%), and parasagittal/falx (17.5%). The intra-axial lesions accounted for 32% of patients. Of the intra-axial tumors, frontal lobe was involved in 11 cases, temporal lobe in 8 cases, while parietal involved in 4 cases. Tumors with contrast enhancement (96.9%), and edema (94.8%) were more common than tumors with cystic change (17.5%), and calcification (12.4%). See Table 3 for details.

Table 3: Preoperative radiographic characteristics of study participants in three selected hospitals, from January 1, 2015 to December 31, 2019 (n=97)

	Postoperative seizure status		
Preoperative Radiologic characteristics	Total (n=97)	Seizure free (Engel class I) (n=64)	Not seizure free (Engel class II-IV) (n=33)
Lateralization			
Right, n (%)	36 (37.1)	20 (31.3)	16 (48.5)
Left, n (%)	53 (54.6)	37(57.8)	16(48.5)
Midline/bilateral, n (%)	8 (8.2)	7 (10.9)	1 (3.0)
Location			
Extra-axial, n (%)	67 (69.1)	47 (73.4)	20 (60.6)
Intra-axial, n (%)	30 (30.9)	17 (26.6)	13 (39.4)
Extra-axial location (meningioma)			
Convexity, n (%)	23 (23.7)	16 (25.0)	7 (21.2)
Parasagittal/falx, n (%)	17 (17.5)	13 (20.3)	4 (12.1)
Sphenoid wing/clinoidal	18 (18.6)	12 (18.8)	6 (18.2)
Tuberculum sellae, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Olfactory groove/planum, n (%)	7 (7.2)	6 (9.5)	1 (3.0)
Others[a] , n (%)	3 (3.1)	1 (1.6)	2 (6.1)
Intra-axial location			
Frontal, n (%)	11 (11.3)	6 (9.5)	5 (15.2)
Temporal, n (%)	8 (8.2)	6 (9.5)	2 (6.1)
Parietal, n (%)	4 (4.1)	3 (4.7)	1 (3.0)
Occipital, n (%)		0 (0.0)	0 (0.0)
Others[b], n (%)	6 (6.2)	1 (1.6)	5 (15.2)
Perilesional edema			
Yes, n (%)	92 (94.8)	61 (95.3)	31 (93.9)
No, n (%)	5 (5.2)	3 (4.7)	2 (6.1)
Tumor size			
< 3 cm, n (%)	4 (4.1)	2	2
3-5 cm, n (%)	39 (40.2)	29	10
> 5 cm, n (%)	54 (55.7)	33	21
Tumor calcification			
Yes, n (%)	12 (12.4)	7 (10.9)	5 (15.2)
No, n (%)	85 (87.6)	57 (89.1)	28 (84.8)
Contrast enhancement			
Yes, n (%)	94 (96.9)	62 (96.9)	32 (97)
No, n (%)	3 (3.1)	2 (3.1)	1 (3)

[a]One lateral ventricle, and 1 tentorial. [b]Two frontotemporal, 1 fronto-parietal and 1 parieto-occipital

5.3. Surgical procedure

Gross total resection was performed on 80.4% of the patients (61 patients with extra-axial lesions and 17 with intra-axial lesions). Subtotal resection was performed on 19.6% of the patients. In 14 of 19 cases of STR, the lesion were intra-axial. Postoperative complications were relatively uncommon. The overall complication rate was 15.5% with the commonest complication being new postoperative weakness which occurred in 9.3% of the study participants. Recraniotomy (for ICH, abscess or brain swelling) and CNS infection were present in 5.2% of patients each. Nine patients (9.3%) experienced early postoperative seizure within 7 days following surgery. Only seven patients were received adjuvant radiotherapy and/ or chemotherapy. Details are presented in Table 4.

