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Original Research Article

Endoscopic endonasal pituitary adenoma surgery: our surgical experience in 116 patients

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ABSTRACT

Background: The primary objective of this study was to evaluate the outcome of excision in terms of gross and partial resection rates compared to the grades of pituitary adenoma (based on Hardy-Vezina classification). We also evaluated the post-operative complications and the effect of resection on visual outcomes and endocrinological remission.
Methods: We retrospectively analysed 116 patients who underwent surgical resection of pituitary adenoma via endonasal trans-sphenoidal approach at Civil Hospital (Ahmedabad) between March 2013 and March 2019 and collected pre-operative and post-operative data in terms of imaging, endocrine function and vision.
Results: According to the postoperative imaging data and endocrine examination results, gross-total resection (GTR) was achieved in 79.3% (92 patients), and partial (PR) in 20.6% (24 patients) which was significant ($p<0.05$). Improvement in vision was seen in 62% (40 patients out of 64 patients). Out of 44 patients having endocrine dysfunction, endocrinological remission was achieved in 32 patients with functional adenomas (72.7%). Sinusitis followed by headache was the most common minor complication seen in the study.
Conclusions: Endoscopic endonasal transsphenoidal surgery is a valuable treatment option for patients having grade 3 or lower pituitary adenomas, which leads to gross total resection in comparison to patients having grade 4 adenoma. It also results in high rate of surgical decompression and better visual outcome. Partial resection may result in endocrinological response in functional tumors.

Keywords: Endoscopic endonasal approach, Pituitary adenomas

INTRODUCTION

Pituitary adenomas account for 10-12% of all intracranial tumors. It is benign histologically but aggressive in nature, resulting in mass effect on the optic apparatus and adjacent structures, giving rise to visual field defects and headaches. The preferred treatment is excision by the trans-sphenoidal route because it is less invasive and provides a direct approach to the pituitary gland. The success rate and visual outcomes following excision depends on the age, the preoperative visual the duration of the visual symptoms and size of the lesion.[1-3] Surgery is done to provide relief of mass effect by obtaining maximal tumor resection to decompress visual pathways and neurovascular structures. The primary objective of this study was to evaluate the outcome of excision in terms of gross and partial resection rates compared to the grades of pituitary adenoma (based on Hardy-Vezina classification). We also evaluated the post-operative complications and the effect of resection on visual outcomes and endocrinological remission.

METHODS

After obtaining approval from the institutional review board; we retrospectively reviewed the hospital records of patients who had undergone endoscopic trans-

sphenoidal surgery for pituitary adenomas at Civil Hospital, Ahmedabad.

Inclusion criteria

Patients diagnosed with pituitary adenoma (postoperative pathologically confirmed diagnosis), treated with trans-sphenoidal surgery, with a documented visual status and having both pre-operative and follow up MRI.

Exclusion criteria

Patients with a pathological diagnosis other than pituitary adenoma were excluded from the study, as were those who underwent combined microscopic/endoscopic surgery.

A total of 116 patients who underwent endoscopic trans-sphenoidal surgery between March 2013 and March 2019 were included.

Data collection

Data collected includes age, sex, clinical characteristics, tumor characteristics, operative details, clinical outcome and surgical complications. Clinical characteristics analysed included visual acuity, visual field deficit, pituitary hyper- and hypofunction syndromes, pan-hypopituitarism, diabetes insipidus, pituitary apoplexy, prior surgery and prior medical management.

