ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE, DEPARTMENTS OF SURGERY,

NEUROSURGERY UNIT

ADDIS ABABA, ETHIOPIA.

Research ON

PROSPECTIVE STUDY ON 30 DAY COMPLICATIONS OF INTRACRANIAL MENINGIOMA SURGERY

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Research proposal submission form

Name of investigator	Dagmawi Sileshi(Dr.)
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List of Abbreviations

CN	**Cranial nerve**
CT	**Computed tomography**
DVT	**Deep vein thrombosis**
EBL	**Estimated blood loss**
ICP	**Intracranial pressure**
GTR	**Gross total resection**
KPS	**Karnofsky performance score**
MRI	**Magnetic resonance imaging**
MCM	**Myungsung chrstian medical**
TASH	**Tikur anbessa specialized hospital**
Pre-op	**Preoperative**
Post-op	**Postoperative**
PE	**Pulmonary embolism**
STR	**Subtotal resection**
VTE	**Venous thromboembolism**
ZMH	**Zewditu memorial hospital**

Abstract

Background: Meningioma is the most common primary intracranial tumor. Even though different management options exist in modern medicine, surgery is still the only cure for this benign tumor. Surgical options are not without risk. Identifying and predicting the short-term complications in an Ethiopian setup might be useful in the decision-making process before surgery for our patients. This study uses a prospective design that aims to assess 30 days of post-operative complications of intracranial meningioma.

Methods: Aprospective study that was conducted at TASH, ZMH & MCM hospital between November 1, 2019, and September 1, 2020. Assessment of postoperative complications was determined in-person using a standard questionnaire in both inpatient & outpatient setup. For the investigation, pathology & Intraoperative findings data were collected from medical charts, radiology, and pathology archives.Data were checked for completeness and quality control after which, it was entered on SPSS version 21 for analysis using logistic regression.

Results:A total of 77 patients were enrolled in the study. The mean age of the patients was 40.94 years. 71 (92%) patients presented with headache and 62 (80.5%) patients had one or more focal neurologic deficits. Tumor was classified based on location and size. 47 (61%) of the tumors were skull base tumors.The surgical mortality rate which was defined as death within one month was 9.1%. Among all patients, 37 (48.1%) had one or more postoperative complications of which new-onset or worsened focal deficit was the commonest. A significant association was seen between skull base tumors and postoperative complications in both bivariate and multivariate analyses witha p-value of 0.01 (OR=5.79, 95% CI: 2.061-16.312.

Conclusion: Even though the complications and mortality rates were high, surgery led to symptom improvement in a large proportion of patients. Skull base meningioma, anesthesia time more than 5 hours, and blood loss more than 1000ml hada significant association with postoperative complications.

1. Introduction

1.1 Background

Meningioma is the most common primary intracranial tumor. The oldest paleopathological evidence of a hyperostotic meningioma is a skull excavated in southwestern Germany estimated to be 365000 years old (1). The first documented attempt at surgical removal of convexity meningioma took place in the eighteenth century (1). Meningioma account for 33.8% of all primary brain tumors reported in the USA between2002-2006 (2).The incidence peaks in the 3rd to 6th decade and shows female predominance with female to male ratio of2:1.60–70% occur along the falx (including parasagittal), along sphenoid bone (including tuberculum sellae), or over the convexity(2).

There are 15 histologic subtypes arranged as WHO grade 1 up to 3. Based upon the pathogenicity, most are benign or WHO grade 1 lesions. Common presentations of meningioma are seizures, headache, behavioral and personality change, confusion, and focal neurologic deficit depending on the location of the tumor.

Surgery is the main treatment modality of this benign tumor which offers the possibility of a cure. Nevertheless, surgery may cause significant complications. Counseling the patient and the family as well about the anticipated clinical course, including the short-term risks, is needed. It is also true that following intracranial surgery, transient neurological deficits may occur. Due to the long-term treatment aim in patients with meningioma (i.e. cure), several studies are reporting on the long-term outcome of patients, but less information is available concerning short-term morbidity. Besides, there is a common dilemma in surgery, weighing the risk of short-term complications and neurological impairment against the natural history of the disease and long-term results. This scenario may be especially challenging and affect our clinical judgment for minimally symptomatic patients with presumed WHO grade I meningioma, where short-term benefit may need to be sacrificed to have a better chance of long-term cure.

Although there are worldwide reports on the complications and short-termoutcomes of meningioma patients, there are very few African studies published on this subject. These real-world data on short-term outcomes may be useful in the decision-making process before surgery for our patients.

1.2 Statement of the Problem

Although there are many retrospective studies concerning meningioma clinical outcomes (4, 12), prospective studies are scarce from the continent of Africa and particularly from Ethiopia.

Intracranial meningiomas are the commonest brain tumors operated in our hospitals (3) &despite the annual mortality & morbidity data we haveconcerning brain tumors, there are very few systematic studies published concerning 1-month postoperative complication of meningioma surgery(3).

We hope that the results of this study will yield an improved standard of care in the treatment of meningioma.

1.3 Significance of the study

This study will assess the 30-day post-operative complications of intracranial meningioma surgery in three Ethiopian hospitals. Wehave identified some of the factors associated with both good and poor surgical outcomes. We will also compare our results with other similar reported studies so that we can identify interventions that may result in improvement.Also, it can be used as a baseline study for future researches concerning short-term or long-term outcomes of meningioma surgery.

2. Literature Review

Intracranial meningioma is one of the oldest known tumors of mankind (1).). There have been many stages in the diagnosis and management of intracranial meningioma, since Harvey Cushing, describesthem in 1922 as most of the tumors are benign (2).

