A retrospective Observational Study Assessing Outcomes after Endoscopic Transsphenoidal Surgery for Non-Functioning Pituitary Adenomas

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Abstract:

Objective: The objective of this study was to examine the remission and preservation of hormones, endocrinological and anatomical problems, and visual improvement following endoscopic transsphenoidal surgery (ETS).

Methods: This observational study looked back at all cases of pituitary adenoma that had endoscopic transsphenoidal surgery (ETS) performed on them in a single 5-year period. Two hundred patients who had pituitary adenoma and had transsphenoidal surgery were a part of this research.

Results: In total, 120 patients had non-functional pituitary adenoma and 80 had functional one. The non-functioning pituitary group had 72 males and 48 females, while the functional group had 44 males and 36 females. Notably, 32 non-functional pituitary adenoma patients were aged 50-59. However, 16 functional pituitary adenoma patients were under 30. Within three months of surgery, 16.66% (n = 20) of non-functioning pituitary adenoma patients reported improvements in eyesight and hormone levels, while 83.34% (n = 100) did not. Twelve patients with cavernous sinus tumors improved their eyesight, while 36 did not. After the operation, 12 individuals had compromised endocrine function, while 36 had normal function. The cohort included 68 acromegaly and 12 Cushing's patients.

Conclusion: In order to assess the success of the operation and the patient's well-being, it is crucial to maintain or restore hormonal function. Modern technology, such as endoscopy and magnetic resonance imaging (MRI), has improved surgical outcomes and decreased postoperative complications.

Keywords:Endoscopy, Pituitary Adenoma, Transsphenoidal Surgery
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1. Introduction

Non-functioning pituitary adenomas (NFPA) are benign tumors that make up approximately one-third of all pituitary neoplasms. They have a prevalence of 7-22 instances per 100,000 population and a normalized incidence rate of 1.02-1.08 per 100,000[1-4].The diagnosis of pituitary hormonal hypersecretion syndromes is not caused by these tumors. Instead, they are typically diagnosed incidentally during radiological imaging for other reasons or when they grow large enough to put pressure on surrounding tissues. This pressure can lead to headaches and/or visual defects due to compression of the optic chiasm[5].Significantly, most individuals exhibit detectable pituitary hormone deficiencies upon initial examination. Studies evaluating the endocrine function in these individuals using different diagnostic criteria have revealed that growth hormone (GH) deficiency is present in 77-88% of patients initially, gonadotropin (Gn) deficiency in 61-78%, while corticotropin (19-53%) and thyrotropin (19-43%) deficiencies are observed to a lesser extent[6].Endoscopic transsphenoidal surgery (ETSS) is a commonly used surgical treatment for removing non-functioning pituitary adenomas (NFPAs)[7-10].Visual field deficits and compression of the optic chiasm are widely accepted reasons for surgery. However, it is uncertain whether surgical treatment is appropriate for patients who only have endocrine

dysfunction[11].This is because the recovery of hormones is uncertain and there is a significant risk of developing new endocrine deficits [12].The rates of postoperative endocrine recovery in individuals who underwent endoscopic transsphenoidal surgery (ETSS) are inadequately defined, and the mechanisms contributing to recovery are not well recognized.

Macroadenomas are classified as non-functioning pituitary adenomas when their diameter exceeds 10mm. Transsphenoidal surgery (TSS) is the preferred treatment for patients with non-functioning pituitary macroadenomas (NFPMA). The goal of this surgery is to preserve or restore vision and achieve long-term control of the tumor. In recent times, the endoscopic endonasal technique has become increasingly popular as the preferred method for surgical debulking, replacing the traditional microscopic approach [13-15].Irrespectiveof the chosen method, it is crucial that surgery is conducted exclusively by a skilled and specialized pituitary surgeon, as this improves the likelihood of success and minimizes complications.[16] However, hypopituitarism is still common in a significant number of patients after surgery and is likely to deteriorate if more pituitary irradiation is needed.