Pre-operative tumor characteristics were obtained from MRI with an imaging protocol, which consisted of 2-3 mm sagittal and coronal planes, T1-weighted images with and without contrast enhancement and T2-weighted images. Tumor size, as defined by its maximum diameter, was classified into microadenoma (<10 mm) and macroadenoma (>10 mm). Macroadenomas were further classified into large macroadenomas (≥20 mm) and giant macroadenomas (≥30 mm). Parameters assessed were, presence or absence of a cystic component, hemorrhagic component, optic nerve compression and hydrocephalus. Images were assessed to determine whether the tumor had suprasellar extension and its relation with the internal carotid artery. These assessments were done based on Hardy-Vezina classification systems. Hardy classification system provides descriptive tool for pituitary adenomas and is often utilized in research studies.[4]

Preoperative pituitary endocrine function laboratory data were collected, including follicle-stimulating hormone, thyroid stimulating hormone (TSH), T3, T4, cortisol, adrenocorticotropic hormone, Growth hormone (GH), insulin-like growth factor-1(IGF-1), and prolactin (PRL) levels.

Post operatively, we assessed free T4 and prolactin within 1-2 weeks of surgery and GH immediately after 6 hours of surgery as GH has half-life of 20-40 minutes and IGF after 3-4 days.[5] Post-operative endocrinological remission was defined as random GH level <1 ug/l and Insulin like growth factor-1IGF-1 level at normal range according to the age and sex simultaneously and normal range for PRL <22.80 ug/l for male, and <30.74 ug/l for female.

Postoperative change in visual acuity was tested using Snellen's chart and visual fields mapping was done. All patients underwent MRI 2 months after surgery, which was used to classify the resections into gross total resection (GTR) and partial resection (PR).

The presence of postoperative complications including syndrome of inappropriate antidiuretic hormone secretion (SIADH), diabetes insipidus, cranial nerve palsy, ICA artery damage, CSF leak, CSF leak requiring a lumbar drain, headache, epistaxis, sinusitis, visual complications, deep venous thrombosis, pulmonary embolism, vasospasm, subdural hygroma, hematoma, seizure, hydrocephalus, meningitis, coma and death were noted.

Data analysis

We used Chi square test and Fischer's exact t test to evaluate the relationship between the tumor resection rate and the tumor invasiveness and extrasellar spread (Modified Hardy classification). A p value <0.05 was considered significant. Statistical analyses were performed using SPSS software (IBM, version 24). Complication rates and clinical/endocrinological response rates were also calculated.

Surgical approach

All patients in this study underwent trans-nasal trans-sphenoidal endoscopic resection of a pituitary adenoma. The objective of surgery was to achieve maximum decompression of the optic apparatus, to achieve maximum resection with care not to injure sensitive neural and vascular structures, and to preserve or restore endocrine function.

Patients were positioned with their heads secured by a Mayfield head holder. The nasal cavity was prepared with adrenalin (1:1000) soaked cottonoids for at least 5 minutes in order to decrease bleeding. The surgical procedure started with the inventory of nasal cavity with a 0-degree 4 mm endoscope. A right middle turbinectomy is done before harvesting mucoperiosteal nasoseptal vascularized flap for skull base reconstruction after tumor resection. A posterior septectomy was undertaken for a two nostril bimanual technique. An anterior sphenoidotomy was then carried out. Its front wall was opened with a fine chisel and expanded with a Kerrison forceps or drilling. Dural exposure was limited by the tuberculum sellae superiorly, clival recess inferiorly, and laterally by the medial walls of the cavernous sinus. Cruciate incision is kept over dura (Figure 1). Tumor was debulked by piecemeal resection (Figure 2) and suction and ultimately the tumor border was defined for bimanual

preparation of the neurovascular structures. The reconstruction of the skull base was performed with autologous fat patch, which was placed in the resection cavity with a special care not to overpack, followed by placement of the nasoseptal mucous flap. Tissue glue was applied to the flap edges and covered with Surgicel (Ethicon) (Figures 3 and 4). A nasal Foley catheter was introduced for packing of the sphenoidal cavity in order to prevent flap migration only in the case of intraoperative CSF leakage or packed with merocoele.

