“A SINGLE INSTITUTIONAL EXPERIENCE WITH PINEAL REGION TUMOUR”

DISSERTATION SUBMITTED FOR THE PARTIAL FULFILMENT FOR THE REQUIREMENT OF THE DEGREE OF
M.CH NEUROSURGERY

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DECLARATION

This thesis titled "A Single Institutional Experience with Pineal Region Tumour" is a consolidated report based on a bonafide study of the period from 1st January 2019 to 31st July 2020, done by me under the Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

This thesis is submitted to SCTIMST in partial fulfilment of rules and regulations of MCh Neurosurgery examination.

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CERTIFICATE

This is to certify that the thesis entitled - "Single Institutional Experience with Pineal Region Tumour" is a bonafide work of Dr. Patel Biren Khimji and was conducted in the Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram (SCTIMST) under my guidance and supervision.

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ABBREVIATIONS

ITSC – Infratentorial supracerebellar approach

OIH – Occipital interhemispheric approach

PCA- Posterior cerebral artery

MPChA - Medial posterior choroidal artery

KPS – Karnofsky performance score

STR – Subtotal resection

NTR – Near total resection

GTR – Gross total resection

ETV- Endoscopic third ventriculostomy

VP shunt – Ventriculoperitoneal shunt

TABLE CONTENTS

SYNOPSIS

Pineal region tumours are rare, technically challenging lesions accounting for 0.5-1.6% of all intracranial tumours. There is paucity of large series in world literature as well in the Indian context with regards to surgical experience in this critical anatomical zone.Objective of this study was to analyse the clinical presentation, and surgical outcome of patients with pineal region lesions operated over a period of 8 years in our centre.Study population was 106 consecutive patients operated for pineal regions lesions. Retrospective analysis was done for 76 patients while 30 patients were studied prospectively. We studied various patient related & tumour related factors & analysed their effect on the clinical outcome of patients. Our study included factors like clinical presentation , Karnofsky Performance Scale (KPS) score on admission, discharge and after 3 months of surgery, tumour volume, presence of hydrocephalus & its management, surgical approach, tumour characteristics, tumour pathology, intra-operative & post-operative complications, extent of resection confirmed 3 months after surgery by MRI imaging, duration of intensive care and hospital stay & need for adjuvant therapy.

Modified Poppen's approach was most commonly employed approach for surgical treatment of pineal region tumours i.e. in 89 patients (83.96%).Gross total or near total resection as per post operative imaging was achieved in 98 patients (92.45 %). An inverse relationship was noticed with age, ICU stay & total hospital length of stay to the KPS score on admission. However, difference was not statistically significant. Significant improvement of the KPS score on discharge & at 3 months of follow up compared to KPS score on admission was noted. On 3 month follow-up, 14 patients (13.2%) had residual lesion & adjuvant therapy was given to 30 patients (28.3%). Visual gaze and field deficits were present in 24.52 % patients in the immediate post operative period which reduced to 9.9 % at 3 months followup.

We conclude that Modified Poppen's approach was found to be an extremely useful approach applicable to majority of pineal region tumours giving good functional outcomes & causing minimal morbidity. KPS score at admission and tumour pathology are the main deciding factors in the surgical outcome of pineal region lesions.

INTRODUCTION

The pineal region tumours are rare, technically challenging lesions accounting for 0.5% to 1.6% of all intracranial tumours (1). Located within the confines of posterior tentorial incisura the pineal region is bounded by highly critical structures. The roof is formed by the lower surface of the splenium of the corpus callosum, the hippocampal commissure and the crus of the fornix. The anterior wall by the tectal plate and the posterior third ventricle. The lateral wall, is made of the pulvinar, the crus of the fornix and the medial surface of the cerebral hemisphere. The floor of the pineal region is formed by the superior surface of the cerebellar vermis. The venous confluence and the pineal gland are the main constituents of the space within. The relatively complex anatomy, depth from the surface relationship with vital structures and the limited corridors renders several challenges to the surgeon (2).

Neuroepithelial tumours, such as pineal parenchymal tumours (PPTs), glial tumours and papillary tumours of the pineal region (PTPRs) represent approximately 50% of tumours in pineal region. Germ cell tumours account for 30% of the pineal region tumours. Miscellaneous neoplastic lesions (meningiomas, metastases) and non-neoplastic lesions (pineal cysts, arachnoid cysts, vascular malformations) account for the remaining 20% of pineal region tumours (3). Epidermoid cyst of pineal gland account for 0.2-1% of all intracranial tumours (4).

Pineal region approaches may be infratentorial or supratentorial. Although once considered a morbid procedure (5,6), application of microsurgical techniques for the infratentorial supracerebellar approach of Krause (7) and for the sub-occipital transtentorial as approached and revisited by Lapras, Yasargil, Brotchi and others have allowed a dramatic reduction in mortality and in morbidity(8-12).

There are very few studies in the literature investigating perioperative management and clinical outcomes of these patients , as well as those on the influence of approach on clinical outcome and functional status. We have investigated on the anatomical factors, clinical presentation and surgical approach in relation with functional status and clinical outcome in the preoperative period and on follow-up.

REVIEW OF LITERATURE

History:

Pineal tumours represent a very challenging pathology owing to the various types of pineal gland tumours, different operative strategies that are required to treat them. For long pineal region tumours were considered inaccessible for surgery due to its deep site & presence of vital structures around it.

Rarity of these tumours (1.2 % of all CNS tumours) along with its diverse histologic variations pose a significant challenge to study tumour biology & outcome (13). Pineal gland has always interested humans for a long time.

In Hindu scriptures, the pineal gland was considered as one of the seven chakra: the crown chakra, representing the centre of spiritual force (14).

The difficulties of surgical approach for pineal tumours can explain that the recommended strategy for their treatment has been the cure of hydrocephalus followed by irradiation for a long time and that is why Dandy stated "Pineal tumours are perhaps the most dangerous of all intracranial tumours to attack surgically" (5).

In 1905, an era of pineal tumour surgery began as Victor Horsley tried to remove a pineal tumour by infratentorial approach unsuccessfully, while in 1904 Harvey Cushing reported bitemporal craniectomy for a patient who some weeks later succumbed to death while the autopsy revealed a quadrigeminal plate tumour (15, 16).

In 1913, the first successful surgery for pineal region tumour was reported by Krause in a 10 year old patient using an infratentorial supracerebellar approach (14). The success of the surgery was due to the preservation of the venous system, developed dorsally, and lateral to the lesion, avoiding the main cause of surgical

morbidity (17,18). The occipital transtentorial approach was popularized by Heppener in 1959, and by Poppen in 1966 (19).

In 1971, the modification of the sub-occipital transtentorial approach was reported by Jammieson modifying the axis of approach that became more medial and modifying the opening of the tentorium permitting a better exposition of the vermian and quadrigeminal arachnoidal space and of the pineal region (20).

Lapras then modified the Jamieson's approach proposing a diamond shaped bone flap with the lateral superior bone hole at the level of the parietal bossing and modifying the retraction of the occipital lobe that improved the exposure of the deep pineal region (21).

The choice of the surgical approach depends on the plane that delineates the pineal region which is represented by the tentorial plane. Advancement & modification of microsurgical techniques for the infratentorial supracerebellar approach and for the sub-occipital transtentorial approach by Lapras, Yasargil, Brotchi and others have led to dramatic reduction in mortality and in morbidity (22-26).

Anatomy :

Pineal region :

The pineal region also known as posterior incisural space or quadrigeminal cistern is a pyramidal shape area whose roof is formed by lower surface of the splenium of the corpus callosum (27) . The superior part of the anterior wall of the pineal region is formed by the pineal body, the habenular trigone and the habenular commissure medially and by the medial portion of the pulvinar laterally. The middle part of the anterior wall is formed by the collicular plate of the quadrigeminal cistern, and the pineal gland is situated between the paired superior colliculi. The inferior part of the anterior wall is formed by the lingula of the vermis on the midline and by the superior cerebellar peduncle laterally. The floor is constituted by the superoventral portion of the cerebellum. The lateral walls are

formed by an anterior part (the crus of the fornix) and by a posterior part (the medial surface of the occipital cortex below the splenium of the corpus callosum). The angle between the floor and the roof is generated where the Galen vein drains into the straight sinus (28-35).

Venous anatomy :

The vein of Galen originates few millimetres behind the pineal body with its length ranging from a few millimetres to 1 inch (29). The vein of Galen runs

postero-superiorly to drain into the straight sinus located around 10 mm from the tip of the pineal body.

The surgically significant vessels draining into the vein of Galen are the following:

A) Internal cerebral veins. These originate in the posterior aspect of the foramen of Monro by union of the anterior septal and thalamostriate veins. Both veins run on the roof of the third ventricle without any connection with bridging veins. They course inferior to the splenium of the corpus callosum and lateral to the pineal body and turn upward before joining to form the vein of Galen.

B) Precentral cerebellar vein and superior vermian vein. These course in the cerebellomesencephalic fissure and over the superior cerebellar peduncle. They can drain separately into the Galen vein or as a single trunk known as the superior cerebellar vein.

C) Basal vein. This runs posteriorly, medially, and inferiorly above the optic tract; courses laterally between the cerebral peduncle and the uncus and then enters the quadrigeminal cistern. It drains into the vein of Galen more inferiorly than the convergence of the internal cerebral veins.

D) Internal occipital vein. This vein originates on the inferior and medial surface of the occipital lobe, drains the medial surface of the occipital lobe, and runs anteromedially to terminate in the lateral part of the vein of Galen, septal and thalamostriate veins (29,30,33).

Arterial anatomy :

Arterial supply of pineal region relevant to ITSC & OIH approach has been described :

A) Medial posterior choroidal artery : It arises from the posteromedial aspect of the proximal part of the PCA in the interpeduncular and crural cistern. It runs in the ambient cistern, parallel to the PCA, supplies the superior-inferior colliculi and the pineal gland, and then travels along the tela choroidea of the third ventricle. The MPChA then turns backward at the foramen of Monro , runs in the choroid plexus of the lateral ventricle, and anastomoses with the lateral posterior choroidal arteries. It supplies the anterior thalamic nucleus, the medial geniculate body, and the pulvinar.
B) Lateral posterior choroidal artery : It arises from the PCA, runs in the ambient cistern, and through the choroidal fissure courses into the choroid plexus of the lateral ventricle to anastomose with the MPChA and the anterior choroidal artery. It supplies the lateral geniculate body and parts of the thalamus.

The quadrigeminal artery arises from the posterior cerebral artery, medial to the junction with the posterior communicating artery. It courses in the ambient cistern to supply the superior colliculus. A branch of the superior cerebellar artery supplies the inferior colliculus. The arteria occipitalis medialis is a distal branch of the posterior cerebral artery. It sends the calcarine artery to the calcarine sulcus and the parieto-occipital artery to the parieto-occipital sulcus (32,33,34).

Most pineal region tumours originate infratentorially and expand into the posterior third ventricle. They can later progress into the thalamus or posteriorly over the dorsal surface of the quadrigeminal plate. Malignant tumours, particularly of glial origin, can invade into the midbrain and thalamus, which ultimately determines the tumour's respectability.

