



Endoscopic versus Microscopic Transsphenoidal Hypophysectomy: Comparison of the Endocrine Outcome – An Institutional Experience

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Abstract

BACKGROUND: The transnasal transsphenoidal endoscopic approach to the sella turcica is an overwhelming alternative to the microscopic approach for the past few decades assuming into prominence as a new technique, reaching nearly gold standard for this pathology. The endoscopic approach to the pituitary has redefined accurate visualization of the sella. The panoramic view afforded by the endoscope is unparalleled as compared with the traditional conical view of the microscope.

AIMS: This study aims to compare both endoscopic and microscopic technologies, including advantages and disadvantages through the results of endocrine outcome.

SETTINGS AND DESIGN: Our retrospective/prospective study included 46 microscopically and 39 endoscopically treated patients during the period of 2010–2018. Tumors were classified according to the diameter and clinical outcomes were evaluated.

RESULTS: Our retrospective/prospective study included 46 microscopically and 39 endoscopically treated patients during the period of 2010–2018. Tumors were classified according to the diameter, hormone activity and clinical outcomes were evaluated. Comparison results revealed more efficacious and effective endocrine control and reestablishing the endocrine homeostasis utilizing the endoscopic technique, especially in secretory active macroadenomas. Further, the extension of the resection, which was better in endoscopic approach undoubtedly contributed to better endocrine control of the disease. Complication rate, including endocrine, was lower following endoscopy compared with microsurgery.

CONCLUSION: This technique evidenced to have a statistically significant reduction in operative time and length of hospital stay, as well as more radical safe resection and complication control. There is also a trend toward improved endocrine outcomes and rate of return of visual defects. These two approaches are still comparable with eloquent advantages and disadvantages, formulated as balanced dialectics. In addition, the use of endoscopes, including multilocular polifilament 3D endoscope, facilitates extended approaches, reaching a delicate skull base lesions that are suprasellar, retrosellar, and parasellar, which permits visualization beyond the abilities of the microscope.

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Introduction

Pituitary adenoma is the third most common intracranial tumor in surgical practice, accounting for approximately 10–25% of all intracranial tumors [1]. Recent epidemiological data suggest that clinically apparent pituitary adenomas have a prevalence of 1/1000 in the general population [2], [3]. Although only very rarely malignant, pituitary tumors may cause significant morbidity in affected patients where why they demand total resection, and their treatment remains challenge [4].

Transsphenoidal surgery of the pituitary evolves continually beginning from the early 20th century, initially assigned by Schmidt *et al.*, which were the first to report a sellar tumor through transsphenoidal route in 1907 [5], [6]. Cushing successively focused and popularized sublabial transseptal transsphenoidal

corridor in the following decades [7]. Abandoned for several decades, this technique revived with Hardy in the early 1960s, introducing the operative microscope nearly becomes a standard approach causes it provided minimal morbidity and mortality [8]. The rapid global expand in the past two–three decades emerged with Jankowski, who proposed fully endoscopic approach to pituitary lesions in 1992 [9]. The current high-tech development of optics, radiodiagnostics, high sensitivity radio essays, informatics, instrumentation, surgical devices, and utility tissue high-tech materials incorporated with human innate sickness for prospect, lead to milestone progress at this field. Endoscopic transsphenoidal surgery presents safe, efficacious, effective, and minimally invasive surgery of the pituitary, which allows surgeons to gain access to central skull base lesions in a secure manner defining probably the gold standard for the future.

Comprehensive cadaveric dissections, with 3D evaluation in the learning curve of the pituitary

surgeons, provided meaningful baseline for expansion in this field [10].

The current endoscopes are two dimensional and cannot provide stereoscopic three-dimensional view compared with the operative microscope. This fact dictates evaluated equivocal rationale and balanced dialectics between these two technologies. The emerging new technology of 3D multilocular polifilament endoscopes supposed to overwhelm this insufficiency.

The purpose of this study was to compare the outcomes and the complications associated with these techniques by comparing endoscopic with microscopic surgery in the treatment of pituitary adenomas, emphasizing the endocrine aspect.

Materials and Methods

Our study included eighty-five patients harboring pituitary adenoma, operated in our institution during the period of 2011–2018. According to the technology, they were separated in two groups. The first group of 46 patients treated with transsphenoidal microscopic and endoscopically assisted microscopic technique and the second group of 39 patients operated on fully endoscopically.