Surgery is the primary treatment modality for these tumors though other non-open surgical methodshave been developed recently(2).Since most of the histologic subtypes are benign, complete surgical excision is said to be the only curative way of management (1).

As stated above surgical treatment is curative, deciding on which types of meningioma consider total excision, which patients are true candidates, and is it worthy of doing the surgery anticipating the post-operative complications and outcome is always not straight forward & require further studies particularly in a set up where minimally invasive surgery, radiation, and chemotherapy areconsidered as luxury(6).

Many have studied the likelihood of complications in intracranial meningioma surgery. The consensus is that safe maximal resection witha short term goal of minimal surgical morbidity and mortality and a long term goal of arresting disease progression (2).

Post-operative complications after intracranial meningioma surgery depend on different factors including the patient's age, preoperative KPS, location & histopathology of the tumor, intraoperative findings, and type of surgery (14).

There are few studies from Africa on 30 days post-operative complications of meningioma surgery, particularly in our setup. In the study done in Ethiopia, at Black Lion Hospital in 2014, by Tsegazeab L et.al (3) ona 5-year retrospective study on Clinical Outcome of Operated Intracranial Meningioma in 91 patients, Tumor size was shown to be related to post-op functional outcome with a p-value of 0.032 and the surgical mortality rate was 14.3%, a higher rate than other internationalfigures. The re-operation rate of this study was 13.2% mainly due to post-operative hematoma and new-onset seizure seen in 10%.This paper also showed that 8% of patients had developed HAI, of which 5.5% was due to surgical site infection. The average duration of hospital stay of patients was 21 days. In another retrospective study done in the same center by Abat

Sahlu et.al (5) on the short term outcome of 100 skull base tumors, 10% of the patients died by the 6th post-operative month and 39% of patients had post-operative complications of Cranial infection, CSF Leak & new-onset neurologic deficit predominate. Eightof the patients required further surgery for hematoma, CSF leak, and inadequate tumor removal. Their rate of post-operative cranial infectionwas 14% and hospital-acquired pneumonia was seen in 2 patients. CSF leak in 11% and 8% of the patients were re-operated due to complications. They also reported that longer anesthesia time was significantly associated with the development of postoperative complications.

In regional retrospective research done by Wilfred C. et al. (6) In Nigeria and published in 2012, on the management of intracranial meningioma, GTR was achieved in 78.8% of patients and post-operative CSF leak, severe brain edema, and postoperative death occurred in 3.9% of patients. They also showed thatthe mean duration of hospital stay was 7.5 days.

A retrospective study in Mauritania, a retrospective study published in 2018 by kleib A.et al. (7), onthe outcome of 32 operated patients showed a mortality rate of 9.4%. The mean hospital stay of the patients was 13 days and Simpson grade 1 resection was achieved in 66% of patients. Even though the sample size is too small for a strong conclusion; this paper is from a country where most of the scenario is presumed to be similar to our country.

In another retrospective study done in Egypt by Aymen E.et.al. onSurgical outcomes and predictors of complication in elderly patients with meningioma, they reported a new onset neurologic deficit of 21.4%, significantlymore than other reports even though only 42 patients were included in this study(19).Total resection in skull base meningioma was associated with a higher incidence of morbidity. The mortality rate was 14.2%. Similar to other African papers most had tumors 4-5cm in diameter and amean hospital stay of 16 days.

In a retrospective study done in Sweden by Alba Corell et.al(4), the 30-day complication rate after 2324 operations for meningioma, 344(14.8%) developed new neurologic deficit, new-onset seizure occurred in 105(4.5%), reoperations due complications were performed in 120(5.2%) patients, VTE occurred in 3% and the post-operative 30-day mortality in the whole cohort was 1.5%(P=0.06) and 2.4% in patients with higher grade(WHO grade 2 & 3)meningioma(P=0.14). According to this research new or worsened neurological deficits were observed in 14% of Simpson grade 1, 12% of Simpson grade 2, 19% in Simpson grade 3, 25% in Simpson grade 4, and 28% in Simpson grade 5. This research has shown that 30-day mortality for higher histologic grade meningioma is different from WHO grade 1 meningioma's and also significant association was observed between Simpson grading and new-onset neurologic deficit (P<0.001). Retrospective studies (5, 6, and 7) had 8.3%- 10.8% post-operative deficit rates, and the range is wider and affected by tumor location and preoperative symptoms. Another study that supports the above finding was done by Andrew P. Jacob Z. et al in 2008, on Retrospective outcome of Surgery for convexity meningioma (8),in 163 operated patients for convexity meningioma over 20 years, there was no death recorded within 30 days, but 11 deaths recorded during the total follow up period (1-13 yrs.), of which all except 1 death were in patients aged 65 years or older, none of the mortality was related to the meningioma or surgery.

In another retrospective study of 257 consecutive patients who were diagnosed with intracranial meningioma at the Vancouver General Hospital (VGH) between 1960 and 1981, on morbidity, mortality, and quality of life following surgery (12), the new post-operative neurologic deficit was 10.8% andnew-onset post-op seizure was seen in 19%,ofwhich significant association was seen in convexity and Para-falcine meningioma. Reoperation was done for 3.1% of patients witha 30-day perioperative mortality rateof 4%.In this study, the new post-operative seizure and the 30-day mortality rate arehigher which can be explained by the small sample size and improvement in surgical and anesthetic techniques in modern neurosurgery. In other research done in Germany by Marcos skardely et.al. in 2018, a total of 634 adult meningioma patients were included in the retrospective single-center cohort studyto study factors of preoperative and early postoperative seizure in meningioma patients (13). Early postoperative seizures occurred in 5% of the patients with no history of preoperative seizures and non-skull base tumors, larger tumor size & edema were associated witha new-onset post-op seizure.

