

“Utility Of Extended Endoscopic Endonasal Approaches To Maximize The Resection Of Giant Pituitary Adenoma”



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DECLARATION

This thesis titled "Utility Of Extended Endoscopic Endonasal Approaches To Maximize The Resection Of Giant Pituitary Adenoma" is a consolidated report based on a bonafide study of the period from 1st January 2021 to 31st July 2021, done by me under the Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

This thesis is submitted to SCTIMST in fulfilment of rules and regulations of post doctoral fellowship in Neurosurgery



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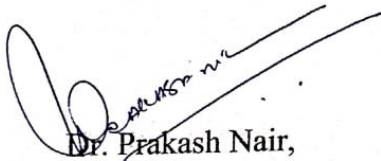
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CERTIFICATE

This is to certify that the thesis entitled - "Utility Of Extended Endoscopic Endonasal Approaches To Maximize The Resection Of Giant Pituitary Adenoma" 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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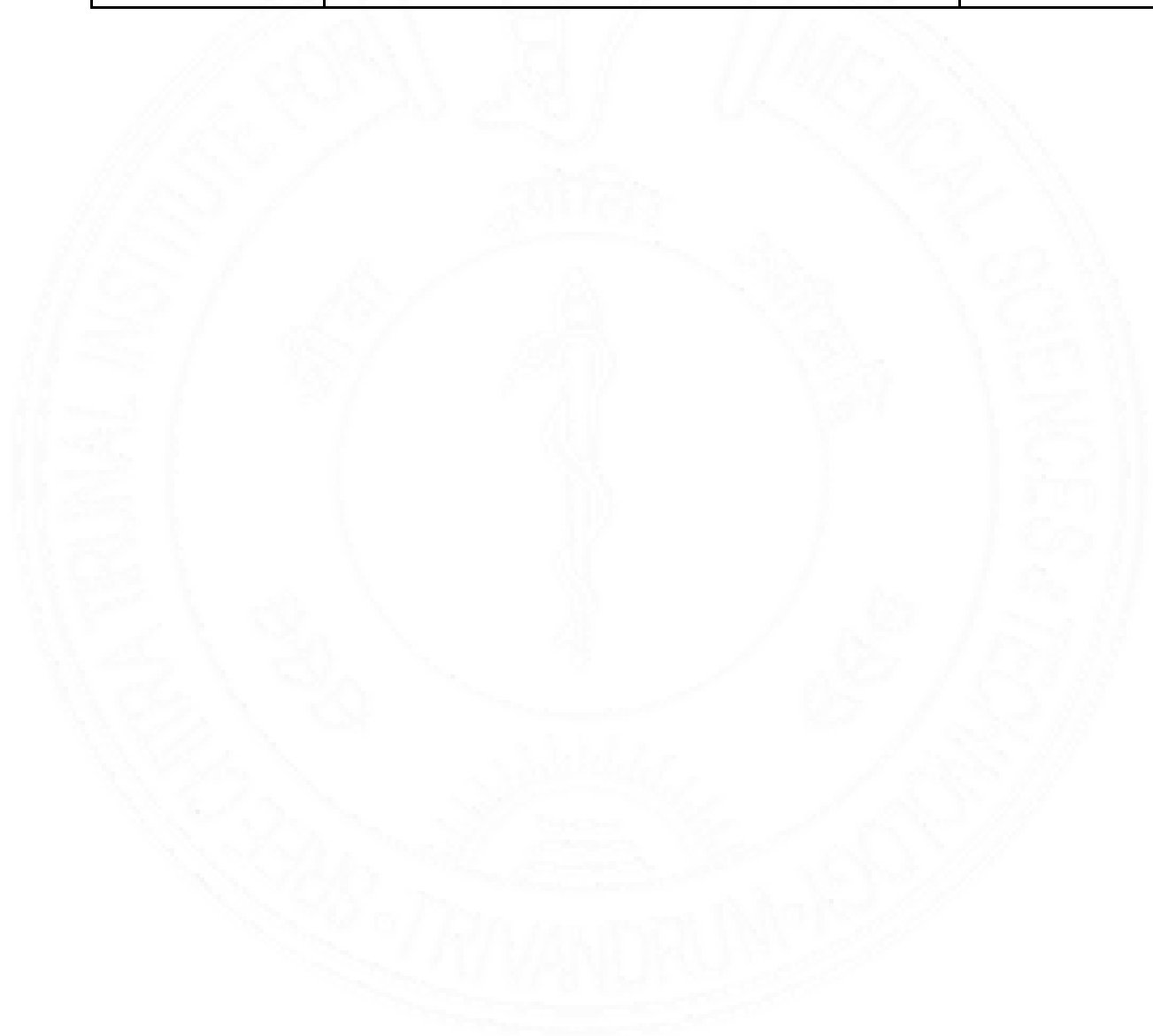
I am very grateful to my family; especially my wife Dr. Asmita and my parents for their constant moral support and help for my every academic activities

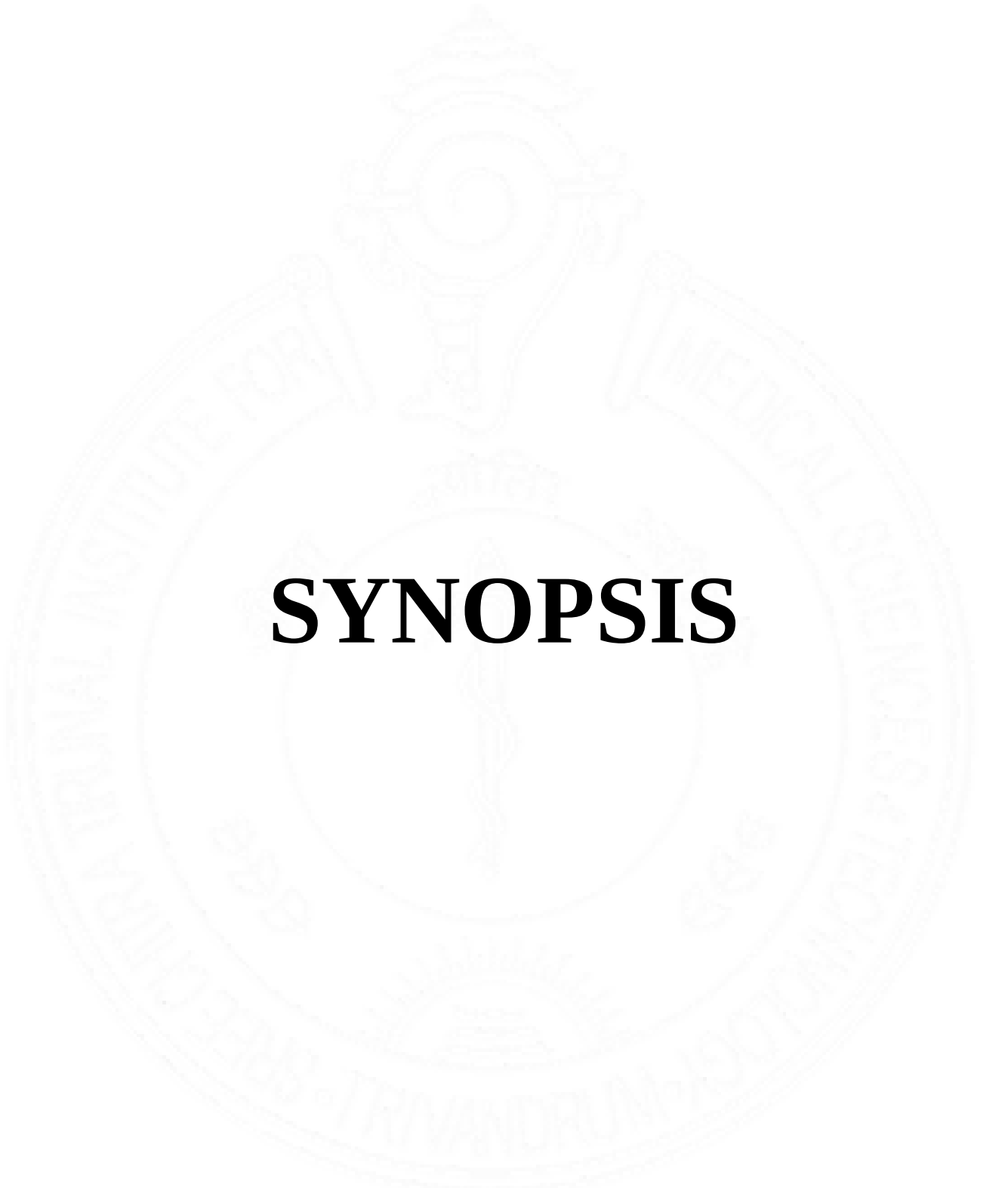
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TABLE CONTENTS

SL. No	TITLE	PAGE NO.
1	Synopsis	7
2	Introduction	9
3	Review of literature	11
4	Aims & Objectives	18
5	Materials And Methods	20
6	Results	22
7	Discussion	30
8	Conclusions	38
9	Bibliography	40

10	Annexure: - Patient proforma - Institutional Ethics Committee Clearance letter	47 51
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SYNOPSIS