Pathology :

The mature pineal gland is made up of pinealocytes arranged in lobules to form the pineal parenchyma. The pinealocytes are surrounded by astrocytes, with endothelial cells forming the vasculature and connective tissue cells forming septa between the lobules. The gland also contains nerve endings from sympathetic nervous innervation to the pinealocytes. The ependymal cells of the third ventricle adjoin the gland along its anterior border (35, 36).

Approximately 11–28% and 50–75% (37,38) of pineal region tumours are of pineal parenchymal origin and germ cell origin, respectively. In addition, glioma, meningioma and mesenchymal tumours are occasionally encountered.

A) Pineal parenchymal tumours : A histologically benign neoplasm composed of cells differentiating to pineal parenchymal cells & corresponding histologically to WHO grade II. It usually affects young adults & constitute approximately 45% of pineal parenchymal tumours . The cut surface of the tumour has been described as white, pink, or gray, granular or gelatinous, sometimes with cysts and focal necrosis. Pineocytoma is a moderately cellular neoplasm with large pseudorosettes and abundant cytoplasmic processes, showing a lobular architecture separated by fibrovascular septa (39).

B) Pineoblastoma : A neoplasm composed of primitive cells originating from the pineal body & corresponding histologically to WHO grade IV. Pineoblastomas tend to occur in the first two decades constituting nearly 45% of pineal parenchymal tumours (38). They are soft, friable, greyish, ill-defined masses with haemorrhage and/or necrosis infiltrating into the adjacent brain tissue. Extensive leptomeningeal dissemination is commonly seen. On microscopy, they are found to be highly cellular. Small undifferentiated cells proliferate diffusely without lobular architecture, mimicking medulloblastoma and PNET arising in other sites. Necrosis is

common. These tumours are associated with rapid recurrence and cerebrospinal dissemination. The projected 1-year, 3-year and 5-year survival rates of patients with pineal parenchymal tumours excluding pineocytoma are 88%, 78% and 58%, respectively (40).

C) Pineal parenchymal tumour of intermediate differentiation and mixed pineocytoma/pineoblastoma : Pineal parenchymal tumours represent a spectrum of tumours composed of primitive parenchymal cells to well-differentiated pinealocytes. Typical pineocytomas and pineoblastomas are composed of well-differentiated neoplastic pinealocytes and poorly differentiated neuroectodermal cells, respectively. However, pineal parenchymal tumours do not always fit the histological appearances of pineocytoma or pineoblastoma. These tumours are divided into two types. First, tumours composed of both poorly differentiated, pineoblastoma-like cells and well differentiated pinealocyte-like cells. Second, tumours consisting of cells with intermediate histological features between pineocytoma cells and the pineoblastoma cells. The first type is referred to as mixed pineocytoma /pineoblastoma & they constitute approximately 10% of pineal parenchymal tumours. The tumours of the second type are moderately hypercellular and the lobular architecture is inconspicuous. Pineocytomatous rosettes are infrequent, and smaller and more variable in shape than those in pineocytomas. Homer Wright rosettes are occasionally observed. The clinical behaviours of this type of pineal tumour are variable with prognosis being indistinct. Occasional leptomeningeal dissemination is present . It appears that mixed pineal parenchymal tumours are more prone to metastasis than pineal parenchymal tumours with intermediate differentiation (40,41).

D) Pineal cyst : A non-neoplastic glial cyst formed within the pineal body. A small asymptomatic cyst is a common incidental finding in adolescents and adults at autopsy or at radiological imaging with its incidence ranging from 25% to 40% at autopsy (37). Large symptomatic cysts are rare. The mean age

of the patients with symptomatic cysts is nearly 30 years (42). Clinical signs and symptoms are related to increased intracranial pressure, CSF obstruction, neuro-ophthalmologic dysfunction and brain stem compression. Rapid enlargement by intracystic haemorrhage may induce sudden death or loss of consciousness. The cysts are unilocular or multilocular, and smooth walled. Pineal parenchymal tissue represents a thin layer or a nodule on the wall. Differentiation of these cysts from other neoplasms is extremely important because misdiagnosis could lead to inappropriate radiotherapy (42). The normal pineal gland usually has a uniform lobular structure and no pineocytomatous rosettes. However, that in the wall of the cysts occasionally loses its original architectures and shows a diffuse cellular arrangement. Complete remission is obtained by surgical excision. Stereotactic drainage may be followed by recurrence in some cases (40,42).

E) Pineal interstitial tumour and other types of neuroectodermal tumour derived from adjacent tissues : Gliomas occurring in the pineal region include fibrillary astrocytoma, pilocytic astrocytoma, anaplastic astrocytoma, glioblastoma, oligodendroglioma, ependymoma and choroid plexus papilloma (43-47). Well-differentiated astrocytomas are more common. Pleomorphic granular cell astrocytoma was suggested to be a peculiar astrocytoma originating from a pineal gland. The well-differentiated form of pineocytoma occasionally contains ganglion cells. This tumour was classified as variant of pineocytoma, i.e. pineocytoma with neuronal differentiation (48). Pineal ganglioglioma and gangliocytoma are other types of tumours with ganglion cells. These pure ganglion cell tumours should be precisely distinguished from pineocytomas with neuronal and/or astrocytic differentiation (49). Primary melanoma in the pineal region constitutes nearly 3.6% of primary malignant melanomas in the central nervous system with almost all cases associated with meningeal dissemination (50). Paraganglioma is one of the rarest tumours arising in the pineal region. As there are no chemoreceptors

such as the carotid body around the pineal gland, the tumour is considered to be derived from the pineal parenchyma (51).

F) Germ cell tumours : The pineal germ cell tumours which are derived from totipotential primordial germ cells constitute 33–63% of the intracranial germ cell tumours (52-54). Germinoma is a tan-white, solid and soft tumour, and is not usually associated with necrosis or haemorrhage. In contrast, embryonal carcinoma is fragile, and necrosis and haemorrhage are commonly present. Massive haemorrhage is observed in choriocarcinoma. Teratoma presents cysts and chondroid foci.

G) Meningeal tumours and other miscellaneous tumours : Pineal meningiomas represent approximately 0.3% of intracranial meningiomas (55). In the pineal region, meningiomas are considered to arise from the velum interpositum. Other rare histological types of the pineal region include malignant rhabdoid tumour , hemangiopericytoma, hemangioma, lipoma and craniopharyngioma .

H) Metastatic tumours : The pineal region is one of the rarest sites in the brain for metastasis of malignant tumours. In a large study of 5021 intracranial metastatic tumours, only 17 (0.3%) metastatic tumours were found in the pineal region (38). The most common site of origin for pineal region metastasis is the lung, followed by the breast, and other organs as melanoma, gastric carcinoma, kidney, gallbladder or colon and myeloma in a review of 75 pineal region metastatic tumours (56). There were no other metastases within the brain in approximately half of the cases. Small cell carcinomas need to be distinguished from pineoblastoma.

Clinical features :

Most common initial symptom is headache, which is associated with obstructive hydrocephalus secondary to compression of the aqueduct of Sylvius. Nausea, vomiting, obtundation, cognitive impairment, papilledema, and ataxia may come with progression of hydrocephalus. Rarely, pineal apoplexy from haemorrhage in a pineal tumour can cause manifestation of all these symptoms abruptly (57-59)

Parinaud's syndrome due to direct compression of the midbrain, particularly at the level of the superior colliculus by tumour can cause disorders of extraocular movement (60).

This syndrome also consist of paralysis of upgaze, convergence or retraction nystagmus and pupillary light-near dissociation. Another syndrome called sylvian aqueduct syndrome from further midbrain compression may also occur manifesting as paralysis of downgaze or horizontal gaze. Dorsal midbrain compression or infiltration can lead to lid retraction (Collier's sign) or ptosis. Symptoms due to hydrocephalus subsides after CSF diversion procedure. Interference with the cerebellar efferent pathways of the superior cerebellar peduncles can cause ataxia and dysmetria (60).

Spread of tumour in hypothalamic area or secondary effects of hydrocephalus manifest rarely as endocrine dysfunction. Diabetes insipidus can occur with a germinoma spreading along the floor of the third ventricle. Even, precocious puberty has been linked historically with pineal masses; however such cases are rare (61).

Diagnosis :

Magnetic resonance imaging (MRI) with gadolinium enhancement is the most important diagnostic test for pineal tumours (62). It reveals the degree of hydrocephalus and allows evaluation of tumour size, vascularity, homogeneity, and anatomic relationships with surrounding structures. It is of paramount importance while planning operative approach for tumour as it gives knowledge

of the relevant anatomic relationships including the position of the tumour within the third ventricle, the amount of lateral and supratentorial extension, and the degree of brainstem involvement.

Operative choice between an infratentorial and a supratentorial approach is influenced by the position of the tumour relative to the deep venous system. Computed tomography along with MRI can further provide details regarding calcification, blood-brain barrier breakdown, and the degree of vascularity (63). Angiography can be done if a vascular anomaly is suspected.

Tumour markers :

The presence of α-fetoprotein or β-HCG, in serum or CSF, is pathognomonic for malignant germ cell elements (57,64). CSF levels tend to be more sensitive than serum levels. Various tumour markers with associated pathology are enlisted in table below (57,64) :

Absence of germ cell markers should be interpreted cautiously because it does not rule out the presence of a germinoma or embryonal cell carcinoma. Tumour markers are useful for monitoring response to adjuvant therapy and also as an early sign of recurrence. As they are reliable indicators of malignant germ cell elements, presence of malignant germ cell markers makes surgery and biopsy unnecessary, and such patients should be managed with radiation therapy and chemotherapy (57,64) .

Surgical Management :

Surgical approaches to pineal region tumour are broadly classified as Supratentorial & Infratentorial approaches (65,66,67). Supratentorial approaches include the transcallosal interhemispheric, the occipital transtentorial, and the rarely used transcortical transventricular (67,68,69,70).The infratentorial approach is through a natural corridor created between the tentorium and the cerebellum (71,72).

The choice of approach depends on the surgeon's experience as well as comfort with the specific technique. Supratentorial approach is used for large tumours extending supratentorially or laterally to the trigone of the lateral ventricle, however surgeon has to work around deep venous system (67).

The location of most pineal tumours infratentorially and in the midline gives the infratentorial supracerebellar approach several natural advantages like tumour can be more easily dissected off the deep venous system and velum interpositum as tumour tends to move down due to gravity, which is often the most technically difficult portion of tumour dissection. Also, location of the deep venous system being dorsal to the mass, makes it more avoidable through most of the tumour dissection. This approach is less favourable if the tumour has a significant supratentorial or lateral extension, although with appropriate extra-long instruments, even tumours extending anteriorly into the third ventricle can be removed (67,72).

A) Occipital Transtentorial approach :

The occipital transtentorial approach which is a variation of the supratentorial approaches was originally described by Horrax and later modified by Poppen (73,74). A three-quarters prone position is generally preferred. This approach to the pineal region uses an oblique trajectory for lesions that are essentially midline, and may therefore be disorienting to surgeons who are not familiar with it. However, by dividing the tentorium, excellent exposure of the quadrigeminal plate is achieved, thus making it particularly useful for tumours that extend inferiorly.

A U-shaped right occipital scalp flap is reflected inferiorly, with the medial vertical limb beginning just to the left of midline at about the level of the torcular (68). A bur hole is placed in the midline over the sagittal sinus just above the torcular, along with another bur hole 6 to 10 cm above this. A craniotome is then used to turn a generous craniotomy extending 1 to 2 cm left of midline.