Table 4: Surgery and postoperative characteristics of study participants in three selected hospitals, from January 1, 2015 to December 31, 2019 (n=97)

	Postoperative seizure status		
Surgery and postoperative variable	Total (n=97)	Seizure free (Engel class I) (n=64)	Not seizure free (Engel class II-IV) (n=33)
Extent of surgery			
GTR, n (%)	78 (80.4)	58 (90.6)	20 (60.6)
STR, n (%)	19 (19.6)	6 (9.4)	13 (39.4)
Surgical complication	15 (15.5)	7 (10.9)	8 (24.2)
New weakness, n (%)	9 (9.3)	2 (3.1)	7 (21.2)
New CN deficit, n (%)	1 (1.0)	1 (1.6)	0 (0.0)
Intracranial hemorrhage	2 (2.1)	0 (0.0)	2 (6.1)
Language deficit, n (%)	3 (3.1)	2 (3.1)	1 (3)
Infarction, n (%)	2 (2.1)	2 (3.1)	0 (0.0)
Cerebral edema, n (%)	1 (1.0)	1 (1.6)	0 (0.0)
CNS infection, n (%)	5 (5.2)	2 (3.1)	3 (9.1)
Recraniotomy, n (%)	5 (5.2)	3 (4.7)	2 (6.1)
Early postoperative seizure			
Yes, n (%)	9 (9.3)	1 (1.6)	8 (24.2)
No, n (%)	88 (90.7)	63 (98.4)	25 (75.8)
Adjuvant therapy			
Radiotherapy, n (%)	5 (5.2)	2 (3.1)	3 (9.1)
Both radiotherapy and Chemotherapy, n (%)	2 (2.1)	1 (1.6)	1 (3.0)
No, n (%)	90 (92.8)	61 (95.3)	29 (87.9)

Histopathology

Meningioma was the most common histopathological type. All the tumors were primary brain tumors except two patients who had metastasis. Meningioma was found in 69 patients, LGG in

12, HGG in 11, metastasis in 2, colloid cyst and hemangiopericytoma in 1 patient each. Details are presented in Table 5.

Table 5: Tumor histopathology of study participants in three selected hospitals, from January 1, 2015 to December 31, 2019 (n=97)

	Postoperative seizure status		
Tumor histopathology	Total (n=97)	Seizure free (Engel class I) (n=64)	Not seizure free (Engel class II-IV) (n=33)
LGG, n (%)	12 (12.4)	5 (7.9)	7 (21.2)
HGG, n (%)	11 (11.3)	6 (9.5)	5 (15.2)
Meningioma, n (%)	69 (71.1)	49 (77.8)	20 (60.6)
Other[a] , n (%)	4 (4.1)	3 (4.8)	1 (3.0)
LGG			
Diffuse astrocytoma	5 (5.2	0 (0.0)	5 (15.2)
ODG, n (%)	3 (3.1)	2 (3.1)	1 (3.0)
Ependymoma , n (%)	1 (1.0)	1 (1.6)	0 (0.0)
Others[b], n (%)	4 (4.1)	3 (4.7)	1 (3.0)
HGG			
GBM, n (%)	8 (8.2)	4 (6.3)	4 (12.1)
Anaplastic Oligoastrocytoma, n (%)	1 (1.0)	0 (0.0)	1 (3.0)
Gliosarcoma, n (%)	2 (2.1)	2 (3.1)	0 (0.0)
Meningeal tumors			
WHO grade I, n (%)	62 (63.9)	46 (71.9)	16 (48.5)
WHO grade II, n (%)	6 (6.2)	4 (6.3)	2 (6.1)
WHO grade III, n (%)	2 (2.1)	0 (0.0)	2 (6.1)

[a]Two metastasis, 1 hemangiopericytoma, and 1 colloid cyst
[b]Three pleomorphic xanthoastrocytoma, and 1 pilomyxoid astrocytoma

5.4. Postoperative Seizure status and Factors Influencing Seizure Control

The median overall follow up duration was 6 months (range 3 months to 3 years). Overall at final follow up 64 patients (66%) were in Engel's class I (free of disabling seizures), 7 had class IV and 26 patients had class II and III Engel's score (Figure 1).