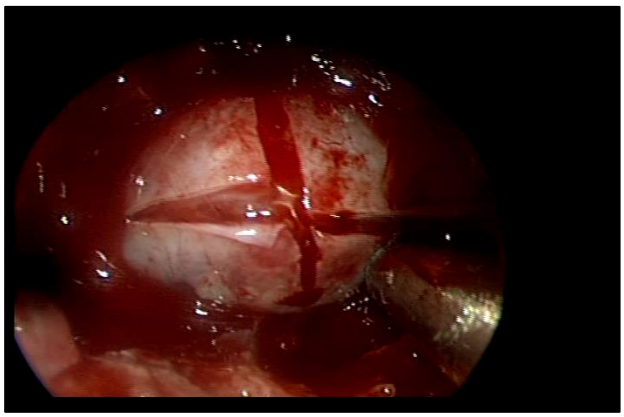

Figure 1: Showing cruciate incision over the dura.

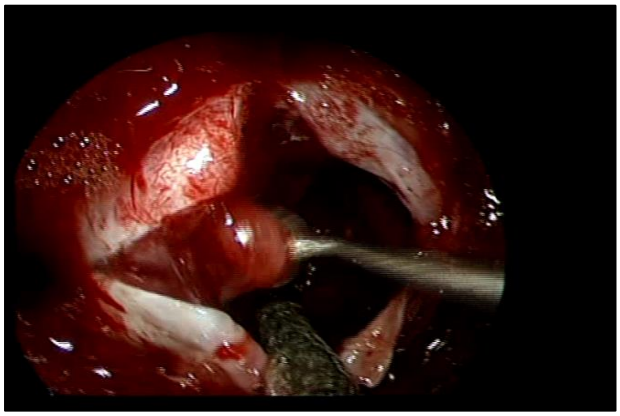

Figure 2: Debulking of tumor.

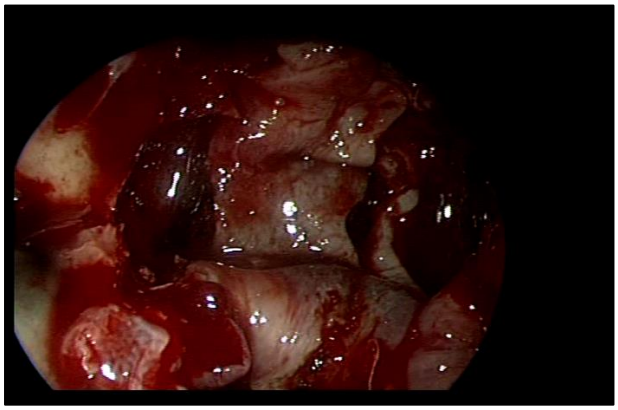

Figure 3: Covered by layer of tissue glue.

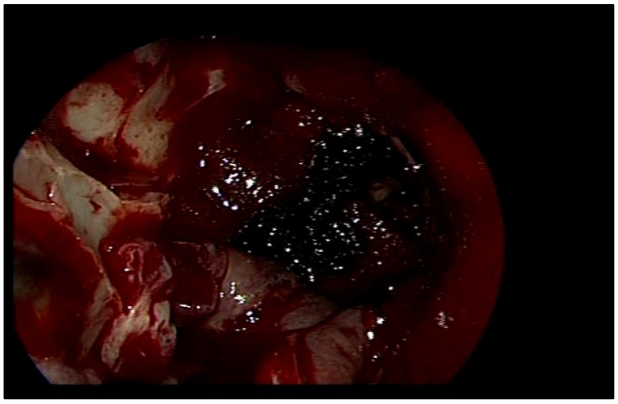

Figure 4: Second layer of surgicel covering the defect.

RESULTS

Endoscopic resection of large pituitary adenomas was performed in 116 patients at our institution between March 1, 2013, and March, 2019. Baseline characteristics of the study population are summarized in Table 1.

Table 1: Summary of the clinical characteristics of 116 patients.

