



Endoscopic Transsphenoidal Hypophysectomy versus Microscopic Transsphenoidal Surgery in the Treatment of Pituitary Adenomas: Evaluation of Results in Terms of Ophthalmic Affection

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Abstract

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BACKGROUND: Neurophthalmologic examination is part of the baseline evaluation of patients with pituitary lesions. The neuro-ophthalmologist quantifies and evaluates the impact that the sellar lesion has on afferent and efferent visual pathways, contributes to the determination of tumor growth dynamics, and monitors the success and possible complications. In cases of vision loss, blurring, damage, or double vision as symptoms of a clinical presentation, the neuro-ophthalmologist is often the first to recognize and define the pituitary lesion.

AIM: The aims of this study are as follows: First, to determine the comparative difference and value of the axis/width of the field of vision in the comparable resection technologies, i.e. fully endoscopic and microscopic/microscopic-assisted hypophysectomy; and second, the extent of resection in both technologies compared with post-operative outcome analysis.

METHODS: The study was designed as a retrospective-prospective clinical trial in the period of 2011–2017. This study enrolled 85 patients, 46 of whom were treated with a microscopic resection, and 39 patients treated only with endoscopic transsphenoidal resection of pituitary adenomas as the subject of this study.

RESULTS: The results of our analysis showed that the achievement of complete, radical, and subtotal resection is significantly higher in the endoscopic technique compared to the microscopic technique. Essentially, better lighting, better viewing angle with no "blind spots," and a perfected toolkit of instruments are the objective factors for progress.

CONCLUSION: The results of our study, comparing the endoscopic version of the microscopic transnasal, transsphenoidal resection of pituitary adenomas, during the period 2010–2018, have unequivocally shown that the endoscopic transnasal transsphenoidal procedure is rational, effective, efficient, and above all safe technique, with a number of favorable advantages that allow for a higher degree of surgical radicality.

Introduction

Microscopic transsphenoidal surgery is a widely accepted and highly effective therapy for pituitary adenomas [1], [2]. In the last decade, more centers have converted from microscopic to completely endoscopic transsphenoidal approach, suggesting that this technique provides more complete tumor resection and/or reduction, controlling the usual complications at the same time [3], [4]. However, only a few worldwide multicentric studies exist to document the results of this procedure.

This study is a comparative overview of both of the above-mentioned surgical procedures in our institution for our population. It presents our experience in the treatment of pituitary adenomas, comparing the two procedures to each other. At the same time, an analogous comparison is made of the outcome of treatment in our institution of patients who have been treated with complete endoscopic transsphenoidal pituitary surgery versus the results of patients treated

with microscopic technique. Its purpose is to establish and implement a procedure that will provide safer, more effective treatment with a better cost-benefit index.

Diagnostic procedures, clinical evaluation

Assessment of patients undergoing surgical treatment of pituitary adenomas begins with a multidisciplinary evaluation of subjective symptoms, objective clinical signs, initially performed by a primary care physician, neurosurgeon, endocrinologist, ophthalmologist, or neurologist. Anatomical and functional assessment of the pituitary gland is of great importance. A neurosurgeon and an endocrinologist evaluate the pituitary lesion. Indications for surgical treatment of pituitary adenomas are based on functional symptoms, objective clinical signs, computed tomography, and magnetic resonance imaging (MRI) findings [5], [6].

Ophthalmic symptoms are manifested by contact or compression of the chiasm and anterior

visual pathways with the lesion [7]. Oculomotor nerve palsy is manifested by penetration and compression of the lesion in the cavernous sinus [8], [9].

Extensive growth of the lesion by suprasellar progression, compression of the third ventricle, compromising the foramen of Monroe, and the liquid flux can potentially cause obstructive hydrocephalus.

Initial symptoms and signs may be discrete latent and are evidenced by sophisticated endocrinological functional tests, but also ophthalmological, and neuroradiological findings.