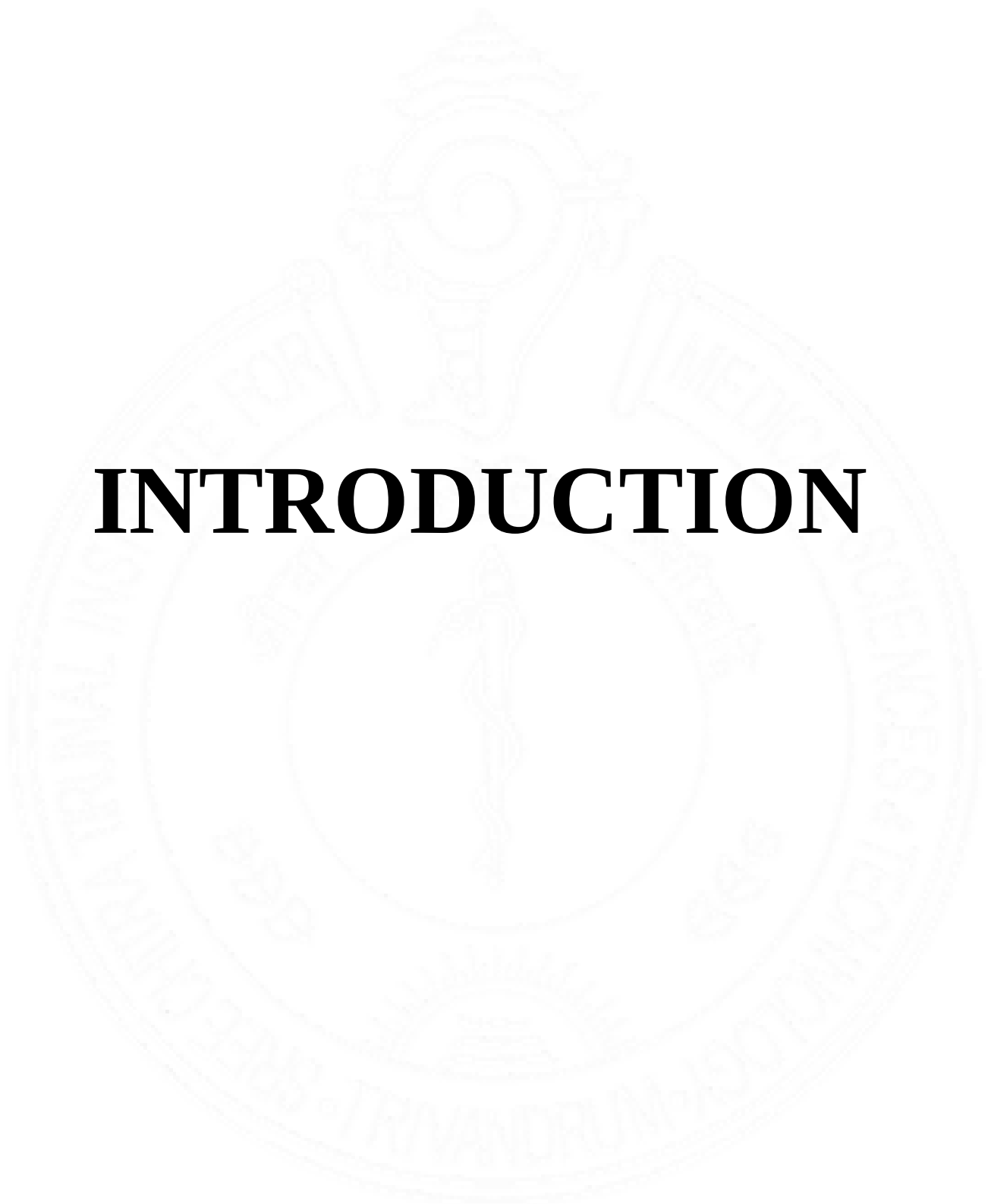
SYNOPSIS

Giant pituitary adenomas are technically challenging lesions that invade multiple vital parasellar and suprasellar structures. 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 particularly with endonasal endoscopic approach.

Objective of this study was to assess the surgical and clinical outcome of using multiple endoscopic endonasal corridors for the resection of giant pituitary adenomas (GPA) and study various factors that limit tumor resection.

A retrospective study of all GPA (defined as minimum diameter > 3 cm and tumor volume > 10 cm³), operated via the endoscopic endonasal approach between January 2015 and December 2020 was performed. The volumetric extent of resection (3D volumetric analysis software) was correlated with various demographic, tumor related, pathological, immunohistochemical factors and its impact on clinical outcome was studied. The study included 106 cases of GPA, out of which, volumetric analysis was performed in 85 patients. The mean extent of resection volume was 79.18 ± 21.75 cm³. Statistically significant tumor related factors affecting the extent of resection were found to be pre-operative tumor volume ($p=0.011$) and Knosp grade ($p=0.022$). The percentage increase in the extent of resection with use of 2 endonasal corridors was 10.6% and with 3 corridors was 14%. Visual improvement was seen in 82% cases and new onset hormonal insufficiency was seen in 2.9% cases. Mortality directly related to surgery was seen in 1.8% cases. We conclude that extended endoscopic endonasal approaches can safely and effectively be used for the gross total resection of giant pituitary adenoma. However, we found that preoperative tumor volume and Knosp grade 3 were significant factors affecting the extent of resection. The utilization of multiple endoscopic endonasal corridors can increase the volumetric extent of tumor resection in giant pituitary adenomas.

INTRODUCTION



INTRODUCTION

Giant pituitary adenomas (GPA) are known to be a challenging group of tumors that constitute about 5% of pituitary neoplasms.¹ Large size, aggressive behaviour, multicompartmental extension, high prevalence of neuroophthalmological deficits, poor response to surgical excision and adjuvant therapy, proximity to vital anatomical structures, high residual and recurrence rate made this tumor a separate entity to counter.^{2,3,4} Traditionally, open craniotomy approaches that need brain retraction and microscopic transsphenoidal approach have been used with suboptimal results.^{5,6,7,8} The evolution of extended endoscopic endonasal approaches (EEA) to tackle these formidable tumors have occurred in the last two decades owing to better illumination, superior image quality, panoramic visualisation, angled endoscopes, image guidance, specialized instruments and better skull base reconstruction techniques.^{9,10,11} However, safety and efficacy of EEA to giant pituitary adenomas have been described by limited studies.¹²⁻²⁴ Factors like tumor pathology, tumor behaviour, invasion and extension of giant pituitary adenoma to surrounding structures also affect the extent of resection and overall prognosis of patient.

The present study is an attempt to consolidate all the demographic factors, various morphological characters of tumor, tumor pathology and correlate them with the extent of resection of giant pituitary adenomas and to assess the ultimate visual and hormonal outcome of the patient.

REVIEW OF LITERATURE



REVIEW OF LITERATURE

Pituitary adenomas accounts for about 7% to 17% of all the intracranial tumors, and are the third commonest primary intracranial tumors after gliomas and meningiomas. These tumors are mostly benign, remaining limited to the sella and diaphragm and produce symptoms due to hormonal secretion, hypopituitarism, local mass effect, or a combination of these. A significant proportion of pituitary adenomas may grow unpredictably and spread to the extrasellar compartments reaching giant size.²⁵

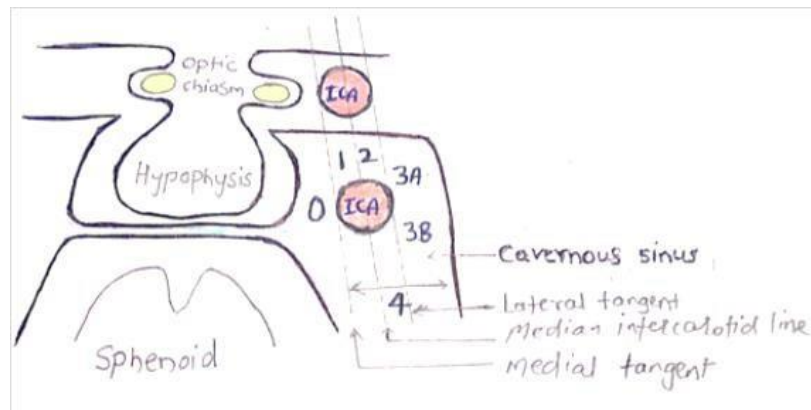
There is still ambiguity in the definition and a clear-cut point of size that is able to define a giant pituitary adenoma. There are no distinct histologic features, rigid criterion is lacking and the description of what constitutes a giant pituitary adenoma has been somewhat variable. Symon and Jakubowski termed giant adenomas as those with extension of more than 40mm above the planum sphenoidale in any direction (essentially 40mm or more of suprasellar extension) or less than 6-mm distance from the highest point of the tumor to the foramen of Monro or multidirectional spread with lobules extending to the suprasellar region in more than 2 directions. This has been the most accepted definition since then.^{26,27} Garibi et al has selected tumors more than 30-mm diameter as giant and according to them, tumors with Hardy grade D should be considered as GPAs.²⁸

Giant pituitary adenoma generally extends posteriorly towards dorsum sella and then towards clivus, anteriorly over tuberculum sella and planum, laterally into the cavernous sinus invading internal cerebral artery and sometimes abuts the temporal lobe, superiorly in the suprasellar cistern and then inside the third ventricle.¹⁷

The tumour are classified based on standard classification systems which are used internationally:

1) Knosp grading²⁹: for tumors extending into cavernous sinus

Grade 0	Medial to medial tangent
Grade 1	Tumor extends to space between the medial tangent and the intercarotid line
Grade 2	Tumor extends to space between the intercarotid line and the lateral tangent
Grade 3	Tumor extends lateral to the lateral tangent
3A	Above the intracavernous ICA into the superior cavernous sinus compartment
3B	Below the intracavernous ICA into the inferior cavernous sinus compartment
Grade 4	Complete encasement of intracavernous ICA



2) Yasargil classification³⁰: for local and loco regional extension

1	Suprasellar-suprachiasmatic: tumors that grow more than 2 cm above the planum sphenoidale and in front of the chiasm
2	Suprasellar-retrosellar: tumors that extend into the interpenduncular cisterns
3	Parasellar-cavernous: tumors that extend into the cavernous sinuses
4	Paninvasive: tumors that extend in all directions

3) Modified Hardy classification⁶: for suprasellar and extrasellar extension

A	Extension into chiasmatic cisterns
B	Extension into the third ventricle
C	3 cm of extension into the third ventricle
D	>3 cm of extension beyond the foramen of Monroe, each with at least 2 cm of extension superior to the jugum sphenoidale
E	Extradural spread (extension into or out of the cavernous sinus)

The division of the giant tumors into tumors having predominant suprasellar extension and tumors having multicompartmental extension has important therapeutic implications, as the former tumors are more amenable to decompression by transsphenoidal route. ²⁵

Although this type of pituitary tumor is rarely malignant or rapid growing, they often present a neurosurgical challenge because of the enormous tumor size and neighbouring critical structures. In many cases, lateral invasion of cavernous sinuses, downward erosion into the sphenoid sinus, and upward suprasellar extension are often obvious on diagnosis.¹⁵

Midline structures surrounding the sella turcica are frequently displaced or eroded and thus pose difficulty when complete resection is attempted. In recent years, there has been an emerging popular technique of endoscopic transnasal transsphenoidal surgery for pituitary adenomas. The most advantageous features of adapting ETTS are the panoramic views through the angled endoscopes.¹⁵ The large dimension of those tumors and their proximity to important neurovascular structures in the skull base justify, partially, the low rates of gross total resection, that is inferior to 50% in some previous studies. Surgical resection is the main treatment option for giant pituitary adenomas. The main objectives in those cases are to achieve maximal tumor resection, improve visual function and other neurological deficits and to preserve the hormonal function of the normal pituitary gland.¹⁶

A favourable outcome of surgery in these lesions is proposed as the resolution of mass effect and reverse of hormonal dysfunction. Historically, standard microscopic transsphenoidal, transcranial, or combined transcranial-transsphenoidal approaches were used for surgical decompression. The narrow corridor of microscopic transsphenoidal approaches limits suprasellar and parasellar visualization. Transcranial and combined approaches are associated with higher risk of panhypopituitarism and vascular and optic nerve injury caused by brain retraction. Regarding the limitations, the rate of GTR in reported series of microsurgical approaches in giant macroadenomas has been reported to be <50%.