With the three-quarters prone position, gravity helps with retraction of the nondominant occipital lobe, which is also facilitated by the lack of bridging veins near the occipital pole. Under the operating microscope, the straight sinus is identified so that the tentorium can be divided adjacent to it. A retractor can be placed over the falx for exposure. The inferior sagittal sinus and falx can be divided to facilitate further falcial retraction. At this point, the arachnoid overlying the tumour and the quadrigeminal cisterns can be seen. Tumour removal proceeds as described earlier while taking care to avoid injury to the deep venous system.

B) Infratentorial Supracerebellar Approach :

The infratentorial supracerebellar approach was first described by Krause at the beginning of the 20th century (75).The infratentorial supracerebellar approach is usually performed with the patient in the sitting position (66,67). A suboccipital exposure is begun through a linear midline incision extending from just above the torcular and external occipital protuberance down to the level of the C4 spinous process. The craniotomy is centered just below the torcular. The dura is opened in a gentle semilunar curve that extends from the lateral aspects of the exposure.

To open the infratentorial corridor, the arachnoidal adhesions and midline bridging veins between the dorsal surface of the cerebellum and the tentorium are cauterized and carefully divided. Under the microscope, the arachnoid overlying the quadrigeminal plate is sharply opened. This is generally an avascular plane, and minimal cautery is necessary. The precentral cerebellar vein is identified as it courses from the anterior vermis to the vein of Galen and should be carefully dissected, cauterized, and divided.

With the posterior surface of the tumour exposed, the central portion is cauterized and opened with a long-handled knife or bayonet scissors. The tumour is then internally debulked with a variety of instruments such as suction, cautery, tumour forceps, and a Cavitron ultrasonic aspirator if necessary. As the tumour is decompressed, the capsule can be separated from the surrounding thalamus. The

dissection continues until the third ventricle is encountered. The tumour is then carefully dissected inferiorly off the brainstem.

Intraoperative decision making regarding the extent of tumour resection depends on the degree of tumour invasion (66,67).

C) Transcallosal Interhemispheric Approach :

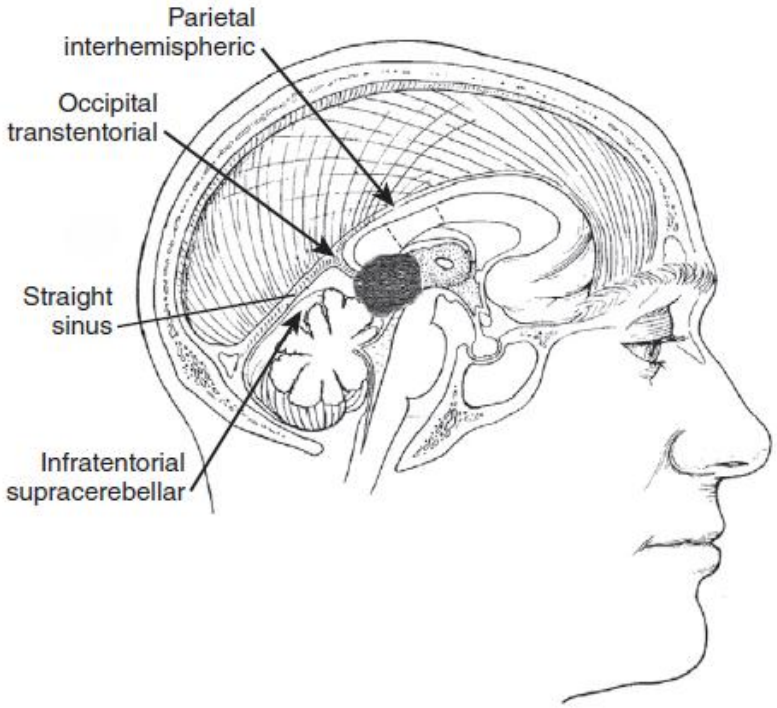
The transcallosal interhemispheric approach was first described by Dandy (11,76) This approach between the falx and hemisphere of the brain involves a corridor along the parieto-occipital junction. Positioning of the bone flap depends on where the tumour is centered in the third ventricle (70). A wide craniotomy roughly 8 cm in length provides flexibility in determining the corridor and avoiding bridging veins whenever possible. A U-shaped scalp flap extending across the midline and reflected laterally provides adequate exposure. The dura is opened in U-shaped fashion and reflected medially toward the sagittal sinus. The bridging veins are inspected, and an approach is chosen that will minimize the number of veins sacrificed.

The corpus callosum is easily identified with the operating microscope by its striking white appearance. The pericallosal arteries are identified as a paired structure running over the corpus callosum. These arteries are retracted either to one side or with separate retractors to each side. The opening into the corpus callosum, centered over the maximal bulge of the tumour, is generally about 2 cm, which is not likely to lead to disconnection syndrome or cognitive impairment Even more posterior openings in the splenium have been performed routinely without deficits. If necessary, the tentorium and falx can be divided to provide additional exposure. Once through the corpus callosum, the dorsal surface of the tumour can be seen, and the veins of the deep venous system must be identified early to prevent damage to them. Once the tumour is exposed, it is debulked and then dissected as described previously.

D) Transcortical Transventricular Approach :

The transcortical transventricular approach was developed by Van Wagenen, who used a trajectory through the right lateral ventricle via a transcortical incision (69). This approach is unpopular because the exposure is limited and the needed cortical incision is undesirable. Stereotactic guidance is often useful with this approach and may be desirable for a tumour that extends into the lateral ventricle.

Figure 1 : Surgical approaches to pineal region tumour



Complications :

In immediate postoperative period, patients frequently have impairment in extraocular movements particularly limited upgaze and convergence (78).

Many of these extraocular problems are transient and resolve within the first few days, some however may persist for several months. Also, ataxia is frequently present but resolves within a few days after surgery.

Overzealous brainstem manipulation can lead to cognitive impairment or, in its extreme form, even to akinetic mutism. Complications are more common in previously irradiated patients, invasive tumours, and those who were progressively symptomatic preoperatively (78,79).

Patients with highly vascular, invasive tumours such as malignant pineal parenchymal tumours are at greatest risk for devastating complication like haemorrhage in tumour bed (78). A large haemorrhage may require immediate evacuation. Such decisions must consider the possibility of obstructive hydrocephalus. Another potential vascular complication is venous infarct, which can extend into the midbrain with devastating consequences. This rare complication is thought to be the result of venous insufficiency in a small subset of patients who cannot tolerate the sacrifice of bridging veins in the cerebellum.

Complications of supratentorial approaches include hemiparesis from brain retraction or from sacrifice of bridging veins (79,80). Parietal lobe retraction can lead to sensory or stereognostic deficits on the opposite side.Occipital lobe retraction during the transtentorial approach can cause visual field defects (68,79,80). Disconnection syndromes with corpus callosum incisions have also been rarely reported (80).

Pineal tumour patients are generally young and have relatively few medical problems. Consequently, the incidence of medical complications such as cardiac or respiratory problems is low.

AIMS AND OBJECTIVES

Our primary objective was to evaluate the various factors related to the post-operative outcome of surgery & comparing them with the pre-operative presentation.

The following characteristics were included in our study:

1) Symptoms at presentation

2) Gender & age at surgery

3) Karnofsky performance score (KPS) at admission

4) Tumour diameter, dimensions, and volume

5) Preoperative hydrocephalus presence and management

6) Surgical approach

7) Extent of tumour removal

8) Tumour characteristics

9) Post-operative visual outcome

10) Intra-operative & Post-operative Complication

11) Tumour pathology

12) Duration of ICU stay

13) Duration of postoperative hospital stay

14) Karnofsky performance score (KPS) at discharge & 3 months follow up

15) Residual lesion at 3 month follow up

16) Use of adjuvant therapy

METHODOLOGY

Study was initiated after obtaining institutional review board approval. We included a total 106 consecutive patients, operated between July 2012 to March 2020. Retrospective study was done of 76 patients operated till December 2018 & prospective analysis was done on 30 patients who underwent surgery from January 2019 to March 2020. Both the adult and paediatric patients were included in the cohort.

We analysed various patient related factors, tumour related factors, intra-operative observations, and postoperative clinical and radiological parameters for their effects on the clinical outcome of patients. Patient factors included clinical presentation, gender, age at surgery, Karnofsky Performance Scale (KPS) score on admission, discharge and after 3 months of surgery. Tumour related factors included tumour diameter & volume, presence of preoperative hydrocephalus & its management. Surgical observations included surgical approach, tumour characteristics, tumour pathology, intra-operative complications. Clinical and radiological parameters included postoperative complication, duration of intensive care post-operative length of stay in hospital, extent of resection confirmed at 3 months after surgery by MRI or CT imaging , & need for adjuvant therapy. Surgical approaches used in this study were Modified Poppen's approach, Supracerebellar Infratentorial (SCIT) approach, Interhemispheric approach & Transcortical approach.

Statistical analysis :

All statistical analyses were carried out in SPSS Statistics for Windows, Version 17.0. Paired sample statistics (t-test) was used for comparing KPS score at admission, discharge & at 3 months follow-up.

RESULTS

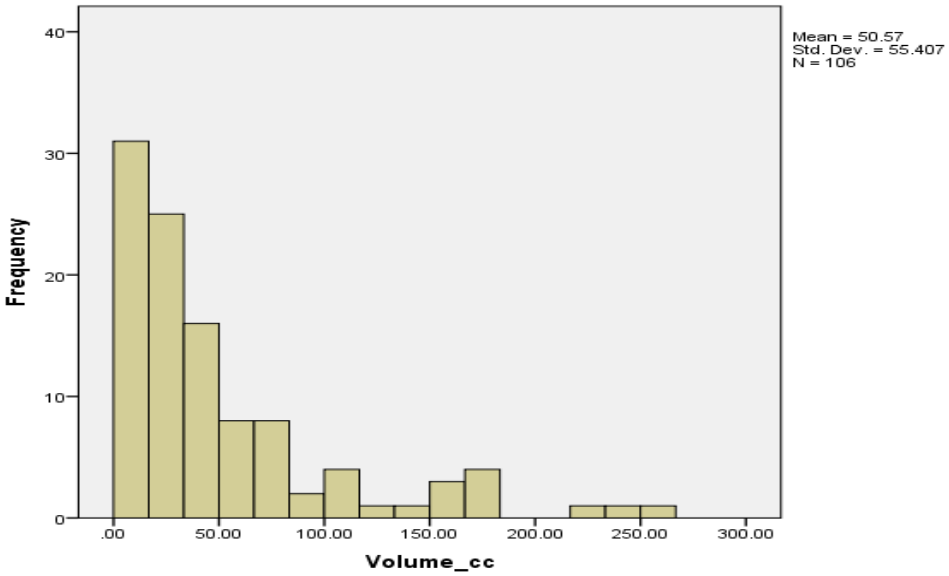
Patient Characteristics:

Out of 106 patients operated , 54 (50.9%)were female and 52 (49.1%) were males . Patients below 20 were 36.8% (39), between 20 - 39 years were 31.1% (33) and above 40 years were 32.1% (34) (Table 1). All surgeries were performed by the corresponding author. 4 patients died in the perioperative period and 1 patient discharged in good condition was lost from followup. KPS score on admission was 71-89 in 74 patients (69.8%), above 90 in 19 patients (17.9%) & less than 71 in 13 patients (12.3%) (Table 1).

