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## Original article

# Surgical Outcome of Endoscopic Transsphenoidal Surgery for Giant Pituitary Adenoma

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## ABSTRACT

**Background:** Pituitary adenomas are benign neoplasms representing 10 to 15% of intracranial lesions. Giant pituitary adenomas describe tumors more than 4 cm in maximum diameter and represent 6-10% of pituitary tumors. The introduction of truly 'extended endonasal' approaches has enabled the pituitary surgeon to achieve a more radical resection safely.

**The aim of the work:** Evaluation of efficacy of the endoscopic endonasal approach in managing giant pituitary adenoma.

**Patients and methods:** Fifteen patients with giant pituitary adenomas were enrolled. They were submitted to full clinical examination, radiological, visual, and hormonal assessment in the pre and postoperative period. A purely endoscopic endonasal approach was used as the primary surgical management for all the patients. The collected data included preoperative data, tumor characteristics, resection rate, clinical outcome, recurrence rate, and need for adjuvant radiotherapy

**Results:** The mean age was 40.7 [range 16-57] years, with a male predominance [60%]. Visual affection was reported in [86.6%] with pituitary hormonal hypersecretion in 53.3%. There was an improvement in 80% of patients with visual field defects and 83.3% of patients with diminished visual acuity. Prolactin hormone levels normalized in 40%, while growth hormone normalized in 33.3%. Follow-up MRI revealed gross total resection [GTR] in 41.6% of patients with suprasellar extension, subtotal removal [about 80% of the tumor] in 50% of patients, partial tumor resection in one patient [8.4%]. In para-sellar extension, subtotal resection achieved [in 66.6%], and partial resection in 33.3%. Postoperative CSF leak occurred in 13.3% due to incomplete reconstruction of the sella. They were reoperated for sella repair and augmentation. Three patients [20%] had transient [for 3 weeks] postoperative diabetes insipidus [DI] in the early postoperative period.

**Conclusion:** Endoscopic endonasal approach is an effective and safe approach for managing giant pituitary adenomas.

**Keywords:** Pituitary; Giant; Transsphenoidal; Endonasal; Endoscopic; Adenoma.

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\* Main subject and any subcategories have been classified according to the research topic.

## INTRODUCTION

The pituitary gland, [also known as a hypophysis], is an organ of neuroendocrine system, situated in the "sella turcica" in the base of the skull. It consists of two main parts [adenohypophysis formed by the anterior and the medial parts; and the neurohypophysis formed by the posterior part. The pituitary gland is responsible for homeostasis, and reproductive function. Thus, its abnormalities lead to a wide spectrum of diseases [1].

Pituitary adenomas represent about 10% to 15% of all intracranial tumors and 50-80% of pituitary tumors. Most benign adenomas arise from the anterior pituitary. In general populations, imaging and postmortem studies recognized an incidence of 20-25% of pituitary adenomas; however, only about one third of them are clinically evident [2-3].

Classically, pituitary tumors are classified into functional [or secreting] and non-functional [non-secreting]. In general secreting tumors tend to present earlier due to symptoms caused by physiologic effects of excess hormones that they secrete. Non-secreting tumors usually do not present until they are sufficiently large enough to cause neurological deficits by mass effect. They also can be classified according to size for microadenoma less than one centimeter, macroadenoma more than 1cm and giant adenoma more than 4cm [4-5]. Giant pituitary adenomas are defined as tumors larger than 4 cm that usually extend within 6 mm of the foramen of Monro. However, this definition has not always been homogeneous in literature. However, the majorities of published studies use the described one. Giant adenomas represent about 6-10% of all pituitary tumors. They are mostly clinically nonfunctioning and occur predominantly in males [6-7].

There are different modalities to manage giant pituitary adenomas. Surgery is considered the first line treatment for most giant pituitary tumors, except for prolactinomas. Its main objective is the maximum possible safe resection, preserving the neurological function. The most used approach routes have been the microscopic transsphenoidal surgery [MTS], and transcranial [TC] approaches, reserved for giant pituitary tumors with important supra- and parasellar extension. However, the development of endonasal endoscopic transsphenoidal surgery [EETS] since the late 1990s has expanded the limits of transnasal

approaches to these tumors and the whole skull base [8].

Today, in most reference centers, EETS is adopted as the first surgical option for the vast majority of giant pituitary adenomas [9]. The first line management of giant prolactinomas is the use of dopamine agonists. Somatostatin analogs could also be used as a therapeutic option in a growth hormone and producing giant tumors, although remission is not achieved in the majority of these conditions. Surgical treatment through transsphenoidal approaches is the standard curative treatment option in most patients [10].

The endoscopic transsphenoidal approach follows the same principle and aims of the standardized microsurgical techniques, i.e., management of apoplexy, removal of mass effect, normalization of hormonal hypersecretion, prevention of recurrence, and sampling of tissues to confirm diagnosis. It can be performed in two ways: the endoscopically assisted approach and a purely endoscopic endonasal transsphenoidal approach [11-12].