Inclusion criteria

The following criteria were included in the study:

- Patients with adenoma over 14 years old
- Patients with clinically evident adenoma
- Patients with sellar lesion, according to the configuration, volume, and anatomy provide safe transsphenoidal endoscopic resection without distortion
- Intact diaphragm
- Patients with supra and parasellar lesion, previously assessed for two steps resection, initially transnasal
- Patients with microadenoma with Cushing disease
- Previously transsphenoidal microscopically operated patients with recurrens and clinical manifestation.

Exclusion criteria

The following criteria were excluded from the study:

- Patients bellow 14 years old
- Lesions unfavorable anatomically for safe endoscopic resection (kissing carotids, high suprasellar and/or parasellar, intraorbital

- propagation, or cavernous sinus engagement)
- Other histopathological lesions
- Microadenomas favorable for conservative treatment
- Previously endoscopically treated patients with evident complication and high risk

Comprehensive neurological examination including motor, sensory, and cranial nerve examination has been performed, including visual field, acuity, fundus, and evoked potentials. Routine blood and basic hormonal profile were performed. Magnetic resonance imaging (MRI) brain and paranasal sinuses including sella computed tomography (CT) were performed in all patients. All patients underwent the standardized microscopic or endoscopic procedure and were provided a uniform post-operative care.

All procedures were performed under general anesthesia with orotracheal intubation.

We used 4 mm diameter sinonasal rigid endoscope, "Karl Storz," Tuttlingen, Germany, spheric 0–0 and 30°. Initial phase was decongestive of the mucosa of the septum and turbinates. Consecutively, the middle meatus and sphenoid rostrum have been identified and drilled to enter the sphenoid. Delicate drilling was to open the sellar floor. The dura was opened in a crucial manner. Further, with delicate dissection with the pituitary instruments, the tumor has been removed, primarily posterior and superior aspect and finally lateral and anterior portion prospectively. Second, the tumor site, the sella has been inspected with a 30° endoscope. After the tumor resection, the basal cisternal arachnoid emerges downward pulsating. Hemostasis is completed usually with Surgiflo liquid surgical. The tumor cavity and sphenoid were packed with fat and sealed with fibrin glue. Nasal packing was done with Meroceol up to the middle meatus. In most cases, lumbar drain has been placed for 72 h.

Microscopic surgery was standardized and similar, except introducing Hardy's nasal speculum and done under visualization with a microscope pp "Pentero," Zeiss, Germany.

The hormonal profile, highly sensitive assays, and visual function evaluation including VEP, MRI, and CT scanning were repeated immediately and after 1 month of surgery and were compared with pre-operative findings, both for endoscopic and microscopic procedures.

Statistical analysis

Statistical analysis was performed with Statistica 7.1 for Windows and SPSS Statistics 23.0 (SPSS Inc., Chicago, IL, USA).

The analysis of the patient series with attributes (gender, clinical diagnosis, pre-operative hormone activity, type of pre-operative hormone activities, quantity of resection of the lesion, post-operative assay

in secretory tumors, and the categorical data) were presented as numbers (percentage - %).

The differences between the two technologies (microscopic transsphenoidal and endoscopic transsphenoidal surgery) were compared using Pearson Chi-square test (p), Pearson's Chi-square test/Monte Carlo sig. (p), and Fisher's exact test/Monte Carlo sig. (p).

The cross-tabulation between the two groups has been performed with Pearson's Chi-square test/Monte Carlo sig. (p), and Fisher's Exact Test/Monte Carlo Sig. (p).

Results

Within the group microscopically treated, 33 were male and 13 female patients. Nineteen were male and 20 were female in the group treated endoscopically.

The mean age of the patients with microscopic procedure was 54.22 ± 12.64 years (ranged 28–75 years).

The mean age of the patients endoscopically treated was 50.87 ± 12.65 years (ranged 12–72 years).

The results of the pre-operative hormone activities in both groups of pituitary adenomas are exposed in Table 1.

Table 1: Pre-operative hormone activities in both groups of pituitary adenomas

Variable	Pre-operative hormone activity		Total
	Non-secretory (non-active)	Secretory (active)	
Procedure			
Microscopic			
Count	13	33	46
%	28.3	71.7	100.0
Endoscopic			
Count	11	28	39
%	28.2	71.8	100.0
Total			
Count	24	61	85
%	28.2	71.8	100.0

Within the group of 46 microscopically treated, 13 (28.30%) were secretory non-active and 33 (71.70%) were functional, secretory active.