Both patient morbidity and mortality are greatly influenced by the occurrence of DVT and/or PE Patients with meningioma have an increased riskof postoperative venous thromboembolism and PE.Dephna Hoefnagel et.al,2014, did a retrospective single-center cohort study lasting for 12 years toassess the incidence of postoperative thromboembolic complications following surgical resection of intracranial meningioma(11) in 581 patients, showing thromboembolic complications in 7.2% (deep venous thrombosis (DVT) 3.5% & pulmonary embolism (PE) 4.6%), all receiving a perioperative protocol with low-molecular-weight heparin. VTE-related mortality was shown to be 11.2% (DVT 5.0%; PE 23.1%). In this research for DVT, only the body mass index, peri-operative blood loss, and postoperative in-hospital mobility status showed univariate significance & in patients with postoperative PE, age, weight, body mass index, and a postoperative in-hospital bedridden status had univariate significance.

In another prospective study by Gebler et al. between 2010-2012,in Frankfurt Germany, to assess the role of postoperative imaging after meningioma removal (12), using postoperative imaging in 113 patients, there were 30 patients (26.5%) who experienced symptoms postoperatively, including prolonged awakening, seizures, and neurological deficit. A total of 28 patients (24.7%) experienced postoperative symptoms and radiological verified hematoma. Two patients underwent reoperation due to a hematoma, which represents 1.8% of the cohort of 113 patients.

In a Norwegian study in 2010, by Torstein R. et al. (16) surgical mortality at 30 days and complications leading to repeat craniotomy in 2630 consecutive craniotomies for intracranial tumors was determined. The mortality rates for high-grade gliomas, low-grade gliomas, meningiomas, and metastases were 2.9%, 1.0%, 0.9%, and 4.5% respectively. Post-operative hematomas accounted for 35% of surgical mortality. 39 patients (1.5%) were re-operated for postoperative infection. Meningiomas had an increased risk of infection compared to high-grade glioma (odds ratio 4.61, $P<0.001$). This study also showed that case selection was a strong predictor of outcome. There was no mortality in meningiomas <3cm, or convexity meningiomas within 30 days following surgery.

In a population-based multicenter retrospective study investigating severe complications in intracranial meningioma surgery(14), by Jiri B, Kirstin S., et al, 2013,from 979 operations, 68 (7%) of the patientshad severe postoperative complication at 30 days.

74% of these procedures last > 4 hours. Multivariable regression analysis revealed that age> 70 and KPS score<70 were independent risk factors for severe perioperative complications.

Post-operative hospital-acquired infection is another concern in geriatric patients and patients with comorbidities or prolonged high dose steroids (4).Tannaz A. et al. did a single-center retrospective study on Post-Operative infection after surgery for brain tumors. They reported a 2-4% post-operative infection rate. The most common pathology was glioma in 41%, followed by meningioma in16% and metastases in 11 %(20).

Cerebrospinal fluid leakage is a risk of cranial surgery with a dural opening. Ina 1-year retrospective analysis of 412 non-trauma cases by Andre G. et.al, theoverall risk was 10.7%.The incidence was less for supratentorial and transsphenoidal procedures and higher for infratentorial procedures and extensive skull base procedures (21). In the other prospective multicenter analysis on CSF leak after cranial surgery by Uwe K. et al. on 545 cranial surgeries(elective and trauma), and found a CSF leak rate of 7.7%. A significant association was seen with the following factors: posterior fossa surgery, in craniectomies more than in craniotomies, if pneumatized spaces were opened,if the dura defect after closure remained larger than 1 cm and in patients younger than 66 years old (22).

Hormuzdiyar H. et al. retrospectively studied the length of stay of11,510 patients and found the median hospital stay was 4 days. Independent predictors of extended hospital stay included age greater than 70 years, African American, and Hispanic race or ethnicity (23).

3. Objectives

3.1. General objective:

- To assess the 30-day post-operative complications of intracranial Meningioma surgery in three Ethiopian hospitals

3.2. Specific objective:

- To describe the common clinical presentations, imaging characteristics & histopathology of intracranial meningioma
- To assess the surgical morbidity and mortality
- To identify factors that predispose to post-operative complications

4. Methodology

4.1. Study setting and design:

A hospital-based multi-center prospective descriptive study on 30-day post-operative complications of intracranial meningioma surgery was done.

The study was conducted at Tikur Anbessa Specialized Hospital (TASH), Zewditu Memorial Hospital (ZMH) & Myungsung Christian medical center (MCM).These are the pioneer hospitals to start neurosurgical practice in Ethiopia in 2006 and now provide neurosurgical services including oncology, pediatric neurosurgery, spine surgery, and vascular neurosurgery. Almost all craniotomies were performed with equipmentthat is obsolete inmodern hospitals.

4.1.1. Pre-operative Assessment

Prior to surgery, patients were evaluated by the neurosurgical resident, and their socio-demographics, presenting complaint, Karnofsky performance score, and pre-operative imaging findings were recorded. Their performance status was determined by the Karnofsky Performance Scale (KPS) which is scaled from 10 to 100 where 10 signifies the severest form of disability with a fatal process progressing rapidly whereas 100 signifies normal with no complaints. The tumor is also classified by location and size determined by pre-operative imaging and the intra-operative findings.

