A RADIOLOGICAL- PATHOLOGICAL CORRELATION OF HYPEROSTOSIS AMONG PATIENTS WITH INTRACRANIAL MENINGIOMAS AT THE KENYATTA NATIONAL HOSPITAL.

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A DISSERTATION SUBMITTED TO THE UNIVERSITY OF NAIROBI IN PARTIAL FULFILLMENT FOR THE AWARD OF THE DEGREE IN MASTER OF MEDICINE IN NEUROSURGERY

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STUDENT DECLARATION

I, DR ADAGI MARJORIE, declare that this dissertation is my original work and to the best of my knowledge, it has not been presented elsewhere for consideration of publication or award of a degree at any other university.

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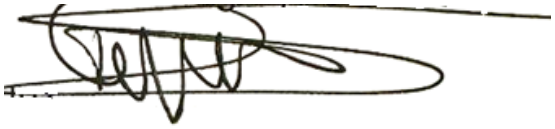
Signature .  Date .....24/5/2023.....

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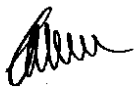
Signature ……  …… Date……21/5/2023……..

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And to Sharon; my pillar of strength.

DEDICATION

Dedicated to my loving parents. Thank you for believing in me. Thank you for your prayers and for holding my hand throughout this journey of life. Because of you, I am.

My mother Terry Mbula Adagi ; my motivator.

My late father Evans Adagi Salamu; the sky will never be the limit.

LIST OF ABBREVIATIONS AND ACRONYMS

A.D.C.- Apparent diffusion coefficient

BMP- Bone Morphogenic protein

COX2- Cyclooxygenase

CT- Computer tomography

DWI- Diffusion-weighted imaging

EANO- European association of Neuro-Oncology

ER- Estrogen receptor

ET-1- Endothelin

FGF- Fibroblast growth factor

HIF- Hypoxia Inducible factor

hTERT- Human telorase reverse transcriptase

IGF- Insulin growth factor

IR- Ionizing radiation

KNH- Kenyatta National Hospital

MRI- Magnetic resonance imaging

MRA - Magnetic Resonance Angiography

NAA- N- acetyl aspartate

NF2- Neurofibromatosis type 2

O.P.G.- Osteoprotegerin

PDGfr- Platelet-derived growth factor

P.E.T.- Positron emission tomography

PR- Progesterone receptor

T2 FLAIR- Fluid attenuated inversion recovery

rCBF- Relative cerebral blood flow

rCBV- Relative cerebral blood volume

VEGF- Vascular endothelial growth factor

WHO- World Health Organisation

DEFINITION OF TERMS

Bone morphogenic proteins – A group of growth factors known as metabologens that induce the formation of bone and cartilage.

Clinical characteristics – patient characteristics such as age, sex, recurrent tumor,

Hyperostosis – Excessive growth of bone.

Osteoprotegerin – Regulatory factor which acts as a decoy receptor for the receptor nuclear activator ligand.

Meningiomas – Primary slow-growing tumor that arises from the arachnoid cap cells.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Background: Meningiomas account for 34.4% of all central nervous system (CNS) neoplasms in Kenya. Hyperostosis has been described in 25% to 44% of meningiomas. The risk of tumor recurrence is largely dependent on the extent of resection. According to Simpson et al, complete bony removal is associated with a 9% recurrence rate over a ten year period. Prior traumatic injury, irritation of bony elements by the tumorous growth without bony invasion, activation of osteoblastic cells in healthy bone by substances produced by neoplastic cells, synthesis of bone fragments by the tumor itself, and vascular abnormalities brought on by the neoplasm are all factors that may contribute to hyperostosis. The purpose of this study was to ascertain whether radiological changes in skull bones observed in cases of meningiomas are solely attributed to tumor invasion.

Study design: This was a prospective cohort study.

Broad objective: To determine the proportion of patients with radiologic hyperostosis who have microscopic tumor invasion in bone .

Study area: Kenyatta National Hospital Neurosurgery and Pathology departments.

Study population: Post-surgical patients who underwent resection of meningiomas.

Materials and methods: This prospective study included all patients with a diagnosis of meningioma with radiological evidence of hyperostosis. Preoperatively, a computed tomography (CT) scan was done by a consultant radiologist in all patients and reviewed by two neurosurgeons for associated bony hyperostosis. Intra-op, a sample of the bone measuring 2cm by 2cm by 2cm displaying features of hyperostosis was harvested. Bone samples were decalcified with 10% formic acid. A consultant neuropathologist thereafter microscopically evaluated the samples to check for bone invasion.

Results: A total of 36 patients underwent resection for intracranial meningiomas during the study period. Radiological evidence of hyperostosis was present in 22 (61.1%)

patients. Out of the 22 patients, female patients were 17(77.3%) while male patients were 5(22.7%).

The median age of the patients at the time of surgery was 45.5 years (range 20-65 years; mean 44.3 ± 11.9 years). On histopathological examination, Meningothelial meningioma was the most common variant (68.2%). Microscopic tumor invasion of the bone was seen in 13 (59.1%) patients.

Conclusion: A significant number of patients with radiological hyperostosis had tumor invasion of the bone. The findings of this study show that one should remove the bone flap whenever possible in order to achieve total excision of the tumor, reduce recurrence rates and perform titanium mesh/ hydroxypartite cement cranioplasty for calvarial reconstruction.

Keywords – Meningiomas, hyperostosis, bony invasion, surgical resection.

CHAPTER ONE

1.0 INTRODUCTION

Meningiomas are neoplastic growths of the brain that develop from the arachnoid cap cells and are characterized by their slow-growing behavior. Meningiomas form thirty-six percent (36.6%) of the primary CNS tumors, of which they still contribute to 53.2% of benign tumors (1).

Meningiomas tend to localize in the supratentorial areas, and 35% of them are found along cortical concavities. Only approximately 10% arise within the posterior fossa, while 17 and 25 percent do so in the frontobasal region (2). The olfactory groove, sella turcica, parasellar area, and petrous part of the temporal bone are the preferred places within the frontobasal region. Within the cerebellopontine angle, 2 to 4 percent of cases occur, as do 5 percent along the convexity of the cerebellum, 2 to 4 percent just at tentorium cerebelli, and 2 to 4 percent elsewhere (2). The ventricular system, as well as the sheath of the optic nerve, are two more uncommon sites. Less than ten percent of meningiomas are spinal meningiomas. Meningiomas localized outside the cranial cavity are extremely uncommon tumors that have been reported in ectopic places like the intraosseous sinuses, scalp, parapharyngeal space, parotid, mediastinum, lungs, or adrenal glands (2).

According to Muriithi et al. (2015) (3), the gender disparity in the prevalence of these tumors at KNH is a 7:3 female to male preponderance. Infratentorial compartment meningiomas comprise 14.1% of all meningiomas, whereas supratentorial meningiomas made up 85.9% of all meningiomas. 51.5 percent of the meningiomas are comprised of neoplasms at the tuberculum sellae (5.9 percent, olfactory groove (20.6 percent), sphenoid wing (25 percent) within the anterior cranial fossa. Patients presenting with

meningiomas may benefit from considering a number of prognostic markers, such as the degree of resection possible, WHO tumor grading, receptor status, cerebral invasion, and cortical bone involvement (4).

It is increasingly acknowledged that meningiomas and hyperostosis are related. However, the reason for these skeletal modifications is still up for debate (5).

According to other writers, hyperostotic alterations are a result of the tumor's initial growth and do not signify its invasion of the bone. The answer to this question will directly affect how these individuals are treated, particularly with reference to surgical issues. It is required to conduct a study relating morphology to radiography in order to more fully examine this subject (6).

CHAPTER TWO

2.0 LITERATURE REVIEW AND BACKGROUND

2.1 History of the term 'Meninges'

The Grecian anatomist and physician to the monarch Seleucus I Nicator of Syria, Erasistratus (304–250 BC), is credited with coining the term "meninges." In their anatomy school in Alexandria, Erasistratus and his colleague Herophilus conducted human dissections and brought objectivity to the study of anatomy by firsthand observation. Their research supported Aristotle's observations that animal brains were encased in a dual-layered membrane, one layer of which was in opposition to the cranium and the other adherent to the outlines of the cerebral cortex. Aristotle lived from 384 to 322 BC (7). Other civilizations, however, did describe the brain's coverings before the Greeks. The depiction of a head trauma patient in the Edwin Smith Papyrus' Egyptian trauma surgery treatise (about 2200 BC) featured a depiction of the membranous layers of tissue encasing the central nervous tissue, which, when ruptured, would spill the "fluid of the inside of the head." According to Al Mefty's book, the arachnoid layer was originally described in detail by Dutch anatomist Gerardu Blasius in 1664 (8). The meninges are now subdivided embryologically into the pachymeninges, that is, the dura mater, and the leptomeninges, that is further comprised of the arachnoid and the pia mater (8).

2.2 Anatomy and biology of the meninges.

2.2.1 Embryology of the meninges

Understanding meningeal developmental biology is essential for improving our insight into the mechanisms driving meningioma initiation and development. The meninges develop early in pregnancy and reach their fundamental adult shapes by the end of the first trimester (9). The neural crest layer and cells arising from the mesoderm will

produce meningeal progenitor cells. When the neural tube closes at the third-week post-conception, a discrete layer of cells envelopes the growing neural axis, with several connections to the neural crest. Starting about day 24 to 28, a wider, less compact layer of mesenchymal cells completely envelops the growing central nervous system by day 33 to 41 (10). The neural crest-derived monocellular layer and the mesodermal-derived cellular primordia will differentiate to form the primitive meninx (primary meninx). Between gestational days 34 and 48, the pluripotent primary meninx splits into two different layers as it grows. The endomeninx, which makes up the inner layer, is more loosely structured than the ectomeninx, which is the external layer. The dural membrane and the bones making up the neurocranium are both derived from the ectomeninx; hence the dura and skull are positioned adjacent to each other because of their similar embryological heritage (10). Between the 45th to 55th-day post-conception, the inner endomeninx, which contains a layer of cells of neural crest origin covering the neural tube, starts to develop the pia. By 55 days of gestation, cavitations (cisternal primordia) start appearing in the outer part of the endomeninx as CSF fluid infiltrates it. The dura, the intermediate arachnoid layer, and the pial layer, the deepest layer in proximity to the cerebral cortex, will eventually form from the primary meninx (10).

2.2.2 Anatomy of the meninges

The dura mater's (Figure 1) two separate and distinct layers are fused together in the majority of its area covering the brain (11). The underlying cranium's periosteum is made up of the outer periosteal (endosteal) dural layer, which is well supplied by lots of blood vessels and tightly attached to it. At suture lines and neural foramina, the outer layer of dura is continuous, with the periosteum protecting the external surface of the neurocranium. At the superior orbital fissure and optic canal, it fuses with the periorbital membrane. The internal meningeal layer of dura also surrounds the cranial nerves as

tubular sheaths as they emerge from the brain, eventually merging with their epineural sheath as they leave through their separate cranial foramina (11). The venous sinus system is formed by multiple reflections of the deeper meningeal dural layer away from the outer periosteal layer. To create dural septa, which divide and keep the positions of the intracranial neuronal structures in place, it folds inward. These dural reflections include the diaphragma sellae, tentorium cerebelli, falx cerebri, and falx cerebelli (11).

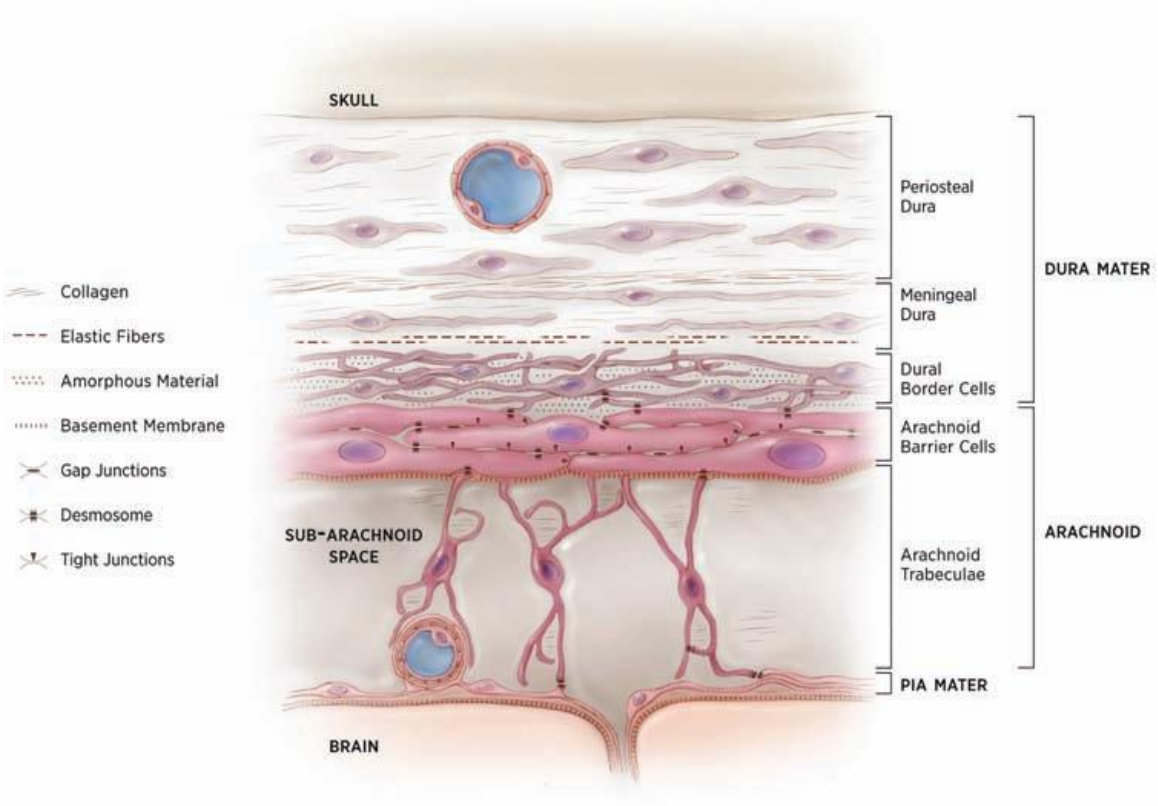


Figure 1: Layers of the meninges

The barrier cell layer of the arachnoid membrane is located close to the border cell layer of the dura. Large, densely packed fibroblasts make up this layer, which has little extracellular space and virtually no collagen. Cell-to-cell junctions are uniquely numerous within this layer. The barrier cell layer is strengthened by the tight interconnections between cells, making it impervious to fluids, substances with high molecular weights, and even certain ions (12). Additionally, an uninterrupted basement

membrane confines the subarachnoid CSF region on the arachnoid's inner surface. Specialized fibroblasts called arachnoid trabecular cells have lengthy protrusions and connections to the arachnoid barrier layer. They span the subarachnoid space via their lengthy, flat, uneven cellular protrusions and can connect with pial cells to establish cellular attachments. The trabecular matrix synthesized from the processes of the arachnoid cells within the subarachnoid space may contain collagen (12).