Recently, the extended endoscopic transsphenoidal approach has been widely used for resection of pituitary adenomas. Wide angled endoscopic views provide better visualization and make the surgeon capable of tumor resection in various directions

under direct visual control, consequently improving the rate of total tumor resection. Although limited data have been reported on the surgical outcome of endoscopic resection of large and giant macroadenomas, reports show promising results.²³

The tumor volume of pituitary adenomas has classically been determined using 2-dimensional (2D) methods based on measuring the largest tumor diameters in the axial, transverse, and sagittal planes. This has been challenged by more recent studies using three-dimensional (3D) methods. These 3D methods have demonstrated that the 2D methods do not precisely reflect the true volume of these tumors.²² Also, Hofstetter et al., demonstrated that the correlation between the diameter-based (2D) and volume-based (3D) thresholds diverges at greater tumor volumes.¹⁴

Such discrepancies between the calculated and measured volumes can be explained, at least in part, by the often irregular shape and differential vectors of growth around the epicenter of these tumors. In addition, it is not clearly known whether pituitary tumors grow equally in all 3 planes or are more prone to grow in 1 particular plane over another, depending on the surrounding anatomy. The inaccuracy of the ellipsoid method for calculating the tumor volume has proved critical regarding the EOR of large and giant pituitary adenomas. The tumor volume has been found by many investigators to be an important determinant of the EOR, with a larger tumor volume associated with a lesser degree of resection. The use of a uniform method to define large and giant pituitary tumors would be indispensable for decision making as tumor factors other than the volume have also been found to influence the EOR.²²

Koutourousiou et al. reported that the resection rate was significantly different for different tumor configurations. The GTR rates were 46.7%, 33.3%, and 6.1% for rounded, dumbbell-shaped, and multilobular adenomas, respectively.¹⁵

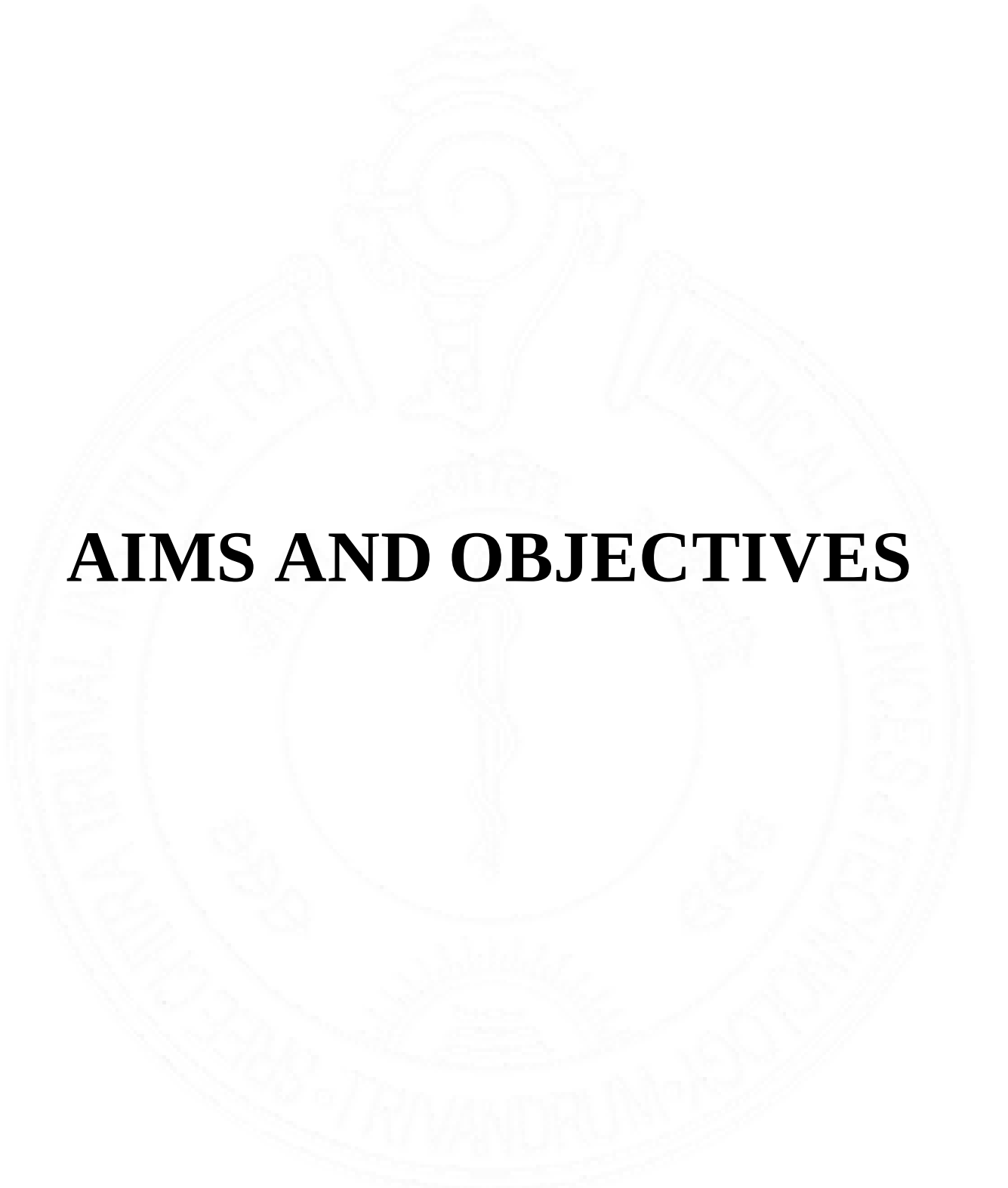
Chohan et al., found that CS invasion was found to be the most significant predictor of the EOR.²⁰ In a previous report by Hofstetter et al., the GTR rate was 92.0% versus 38.1% for adenomas without and with CS invasion, respectively.³⁰

Similarly, Chabot et al. reported the Knosp grade was significantly related to the degree of resection, with lower Knosp grades more likely to be associated with GTR.¹⁸ In their analysis, the correlation held true when analyzing the Knosp grades individually and in groups. Azab et al demonstrated that a soft consistency is a statistically significant predictor of GTR.²²

The complications related to surgery on giant pituitary adenoma are less commonly seen with the less invasive transsphenoidal approach as compared with the transcranial approaches. The reports of high surgical mortality in these tumors have been attributed to the breach of subarachnoid spaces usually above the diaphragma sella into the chiasmatic cistern, ischemia of the hypothalamus, brainstem or cerebral hemispheres due to small or large vessel traction and subtotal resection of the tumor leading to infarction and edema of the residual tumor, (postoperative pituitary apoplexy) causing compression of vital structures or acute obstructive hydrocephalus.

The mortality in our series was 11.8%.

The surgical outcome in GPAs remains poor when compared with the usual pituitary adenomas, with mortality ranging from 4.2% to 18% One of the leading causes of postoperative death is apoplexy of the residual adenoma.²⁵



AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

To study extent of resection, visual and endocrinological improvement in patients operated for giant pituitary adenoma using multiple extended endonasal corridors.

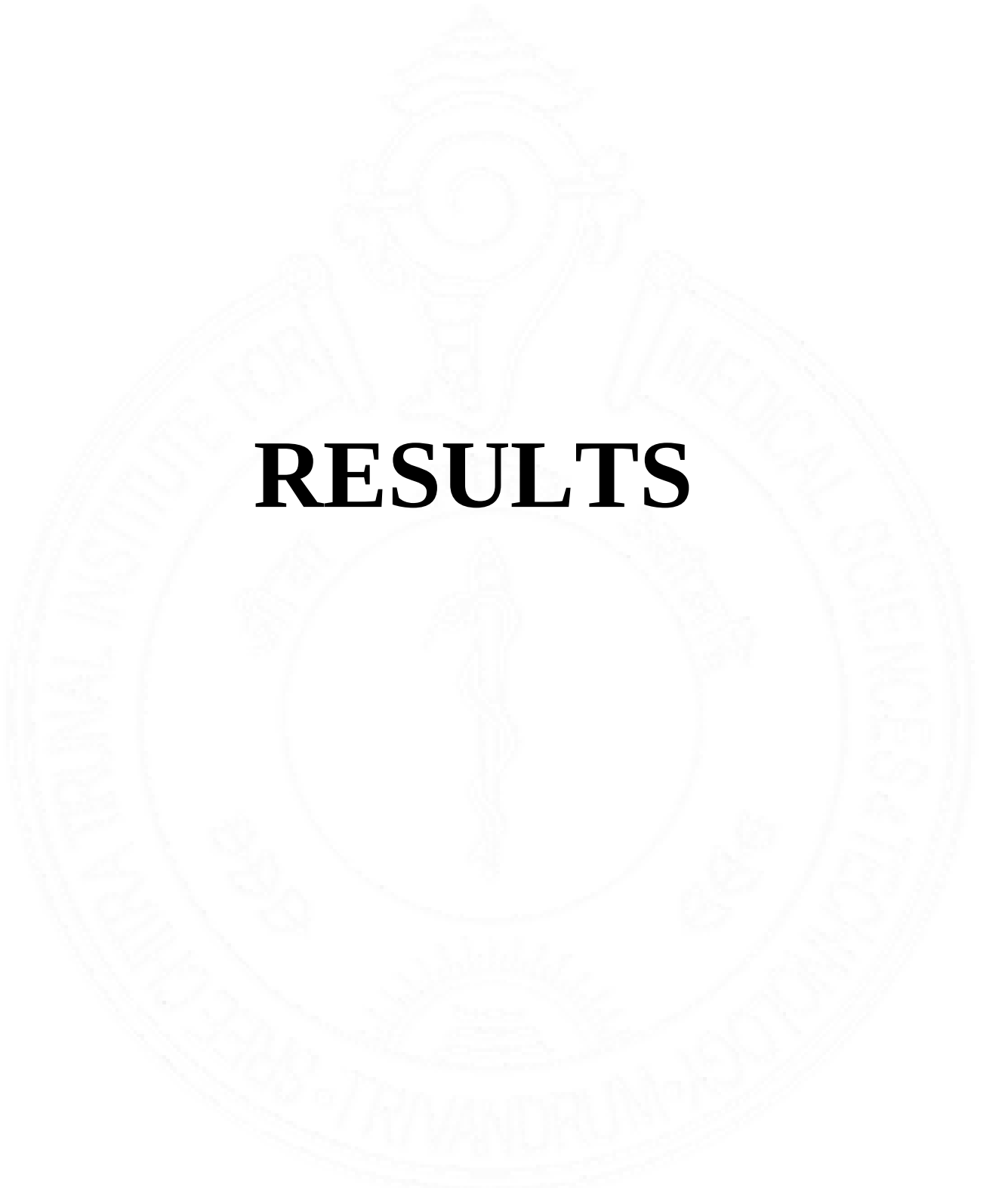




METHODOLOGY

METHODOLOGY

A retrospective study was carried out to review all the consecutive cases of pituitary adenoma that had a minimum diameter of more than 3 cm and total volume more than 10 cm³ on pre-operative MRI between January 2015 and December 2020. The volumetric extent of resection (3D volumetric analysis software) that was done in 85 patients was correlated with various demographic, tumor related, pathological, immunohistochemical factors and its impact on clinical outcome was studied. Quantitative variables were measured using mean and standard deviation. Categorical variables were measured and expressed using proportion and percentages. The student's t-test was used to compare the means of two groups. ANOVA was used to compare the means of variables with more than two groups. Chi-square test was used to examine the difference between categorical variables. The Pearson correlation coefficient was used to understand the linear relationship between two continuous variables. A p-value of 0.05 was considered as significant. Data was collected using a structured proforma and entered in Microsoft Excel and was analysed using the statistical software SPSS Version 22.0. Patient consent was not required for retrospective study as per our institutional policy.