Patients were also evaluated by the anesthesia team before surgery. Patients were managed to co-morbidities and optimized to the surgery. Baseline investigations are completed beforehand including pre-operative imaging, cost-effectively, and affordably to the patients (Ct-scan or MRI or both). The imagings were used to characterize tumors based on their location and size.

All patients were given intravenous dexamethasone pre-operatively. Some of the patients were also given prophylactic anticonvulsants. Prophylactic antibioticswere given to all patients.

4.1.2 Post-operative Assessment

Following surgery, the extent of surgical resection was determined by the surgeon using Simpson's grading system as grade 0 refers to complete tumor resection along with a 2 cm margin of duraplasty and grade 5 refers to biopsy only. Other intraoperative findings including intraoperative complications were recorded. Surgical time, anesthesia time, and estimated blood loss were obtained from the anesthesia record

Intensive Care Unit (ICU) care was decided according to the duration of anesthesia and the relative risk of the operation depending on the tumor location. It was impossible to admit all operated patients to the ICU due to resource limitations. The postoperative neurologic and medical conditions were recorded to detect any complications related to the procedure done. Patients were kept in the wards until they were stabilized and post-operative complications ruled out after which time they were discharged with a follow-up appointment.

4.1.3. Clinical Follow-up

Patients were seen in the neurosurgical clinic for follow-up on their 30th post-operative. The histopathological findings were reviewed.

4.2. Study period:

The study was done from November 1, 2019, to September 1, 2020.

4.3. Source and study population:

- **Source population:**All patients who were operated on for intracranial meningioma in three selected hospitals.
- **Study population:**All patients who were operated on for intracranial meningioma in three selected hospitals within thestudy period and fulfilling the inclusion criteria.

4.4. Inclusion criteria:

- All patients who were operated on for intracranial meningioma in the stated study period &fulfilling the parameters included in the questionnaire were included in the study.

4.5. Exclusion criteria

- Patients with recurrence and reoperation
- Patients who refuse to participate in the study

4.6. Sampling method:

- Convenience sampling was used. All surgically managed patients in these three hospitals within the study period and fulfilling the inclusion criteria were enrolled in the study.

4.7. Study variables:

4.7.1. Independent variables:

- Age, Sex, Symptom at diagnosis, KPS, Tumor size, Tumor site, Multifocality, Simpson grade, Comorbidity, Duration of steroid use before surgery, Surgical time, Anesthesia time, EBL, Intraoperative complications, Histopathology

4.7.2 Dependent Variables:

- Complications within 30 days

4.8. Operational definitions

- **Brain tumor**: A tissue mass in the brain consisting of collection of abnormal cells.
- **Meningioma**: A benign brain tumor consisting of meningeal cells that for purposes of this study has been diagnosed radiologically or intraoperatively.
- **Post-operative Complication**: any deviation from the normal postoperative course occurring within 30 days of surgery.
- **Focal neurologic deficit:** a neurological findingthat for this study includes a motor, sensory, language, visual, cranial nerve deficit,orfrontal lobe syndrome.
- **Neurologic worsening**: Any deterioration in a neurologic function compared to pre-operative status.
- **Surgical time:** Time from skin incision to closure.
- **Anesthesia time:** Time from intubation until the patient leaves the operation theater.
- **Surgical mortality**: Death from any cause within 30 days of surgery.

4.9. Data collection and analysis:

Data was collected by taking a history using a standard questionnaire during admission and the course during hospital stay including new physical findings, diagnosis, and condition at dischargewere recorded.

Investigation and operative data were collected from the patients' medical records, surgical and radiologic records.

The assessment of complications was determined in theclinic on the 30^{th} postoperative day or 30 days following surgery if they were still hospitalized. The statistical analyses were performed using SPSS for Windows software (version 23.0; SPSS, Inc., Chicago, IL).

A multivariate analysis, using the factors that are found to be significant on univariate analysis, was done. The strength of association was evaluated using an adjusted odds ratio (AOR) and 95% confidence interval (95% CI). A p-value of less than 0.05 was considered significant.

4.10. Ethical consideration:

Ethical clearance was obtained from Departmentof surgery research committee and Institutional Review Board (IRB) of the College of Health Sciences. This study was conducted following the ethical principles stated in applicable guidelines for good clinical practice, whichever represents the greater protection of the individual. Patients' data were kept anonymously; the data was stored in a secure place so that confidentiality was not breached. The medical director of TASH, ZMH, MCM, and involved departments especially the department of surgery was notified by letter.

5.1. Results

5.1.1. Patient Characteristics

A total of 77 patients were operated for intracranial meningioma during the study period.76.6% of the patients were operatedat BLH, 20.7% of the patients were operatedat MCM and the remaining 2.5% of patients were from ZMH. 75 of the patients hada biopsy-proven meningioma, 1 patient was a metastasis from follicular thyroid cancer and 1 patient was WHO grade 2 Hemangiopericytoma.

Table 1- Histopathology of the tumor

WHO grading	Total
WHO 1, n (%)	**70(90.9)**
Meningiothelial n (%)	58(75.3)
Transitional n (%)	10(13)
Fibroblastic n (%)	2(2.6)
WHO 2, n (%)	**4(5.2)**
Chordoid n (%)	2(2.6)
Atypical n (%)	2(2.6)
WHO 3, n (%)	**1(1.3)**
Anaplastic	**1(1.3)**
Other histology	**2(2.6)**

5.1.1.1. Age and Gender

32(41.6%) of the patients were age group 31- 40 which contains the majority, followed by 15(19.5%) patientswere age 41-50.The mean age at presentation of the patients was 40.94±13.6 years with a rangefrom 18-86 years.52 (67.5%) of the patients were female and 25(32.55) males with a female to male ratio of 2.08:1.