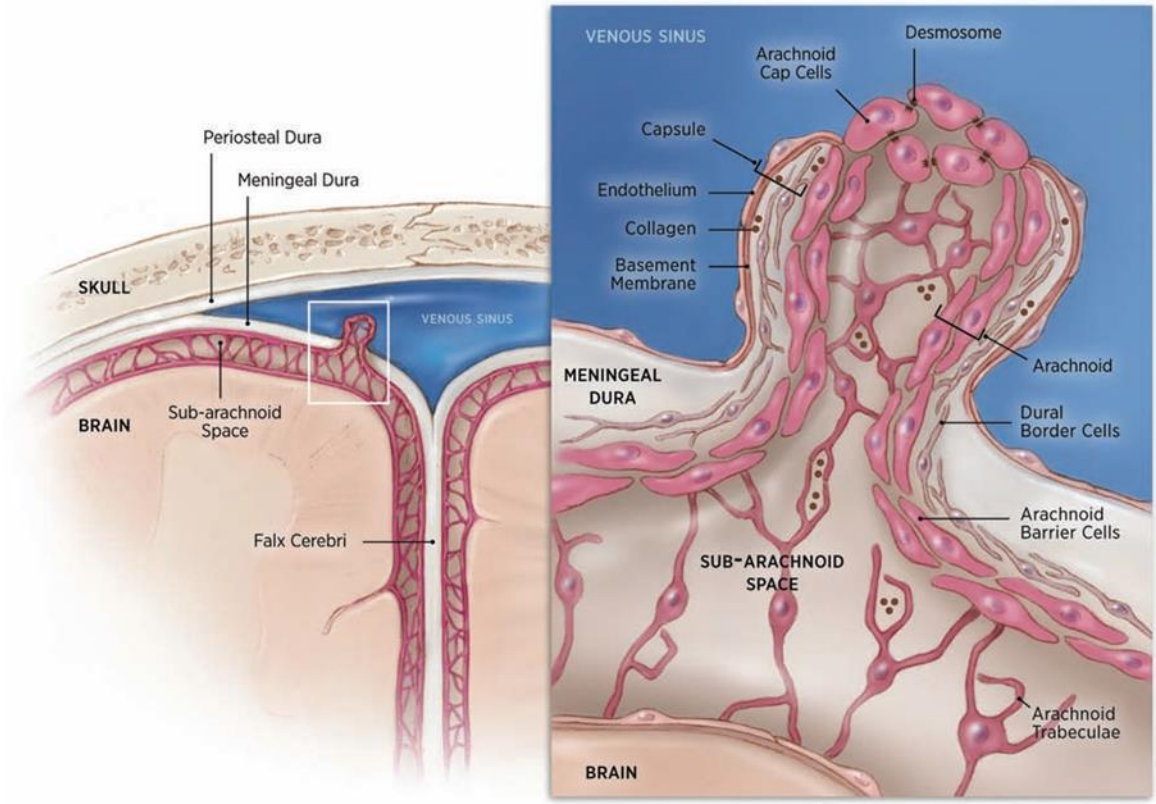


Figure 2: Detailed view of the subarachanoid layer

The subarachnoid space is delineated from the sub-pial and cerebral perivascular spaces by the pia mater, a very thin sheet-like membrane of spindle-shaped fibroblasts. The sub-pial space is formed because the pia is separated from the neural tissue deep to it by the basement membrane of the external cell layer of glia of both the brain and spinal cord, known as glia limitans. The pia becomes impervious to particle materials, such as blood, when these atypical fibroblasts of the pia form cell-to-cell complexes at their edges

(11,12). The meningeal arteries supply the dura and the nearby cranium from the carotid arteries and vertebrobasilar system. These arterial branches offer intersecting vascularization configurations that are more intricate near the base of the skull than over the convexity of the brain. The recurrent ophthalmic artery, the ethmoidal arteries, and the lacrimal arteries all from the internal carotid system supply the paramedian dura of the anterior and middle cranial fossae. The middle and accessory meningeal arteries and the ascending pharyngeal arteries all supply the more lateral sections of the three cranial fossae with blood from the external carotid system (12).

Table 1: Arterial supply of the meninges

Anatomic Site	Branch in Fossa	Foramen	Parent Vessel	Source
Anterior fossa	Meningeal branch		Cavernous part of internal carotid	Common carotid
	Meningeal branch	Anterior and posterior ethmoidal	Anterior and posterior ethmoidal branches of ophthalmic	Ophthalmic from internal carotid
	Meningeal branch	Lacerum	Ascending pharyngeal	External carotid
Middle fossa	Middle meningeal artery	Spinosum	Maxillary	External carotid
	Accessory meningeal artery	Ovale	Maxillary or middle meningeal	External carotid
	Recurrent meningeal ramus	Superior orbital fissure	Lacrimal	Ophthalmic from internal carotid
Posterior fossa	Meningeal branch	Jugular, hypoglossal canal	Ascending pharyngeal	External carotid
	Meningeal branch	Jugular, condylar canal	Occipital	External carotid
	Meningeal branch		Vertebral	Subclavian

Through both the anterior and posterior meningeal arteries, as well as the subarcuate artery, the vertebrobasilar system provides the vasculature to the midline tissues at the posterior cranial fossa, including the area around the foramen magnum. The chief meningeal artery provides the majority of the blood supply to the dura covering the convexity of the brain (13).

Numerous cranial and spinal nerves, including the trigeminal nerve, glossopharyngeal nerve, vagus nerve, and cervical spinal nerves one through three, supply the cranial dura with extensive innervation (12).

Table 2: Dural innervation

Trigeminal nerve	Ophthalmic nerve	Innervation of dura over cribriform plate, medial orbital roof, crista galli, diaphragma sellae, tentorium, falx cerebri, inferior and superior sagittal, transverse and straight sinuses
	Maxillary nerve	Innervation of dura of the anterior floor of the middle fossa
	Mandibular nerve	Innervation of dura over the lateral floor of the middle cranial fossa and most of the convexity of the cranium
Upper three cervical roots	Ascending meningeal rami	Innervation of dura lining anterior floor of posterior fossa, clivus, and ventral craniospinal junction
	Recurrent meningeal branch of vagus	Innervation of walls of sigmoid sinus, occipital sinus, falx cerebelli, dura over the petrous surface of temporal bone, and suboccipital cerebellar surface
	Hypoglossal nerve	Innervation of dura of posterior fossa up to inferior petrosal sinus

2.3 Risk Factors associated with meningiomas

2.3.1 Ionizing radiation

Ionizing radiation (IR) exposure is currently the main environmental risk factor for meningioma, with reported risks ranging from six to ten times higher than the general population. Israelite children who received radiation treatment for fungal infections of the scalp during the period mainly in the 1950s (the Tinea Capitis Cohort) were found to be ten times more likely to develop a meningioma, according to one of the most well-known studies on the relationship between ionizing radiation exposure and risk of developing meningioma (14). According to case-control research involving 200 meningioma patients, those who had orofacial X-ray imaging had a disproportionately higher chance of developing the disease (OR 2.06, 95 percent CI 1.03, 4.17) even though there was insufficient proof of a dose-response relationship (P for trend = 0.33) (15).

2.3.2 Hormones

The higher incidence of the tumor in women of reproductive age than in men (2:1), a ratio that peaks at 3.15 to 1 during the peak reproductive years, the positive presence of progesterone receptors, androgen hormone receptors, and estrogen receptors on certain meningiomas, a positive correlation between breast malignancies and meningiomas, and signs that meningiomas alter in volume periodically, coinciding with the luteal phase of the normal menstrual cycle, are just a few findings that point to a hormonal link between meningioma (16,17).

The progesterone receptor (PR) status was found to be more significantly and positively related to the expression of genes than the estrogen receptor (ER), according to a pioneering investigation of meningiomas. The most often observed expression variation was found in genes localized along the long arm of chromosome 22 and close to the NF2 gene (22q12), and considerable upregulation in PR+ versus PR- lesions suggested a higher probability of 22q loss in PR- lesions (18).

2.3.3 Head Trauma

Traumatic injury to the head, going all the way back to Harvey Cushing's era, has commonly been cited as a possible risk factor for meningioma, albeit findings from different investigations are inconsistent. At the same time, some modest case-control studies suggest that both boys and girls who sustain head trauma have an increased chance of developing meningioma (19). The incidence ratio, standardized for meningioma, after year one post-trauma, averaged 1.2 in an investigation of 228,055 Dane citizens hospitalized for cranial fractures, concussions, or general traumatic head injuries the years 1977 to 1992 and monitored for a mean of approximately eight years (95 percent CI 0.8, 1.7). Meningioma and head injury relationships may therefore demonstrate detection bias, as was previously indicated (20).

2.3.4 Cell phone Use

The general public continues to be very interested in the issue of whether using a cell phone increases the risk of developing meningioma. The relationship between cell phone use and CNS neoplasms has been investigated in at least ten published research projects. Little evidence supports a connection between the two at the present time. The follow-up period following the beginning of mobile-phone use may be brief, and, in some cases, the quantification of cellular telephone use is quite poor, despite the fact that population samples unique to meningiomas are comparatively small (21,22).

2.3.5 Family history of meningioma

The association between the risk of presenting with a meningioma and a familial preponderance of meningioma has only been briefly studied. Malmer et al. (2003) studied, in Sweden, the likelihood of malignancy development in marital partners and close relatives of patients with brain neoplasms and found that a diagnosis of meningioma increased the probability of developing the disease twofold for first-degree relatives but not for spouses of those affected (23). The overall frequency of families with several members having meningioma diagnoses is low (denoting, partially, a broad continuum of phenotypic variation with regard to diagnostic and therapeutic import and therefore screening conducted), and the majority of such families are currently thought to be due to inherited NF2 mutations, regardless of the reality that close to up to 3% of adults could be living with a meningioma (24).

2.3.6 Association with breast cancer

Several research studies have investigated a connection between meningioma and breast cancer. Predisposing factors, such as intrinsic and exogenous hormones, as well as familial predilection, including mutant DNA repair genes, have all been put out as possible explanations for this link (25). Custer et al. (2002) used information from the cancer registry in Washington State to examine the literature and analyze the connection between meningioma and breast malignancies (26). The majority of the reported relative hazards in the existing research are statistically significant and range from 1.5 to 2.0. None of these studies have been able to assess the connection while taking into account potential confounders such as factors directly related to the pregnancy and the menstrual cycle and supplemental hormone use, which are anticipated to be shared by the two neoplasms. The bulk of these studies have relatively small sample sizes and have employed tumor registry data. Studies linking meningioma to breast cancer risk and vice

versa show comparable magnitude increases in risk, demonstrating that there is not a direct causal relationship between these tumors but rather that they are both at risk for developing them due to the same factors, including biological sex, maturity level, hormone induction, and possibly other demographic variables.

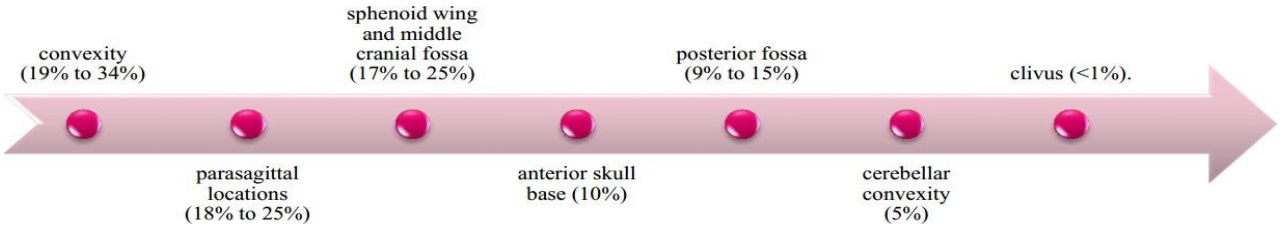
2.3.7 Occupation/ Diet /Allergy

Meningiomas in patient groups in which the etiology is suspected to be due to occupational or industrial exposure to carcinogens have not been definitively linked to any specific chemicals in attempts to do so (27). A broad controlled study with 332 participants discovered no link between nutrition or dietary factors and meningioma (28). Little proof exists for such an association for meningioma, despite several studies examining the relation between glial brain neoplasms and autoimmune conditions like asthma and eczema finding evidence for an association (29).

2.4 Classification of Meningiomas

Meningiomas can be classified according to the location and histopathological grading of the tumor, cerebral convexity meningiomas, and parasagittal meningiomas being the most common intracranial meningiomas by location.

Figure 3: Frequency of location of meningiomas



Adapted from Yamashita, Recurrence of intracranial Meningiomas, 2016

Meningioma histopathology is graded according to proliferative rate, cerebral infiltration, or particular microscopic characteristics. While brain invasion was added as a new parameter for atypical meningioma WHO grade 2 in the 2016 WHO categorization,

multiple recent studies have called into question the predictive value of this criterion (30). However, in the WHO classification for 2021, brain invasion is still a separate requirement for atypical meningioma WHO grade 2. In contrast to earlier classifications, molecular biomarkers are currently included in the grading of a couple of subtypes. Secretory meningiomas can now be identified based on KLF4/TRAF7 mutation detection in addition to histological features. Similarly, regardless of the histopathological criteria for anaplasia, any meningioma with a TERT promoter mutation and/or CDKN2A/B homozygous deletion is assigned to WHO grade 3. Furthermore, rhabdoid meningiomas and papillary meningiomas, two subtypes formerly connected to WHO grade 3, would heretofore not be assigned to a particular grade only on the subtype-specific histology. Similar criteria for atypia and anaplasia that apply to other meningioma variants are now used to grade these two subtypes.

2.5 Clinical Presentation of meningiomas

Like many other CNS tumors, the clinical presentation of meningiomas depends on their size and location. Meningiomas do not have a pathognomonic presentation, but typical clinical symptoms include headache brought on by secondarily raised intracranial pressures, localized neurological impairments, or generalized and partial convulsions brought on by elevated intracranial pressure. Particularly in frontal or parasagittal meningiomas, bizarre alterations in personality, disorientation, and obtundation can be noted; these may first be mistaken for dementia or depression, according to Robin et al. 2018.

2.6 Imaging findings in Meningiomas

The gold standard for the radiologic diagnostic identification and follow-up of meningioma is the magnetic resonance imaging (MRI) modality. It often reveals a well-circumscribed lesion that is extra-axial, dural, and homogenously enhancing. On non-

contrast sequences, these neoplasms are usually isointense/hypointense to gray matter and have a thicker, contrast-enhancing dural tail that is diagnostic of benign meningiomas. Sometimes a CSF fissure can be visible right next to the tumor. On T2 and T2-FLAIR CT images, peritumoral edema might be visible, especially in meningiomas of the secretory subtype and in more invasive meningiomas that enter the brain.