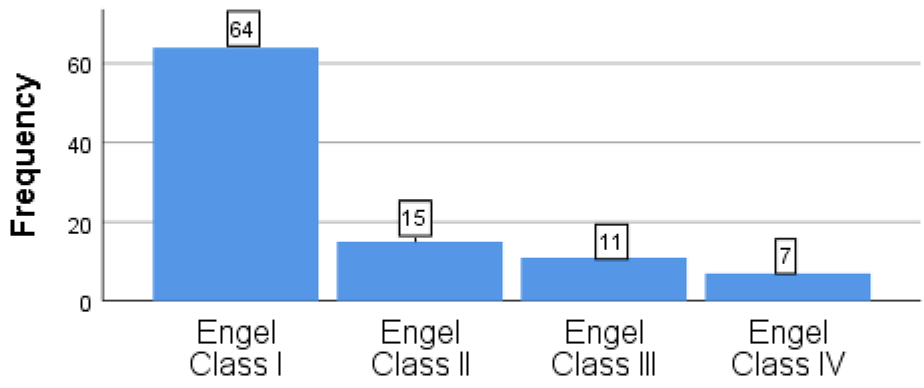

Figure 1: Bar graph showing the postoperative seizure status of study participants in three selected hospitals, from January 1, 2015 to December 31, 2019 at final follow up using the Engel classification (n=97)

In patients with meningioma the seizures control was 71% at final follow up. Moreover, in patients with intra-axial tumor only 53.5% patients gained Engel's class I (completely seizure free).

Among patients with controlled preoperative seizures, their occurrence was rare in the postoperative period, where only 18.8% of patients reported seizures at final follow up postoperatively (Figure 2). The majority of patients (81.8%) remained seizure-free (class I) postoperatively; 11.4% had rare seizures (class II), 4.5% had meaningful seizures (class III), and 2.3% patients had worsening seizures (class IV).

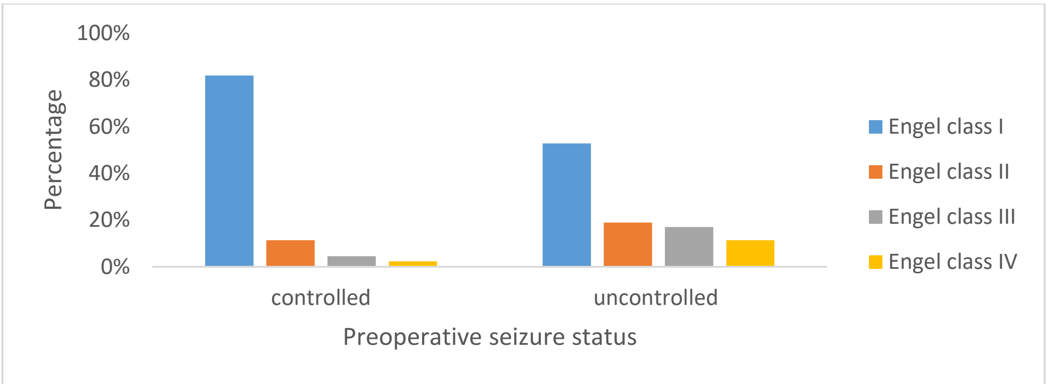

Figure 2: Graph illustrating postoperative seizure status (Engel class) stratified by preoperative seizure control of study participants in three selected hospitals, from January 1, 2015 to December 31, 2019 at final follow up (n=97).

The preoperative presence of uncontrolled seizures was associated with poorer postoperative seizure control.

To determine which preoperative factors influenced postoperative seizure status, outcomes were dichotomized as Engel I (completely seizure free or controlled seizure) versus Engel II–IV (not seizure free or uncontrolled seizure) at final follow up following surgery. Potential prognosticators were evaluated using a univariate analysis (Tables 6). Gross total resection and preoperative seizure duration ≤ 1 year associated with better control (*P*=0.001 and 0.024 respectively), whereas early postoperative seizure in the first week after surgery, presence of uncontrolled preoperative seizure, and new postoperative weakness were associated with uncontrolled postoperative seizure status (*P*=0.001, 0.005, and 0.007 respectively). Other factors related to lesion location, imaging characteristics, and histopathological characteristics as well as chemotherapy and radiation therapy were not associated with postoperative seizure control.