<u>Table 2- Sociodemographic data</u>

Variables	Total
Age, mean(SD)	40.93(13.6)
Under 20, n (%)	3(3.9)
21-30	11(14.3)
31-40	32(41.6)
41-50	15(19.5)
51-60	10(13)
61-70	4(5.2)
71-80	1(1.3)
81-90	1(1.3)
Male n, (%)	25(32.5)
Female n, (%)	52(67.5)

5.2. Clinical Presentation

The commonest presentation of patients was a headache in 71 (92.2%) of the patients and next was a focal neurologic deficit in 62(80.5%) patients. Of all the focal deficits extremity weakness was seen in 19(24.4%) patients and cranial nerve palsies in 46(59.7.Sensory symptoms in

2(2.6%) patients, Cerebellar symptoms occurred in 6(7.8%) patients, behavioral change in 5 (6.5%), and aphasia 1(1.3%) patient.Seizureoccurred in 13(16.4%) patients.

Table 3 Pre-operative data

Clinical presentation	Total
Headache n,%	71 (92.2)
Focal neurologic deficit n,%	62 (80.5)
Seizure n,%	13 (16.4.)
Karnofsky Performance scale (KPS)	
50, n (%)	1(1.3)
60, n (%)	2(2.6)
70, n (%)	12(15.6)
80, n (%)	31(40.3)
90, n (%)	31(40.3)
Medical comorbidity, n (%)	6(7.8)
Duration of steroid use before surgery	
Less than 2 weeks, n (%)	71(92.2%)
2-4 weeks, n (%)	6(7.8%)
Tumor Laterality	
Left n (%)	29(37.7)
Right n (%)	23(29.9)
Midline n (%)	25(32.5)
Multifocal tumor n (%)	3(3.9)
Skull base tumor n (%)	47(61)
Tumor size	
Less than 4cm, n (%)	20(26)
4cm-6cm, n (%)	36(46.8)
Greater than 6cm, n (%)	21(27.3)

The Karnofsky scale (KPS) was assessed in all patients and 4(5.2%) patients had a score of less than 60 while 73(94.8%) patients had a KPS greater than 70.

Medical comorbidity occurred in 6(7.8%) patients, of which 2(33.3%) were diabetic, 3(50%) were hypertensive and 1(16.6%) patient were both diabetic and hypertensive.

Preoperative steroid was given for less than 2 weeks in 71(92.2%) of the patients and 6(7.8%) patients were treated between 2 and 4 weeks prior to surgery.

5.3. Tumor Characteristics

Based on the pre-operative imaging reports and the surgeon's intra-operative observation, the tumors were characterized according to their size and location.

Tumors were located on the left side in 29(37.7%) patients and on the right in 23(29.9%) patients. 25(32.5%) patients had midlinetumors. 3(3.9%) of patients had a multifocal tumor.

The estimated tumor size was less than 4 cm in 20(26%) of the patients, while 36(46.8%) had tumor size of 4- 6cm. Only 21(27.3%) of the patients had a tumor size greater than 6cm.

Convexity meningiomais the commonest to be operated on comprising 16 (20.8%) of the patients while 15 (19.5%) patients had Tuberculum sellae meningioma. Parasagittal and falx meningioma was found in 8(10.4%) and 2(2.6%) of the patients, respectively. Olfactory groove meningioma was found in 9(11.7%) of the patients while medial and lateral sphenoid wing meningioma was found in 9(11.7%) and 2(2.6%) of patients, respectively. From the posterior fossa meningioma, Five (6.5%) patients had CPA meningioma, three (3.9%) patients were diagnosed to have foramen magnum meningioma, two (2.6%) patients with tentorial meningioma, and 3(3.9%) had petroclival meningioma. Of all the tumors 47(61%) were skull base meningioma. Skull base tumor has a significant association with apostoperative complication with a p-value of 0.01 (OR=5.79, 95% CI: 2.061-16.312,) on both bivariate and multivariate analysis.The tumor locations are summarized in Table 4.

__Table 4 Tumor based on location__

Tumor Location	Total
Convexity Meningioma, n (%)	16(20.8)
Tuberculum sellae meningioma, n (%)	15(19.5)
Medial SWM, n (%)	9(11.7)
Olfactory groove meningioma, n (%)	9(11.7)
Parasagittal Meningioma, n (%)	8(10.4)
CPA Meningioma, n (%)	5(6.5)
Foramen magnum meningioma, n (%)	3(2.6)
Sphenorbital Meningioma, n (%)	3(3.9)
Petroclival meningioma, n (%)	3(3.9)
Tentorial meningioma, n (%)	2(2.6)
Lateral SWM, n (%)	2(2.6)
Falx Meningioma, n (%)	2(2.6)

5.4. Surgical Treatment

5.4.1. Simpson grading

Tumor removal was graded based on Simpson's Grading system. GTR which is considered as Simpson grade 1-3 was achieved for 76.6% of the cases. Grade 0 removal was achieved in 3(3.9%) of all patients. Grade I removal was achieved in 12(15.6%) of all patients while Grade II removal was possible in 44(57.1%) of patients. Grade 4 and 5 resections were achieved in 16(20.8%) and 2(2.6%) of the patients, respectively.