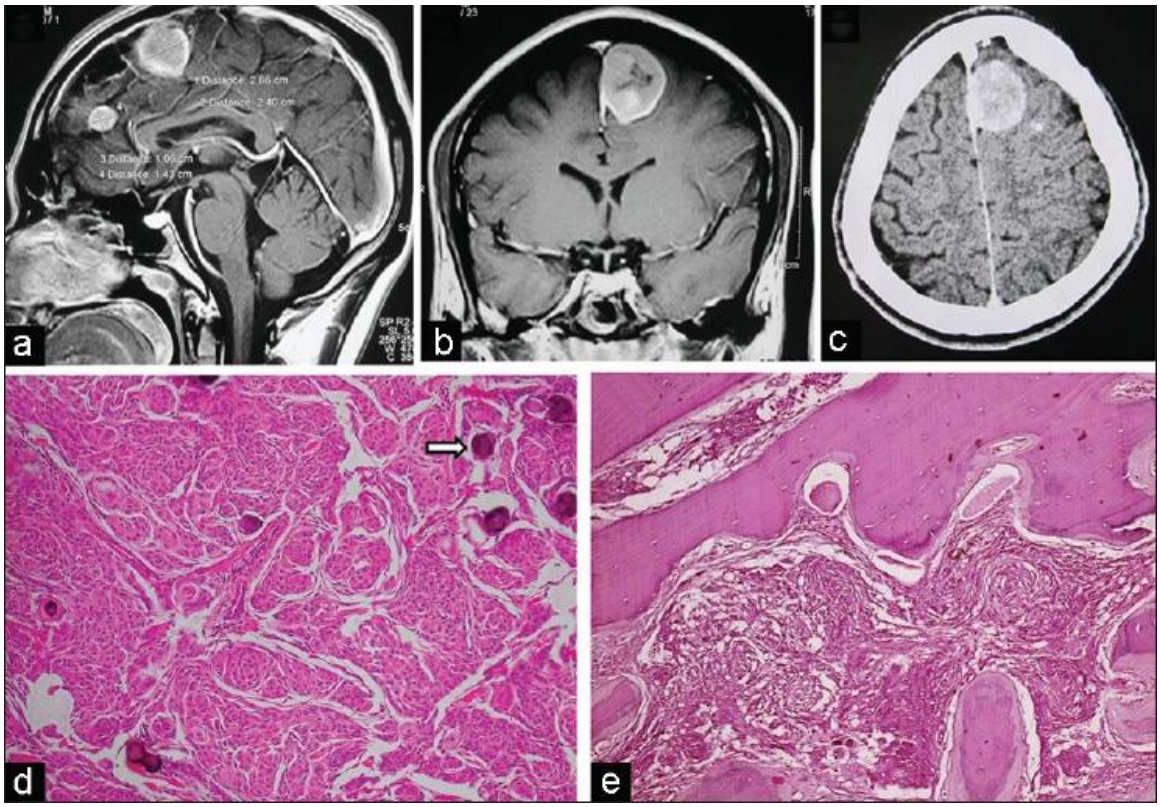


Figure 4: Imaging and histopathological features of meningiomas

The apparent diffusion coefficient (ADC) estimates of meningiomas in diffusion-weighted imaging (DWI) usually vary; however, ADC may be rather low, especially in higher grade tumors but also in grade I meningiomas. According to Kousi et al. (2012), higher choline and alanine levels and lower N-acetyl aspartate (NAA) levels are expected on MR spectroscopy (31). Relatively high cerebral cortical blood flow (rCBF) and relative cerebral blood volume (rCBV) are typically seen in perfusion imaging.

A Magnetic Resonance Angiography (MRA), a vascular-based imaging modality, can assist in defining how the tumor's vasculature interacts with it. For parasagittal tumors that may directly invade the superior sagittal sinus or indirectly cause sinus compression or thrombosis, an MR venogram may be helpful.

On a CT scan, intralesional calcification is frequent, and bone alterations, such as hyperostosis and a deformed skull that looks "beaten brass," can also be visible in tumors that are positioned along the convexity.

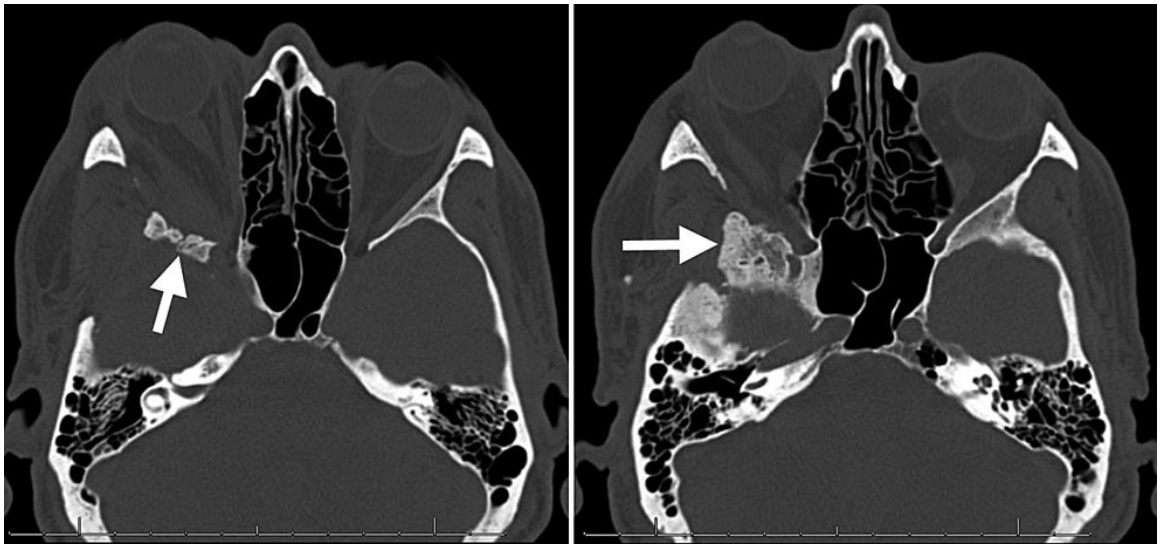


Figure 5: Imaging features of hyperostosis

According to Wong et al. (2002), PET is an imaging technique that can provide physiological and biochemical information about a tumor (32). 2-[18F]-fluoro-2-deoxy-D-glucose (F-FDG), a glucose analog actively delivered into metabolically active cells, is the radioisotope utilized most frequently in PET imaging. For grading of the tumour, prognosis, and separating recurring tumors from radiation necrosis in patients with initial brain tumors, FDG-PET has been employed.

When a surgical biopsy is not an option, positron emission tomography (PET), which uses, for instance, a 68-Gallium-labeled somatostatin-receptor analog (68-Ga-DOTATE), can play a role in tracking potential reappearance in previously radio treated meningiomas and in assisting with diagnosis (33).

2.7 Management of Meningiomas

One of the most frequently diagnosed cerebral tumors is meningioma. To support clinical decision-making, only a small number of controlled clinical studies have been carried out, leading to disparities in management among different locations. Clinical trial findings and recent advancements in molecular genetics serve to improve the diagnosis and treatment approach to meningiomas. The European Association of Neuro-Oncology (EANO) modified its guidelines for the identification and management of meningiomas as a result.

2.8 Molecular biology of meningiomas

Typically, meningiomas are described as slow-growing tumors. Based on histological characteristics, meningiomas are classified as benign (about 92 percent of meningiomas), atypical (6 percent), or anaplastic/malignant (4 percent). More recently, it has been discovered that tumor grade and molecular variables are related.

Patients with NF2 were the first to suspect a connection between meningiomas and chromosome 22 anomalies. Acoustic schwannomas on both sides are the disease's defining feature. In about 50% of NF2 patients, meningiomas develop. Cytogenetic and molecular research has uncovered the NF2 tumor suppressor gene, which is found on chromosome 22q12.1, and its proteinaceous product, schwannomin or merlin. Moesin, ezrin, and a radixin-like protein designated as the schwannomin/merlin tumor suppressor (TuS) protein that is expressed by the NF2 gene, are among the families of band 4.1 cytoskeleton-associated proteins. The roles of schwannomin/merlin in cytoskeletal

processes (such as contact inhibition) and auxiliary signaling pathways (such as Ras) carcinogenesis are among their potential biological functions.

The second most frequent alteration identified by the cytogenetic study of meningioma is deletions on the short arm of chromosome 1. According to FISH investigations, deletion of chromosome 1p is correlated with the evolution of meningiomas in roughly 70% of atypical and virtually 100% of anaplastic cases.

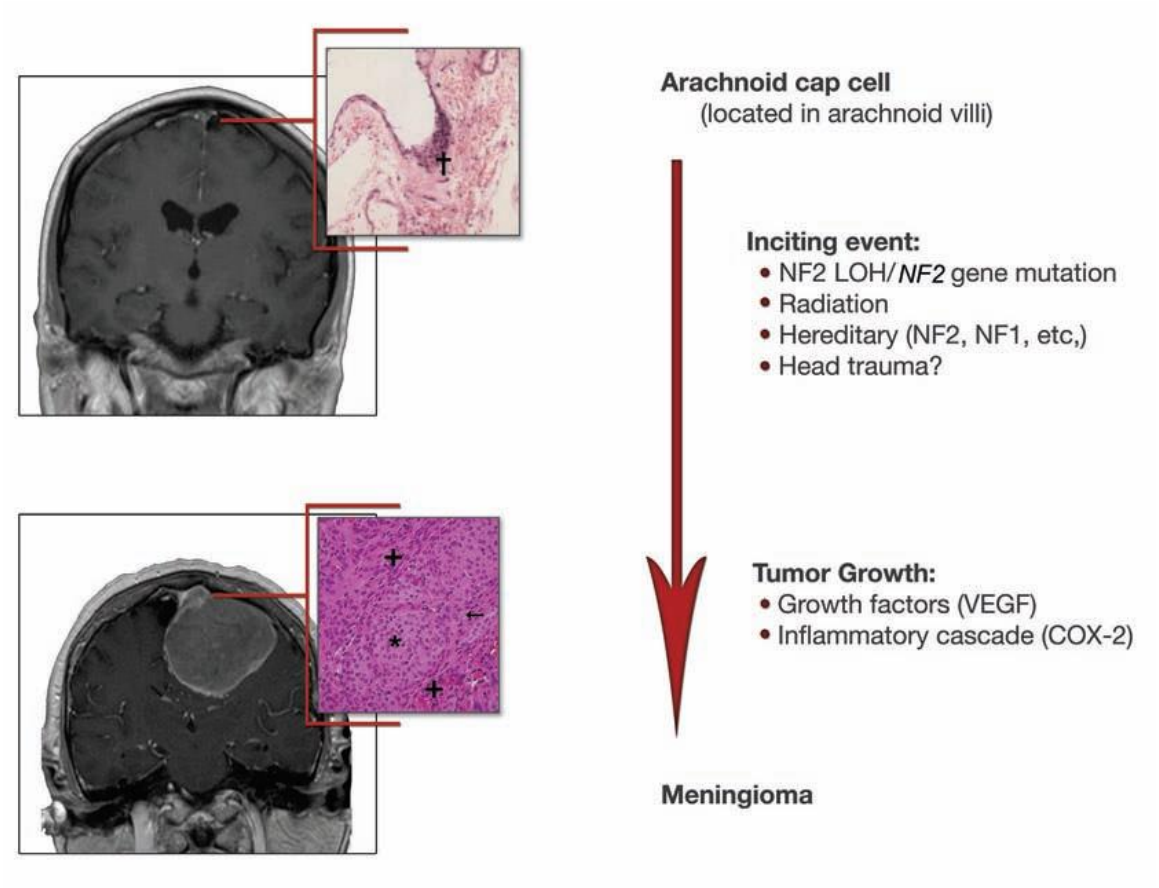


Figure 6: Growth of meningiomas

The c-sis and c-myc oncogenes have increased expression in human meningiomas. The tumor suppression genes that typically regulate the transcription-regulating genes c-myc and c-fos are deleted in meningiomas, which causes >70% of the time for proto-oncogene mRNA expression for c-myc and c-for. The bcl-2 proto-oncogene is also associated with

higher grades, and the TP53 mutation in the tumor suppressor gene is a biomarker for malignant meningioma tumorigenesis. Most atypical and aggressive meningiomas and only about half of benign tumors exhibit telomerase activity. The catalytic component of the telomerase complex is encoded by the human telomerase reverse transcriptase (hTERT) gene, whose overexpression is correlated with a worsening meningioma grade. When telomeric DNA shortens due to persistent mitotic division, normal cells stop dividing. Cancer cells can prevent terminal differentiation and senescence by continuously extending the telomeres on their DNA.

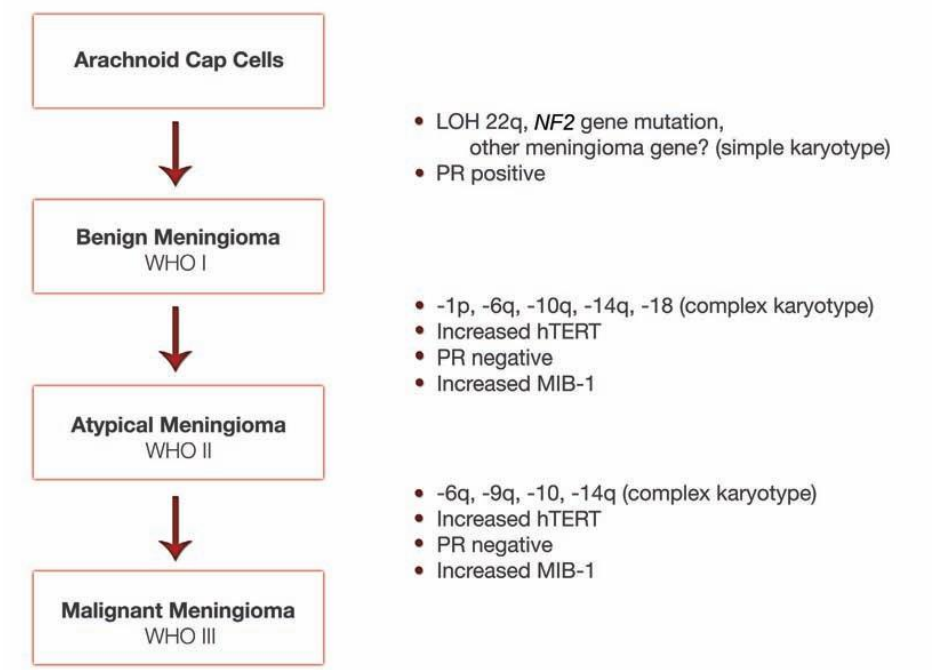


Figure 7: Transformation of meningioma and associated molecular markers.

In human meningioma cultures, exposure to EGF activates signaling pathways that promote cell proliferation and DNA synthesis.

The majority of meningiomas examined express PDGFr or platelet-derived growth factor receptors. In human meningioma cultures, PDGF promotes growth and DNA synthesis via a process that involves the oncogene c-fos. In every meningioma that has been

examined, fibroblast growth factor (FGF) receptors and FGF protein have been discovered. FGF has been shown to promote DNA synthesis and cell proliferation in patient meningioma cultures. Meningiomas are more frequent in acromegaly patients than in the normal population. Meningiomas have been discovered to contain IGF I and II receptors. 30/39 of the examined meningiomas tested positive for IGF-I, while 11/16 tested positive for IGF-II, or 77%. Meningiomas in serum-free media exhibited accelerated development after insulin exposure, as initially shown by Glick et al. (34). Meningiomas have a high density of somatostatin receptors, and adding somatostatin in a lab setting prevents the growth of meningioma cells. According to research by Schulz et al., 29 out of 40 meningiomas tested positive for the somatostatin receptor subtype sst2A (35,36). All other somatostatin receptors, in contrast, were found to stain intermittently and poorly. Three patients with unresectable meningiomas were treated clinically with the long-acting somatostatin agonist octreotide by Garcia-Luna et al. (37). Results also showed a subjective relief of symptoms but no change in computed tomographic (CT) assessments of the meningioma size.

Meningiomas produce VEGF, and two of the primary VEGF receptors have been found on the intratumoral blood vessels of these tumors. VEGF protein or VEGFr positivity is a common discovery in meningiomas. Meningioma peritumoral edema and angiogenesis have been linked to VEGF. The transcription factor hypoxia-inducible factor-1 primarily controls VEGF (HIF-1). We have demonstrated that embolized meningiomas have higher levels of HIF-1 and VEGF, but not in healthy tissues. Several case studies and epidemiological studies that identified traumatic head injury as a predisposing factor for meningioma development prompted researchers to start looking into the potential function of the inflammatory response in meningiomas. Cyclooxygenase is the rate-limiting enzyme in the inflammatory pathway that produces prostaglandins from

arachidonic acid. Prostaglandins, which are biologically active lipid mediators that belong to the eicosanoid family, control a number of vital cellular processes, including proliferation, adhesion, angiogenesis, the inhibition of apoptosis, and inflammation. A key inducible enzyme in mediating inflammatory reactions is cyclooxygenase-2 (Cox-2). Cox-2 overexpression in breast, lung, and colon cancers has also previously been used to illustrate the function of Cox-2 in carcinogenesis. Cox-2 is widely and intensely expressed in meningiomas, according to Ragel et al. (38). Eicosanoids' abnormal activity may thus have a role in the initiation and progression of tumors.