RESULTS

RESULTS

A total of 243 patients underwent EEA for PA in the study period (December 2015-2020). Of these, 106 patients had PA measuring more than 3 cm in the minimum dimension. In the study population, 61(57.5 %) were male and 45(42.4 %) were females. The mean age at presentation was 43.1 ± 12.7 years (range 8 -71 years). Average maximum dimension of the PA on MR Imaging was 4.1 ± 0.85 cm (range 3-7.7 cm).

Table 1: Correlation of demographic characteristics with extent of resection

	Grade I resection (>90% volume) (n=33)	Grade II & III resection (<90% volume) (n=52)	p value
Age	42.39	42.21	0.557
Sex:			
- Male	17 (51.5%)	28 (53.8%)	0.957
- Female	16 (48.5%)	24 (46.1%)	
Time from onset of symptoms till surgery (months)	9.64	23.03	0.456
Type of Tumour			
- First surgery	27 (81.8%)	37 (71.1%)	0.828
- Re-operation	6 (18.2%)	15 (28.9%)	

Post-operative length of stay (days)	13.57 +/- 7.3	13.09 +/- 9.9	0.198

Clinical presentation:

Visual deterioration was the commonest presentation seen in all 106 (100%) patients, other complaints at presentation included headache in 58 (54.7%), hormonal disturbances in 24 (22.64%) and cranial nerve deficit in 3(2.8%) patients. The mean average time from the onset of symptoms till surgery was 16.17 ± 25.82 months (6 days to 6 months). The average follow-up period was 20.6 months (1-58 months). One patient was lost to follow up.

Primary tumor resection was performed in 83 (78.3%) patients and the other 23 (21.7%) were re-surgeries. Prior procedures included 10 patients who had undergone tumor excision by an endoscopic endonasal route, 8 patients by transcranial route, 4 patients by transnasal microscopic route and one patient by sublabial rhinoseptal route with endoscopic assistance. **(Table 1).**

Table 2: Correlation of tumor characteristics with extent of resection group:

	Grade I resection (>90% volume) (n=33)	Grade II & III resection (<90% volume) (n=52)	p value
Tumor size (maximum width in cm)	4.09+/- 0.73	4.18 +/- 0.84	0.954
Pre-operative tumor volume (cm ³)	16.32+/- 6.74	21.53 +/- 12.9	0.011
Knosp score			
- Grade 0	1 (3.0%)	1(1.9%)	0.022
- Grade 1	8 (24.2%)	11 (21.1%)	
- Grade 2	10 (30.3%)	8(15.3%)	
- Grade 3	7 (21.2%)	4 (7.7%)	
- Grade 4	7 (21.2%)	28 (53.8%)	
Tumor shape			
- Rounded	3 (9.1%)	4 (7.7%)	0.688
- Dumbbell shaped	13 (39.4%)	20 (38.5%)	0.841
- Multilobular	17 (51.5%)	28 (53.8%)	0.976
Tumor extension			
- Sphenoid sinus	20 (60.6%)	29 (55.8%)	0.74
- Suprasellar	33 (100%)	52 (100%)	
- Frontal lobe	3 (9.1%)	3 (5.8%)	
- Temporal lobe	7 (21.2%)	13 (25.5%)	
- Posterior fossa	0 (0.0%)	1 (1.9%)	
- Clivus	6 (18.2%)	11 (21.2%)	
- Orbit	0 (0.0%)	1 (1.9%)	
- Cavernous sinus	32 (96.9 %)	51 (98 %)	
Tumor consistency			
- Soft	27 (81.9%)	44 (84.6%)	0.434
- Firm	2 (6 %)	5 (9.6%)	0.698
- Mixed	4 (12.1%)	3 (5.8%)	0.207
Surgical Corridor used			
- Trans-sellar	33 (100%)	52 (100%)	0.228
- Transplanum	3 (9.1%)	3 (5.8%)	
- Transclival	1 (3.0%)	1 (1.9%)	
- Transtuberculum	5 (15.1%)	7 (13.5%)	
- Transpterygoid	2 (6.1%)	0	

Tumor volume:

Volumetric analysis (3D) was performed in 85 cases in whom complete set of imaging sequences were available. The total average pre-operative tumor volume in these 85 cases was $19.51 \pm 11.3 \text{ cm}^3$ ($10.16 - 65.1 \text{ cm}^3$) and post-operative tumor volume was $4.76 \pm 7.50 \text{ cm}^3$ ($0 - 53.75 \text{ cm}^3$). The mean extent of resection was $79.18 \pm 21.75 \text{ cm}^3$ ($17.4 - 100 \text{ cm}^3$). Pre-operative tumor volume ($p=0.011$) was found to be statistically significant factor affecting the extent of resection

Factors affecting resection:

Based on the volumetric analysis, Extent of resection was categorized as Grade 1 where more than 90% tumor volume resection was achieved, Grade 2 where less than 90 % but more than 50% tumor volume resection was achieved and Grade 3 where less than 50% tumor resection was achieved.

Grade 1 resection was seen in 33(38.82 %) patients, Grade 2 resection was seen in 41 (48.23 %) patients and Grade 3 resection was seen in 11(12.94 %) patients. Extent of resection was found to be 100 % in 22 (25.9%) patients. **(Table 2).**

Implication of height from tuberculum:

The maximum height of tumor from the tuberculum sellae was calculated in 82 cases. It was 1.59 ± 0.7 cm in the Grade 1 resection and 1.43 ± 0.7 cm in the Grade 2 & 3 resection group. No statistical significance was found between the maximum height of tumor and the extent of resection.

Implication of invasion into adjacent areas:

Out of 85 cases with volumetric analysis, tumor extension into adjacent regions occurred into the 1) Sphenoid sinus in 49 (57.64%), 2) Suprasellar in 85 (100%), 3) Frontal lobe in 6 (7.05%), 4) Temporal lobe in 20 (23.5%), 5) Posterior fossa in 14 (16.5%) 6) Clivus in 17 (20%) & 7) orbit in 1 (1.2%) patient.

The cavernous sinus was invasion in 99.05% patients. The Knosp grade was 0 in 2 (2.35%) patient, grade 1 in 19 (22.3%) patients, grade 2 in 18 (21.2 %) patients, grade 3 in 11 (12.9%) patients and grade 4 in 35 (41.2%) patients (Table 2).

Patients with a higher grade of cavernous sinus invasion (Knosp Grade 3 and 4) had a lesser extent of resection when compared to patients with lower grade of cavernous sinus invasion (Knosp 0-2) ($p=0.022$).

Implication of shape:

The tumor was classified as dumbbell shaped, rounded and multilobulated. No statistically significant association was seen with the extent of resection and shape.

Implication of using multiple corridors:

Additional surgical corridors apart from transsellar corridor were used in 22 (25.9%) out of 85 cases. Trans-tuberculum corridor was used in 16 cases and in addition transplanum was used in 6 cases, transclival in 2 cases, transpterygoid in 2 cases and transmaxillary in one case. The mean extent of resection volume with the use of single corridor was 76%, with use of 2 corridors was 85.3% and with the use of three corridors was 88%. The result signifies that the use of multiple corridors increases the volume of resection (**Table 2**).

Table 3: Correlation of tumor pathology and immunohistochemical characteristics with the extent of resection groups

	Grade I resection (>90% volume) (n=33)	Grade II & III resection (<90% volume) (n=52)	p value
Cell type:			
- Gonadotroph	7 (21.2%)	18 (34.6%)	0.364
- Corticotroph	11 (33.3%)	12 (23.1%)	0.652
- Lactotroph	1 (3.0%)	1 (1.9%)	0.660
- Null cell adenoma	0	6 (11.5%)	-
- Pit-1 pleurohormonal	1(3.0%)	1 (1.9%)	-
- Oncocytic	0	0	-
- Somatotroph	3 (9.1%)	1 (1.9%)	0.089
- Crooke cell adenoma	0	1 (1.9%)	-
- Unknown	6 (18.2%)	6 (11.5%)	0.250
- Pleurohormonal	4 (12.1%)	5 (9.6%)	0.544
- Mammosomatotroph	0	1 (1.9%)	-
MIB-1 index			
<3	6 (20%)	14 (27%)	0.571
>= 3	22 (66.7%)	30 (57.7%)	0.443
Unknown	5 (13.3%)	8 (15.4%)	0.711
Invasiveness			0.793
- Invasive	14(42.2%)	24 (46.1%)	
- Non-invasive	19 (57.6%)	28 (53.8%)	
Cam 5.2	8	20	0.164
P53	4	5	0.727

Histopathological Outcome:

Out of 106 total cases, non-invasive pituitary adenoma was seen in 59(55.7%) cases and invasive in 47(44.3%) cases. Immunohistochemical examination of the specimens revealed that gonadotroph adenoma seen in 33 cases was the most common subtype. Corticotroph adenoma was seen in 27 cases, plurihormonal adenoma in 10 cases, null cell adenoma in 6 cases, somatotroph adenoma in 5 cases, lactotroph adenoma in 3 cases, Pit-1 plurihormonal adenoma in 2 cases, crooke cell adenoma in 1 case and mammosomatotroph adenoma in 1 case. MIB index was found to be equal or more than 3 % in 65 patients and less than 3 % in 25 cases. MIB status was unknown in remaining 3 cases. Almost 36.5 % tumors were found to be ‘high risk’ tumors as per WHO 2017 classification (**Table 3**).

Table 4: Clinical outcome of patients

	Grade I resection (>90% volume) (n=33)	Grade II & III resection (<90% volume) (n=52)
Vision:		
- Improved	29 (87.9%)	44 (84.6%)
- Stable	4 (12.1%)	5 (9.6%)
- Worsened	0	1 (1.9%)
- CNBT	0	2 (3.8%)
Hormonal status		
- Controlled without medication	29 (87.9%)	50 (96.2%)
- Controlled with medication	3 (9.1%)	0
- Uncontrolled	1 (3.0%)	1 (1.9%)
- CNBT	0	1 (1.9%)
Post-operative complications:	8 (24.2%)	14 (26.9%)
- Permanent Diabetes Insipidus	3 (9.1%)	0
- Meningitis	0	1 (1.9%)
- Sino-nasal symptoms	4 (12.1%)	10 (19.2%)
- Post op CSF leak	1(3.0%)	1 (1.9%)
- Third cranial nerve palsy(transient)	0	1 (1.9%)
- Sixth cranial nerve palsy (transient)	0	1 (1.9%)
Need for adjuvant therapy	1(3.0%)	11 (21.1%)
- Recurrence	0	6 (11.5%)
- Residual	0	4 (7.7%)
- Uncontrolled hormonal status	1 (3.0%)	1 (1.9%)
Mortality (number)	0	1 (1.9%)

Surgical outcomes:

Vision:

Postoperatively, improvement in vision was seen in 87 (82%) out of 106 patients, stable vision was seen in 15 (14.1%) patients, worsening of vision was seen in only one (0.94%) patient and visual assessment was not possible in 3 patients.