Table 1: Patient Characteristics

Category	Subgroup	N(%)
Gender	Male	52 (49.1%)
	Female	54 (50.9%)
Age(years)		
	< 20 years	39 (36.8%)
	20-39 years	33 (31.1%)
	>40 years	34 (32.1%)
Admission KPS		
	90 +	19 (17.9%)
	71-89	74 (69.8%)
	<71	13 (12.3%)
Tumour volume ($cm^{3)}$		
	<5	7 (6.6%)
	5-9	12 (11.3%)
	10 +	87 (82.1%)
Extent of resection		
	STR	8 (7.5%)
	GTR or NTR	98 (92.45%)
ICU Length of stay (days)	4.65 days (mean) 3 days (median)	
	0-1 days	21 (19.8%)
	2-7 days	71 (67.0%)
	8+ days	14 (13.2%)
Total Post-operative length of stay (days)	11.86 days (mean) 10.5 days(median)	
	0-7	37 (36.3%)
	8-14	42 (41.2%)
	15 +	23 (22.5%)

Figure 2 : Tumour Volume



As per operative notes,Gross total or near total resection of tumour was achieved in 98 patients (92.45 %) & sub-total resection in 8 patients (7.5%). However imaging evidence of residual lesion was seen in 13.2% patients (14)

The mean ICU length of stay was 4.65 days & median value was 3 days. The mean postoperative length of stay was 11.86 days and the median was 10.5 days (Table 1). Mean duration of ventilation was 0.8 days and the median duration was 0 days.

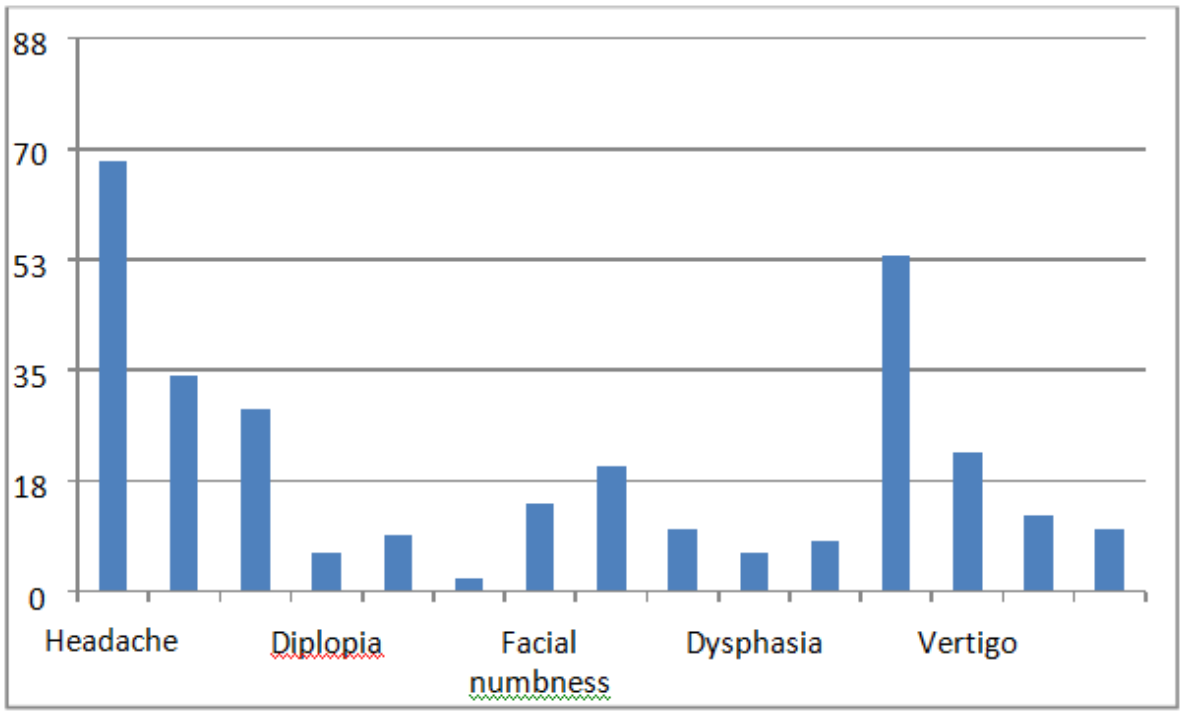
Clinical presentation:-

The most common presenting symptom was headache in 80 patients (75.5%). Gait unsteadiness was present in 34 patients (34.1%), blurring of vision in 26 patients (24.5%), vomiting & diplopia in 21 patients (19.8%). Other symptoms with their frequency have been enlisted in Table 2.

.Table 2: Presenting symptoms of Pineal region tumours

Presenting symptoms	N	%
Headache	80 / 106	75.5
Blurring of vision	26 / 106	24.5
Vomiting	21 / 106	19.8
Seizure	6 / 106	5.7
Gait Unsteadiness	34 / 106	32.1
Nystagmus	1 / 106	0.9
Diplopia	21 / 106	19.8
Memory Disturbances	9 / 106	8.5
Facial Palsy	4 / 106	3.8
Decreased Speech	1 / 106	0.9
Loss Of Consciousness	1 / 106	0.9
Hearing Loss	3 / 106	2.8
Incidental	2 / 106	1.9
Developmental Delay	1/106	0.9
Urinary Incontinence	2/106	1.9
CSF Rhinorrhea	1/106	0.9
Anosmia	1/106	0.9
Disorientation	1/106	0.9
Endocrine Dysfunction	1/106	0.9
Neck Pain	1/106	0.9
Dizziness	1/106	0.9

Figure 3 : Frequency of Symptoms



Presence & management of Hydrocephalus:

Hydrocephalus was present in 83 patients (78.3%) with mean KPS score of 79.52 . The rest 23 patients (13.47 %) had no hydrocephalus and their KPS mean score was 82.17. Hydrocephalus had a marginal statistically insignificant influence on KPS score (Figure 4).

Among 83 patients with hydrocephalus, 55 (51.8%) underwent pre-operative CSF diversion procedure. Ventriculo-peritoneal shunt placement was done for 27.3% (29)patients, 19 patients (17.9%) underwent endoscopic third ventriculostomy & 7 patients (6.6%) required both ETV & Ventriculo-peritoneal shunt (Table 4) . Post-operatively, 8 out of 101 patients (7.92%) required CSF diversion procedure. Out of which, 5 patients underwent VP shunt and 1 patient a subduroperitoneal shunt within 3 months of surgery and 2 patients had a VP shunt placement after 3 months of surgery

Table 3: Hydrocephalus as a Predictor for Karnofsky Performance Score on admission

Preop hydrocephalus	Patients (n)	Mean KPS ± SD	*P*-value
No	23	82.17 (13.47)	0.238
Yes	83	79.52 (8.10)	

Figure 4 : Graph correlating hydrocephalus with KPS score on admission

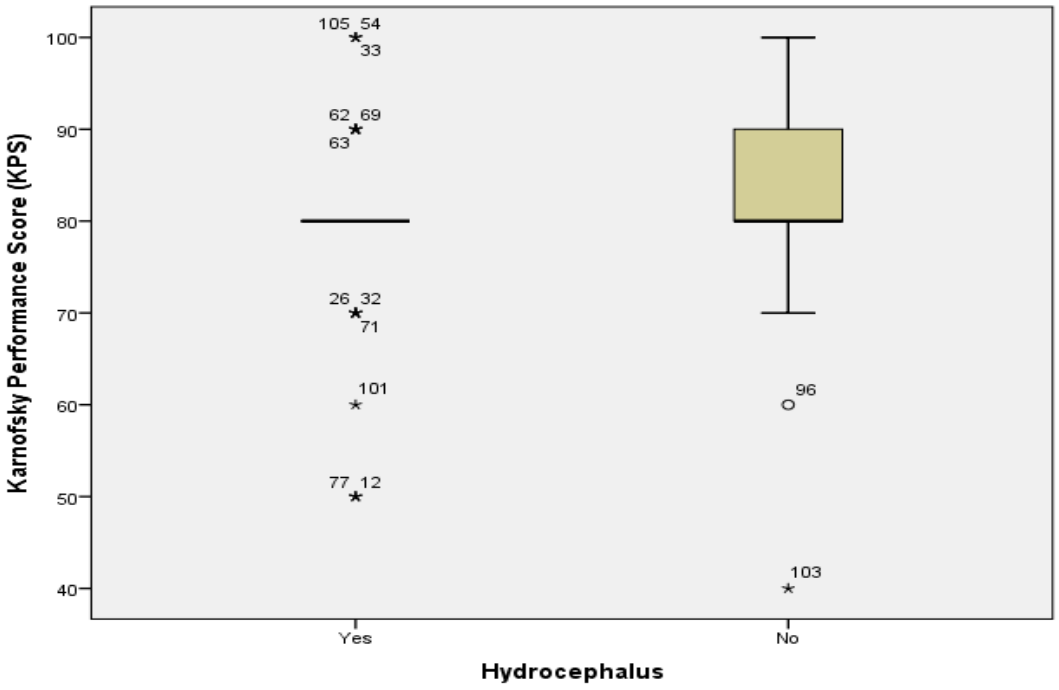


Table 4 : Preoperative Hydrocephalus and Treatment Plan Rates

Preoperative hydrocephalus management	N(Number of patients)	%
Hydrocephalus	83	78.3
ETV	19	17.9
VPS	29	27.3
Both	7	6.6
No Hydrocephalus	23	21.7

Tumour Characteristics :

Tumour characteristics like presence or absence of calcification, vascularity & consistency of tumour are routinely noted in the operative notes. Calcification was found in 10 patients (9.4%). 56.6% (60)of tumours were moderately vascular while 37 lesions (34.9%) were highly vascular, low vascularity or avascular lesions were 8.5 % (9).

Tumour was both suckable & causable in 40 patients (37.35%) , suckable in 34 patients (32.1%) & cusable in 18 patients (17%) (Table 5).

Table 5 : Tumour characteristics

Imaging characteristic	Number of patients	Percent (%)
Calcification	10	9.4
High vascularity	37	34.9
Moderate vascularity	60	56.6
Avascular	9	8.5
Suckable	34	32.1
Cusable	18	17
Both Suckable & Cusable	40	37.35

Surgical approaches :

Modified Poppen's approach was most commonly employed approach for surgical treatment of pineal region tumours i.e. in 89 patients (83.96 %). Posterior interhemispheric approach was used in 8 (7.56 %) patients, Supracerebellar Infratentorial approach used in 7 (6.6%) patients & Transcortical approach in 2 (1.9%) patients.

Table 6. Definitive Surgical Approaches Employed

Surgical approach	N (No.of patients)	Percentage (%)
Modified Poppen's approach	89	83.96 %
Supracerebellar Infratentorial approach	7	6.6%
Posterior Interhemispheric approach	8	7.56%
Transcortical approach	2	1.9%

Tumour Pathology :

Various pathologies were found on histopathological examination of tumour, which are enlisted in the table below. Of over 11 different pathologies, 32 tumours were of pineal parenchyma origin, 32 lesions were of glial origin, 16 were meningiomas and 5 were germ cell lesions.