2.9 Hyperostosis and Meningiomas

Meningiomas and hyperostosis are frequently linked, and it has been noted in as many as 25% to 49% of meningiomas. According to a theory, they frequently penetrate nearby bone, which is evident on radiographs by the appearance of thicker bone. Numerous investigations have shown that meningioma can invade the Haversian canals of hyperostotic bone.

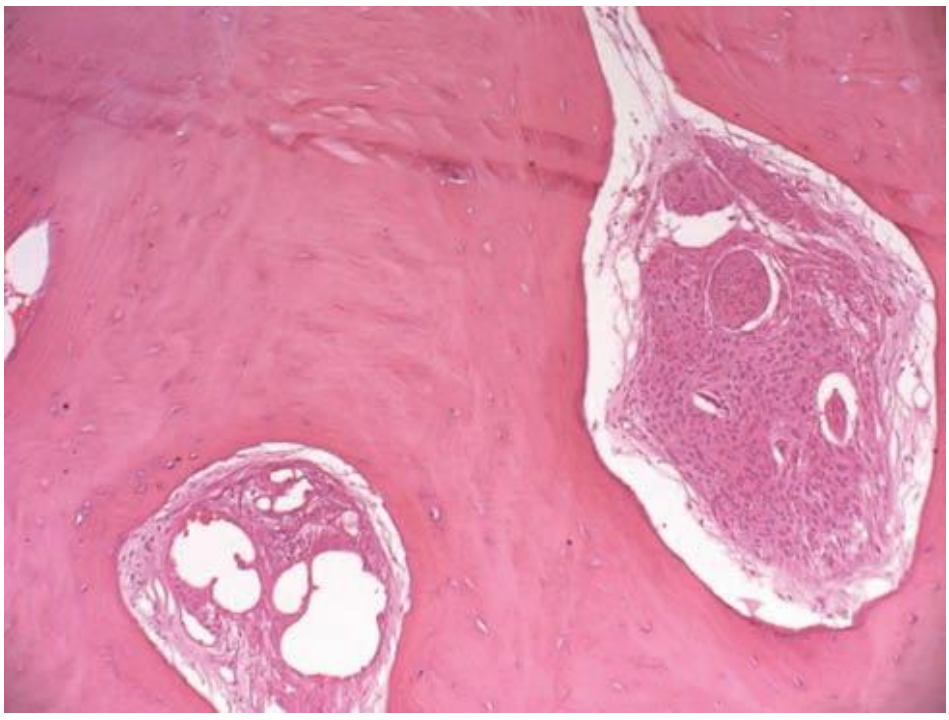


Figure 8: Hematoxylin and Eosin (H&E) stain of hyperostotic bone showing meningioma tumor invasion into the Haversian canals

On CT scans, Terstegge et al. (Figure 8) characterized hyperostosis as a compact, dense, whorl-shaped, and nonhomogeneous structure with local laminar bone structural loss. The osseous calcification density is likely to have significantly increased as a result of the changes to the fine structure of the bone.

When compared to the contralateral bone, MR reveals marginally or occasionally considerably elevated signal intensities of the hyperostosis that was demonstrated by CT. The locations where CT had shown high density and likely dense calcification were the same ones where contrast-free pictures showed a slightly enhanced signal intensity. Signal intensity increases cannot be attributed to increasing calcification alone. The correlation between comparable CT densities and MR signal intensities in locations of cerebral calcifications has been shown to be less than perfect. Although the exact relationships are unclear, it has been hypothesized that either calcium-independent soft tissue features or the concentration of specific trace elements (Fe) in the calcification may affect the signal intensity in such locations. Only a speculative relationship between the slightly elevated signal intensity in the hyperostotic tissue and tumor tissue in the bone, specifically in the Haversian channels, is possible.

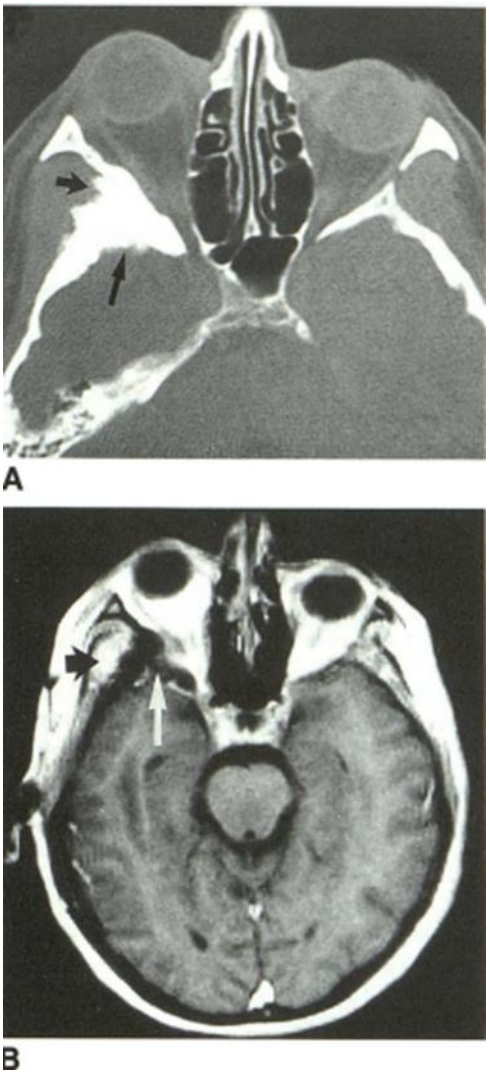


Figure 9: Hyperostosis in meningiomas

Kim et al. identified five hyperostotic radiologic patterns.

(1) Homogeneous pattern: homogeneous density with distinct inner, middle, and exterior tables

(2) Periosteal pattern: The outer and/or inner surfaces of the skull were found to have hyperostosis. The less-dense hyperostotic bone could be distinguished from the surrounding table of the dense cortical bone. The diploe's thickness and density were normal, as were those of the next table.

(3) Three-layer pattern: All three layers were affected by hyperostosis. The diploe continued to be less dense than the inner and outer tables, allowing for the separation of the three layers. In this pattern, the hyperostotic bone's total thickness was quite mild.

(4) Diploic pattern: The thickened and sclerotic diploe was affected by hyperostosis. Hyperostotic diploe, which would be a little less thick than the outer and inner tables of the compact bone, can be distinguished from the outer and inner tables. The inner and outer tables retain their cortical definition.

Forty individuals who had resection for intracranial meningiomas were the subject of a study by Goyal et al. (5). Thirty patients (75%) had radiological evidence of hyperostosis. Eight (20%) of the patients had tumor infiltration of the bone as determined by histopathology.

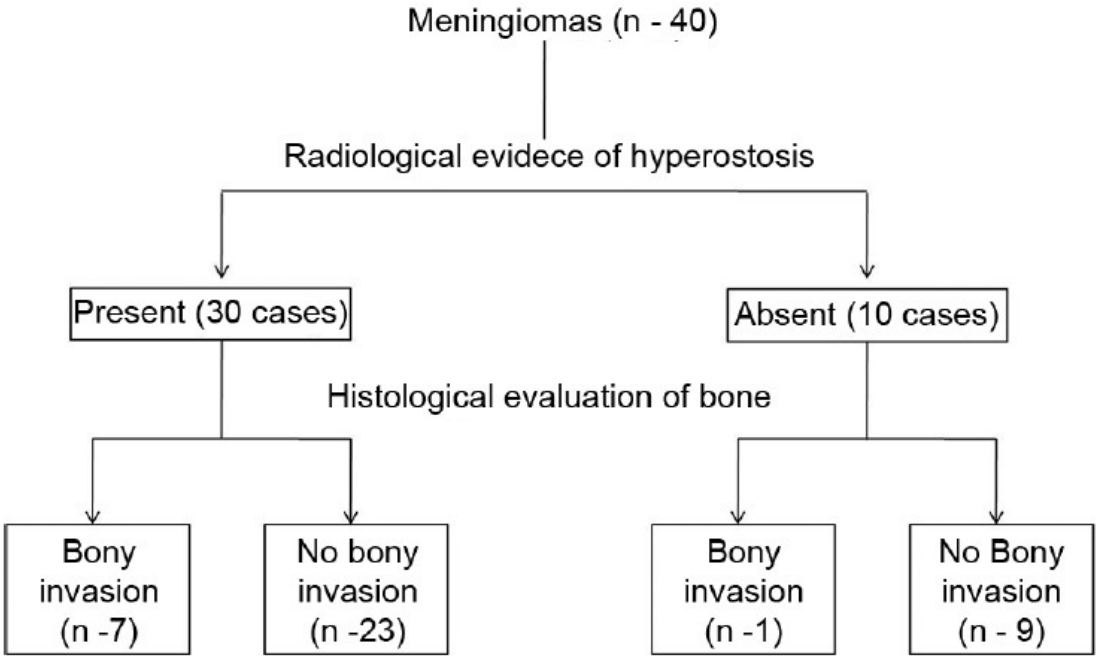


Figure 10: Occurrence of hyperostosis

There has long been controversy around the etiology of hyperostosis in meningiomas. According to other writers, hyperostotic alterations are a byproduct of the tumor's initial growth and do not signify the tumor's invasion of the bone (39).

Various explanations for this phenomenon have been put forth, including previous traumatic injury, secondary inflammation of the bony tissue without bony incursion, activation of osteoblastic cells in healthy bone tissue by substances produced by cancerous cells, synthesis of bone by the tumor of its own, and vascular disruptions brought on by the tumor. According to Nishant et al. (2012), Echlin made the suggestion that hyperostosis and malignant incursion into bone were directly related in 1934. In a study, Cristofori et al. looked into the functions of bone morphogenetic proteins (BMP) 2 and 4 as well as osteoprotegerin (OPG), insulin-like growth factor 1 (IGF-1), endothelin 1 (ET-1), and osteoprotegerin (IGF-1). According to his findings, the overexpression of osteoprotegerin (OPG) and insulin growth factor (IGF)-1 was linked to the emergence of hyperostosis. According to his research, tumor infiltration is not always the source of hyperostosis but rather the overexpression of osteogenic chemicals that affect osteoblast/osteoclast activity. In adult leptomeninges, bone morphogenetic protein four was occasionally found, by Western blot and immunohistochemistry, in 89 or 84 percent of Grade I meningiomas and in 60 percent of Grade II meningiomas, respectively. In addition, Johnson et al. reported finding activated Smad1 in all of the meningiomas they examined, as well as bone morphogenetic protein receptors IA and II in the leptomeninges. BMP 4 was found in the conditioned medium from 4 out of 7 cultures, and it was shown to enhance meningioma cell proliferation and phosphorylation/activation of Smad1 and not p38 MAPK or p44/42 MAPK in vitro.

A 56-year-old man who came with a meningioma and hyperostotic bone with minimal tumor cell infiltration became the subject of a case study by Jun Hon et al. Large portions of the tumor, and the damaged bone was removed. Rhabdoid meningioma was confirmed by histological analysis. However, there was no tumor cell infiltration in the hyperostotic bone. Although the exact etiology of the hyperostosis brought on by meningioma is

unknown, tumor invasion is thought to be the likely culprit. Since there was no tumor cell infiltration in this instance, it is possible that another mechanism was at play.

Simpson thoroughly explained the significance of the degree of resection in preventing meningioma recurrence in his seminal work, which was published in 1957. In Simpson Grades I through IV, he observed recurrence rates of 9, 19, 29, and 40%, respectively. Despite the fact that the series was published before the development of CT, MRI, and micro neurosurgery, numerous subsequent investigations on the rate of meningioma recurrence have supported the idea that clinical success in meningioma surgery is correlated with the depth of resection. Therefore, it's also important to remove any bone that the neoplastic growth has infiltrated in order to achieve total excision and ensure a lower recurrence rate. To ensure total removal and tumor-free bone margins in grade I and II meningiomas, Fathalla et al. (2020) advised removal of the center of hyperostotic bone and the adjoining 2 cm margin (40). However, because invasion can occur without radiographic evidence of hyperostosis and because it is not practical to examine bones in frozen sections, it is not possible to predict which patients will likely exhibit bone invasion based on preoperative radiology or intraoperative pathological evaluation. Therefore, wherever possible, one should remove as much bone in touch with the tumor as possible in order to attain a higher Simpson grade of tumor excision (5).

2.10 Study Justification

According to Mwang'ombe et al., meningiomas account for 34.9 percent of cerebral malignancies in our health system (41). According to Donald Simpson's seminal study from 1957, the degree of bone excision in meningiomas directly affects recurrence rates (42). His advice to maximize the area of resection and reduce morbidity is still applicable, although his eponymous index is no longer appropriate in contemporary

meningioma surgery, according to Schwartz et al. 2020 (43). Nishant et al. in 2012, documented hyperostosis in 25–49% of meningiomas (5). It is yet unclear what causes hyperostosis. Many authors have proposed the possibility that hyperostosis is a symptom of tumor invasion. Some individuals, however, think that these skeletal modifications are merely reactive. In situations of intracranial meningiomas, neurosurgeons frequently drill the hyperostotic bone and replace the bone flap. The degree of microscopic bone invasion in meningiomas will ultimately affect surgical care, which will have a positive effect by lowering tumor recurrence rates.

2.11 Research Question

Does radiologic evidence of hyperostosis in meningiomas always signify microscopic tumor invasion?

2.12 Hypothesis

Radiological evidence of hyperostosis seen in meningioma is due to microscopic tumor invasion.

2.13 Objectives

2.13.1 Main

To determine the proportion of patients with radiologic hyperostosis with microscopic tumor invasion in bone .

2.13.2 Specific

1. To assess the proportion of meningioma patients with hyperostosis as seen at the Kenyatta National Hospital.
2. To assess the extent of resection of meningiomas at the K.N.H
3. To determine the histopathologic subtypes/ grading of meningiomas among patients seen at KNH.

4. To correlate the histopathologic subtypes/ grading of meningiomas and bony invasion among patients seen at KNH.

2.14 Conceptual framework

The conceptual framework demonstrates interaction between various variables. In this study, a correlation will be made to assess the histopathological subtype of tumor and whether there is hyperostosis. Confounder to this relationship is occurrence of bony pathology resulting to inflammation that is not directly associated with the meningioma.

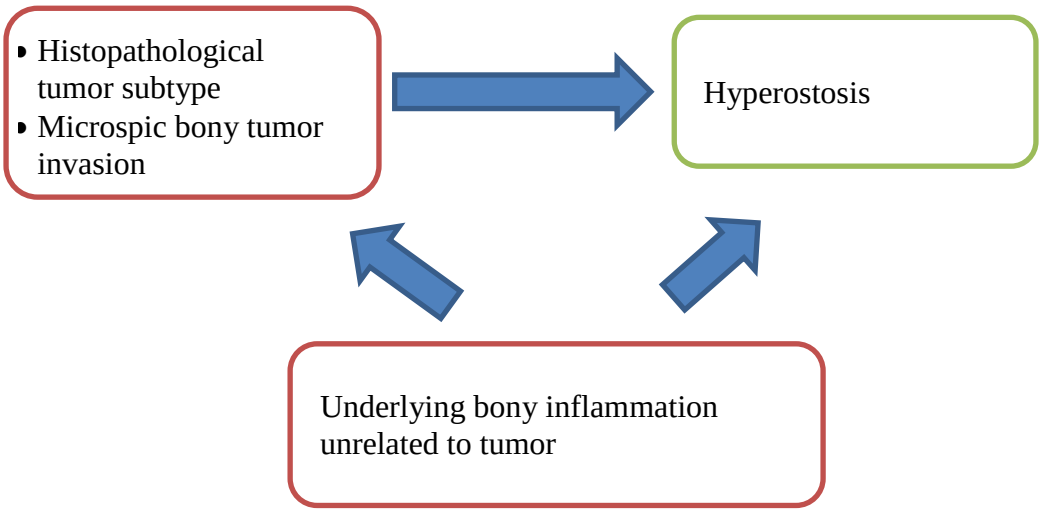


Figure 11: Conceptual framework demonstrating relationship between hyperostosis and tumor subtype and potential confounders.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

Prospective cohort study design. Patients were recruited prior to undergoing surgery for intracranial meningiomas.