Endocrine:

New onset persistent hormonal insufficiency was seen in 3(2.9%) out of 103 cases. One patient developed hypocortisolism post-surgery, for which steroid replacement was needed on follow up. One female patient required progesterone for amenorrhea and other male patient required regular testosterone supplementation. Transient diabetes insipidus was seen in 13 patients and 4 patients had chronic diabetes insipidus. One patient developed hypocortisolism post-surgery, for which steroid replacement was needed on follow up.

Complications:

A total of 29 out of 106 (27.3%) patients had post-operative complications. Out of this 29 patients, 19(17.9%) patients had sinonasal symptoms, 4(3.8%) patients had permanent diabetes insipidus, 2(1.9%) patients had postoperative CSF rhinorrhea, 2(1.9%) patients had meningitis, 1(0.94%) patient had transient sixth cranial nerve palsy and transient third cranial nerve palsy was seen in one (0.94%) patient.

Adjuvant therapy in the form of radiotherapy was required in 14 out of 106 (13.2%) patients. Six (5.6 %) patients required it for recurrence of tumor (4 out of this 6 patients had Mib index >3%), five(4.7%) patients required it for residual tumor, two (1.9%) patients required it for aggressive pathology and one (0.94 %) patient required it for uncontrolled hormone levels. The mortality rate was 2.8% (**Table 4**).



DISCUSSION

DISCUSSION

The original description of giant pituitary adenoma was given about 60 years ago by Jefferson. Their size, aggressive behaviour, neurological deficits in patients and poor response to treatment raised a complex management issue and established it as a distinct entity to treat.² Various definition of giant pituitary adenoma have been quoted by numerous authors as the term 'giant' is still ambiguous.²⁵⁻²⁸ As these tumors are irregular in shape, solely relying on maximum tumor diameter may not reflect the true reach of the tumor to its surrounding structure.^{20,31} So, in the present study, we have considered both the tumor diameter more than 3 cm and minimum volume more than 10 cm³ that is known to be the modern definition of giant pituitary adenoma by Hofsetter et al¹⁴, to precisely define giant adenomas and for better quantification of extent of resection.^{4,20,27}

Traditionally, transcranial approaches has been advised for giant pituitary adenomas that have dumbbell shape or irregular adenomas and have tumor extension into the subfrontal region, retrochiasmatic area, temporal region, or posterior fossa.³²⁻³⁵ The panoramic view of endoscope that provides visualization of the cavernous sinuses and parasellar and suprasellar regions have led to resection of giant adenomas that have extensive invasion.^{36,37} This advantage of endoscope over traditional approaches could theoretically translate into greater extent of resection (EOR). Still, the reported resection rate for large and giant pituitary adenomas are much lower as compared to the EOR of small adenomas.²² Cavernous sinus invasion should be one of the main reason for this as it is a well-known factor that avoids GTR of these challenging tumors.¹⁵ In our study, cavernous sinus invasion was found to be in 99.05% cases with Knosp grade 4 occupying 38.6% cases. These two factors may have led to relatively less Grade I resection in our study, which is 38.82 %.^{15-18,38} We found that Knosp grade 3 and grade 4 were the main limitations while achieving Grade I resection for giant pituitary adenomas ($p = 0.022$). Interestingly, we were able to achieve 100% resection in 2 cases of knosp grade 4 tumor with one patient developing transient 3rd nerve palsy. Though one should try to achieve maximum resection of these tumors to avoid life threatening complications like bleed from residual tumor, main goal of surgical resection should always be to improve visual function and preserve hormonal

function without causing any neurological deficit.^{16,18,23} Though challenging, still, it is possible to excise tumor from the medial part of cavernous sinus to increase the extent of resection. In our study, we were able to achieve 100% resection as per volumetric analysis in 22(25.9%) out of 85 cases. The surgeon should be cautious while venturing into the lateral part of cavernous sinus to get GTR as it may prove to be more harmful than useful. Moreover, numerous studies have shown extremely good results with stereotactic radiosurgery(SRS) for treating the cavernous sinus residue.³⁹⁻⁴¹ The best strategy to deal with GPA having knosp grade 3 or 4 invasion is to excise tumor from the medial part of cavernous sinus as much as possible without injuring the cranial nerves and the residual tumor should be treated with SRS.

GPA generally extends posteriorly towards dorsum sella and then towards clivus, anteriorly over tuberculum sella and planum, laterally into the cavernous sinus invading internal cerebral artery and sometimes abuts the temporal lobe, superiorly in the suprasellar cistern and then inside the third ventricle.¹⁷ There is great difficulty in reaching such multi-compartment tumors using purely transsellar approach. So, there is always need for multiple extensions of usual transphenoid approach in each patient like transpterygoid, transtuberculum, transplanum, transcavernous, transclival for better dissection, visualization and preservation of vital structures like cranial nerves, internal carotid artery, optic chiasm etc.²⁸ Due to availability of advanced instrumentation and increasing demand from patients even in developing countries like India, minimally invasive endoscopic approaches have great value for the resection of large intracranial skull base tumors. It is important to study the utility of these multiple endoscopic endonasal corridors in each patient to show their feasibility and comparable or good outcome compared to traditional transcranial approaches.⁴² Inadequate bone removal is one of the most common cause of subtotal tumor resection. This principle is especially applicable to giant tumors that resist the descent of their suprasellar portion if their lateral extensions into the sella are not addressed because of restricted bone exposure.

We used 3D volumetric analysis to calculate the tumor volume and the extent of resection as volumetric analysis is known to give more accurate measurement of extent of resection than ellipsoidal volume calculation as volume.¹⁷ EOR was then correlated with the shape and extensions of giant adenomas in various compartments. However, we did not find any statistically significant difference between the various grades of resection in our study while comparing these factors. We believe that utilization of multiple endonasal corridors based on the shape and extension of tumor that is studied in detail in the pre-operative planning might be the reason as we were able to expand the traditional midline corridor of transsphenoidal route to reach the borders of many such complex giant adenomas. We employed multiple corridors in 25.9 % patients depending on the tumor extension and were able to achieve Grade I resection in 50% of patients in whom multiple corridor was used. The mean extent of resection volume with the use of single corridor was 76%, with use of 2 corridors was 85.3% and with the use of three corridors was 88%. Thus, the percentage increase in the extent of resection with use of 2 endonasal corridors was 10.6% and with 3 corridors was 14%. In our experience, the use of multiple corridors can make a valuable difference in the extent of resection of complex giant adenomas that have irregular extensions. This opinion have been supported by few studies in the literature that concludes that the extended endoscopic approach are able to overcome the classic limitations of traditional unicorridor endoscopic approach like dumbbell shape, suprasellar adenomas and fibrous tumors and provide greater EOR.^{12-17,21} We have also described our experience regarding the safe and efficient role of extended endonasal endoscopic approach for single stage excision of GPA that disrupt the diaphragm and extend into the third ventricle in our other study.⁴³

Pre-operative tumor volume ($p=0.011$) was one of the statistically significant predictor of Grade II and Grade III resection in our study as also found in few other studies.^{14,17,}

²⁰ Though not statistically significant, we found a positive correlation between the maximum height of tumor from the tuberculum sellae to the extent of resection. It meant that as the tumor height increases above tuberculum, the extent of resection proportionately decreases.

We also found that the tumor consistency did not affect the extent of resection. Our results are in contradiction to the observations made by Ajab et al²² who concluded that consistency of tumor, rather than the preoperative tumor volume was a significant predictor for the extent of resection. The use of meticulous microscopic dissection to preserve the vessels and nerves adherent to tumor while separating tumor from them is a possible reason for making tumor consistency non-significant while increasing the extent of resection.

There is a lack of understanding of the various factors involved in this tumor's regrowth, invasiveness and high rate of recurrence.³⁰ In our study, we tried to find the reasons for the aggressive behaviour of giant adenomas by studying their histopathological subtype and MIB-1 index in detail as both of these are known to be reliable tools to predict tumor behavior.³¹ However, we did not find any statistically significant difference between histological subtypes and MIB-1 index in the resection groups. However, 31 (36.5%) patients were found to be 'high risk' tumors as per WHO 2017 classification.⁴⁴ Also, five out of six patients who required adjuvant therapy for recurrence of tumor had MIB-1 index more than 3%. Radiotherapy was required only in 13.2% patients, which is less than that reported by other authors.^{4,15}

Visual improvement was seen in 82% of cases that is comparable with rates reported by various other authors.^{12,14,15,18} New onset persistent hormonal insufficiency was seen in 2.9% patients, which is less than that reported by other authors.^{13,15,14,18,23,24} Permanent diabetes insipidus was observed in 3.9% of patients which is comparable to other studies.^{19,21} Mortality rate in our study was 2.8% (3 out of 106 patients). One patient died because of pituitary apoplexy in the residual tumor and second patient succumbed to septicemia. Death of third patient because of myocardial infarction in the post-operative period was unrelated to surgery.

