

A Retrospective Observational Assessment of the Endocrine Outcomes after Endoscopic Transsphenoidal Surgery for Non- Functioning Pituitary Adenomas

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to analyze the remission and preservation of hormones, endocrinological and anatomical complications and visual improvement after endoscopic transsphenoidal surgery (ETS).

Methods: The present retrospective observational study consisted of all consecutive cases of pituitary adenoma treated with endoscopic transsphenoidal surgery (ETS) in Department of Neurosurgery, Kashi Neuron Multispeciality Hospital Ramnagar Varanasi UP, India for the period of 1 year, a total of 50 patients, diagnosed with pituitary adenoma and underwent transsphenoidal surgery, were included.

Results: Of these, 30 patients were diagnosed with non-functioning pituitary adenoma, and 20 were diagnosed with functioning pituitary adenoma. The non- functioning pituitary group consisted of 18 males and 12 females, while the functioning pituitary group consisted of 11 males and 9 females. 8 of non-functioning pituitary adenoma patients were 50–59 years-old, while 8 of the functioning pituitary adenoma patients were < 30 years-old. In the non-functioning pituitary adenoma group, vision and hormones improved in 16.66% (n = 5) patients, while 83.34% (n = 25) did not report any changes within three months postoperation. In the group of patients with tumour that has invaded into the cavernous sinus, vision was improved in 3 patients, while 9 patients did not exhibit any changes. Of these, 3 patients experienced impaired endocrine function post-operatively, while that in the remaining 9 remained normal. The functioning group consisted of 17 acromegaly patients and 3 cushing disease patients. All the hormones were normalised after decompression surgery. This phenomenon was apparent for cortisol, thyroxine, TSH, and prolactin. All the hormones were normalised after decompression surgery. This phenomenon was apparent for cortisol, thyroxine, TSH, and prolactin.

Conclusion: Hormonal preservation and recovery are crucial for assessing the outcome of the surgery and the quality of life of the patient. With the advancement of endoscopy, MRI, and other modern technologies, the operation outcome has significantly improved with fewer post-operative complications.

Keywords: Endoscopy, Pituitary Adenoma, Transsphenoidal Surgery.

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Introduction

Non-functioning pituitary adenomas (NFPAs) are among adulthood's most common benign central nervous system neoplasms, accounting for 15 % of all intracranial tumors, behind meningiomas and gliomas. [1] Although NFPAs are hormonally inactive and relatively benign, they have a propensity for growth and expansion and may directly compromise neurovascular structures closely associated with the pituitary gland. In addition, hypopituitarism may also result from direct mechanical compression and ischemia of the pituitary gland or disruption of the adenohypophyseal portal system. Although endocrine deficits are known to be expected in patients with NFPAs [2], the incidence of hypopituitarism by individual endocrine axes varies

significantly, and a wide range of rates of anterior hypopituitarism has been reported by previous studies. [3-6]

Endoscopic transsphenoidal surgery (ETSS) [7] is a standard surgical procedure performed for the resection of NFPAs. [8-10] Visual field deficits and compression of the optic chiasm are relatively uncontroversial indications for surgery; however, it is unclear if surgical treatment is indicated for patients presenting solely with endocrine dysfunction [11], as hormonal recovery is uncertain [12] and there is a significant risk of the development of new endocrine deficits. The rates of postoperative endocrine recovery of patients who underwent ETSS are poorly characterized, and the

factors associated with recovery are poorly understood.

Non-functioning pituitary adenomas are categorized as macroadenomas when larger than 10mm in diameter. The treatment of choice in patients with non-functioning pituitary macroadenomas (NFPMA) is transsphenoidal surgery (TSS), aiming for preservation or restoration of vision and long-term tumour control. More recently, the endoscopic endonasal technique is emerging as the primary choice for surgical debulking as an alternative to the microscopic approach. [13-15] Regardless of either technique, surgery should only be performed by an experienced dedicated pituitary surgeon as this enhances success rate and reduces complications. [16] Nonetheless, hypopituitarism prevails in a considerable portion of patients following surgery and is expected to worsen if adjuvant pituitary radiotherapy is required.

The aim of the present study was to analyze the remission and preservation of hormones, endocrinological and anatomical complications and visual improvement after endoscopic transsphenoidal surgery (ETS).

Materials and Methods

The present retrospective observational study consisted of all consecutive cases of pituitary adenoma treated with endoscopic transsphenoidal surgery (ETS) in Department of Neurosurgery, Kashi Neuron Multispeciality Hospital Ramnagar Varanasi UP, India for the period of 1 year, a total of 50 patients, diagnosed with pituitary adenoma and underwent transsphenoidal surgery, were included.