Within the group of 39 endoscopically treated, 11 (28.20%) were preoperatively inactive, non-secretory and 28 (71.80%) were secreting active adenomas.

By Pearson's Chi-square = 0.00 and $p < 0.05$ ($p = 0.99$), no significant difference according to the secretory activity has been noted.

Compared results postoperatively, according to the radicality of resection associated with secretory active adenomas are revealed in Table 2.

In the group of 33 secretory active microscopically treated lesions, 5 (15.20%) remained unchanged, 18 (54.50%) experienced partial non-significant

Table 2: Postoperatively results, according to the radicality of resection associated with secretory active adenomas

Variable	Post-operative assay in hormone secretory adenomas		Total
	Significant improvement	Normalized	
Radicality of resection			
Up to 90%			
Count	7	3	10
%	70.0	30.0	100.0
Over 90%			
Count	6	12	18
%	33.3	66.7	100.0
Total			
Count	13	15	28
%	46.4	53.6	100.0

improvement, 9 (27.30%) experienced significant improvement, and 1 (3.00%), the vision was normalized.

In the group of 28 secretory active endoscopically treated lesions, 13 (46.40%) post-operative vision has been significantly improved and 15 (53.60%) had normalization of the vision.

For Fisher's exact test = 40.22 and $p < 0.001$ ($p = 0.000$)/Monte Carlo sig./0.000–0.000/there is a significant difference in post-operative assay between the groups of hormone active lesions treated microscopically and endoscopically.

The results of the post-operative assay of the group with endocrine active lesion microscopically treated, associated with the quantity degree of resection are evident in Table 3.

In the group of 33 patients with hormonally active microscopically treated lesion, in 7 (21.21%), the resection has been achieved up to 50%, in 22 (66.67%) up to 75%, and in 4 (12.12%) subtotal resection up to 90%.

Postoperatively, within the group of 7 patients with resection up to 50%, in 4 (57.10%), the hormone activity remained unchanged, and in 3 (42.90%), the hormone activity improved partially.

In the same group, where the resection has been performed up to 75%, in 1 (4.50%) hormone activity remained unchanged, in 13 (59.10%) partially improved, in 7 (31.80%) significantly improved, and in 1 (4.50%), the hormone activities have been normalized.

In four patients of this group, where the resection has been achieved up to 90%, in 2 (50.00%), the hormone activity has been partially improved and in 2 (50.00%) significantly improved.

The cross-tabulation of the results between the degree quantity of resection and post-operative hormone activity for the lesions treated with transsphenoidal microscopic surgery for Fisher's exact test = 11.43 and $p < 0.05$ ($p = 0.033$) / Monte Carlo sig./0.028–0.037/ delineated significant difference.

The group of 28 patients with pre-operative secretory active adenomas, treated with transsphenoidal endoscopic resection, comprised 10 (35.71%) with subtotal resection up to 90% and 18 (64.29%) with resection over 90%.

Postoperatively, of the subgroup with subtotal resection up to 90%, in 7 (70.00%), the hormone

Table 3: Post-operative assay of the group with endocrine active lesion microscopically treated, associated with the quantity degree of resection

Variable	Post-operative assay in secretory active adenomas				Total
	Unchanged	Partially improved	Significantly improved	Normalized	
Type of hormone activity preoperatively					
STH secretory					
Count	0	7	1	0	8
%	0.0	87.5	12.5	0.0	100.0
PLC secretory					
Count	3	1	0	0	4
%	75.0	25.0	0.0	0.0	100.0
ACTH secretory					
Count	0	1	0	0	1
%	0.0	100.0	0.0	0.0	100.0
TSH secretory					
Count	0	0	1	0	1
%	0.0	0.0	100.0	0.0	100.0
STH, PLC secretory					
Count	2	9	7	1	19
%	10.5	47.4	36.8	5.3	100.0
Total					
Count	5	18	9	1	33
%	15.2	54.5	27.3	3.0	100.0

activity was significantly improved and in 3 (30.00%) normalized.

The compared results of post-operative hormone assay of the two groups of patients treated microscopically and endoscopically are exposed in Table 4.