Table 6: Univariate predictors of postoperative seizure status of study participants in three selected hospitals, from January 1, 2015 to December 31, 2019 (n=97)

	Postoperative seizure status			
Variables	Total (n=97)	Seizure free (Engel class I) (n=64)	Not seizure free (Engel class II-IV) (n=33)	p-Value
Sociodemographic variable				
Sex				
Female, n (%)	60 (61.9)	40(62.5)	20(60.6)	1.000
Age in years, mean ± SD		42.8±13.9	39.9±12.6	0.260
Preoperative seizure characteristics				
Preoperative seizure duration				
≤ 1year, n (%)	65 (67.0)	48 (75)	17 (51.5)	.024*
Seizure type				
Simple partial, n (%)	15 (15.5)	9 (14.1)	6 (18.2)	.08
Complex partial, n (%)	7 (7.2)	2 (3.1)	5 (15.2)	
Primary generalized, n (%)	52 (53.6)	39 (60.9)	13 (39.4)	
Secondary generalized, n (%)	23 (23.7)	14 (21.9)	9 (27.3)	
Seizure frequency				
1 seizure ever, n (%)	12 (12.2)	8 (12.5)	4 (12.1)	.122
≥1/year, n (%)	32 (33.0)	26 (40.6)	6 (18.2)	
≥1/month, n (%)	43 (44.3)	25 (34.1)	18 (54.5)	
≥1/week, n (%)	10 (10.3)	5 (7.8)	5 (15.2)	
Preoperative AEDs use				
Yes, n (%)	63 (64.9)	42 (65.6)	21 (63.6)	.846
Seizure in 1 month before surgery (uncontrolled seizure)				
Yes, n (%)	54 (55.5)	29 (45.3)	25 (75.8)	.005*
Associated sign and symptoms				
Headache, n (%)	82 (84.5)	55 (85.9)	27 (88.8)	.768
Neurologic deficit, n (%)	45 (46.4)	28 (43.8)	17 (51.5)	.523
Preoperative Radiologic characteristics				
Location				
Extra-axial, n (%)	67 (69.1)	47 (73.4)	20 (60.6)	.247

Table 6 continued

Variable	Postoperative seizure status Total (n=97)	Seizure free (Engel class I) (n=64)	Not seizure free (Engel class II-IV) (n=33)	p-Value
Extra-axial location (meningioma)				
Convexity, n (%)	23 (23.7)	16 (25.0)	7 (21.2)	.587
Parasagittal/falx, n (%)	17 (17.5)	13 (20.3)	4 (12.1)	
Sphenoid wing/clinoidal	18 (18.6)	12 (18.8)	6 (18.2)	
Tuberculum sellae, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	
Olfactory groove/planum	7 (7.2)	6 (9.5)	1 (3.0)	
Intra-axial location				
Frontal, n (%)	11 (11.3)	6 (9.5)	5 (15.2)	.158
Temporal, n (%)	8 (8.2)	6 (9.5)	2 (6.1)	
Parietal, n (%)	4 (4.1)	3 (4.7)	1 (3.0)	
Occipital, n (%)		0 (0.0)	0 (0.0)	
Perilesional edema				
Yes, n (%)	92 (94.8)	61 (95.3)	31 (93.9)	1.000
Tumor size				
< 3 cm, n (%)	4 (4.1)	2	2	.340
3-5 cm, n (%)	39 (40.2)	29	10	
> 5 cm, n (%)	54 (55.7)	33	21	
Tumor calcification				
Yes, n (%)	12 (12.4)	7 (10.9)	5 (15.2)	.535
Contrast enhancement				
Yes, n (%)	94 (96.9)	62 (96.9)	32 (97)	1.000
Surgery and postoperative variable				
Extent of surgery				
GTR, n (%)	78 (80.4)	58 (90.6)	20 (60.6)	.001*
Surgical complication	15 (15.5)	7 (10.9)	8 (24.2)	.136
New weakness, n (%)	9 (9.3)	2 (3.1)	7 (21.2)	.007*
CNS infection, n (%)	5 (5.2)	2 (3.1)	3 (9.1)	.333
Early postoperative seizure				
Yes, n (%)	9 (9.3)	1 (1.6)	8 (24.2)	.001*
Tumor histopathology				
LGG, n (%)	12 (12.4)	5 (7.9)	7 (21.2)	.172
HGG, n (%)	11 (11.3)	6 (9.5)	5 (15.2)	
Meningioma, n (%)	69 (71.1)	49 (77.8)	20 (60.6)	
Other[a] , n (%)	4 (4.1)	3 (4.8)	1 (3.0)	