The initiation of the endonasal endoscopic approach to resect pituitary adenomas is one of the most crucial milestones for the management of pituitary tumors since 1997. After the initial reports of endoscopic pituitary surgery by Cappabianca and his colleagues, the technique has gained wide acceptance worldwide and represents the standard surgical approach for sellar lesions [13].

A panoramic vision of the surgical site, a near close-up of the anatomy, and a better working angle are some advantages of endoscope use for pituitary surgery. Nevertheless, fewer nasal cavity injuries, without the use of nasal speculum or fluoroscopy, and patient's fast recovery are also another benefits. Compared to the sub-labial incision, morbidity is reduced, mainly related to reduction of the upper lip and nasal complications [14].

The combination of endoscopic technique with extended transsphenoidal approaches allowed more effective resection of the large and giant pituitary adenomas extending into the suprasellar and parasellar regions previously considered to be done using a transcranial approach or only for surgical debulking using the transsphenoidal approach [9].

The results of the pure endoscopic endonasal

approach for tumor resection and clinical outcome in pituitary macroadenomas have been reported extensively in the literature in the last decade; it has also been extensively compared to the results obtained by microsurgery<sup>[15]</sup>.

### AIM OF THE WORK

Evaluation of efficacy of the endoscopic endonasal approach in managing giant pituitary adenoma in regards to the resection rate and clinical outcome. Assessment of the safety of the approach and the complication rate.

### PATIENTS AND METHODS

This study included 15 patients with giant pituitary adenomas with suprasellar and parasellar extensions. They were treated in the neurosurgery department [Al-Azhar University Hospital, Damietta, Egypt] between January 2019 and Dec 2020. The patient must have a pituitary adenoma of more than 4 cm to be included. However, if the size is smaller than 4 cm, or the sphenoid sinus was nonpneumatized, the patient was excluded from the study. The preoperative assessment was clinical, laboratory [hormonal and routine], and radiological. The preoperative clinical assessment was complete medical history, physical examination, and detailed neuro-ophthalmological examination. The visual field, visual acuity, and fundus examination were carried out. The lab workup formed of full pituitary hormones [serum prolactin level, serum Adrenocorticotrophic hormone [ACTH] and cortisol levels, serum growth hormone [GH] and Insulin-like growth factor I [IGF-I] levels, thyroid-stimulating hormone [TSH], Follicle-stimulating hormone [FSH], Leutinizing hormone [LH] assessment and routine laboratory investigations. Also, thyroxin hormones [T3 and T5] and testosterone levels were assessed. Finally, all patients had radiological investigations by CT brain, CT nasal and paranasal sinuses, and the MRI brain. Visual assessment was repeated in the postoperative period before discharge, three months after surgery, and then annually. The ocular motility was tested before and after surgery. The hormonal assessments were repeated on the third week and three months later during the follow-up and then annually. All the 15 patients had multislice parasagittal, coronal, and axial CT scan cuts of the nose, paranasal sinuses, and sellar area; this diagnostic technique was the basic study to determine the precise anatomic

features of the surgical route. Tumor size was evaluated by high-resolution MR imaging for all cases. MRI in axial, sagittal, and coronal images before and after gadolinium diethylenetriamine penta-acetic acid intravenous injection. The grade and stages of the pituitary tumors were classified using Hardy's classification system<sup>[16]</sup>.

Surgical procedures: Endoscopic endonasal transsphenoidal approach [EETA] was completed as described by Sankhla *et al.*<sup>[17]</sup>

Postoperative evaluation: Uncomplicated cases stayed in the hospital for 3 to 5 days, nasal packs were removed on the third to fifth postoperative day. The patient was monitored for nasal or post-nasal CSF drainage for at least several hours after removing the packs. Postoperative ophthalmologic assessments included visual acuity using Snellen Wallchart, ocular motility, and visual field using Goldman Kinetic Perimeter or confrontation method. Patients with pituitary adenoma rather than ACTH secreting adenoma were given hydrocortisone 100 mg every 8 hours and tapered on the next 5 days. Prophylactic antibiotics with intravenous third-generation cephalosporins continued until removing the nasal packing, with frequent body temperature monitoring. CT and MRI brain were done in severe headaches, sudden deterioration of vision, or deterioration of the conscious level.

A protocol for monitoring fluid balance and detecting diabetes insipidus [DI] during the postoperative period had been well established. A Foley catheter was routinely inserted on the first day, fluid intake and output were carefully recorded, and patients were questioned regarding thirst. Blood glucose and serum electrolytes [including sodium, potassium] were determined. Serum sodium may be evaluated more frequently when indicated. DI was diagnosed if the patients' urine-specific gravity is 1.004 and had documented voluminous urine output more than [3cc/Kg/hour] for 3 consecutive hours and in the absence of glycosuria. If the patient was diagnosed with DI, the patient had replacement therapy first by IV fluid then by ADH by minrin 0.2% every 6, 8, or 12 hours according to the patient's condition. The patient neurological condition, vital signs, CSF leakage, urine output, hormonal profile, laboratory investigation, the pathological diagnosis of the tumor, and the patient medication at home were reviewed and recorded in the

hospital records before discharging the patient from the hospital to be used in the follow-up period of the patient.