The objective of this study was to examine the remission and preservation of hormones, endocrinological and anatomical problems, and visual improvement following 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) for the period of 5 years. This study was approved by the Research and Ethics committee. In this study, a total of 200 patients, diagnosed with pituitary adenoma and underwent transsphenoidal surgery, were included.

INCLUSION AND EXCLUSION CRITERIA

This study covered all individuals who were diagnosed with both functional and non-functional pituitary adenoma and were treated with ETS.

Additionally, patients who underwent treatment for pituitary adenoma using transcranial and microscopic approaches, as well as those treated with endoscopic transsphenoidal procedures but did not have any pituitary adenoma reported in their histological examination (HPE), were excluded.

METHODOLOGY

Patients were treated using a multidisciplinary approach involving a team of medical professionals including a neurosurgeon, endocrinologist, neuroradiologist, and ORL surgeon. The pre-operative examination involved evaluating the hormonal profile and optimizing the patient's condition before surgery, with the assistance of both the endocrinologist and the anesthetist. The radiographic assessment involved conducting a pre-operative magnetic resonance imaging (MRI) scan, both with and without contrast. This scan was then repeated every 3-6 months in the first year, and then once a year. The medical records were examined to assess the hormonal status before and after the operation, pathology reports, MRI features, surgical notes, and clinic follow-up notes from the patient's neurosurgeon and endocrinologist. Every patient was mandated to undergo a minimum of three months of post-operative follow-up.

HORMONAL RANGE

Each patient got an initial pre-operative pituitary panel and a follow-up hormonal examination at least three months after surgery. This retrospective analysis aimed to assess the overall effect on pituitary gland function. The established range of hormones was determined using the local laboratory findings.

Prior to the procedure, every patient received a comprehensive hormonal and clinical evaluation conducted by an endocrinologist. Acromegaly's biochemical remission is characterized by a reduction in growth hormone (GH) levels to less than 5.0 ng/mL in functional pituitary adenomas within 12 days after surgery [17].Furthermore, the term "remission" in the context of Cushing's illness refers to a situation when the cortisol level in the morning (AM) is less than 137 nmol/L within seven days after the surgery [18].The current protocol for HKL involves measuring the AM cortisol level on the first day after surgery. If the morning cortisol level is elevated, the test is subsequently conducted 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 Humphey'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. McNemar 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

Variables		Non-functioning pituitary adenoma	Functioning pituitary adenoma
Male		72	44
Female		48	36
Age (years)	< 30	12	32
	30–39	20	12
	40–49	28	8
	50–59	32	24
	> 60	28	4
Improvement of non-functioning pituitary adenoma post-operation			
Improve		20 (16.66%)	
Deteriorated		0	
No changes		100 (83.34%)	

Of these, 120 patients were diagnosed with non-functioning pituitary adenoma, and 80 were diagnosed with functioning pituitary adenoma. The non- functioning pituitary group consisted of 72 males and 48 females, while the functioning pituitary group consisted of 44 males and 36 females. 32 of non-functioning pituitary adenoma patients were 50-59 years-old, while 16 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 = 20) patients, while 83.34% (n = 100) 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

		Invasion to Cavernous Sinus	
		Yes	No
Non-functioning	Improvement	12	8
	Deteriorated	0	0
	No	36	64

In the group of patients with tumour that has invaded into the cavernous sinus, vision was improved in 12 patients, while 36 patients did not exhibit any changes.

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

Tumour subtype	Normal/Normal	Impaired/ Recovered	Impaired/ Impaired	Impaired/ Worse	Normal/ Impaired	Grand total
Functioning	-	30	50	-	-	80
Acromegaly	-	26	42	-	-	68

Cushing disease	-	8	4	-	-	12
Non-functioning	36	70	-	2	12	120
Grand total	36	104	46	2	12	200

Of these, 12 patients experienced impaired endocrine function post-operatively, while that in the remaining 36 remained normal. The functioning group consisted of 68 acromegaly patients and 12 cushing disease patients.