All patients diagnosed with functional and non-functional pituitary adenoma treated with ETS were included in this study. Moreover, patients with pituitary adenoma treated with transcranial and microscopic approach and patients treated with endoscopic transsphenoidal procedure but the histopathological examination (HPE) did not report any pituitary adenoma, were excluded.

Patients were managed through a multidisciplinary approach together with neurosurgeon, endocrinologist, neuroradiologist, and ORL surgeon. Pre-operative assessment included hormonal profile and pre-operative optimisation by the endocrinologist and the anesthetist. The radiographic evaluation consisted of a magnetic resonance imaging (MRI) scan, with and without contrast, performed pre-operatively and repeated every 3–6 months during the first year and subsequently every year. The medical records were reviewed to evaluate pre- and post-operative hormonal status, pathology reports, MRI characteristics, operative notes, and clinic follow-up notes from the patient's neurosurgeon and

endocrinologist. All patients were required to have a minimum of three months of post-operative follow-up.

Hormonal Range

All patients underwent a baseline pre-operative pituitary panel and post-operative hormonal evaluation (minimum three months post-surgical follow-up) in a retrospective manner to determine the overall impact on the pituitary gland function. The normal range of hormones was set based on the local lab results.

Before the operation, all patients underwent a hormonal and clinical assessment by an endocrinologist. The biochemical remission of acromegaly is defined as a decrease in growth hormone (GH) < 5.0 ng/mL of functioning pituitary adenomas within 12 days post-operatively. [17] Moreover, the remission of Cushing's disease is defined as the morning (AM) cortisol level < 137 nmol/L within seven days post-operation. [18] For HKL, the current practice is to measure the AM cortisol level on post-operative day 1. If the AM cortisol level is high, the test is repeated on days 3, 7, 14, and 28.

Imaging Characteristics

The pre-operative and post-operative MRI and CT brain reports were reviewed. The formula ABC/2 was used, where A = maximum tumour diameter, B = diameter of the tumour perpendicular to A, and C = maximum height of the tumours as reported on the MRI scan. The degree of resection was calculated by measuring the residual tumour volume in the post-operative scan, which was corroborated by reviewing the surgeons' operation report. [19]

Visual Assessment

The Humphrey's chart is used by a dedicated neuro-ophthalmologist to interpret the visual field and assess the visual acuity pre-operatively, post-operatively, at 3–6 months for the first year, and yearly thereafter.

Complications

The complications, such as rhinological features, CSF leaks, infection, and vascular complications (bleeding), were classified according to the anatomical structures involved in the operative stages. [20,21]

Statistical Analysis

Descriptive analysis was performed using SPSS version 20. Chi-square test was used to study the association between the study groups with respect to the gender and age of the participants, while Fisher's exact test was used to study the association between the study groups and improvement in the vision field. A combination of

chi-square test and Fisher's exact test was used to study the correlation between the study groups and their complications. The pre- and post-operative endocrine outcomes were tabulated in Microsoft Excel. Mc Nemar test was used to evaluate the pre-

and post-operative endocrine outcomes for non-functioning pituitary adenoma patients.

Results

Table 1: Demography for functioning and non-functioning pituitary adenoma patient and Improvement in vision field in non-functioning pituitary adenoma post-operation and preservation of hormone

		Non-functioning pituitary adenoma	Functioning pituitary adenoma
Male		18	11
Female		12	9
Age (years)	< 30	3	8
	30–39	5	3
	40–49	7	2
	50–59	8	6
	> 60	7	1
Improvement of non-functioning pituitary adenoma post-operation			
Improve		5 (16.66%)	
Deteriorated		0	
No changes		25 (83.34%)	

Of these, 30 patients were diagnosed with non-functioning pituitary adenoma, and 20 were diagnosed with functioning pituitary adenoma. The non-functioning pituitary group consisted of 18 males and 12 females, while the functioning pituitary group consisted of 11 males and 9 females. 8 of non-functioning pituitary adenoma patients

were 50–59 years-old, while 8 of the functioning pituitary adenoma patients were < 30 years-old. In the non-functioning pituitary adenoma group, vision and hormones improved in 16.66% (n = 5) patients, while 83.34% (n = 25) did not report any changes within three months post-operation.

Table 2: Improvement in vision field (non-functioning pituitary adenoma) post-operation and invasion to cavernous sinus

Non-functioning	Invasion to Cavernous Sinus	
	Yes	No
Improvement	3	2
Deteriorated	0	0
No	9	16

In the group of patients with tumour that has invaded into the cavernous sinus, vision was improved in 3 patients, while 9 patients did not exhibit any changes.