Surgical treatment of primary adenomas needs to be critically compared to other treatment options such as medical therapy, and sometimes radiotherapy and/or gamma knife, which is often performed as an alternative procedure. An indication for operative treatment is either tumor recurrence or progressive growth in a residual tumor [10].

Study design

This study is a retrospective-prospective randomized clinical trial, evaluating both treatment technologies. The randomization is performed with the patient's free choice of the operative team.

In the period of 2011–2018, 85 patients were treated, respectively, with microscopic and/or endoscopic-assisted technology, as well as endoscopic transsphenoidal resection of pituitary adenomas, that is now the subject of this study. They are processed with inclusive and exclusive criteria. Patients were randomized into two groups. The first group is patients treated with transsphenoidal microscopic and microscopically assisted hypophysectomy. The second group includes patients surgically treated with a fully transsphenoidal endoscopic technique.

The subject of this study will be patients with a recorded lesion, pituitary adenomas, hormonally active as well as hormonally inactive, or dysfunctional. A retrospective review of patient records, post-operative, clinical, and outpatient data was used, and prospective patients will be used to determine the outcome of treatment.

The first group, the majority of treated patients were retrospectively analyzed, until 2014, treated with transsphenoidal microscopic and microscopically assisted hypophysectomy. The second group includes patients surgically treated with a fully transsphenoidal endoscopic technique.

There are several goals defined in this study: First, to determine the prevalence of pre-operative visual acuity affection; second, to determine the type of visual acuity; and third, to determine post-operative ophthalmologic status comparatively in both operating methods.

Materials and Methods

The study was conducted in the University Clinic of Neurosurgery at the Clinical Center Mother Teresa, Skopje, Macedonia. Designed as a retrospective-prospective clinical trial, aiming to evaluate and compare both technologies in the period 2011-2018.

This study treated 85 patients, 46 of whom were treated with microscopic and/or endoscopic-assisted microscopic resection and 39 patients treated only with endoscopic transsphenoidal resection of pituitary adenomas as the subject of this study. Initially treated patients were mainly treated with a microscopic transnasal technique as the only possible option in our institution until 2014.

The procurement of the necessary equipment and resources has opened the possibility for endoscopic assisted and fully endoscopic technology for resection of pituitary adenomas.

Inclusion criteria

The following criteria were included in the study:

- Patients over 14 years of age of both sexes;
- Patients with clinically diagnosed adenomas;
- Patients with sellar lesions which, by configuration, volume and anatomic configuration without distortion, provide safe transsphenoidal resection;
- Patients with lesions in which the diaphragm of the sella is intact;
- Patients with invasive lesions, penetrating over the diaphragm of the sella, but with prior strategy and consent for double phase resection, the first of which is transnasal endoscopic approach;
- Patients with microadenomas with Cushing's disease as life threatening; and
- Patients previously treated with transnasal transsphenoidal microscopic approach, and endoscopically assisted resection with diagnosed recurrence with clinical manifestation.

Exclusion criteria

The following criteria were excluded from the study:

- Patients under 14 years of age of both sexes;
- Patients with lesions with unfavorable anatomical configuration for safe resection along this corridor (close carotid artery, high suprasellar, parasellar tumor extension, cavernous sinus involvement...);

- Patients with sellar lesions of other histological and etiopathogenic structure;
- Patients with microadenomas that are favorable for conservative treatment; and
- Patients with previous operative procedures across this corridor with reported complications and high risks.

Results

Neuroendoscopy is an impressive high-tech surgical procedure, with relaxed, comfortable accessibility, and simplicity, at the same time complemented by continuous expertise in continuous medical education and training, provided with improved field of vision, angle of view, brightness, bimanual manipulation, and better potential for manipulation in case of complications, ensuring marked improvement in the outcome of treating patients with hypophyseal adenomas.

Namely, with the implementation of neuroendoscopy in our institution, the expectations are that there will be a significant improvement and facilitation in the management of sellar pathology, in terms of volume of resection, i.e., less voluminous residual tumor, reduced risk for recurrence, general extended grace period in case of recurrence, improvement of hormonal status, reducing the risk of complications, shortening hospital treatment, or better cost-benefit index.