Table 7 : Tumour Histopathology

Histopathology	Frequency	Percent (%)
Pineal Parenchymal tumours	32	30.18
Pineal tumours oif glial origin	32	30.18
Germ cell tumours	5	4.72
Non germinamatous germ cell tumours	7	6.6
Meningioma	16	15.09
Epidermoid cyst	5	4.72
Arachnoid cyst	2	1.89
Hemangioblastoma & Hemangiopericytoma	4	3.77
Medulloblastoma	1	0.94
Neurocytoma	1	0.94
Squamous cell carcinoma	1	0.94

Surgical Approaches and Extent of Resection :

Modified Poppen's approach was most commonly employed surgical approach with 89 patients (83.96%) operated through this route . Inter-hemispheric approach was used in 8 patients (7.56%), Supracerebellar Infratentorial approach used in 7 patients (6.6%) & Transcortical approach in 2 patients (1.9%) (Table 8).

Table 8 : Surgical approaches & extent of resection

Surgical approach	Gross total or Near total resection	Subtotal resection	Total (N=106)
Modified Poppen's approach	82 (92.13 %)	7 (7.87 %)	89 (83.96 %)
Supracerbellar-Infratentorial approach	6 (85.71 %)	1 (14.29%)	7 (6.60%)
Interhemispheric approach	8 (100 %)	0	8(7.56 %)
Transcortical approach	2 (100 %)	0	2 (1.89 %)
Total	98 (92.45%)	8 (7.55 %)	106 (100%)

Extent of Resection as a Function of World Health Organization Grade :

Extent of Resection as a Function of World Health Organization Grade:

As per Table 9, 42 (39.62%) lesions were WHO grade 1. Gross total or near total resection was obtained in 38 patients(90.47%) . Even in WHO Grade 2/3 tumours which constituted 42 patients (39.62%), gross total or near total resection was possible in 39 patients (92.85%) . In WHO grade 4 group which comprised of 22 patients (20.75%), gross total or near total resection was achieved in 21 patients (95.45%).These results suggest that gross total or near total resection is possible in majority of patients irrespective of the WHO grade of the tumor.

Table 9 : Extent of Resection as a Function of World Health Organization Grade

WHO Grade of Tumour	Gross & Near total resection	Subtotal resection	Total (percentage out of total study population)
WHO Grade 1	38(90.47%)	4 (9.52%)	42 (39.62%)
WHO Grade 2/3	39(92.85%)	3 (7.15%)	42(39.62%)
WHO grade 4	21(95.45%)	1 (4.54%)	22 (20.75%)
Total	98 (92.45%)	8(7.54 %)	106 (100%)

Wound related complications :

In our study, 11.32 % patients experienced wound related complications in the post-operative course with pseudomeningocele 8 (7.54 %) being the most common complication f/b meningitis which was seen in 2(1.89 %) patients & bone flap infection which was seen in 2 (1.89%) patients.Both the patient s with bone flap infection underwent bone flap removal.

Table 10 : Wound related complications

Complications	Frequency (N)	Percentage (%)
Bone flap infection	2	1.89%
Meningitis	2	1.89%
Pseudomeningocele	8	7.54%
Total	12/106	11.32%

Vision related complications at discharge :

Out of 106 patients, 26 (24.52%) patients had fresh visual deficits in immediate post operative course & at discharge. Bilateral upgaze palsy was found to be most common complication, seen in 15 (14.15%) patients. Other complications are listed in the table below.

Table 11 : Vision related complications at discharge

Visual deficits	N (Number of patients)	Percentage (%)
B/L upgaze palsy	15	14.15%
B/L downgaze palsy	1	0.94%
B/L upgaze + downgaze palsy	2	1.89%
B/L lateral rectus palsy	1	0.94%
B/L ptosis	3	2.83%
Hemianopia	4	3.77%
Total	26/106	24.52%

Vision related complications at 3 month follow up :

Many patients had significant improvement in their visual deficit at 3 month of follow up when compared to discharge i.e from 24.52 % patients with visual deficit at discharge, only 9.9 % were found to have the same at 3 month of follow up. Again, bilateral upgaze palsy was found to be most common visual deficit at 3 month of follow up.

Table 12 : Vision related complications at 3 month follow up

Visual deficits	N (Number of patients)	Percentage (%)
B/L upgaze palsy	7	6.93%
B/L ptosis	2	1.98%
Hemianopia	1	0.99%
Total	10/101	9.9 %

Post-operative stay :

In the post operative course,ventilator support was required for the mean of 0.8 days, mean ICU length of stay was 4.65 days & mean post-operative length of stay was 11.86 days.

Table 13 : Post operative length of stay

Number of Days	Mean (days)	Median (days)
Ventilator support	0.802	0
ICU stay	4.65	3
Post-op hospital stay	11.86	10.5

Residual Lesion :

On 3 months of follow-up,14 (13.2%) patients were found to have residual lesion on MRI Brain imaging & 87 (82.07%) were found to have no residual lesion.

Table 14 : Residual lesion at 3 month follow up

Residual lesion	N (Number of patients)	Percentage (%)
Yes	14	13.2%
No	87	82.07%
Death	4	3.77%
Lost to follow up	1	0.94%
Total	106	100

Adjuvant Therapy :

Adjuvant therapy was received by 30 (28.3%) patients & in majority of patients i.e. 71(67%) , there was no need for adjuvant therapy.

Table 15 : Adjuvant therapy

Adjuvant therapy	N (Number of patients)	Percentage (%)
Yes	30	28.3%
No	71	67%
Death	4	3.77%
Lost to follow up	1	0.94%
Total	106	100

Relationship of KPS score to various parameters :

Various factors like age, tumour volume, ICU length of stay & total hospital stay were co-related with KPS score on admission. There was inverse relationship between age, ICU length of stay & total hospital length of stay with KPS score on admission. However, difference was not statistically significant. Interestingly, tumour volume had direct relationship with KPS score on admission & also the difference was found to be statistically significant.

Table 16. Regression Analysis of various factors with KPS score on admission

Relationship	Value	95% CI (low)	95% CI (high)	P-value
Effect of age on admit KPS	0.064 KPS per each year of age	-0.029	0.157	0.178
Effect of tumour volume on admit KPS	0.046 KPS per each additional 1 cm3	0.015	0.077	0.004
Effect of admit KPS on ICU LOS	0.3 days additional ICU stay per 10-point admission KPS	-0.95	1.00	0.959
Effect of admit KPS on post-operative hospital LOS	0.79 days additional post-operative hospital LOS per 10-point admission KPS	-0.71	2.3	0.298

Figure 5 : Graph correlating tumour volume with KPS score on admission

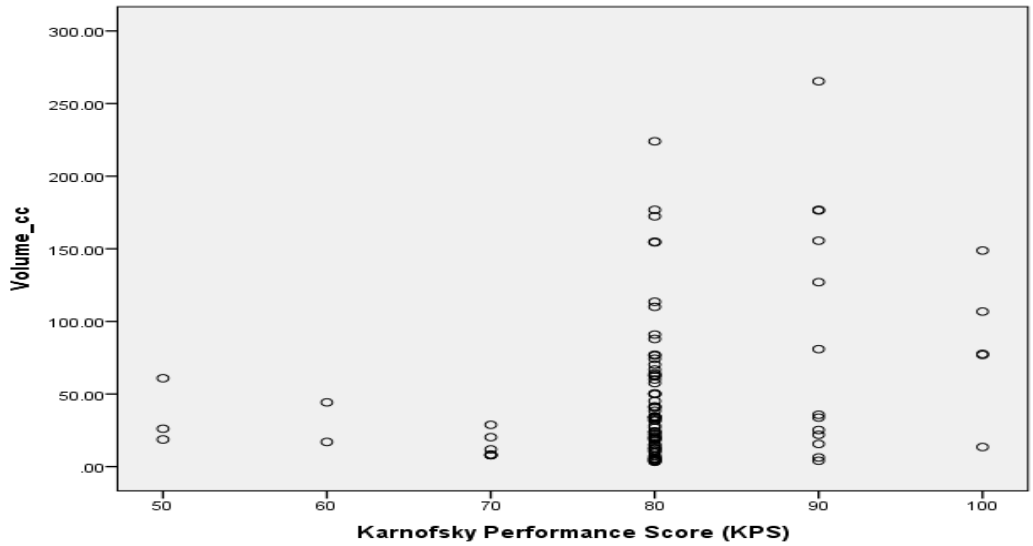
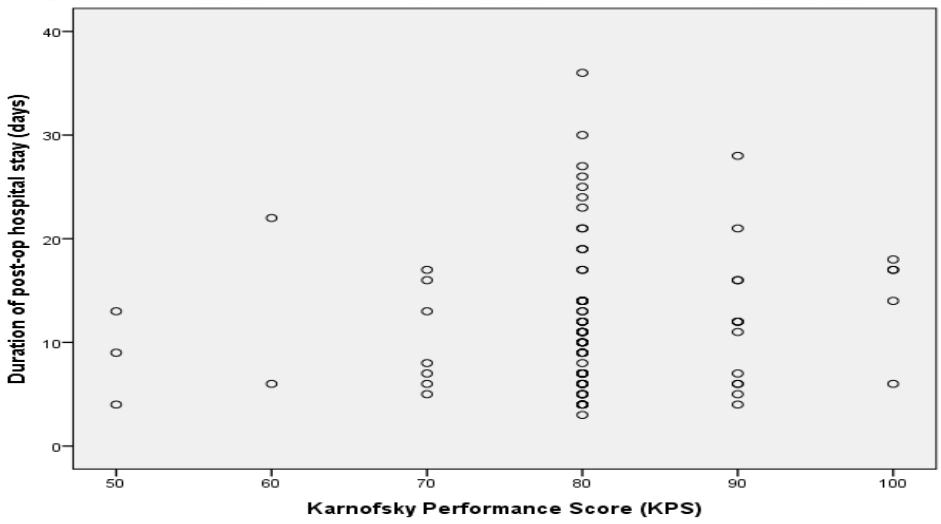


Figure 6 : Graph correlating post-operative length of stay with KPS score on admission



Improvement of KPS score :

Statistical analysis of KPS score was done comparing difference in the KPS score between KPS score at admission with KPS score at discharge, KPS score at admission with KPS score at 3 months of follow up & KPS score at discharge with KPS score at 3 months of follow up. On analysis, all 3 differences in the KPS score were found to be statistically significant.

There was improvement of the KPS score on discharge & at 3 months of follow up compared to KPS score on admission. Also, there was improvement in KPS score at 3 month of follow up compared to KPS score at discharge.