* *p*-value<0.05 indicates statistical significance

[a]Two metastasis, 1 hemangiopericytoma, and 1 colloid cyst

The strength of association between potential factors and seizure-free outcome as evaluated by multivariate analysis using a backward stepwise logistic regression is shown in Table 7. Of several analyzed variables, four factors were found to be significantly associated with seizure-free outcome. Gross total resection (adjusted OR 6.24, 95% CI: 1.79-21.71, P=0.004) and seizure duration ≤ 1 year before surgery (adjusted OR 3.60, 95% CI: 1.20-10.82, P=0.022) were significant independent predictors associated with better seizure control. Occurrence of postoperative weakness after surgery (adjusted OR 16.23, 95% CI: 2.57-103.09, P=0.003) and uncontrolled preoperative seizure (adjusted OR 4.69, 95% CI: 1.49-14.75, P=0.008) were found to be significant independent predictors associated with uncontrolled postoperative seizure status.

Table 7: Multivariate analyses of predictors for postoperative seizure status of study participants in three selected hospitals, from January 1, 2015 to December 31, 2019 (n=97)

Variables	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Gross total resection	6.28 (2.12-18.74)	.001*	6.24 (1.79-21.71)	.004*
Seizure duration ≤ 1 year	2.82 (1.16-6.85)	.024*	3.60 (1.20-10.82)	.022*
Presence of postoperative weakness	0.12 (0.02-0.62)	.007*	0.06 (0.01-0.37)	.003*
Uncontrolled preoperative seizure	0.26 (0.10-0.68)	.005*	0.21 (0.07-0.67)	.008*

* *p*-value <0.05 indicates statistical significance
Abbreviations: CI, confidence interval; OR, odds ratio.
In addition to the variables listed in Table 7, the following variables were included in multiple backward binary logistic regression analysis: age in years, seizure type, seizure frequency, tumor side and location, tumor histopathology, surgical complication and early postoperative seizure.

At final follow up after surgery, 11.3% of the study population no longer required the use of AEDs. The remaining 88.7% of the study population continued to take AEDs after surgery; of this group, 38.4% continued to experience seizures while taking medications. Although this was a relatively high rate of postoperative AED use, it should be noted that AEDs were typically discontinued at the discretion of the outside referring physicians. Thus, it was difficult for us to assess whether seizure-free outcomes depended on the ongoing use of AEDs. Use of AEDs is thus unlikely to be a good surrogate indicator of the effectiveness of surgery.

6. Discussion

Many patients with brain tumor have seizure as a primary clinical presentation. Uncontrolled and frequent seizures impair patient quality of life. Radical tumor resection without risk of additional neurological damage is the surgical objective. Tumor resection relieves compressive symptoms caused by the tumor, delays tumor growth, improves survival, and achieves postoperative seizure control (38). In patients with medically intractable seizure, concurrent resection of both the tumor and epileptogenic brain tissue renders significantly better seizure control than tumor resection alone (1).