The results regarding pre-operative visual acuity in both patient groups are shown in Table 1.

Table 1: Pre-operative visual acuity affection

Procedure	Pre-operative visual acuity affection		Total
	No affection	Affected visual acuity	
Microscopic			
Count	12	34	46
%	26.1%	73.9%	100.0%
Endoscopic			
Count	16	23	39
%	41.0%	59.0%	100.0%
Total			
Count	28	57	85
%	32.9%	67.1%	100.0%

In the group of 46 patients treated with microscopic transsphenoidal surgery, 12 (26.10%) patients were preoperatively unaffected and 34 (73.90%) patients were afflicted. In the group of 39 patients treated with endoscopic transsphenoidal approach, 16 (41.00%) patients were preoperatively without visual acuity affection and 23 (59.00%) patients had affected visual acuity.

For Pearson Chi-square = 2.13 and $p > 0.05$ ($p = 0.14$), there was no significant difference between the two groups of patients in terms of pre-operative visual acuity.

Results for the type of visual acuity in the two patient groups are shown in Table 2.

Table 2: Type of visual affection

Procedure	Type of visual affection						Total
	Scotoma	Hemianopsia	Reduced acuity	Amblyopia	Amaurosis	Diplopia	
Microscopic							
Count	9	11	7	0	6	1	34
%	26.5%	32.4%	20.6%	0.0%	17.6%	2.9%	100.0%
Endoscopic							
Count	1	6	8	5	3	0	23
%	4.3%	26.1%	34.8%	21.7%	13.0%	0.0%	100.0%
Total							
Count	10	17	15	5	9	1	57
%	17.5%	29.8%	26.3%	8.8%	15.8%	1.8%	100.0%

In the group of 34 patients undergoing microscopic transsphenoidal surgery, the following results were obtained with regard to the type of visual acuity: 9 (26.50%) patients had visual field scotoma, 11 (32.40%) patients had hemianopsia, 7 (20.60%) patients had reduced acuity, 6 (17.60%) patients had amaurosis, and 1 (2.90%) patients had diplopia.

In the group of 23 patients treated with endoscopic transsphenoidal approach, the following results were obtained in terms of the type of visual acuity: 1 (4.30%) patients had visual field scotoma, 6 (26.10%) patients had hemianopsia, 8 (34.80%) patients had reduced acuity, 5 (21.70%) amblyopia, and 3 (13.00%) patients had amaurosis.

For Fisher's exact test = 12.89 and $p < 0.05$ ($p = 0.015$)/Monte Carlo Sig./0.012–0.018/there is a significant difference in the type of visual acuity in patients treated with both operating methods.

Results regarding post-operative ophthalmologic status in patients with pre-operative visual acuity treated with both operating methods are shown in Table 3.

Table 3: Post-operative ophthalmologic status in patients with pre-operative visual affection

Procedure	Post-operative ophthalmologic status				Total
	Unchanged	Partially improved	Significantly improved	Normalized	
Microscopic					
Count	14	14	6	0	34
%	41.2%	41.2%	17.6%	0.0%	100.0%
Endoscopic					
Count	0	2	14	7	23
%	0.0%	8.7%	60.9%	30.4%	100.0%
Total					
Count	14	16	20	7	57
%	24.6%	28.1%	35.1%	12.3%	100.0%

Of the 34 patients treated with microscopic transversal surgery, in 14 (41.20%), the post-operative ophthalmologic status remained unchanged; in 14 (41.20%), the post-operative ophthalmologic status partially improved; and in 6 (17.60%), the post-operative ophthalmologic status was significantly improved.

Of the 23 patients treated with endoscopic transsphenoidal approach, in 2 (8.70%), the post-operative ophthalmologic status was partially improved; in 14 (60.90%), the post-operative ophthalmologic

status improved significantly; and in 7 (30.40%), the post-operative the ophthalmic operating status was normalized.