Variables	Number	Percentage
Sex		
Male	57	49
Female	59	51
Clinical presentation		
Decrease vision	64	55
Headache	61	52.5
Visual field defect	38	33
Coarse fascial features	5	4
Giddiness	8	7
Amenorrhea	13	11
Weight gain	4	3
Loss of libido	2	2
Others	5	4

The average age of the study population was 54.5 years, and the study population had a high female/male ratio (50.8% female, 31.5% male). The majority of patients in this series presented with visual acuity (55.1%) and/or visual field (32.7%) deficits and headache (52.5%). Forty-four patients (38%) were found to have endocrine dysfunction prior to surgery. Prior to surgery, 2.58% had apoplexy (defined by clinical presentation and confirmed by radiographic and intraoperative findings); 4.4% of patients had prior surgery. Cabergoline (5.1%) was used as an attempt to induce tumor remission.

As expected, majority of the tumors in this series were non-functioning pituitary adenomas (59.4%). Among the functional tumors, prolactinoma was the most common cell type (50%), followed by growth hormone adenomas (36.3%) and corticotrophs (11.3%) as summarized in Table 2.

Table 2: Tumor characteristic and tumor extension.

Variables	Number	Percentage
Tumor characteristics		
Apoplexy	3	2.6
Non functional	69	59.4
Functional		
Growth hormone	16	
Prolactin	22	
TSH	0	
ACTH	6	
Total	44	38
Tumor extension		
Suprasellar Extension	61	52.5
Optic nerve compression	22	19
Encasement of cavernous sinus and ICA	23	20
Intracranial optic nerve invasion	2	1.7

The tumor resection rates were estimated by assessment of postoperative MRI exams, which were performed two months after surgery. Gross-total resection (GTR) was achieved in 79.3% (92 patients) and partial resection (PR) in 20.6% (24 patients) as shown in Table 3 and Table 4.

Table 3: Showing relation of grade of pituitary adenoma to surgical outcome.

Variables	Grade I to III	Grade IV	Marginal row totals
Partial resection	9	15	24
Complete resection	60	32	92
Marginal column totals	69	47	116 (grand total)

Table 4: Surgical outcome.

Variables	Number	Percentage
Hardy classification		
Grade I-II	8	6.8
Grade III	61	52.5
Grade IV	47	40.5
Extent of resection		
Total excision	92	79
Near total excision	24	21

There was a significant difference in outcome of patients with grade I to III pituitary adenoma as compared to those having grade IV pituitary adenoma. Out of the 47 patients having grade IV pituitary adenoma, post-operative MRI showed that 31.9% (n=15) had undergone partial resection and 68% (n=32) had undergone complete resection, while of the 69 patients having grade 3 or less tumors, 86.9% (n=60) had undergone complete resection and only 13% (n=9) had undergone gross total resection. A chi-square test of independence was performed to examine the relation between tumor grade and the surgical outcome (partial resection or gross total resection). The relation between these variables was significant, p=0.013.

Improvement in vision (VA), tested using Snellen's chart, was seen in 62% (40 patients out of 64 patients) who had complained of decrease in vision, was unchanged in 18 patients and had worsened in 6 patients (9%). Rest 52 patients had no complaints of decreased vision and this remained unchanged after the operation. Visual field improvement was seen in 38 patients (60%) and remained unchanged in 26 patients. Out of 44 patients having endocrine dysfunction, endocrinological remission was achieved in 32 patients (72.7%).

Sinusitis followed by headache was the most common minor complication. Two (2%) patients incurred postoperative CSF leakage, which was resolved after lumbar drainage. After surgery, 18 (15.5%) patients incurred transient DI, of which one patient developed persistent DI, which was treated with Minirin. Meningitis occurred in two (2%) patients who were treated by a third-generation cephalosporin. There were no cases of intracranial haematoma, reoperation or death (Table 5).

Table 5: Postoperative complications.