In this retrospective study, we have documented postoperative seizure status and the factors associated with postoperative seizure control in patients with brain tumor and seizure. We present a first series of patients with brain tumor and seizure who were treated at three teaching hospital, in central Ethiopia.

In our study, the rate of seizure freedom after brain tumor surgery was 66%, which is comparable to the 60 to 90% seizure freedom rates reported in previous studies (3,4,32,38). Overall, 88% of the population continued to take AEDs at final follow up after surgery, a rate roughly comparable to that observed in another series (33). We identified four important factors significantly associated with freedom from seizures: controlled preoperative seizure, gross total resection, seizure duration ≤ 1 year, and absence of postoperative weakness.

We observed a statistically significant association between the extent of tumor resection and seizure outcome, with GTR being associated with greater rates of seizure freedom than STR. The present study is consistent with previous studies that have also reported better seizure outcomes after GTR than STR (33,38,43). From our review of the literature, radiotherapy and chemotherapy also influence seizure outcome. Chemotherapy was found to be beneficial for seizure reduction, with seizure freedom observed in some patients (39). Kahlenberg et al reported valuable effect of radiation ($p = 0.02$) and chemotherapy ($p = 0.03$) for seizure control. Patients with presurgical seizures who received radiation or chemotherapy had significantly better seizure outcomes than those who did not (35); however, these correlations were not observed in our study, possible because the number of patients who received chemo-radiotherapy were too small for statistical comparison.

Regarding duration of preoperative seizure, our result was similar to that of the other studies that reported significantly higher rates of seizure-freedom in patients with <1 year duration of seizure (6,49). Our study showed that seizure duration ≤1 year was significantly associated with favorable outcome (AOR 3.60, 95% CI: 1.20-10.82, P=0.022). This may argue for earlier resection of brain tumors associated with seizures even when other clinical factors (small lesion or lack of progression on neuroimages) do not suggest a need for early surgery.

Some previous studies reported preoperative seizure control as a predictor of seizure outcome after brain tumor resection (29,34). Our study also found that the patients with poorly controlled preoperative seizures were more than four times likely to have seizure recurrence after surgery. This propensity for seizure recurrence, regardless of extent of resection, may be due to the lowered seizure threshold for these patients. This lowered threshold may make it easier for precipitating factors to elicit seizures (29). This may also emphasize the need for early surgical resect of tumors at risk of causing seizures and appropriate preoperative seizure control bring about better seizure outcomes.

In our study, the presence of new postoperative weakness was a significant factor correlated with poor postoperative seizure control. This has been seen in other studies as well (41). Intraoperative injury due to excessive brain retraction or sacrifice of major draining or bridging veins may induce new postoperative weakness, which in turn increase the risk of postoperative seizures (41). Chozick et al. (29) reported that irreversible surgical complication was significantly related to postoperative seizures by univariate statistics, but not by multiple logistic regression statistics. We suggest that reducing surgical cerebral or vascular injury may lead to better long-term seizure outcome.

Previous studies have observed an association between preoperative seizure types and postoperative seizure outcomes. A lower rate of seizure freedom after surgery was correlated with presence of simple partial seizure (OR: 0.46, 95% CI: 0.26 to 0.80; $p = 0.002$) (6) and secondarily generalized seizure (OR: 0.40, 95% CI: 0.24 to 0.66; $p<0.001$) (49). The same was observed by Radhakrishnan et al. (2016) in cases of brain tumor related seizure, those with pre-operative secondary generalized seizures had less favorable seizure outcome (20). In the present study, we observed no statistical association between preoperative seizure types and postoperative seizure outcomes, again possible because the number of patients with seizure of certain types was too small for statistical comparison.

The relationship between tumor location and seizure-free outcome is variable. Radhakrishnan et al reported significant unfavorable outcome in temporal location of long-term epilepsy-associated brain tumor ($p = 0.008$) (20). Other studies (including the present study) found no association between tumor location and seizure outcome (6,10,38,41,49), and we found no significant association between specific location of tumor and seizure outcome, possible because the number of patients with tumors at certain sites was too small for statistical comparison.