Table 4: Hormones that improved after ETS

Condition	Improved	Normal
Cortisol level	12	110
Thyroxine level	12	110
TSH level	12	110
ACTH level	4	2
GH level	12	68
PRL level	12	104
LH level	12	96
FSH level	12	96
Testestrone level	6	44
Estradiol level	4	20

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	Yes/No	Non-functioning pituitary adenoma	Functioning pituitary adenoma	P
Bleeding	No	120	74	0.068
	Yes	0	6	
CSF leak	No	112	72	0.840
	Yes	8	8	
Meningitis	No	120	80	n/a
	Yes	0		
Rhinological	No	120	74	0.182
	Yes	0	3	
Visual deterioration	No	120	80	0.175
	Yes	0	0	

There were more complications for functioning pituitary adenoma with 6 of the patients suffering post- operative bleeding, CSF leak 8 and rhinological problem 6 as compared to non-functioning pituitary adenoma, wherein only 8 of the patients suffered post-operative complications due to CSF leak.

DISCUSSION

Surgery is a widely accepted and commonly used initial treatment for various pituitary abnormalities. Performing surgical decompression of the pituitary gland and its stalk has the potential to restore normal pituitary function in up to 60% of individuals with hypopituitarism caused by any type of adenoma. The main objective of surgery for pituitary lesions is to achieve the most extensive excision of the tumor while maintaining the function of the gland [22].

When comparing the current study to Karppinen's study [23],we found similar ratios of females to males and age groups. However, in comparison to Maric et al. [19] study had a higher proportion of females than males, and the group with functioning pituitary glands was larger than the group without functioning glands. Additionally, examining the pre-operative position of the healthy gland is a crucial aspect of the planning and surgical approaches, particularly when the objective is to preserve the functionality of the pituitary gland. For numerous cases, preserving the intact gland takes precedence over removing the tumor [24].Out of the total, 120 patients were identified as having non-functional pituitary adenoma, whereas 80 patients were

diagnosed with functioning pituitary adenoma. The non-functional pituitary group comprised 72 males and 48 females, whereas the functional pituitary group comprised 44 males and 36 females. Out of the patients with non-functional pituitary adenoma, 32 were between the ages of 50 and 59. On the other hand, among the patients with functioning pituitary adenoma, 16 were less than 30 years old. Among the patients with non-functioning pituitary adenoma, 16.66% (n=20) saw improvements in eyesight and hormones, while 83.34% (n=100) did not report any changes within three months after the operation. Among the cohort of patients with a tumor that had infiltrated the cavernous sinus, 12 individuals saw an improvement in eyesight, while 36 individuals did not demonstrate any alterations. Out of these patients, 12 individuals encountered reduced endocrine function after the operation, while the remaining 36 patients maintained normal endocrine function. The group comprised 68 patients with acromegaly and 12 people with Cushing's syndrome. The hormone levels were restored to normal following decompression surgery. When there are no established medical treatments that can consistently decrease the size of NFPMA tumors, the first step is to examine the patient's condition and monitor their nervous system using MRI scans. Another option is to surgically remove the tumor. Prior published data indicate that the rates of tumor regrowth range from 15% to 50% within a period of 5 years following surgery without any additional treatment [25, 26].The size of the remaining tumor after surgery is a crucial factor in determining its regrowth [25].

Subsequent to partial removal, regrowth rates of 50-60% were noted in the absence of additional treatment. After complete removal, regrowth rates above 20% were observed, with a higher percentage seen as the duration of monitoring extended [26, 27].

The presence of this phenomena was evident for cortisol, thyroxine, TSH, and prolactin. The occurrence of complications was higher in patients with functioning pituitary adenoma compared to those with non-functioning pituitary adenoma. Specifically, 6 patients experienced post-operative bleeding, 8 had CSF leak, and 6 had rhinological problems in the former group. In contrast, only 8 patients in the latter group had post-operative difficulties related to CSF leak. In comparison to the study conducted by Tabaee A et al. [28], which analyzed several extensive groups of participants, the death rate recorded for traditional surgery was less than 1%. The incidence rates of both epistaxis and CSF leak revealed in the present investigation were comparable to the rates of 1%-4% [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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