Variables	Number	Percentage
Major complication		
Meningitis	2	2
Hydrocephalus	1	1
CSF leak	2	2
Minor complication		
SIADH	18	15.5
Headache	37	32
Epistaxis	5	4.3
Sinusitis	47	40.5

DISCUSSION

Complete resection is often a technical challenge, even for experienced ENT specialists and neurosurgeons, considering that large and giant tumors may present with a high degree of invasion of neurovascular structures and large areas of supra- and parasellar extension. In this way, the primary objective of surgery of these tumors includes relief of mass effect by obtaining maximal tumor resection in order to decompress visual pathways, neurovascular structures and the pituitary gland.

Although pituitary adenomas are benign, they have a high recurrence rate, which is generally believed to result from incomplete resection. Cappabianca et al estimated that surgical treatment of pituitary tumors had a 30% recurrence rate, while incomplete tumor resection was associated with a recurrence rate as high as 75%.[6] Thus, for patients with pituitary adenomas complete resection of the tumor is critical. However, complete resection via

the endonasal trans-sphenoidal endoscopic approach is sometimes difficult, as tumors are often invasive, growing within or beyond the sella, involving the dura mater or cavernous sinuses, and/or have a tough texture and may present with irregular shapes. According to recent literature, the endoscopic approach for pituitary adenomas- including prolactinomas- can achieve a complete resection rate of 77%-96%.[7]

Here, we summarize our experience with endonasal endoscopic trans-sphenoidal surgery in 116 pituitary adenoma cases. Postoperative MRI review showed good overall therapeutic effect, with total tumor excision achieved in 92 cases i.e. 79%. These rates of resection correlate well with some other recent studies on endoscopic trans-sphenoidal surgery, such as that by Darwisha et al who reported gross total resection rate of 87%, Shou et al who achieved a 72.5% GTR.[8,9] Sun et al showed 31 cases out of 42 cases had gross total resection. Komotar et al found that the endoscopic cohort had higher rates of gross total resection (GTR) (47.2%) and improved visual outcome (91.1%).[11]

As for patients with preoperative visual field disturbances, complete recovery of vision was seen in 40%-50% of the cases and improvement in 39%-51% of the cases in two large endoscopic series.[12,13] In our series, 64 patients with postoperative visual acuity assessment (excluding those without pre- or postoperative visual acuity deficit), 40 (62%) experienced improvement, while only 6 (9.3%) worsened and 18 (28%) experienced no change.

According to Cohen et al better visual acuity outcome was seen in patients with lesser degree of preoperative visual acuity compromise.[1] Gnanalingham et al reported that the extent of the visual field recovery was mainly dependent on the preoperative visual field deficit.[2] Sullivan et al in their retrospective study of 45 patients concluded that the preoperative visual acuity was not predictive of postoperative visual acuity.[14] Powell in his series of 67 patients reported that preoperative visual defect did not correlate with the postoperative visual recovery.[15] Sinusitis followed by headache was the most common complication encountered in this study. One other common complication is transient diabetes insipidus. Permanent diabetes insipidus is less common around 1% of the cases.[16] Postoperative CSF leak rate ranges around 2%-4%, and in the 200 patients reported by Dehdashti et al it was 3.5% which correlates with the figures of our study (2%).[12,16]

Our study has a number of limitations, most significant of which is its retrospective nature. Another important drawback is that separate grading systems were not used for classifying cavernous sinus invasion (included in grade IV in this study).

CONCLUSION

As endoscopic trans-sphenoidal surgery has emerged as the standard treatment of pituitary adenomas, particularly in experienced tertiary care centres, surgeon comfort and experience with this technique has expanded the indications for trans-sphenoidal approaches to pituitary adenomas.

Recommendations

Redefining the goals and expectation of outcomes following surgery is important, such that partial resection with decompression the optic apparatus is the expected surgical outcome and presence of residual tumor is an accepted result, in particular in patients with comorbidities or older age where progression of residual tumor is not clinically concerning. Further reports of institutional experiences, longer follow-up, and investigations are needed to validate our results. Extending our endoscopic approach with innovative approaches to overcome current limitations of the endoscopic approach is also important.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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