Table 17 : Paired Samples Statistics (T test)

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Karnofsky Performance Score (Pre-op)	80.2941	102	8.61220	.85274
	Karnofsky performance score (DISCHARGE)	89.7059	102	17.76947	1.75944
Pair 2	Karnofsky Performance Score (Pre-op)	80.2970	101	8.65511	.86122
	Karnofsky performance score(3 MONTHS)	93.0693	101	14.33475	1.42636
Pair 3	Karnofsky performance score (DISCHARGE)	89.6040	101	17.82811	1.77396
	Karnofsky performance score(3 MONTHS)	93.0693	101	14.33475	1.42636

Table 18 : Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	Karnofsky Performance Score (Pre-op) & Karnofsky performance score (DISCHARGE)	102	.182	.068
Pair 2	Karnofsky Performance Score (Pre-op) & Karnofsky performance score(3 MONTHS)	101	.178	.075
Pair 3	Karnofsky performance score (DISCHARGE) & Karnofsky performance score(3 MONTHS)	101	.631	.000

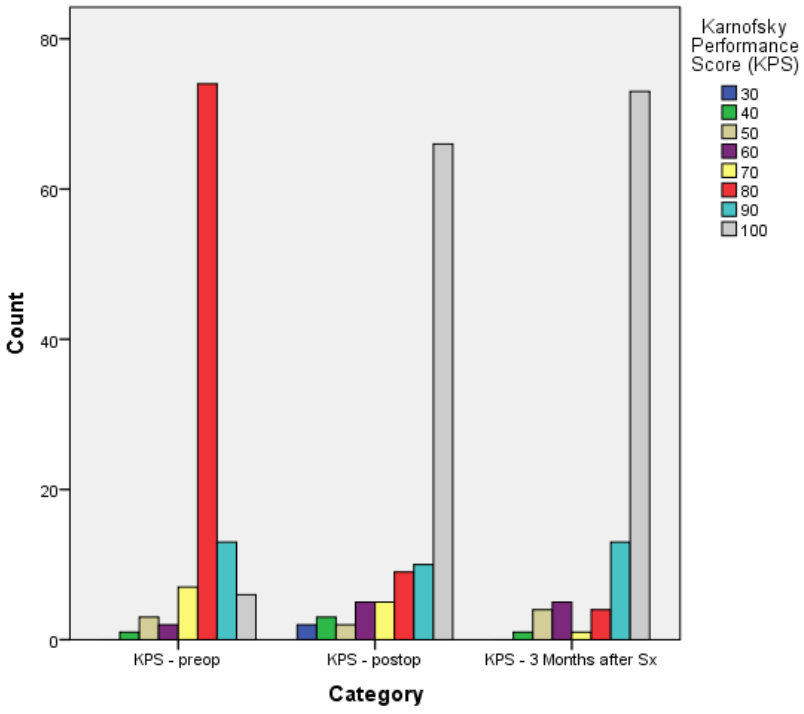
Table 19 : Paired Samples Test

		Paired Differences			
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference
					Lower
Pair 1	Karnofsky Performance Score (Pre-op) - Karnofsky performance score (DISCHARGE)	-9.41176	18.28398	1.81038	-13.00308
Pair 2	Karnofsky Performance Score (Pre-op) - Karnofsky performance score(3 MONTHS)	-12.77228	15.37002	1.52937	-15.80651
Pair 3	Karnofsky performance score (DISCHARGE) - Karnofsky performance score(3 MONTHS)	-3.46535	14.17291	1.41026	-6.26326

Table 20 : Paired Samples Test

		Paired Differences	t	df	Sig. (2-tailed)
		95% Confidence Interval of the Difference			
		Upper			
Pair 1	Karnofsky Performance Score (Pre-op) - Karnofsky performance score (DISCHARGE)	-5.82045	-5.199	101	.000
Pair 2	Karnofsky Performance Score (Pre-op) - Karnofsky performance score(3 MONTHS)	-9.73804	-8.351	100	.000
Pair 3	Karnofsky performance score (DISCHARGE) - Karnofsky performance score(3 MONTHS)	-.66744	-2.457	100	.016

Figure 7 : Graph showing Improvement in the KPS score



DISCUSSION

Pineal region tumour surgery is known to be technically challenging as well as requires consideration of various patient related & tumour related factors so as to select the best surgical approach from surgeon's armamentarium. There are few studies in the literature presenting their experience with this difficult tumour. However, they are limited by focusing on single surgical approach or on single pathology of pineal region (81).

In our study, we have addressed limitations of other studies by including various surgical approaches to this tumour, not limiting study to specific set of pathologies as well as we have considered various pre-operative, intraoperative & postoperative factors & have studied their effect on patient outcome by using statistical analysis.

There was study published by Maselli et al (82) reviewing their experience with Occipital transtentorial approach in posterior fossa tumours. Out of 14 patients they included in their study, only 2 patients had actual pineal region tumour. Also,that study was limited by small sample size, majority being small tumours (<3cm) ,use of single approach, lack of information regarding follow up. Functional outcomes of all patients was described as good to excellent. Our study, in contrast, has a very large sample size of 106 patients with use of 4 surgical approaches depending on the regional & vascular anatomy of tumour with all tumours arising in pineal region of various size with majority of tumour (82.1%) having volume more than 10 cm^3 (Refer Table 1) . Similar to Maselli et al, our study population also had improvement in functional outcome which was measured by using Karnofsky performance score at discharge as well as at 3 months of follow up.

Another study done by Oliveira et al (83) focused on the use of Supracerebellar infratentorial approach for resection of pineal region tumours. In their study, gross total resection was achieved in 15 patients (45.45%) & subtotal resection in 7

patients (21.21%) out of total study population of 33 patients. In our study, SCIT approach was used in 7 patients & we were able to achieve gross total or near total resection in 6 out of 7 patients (85.71 %) which is more than that reported by Oliveira et al.

In 2014, Qui et al (84) reported a case series of 15 patients who underwent unilateral Occipital transtentorial approach for pineal region meningiomas. There was no mortality & they reported visual deficits in 3 patients. Two patients had homonymous out of which, one patient had gradual improvement & third patient had parinaud syndrome with diplopia. In our series,16 patients had pineal region meningioma, all patients underwent Modified Poppen's approach (Occipital Transtentorial) with no mortality similar to the series of Qui et al. However, in our study in contrast to result of Qui et al ,only one patient had lateral hemifield defect that too resolved at follow up after 3 months of surgery.

In 2008, Hernesniemi et al (80) published his experience with 107 cases of pineal region tumour using Supracerebellar infratentorial route. He achieved gross total resection in 88 % cases with zero mortality. In our study, gross total resection was achieved in 98 patients (92.45%) with mortality rate of 3.77 % (4 patients).In study by Hernesniemi et al, 2 patients had meningitis & 3 patients had wound infection which is almost similar to our series. Visual deficit was seen in 9 patients in study by Hernesniemi et al. Post operative visual deficit was seen in 26 patients in our study which is almost three times of that seen in Herniesniemi et al. However, majority of patients had improvement in visual deficits with only 10 patients had persistent visual deficit at 3 month of follow up. All patients with benign lesion survived at 3.5 yrs of follow up in Hernesniemi study which is similar to the result seen in our study thus emphasizing on the importance of surgical treatment as the first line option while dealing with pineal region tumours. Though this study by Herniesmi et al had large sample size but utilization of a single approach for all tumours act as a major limiting factor as it implies the importance given to surgeon's comfort with a particular single approach rather than the judicious use of another approach which may be more

safe and efficacious when patient specific & tumour specific factors are considered for the tumour.

A very large series of 233 patients of pineal region tumour operated between 1982 to 2012 using Sub-occipital Transtentorial approach was published by Mottolese et al (85) in 2014.

In this series, gross total resection was achieved in 135 patients (58%) and subtotal resection in 60 patients (26%) In our study, we achieved comparatively higher rate of gross total or near total resection by using same approach i.e. in 98 patients (92.45%) & subtotal resection was obtained in only 8 patients(7.54%). Mortality rate of Mottolese et al series was 0% compared to mortality rate of 3.77% in our study. Also, since all patients in Mottolese et al series were operated in sitting position, there was 4% incidence of severe pneumocephaly which required prolonged intensive care hospitalization. In our series, all patients operated by Modified Poppen's approach had prone position during surgery & we had no patient with significant pneumocephaly in the post-operative period. Hence, prone position should be preferred for these tumours by occipital transtentorial approach to decrease incidence of significant pneumocephaly.

Mottolese et al found sub-occipital transtentorial approach to be the best approach for pineal tumours because it permits a large exposition of the pineal region favoring the removal of the tumour with a lateral extension and also for tumours extending low into the posterior cranial fossa. So, it was their preferred approach & was used in a large majority of cases. We share similar opinion regarding the choice of approach, however we also emphasize familiarity with other approaches as well so as to get maximum resection of tumour & best possible functional outcome to patient.

Motollese et al (86) also published his experience in pineal region tumours using Supracerebellar infratentorial approach in 31 patients. Postoperative complications included symptomatic diffuse cerebellar edema (one patient) which completely resolved with a mild residual cerebellar syndrome; double vision

secondary to fourth nerve palsy in one patient, transitory Parinaud's syndrome in 2 patients and cerebellar gait in 2 patients which nearly completely recovered at respectively six and twelve months. In our experience with Supracerebellar infratentorial approach which was used in 7 patients, one patient had parinaud syndrome which was found to be absent at 3 months follow up & one patient with bilateral upgaze palsy which also resolved at 3 month follow up. Also, all patients had improvement in their KPS score at 3 month of follow up with no mortality. Thus, we agree with the conclusion of Motollese et al that Supracerebellar infratentorial approach is a safe approach to use for this group of tumours when needed.

A series of 160 pineal region operations on 154 patients was published by Bruce et al (87) using the SCIT approach in 86% of patients with a 4% mortality. Though, in our series Modified Poppen's approach was used for majority of cases i.e. in 89 (83.96%) patients, mortality rate of 3.77% is comparable to series of Bruce et al. In series by Bruce et al, gross total resection was achieved in 45% of cases and only in 29% of malignant tumours. However, in our series gross or near total resection was much higher i.e. in 98 patients (92.45%) patients & also it was achieved in 21 out of 22 cases (95.45 %) of malignant WHO grade 4 tumours

In study published by Abecassis et al (88) about their experience with 50 pineal region tumours,most common approach used was Supracerebellar infratentorial approach (32%) followed by posterior interhemispheric transsplenial (26%) and ETV with biopsy (22%). Gross total resection (GTR) was achieved in 62% of the tumours approached with microsurgery and subtotal resection (STR) in 38% of tumours. In our study, we achieved gross total or near total resection in 98 patients (92.45%) patients & subtotal resection was obtained in only 8 patients (7.54%).

Abecassis et al found by univariate analysis that admission KPS scores were significantly related to patient age, tumour volume, presence of preoperative hydrocephalus, ICU length of stay & total length of stay. Moreover, regression analysis showed that increased patient age and tumour volume were predictive of

lower admission KPS scores with each additional 10 years of patient age and each 10 cm^3 increase in tumour volume, corresponding to 2.4 and 4.9 point lower admission KPS scores, respectively. However, in our study there was no statistically significant relationship found between admission KPS score with patient age, presence of pre-operative hydrocephalus, ICU & post-operative length of stay. The only significant relationship found was effect of tumour volume on admission KPS score which again was in contrast to the result by Abecassis et al i.e. there was increase of KPS score by 0.046 per each additional 1 cm^3 (Table 16).

Also, Abescassis et al found that patients with radiographic evidence of hydrocephalus on admission had average KPS scores of 75 ± 17 compared with 88 ± 9 in patients without evidence of hydrocephalus. We also found similar result as patients without hydrocephalus on admission had slightly better KPS score i.e. 82.17 ± 13.47 than patients with hydrocephalus i.e. 79.52 ± 8.10 (Table 3).

Also all patients with hydrocephalus in series by Abescassis et al underwent CSF diversion procedure. However in our study ,55 patients out of 83 (66.26%) required CSF diversion procedure with ventriculoperitoneal shunt being most commonly used procedure i.e. in 36 out of 55 patients (65.45%) (Table 4).