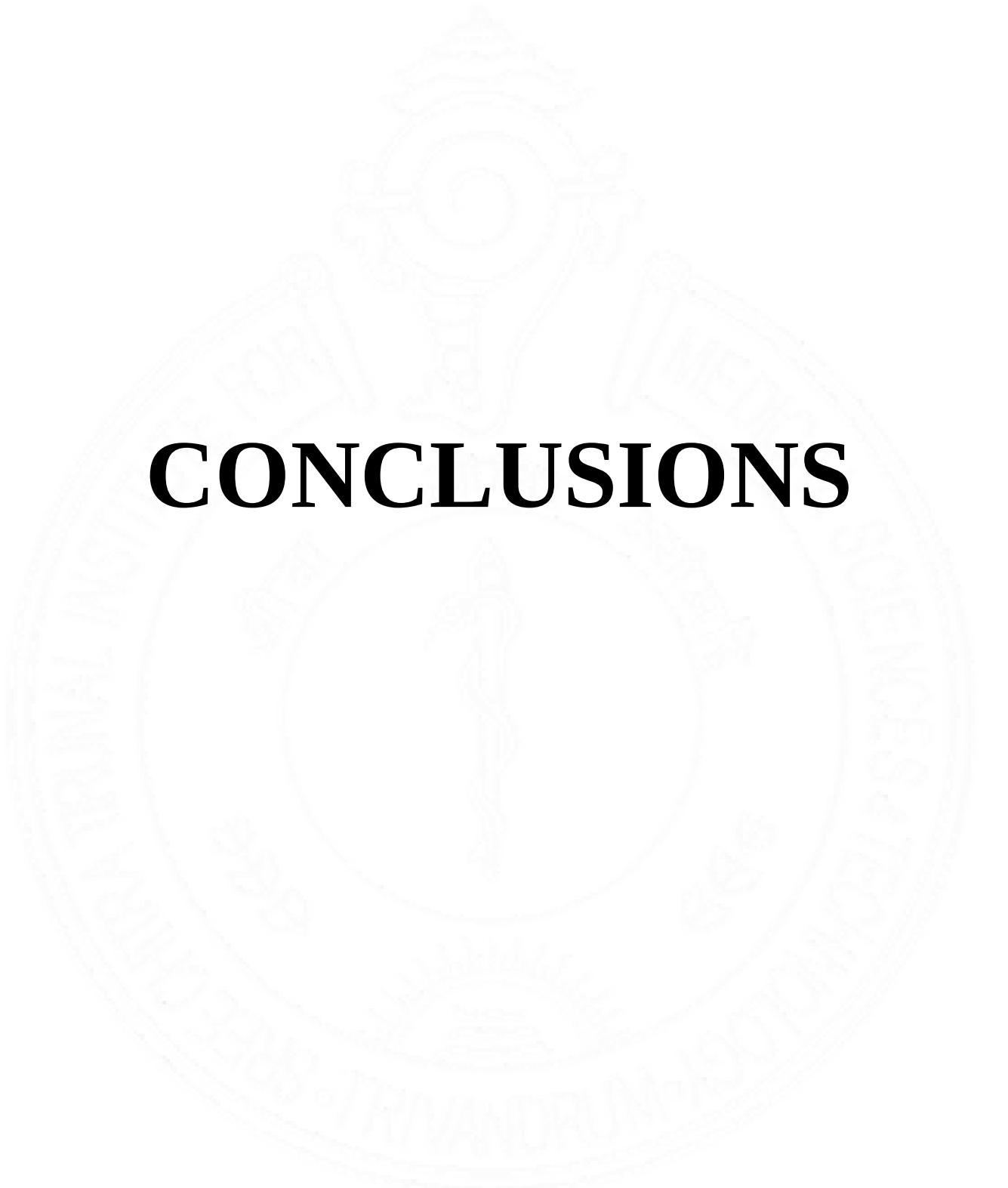
The outcomes following EEA for giant pituitary adenoma were compared against the recent body of literature (Table 5) and it was found that in many studies EEA was associated with higher rates of GTR along with better visual outcome and preserved

pituitary function.¹²⁻²⁴ Endoscopic skull base surgery is growing into a well-established alternative to the traditional open micro-surgical approach, however, it demands careful case selection. Once proper case has been selected, we also propose further, selection of an additional endonasal corridor as per the pre-operative imaging for increasing the extent of resection. The outcome of this study can be used to validate the approach for giant pituitary adenomas as a future standard of care.

Table 5: Literature review of studies utilising EEA for giant pituitary adenoma

Sl. No.	Study	Definition of Cases	No. of cases	GTR	NTR (>90%)	STR (<90%)	PD/ Biopsy	New hormonal deficit	Diabetes Insipidus (%)	Visual improvement (%)	Postop CSF rhinorrhea (%)	New neurological deficit (%)	Mortality (%)
1.	Di Maio et al 2011 ¹²	-	20	60	20	15	5	-	-	85.7	5	-	0
2.	Nakao and Itakura 2011 ¹³	Suprasellar extension > 20 mm	43	47*	-	53	-	4.7	0	97.7		-	0
3.	Cusimano et al 2012 ⁴	Tumor volume >10 cm ³	29	20.7	-	79.3	-	0.31	0.07	96.2	27.6		0
4.	Hofstetter et al 2012 ¹⁴	Tumor volume >10 cm ³	43	48.8	-	51.2	-	13.9	13.9	85.7	0		4.6
5.	Koutourousiou et al 2013 ¹⁵	Minimum size >4cm	54	20.4	66.7	-	12.9	16.7	9.6	80	16.7	4.4	0
6.	Gondim et al 2014 ¹⁶	Minimum size >4cm	50	38	18		44	0.36	0.1	76	8		4
7.	Juraschka et al 2014 ¹⁷	Minimum size >3cm	66	24.2	16.7	36.4	22.7	5.5	Included in new	73	9.6	2.7	0

									hormonal deficit				
8.	Chabot et al 2015 ¹⁸	Minimum size >3cm	39	56.4%	28.2	15.4	-	12.8	7.7%	79	10.3	0	0
9.	Kuo et al 2016 ¹⁹	Minimum size >4cm & tumor volume > 10 cm ³	38	21.1	78.9	-	-	26.4	2.6	71.1	0	5.3	0
10.	Chohan et al 2016 ²⁰	Minimum size >3cm	62	46.7	53.3	-	-	13	18	63	2	-	0
11.	Constantino 2016 ²¹	Minimum size >3cm	28	14.3	10.7	39.3	35.7	35.7	3.6	32.1	17.8	-	7.1
12.	Azab 2019 ²²	Minimum size >3cm	28	28.6 %	32.1 %	39.3 %	-	-	-	-	-	-	-
13.	Elshazly 2019 ²³	Minimum size >4cm	55	44 %	47%	-	-	17	7%	66	1.8	1.8	1.8
14.	Fallah 2019 ²⁴	Minimum size >3cm	80	82.5%	12.5	5 %	-	16.4	7.5	76.8	5	-	3.8
15	Present study	Minimum size >3cm & tumor volume >10 cm ³ (volume in 85 cases)	106	25.9%	9.4 %	51.8%	12.9%	2.9	3.9	83	1.9	-	2.8

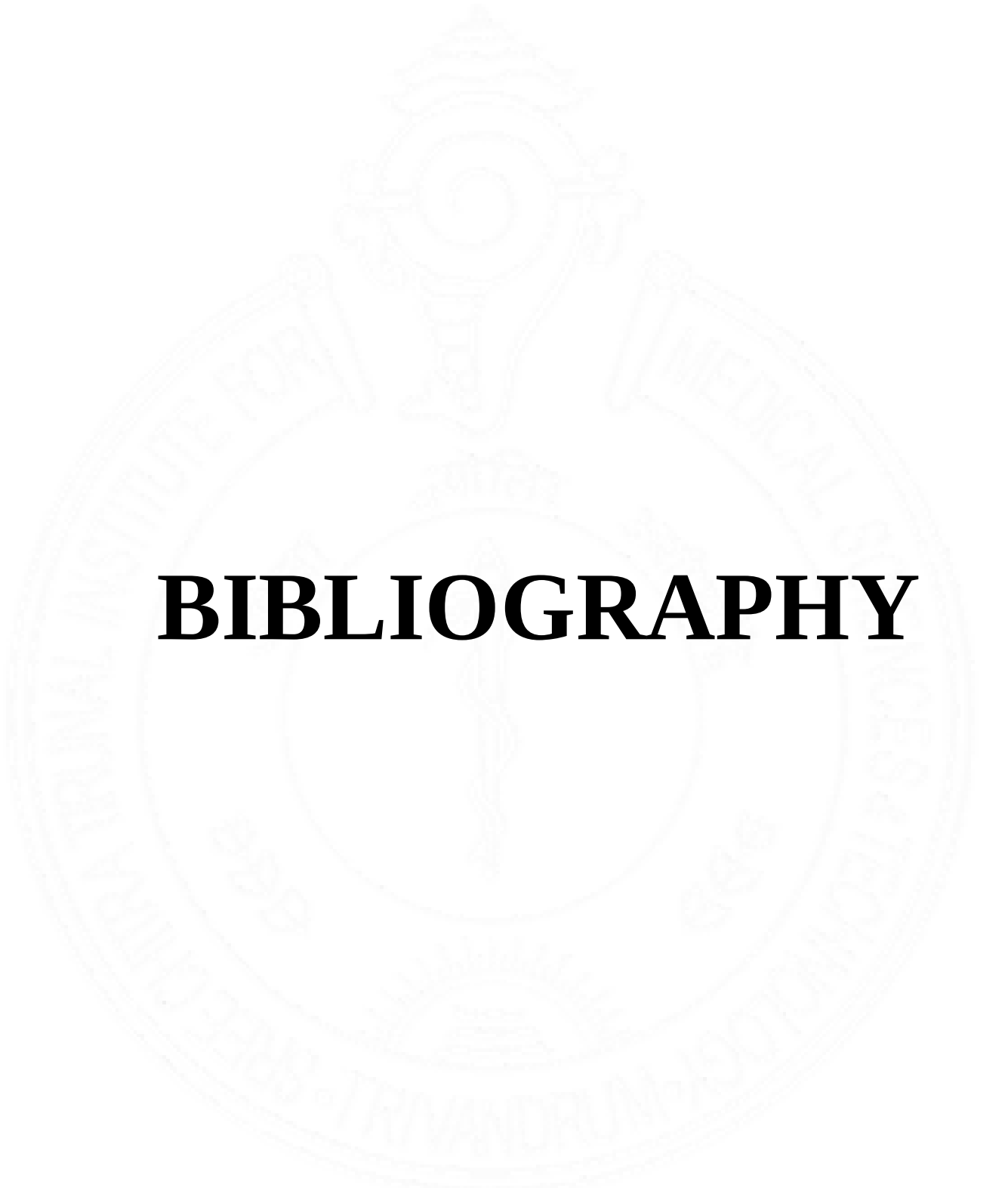


CONCLUSIONS

CONCLUSIONS

Extended endoscopic endonasal approaches can safely and effectively be used for the gross total resection of giant pituitary adenoma. However, we found that a preoperative tumor volume and Knosp grade 3 & grade 4 were statistically significant factors determining the extent of tumor resection. The utilization of multiple endoscopic endonasal corridors can increase the volumetric extent of tumor resection in giant pituitary adenomas. Visual improvement and preservation of hormonal axis with no neurological deficit should be the ultimate goal while managing these tumors.





BIBLIOGRAPHY

BIBLIOGRAPHY

1. Ezzat S, Asa SL, Couldwell WT, Barr CE, Dodge WE, Vance ML, McCutcheon IE (2004) The prevalence of pituitary adenomas: a systematic review. *Cancer* 101(3):613–619.
2. Jefferson G. Extrasellar extensions of pituitary adenomas. *Proc R Soc Med.* 1940;33:433–458.
3. Cappabianca P, Cavallo LM, Esposito F, De Divitiis O, Messina A, De Divitiis E: Extended endoscopic endonasal approach to the midline skull base: the evolving role of transsphenoidal surgery. *Adv Tech Stand Neurosurg* 33:151–199, 2008
4. Cusimano MD, Kan P, Nassiri F, Anderson J, Goguen J, Vanek I, et al: Outcomes of surgically treated giant pituitary tumours. *Can J Neurol Sci* 39:446–457, 2012
5. Sinha S, Sharma BS: Giant pituitary adenomas—an enigma revisited. Microsurgical treatment strategies and outcome in a series of 250 patients. *Br J Neurosurg* 24:31–39, 2010
6. Mohr G, Hardy J, Comtois R, et al. Surgical management of giant pituitary adenomas. *Can J Neurol Sci* 1990;17:62–6.
7. Mortini P, Barzaghi R, Losa M, et al. Surgical treatment of giant pituitary adenomas: strategies and results in a series of 95 consecutive patients. *Neurosurgery* 2007;60:993–1004.
8. Saito K, Kuwayama A, Yamamoto N, et al. The transsphenoidal removal of nonfunctioning pituitary adenomas with suprasellar extensions: the open

sellar method and intentionally staged operation. *Neurosurgery* 1995;36:668–76.