Table 4: Results of post-operative hormone assay of the two groups of patients treated microscopically and endoscopically

Variable	Post-operative assay in secretory active adenomas				Total
	Unchanged	Partially improved	Significantly improved	Normalized	
Procedure					
Microscopic					
Count	5	18	9	1	33
%	15.2	54.5	27.3	3.0	100.0
Endoscopic					
Count	0	0	13	15	28
%	0.0	0.0	46.4	53.6	100.0
Total					
Count	5	18	22	16	61
%	8.2	29.5	36.1	26.2	100.0

In 33 patients microscopically treated, 5 (15.20%) remained unchanged, 18 (54.50%) experienced partial improvement, 9 (27.30%) experienced significant improvement, and in 1 (3.00%), post-operative secretory activity was normalized.

In 28 patients endoscopically treated, 13 (46.40%) experienced significant improvement, and in 15 (53.60%), the post-operative hormone activity was normalized.

The Fisher's exact test = 40.22 and $p < 0.001$ ($p = 0.000$)/Monte Carlo Sig./0.000–0.000 depicted significant difference in the outcome pp post-operative hormone assay in the compared groups treated microscopically and endoscopically.

Discussion

Pituitary tumors surgery still represent a significant challenge, despite the highly refined nature, evolved high technology, informatics, and training

and learning advance of the contemporary micro and endoscopic surgery. The endoscope as a device introduced to this technology has been widely accepted for the past three decades. High technology evolution of the optics provides progressive trends toward less invasive approach. Evidently, the endonasal endoscopic approach is less invasive, efficacious, safe, and effective to the pituitary gland and local surrounding structures, supplemented with better intraoperative illumination, image, angle, and wideness of surgical and working field.

Guiot is the recognized first pioneering surgeon introducing endoscope in transsphenoidal approach [11].

Reisch *et al.* defined that the endoscope contributes to comprehensive panorama to the anatomy, introducing the concept of minimally invasive surgery [12]. Song *et al.*, in 1992, introduced the fully endoscopic concept as an approach to sellar region [13].

Keyworth *et al.* with largest prospective study series (215 patients) and Khan *et al.*, with series of 170 patients traced the pathway of this technology as dominant and safe [14], [15].

First comparison between microscopic and endoscopic technique performed by Khan *et al.*, in a retrospective study in 1999 [2], [15].

Yadav *et al.*, presented comparison of the two technologies with evident improvement and advance of the transsphenoidal endoscopic versus transsphenoidal microscopic technology, concerning visuality, quantity of resection, and complication control [16].

Schwartz *et al.* proceeded step forward, defining the concept of balanced dialectics of both technologies.

Endoscopic transsphenoidal pituitary surgery is developing technique becoming nearly standard procedure for pituitary lesions, and consequent comparison with microscopic transsphenoidal surgery is and will be committed only to delineate the advantages and disadvantages.

Three-dimensional visibility and almost unnecessary additional training for microneurosurgeons are still the advance.

On the other hand, endoscope provides full exquisite panorama of the surgical site, minimal damage to the nasal cavity, no invisible angle, better illumination, better vision and distinguishability of the lesion surface, better bleeding control, better bimanual manipulation, no speculum, in addition much wider surgical operating field better resection, less complication, less operative time, and early discharge.

Certainly, learning curve and process of training much more demand for this technology.

Furtheron, introducing the multifocal multifilament endoscope as a technological innovation provides 3D vision of the surgical field, eliminating the handicap compared to 3D operative microscope.

In our study, we present a comparison of these two technologies, the ability and quantity of resection, associated with endocrine function outcome compared pre- and postoperatively.

In the present study, there was safer and significantly more radical resection accomplished within the group endoscopically treated, consequently with better endocrine outcome and less complication.

This result is entirely compatible with the recent studies, pp previous prospective study done by Jain *et al.* who concluded less post-operative complication, less operative time in endoscopic transsphenoidal group as compared to transsphenoidal microscopic technology.

Conclusion

For the past decades, the endoscopic transsphenoidal pituitary surgery becomes a milestone in operative treatment of pituitary lesions mostly comprising adenomas. It provides direct endonasal minimally invasive corridor, panoramic view inside the sphenoid cavity, and sella. Endoscopic transsphenoidal pituitary adenoma surgery is defined as safe, efficacious, effective, minimally invasive, with wider and direct anatomical control of the operative field, better illumination, wide angle without blind angle field, resulting with greater, faster and safer potential of tumor excision with respect to the sphenoid, and sellar and parasellar anatomical structures. Conclusively, higher possibility and potential for more radical resection provided better general outcome result and free of disease interval including much better in our study, endocrine overall outcome.

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