In Abescassis et al study, the average postoperative (2 months and most recent follow-up) KPS score was 88 ± 21, with a median of 90. In our study, the average KPS score at admission was 80.09 ± 9.51. The average postoperative KPS at discharge was 86.32 ± 24.47 that was statistically significant compared to KPS at admission. There was further statistically significant improvement in KPS at 3 month follow up which was 93.07 ± 14.33.

Also, the specific surgical approach did not uniformly relate to extent of resection based on MRI which was similar finding in our study too. Abescassis et al found that tumour pathology based on World Health Organization grade was unrelated to extent of resection on a statistical level. Even in our study, extent of resection was unrelated to WHO grade of tumour.

There was no surgical mortality defined as death within 30 days in Abescassis et al series. However , in our study three patients succumbed to death within 30 days of surgery out of which one patient already had a poor KPS score at admission (KPS = 40) , other patient was a recurrent tectal plate lesion with thalamic extension operated at outside hospital.

Third patient was a 9 month old child with extensive lesion whose histopathology was pineoblastoma. Fourth patient who succumbed to death in our series at postoperative day 50 had left cerebellar & hemipons infarct due to venous sinus thrombosis & vasospasm & histopathology of tumour was glioblastoma.

The complications in Abescassis et al series included a 6% risk of CSF leak with meningitis and a 10% rate of surgically induced ocular dysfunction (6% new/transient, and 4% new/permanent). In our study, meningitis was seen in 2 (1.89%) patients & bone flap infection was seen in 2 (1.89%) patients. Also, in our study, 24.52% patients had fresh visual deficits in immediate post operative course & at discharge, while only 9.9% had the same at 3 months of follow up implying majority of such visual deficit postoperatively to be transient.

Limitations :

In the retrospective review of patients, KPS score was collected from admission notes, discharge paper & from OPD notes at 3 months of follow up. Therefore, this data was not standardized & thus there can be scope of bias. Also, follow up data was limited to 3 months of follow up, as we included prospective review of patients as well. A prospective long term follow up study can address these limitations.

CONCLUSIONS

Modified Poppen's approach was found to be an extremely useful approach applicable to majority of pineal region tumours giving good functional outcomes & causing minimal morbidity. KPS score at admission and tumour pathology are the main deciding factors in the surgical outcome of pineal region lesions.

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.

ANNEXURE

Patient Proforma Form

A. GENERAL INFORMATION -

Anonymized Patient Hospital ID:

Age

Gender

B.CLINICAL DETAILS -

GCS on admission:

Karnofsky performance score

Symptoms at presentation

Hydrocephalus

Size of tumour (in mm) with extent of tumour

Preoperative Vision profile

Radiological investigations

C.INTRAOPERATIVE EVENTS-

Surgical approach

Extent of tumour resection

Tumour Characteristics

-Calcification:

-vascularity:

-consistency:

D. POST-OPERATIVE EVENTS

Infection

CSF leak

Pseudomeningocele

Re-exploration / Decompression

Other complication :

Duration of the ventilator support:

Duration of ICU stay (days)

Duration of post-op hospital stay (days)

Tumour pathology

Postoperative vision profile

E. STATUS ON DISCHARGE

Karnofsky performance score:

Motor and speech status

Any other deficit

F.STATUS ON FOLLOW UP ON 3 MONTHS

Karnofsky performance score:

Motor and speech status

Any other deficit

Radiological follow up

Patient Information Sheet

"A Single-Institution Experience with Pineal RegionTumor"

INVESTIGATORS:
PRINCIPAL INVESTIGATOR: Biren Khimji Patel (Dr) M.S (General Surgery) Address: Senior Resident, Department of Neurosurgery, SCTIMST, Medical college P.O., Thiruvananthapuram, Kerala, India, Pin – 695011
CO-PRINCIPAL INVESTIGATOR: Mathew Abraham (Dr) M.S., M.Ch (Neurosurgery), FRCS (Edin.) Address: Professor & Head, Department of Neurosurgery, SCTIMST, Medical college P.O., Thiruvananthapuram, Kerala, India, Pin – 695011

You are planned for surgery for the disease you are suffering from, after personally verifying and discussing the data obtained from your clinical history, examination and imaging. You have also expressed your willing for surgical management of your disease condition.

The pineal region is a challenging surgical location, in part due to the rarity of pineal region neoplasms, which comprise only 0.5% to 1.6% of all intracranial tumors . The pineal tumors are nowadays treated surgically in many center and even though the surgical approach of this region is challenging this surgery can be realized with good results and acceptable postoperative morbidity mainly in cases of benign lesions in children and adults patients. There are very few studies in the literature investigating peri-operative management and clinical outcomes in this population as well as whether or not surgical approach affects functional status. We will be studying whether or not certain anatomical and clinical features at presentation and surgical approach were associated with functional status at presentation and at most recent follow-up.

Prior to undergoing surgery, you will be evaluated,imaged via MR and CT as per standard protocol. Immediate postoperative CT imaging and a follow-up MRI shall also be done as per standard protocol. Routine follow up visits are required.

What if you consent for the study?

Based on your totally voluntary choice, as per this study, you shall be assessed at appropriate timeframes. This includes preoperative clinical evaluation and imaging analysis. Observations shall be made during surgery such as appearance of tumor,vascularity & presence or absence of calcification. Immediate postoperative evaluation and imaging as well as follow-up evaluation and imaging shall be studied. There will be no interference on your follow up dates for the study. There will be no additional imaging or cost burden to the patient.

What if you do not consent for the study?

Even if you do not consent for this study, you will undergo surgery as usual without any change in the timing or plan of surgery you were supposed to undergo.

Will you have to pay for the investigations?

Imaging investigations required for the purpose of the study are part of routine protocol for the surgery. No added imaging shall be done and there will no additional cost to you. You will need to come only on your usual review date for the study. Routine follow up visits are required.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, people associated with the study, without your additional permission, may review your medical notes.

If you have any further questions, please ask Dr. Biren Khimji Patel, Senior Resident, Department of Neurosurgery, SCTIMST (Ph: 07021805864, Email: birenpatel13@ yahoo.com). For any clarifications regarding the study's ethics clearance you may contact the Member Secretary of the SCTIMST-IEC. The phone number is: 0471- 2524234 and the email id is iec.mem.sec@sctimst.ac.in

Dr Biren Khimji Patel
Principal investigator

രോഗിക്കുള്ള വിവര പത്രിക

"പിനിയൽ റിജിയൻ ട്യൂമറുമൊത്തുള്ള ഒരു ഒറ്റ-സ്ഥാപന അനുഭവം"

അന്വേഷകർ:
മുഖ്യ അന്വേഷകൻ: ബിരേൻ ഖിംജി പട്ടേൽ (ഡോ) എം.എസ്. (ജനറൽ സർജറി) മേൽവിലാസം: സീനിയർ റെസിഡന്റ്, ഡിപാർട്ട്മെന്റ് ഓഫ് ന്യൂറോസർജറി, എസ്.സി.ടി.ഐ.എം.എസ് മെഡിക്കൽ കോളജ് പി.ഒ., തിരുവനന്തപുരം, കേരള, ഇന്ത്യ, പിൻ - 695011
സഹ-മുഖ്യ അന്വേഷകൻ: മാത്യു ഏബ്രഹാം (ഡോ) എം.എസ്. എം.സി.എച്. (ജനറൽ സർജറി), എഫ്.ആർ.സി.എസ്. (എഡിൻ) മേൽവിലാസം: പ്രൊഫസർ & ഹെഡ്, ഡിപാർട്ട്മെന്റ് ഓഫ് ന്യൂറോസർജറി, എസ്.സി.ടി.ഐ.എം.എസ് മെഡിക്കൽ കോളജ് പി.ഒ., തിരുവനന്തപുരം, കേരള, ഇന്ത്യ, പിൻ - 695011

നിങ്ങളുടെ ക്ലിനിക്കൽ ചരിത്രം, പരിശോധന, ഇമേജിംഗ് എന്നിവയിൽ നിന്ന് കരസ്ഥമാക്കിയ ഡാറ്റ വ്യക്തിപരമായി പരിശോധിക്കുകയും ചർച്ച ചെയ്യുകയും ചെയ്ത ശേഷം, നിങ്ങൾ ബുദ്ധിമുട്ടനുഭവിക്കുന്ന രോഗത്തിനായി നിങ്ങൾക്ക് ശസ്ത്രക്രിയ നടത്താൻ പദ്ധതിയിട്ടിരിക്കുകയാണ്. നിങ്ങളുടെ രോഗാവസ്ഥയുടെ ശസ്ത്രക്രിയാ മാനേജ്മെന്റിനുള്ള നിങ്ങളുടെ സന്നദ്ധത നിങ്ങൾ പ്രകടിപ്പിച്ചിട്ടുള്ളതുമാണ്.

പിനിയൽ പ്രദേശം വെല്ലുവിളി ഉയർത്തുന്ന ഒരു ശസ്ത്രക്രിയാ സ്ഥാനമാണ്. ഭാഗികമായി അതിന്റെ കാരണം തലയോട്ടിയ്ക്കുള്ളിലെ എല്ലാ ട്യൂമറുകളിലും 0.5% മുതൽ 1.6% വരെ മാത്രം അടങ്ങുന്നതായി പിനിയേൽ പ്രദേശ നിയോപ്ലാസങ്ങളുടെ അപൂർവ്വതയാണ്. പിനിയേൽ ട്യൂമറുകൾ ഇക്കാലത്ത് പല കേന്ദ്രങ്ങളിലും ശസ്ത്രക്രിയയിലൂടെ ചികിത്സിക്കുന്നുണ്ട്. ഈ പ്രദേശത്തിന്റെ ശസ്ത്രക്രിയാപരമായ സമീപനം വെല്ലുവിളിയുയർത്തുന്നതാണെങ്കിലും, ഈ ശസ്ത്രക്രിയ നല്ല ഫലങ്ങളോടെയും സ്വീകാര്യമായ ശസ്ത്രക്രിയാനന്തര രോഗാതുരതയോടെയും സാക്ഷാത്കരിക്കാനാവുന്നതാണ്, വിശേഷിച്ചും കുട്ടികളും മുതിൽന്നവരുമായ രോഗികളിലെ അപകടകരമല്ലാത്ത ക്ഷതങ്ങളുടെ സാഹചര്യങ്ങളിൽ. പെരി-ഓപ്പറേറ്റീവ് മാനേജ്മെന്റും ഈ ജനതതിയിലെ ക്ലിനിക്കൽ പരിണിതഫലങ്ങളും, അതുപോലെതന്നെ ശസ്ത്രക്രിയാപരമായ സമീപനം പ്രവർത്തന സ്ഥിതിയെ ബാധിക്കുമോ ഇല്ലയോ എന്നും അന്വേഷിക്കുന്നതായ വളരെ കുറച്ചു പഠനങ്ങളെ സാഹിത്യത്തിലുള്ളൂ. അവതരണത്തിലെ ചില അനാട്ടമിക്കലും ക്ലിനിക്കലുമായ സവിശേഷതകളും ശസ്ത്രക്രിയാപരമായ സമീപനവും പ്രവർത്തനപരമായ സ്ഥിതിയുമായി ബന്ധപ്പെട്ടിരുന്നോ ഇല്ലയോ എന്ന് അവതരണത്തിലും ഏറ്റവും സമീപകാലത്തുള്ള തുടരന്വേഷണത്തിലും ഞങ്ങൾ പഠിക്കുന്നതാണ്.