Furthermore, in our study, patients with extra-axial tumor tended to have seizure-free outcome, because most of the extra-axial tumors were meningioma, with seizure freedom being achieved in 48 of 67 meningioma patients (71.6%) which is comparable with other studies (3,41). In contrast, most of the intra-axial tumors in our study were glioma, with seizure freedom being achieved in only 15 of 28 patients (53.6%) which is lower than those reported in the study by Chang et al (2008) (38), which reported 67% seizure free after supratentorial surgery for gliomas, and it may be because we have no intra operative monitoring and electrocorticography facilities. However, this difference in tumor locations did not achieve statistical significance.

Some studies also reported a significant relationship between the frequency of preoperative seizures and the occurrence of postoperative seizures (43), but, as in our study, others have not observed such correlation (41), a discrepancy that may be explained by the different primary etiologies of seizure in these patient groups (meningioma versus non-meningioma).

7. Limitations of the study

The retrospective nature of the study was associated with inherent problems related to data quality, selection bias, and lower chart retrieval rates. We have tried to mediate these problems by using in-person or in-depth phone interviews to complement the Engel scores calculated from follow-up notes documented in the patients' charts. Additionally, we tried to create a uniform patient population by using strict inclusion and exclusion criteria. However, this resulted in small number of sample size which made it difficult to detect statistical differences in seizure outcomes between the various grouping variables. Furthermore, the present series represented a broad range of tumor locations (extra-axial and intra-axial), which makes its comparison to other case series more difficult. Despite these limitations, we believes that this study provides credible contributions as it is the first of its kind in Ethiopia.

8. Conclusion

In this retrospective study, we have demonstrated that surgical resection is an effective means of reducing seizure burden on patients with brain tumors and seizure. Approximately two third of patients with brain tumor and seizure became seizure-free after surgery. Independent factors significantly associated with the seizure-free outcome included gross total resection, preoperative seizure duration of ≤1 year, and controlled preoperative seizure. The emergence of new postoperative weakness is a major risk factor for poor postoperative seizures control, underscoring the importance of cerebral or vascular injury in postoperative seizure outcome. Furthermore, with an increase in more cases of epilepsy secondary to cerebral tumors with the introduction and installation of CT in some tertiary institutions in several sub-Saharan African countries, the importance of predicting seizures and seizure control is more apparent.

9. Recommendations

Based on our findings, we recommend that strict control of preoperative seizure and total resection of the tumor be done in patients with brain tumors and seizure. Additionally, reducing cerebral or vascular injury during surgery is of paramount importance.

Emphasis should also needs to be given to early surgical intervention to achieve a better postoperative seizure control. Thus, an early identification of structural alterations associated with seizure, followed by a prompt referral to neurosurgical centers, provides the best chance for curing seizure.

We also encourage future large scale multicenter well-designed prospective studies with long follow up to be done on this area. This will answer many provoking questions raise by this research, including when to discontinue AED after surgery.

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ANNEX I: Questionnaire

Questionnaire for institutional based study on postoperative seizure outcome in brain tumors patients with epilepsy

I. Socio-demographic data

1. Name……………………………..	5. Hospital……………………………
2. Card no. …………………..	6. Phone no ……………………….
3. Age ……………	7. Occupation. ………………………..
4. Sex ………..	8. Address……………………………

II. Preoperative status

Seizure history

1. When was the first seizure onset (duration of seizure in months)? -------------------
2. Seizure type 1. Simple partial (focal aware seizure) 2. Complex partial (focal impaired awareness seizure) 3. Secondary generalized (focal to bilateral tonic-clonic) 4. Generalized seizure 5.unkown onset
3. Any anti-epileptic drug use? 1. Yes _________ 2. No.

   If yes since when? ______ and Type of AEDs used _____________________

4. Seizure frequency 1. One seizure ever 2. ≥1/year 3. ≥1/month 4. ≥1/week
5. Seizure in the last 1 month before operation? 1. Yes 2. No.