Table 5 Intraoperative and postoperative data

Simpson grading	**Total**
Simpson grade 0, n (%)	3(3.9)
Simpson grade 1, n (%)	12(15.6)
Simpson grade 2, n (%)	44(57.1)
Simpson grade 4, n (%)	16(20.8)
Simpson grade 5, n (%)	2(2.6)
Surgical time, mean(SD)	5(1.98)
Anesthesia time, mean(SD)	6(2.25)
EBL, mean(SD)	1125.9(751.5)
Less than 500ml, n (%)	10(13)
500ml-1000ml, n (%)	38(49.4)
Greater than 1000ml, n (%)	29(37.7)
Intraoperative accident, n (%)	8(10.4)
Post-operative complication, n (%)	37(48.1)
New or worsened neurologic deficit, n (%)	24(31.2)
New onset post-operative seizure, n (%)	3(3.9)
Post-operative HAI, n (%)	9(11.7)
CSF Leak, n (%)	8(10.4)
Wound related complication, n (%)	4(5.2)
Reoperation, n (%)	11(14.3)
Post-operative DI	8(10.4)
Steroid-induced hyperglycemia	1(1.2)
Bed soar	4(5.2)
VTE	0
Hospital stay, mean(SD)	19(1.5)
30-day mortality	7(9.1)

We also evaluated if complications were associated with Simpson grading. There was no association between Simpson grade and new-onset seizure, postoperative infection, or reoperation. However, there was a significant association between GTR and new or worsened neurological deficits ($p < 0.049$).

5.4.2. Surgical time,anesthesia time & Estimated blood loss

The mean surgical time of all operated patients was 5 hours with the range being 2-14 hours. The mean anesthesia time was 6 hours with a range of 2.3 - 15.5 hours. The mean estimated blood loss was 1125.97ml with a range of 200ml 5000ml.

Our study shows that anesthesia time has a significant association with postoperative complications with a p-value of 0.014(95% CI: 1.2-8.5). The probability of post-op complications in patients with more than 5 hours of anesthesia time is 1.194 times that of patients with anesthesia time of less than 5 hours.

Estimated blood loss has a significant association with a postoperative complication with a p-value of 0.037(95% CI: 1.237-99.15). The odds of post-op complications in patients who bleed more than 1000ml (95% CI: 1.237-99.15) is 11.07 times than that of patients with blood lossless than 1000ml.

5.4.3.Intraoperative and Postoperative complications

Intraoperative complications were reported in 8(10.4%) of the operations. Brain swelling occurred in 4(44.4%) patients, cranial nerve injury in 2(22.2%) patients, MCA injury in 2(22.2%) patients, and Transverse sinus injury was reported in 1(11.1%) patient.

Of the 77operated patients, 37(48.1%) patientshad 1 or more postoperative complications. Of the complications, new-onset orworsened focal deficit was the commonest and it's seen in 24(31.2%) patients. Of all these deficits, 12(15.6%) were extremity weakness, 10(13%)were cranial nerve deficit, 3(3.9%) were frontal lobe syndrome, 1(1.3%) with aphasia, and 1(1.3%) cerebellar symptom.Wefound a significant association between new-onset neurologic deficit following surgery with skull base tumors (OR=4.8, 95% CI: 1.449-16.002, P= 0.07) and GTR (OR= 0.341, 95%CI: 0.114-1.108, P=0.049).

Table 6 Patterns of neurologic deficit

Type of deficit	Total
Extremity weakness, n (%)	12(15.6)
CN deficit, n (%)	10(13)
Frontal lobe syndrome, n (%)	3(3.9)
Aphasia, n (%)	1(1.3)
Cerebellar symptom, n (%)	1(1.3)

New-onset seizures developed postoperatively in 3.9% of the operated cases. There was no correlation with tumor location or size of the tumor.

Hospital-acquired infection was documented in 9(11.7%) patients of whom 5 had Chest infectionsand 1(9%) patient had meningitis. 2 patients had both chest infection and meningitis which accounted for 36.6% of the infections.1(9%) patient had an infection of unknown focus. The post-operative hospital-acquired infection rate is significantly associated with skull base tumor (OR=1.789, 95%CI=1.449-2.210, P=0.01) and anesthesia time more than 5 hours (OR=1.889, 95%CI= 1.510-2.363, P=0.09).

Post-operative CSF Leak was seen in 8(10.4%) patients.3 (37.5%) patients leaked through the wound, 4(50%) patients had CSF Rhinorrhea, and 1(12.5%) leaked CSF through the drain. There was asignificant association between reoperation and post-operative CSF Leak (OR= 2.181, 95%CI=1.804-43.4, P= 0.07).

Wound-related complications occurred in 4(5.2%) patients, half of them required wound debridement and reclosure.1 (25%) patient had surgical site infection requiring abscess evacuation with debridement, and 1(25%) patient had superficial wound infection.

Re-operation was necessary in 14.3% of all the operated cases. Causes included decompression craniectomy in45.4%, ventricular diversion in 36.3%, and acute epidural hematoma in 7.14%. There was a significant association between reoperation and skull base tumor (OR=7.8, 95% CI: 0.947-64.78, P=0.04,) and post-operative complication (P=0.01, 95% CI: 1.154-1.755, OR=1.423).

10.4% of operated patients developed diabetes insipidus, of which 62.5% of the patients were operated on for Tuberculum sellae meningioma, 25% for olfactory groove meningioma, and 12.5% for lateral tentorial meningioma. Steroid-induced hyperglycemia was seen in only 1 patient and 4(5.2%) patients had bedsores. There was no single case of VTE in the follow-up period.