Table 3: Pre-/post-operative endocrine outcomes for pituitary adenoma patients

Tumour subtype	Normal/Nor-mal	Impaired/Recovered	Impaired/Impaired	Impaired/Worse	Normal/Impaired	Grand total
Functioning	-	8	12	-	-	20
Acromegaly	-	7	10	-	-	17
Cushing disease	-	2	1	-	-	3
Non-functioning	9	17	-	1	3	30
Grand total	9	26	11	1	3	50

Of these, 3 patients experienced impaired endocrine function post-operatively, while that in the remaining 9 remained normal. The functioning group consisted of 17 acromegaly patients and 3 Cushing disease patients.

Table 4: Hormones that improved after ETS

Condition	Improved	Normal
Cortisol level	3	14
Thyroxine level	2	14
TSH level	3	14
ACTH level	2	1
GH level	3	8
PRL level	3	13
LH level	3	12
FSH level	3	12
Testosterone level	1	5
Estradiol level	1	5

All the hormones were normalised after decompression surgery. This phenomenon was apparent for cortisol, thyroxine, TSH, and prolactin.

Table 5: Complications post-endoscopic transsphenoidal excision of pituitary adenoma

Complication	Study group			
	Yes/No	Non functioning pituitary adenoma	Functioning pituitary adenoma	P
Bleeding	No	30	18	0.064
	Yes	0	2	
CSF leak	No	28	18	0.832
	Yes	2	2	
Meningitis	No	30	20	n/a
Rhinological	No	30	18	0.182
	Yes	0	2	
Visual deterioration	No	30	20	0.175
	Yes	0	0	

There were more complications for functioning pituitary adenoma with 2 of the patients suffering post-operative bleeding, CSF leak 2 and rhinological problem 1 as compared to non-functioning pituitary adenoma, wherein only 2 of the patients suffered post-operative complications due to CSF leak.

Discussion

Surgery is a well-established first-line treatment for a host of pituitary lesions. Surgical decompression of the pituitary gland and its stalk may lead to the recovery of hypopituitarism caused by all forms of adenoma in up to 60% of the patients. The primary goal of surgery in pituitary lesions is the maximal removal of the tumour while preserving the gland function. [22]

The comparison of the present study with that of Karppinen [23] revealed a similar female and male ratio and age group; however, compared to the study by Marić et al¹⁹ in 2011, Marić et al.'s study consist of more females than males, and the functioning pituitary group was larger than the non-functioning group. Furthermore, analysing the pre-operative position of the normal gland is a major step of the planning and surgery techniques, especially if the goal is to maintain the function of the pituitary gland. For many patients, maintaining the normal gland has higher priority as compared to the

resection of the tumour. [24] Of these, 30 patients were diagnosed with non-functioning pituitary adenoma, and 20 were diagnosed with functioning pituitary adenoma. The non-functioning pituitary group consisted of 18 males and 12 females, while the functioning pituitary group consisted of 11 males and 9 females. 8 of non-functioning pituitary adenoma patients were 50–59 years-old, while 8 of the functioning pituitary adenoma patients were < 30 years-old. In the non-functioning pituitary adenoma group, vision and hormones improved in 16.66% (n = 5) patients, while 83.34% (n = 25) did not report any changes within three months post-operation. In the group of patients with tumour that has invaded into the cavernous sinus, vision was improved in 3 patients, while 9 patients did not exhibit any changes. Of these, 3 patients experienced impaired endocrine function post-operatively, while that in the remaining 9 remained normal. The functioning group consisted of 17 acromegaly patients and 3 cushing disease patients. All the hormones were normalised after decompression surgery. In the absence of proven medical therapies that can reliably reduce NFPMA tumour mass, initial management is limited to clinical assessment and neurosurveillance with MRI scanning, or surgical resection of the tumour. Previously published data suggest tumour regrowth rates of 15–50% within 5 years after surgery alone [25,26]; size of the post-

operative tumour remnant being a major determinant of regrowth.²⁵ Without adjuvant treatment, regrowth rates of 50–60% were observed after subtotal resection and upwards of 20% after gross total resection with increased length of follow-up. [26,27]

This phenomenon was apparent for cortisol, thyroxine, TSH, and prolactin. There were more complications for functioning pituitary adenoma with 2 of the patients suffering post-operative bleeding, CSF leak 2 and rhinological problem 1 as compared to non-functioning pituitary adenoma, wherein only 2 of the patients suffered post-operative complications due to CSF leak. When compared to the study by Tabae A et al [28], which was based on multiple large cohorts, the reported mortality rate for traditional surgery was < 1%. The 1%–4% reported incidences for both epistaxis and CSF leak were almost similar to the results obtained from the present study. [24]

Conclusion

Hormonal preservation and recovery are crucial for assessing the outcome of the surgery and the quality of life of the patient. With the advancement of endoscopy, MRI, and other modern technologies, the operation outcome has significantly improved with fewer post-operative complications. In the current study, the outcome for the preservation and hormone recovery in the non-functioning pituitary adenoma group was satisfactory. Any visual deterioration and mortality were not observed throughout the study.

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