Associated sign and symptoms

1. Headache

2. Neurologic deficit 1, YES 2. NO. if yes what is/are the deficit

I. Motor weakness

II. Cranial nerve deficit ___________

III language deficit

IV. Visual deficit

V. sensory deficit

III. Tumors radiographic characteristics

1. Locations and lateralization 1. right 2. left 3. midline/bilateral

2. Imaging diagnosis 1. meningioma (extra-axial) 2. intra-axial tumors__ 3. Others------------

-If intra-axial 1. Frontal 2. Temporal 3. Parietal 4. Occipital 5. others (specify)__________

-If meningioma (extra-axial) 1. convexity 2. parasagittal/falx 3. Sphenoid wing/clinoidal

4. tuberculum sella 5. olfactory groove/planum

6. others (specify)

3. Size maximum diameter 1. <3cm 2. 3-5cm 3. >5cm

4. Contrast enhancement 1. Yes 2. No

5. Peritumoral edema 1. Yes 2. No

6. Tumor calcification 1. Yes 2. No

7. Cystic component 1. Yes 2. No

IV. Surgical treatment

Date of surgery ___________________

Extent of resection 1. Gross total resection (GTR) 2. Subtotal resection

Simpson grade for meningioma 1. I 2. II 3. III 4. IV

V. Tumor pathology (histology) 1. Astrocytoma 2. oligodendroglioma 3. Oligoastrocytoma
. 4. Meningioma 5. Ganglioglioma 6. DNETs 7. Others ______________________

WHO grade of the tumor 1. I 2. II 3. III 4. IV

VI. Postoperative status

1. Surgical complications 1. Yes 2. No

If Yes what are/is the complication?

1. New post-op weakness 2. New CN deficit 3. New language deficit 4. Intracranial Hemorrhage 5. Infarction 6. Cerebral edema 7. CNS infection (meningitis, ventriculitis, or brain abscess) 8. Recraniotomy (for ICH, absecess, or brain swelling)

2. Early postoperative seizure in the hospital 1. Yes 2. NO

3. Adjuvant therapy 1. chemotherapy 2. radiotherapy 3. No

4. Postoperative AEDs use 1. YES 2. NO.

If yes what type of AEDs? _______________________________

5. Seizure status at final postoperative follow up

(Engel Outcome Scale*) encircle on class*

Class I- Free of disabling seizures

Seizure free or no more than a few early, nondisabling seizures; or seizures upon drug withdrawal only

Class II - Rare disabling seizures ("almost seizure-free")

Disabling seizures occur rarely during a period of at least 2 years; disabling seizures may have been more frequent soon after surgery; nocturnal seizures

Class III - Worthwhile improvement;

Seizure reduction for prolonged periods but less than 2 years

Class IV- No worthwhile improvement; some reduction, no reduction, or worsening are possible

ANNEX II: Engel Outcome Scale

(**Engel Outcome Scale) Epilepsy Surgery Outcome Scales**

Class I**:** Free of disabling seizures
- IA: Completely seizure-free since surgery
- IB: Non disabling -simple partial seizures only since surgery
- IC: Some disabling seizures after surgery, but free of disabling seizures for at least 2 years
- ID: Generalized convulsions with antiepileptic drug withdrawal only

Class II: Rare disabling seizures ("almost seizure-free")
- IIA: Initially free of disabling seizures but has rare seizures now
- IIB: Rare disabling seizures since surgery
- IIC: More than rare disabling seizures after surgery, but rare seizures for at least 2 years
- IID: Nocturnal seizures only

Class III: Worthwhile improvement
- IIIA: Worthwhile seizure reduction
- IIIB: Prolonged seizure-free intervals amounting to greater than half the follow-up period, but not less than 2 years

Class IV: No worthwhile improvement
- IVA: Significant seizure-free reduction
- IVB: No appreciable change
- IVC: Seizures worse

From: Surgical Treatment of Epilepsies, 2nd Edition. Engel J., Editor. Raven Press, 1993. Page 615.