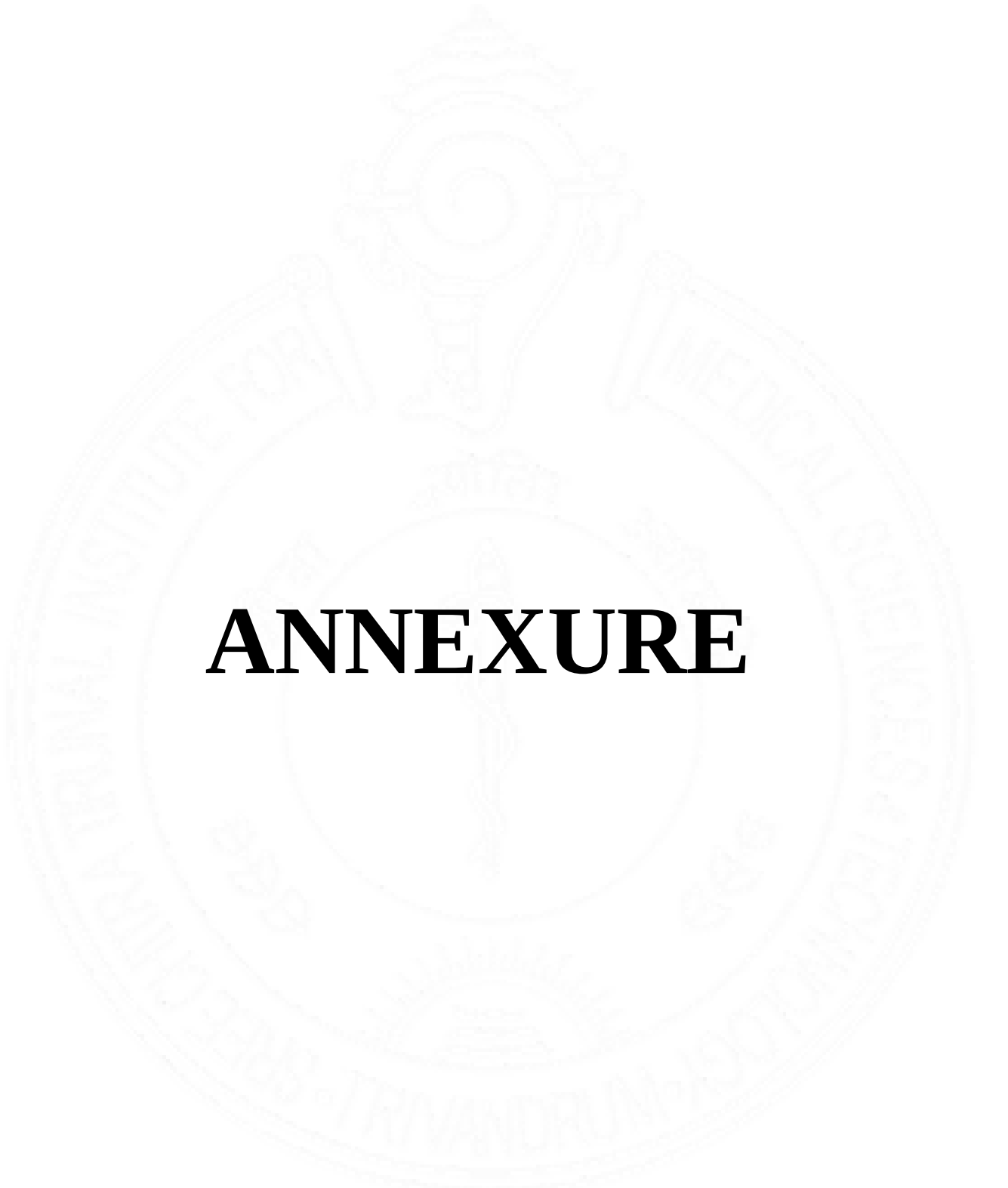
9. Cavallo LM, Prevedello DM, Solari D, Gardner PA, Esposito F, Snyderman CH, et al: Extended endoscopic endonasal transsphenoidal approach for residual or recurrent craniopharyngiomas. Clinical article. *J Neurosurg* 111:578–589, 2009
10. de Divitiis E, Cavallo LM, Esposito F, Stella L, Messina A: Extended endoscopic transsphenoidal approach for tuberculum sellae meningiomas. *Neurosurgery* 62 (6 Suppl 3):1192–1201, 2008
11. Dehdashti AR, Ganna A, Witterick I, Gentili F: Expanded endoscopic endonasal approach for anterior cranial base and suprasellar lesions: indications and limitations. *Neurosurgery* 64:677–689, 2009
12. Di Maio S, Cavallo LM, Esposito F, Stagno V, Corriero OV, Cappabianca P. Extended endoscopic endonasal approach for selected pituitary adenomas: early experience. *J Neurosurg*. 2011 Feb;114(2):345-53
13. Nakao N, Itakura T. Surgical outcome of the endoscopic endonasal approach for non-functioning giant pituitary adenoma. *J Clin Neurosci*. 2011 Jan;18(1):71-5.
14. Hofstetter CP, Nanaszko MJ, Mubita LL, Tsiouris J, Anand VK, Schwartz TH. Volumetric classification of pituitary macroadenomas predicts outcome and morbidity following endoscopic endonasal transsphenoidal surgery. *Pituitary*. 2012; 15:450-463.

- 15.Koutourousiou M, Gardner PA, Fernandez, Miranda JC, Paluzzi A, Wang EW, Snyderman CH. Endoscopic endonasal surgery for giant pituitary adenomas: advantages and limitations. *J Neurosurg.* 2013;118:621-631.
- 16.Gondim JA, Almeida JP, Albuquerque LA, Gomes EF, Schops M. Giant pituitary adenomas: surgical outcomes of 50 cases operated on by the endonasal endoscopic approach. *World Neurosurg.* 2014;82:e281-e290.
- 17.Juraschka K, Khan OH, Godoy BL, et al. Endoscopic endonasal transsphenoidal approach to large and giant pituitary adenomas: institutional experience and predictors of extent of resection. *J Neurosurg.* 2014;121:75-83.
- 18.Chabot JD, Chakraborty S, Imbarrato G, Dehdashti AR. Evaluation of outcomes after endoscopic endonasal surgery for large and giant pituitary macroadenoma: a retrospective review of 39 consecutive patients. *World Neurosurg.* 2015;84: 978-988.
- 19.Kuo CH, Yen YS, Wu JC, et al. Primary endoscopic transnasal transsphenoidal surgery for giant pituitary adenoma. *World Neurosurg.* 2016;91:121-128.
- 20.Chohan MO, Levin AM, Singh R, et al. Threedimensional volumetric measurements in defining endoscope-guided giant adenoma surgery outcomes. *Pituitary.* 2016;19:311-321.
- 21.Constantino ER, Leal R, Ferreira CC, Acioly MA, Landeiro JA. Surgical outcomes of the endoscopic endonasal transsphenoidal approach for large and giant pituitary adenomas: institutional experience with special attention to approach-related complications. *Arq Neuropsiquiatr.* 2016 May;74(5):388-95.

22. Azab WA, Nasim K, Abdelnabi EA, Yousef W, Najibullah M, Khan T, Zaidan SN, Bokeris AA, Mostafa KH, Geng D. Endoscopic Endonasal Excision of Large and Giant Pituitary Adenomas: Radiological and Intraoperative Correlates of the Extent of Resection. *World Neurosurg.* 2019 Jun;126:e793-e802.
23. Elshazly K, Kshetry VR, Farrell CJ, Nyquist G, Rosen M, Evans JJ. Clinical Outcomes After Endoscopic Endonasal Resection of Giant Pituitary Adenomas. *World Neurosurg.* 2018 Jun;114:e447-e456.
24. Fallah N, Taghvaei M, Sadaghiani S, Sadrhosseini SM, Esfahanian F, Zeinalizadeh M. Surgical Outcome of Endoscopic Endonasal Surgery of Large and Giant Pituitary Adenomas: An Institutional Experience from the Middle East. *World Neurosurg.* 2019 Dec;132:e802-e811.
25. Sharma, B. S. MCh; Sinha, Sumit MCh; Suri, Ashish MCh Treatment of Giant Pituitary Adenomas, *Neurosurgery Quarterly*: June 2007 - Volume 17 - Issue 2 - p 120-127.
26. Symon L, Jakubowski J. Transcranial management of pituitary tumors with suprasellar extension. *J Neurol Neurosurg Psychiatry.* 1979;42:123–133.
27. Symon L, Jakubowski J, Kendall B. Surgical treatment of giant pituitary adenomas. *J Neurol Neurosurg Psychiatry.* 1979;42:973–982.
28. Garibi J, Pomposo I, Villar G, et al. Giant pituitary adenomas: clinical characteristics and surgical results. *Br J Neurosurg.* 2002;16:133–139.
29. Alexander s. g. micko, Adelheid wohrer. Invasion of the cavernous sinus space in pituitary adenomas: endoscopic verification and its correlation

- with an MRI-based classification. *J Neurosurg.* 2015;122:803–811.
30. Hofstetter CP, Moshel Y, Nanaszko M, Anand VK, Schwartz TH. Extended endonasal, endoscopic transphenoidal approach versus craniotomy for giant pituitary macroadenomas (chapter 24), in Schwartz TH and Anand VK (eds): *Endoscopic Pituitary Surgery. Endocrine, Neuro-ophthalmologic, and Surgical Management.* American Association of Neurological Surgeons and Thieme, 2012, pp 248-261.
31. Davies BM, Carr E, Soh C, Gnanalingham KK. Assessing size of pituitary adenomas: a comparison of qualitative and quantitative methods on MR. *Acta Neurochir.* 2016;158:677-683.
32. Buchfelder M, Kreutzer J: Transcranial surgery for pituitary adenomas. *Pituitary* 11:375–384, 2008.
33. Mortini P, Barzaghi R, Losa M, Boari N, Giovanelli M: Surgical treatment of giant pituitary adenomas: strategies and results in a series of 95 consecutive patients. *Neurosurgery* 60: 993–1004, 2007
34. Tindall GT, Woodard EJ, Barrow DL: Pituitary adenomas: general considerations, in Apuzzo ML (ed): *Brain Surgery: Complication Avoidance and Management.* New York: Churchill Livingstone, 1993, pp 269–312.
35. Youssef AS, Agazzi S, van Loveren HR: Transcranial surgery for pituitary adenomas. *Neurosurgery* 57 (1 Suppl):168–175, 2005
36. Cappabianca P, Alfieri A, de Divitiis E. Endoscopic endonasal transsphenoidal approach to the sella: towards functional endoscopic pituitary surgery (FEPS). *Minimally invasive neurosurgery : MIN.* 1998;41(2):66-73.