3.2 Study Site

The study was conducted at the Kenyatta national hospital Neurosurgery unit(Ward 4C/ clinic) and pathology departments.

KNH is a national referral hospital providing specialist neurosurgical services. It has availability of neurosurgeons and necessary equipment to operate complex cases such as meningiomas.

On average, 25 patients are seen with meningiomas in a year and also undergo operation for the same as per the brain tumor association of Kenya statistics.

3.3 Study population

All patients that were surgically treated for an intracranial meningioma were recruited into the study.

3.4 Inclusion and Exclusion Criteria

3.4.1 Inclusion criteria

i. All patients with radiological and histopathological diagnoses of intracranial meningiomas.
ii. Criteria for radiologic invasion shall include CT/ MRI evidence of hyperostosis as described earlier.
iii. Patients with recurrent meningiomas.

3.4.2 Exclusion Criteria

i. Intracranial tumors other than meningioma on histopathology.

ii. Patients with radiological diagnosis of hyperostosis not adjacent to tumor.

iii. Patients who presented with a diagnosis of hyperostosis frontalis interna.

iv. Patients who presented with extracranial meningiomas.

v. Patients who didn't consent to the study.

3.5 Sample Size Determination

A census of all consenting eligible participants was used.

The sample size was calculated as shown using Cochrane's Formula:

$$n_0 = \frac{Z^2 pq}{e^2}$$

Where:

n_o= desired size of the sample

Z= The 95% confidence interval (1.96)

e= Margin of error allowed (0.05)

P=The proportional estimate of patients with hyperostosis with meningiomas, thus p as 25%.

q= 1-P

Adjustment for the infinite population.

Sample size= 43

3.6 Sampling Procedure

A consecutive sampling of study participants as they underwent surgical treatment for meningioma.

3.7 Variables

3.7.1 Dependent variables

Hyperostosis in meningioma

3.7.2 Independent variable

Age

Sex

Histopathological tumor subtype

Microscopic bony invasion of tumor

3.8 Data Collection

A structured data collection tool was used and had various components.

Patients were recruited after admission to the Neurosurgical unit to undergo surgery for intracranial meningioma.

The study procedure, the risks and benefits associated with it were clearly explained to the patients. After accepting to participate in the study, they signed an informed consent.

After signing the informed consent, a structured questionnaire was administered to the study participants to collect information on clinical characteristics.

3.9 Study Procedure

3.9.1 Consenting and Study Enrollment

All study participants received an oral summary of the investigation's purpose, and afterward, written informed consent was sought from them.

3.9.2 Sample retrieval, transport, and laboratory processing

Participants going for meningioma resection who were recruited and consented to the study were wheeled to the operating theatre.

They were positioned based on the location of the tumor.

Proper skin preparation was done with an alcohol-based solution.

Cleaning and draping was done aseptically.

A skin incision was made depending on the tumor location, and the scalp was opened in two layers.

A craniotomy was fashioned.

An area of bone measuring 2cm by 2cm by 2cm, which was hyperostotic, was measured using a sterile measuring tool and was harvested using a high-speed drill and craniotome prior to dural opening by the principal investigator.

Once the durotomy was done, early tumor devascularisation,dedressing and internal decompression ensued.

The extent of tumor resection based on the Kobayashi Okudera/ Simpson grading classifications was recorded.

Following tumor resection, closure of dura, anchorage of bone, and closure of scalp in two layers was done.

Both tumor and bone samples collected intraoperatively were stored in separate sample bottles containing 3% formalin solution for preservation and sent to the histopathology lab together with a standard laboratory request form detailing the patient data details and investigation required.

Decalcification of the bone samples with 10% formic acid was done, which allowed tissues to be amenable for sectioning.

After which, tissue fixation and processing was done.

Hematoxylin and eosin staining was used to determine microscopic tumor invasion (44).

3.9.3 Training Procedures

The tools were taught to a suitable research assistant who is a neurosurgery resident and has experience in data collecting.

3.9.4 Quality Control

To ascertain the reliability and both internal and external validity of the study, laboratory and imaging reporting followed the standard protocols recommended by the hospital. All images were reported by a qualified consultant radiologist. The surgeries were performed by a qualified consultant neurosurgeon. The specimens collected were analyzed by a qualified consultant neuro- pathologist in a state-of-the-art pathology lab.

3.10 Ethical Consideration

Ethical approval and permission to proceed with the study was sought from the Kenyatta National Hospital/the University of Nairobi Ethical, Research, and Standards (KNH/UON ERC) review committee. The study was conducted in compliance with the principles of Human research as outlined in the Declaration of Helsinki and the Belmonte Report.

Confidentiality: The information gathered from this study project has been kept strictly confidential. The information gathered about the respondents during the investigation and data collection procedures has been kept strictly private and used solely for the objectives of this research. Any information about the patients has a unique number on it instead of the patient's name. All the information stored in soft copy has been kept secured using a password.

Both the research team and the patient used proper personal protective equipment and followed safety protocols during the interview process to prevent the spread of COVID-19 and any other infectious diseases.

3.11 Data Management

Data was entered into password-protected Ms. Access. Only the principal investigator and the authorized personnel were allowed to access the data.

Structured data collection tools have been stored in a safe after data entry.

3.12 Data Analysis

IBM SPSS Version 26 was used for data analysis.

Descriptive statistics such as means and medians were used to analyze quantitative data to characteristics of the study participants. Categorical variables were reported in proportions and percentages.

The Student T-test was employed in hypothesis testing to evaluate the relationships between continuous independent factors and categorical outcome variables, such as age and presence of hyperostosis. To evaluate relationships between two categorical variables, such as the existence of hyperostosis versus sex or age groups or microscopic invasiveness of tumor, the Chi-square test of independence was utilized.

A <0.05 p-value was deemed statistically significant.

Data has been presented in frequency tables, histograms, bar charts, pie charts, and written reports.

3.13 Data dissemination

The study findings shall be disseminated in conferences and professional meetings. The manuscript shall also be published in a peer-reviewed journal. Hard copies of this study have been submitted to the department of surgery, Unit of Neurosurgery. An electronic copy of this research will be available at the university of Nairobi e- repository.

3.14 Limitations of the study

The following limitation was encountered during the study-;

1. Sample size- Not all meningiomas presented with hyperostosis. However, all cases of meningioma undergoing surgery were investigated for hyperostosis. Due to the limited number of patients with meningiomas, attempts were made to recruit all patients presenting with the condition to ensure maximal capture of the sample size.

CHAPTER FOUR

4.0 RESULTS

A total of 36 patients underwent meningioma surgery during the study period. Fourteen of these patients did not have radiological evidence of hyperostosis and were therefore excluded from the study. The remaining 22 patients were enrolled in this study.

4.1 Demographic and clinical characteristics

4.1.1 Sex distribution

Of the 22 patients recruited to the study, females patients were 17(77.3%) while male patients were 5(22.7%) with a ratio of female to male preponderance at 8:2.

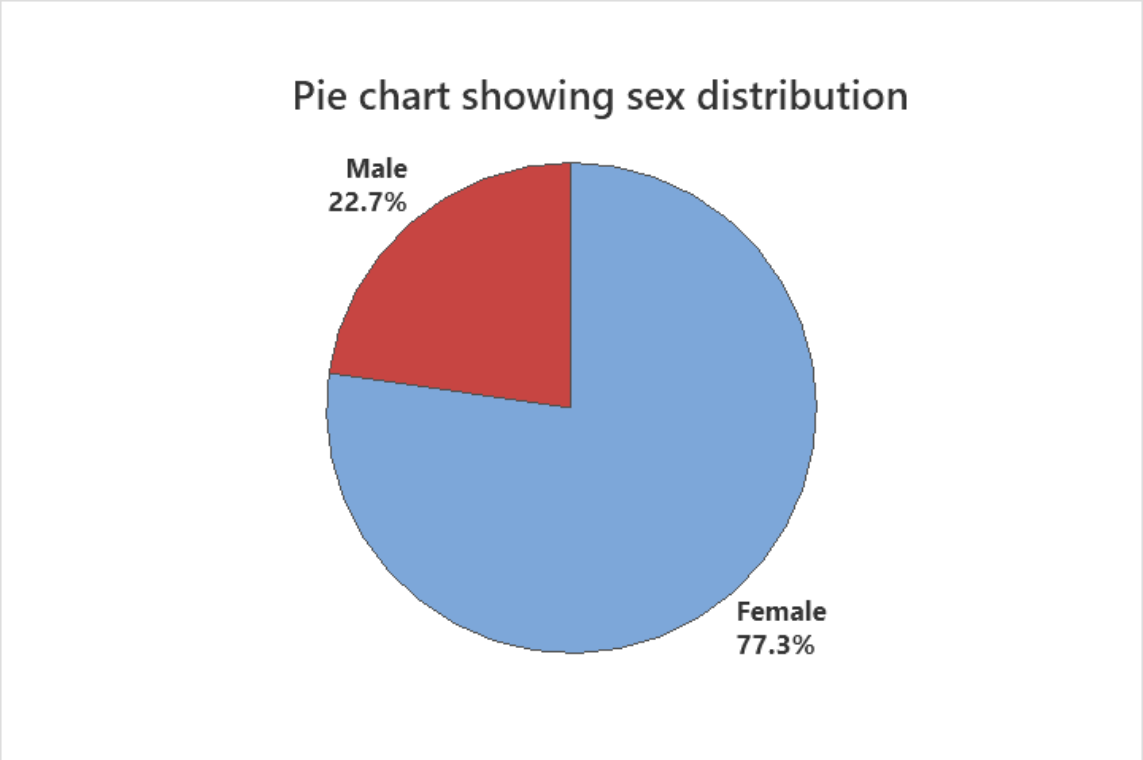


Figure 12: Sex distribution in meningioma cases

4.1.2 Age distribution

The median age of the patients at the time of surgery was 45.5 years (range 20-65 years; mean 44.3 ± 11.9 years) [Table 1]. Majority of the patients 9(40.9%) belonged to the age group 31-40.

Table 3: Distribution of age groups

Age group	Count	Percentage
21-30	2	9.1
31-40	9	40.9
41-50	6	27.3
51-60	3	13.6
61-70	2	9.1

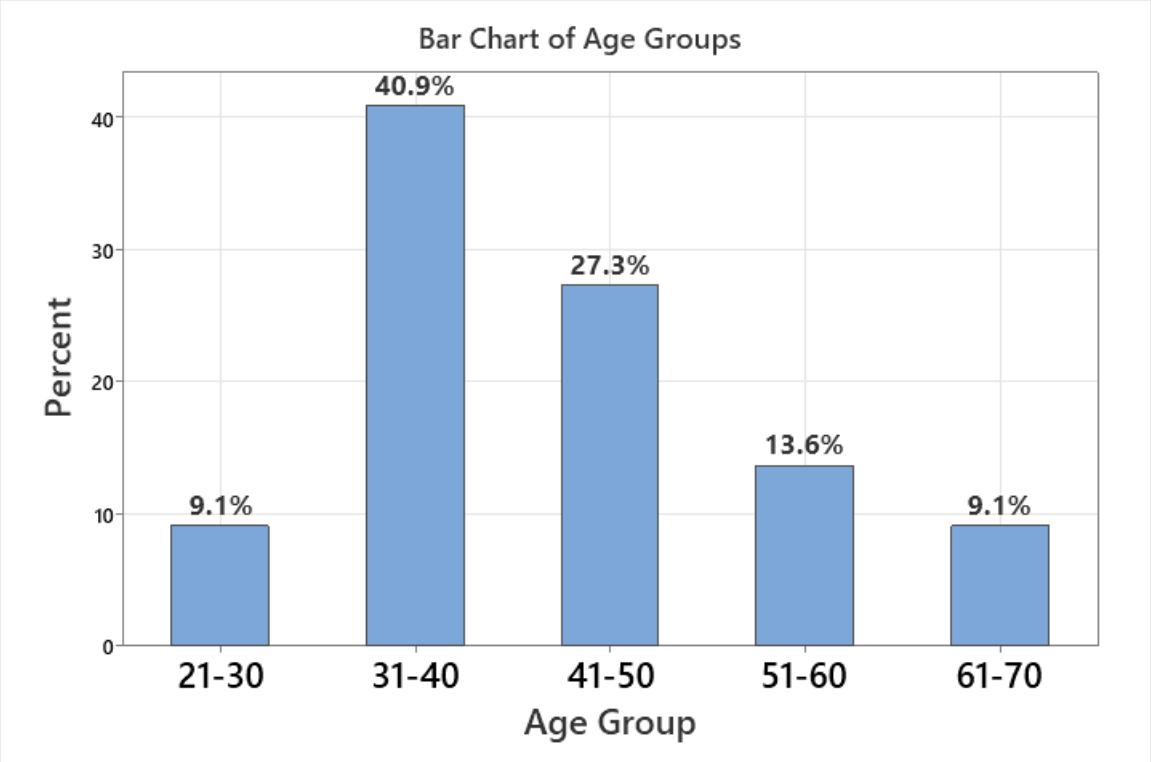


Figure 13: Distribution of age groups.

4.1.3 Location of meningiomas

Convexity meningiomas were most common (8 cases), followed by outer sphenoid wing meningiomas (4 cases) . Parasagittal and Olfactory groove meningiomas were 2 each, and one case each of falcotentorial, foramen magnum, planum sphenoidale and sphenoorbital meningiomas [Table 1].

Radiological evidence of hyperostosis was present in all the 22 patients [Table 2], [Figure 1]. In all these cases, the hyperostosis was confirmed intra-operatively.

Table 4: Location of meningiomas

Tumor location	Count	Percent
Convexity	8	36.4
Falcotentorial	1	4.6
Foramen Magnum	1	4.6
Olfactory Groove	2	9.1
Outer Sphenoid wing	4	18.2
Parasagittal – middle 1/3	2	9.1
Planum Sphenoidale	1	4.5
Spheno orbital	1	4.5
Total	22	100%

4.1.4 Tumor recurrence

Only 1(4.5%) of the patients had tumor recurrence while 21(95.5%) of the patients were presenting for the first time (Figure 14).