ശസ്ത്രക്രിയയ്ക്കു വിധേയമാകുന്നതിനു മുമ്പ്, നിങ്ങളെ വിലയിരുത്തുന്നതും, മാനക പ്രോട്ടോകോൾ അനുസരിച്ച് എ.ആർ., സി.ടി. എന്നിവ വഴിയായി ഇമേജ് ചെയ്യുന്നതുമാണ്. ശസ്ത്രക്രിയാനന്തരം ഉടനടി നടത്തുന്ന സി.ടി. ഇമേജിംഗും ഒരു തുടരന്വേഷണ എം.ആർ.ഐ.യും കൂടി മാനക പ്രോട്ടോകോൾ അനുസരിച്ച് നടത്തുന്നതാണ്. പതിവ് തുടരന്വേഷണ സന്ദർശനങ്ങൾ ആവശ്യമാണ്.

പഠനത്തിന് നിങ്ങൾ സമ്മതിക്കുകയാണെങ്കിൽ എന്തൊക്കെയാണ് സംഭവിക്കുന്നത്?

പൂർണ്ണമായും സ്വമേധയാലുള്ള നിങ്ങളുടെ തെരഞ്ഞെടുപ്പിന്റെ അടിസ്ഥാനത്തിൽ, ഈ പഠനം അനുസരിച്ച്, അനുയോജ്യമായ സമയങ്ങളിൽ നിങ്ങളെ വിലയിരുത്തുന്നതാണ്. ഇതിൽ ശസ്ത്രക്രിയാപൂർവ്വ ക്ലിനിക്കൽ മൂല്യനിർണ്ണയവും ഇമേജിംഗ് വിശകലനവും ഉൾപ്പെടുന്നു. ശസ്ത്രക്രിയാ വേളയിൽ ട്യൂമറിന്റെ പ്രത്യക്ഷത, വാസ്കുലാരിറ്റി, കാൽസിഫിക്കേഷന്റെ സാന്നിദ്ധ്യം അല്ലെങ്കിൽ അസാന്നിദ്ധ്യം എന്നിവ നിരീക്ഷിക്കുന്നതാണ്. ശസ്ത്രക്രിയാനന്തരം ഉടനടി നടത്തുന്ന മൂല്യനിർണയവും ഇമേജിംഗും അതുപോലെതന്നെ തുടരന്വേഷണ മൂല്യനിർണയവും ഇമേജിംഗും പഠിക്കുന്നതാണ്. പഠനത്തിനായുള്ള നിങ്ങളുടെ തുടരന്വേഷണ തീയതികളിൽ ഇടപെടലുകളൊന്നും ഉണ്ടായിരിക്കുന്നതല്ല. അധിക ഇമേജിംഗ് അല്ലെങ്കിൽ രോഗിക്ക് ചെലവ് ഭാരം ഉണ്ടായിരിക്കുന്നതല്ല.

പഠനത്തിന് നിങ്ങൾ സമ്മതിക്കുന്നില്ലെങ്കിൽ എന്തൊക്കെയാണ് സംഭവിക്കുന്നത്?

ഈ പഠനത്തിന് നിങ്ങൾ സമ്മതിച്ചില്ലെങ്കിൽ പോലും, നിങ്ങൾ വിധേയമാകുമെന്ന് പ്രതീക്ഷിക്കപ്പെട്ടിരിക്കുന്ന ശസ്ത്രക്രിയയ്ക്ക് അതിന്റെ സമയത്തിലോ പദ്ധതിയിലോ ഒരു വ്യത്യാസവും കൂടാതെ സാധാരണഗതിയിൽ നിങ്ങൾ വിധേയമാകുന്നതാണ്.

പരിശോധനകൾക്ക് നിങ്ങൾ പണമടയ്ക്കേണ്ട ആവശ്യമുണ്ടോ?

പഠനത്തിന്റെ ഉദ്ദേശ്യത്തിനായി ആവശ്യമായിരിക്കുന്ന ഇമേജിംഗ് പരിശോധനകൾ ശസ്ത്രക്രിയയുടെ പതിവ് പ്രോട്ടോകോളിന്റെ ഭാഗമാണ്. കൂടുതൽ ഇമേജിംഗ് ഒന്നും നടത്തുന്നതല്ല, നിങ്ങൾ അതിനായി കൂടുതലൊന്നും ചെലവാക്കേണ്ടതുമില്ല. പഠനത്തിനായി നിങ്ങൾ നിങ്ങളുടെ പതിവ് അവലോകന തീയതിയിൽ മാത്രം വന്നാൽ മതിയാകും. പതിവ് തുടരന്വേഷണ സന്ദർശനങ്ങൾ ആവശ്യമാണ്.

പരിശോധനകൾക്ക് നിങ്ങൾ പണമടയ്ക്കേണ്ട ആവശ്യമുണ്ടോ?

പഠനത്തിന്റെ ഉദ്ദേശ്യത്തിനായി ആവശ്യമായിരിക്കുന്ന ഇമേജിംഗ് പരിശോധനകൾ ശസ്ത്രക്രിയയുടെ പതിവ് പ്രോട്ടോകോളിന്റെ ഭാഗമാണ്. കൂടുതൽ ഇമേജിംഗ് ഒന്നും നടത്തുന്നതല്ല, നിങ്ങൾ അതിനായി കൂടുതലൊന്നും ചെലവാക്കേണ്ടതുമില്ല. പഠനത്തിനായി നിങ്ങൾ നിങ്ങളുടെ പതിവ് അവലോകന തീയതിയിൽ മാത്രം വന്നാൽ മതിയാകും. പതിവ് തുടരന്വേഷണ സന്ദർശനങ്ങൾ ആവശ്യമാണ്.

നിങ്ങളുടെ വ്യക്തിപരമായ വിവരങ്ങൾ രഹസ്യാത്മകമായി സൂക്ഷിക്കുമോ?

ഈ പഠനത്തിന്റെ ഫലങ്ങൾ ഒരു മെഡിക്കൽ ജേർണലിൽ പ്രസിദ്ധീകരിക്കുന്നതാണ്, എന്നാൽ ഏതെങ്കിലും പ്രസിദ്ധീകരണത്തിലോ ഫലങ്ങളുടെ അവതരണത്തിലോ നിങ്ങളെ നിങ്ങളുടെ പേരിനാൽ തിരിച്ചറിയുന്നതല്ല. എന്നിരുന്നാലും പഠനവുമായി ബന്ധപ്പെട്ട ആളുകൾ, നിങ്ങളുടെ അധിക അനുവാദം കൂടാതെ, നിങ്ങളുടെ മെഡിക്കൽ കുറിപ്പുകൾ അവലോകനം ചെയ്തേക്കാവുന്നതാണ്.

നിങ്ങൾക്ക് കൂടുതൽ എന്തെങ്കിലും ചോദ്യങ്ങളുണ്ടെങ്കിൽ, ദയവായി ഡോ. ബിരേൻ ഖിംജി പട്ടേൽ, സീനിയർ റെസിഡന്റ്, ഡിപാർട്ട്മെന്റ് ഓഫ് ന്യൂറോസർജറി, എസ്.സി.ടി.ഐ.എം.എസ്.ടി. (ഫോ: 07021805864, ഇമെയിൽ: birenpatel13@ yahoo.com) നോട് ചോദിക്കുക. പഠനത്തിന്റെ എത്തിക്സ് ക്ലിയറൻസ് സംബന്ധിച്ച ഏത് സ്പഷ്ടീകരണങ്ങൾക്കും നിങ്ങൾക്ക് എസ്.സി.ടി.ഐ.എം.എസ്.ടി.-ഐ.ഇ.സി.യുടെ മെംബർ സെക്രട്ടറിയെ ബന്ധപ്പെടാവുന്നതാണ്. ഫോൺ നമ്പർ: 0471 – 2524234; ഇമെയിൽ ഐ.ഡി.: iec.mem.sec@sctimst.ac.in

ഡോ. ബിരേൻ ഖിംജി പട്ടേൽ
മുഖ്യ അന്വേഷകൻ

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
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Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1310/DECEMBER-2018 16.03.2019

Dr. Patel Biren
Senior Resident
Department of Neurosurgery
SCTIMST, Thiruvananthapuram

Dear Dr. Patel Biren,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "A SINGLE-INSTITUTION EXPERIENCE WITH PINEAL REGION TUMORS (IEC/1310)" on 15th December, 2018.

The following documents were reviewed:

Original submission

1. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 26.09.2018 with checklist*
2. *Forwarding letter from the HOD*
3. *TAC Approval Letter*
4. *IEC Application Form*
5. *Project Proposal*
6. *Proforma*
7. *Patient Information Sheet and Informed Consent Form in English and Malayalam*
8. *CV of Principal Investigator and Co- Principal Investigators*

Revised submission

1. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 08.03.2019 with checklist*
2. *Forwarding letter from the HOD*
3. *TAC Approval Letter*
4. *IEC Application Form*
5. *Project Proposal*
6. *Proforma*
7. *Patient Information Sheet and Informed Consent Form in English*
8. *Modified Patient Information Sheet and Informed Consent Form in Malayalam*
9. *CV of Principal Investigator and Co- Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 15th December, 2018 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
3.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
4.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
5.	Dr. Harikrishna Varma PR	Ph.D(Materials Science)	Male	Medical Technology	Yes
6.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
7.	Dr. S S Giri Sankar	LL.M. Ph.D.	Male	Legal Expert	No
8.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
9.	Dr. P. Manickam	BSMS, MSc (Epid).,PhD	Male	Health Science Expert/ Social Scientist	No
10.	Mr. Satheesh Chandran	MSW, PGDPM	Male	Lay person/ NGO/ Social Scientist	No
11.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
12.	Dr. Anand Kumar A	MD, DM	Male	Clinician	No
13.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
14.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

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SYNOPSIS Pineal region tumors are rare, technically challenging lesions accounting for 0.5- 1.6% of all intracranial tumors. There is paucity of large series in world literature as well in the Indian context with regards to surgical experience in this critical anatomical zone.Objective of this study was to analyse the clinical presentation, and surgical outcome of patients with pineal region lesions operated over a period of 8 years in our centre.Study population was 106 consecutive patients operated for pineal regions lesions.

Retrospective analysis was done for 76 patients while 30 patients were studied prospectively. We studied various patient related & tumor related factors & analysed their effect on the clinical outcome of patients. Our study included factors like clinical presentation , Karnofsky Performance Scale (KPS) score on admission, discharge and after 3 months of surgery, tumor volume, presence of hydrocephalus & its management, surgical approach, tumor characteristics, tumor pathology, intra-operative & post-operative complications, extent of resection confirmed 3 months after surgery by MRI imaging, duration of intensive care and hospital stay & need for adjuvant therapy.

Modfi Popp'spach motny elyedroach surgical treatment of pineal region tumors i.e. in 89 patients (83.96%).Gross total or near total resection as per post operative imaging was achieved in 98 patients (92.45 %). An inverse relationship was noticed with age, ICU stay & total hospital length of stay to the KPS score on admission. However, difference was not statistically significant. Significant improvement of the KPS score on discharge & at 3 months of follow up compared to KPS score on admission was noted. On 3 month follow-up, 14 patients (13.2%) had residual lesion & adjuvant therapy was given to 30 patients (28.3%).

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