Hospital stay ranged from 6-66 days, with a mean of 19.05±13.55 days.

There were seven postoperative deaths of which the majority (85.7%) had skull base meningioma. Tuberculum sellae meningioma accounted for 3(42.8%) and clinoidal meningioma accounted for 2 (28.5%)of the deaths. Significant association was seen with GTR (OR=0.188, 95%CI=0.38-0.936, P value=0.048).

5.5. Discussion

In this multicenter prospective study of patients undergoing surgery for intracranial meningioma, we benchmark the 30-day complication rate for clinically relevant complications. 37(48.1%) patients had 1 or more postoperative complications. Anesthesia time more than 5 hours and blood loss more than 1000ml were significantly associated with a postoperative complication on bivariate analysis. Skull base tumors had asignificant association with a postoperative complication on multivariate analysis.

We identified thepatient'ssocio-demographic characteristics, common presentation, performance status, and co-morbidities. The tumor was characterized according to the size, location, and histopathology. Intraoperative findings and complications related to the surgery were also identified.

5.5.1. Sociodemographic factors

Femalecomprised 67.5% of the population which coincides with other studies done (3, 4, 5), and the age of our patients showed that 93.5% of them were under 60 with a mean age of 40.94(range 18-86).Unlike reports from Europe (4), our study shows a younger population that matches other studies done in Nigeria and Mauritania (3, 5, 6,7).This could be due to a large younger population and shorter life expectancy in African countries compared with HIC and similar to the other studies, our study showed no significant association between age and postoperative complications (3, 4, 5).

5.5.2. Clinical presentation & Tumor characteristics

Themost common presentationwas headache (92.2%), which is similar to other studies (3, 5).Focal neurologic deficit occurred in 62(80.5%) and Seizure was evident in 13(16.4%) patients as a presenting symptom.

Of all patients, 61% of them were operated on for skull base meningioma since most of the tumors were operated on in a tertiary hospital. This number is almost double that of a previously done study in the same setup (3), which shows more difficult tumors, are being operated on recently than before.

Our study has also revealed that 74.1% of patients had a tumor greater than 4cm in diameter. This is similar toa paper from the same setup and other African countries (3, 5, 6, 7) and the opposite is a common scenario in papers from high-income countries likeNorway (4,16).This can be explained by less medical seeking behavior, shortcomings in diagnostic resource capacity, the patients' lack of resources to pay for imaging, andvery few neurosurgical centers in low-income countries.

5.5.3. Perioperative outcomes

We found that the most common postoperative complication to be a new-onset/worsened focal neurological deficit, which concurs with other local and international studies (3, 4, 5, 6, 9). In the literature, the proportion experiencing a new or worsened deficit in unselected patients with meningioma is 8.3–9.3 %(12, 16) and even some high-income countriesreport 14.8 %(4).Retrospective single-center studies fromEthiopia and Egypt havereported a new onset neurologic deficit of 8% and 21.4% respectively, and thus, our data with 31.2% of new or worsened deficit appears unfavorable(5,19). Even though these papers are retrospective in nature and they calculated only new-onset deficit (not worsened), they are comparable where only basic neurosurgical equipment was used for all tumor surgeries.In other studies, the range is wider and much affected by tumor location and preoperative symptomatology [4, 6, 9]. The short-term neurological deficit may also predispose to other medical complications in the postoperative period, the literature reports improvement of neurological deficits in most patients during the initial follow visit after surgery [4, 9].

We founda significant association between new-onset neurologic deficit with skull base tumors and GTR.This finding is supported by another report from Egypt thateven though complete tumor resection is the goal, the extent of resection should be tailored to each patient depending on the tumor pathoanatomy(19).

The onset of seizures after meningioma surgery dictates prophylactic treatment with antiepileptic drugs (AED), although the current evidence indicates no clear benefits in the prevention of postoperative seizures with routine perioperative AED administration (12,13). Routine perioperative administration of AED is performed at our institution, particularly for supratentorial meningioma. In this study, new-onset seizures occurred in 3.9% of patients.This is similar to the existing literature where new-onset seizure postoperatively was reported in the range 1.9 to 19.4 %(4, 12, 13). This large variability between the reported seizure frequencies in the literature may be due to different lengths of follow-up, meningioma location, non-uniform use of prophylactic AED drugs,and pattern of evaluation because retrospective cross-sectional studies may capture different data than standardized and prospective reporting.

Post-operative hospital-acquired infection is another concernin determining the outcome of meningioma patients. In this study, hospital-acquired infection was seen in 16.8% of patients, of which 5.2% was due to surgical site infection. In most European literaturethe proportion of HAI ranges from 1.6%-4 % and reportsfrom the same setup and some African countries have shown a range of 8% -16 %(3, 5, 16). This shows that post-operative hospital-acquired infection is high compared to international literature. This could be due to different choices and use of prophylactic antibiotics in our study, less satisfactory hygienic standards in our operating room, and crowded ICU andwards(5). Therefore more cases of infection are expected in our studycompared with the westerns countries.

We have identified a significant association between HAI with skull base tumor and anesthesia time greater than 5 hours, which is supported by another study by Tannaz et al, showing an association between infection and surgery duration longer than 4 hours (20).

Cerebrospinal fluid (CSF) leaks are well known and frequent complications in neurosurgical procedures. In this study, a postoperative CSF leak occurred in 10.4%, and reviewing the literature CSF leak was reported in the range of 7.7% to 11 %(5, 20, 21). Accordingly, our result is in line with the existing literature.