For Fisher's exact test = 34.16 and $p < 0.001$ ($p = 0.000$)/Monte Carlo Sig., there is a significant difference in post-operative ophthalmologic status in patients treated with both operating methods.

Discussion

Pituitary adenoma surgery has gradually evolved toward less invasive approaches, primarily the transsphenoidal corridor, with endoscopic technique. There has been more and more evidence that endoscopic surgery is a safe, minimally invasive alternative for the treatment of pituitary adenomas [11], [12], [13], [14], [15], [16]. Endoscopy is already expanding borders, eliminating surgical limitations, improving performance, primarily by improving visualization, lighting, and reliability, allowing removal of lesions that were inaccessible by prior technology and corridors. It is already clearly noted that the feature of minimal invasiveness significantly affects the positive outcomes and lowers the post-operative complications in endoscopic procedures compared to the microscopic approach [17].

The results of our meta-analysis clearly favor endoscopic technology for pituitary surgery compared to microscopic technique. The endoscopic approach was a significant improvement in the extend of resection, with a markedly reduced number and volume of lesion residues, and thus a reduced number and volume of recurrent adenomas, followed by shorter hospital stay/treatment, less incidence of defects, and bleeding. Furthermore, there was a significant improvement in complications such as meningitis, cerebrospinal fluid (CSF) fistula, hypopituitarism, and diabetes mellitus.

Preoperatively, visual acuity is almost identical in both groups. Post-operative ophthalmologic examinations (ophthalmologic examination, visual acuity, perimetry, fundus, and VEP), by comparison, showed a significant difference.

Namely, of 34 patients with preoperatively affected visual acuity that was treated microscopically, 14 remained unchanged, 14 had partial improvement, and 6 had significant benefit.

The group treated with the endoscopic approach reported improvement in almost all patients. In 2 patients, there was a partial improvement in 14 significant improvements and in 7 patients, post-operative normalization was achieved.

In addition, comparing cross-tabulation findings, volume of resection and post-operative ophthalmologic status in patients with pre-operative

visual acuity affection, there is a significant difference in favor of endoscopic technology.

In our opinion, this difference is due to a number of objective and subjective factors. Endoscopic technology, although two-dimensional, provides the full panorama of a well-lit field of vision in the sella itself, supra and partially antero-sellarly, with a clear view of the chiasm, as well as optic nerves securely decompressed by radical resection, with preservation of the arachnoid and their anatomic CSF cisterns, documented with post-operative MRI which is only partially possible or not at all possible with microscopic technology. This option is certainly a result of technical progress as well as continuous training of the team itself, with growing agility, security, reliability, and expertise.

Conclusion

The results of our study, comparing the endoscopic versus microscopic transnasal, transsphenoidal resection of pituitary adenomas, have unequivocally shown that the endoscopic transnasal transsphenoidal procedure is a rational, effective, efficient, and above all safe technique, with numerous favorable advantages that allow for a higher degree of radicality.

Safe radical resection – gross total resection is the primary goal of every surgical oncologist, including this procedure, by providing neoplasm resection, preventing recurrence, and minimizing complications, thereby reducing/eliminating residuals, prolonging the grace period, i.e., tumor-free interval, better endocrinological, ophthalmologic and oncologic results, reduction of hospital days of patient stay, reduction of frequency and hazard of intra- and post-operative complications, and crucial to improve the general and specific quality of life of patients. These are inevitable factors for the promotion and establishment of endoscopic transsphenoidal resection of pituitary adenomas in the future as a possible gold standard in the treatment of these lesions.

Certainly, nowadays, both technologies still have their place in the treatment of pituitary adenomas, but the technological evolution of optical equipment, and in symbiosis with continuous education and training of pituitary surgeons, will inevitably become a new global standard in the treatment of pituitary adenomas.

It is undisputed that this complex procedure is possible only as team collaboration with an endocrinologist, ophthalmologist, otorhinolaryngologist, neuroradiologist, anesthesiologist, oncologist, and as a long-term, comprehensive, and complex process of treating patients.

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