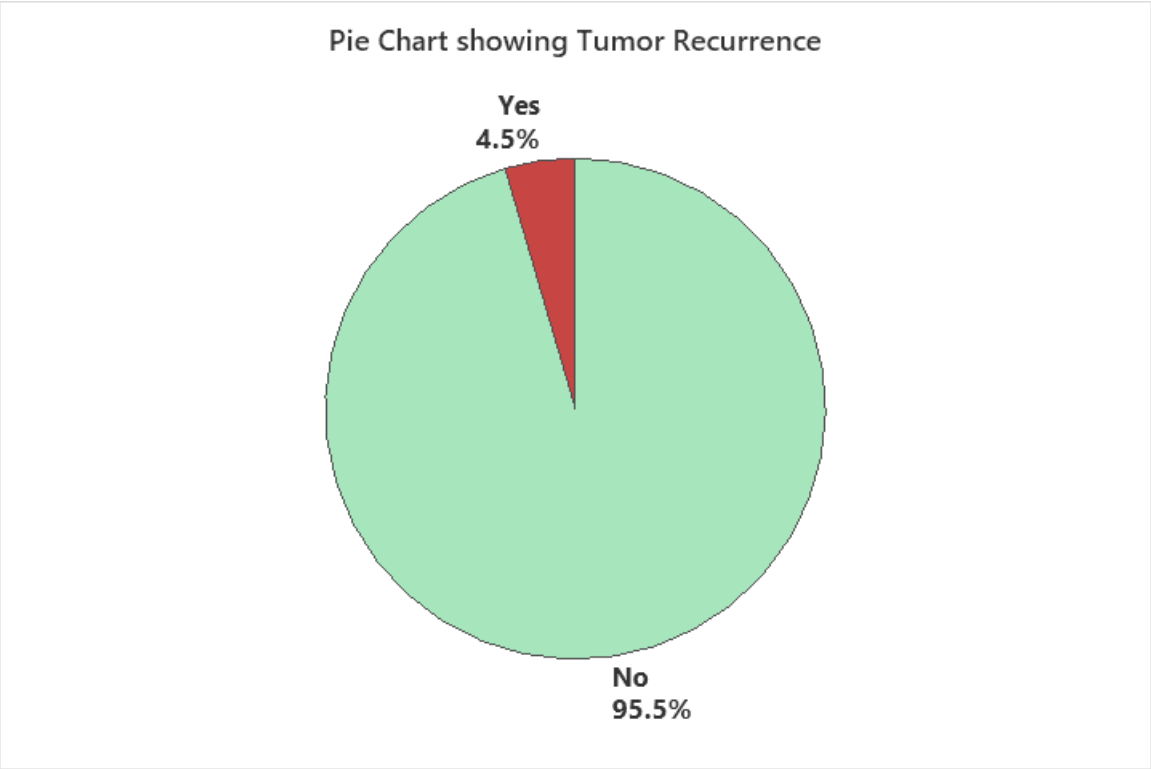


Figure 14: Tumor recurrence

4.2 Objective 1: To determine the proportion of patients with radiologic hyperostosis with microscopic tumor invasion in bone .

All the 22 patients included in the study had radiological evidence of hyperostosis. 13(59.1%) of the patients had microscopic tumor invasion in bone while 9(40.6%) did not (Figure 15).

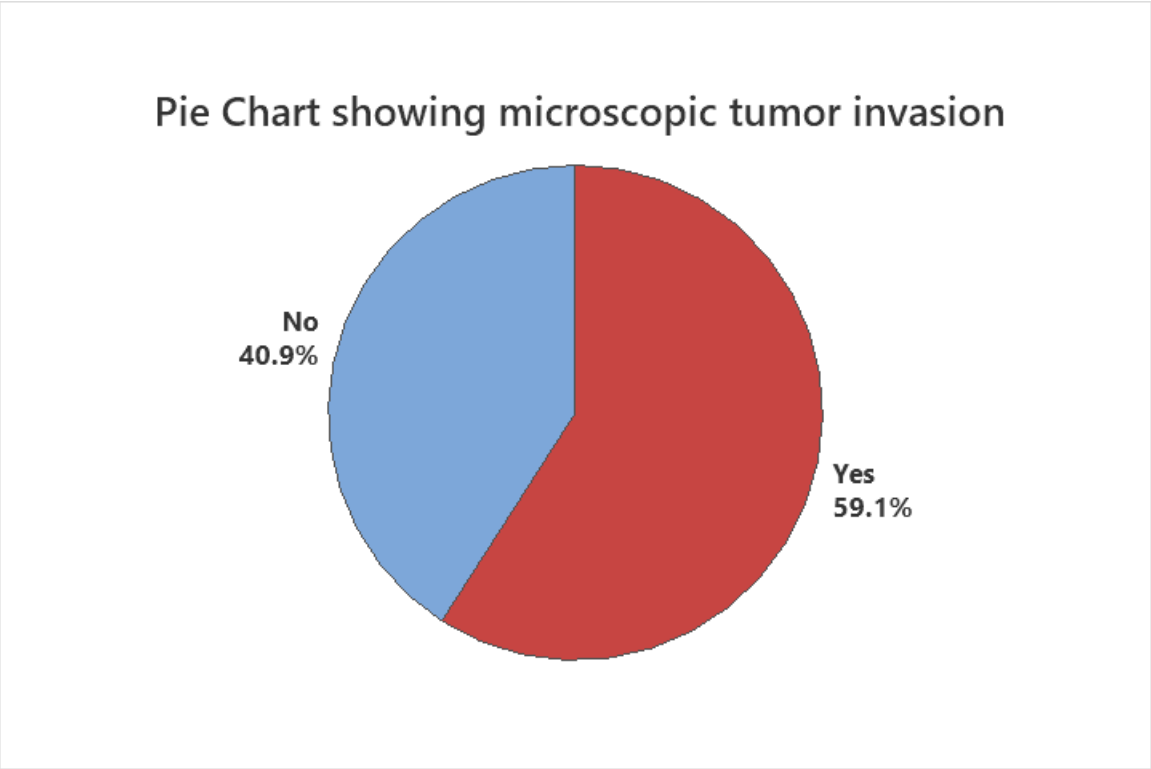


Figure 15: Proportion of patients with microscopic tumor invasion in bone

4.2 Objective 2: To assess extent of resection of meningiomas

Majority of patients had grade 2 extent of resection by both Kobayashi and Simpson grading (Table 3 & 4)

i) Kobayashi grading

The table below shows the extent of Kobayashi grading

Table 5: The extent of resection by Kobayashi grading

Kobayashi Grading	Count	Percentage
1	3	13.6
2	16	72.7
3	2	9.1
4	1	4.5
5	0	0

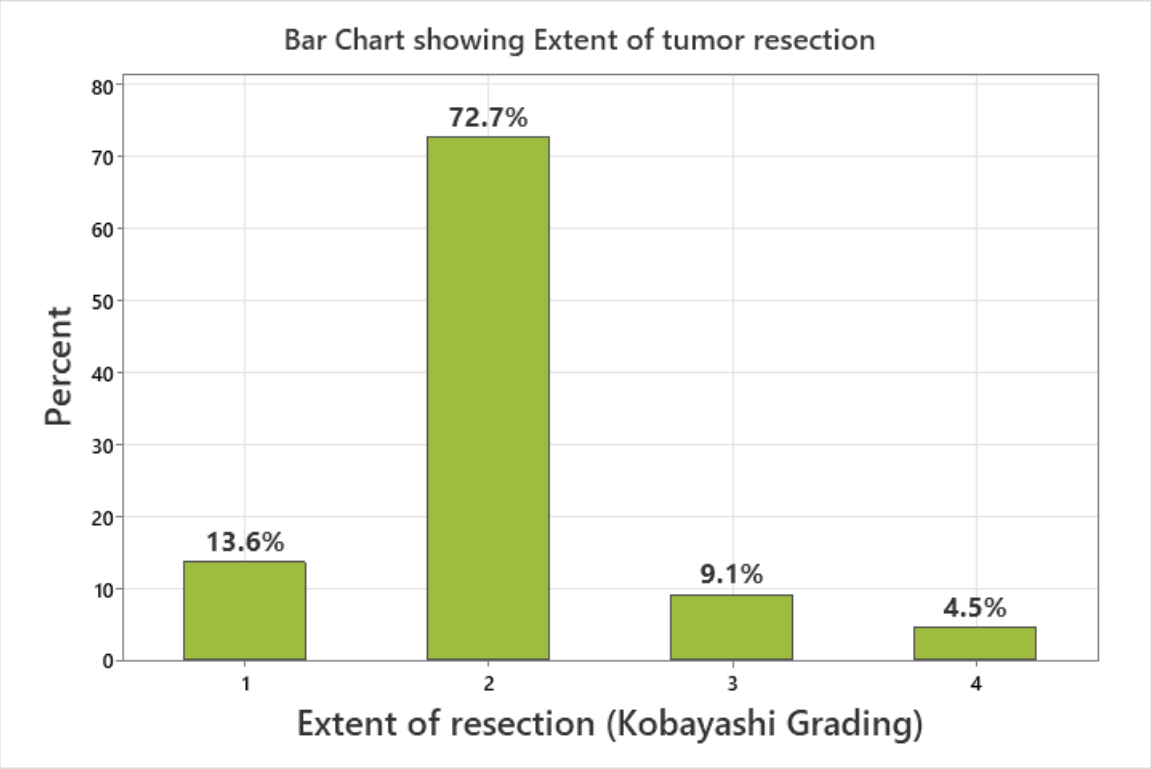


Figure 16: Kobayashi grading extent of resection

ii) Simpson grading

Table 6: The extent of resection by Simpson grading

Simpson Grading	**Count**	**Percentages**
1	3	13.6
2	16	72.7
3	2	9.1
4	1	4.5
5	0	0

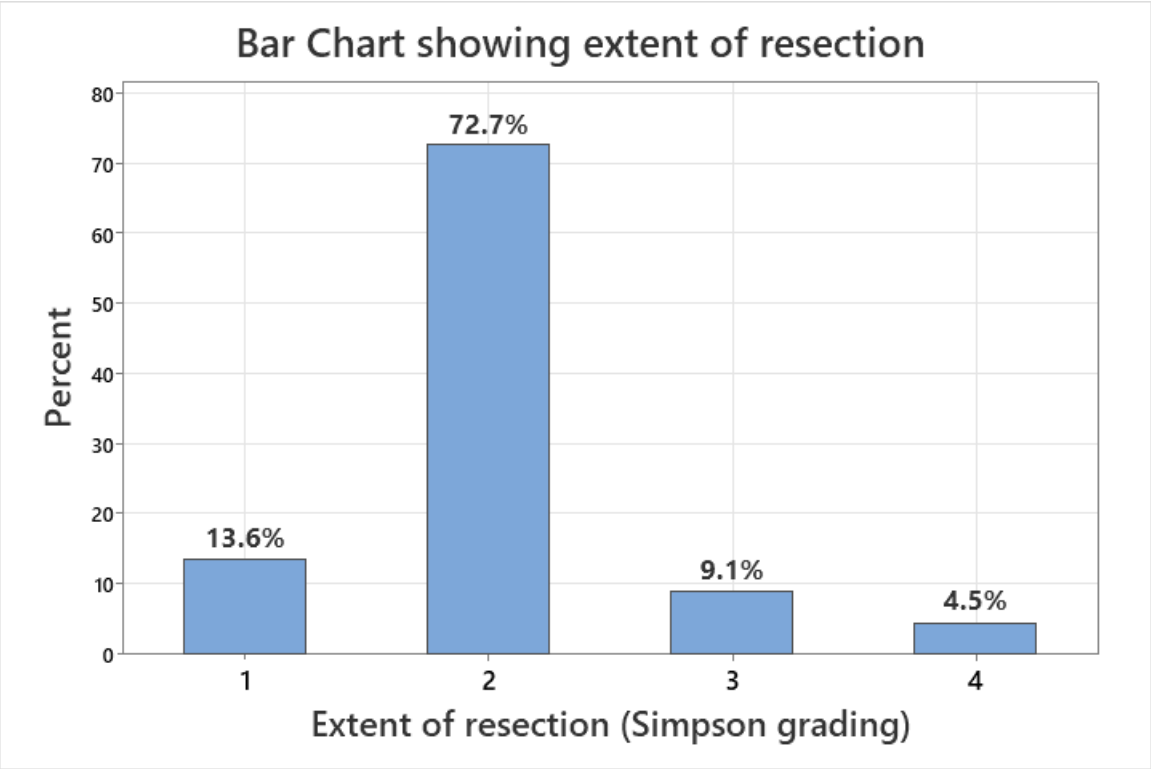


Figure 17: Simpson grading extent of resection

4.3 Objective 3: Histopathologic grading/subtypes of meningiomas among patients seen at KNH

The most common histological subtype of meningiomas was the meningothelial variant at 15 (68.2%) (Table 7).

Table 7: Histopathologic subtypes of meningiomas

Histological	Count	Percentage
Anaplastic	1	4.6
Atypical	1	4.6
Fibroblastic	3	13.6
Meningothelial	15	68.2
Transitional	2	9.1

4.3.1 WHO Grading of Meningiomas

There were 20(90.9) % patients with Grade 1 while only 2(9.1%) had grade 3 as per the WHO 2021 grading.

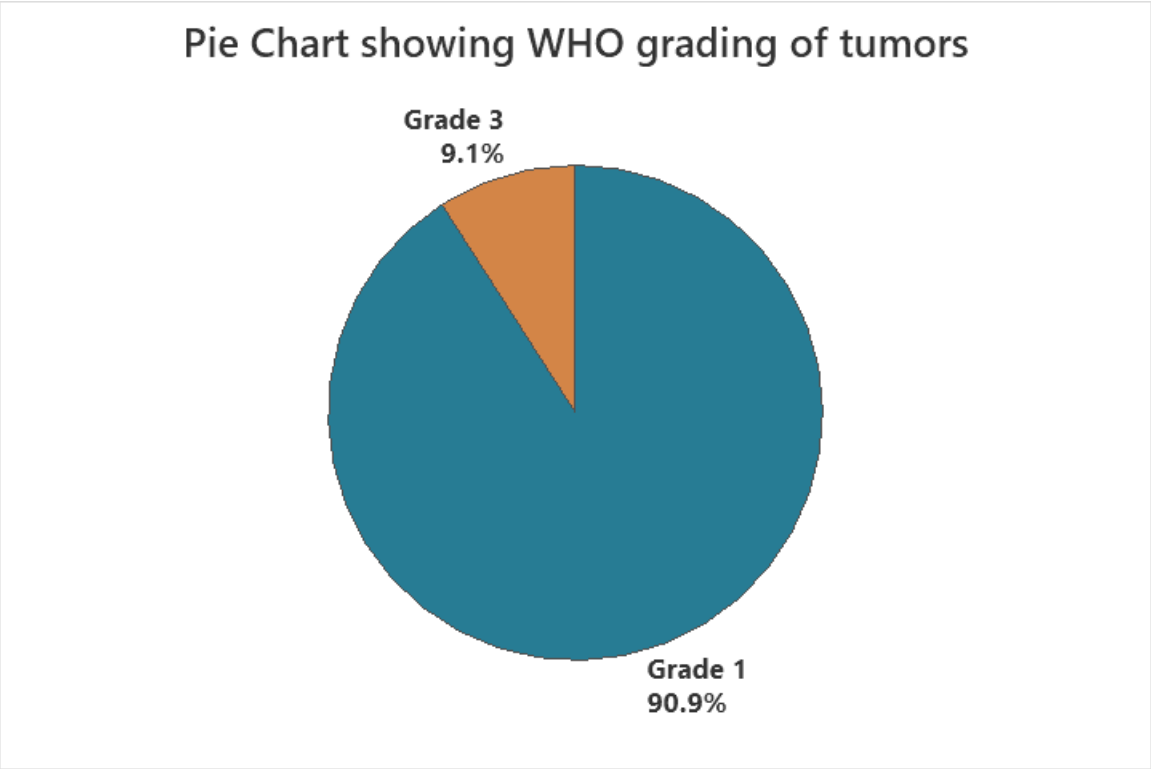


Figure 18: WHO grading of meningiomas

4.4 Objective 4: Correlation of the histopathologic subtype / grading of meningioma and bony invasion among patients seen at KNH.

The association between the histologic subtype and microscopic tumor invasion in bone demonstrates that no specific histologic subtypes were associated with microscopic tumor invasion (Table 6). The fibroblastic variant however had a p value of 0.049 suggesting that it may possibly be least likely associated with microscopic tumor invasion in bone. Further studies are needed to test this association.

Table 8: Association of histopathologic subtype and microscopic tumor invasion.