37. Carrau RL, Jho HD, Ko Y. Transnasal-transsphenoidal endoscopic surgery of the pituitary gland. *Laryngoscope*. 1996;106(7):914-918.
38. Komotar RJ, Starke RM, Raper DM, Anand VK, & Schwartz TH: Endoscopic endonasal compared with microscopic transsphenoidal and open transcranial resection of giant pituitary adenomas. *Pituitary* 15:150–159, 2012.
39. Shin M, Kurita H, Sasaki T, Tago M, Morita A, Ueki K, Kirino T. Stereotactic radiosurgery for pituitary adenoma invading the cavernous sinus. *J Neurosurg*. 2000 Dec;93 Suppl 3:2-5.
40. Ikeda H, Jokura H, Yoshimoto T. Gamma knife radiosurgery for pituitary adenomas: usefulness of combined transsphenoidal and gamma knife radiosurgery for adenomas invading the cavernous sinus. *Radiat Oncol Investig*. 1998;6(1):26-34.
41. Garg K, Singh M. Role of Stereotactic Radiosurgery in Pituitary Adenomas. *Neurol India*. 2020 May-Jun;68(Supplement):S123-S128.
42. Han-Shun Deng, Zhi-Quan Ding. Surgical therapeutic strategy for giant pituitary adenomas. 2017; 28 (19): 8284-8288.
43. Jamaluddin MA, Patel BK, George T, Gohil JA, Biradar HP, Kandregula S, Hv E, Nair P. Endoscopic Endonasal Approach for Giant Pituitary Adenoma Occupying The Entire Third Ventricle: Surgical Results and A Review of Literature. *World Neurosurg*. 2021 Jul 19:S1878-8750(21)01017-2.
44. Mete O, Lopes MB. Overview of the 2017 WHO Classification of Pituitary Tumors. *Endocr Pathol*. 2017 Sep;28(3):228-243



ANNEXURE

Patient Proforma Form

Proforma

Serial no :

Age :

Sex:

Time from onset of symptoms till surgery:

Pre-operative Symptoms:

- 1) Visual acuity
- 2) Visual defects
- 3) Cranial nerve deficits
- 4) Hormonal disturbances
- 5) Headache
- 6) Neurological deficits
- 7) Others

Pre-operative Hormonal replacement: Yes / NO

Co-morbidities:

Type of tumor: Primary/ Recurrent /Residual

Functional status: Type – Functioning

Nonfunctioning

Previous surgery: Transcranial /Transnasal microscopic/ Endoscopic endonasal/

Radiological characteristics:

- 1) Maximum width :
- 2) Knosp Score:
- 3) Modified Hardy Classification stage:
- 4) Tumor characteristic: Optic nerve compression/.Hydrocephalus/apoplexy
- 5) Tumor shape : Rounded/Dumbbell shaped/Multilobar
- 6) Tumor invasion: Sphenoid/cavernous sinus/3rd ventricle/Bone (clivus/anterior skullbase/orbit) / Brain parenchyma

Tumor extension: Suprasellar / Intraventricular/Anterior cranial fossa/ Temporal lobe / Posterior fossa

Surgical approach: Trans-sellar/Transplanum /Transclival /Transtuberculum/Transpterygoid

Need for lumbar drain intra-operatively:

Tumor characteristics:

Use of Neuronavigation : Yes/No

Intra-op Complications :

Intra-op CSF leak:

Extent of resection: Gross total resection/Sub-total resection/ Near total resection

Repair Technique:

Post-op CSF leak:

Post-op Diabetes Insipidus:

Meningitis:

Sino-nasal symptoms:

Other complications:

Post-op Visual acuity (immediate postop):

Post-op Visual field (immediate postop):

Post-op Length of stay

Histopathological diagnosis:

Post-op MRI (extent of resection): GTR/ NTR/ STR

Post-op Hormonal status:

Need for adjuvant therapy:

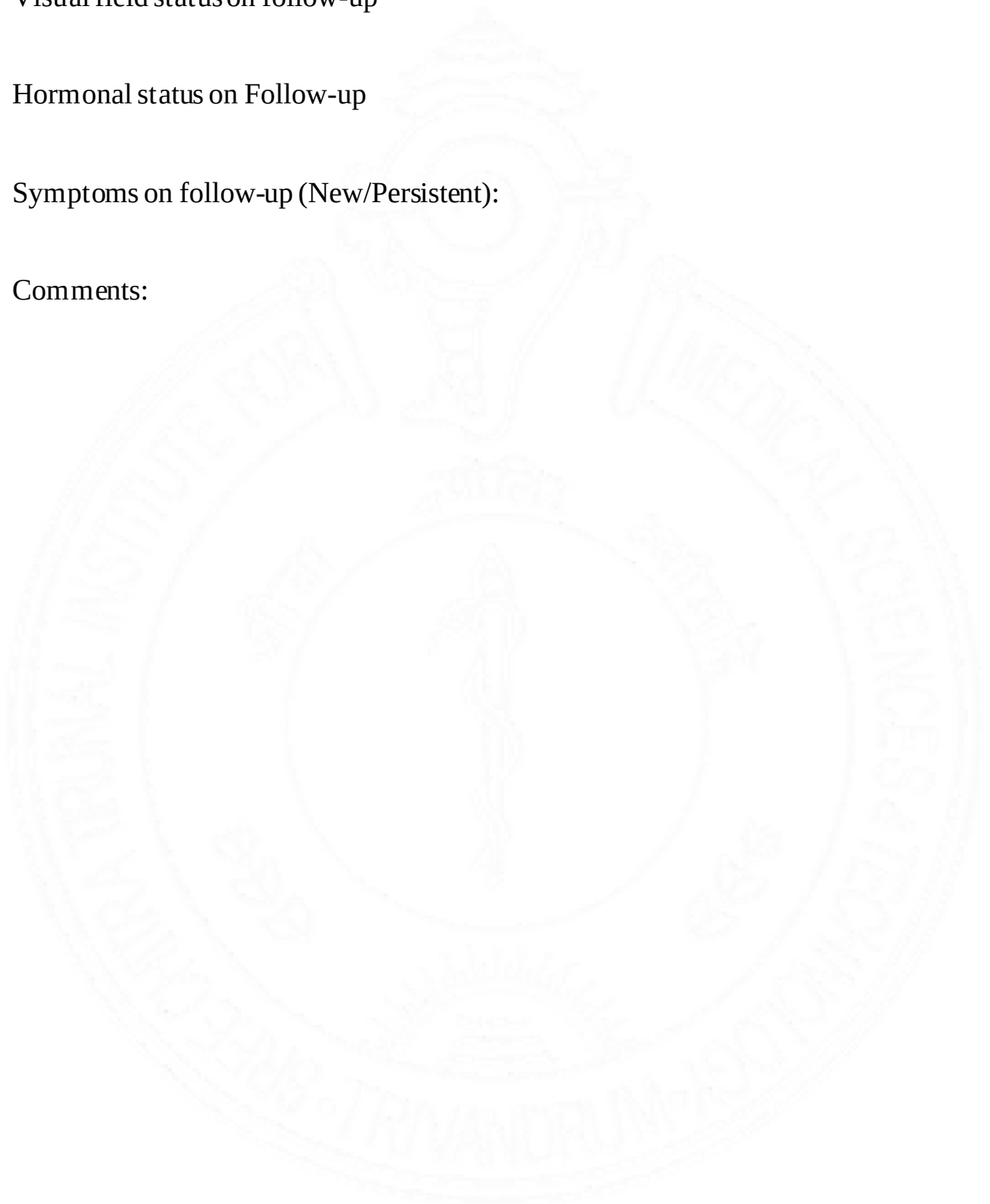
Visual acuity on follow-up

Visual field status on follow-up

Hormonal status on Follow-up

Symptoms on follow-up (New/Persistent):

Comments:





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

SCT/IEC/1703/AUGUST-2021

31.08.2021

Dr. Biren Patel
Post Doctoral Fellow
Department of Neurosurgery
SCTIMST Thiruvananthapuram

Dear Dr. Biren Patel,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "UTILIZATION OF MULTIPLE ENDONASAL CORRIDORS FOR RESECTING LARGE AND GIANT PITUITARY ADE- NOMAS: AN ASSESSMENT OF EXTENT OF RESECTION, VISUAL RECOVERY AND ENDOCRINOLOGICAL OUTCOME (IEC/1703)" on 18th August, 2021.

The following members of the Ethics Committee were present at the meeting held on 18th August, 2021 at Residences and Offices of IEC Members via Video Conference

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Prof. C.C. Kartha	MBBS,MD	Male	Basic Medical Scientist (Chairman)	No
2.	Dr. Kala Kesavan P	MBBS,MD	Female	Basic Medical Scientist	No
3.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
4.	Dr. Pradeep S	MBBS, MD	Male	Basic Medical Scientist	No
5.	Dr. Achuth Sankar S. Nair	Ph.D (i.Engineering ii.Music)	Male	Social Scientist	No
6.	Dr. Rejnish Kumar	MBBS,MD ,DNB	Male	Clinician	No
7.	Adv. N Anand	BAL, L.LB	Male	Legal Expert	No
8.	Adv. Priya Kaimal	LLM, MBL	Female	Legal Expert	No
9.	Dr. Harikrishna Varma P. R	Ph.D (Materials Sciences)	Male	Medical Technology	Yes
10.	Dr. Manikandan.S	MBBS,MD,PDCC	Male	Clinician	Yes
11.	Dr. Narayanan Namboodiri. K K	MBBS,MD,DM	Male	Clinician	Yes
12.	Dr. Biju Soman	MBBS,MD, DPH, MSc, DLSHTM	Male	Basic Medical Scientist	Yes
13.	Dr. Srinivas G	PhD	Male	Basic Medical Scientist (Member Secretary)	Yes

The following documents were reviewed:

1. Covering letter addressed to the Chairperson, IEC, SCTIMST
2. IEC Application form
3. Project Proposal
4. Proforma
5. TAC Approval Letter
6. Request for consent waiver
7. CV of PI and Co-PIs
8. Declaration Form
9. TCMC Registration certificate of Dr. Biren Patel

IEC Decision

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

This approval is in continuation of IEC Regn No. ECR/189/inst/KL/2013/RR-16, subject to IEC Renewal pending process with CDSCO

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,



G. Srinivas
Member Secretary, IEC