Meningioma is known to be associated with VTE (14). Venous thromboembolism has been reported in 3-7.6% in the literature and most of the cases were diagnosed three to four weeks after surgery (4, 14).We had no patient with confirmed DVT or PE in the follow-up period. This could be due to the short-term follow-up of our patients, the asymptomatic nature of the disease in the majority, and sometimes needs advanced diagnostic studies such as D-dimer and spiral CT scan.

The risk of reoperation within 30 days of surgery due to complications was 14.3%, of which decompressive craniectomy and ventricular diversion procedure being the two common reasons. The literature shows thatthe reoperation rate for operated patients due to complications ranges from 5.2% - 13.2 %(3, 4, 5). This shows that our reoperation rate is higher than both local and international literature and this could be due toincreased postoperative complications and the majority of operated tumors were skull base tumors as we have identified a significant association between reoperation with post-operative complication and skull base tumors.

The length of hospital stay is often used as a measure of the quality of care and efficient service (23). In this study, the mean duration of hospital stay was 19.04±13.55 days. In the literature, the mean duration of hospital stay ranges from 4 - 21 days (3, 6, 7, 23). Even though this is in line with our figure, it's the highest when compared to other African countries. This is likely due to scarce ICU facilities in the hospitals in this study which forced the surgery to be delayed.

The 30-day mortality in our study was 9.1%. In a Norwegian study the overall surgical mortality of intracranial tumor surgery within 30 days was 2.3% and for meningioma was 0.9 % (16). In another study from Sweden, the 30-day mortality after surgery for intracranial meningioma was 1.5 %(4). A study seven years ago in this hospital showed 30-day postoperative mortality of 14.3 %(3) and a study from Egypt showed a mortality rate of 14.2(19). Our finding is better than a prior study done in the same setting but far higher when compared to international literature. 71% of the deaths were due to tuberculum sellae and clinoidal meningioma. Case selection was a strong predictor of the outcome. We had only 1 death of lateral sphenoid wing meningioma while the rest were all skull base tumors, similar to other studies (4, 16).

5.6. Limitationsof the study

This studylacks long-term data regarding the duration of neurologic deficit. The inclusion of skull base and non-skull base tumors, the small sample size and the inclusion of non-meningioma tumors compromises the reliability of some of the findings.

5.6. Conclusion

This study showed a higher incidence of intracranial meningioma in younger patients compared to European studies. Surgical morbidity & mortality were higher compared to otherstudies. The majority of operated tumors were skull base meningioma. Significant associations were found between Postoperative complications and Anesthesia time more than 5 hours, estimated blood loss more than 1000ml, and skull base meningioma. Since careful consideration is needed for a surgical decision on short-term risk versus long-term benefit, this information may be useful for both physicians and patients.

5.7. Recommendations

- Modern Neurosurgical instruments like electronic drills andultrasonic aspirators are vital to minimize anesthesia time and blood loss. These should not be luxury anymore.
- The majority of the deaths were from skull base meningioma (Tuberculum sellae and Clinoidal meningioma). Preoperative planning is essential to prevent this.
- The duration of hospital stay is persistently high and it should be minimized with an effective preoperative schedule.

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Annex 1: Questionnaire

1. Socio-demographic data

1. Card no. …………………..

2. Age ……………

3. Sex ………..

4. Address ……………………….

5. Phone no. ………………………..

6. Occupation ………………………..

7. Date of operation…………………..

2. Preoperative clinical data

2.1 Symptom at diagnosis

1. Asymptomatic (yes/no)

2. Focal deficit (yes/no)

3. Seizure (yes/no)

4. ICP related (e.g., headache, cognition) (yes/no)

3. KPS

100- Healthy, no symptom or sign of disease

90- Capable of normal activity, few symptoms or sign of disease

80- Normal activity with some difficulty, some symptom or sign

70- Caring for self, not capable of normal activity or work

60- Requiring some help, can take care of most personal requirements

50- Requires help often, requires frequent medical care

40- Disabled, requires special care and help

30- Severely disabled, hospital admission indicated but no risk of death

20- Very ill, urgently requiring admission, requires supportive measures or treatment

4. Comorbidity (yes/no)

5. Duration of Steroid use before surgery

1. <2 weeks

2.2-4 weeks

3. >4 weeks

7. Imaging

7.1 Laterality

1. Left

2. Right

3. Bilateral

8. Multifocality (Yes/no)

9. Diameter of tumor

1. < 4 cm

2. 4–6 cm

3. > 6 cm

10. Intraoperative data

10.1 Simpson grade

1. Grade I, total removal

2. Grade II, tumor removal and coagulation of attachment

3. Grade III, tumor removal without coagulation

4. Grade IV, subtotal removal

5. Grade V, decompression/biopsy

11. Surgical time……………………

12. Anesthesia time ………………….

13. EBL ………………………………

14. Intra operative accident…………………

15. Post-operative data

1.1 New or worsened focal deficit within 30 days (Yes/no)

1.2 New-onset seizure within 30 days (Yes/no)

1.3 Any infection within 30 days (Yes/no)

1.4 Any VTE within 30 days (Yes/no)

1.5 Any hematoma requiring surgery within 30 days (Yes/no)

1.6 CSF Leak (Yes/no)

1.7 Wound related complications (Yes/no)

1.8 New or Worsened HCP requiring intervention(Yes/no)

1.9 DI(Yes/no)

1.10 Steroid-induced hyperglycemia (Yes/no)

1.11 Bed soar (Yes/no)

1.12 Complication leading to reoperation within 30 days (Yes/no)

1.13 Duration of hospital stay in days______________

16. **Histopathology result________**