Histologic Subtype	Microscopic Tumor invasion in bone		P value*
	Yes	No	
Anaplastic	0	1/1(100%)	0.409
Atypical	1/1(100%)	0	0.439
Fibroblastic	0	3/3(100%)	0.049
Syncytial/meningothelial	10/15 (66.7%)	5/15 (33.3%)	0.376
Transitional	2/2(100%)	0	0.494

*Fishers exact p value

The table below represents the association W.H.O Grade and Microscopic Tumor invasion in bone**.**

Table 9: WHO grades and microscopic tumor invasion

W.H.O Grade	Microscopic Tumor invasion in bone		P-Value
	Yes	No	0.784
Grade 1	12/20(60%)	8/20 (40%)	
Grade 3	1/2 (50%)	1/2 (50%)	

4.4.1 Evaluation of the relationship between age groups and presence of microscopic invasiveness of tumor.

Fishers' exact test of association was used and it indicates that there is an association between the age groups 31 – 40 where the age group was least likely to have microscopic tumor invasion in bone. The odds ratio is 0.05 (0.03 – 0.564) (Table 9).

Table 10: Associations between age groups and microscopic bone tumor invasion

Age group	Microscopic tumor invasion in bone		P value*	Odds ratio
	Yes	No		
21-30	1/2 (50%)	1/2 (50%)	0.662	n/a
31-40	2/9 (22.2%)	7/9(77.8%)	0.012	0.05 (0.03 – 0.564)
41-50	5/6 (83.3%)	1/6(16.7%)	0.178	n/a
51-60	3/3(100%)	0	0.186	n/a
61-70	2/2(100%)	0	0.338	n/a

*Fishers exact test p value; n/a – not applicable since p values not significant

CHAPTER FIVE

5.0 DISCUSSION

5.1 Discussion

The association between meningioma and hyperostosis is well known. Nishant et al documented hyperostosis in 25-49% of meningiomas (5) and was present in 59.1% of cases of meningioma studied in this series. The incidence in our series was higher owing to a greater number of meningomas involving the convexities and sphenoid wing, which are known to be associated more frequently with hyperostosis (6) .

Meningiomas are generally thought to affect the female population more than the male population. In this study we found a female to male ratio of 8:3 which compares well with Muriithi et al. findings in (2015), where he found the gender disparity in the prevalence of these tumors at KNH to be 7:3 (3).

The cause of hyperostosis in meningiomas has long been a matter of debate (5). There are various hypotheses which aim at explaining this phenomenon including prior traumatic injury, irritation of bony elements by the tumorous growth without bony invasion, activation of osteoblastic cells in healthy bone by substances produced by neoplastic cells, synthesis of bone fragments by the tumor itself, and vascular abnormalities brought on by the neoplasm are all factors that may contribute to hyperostosis (19) . In 1934, Echlin suggested a direct association between hyperostosis and tumor invasion of the bone. Since then, microscopic tumor invasion in the harvesian canals as a cause of hyperostosis has been gaining traction among many surgeons worldwide. Our study shows the presence of tumor cells in the bone overlying a meningioma in 59.1% of the cases. These results indicate that tumor invasion into the bone is present in a significant number of patients with meningioma who have hyperostosis. However , the reason why 41.9% of the patients who had evidence of radiological hyperostosis did not have

microscopic tumor invasion into bone remains a mystery. It remains to be elucidated whether tumor invasion is the cause or the result of bony changes. It also negates the possibility that the invading tumor cells are responsible for the increased bone production. It is more likely that reactionary changes in the bone due to the close proximity to the tumor and their shared blood supply lead to production of growth factors which stimulate bone production, leading to hyperostotic changes with attendant release of chemotactic factors that attract the tumor cells into the bone matrix (5). We hypothesize that there may be another pathogenetic pathway, yet to be explained, which leads to both the bony changes and tumor invasion into the bone.

Simpson thoroughly explained the significance of the degree of resection in preventing meningioma recurrence in his seminal work, which was published in 1957. In Simpson Grades I through IV, he observed recurrence rates of 9, 19, 29, and 40%, respectively. Despite the fact that the series was published before the development of CT, MRI, and micro neurosurgery, numerous subsequent investigations on the rate of meningioma recurrence have supported the idea that clinical success in meningioma surgery is correlated with the depth of resection. These findings were further supported by Okudera/Kobayashi in 1992 (43).

Therefore, it's important to remove any bone that the neoplastic growth has infiltrated in order to achieve total excision and ensure a lower recurrence rate. To ensure total removal and tumor-free bone margins in grade I and II meningiomas, Fathalla et al. (2020) advised removal of the center of hyperostotic bone and the adjoining 2 cm margin (40). However, because invasion may or may not occur with radiographic evidence of hyperostosis and because it is not practical to examine bones in frozen sections, it is not possible to predict which patients will likely exhibit bone invasion based on preoperative radiology or intraoperative pathological evaluation. Therefore, wherever possible, one

should remove as much bone in touch with the tumor as possible in order to attain a higher Simpson grade of tumor excision (5).

In skull base meningiomas, this can be achieved by drilling the bone, especially the hyperostotic areas and subsequent reconstruction of the cranial base. In cases of convexity, sphenoid wing meningiomas, one should not replace the bone flap and instead use an artificial bone flap to cover the defect.

5.2 Conclusion

Our study shows that a significant number of patients with radiological hyperostosis (59.1%) had tumor invasion into the bone. However, the presence of hyperostosis does not always indicate presence of microscopic tumor invasion into bone.

5.3 Recommendations

In order to reduce recurrence rates, we recommend that one should remove the bone flap whenever possible so as to achieve total excision of the tumor and use titanium mesh/ hydroxypartite cement cranioplasty for calvarial reconstruction.

A follow up study on the molecular pathways to determine causes of hyperostosis other than tumor invasion into harvesian canals is also recommended.

REFERENCES

1. Buerki RA, Horbinski CM, Kruser T, Horowitz PM, James CD, Lukas RV. An overview of meningiomas. Future Oncol [Internet]. 2018 Sep [cited 2022 Jul 30];14(21):2161–77. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6123887/

2. Krishnan V, Mittal MK, Sinha M, Thukral BB. Imaging spectrum of meningiomas: a review of uncommon imaging appearances and their histopathological and prognostic significance. Pol J Radiol [Internet]. 2019 Dec 29 [cited 2022 Jul 30];84:e630–53. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7016363/

3. Muriithi S, Kiboi J, Mwang'ombe N. Pattern of brain tumours in Kenyatta National Hospital: A 3 year cross-sectional study. University of Nairobi repository; 2015.

4. Eckert F, Clasen K, Kelbsch C, Tonagel F, Bender B, Tabatabai G, et al. Retrospective analysis of fractionated intensity-modulated radiotherapy (IMRT) in the interdisciplinary management of primary optic nerve sheath meningiomas. Radiat Oncol Lond Engl. 2019 Dec 27;14(1):240.

5. Goyal N, Kakkar A, Sarkar C, Agrawal D. Does bony hyperostosis in intracranial meningioma signify tumor invasion? A radio-pathologic study. Neurol India. 2012 Jan 1;60(1):50.

6. Al-Mefty O, Kadri PA, Pravdenkova S, Sawyer JR, Stangeby C, Husain M. Malignant progression in meningioma: Documentation of a series and analysis of cytogenetic findings. J Neurosurg. 2004;101:210–8.

7. Chamberlain: Primary Central Nervous System Tumors:... - Google Scholar [Internet]. [cited 2022 Jul 30]. Available from: https://scholar.google.com/scholar_lookup?title=Primary+Central+Nervous+System+Tumors:+Pathogenesis+and+Therapy&author=MC+Chamberlain&publication_year=2011&

8. Franco DeMonte, Michael W. McDermott, Ossama Al-Mefty. Al-Mefty's Meningiomas [Internet]. 2nd ed. Thieme; 2011 [cited 2022 Nov 7]. 448 p.

9. Boetto J, Peyre M, Kalamarides M. Meningiomas from a developmental perspective: exploring the crossroads between meningeal embryology and tumorigenesis. Acta Neurochir (Wien). 2021 Jan;163(1):57-66. doi: 10.1007/s00701-020-04650-w. Epub 2020 Nov 20. PMID: 33216210.

10. Lopes MBS. Meninges: Embryology. In: Lee JH, editor. Meningiomas [Internet]. London: Springer London; 2009. p. 25–9. Available from: https://doi.org/10.1007/978-1-84628-784-8_4

11. Sehgal I, Das JM. Anatomy, Back, Spinal Meninges [Internet]. StatPearls [Internet]. StatPearls Publishing; 2022 [cited 2022 Jul 30]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK547755/

12. Purves D, Augustine GJ, Fitzpatrick D, Katz LC, LaMantia AS, McNamara JO, et al. The Meninges. Neurosci 2nd Ed [Internet]. 2001 [cited 2022 Jul 30]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK10877/

13. Ghannam JY, Kharazi KAA. Neuroanatomy, Cranial Meninges [Internet]. StatPearls [Internet]. StatPearls Publishing; 2021 [cited 2022 Jul 30]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539882/

14. Banerjee J, P" a "akk" o E, Harila M, Herva R, Tuominen J, Koivula A, et al. Radiation-induced meningiomas: A shadow in the success story of childhood leukemia. Neuro-OncolOct. 2009;11(5):543–9.

15. Longstreth WT, Dennis LK, McGuire VM, Drangsholt MT, Koepsell TD. Epidemiology of intracranial meningioma. Cancer. 1993 Aug 1;72(3):639–48.

16. Vadivelu S, Schulder M. Intracranial Meningiomas: Role of Exogenous Hormones. In: Hayat MA, editor. Tumors of the Central Nervous System, Volume 7: Meningiomas and Schwannomas [Internet]. Dordrecht: Springer Netherlands; 2012 [cited 2022 Jul 24]. p. 29–38. (Tumors of the Central Nervous System). Available from: https://doi.org/10.1007/978-94-007-2894-3_4

17. Vadivelu S, Sharer L, Schulder M. Regression of multiple intracranial meningiomas after cessation of long-term progesterone agonist therapy: Case report. J Neurosurg. 2010 May 1;112(5):920–4.

18. Claus EB, Park PJ, Carroll R, Chan J, Black PM. Specific Genes Expressed in Association with Progesterone Receptors in Meningioma. Cancer Res. 2008 Jan 1;68(1):314–22.

19. Phillips LE, Koepsell TD, van Belle G, Kukull WA, Gehrels JA, Longstreth WT. History of head trauma and risk of intracranial meningioma: population-based case-control study. Neurology. 2002 Jun 25;58(12):1849–52.

20. Inskip PD, Tarone RE, Hatch EE, Wilcosky TC, Shapiro WR, Selker RG, et al. Cellular-telephone use and brain tumors. N Engl J Med. 2001 Jan 11;344(2):79–86.

21. Muscat JE, Malkin MG, Thompson S, Shore RE, Stellman SD, McRee D, et al. Handheld cellular telephone use and risk of brain cancer. JAMA. 2000 Dec 20;284(23):3001–7.

22. Swerdlow AJ, Feychting M, Green AC, Kheifets L, Savitz DA. Mobile Phones, Brain Tumors, and the Interphone Study: Where Are We Now? Environ Health Perspect. 2011 Nov;119(11):1534–8.

23. Malmer B, Henriksson R, Grönberg H. Familial brain tumours—genetics or environment? A nationwide cohort study of cancer risk in spouses and first-degree relatives of brain tumour patients. Int J Cancer. 2003;106(2):260–3.

24. Krampla W, Newrkla S, Pfisterer W, Jungwirth S, Fischer P, Leitha T, et al. Frequency and risk factors for meningioma in clinically healthy 75-year-old patients:

results of the Transdanube Ageing Study (VITA). Cancer. 2004 Mar 15;100(6):1208–12.

25. Bethke L, Murray A, Webb E, Schoemaker M, Muir K, McKinney P, et al. Comprehensive Analysis of DNA Repair Gene Variants and Risk of Meningioma. JNCI J Natl Cancer Inst. 2008 Feb 20;100(4):270–6.

26. Custer BS, Koepsell TD, Mueller BA. The association between breast carcinoma and meningioma in women. Cancer. 2002;94(6):1626–35.

27. Claus EB, Bondy ML, Schildkraut JM, Wiemels JL, Wrensch M, Black PM. Epidemiology of intracranial meningioma. Neurosurgery. 2005 Dec;57(6):1088–95; discussion 1088-1095.

28. Terry MB, Howe G, Pogoda JM, Zhang FF, Ahlbom A, Choi W, et al. An international case-control study of adult diet and brain tumor risk: a histology-specific analysis by food group. Ann Epidemiol. 2009 Mar;19(3):10.1016/j.annepidem.2008.12.010.

29. Berg-Beckhoff G, Schüz J, Blettner M, Münster E, Schlaefer K, Wahrendorf J, et al. History of allergic disease and epilepsy and risk of glioma and meningioma (INTERPHONE Study Group, Germany). Eur J Epidemiol. 2009 Jun 1;24:433–40.

30. Baumgarten P, Gessler F, Schittenhelm J, Skardelly M, Tews DS, Senft C, et al. Brain invasion in otherwise benign meningiomas does not predict tumor recurrence. Acta Neuropathol (Berl). 2016 Sep;132(3):479–81.

31. Kousi E, Tsougos I, Fountas K, Theorou K, Tsolaki E, Fezoulidis I, et al. Distinct peak at 3.8 ppm observed by 3T MR spectroscopy in meningiomas, while nearly absent in high-grade gliomas and cerebral metastases. Mol Med Rep. 2012 Apr;5(4):1011–8.

32. Wong TZ, Westhuizen GJ van der, Coleman RE. Positron emission tomography imaging of brain tumors. Neuroimaging Clin. 2002 Nov 1;12(4):615–26.

33. Rachinger W, Stoecklein VM, Terpolilli NA, Haug AR, Ertl L, Pöschl J, et al. Increased 68Ga-DOTATATE uptake in PET imaging discriminates meningioma and tumor-free tissue. J Nucl Med Off Publ Soc Nucl Med. 2015 Mar;56(3):347–53.

34. Unterman TG, Glick RP, Waites GT, Bell SC. Production of Insulin-like Growth Factor-binding Proteins by Human Central Nervous System Tumors1. Cancer Res. 1991 Jun 1;51(11):3030–6.

35. Tollefsen SE, Jarmund AH, Ytterhus B, Salvesen Ø, Mjønes P, Torp SH. Somatostatin Receptors in Human Meningiomas—Clinicopathological Aspects. Cancers. 2021 Nov 15;13(22):5704.

36. Schulz S, Pauli SU, Schulz S, Händel M, Dietzmann K, Firsching R, et al. Immunohistochemical determination of five somatostatin receptors in meningioma reveals frequent overexpression of somatostatin receptor subtype sst2A. Clin Cancer Res Off J Am Assoc Cancer Res. 2000 May;6(5):1865–74.

37. García-Luna PP, Relimpio F, Pumar A, Pereira JL, Leal-Cerro A, Trujillo F, et al. Clinical use of octreotide in unresectable meningiomas. A report of three cases. J Neurosurg Sci. 1993 Dec;37(4):237–41.

38. Ragel BT, Couldwell WT. Emerging Treatment Modalities I: Cyclooxygenase-2 as a Therapeutic Target for Meningioma Tumor Growth. In: Lee JH, editor. Meningiomas [Internet]. London: Springer; 2009 [cited 2022 Jul 24]. p. 177–83. Available from: https://doi.org/10.1007/978-1-84628-784-8_15

39. Pieper DR, Al- Mefty O, Hanade Y, Buencher D. Hyperostosis associated with meningioma of the cranial base: Secondary changes or tumor invasion. Neurosurgery. 1999;44:742–7.

40. Fathalla H, Tawab MGA, El-Fiki A. Extent of Hyperostotic Bone Resection in Convexity Meningioma to Achieve Pathologically Free Margins. J Korean Neurosurg Soc. 2020 Nov;63(6):821–6.

41. Mwang'ombe N juniahs, Ombachi R. Brain tumours at the Kenyatta National Hospital, Nairobi. East Afr Med J. 2000 Sep 1;77:444–7.

42. Simpson D. The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry. 1957 Feb;20(1):22–39.

43. Schwartz TH, McDermott MW. The Simpson grade: abandon the scale but preserve the message. J Neurosurg. 2020 Oct 9;135(2):488–95.

44. Backer-Grøndahl T, Moen BH, Torp SH. The histopathological spectrum of human meningiomas. Int J Clin Exp Pathol [Internet]. 2012 Mar 25 [cited 2022 Jul 30];5(3):231–42. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3341686/

LIST OF APPENDICES

Appendix 1: Data collection tool

1. Specimen No:
2. Age:……years
3. Date of birth (dd/mm/year):
4. Sex: male / female
5. Radiologic evidence of hyperostosis Yes / No
6. Tumor Recurrence: Yes / No
7. Duration of period from initial surgery: ……. months
8. Tumor location:

Tumor location	✓
Convexity	
Sphenoid wing	
Para-sagittal	
Posterior fossa	
Base of skull	
• Tuberculum sellae	
• Olfactory groove	
• Foramen magnum	
• Clival	
• Dorsum sellae	

9. Extent of resection:
    i. Kobayashi Grading: 1, 2, 3a, 3b,4, 5
    ii. Simpson Grading: 1, 2, 3, 4, 5
10. Histologic subtype:

Histologic subtype	✓
Meningothelial	
Fibrous	
Transitional	
Psammomatous	
Angiomatous	
Microcystic	
Secretory	
Metaplastic	
Lymphoplasmacyte rich	
Chordoid	
Clear cell	
Rhabdoid	
Papillary	
Atypical	
Anaplastic	

11. WHO grade: 1 2 3

12. Microscopic tumor invasion on bone: Present / Absent

Appendix 2: Informed consent form

PARTICIPANT INFORMATION AND CONSENT FORM FOR ENROLLMENT IN THE STUDY

This Informed Consent form is patients undergoing surgical treatment for meningioma. It will be administered to eligible participants. We are requesting you to participate in this research project whose title is "A radiology pathological correlation of bony invasion among patients with meningiomas at the KNH."

Principal Investigator: Dr. Adagi Marjorie

Institution: The Department of Surgery, Faculty of Health Sciences, University of Nairobi.

This Informed Consent Form has three parts:

I. Information Sheet (informs you in a brief overview about the research with you).
II. Certificate of Consent (for you to sign if you agree to take part).
III. Statement by the researcher/person taking consent.

A copy of the informed consent form will be provided.

PART I: Information Sheet

Introduction

My name is Dr. Adagi Marjorie, a postgraduate student in Neurosurgery; department of surgery at the University of Nairobi. I am carrying out research to correlate radiological and pathological feautures of bony invasion among patients with meningiomas at the KNH".

Purpose of the research

I will provide information and invite you to be a participant in this research. There may be some words that you don't comprehend. Please ask me to explain as we go through the information and I will explain. After receiving the information concerning the study, you are encouraged to seek clarification in case of any doubt. This study will elucidate the validity of cadaveric dissection in post graduate neurosurgical training. The study will also aim to justify the establishment of appropriate management protocols on individualized cadaveric training courses in various departments.

Type of Research Intervention

This research will involve use of questionnaires.

Voluntary participation/right to refuse or withdraw

It is your decision to participate or not. If you decide against participating, you will still proceed with the surgery. You have a choice to refuse or withdraw your participation in this study at any point.

Confidentiality

The information obtained in this study will be treated with confidentiality and only be available to the principal investigator and the study team. Your name will not be used. Any personal information will have a number on it instead of your name. We will not be sharing the identity of those participating in this research.

Study procedure

After agreeing and consenting to participate in the study, a structured questionnaire will be administered for purposes of data collection.

Sharing the results

The knowledge obtained from this study will be shared with the policymakers in KNH and doctors through publications and conferences. Confidential information will not be shared.

Benefits

The benefits of joining the study include:

- Impact new knowledge on bony invasion in meningiomas in our set up.
- Help guide on surgical planning and extent of tumor resection.

Cost and compensation

There will be no extra cost incurred for participating in this study nor is there compensation offered.

This research proposal has been reviewed and approved by the UoN/KNH Ethics Committee, which is a Committee whose task is to make sure that research participants are protected from harm.

Who to contact

If you wish to ask any questions later, you may contact:

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PART II: Certificate of Consent

I have read and understood the above information/the above information has been read out to me. I have had the opportunity to ask questions and the questions that I have asked have been answered satisfactorily. I voluntarily agree and consent to participate in this research.

Print Name of Participant _____

Signature of Participant _____

Date _____

PART III: Statement by the researcher

I have read out the information sheet to the participant, and made sure that the participant understands that the following will be done:

A decision to refuse to participate or withdrawal from the study will not in any way compromise the care of treatment.

All information given will be handled with confidentiality.

The results of this study might be published to facilitate research and improved clinical guidelines. I can confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the approval has been given voluntarily.

A copy of the Informed Consent Form has been provided to the participant.

Name of researcher/person taking consent _____

Signature of researcher/person taking consent_____

Date_____

Appendix 3: Informed consent Swahili version - Fomu ya Idhini Ili Kushiriki Katika Utafiti- (Watu Wazima)

Kichwa Cha Utafiti: A RADIOLOGY- PATHOLOGICAL CORRELATION OF HYPEROSTOSIS AMONG PATIENTS WITH INTRACRANIAL MENINGIOMAS AT THE KENYATTA NATIONAL HOSPITAL

Mpelelezi Mkuu Na Ushirika Wa Kitaasisi: Dr.Marjorie Adagi, Mwanafunzi wa Shahada ya Uzamili Katika Neurosurgery. Chuo Kikuu Cha Nairobi, Idara ya Magonjwa ya ubongo

Mimi ni Daktari Adagi Marjorie, kutoka chuo kikuu cha Nairobi, Idara ya upasuaji, sehemu ya ubongo. Ninafanya utafiti kuchunguza 'a radiology pathological correlation of hyperostosis among patients with intracranial meningiomas at the Kenyatta National Hospital' yaani kubainisha kiwango ambacho mfupa wa kichwa unaathiriwa na mgonjwa aliye na meningioma

Ningependa kukuambia juu ya utafiti unaofanywa na mtafiti aliyeorodheshwa hapo juu. Madhumuni ya fomu hii ya idhini ni kukupa habari za kutosha ili kukusaidia kuamua iwapo utakuwa mshiriki wa utafiti au la. Uko huru kuuliza maswali yoyote juu ya utafiti, madhumuni yake, ni nini maana ya wewe kushiriki katika utafiti, ikiwa kuna hatari yoyote inayohusika na faida yoyote, haki za kujitolea, na habari yoyote iliyoongezwa isiyojumuishwa katika fomu hii na inahitaji ufafanuzi. Baada ya kujibu kwa kuridhisha maswali yako yote, unaweza kuamua kushiriki katika utafiti au la. Utaratibu huu unajulikana kama 'idhini ya habari'. Baada ya kukubali kushiriki katika utafiti huu, nitakuomba utie sahihi jina lako kwenye fomu hii.

Unapaswa kuelewa kanuni za jumla ambazo zinatumika kwa washiriki wote katika utafiti wa matibabu:

i. Kushiriki katika utafiti ni kwa hiari.
ii. Wakati wowote unaweza kuamua kujiondoa kwenye utafiti.
iii. Ukikataa kushiriki katika utafiti, hii haiathiri huduma unayopewa katika kituo hicho au kituo kingine chochote cha afya.

Tutakupa nakala ya fomu hii kwa rekodi zako.

Naweza kuendelea? NDIO AULA

Utafiti huu umeidhinishwa na Itifaki ya Kamati ya Maadili na Utafiti ya Hospitali ya Kitaifa ya Kenyatta-Chuo Kikuu cha Nairobi Nambari_____

Utafiti Huu Unahusu Nini?

Kuulizwa maswali kuhusu ugonjwa wako, kutumia picha zako kuangalia mambo kadhaa kuhusu ugonjwa wako na kupata mfupa ulio karibu na uvimbe uliomo ndani ya kichwa. Kutakuwa na takriban washiriki arobaini na tatu katika utafiti huu ambao wamechaguliwa bila mpangilio. Tunaomba idhini yako kufikiria kushiriki katika utafiti huu.

Je, Nini Kitatokea Ukiamua Kuwa Kwenye Utafiti Huu?

Ikiwa unakubali kushiriki katika utafiti huu, yafuatayo yatatokea:

Utahojiwa katika eneo ambalo faragha yako imehakikishiwa na unahisi vizuri kujibu maswali. Mahojiano yatachukua dakika chache. Baada ya mahojiano kumalizika, nitaomba uniwekee sahihi katika fomu hii. Ikibidi, tutauliza nambari yako ya simu kuwasiliana nawe. Maelezo yoyote ya mawasiliano utakayotoa yatatumika tu na watu wanaofanya utafiti huu na hawatashirikiwa na wengine kamwe.

Je, Kuna Athari Zozote, Madhara, Usumbufu Zinazohusiana Na Utafiti Huu?

Kwa ujumla, utafiti wa matibabu una uwezo wa kuanzisha hatari za kisaikolojia, kijamii, kihemko na kiafya. Moja ya hatari ya kuwa katika utafiti huu ni kupoteza faragha. Habari yoyote unayotupatia ni ya siri na itachukuliwa kama siri.

Tutatumia nambari ya kukutambulisha kwenye hifadhidata ya kompyuta inayolindwa na nywila na rekodi zetu zote za karatasi zitahifadhiwa kwenye baraza la mawaziri iliyofungwa. Una haki ya kukataa mahojiano au maswali yoyote yanayoulizwa katika mahojiano. Pia, wafanyikazi wetu wote wanaofanya utafiti huu ni wataalamu wenye mafunzo katika mitihani / mahojiano haya.

Je, Kuna Faida Zozote Ziko Katika Utafiti Huu?

Utafiti huo utatusaidia kuelewa vizuri jinsi kubainisha kiwango ambacho mfupa wa kichwa unaathiriwa na mgonjwa aliye na uvimbe wa meningioma. Hii itapanua zaidi ufahamu wetu kuweza kujua jinsi ya kutibu ugonjwa huu.

Je, Kuna Gharama Kuwa Katika Utafiti Huu?

Hakuna gharama za ziada zitakazopatikana.

Je, Ninaweza Kuondoka Kwenye Utafiti Wakati Wowote?

Kushiriki katika utafiti ni kwa hiari na una haki ya kujiondoa kutoka kwa utafiti na kwamba wakati wowote unaweza kuamua kujiondoa kwenye utafiti bila lazima kutoa

sababu ya kujitoa kwako. Hii haiathiri kwa vyovyote huduma unazopewa katika kituo hicho au katika kituo kingine chochote cha afya.

Kwa habari zaidi juu ya haki zako kama mshiriki wa utafiti unaweza kuwasiliana na watu wafuatao:

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Ama,

Katibu,

Kenyatta National Hospital-University of Nairobi Ethics and Research Committee

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Kichwa Cha utafiti: A RADIOLOGY- PATHOLOGICAL CORRELATION OF HYPEROSTOSIS AMONG PATIENTS WITH INTRACRANIAL MENINGIOMAS AT THE KENYATTA NATIONAL HOSPITAL

Jina la Mtafitu: Dr. Marjorie Adagi, mwanafunzi wa Shahada ya Uzamili Katika Neurosurgery Chuo Kikuu cha Nairobi, Idara ya Upasuaji

1. Nimesoma fomu hii ya idhini au nimesomewa yaliyomo na nilielewa.
2. Nimepewa nafasi ya kuuliza maswali juu ya utafiti huu.
3. Nimejibiwa maswali yangu vya kutosha katika lugha ninayoelewa.
4. Hatari na faida zinazowezekana nimeelezewa kwa njia wazi.

5. Ninaelewa kuwa mimi hushiriki katika utafiti huu kwa hiari na kwamba ninaweza kujiondoa wakati wowote.

Kwa kusaini fomu hii ya idhini, sijatoa haki yoyote ya kisheria ambayo ninayo kama mshiriki wa utafiti.

Ninakubali kushiriki katika utafiti huu: Ndio / Hapana

Ninakubali kutoa habari ya mawasiliano kwa ufuatiliaji: Ndio / Hapana

Jina la mshiriki aliyechapishwa:

_____

Mawasiliano (nambari ya rununu): _____

Saini ya mshiriki / Stempu ya kidole gumba _____ Tarehe _____

Kauli ya mtafiti

Mimi, aliyesainiwa chini, nimeelezea kabisa maelezo yanayofaa ya utafiti huu kwa mshiriki aliyetajwa hapo juu na ninaamini kwamba mshiriki ameelewa na kwa hiari ametoa idhini yake.

Jina la mtafiti: Daktari. Marjorie Adagi: 0789853588.

Saini

_____

Wajibu katika utafiti: Mchunguzi mkuu.

Kwa habari zaidi, wasiliana na: Daktari Vincent Wekesa 0721585535

Fomu Ya Makubaliano Ya Kujiunga Na Utafiti

Fomu ya makubaliano

Nimeelezewa utafiti huu kwa kina. NakubaIi kushiriki utafiti huu kwa hiari yangu.

Nimepata wakati wa kuuliza maswali na nimeelewa kuwa iwapo nina maswali zaidi, ninaweza kumwuliza mtafiti mkuu au watafiti waliotajwa hapa juu.

Jina la Mshiriki_____

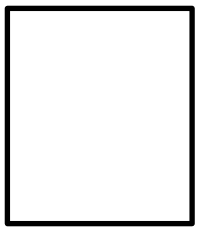
Sahihi ya mshiriki _____

Tarehe_____

Kwa wasioweza kusoma na kuandika:

Nimeshuhudia usomaji na maelezo ya utafiti huu kwa mshiriki. Mshiriki amepewa nafasi ya kuuliza maswali. Nathibitisha kuwa mshiriki alipeana ruhusa ya kushiriki bila ya kulazimishwa.

Jina la shahidi_____ Alama ya kidole cha mshiriki



Sahihi la shahidi_____

Tarehe _____

Ujumbe kutoka kwa mtafiti

Nimemsomea mshiriki ujumbe kiwango ninavyoweza na kuhakikisha kuwa mshiriki amefahamu yafuatayo:

Kutoshiriki au kujitoa kwenye utafiti huu hautadhuru kupata kwake kwa matibabu.

Ujumbe kuhusu majibu yake yatahifadhiwa kwa siri.

Matokeo ya utafiti huu yanaweza chapishwa ili kuwezesha kuzuia na kutibu matatizo yanayosababishwa na prostate biopsy.

Ninathibitisha kuwa mshiriki alipewa nafasi ya kuuliza maswali na yote yakajibiwa vilivyo.

Ninahakikisha kuwa mshiriki alitoa ruhusa bila ya kulazimishwa.

Mshiriki amepewa nakala ya hii fomu ya makubaliano.

Jina la mtafiti _____

Sahihi ya Mtafiti _____

Tarehe_____

Appendix 4: Letter to collaborating institution seeking permission to conduct study.

I Dr. Adagi Marjorie, a registrar in the Department of Surgery, division of Neurosurgery, University of Nairobi, would like to seek consent from the Research and Administration department/Office of the Kenyatta National Hospital to Conduct a research study entitled, radiology pathological correlation of bony invasion among patients with intracranial meningiomas at the Kenyatta National Hospital.

This study entails correlation of radiological and pathological features of bony invasion in meningiomas.

No patient identifying information will be collected.

Results of this study was shared with the hospital management among other stakeholders to help improve local policies and guidelines on the management of meningiomas.

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Hospital representative

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Principal Investigator