**Patients follow-up:** The patients were re-examined in the follow-up period by an attending neurosurgeon and otolaryngologist one month after surgery, 3 months, and then 6 months.

Data obtained in the follow-up

**Hormonal outcome:** The postoperative hormonal values were done 3 weeks postoperatively. The lowest values were documented after long-term follow-up. For prolactinomas, tumor remission was defined as a normal serum PRL level less than 20ng/ml; for GH secreting adenoma, remission was defined as normal age-corrected IGF-I values.

**Radiological outcome:** For uncomplicated cases, a follow-up MRI was done three months postoperatively, the pre and postoperative MRI were compared for residual or recurrent tumor existence. The radiological outcome was classified into; total, subtotal [80% tumor removal], partial removal, and cavernous residual.

**Visual and another clinical outcome:** was classified into; improved, stationary, and worse. The outcome was verified by submitting clinical, hormonal, and radiological findings.

**Ethical considerations:** The institutional review board [Faculty of Medicine, Al-Azhar University] approved the study protocol. The study was also completed according to the research ethics codes provided by World Health Organization [2017].

**Statistical considerations:** the sampling size determination was completed by convenient sample due to the rarity of the condition. Data were summarised by statistical measures according to the data type: quantitative data presented as mean and standard deviations, while categorical variables presented as relative frequency and percentages.

## RESULTS

This work was carried out on 15 patients operated upon for giant tumors. Their age ranged between 16 and 57, the mean age 40.7 years, and 60 % were males. The clinical presentation was mainly by visual complaints [86.7%], headache [73.3%], endocrinal [53.3%], and the least was cranial nerve affection [13.3%]. The reduced visual acuity was reported

among 80.0% [53.3% bilateral and 26.7% unilateral] and visual field defects reported among 66.7% [bi-temporal hemianopia 53.3% and mono-temporal hemianopia 13.3%]. Third cranial nerve palsy reported in 6.7% and six nerve in 6.7%. Clinically nonfunctioning pituitary adenoma [CNFPA] was the commonest tumors [7 patients; 46.7%], and prolactinoma was the commonest functioning adenoma [5 patients; 33.3%]. The other three patients had growth hormone-secreting adenoma. The sphenoid sinus pneumatization was sellar [80.0%] and pre-sellar in 20.0%. Preoperative assessment of tumor extension results in 80.0% of supra-sellar extension and 20.0% of parasellar extension. Two patients [13.3%] were staged A, 26.7% stage B, 40% stage C, and 20% were stage E.

Regarding peri-operative data, the median operative time was two hours, and no patient needed an intraoperative blood transfusion. Three patients [20%] had postoperative facial pain and discomfort, and all patients had postoperative nasal packs. The hospital stay duration ranged between 3 to 5 days for non-complicated and from 7 to 10 days for complicated cases.

The main intraoperative problems were SCF leak, difficult tumor resection [tough], bleeding and nose problems [septal deviation and hypertrophied turbinate] among 3, 3, 1, and 3 patients, respectively

The postoperative complications are presented in table [1]. Diabetes insipidus [DI] was the commonest postoperative complication followed by cerebrospinal fluid [CSF] leak. Postoperative Diabetes insipidus [DI] was a temporary event and reversible within three weeks, and there are no permanent DI cases in our study. In this study, the only death case complicated intraoperative by excess bleeding and CSF leak developed 3<sup>rd</sup> day postoperative disturbed conscious level, urgent CT brain showed interventricular hemorrhage [IVH], follow up CT brain showed obstructed hydrocephalus underwent VP shunt 5<sup>th</sup> day postoperative but she died.

In the present study, three cases needed postoperative 2<sup>nd</sup> surgical intervention, two of them complicated postoperative by CSF leak needed surgical intervention for sellar repair. The other patient complicated postoperative by interventricular hemorrhage then obstructed hydrocephalus underwent VP shunt 5<sup>th</sup> day postoperative.

The vision improved in 10 patients [83.3%] out of 12 patients, stationary only in 2 patients [Table 2]. Prolactin level returns to normal in 2 patients out of 5 patients. The remaining three patients' prolactin levels decreased but did not return to its normal value, and they received medical treatment postoperatively to control high prolactin levels. Growth hormone level normalized in 1 patient out of 3 patients suffered from acromegaly in the other patient decreased but did not return to its normal level [Table 3].

The radiological outcome of suprasellar giant adenoma revealed that gross total resection was completed for 41.6%, subtotal resection for 50.0%, and partial resection for 8.4%. On the other line, gross total resection could not be achieved for any cases with para-sellar giant adenoma, subtotal resection achieved for 66.7%, and partial resection for 33.3%.

At the end of the one-year follow-up, two patients in this study received gamma knife radiosurgery for the tumor's remnant part. Two patients showed recurrence of the tumor and performed 2<sup>nd</sup> surgery in less than one year; one received a gamma knife later after the second operation.

Here are some illustrative cases; the first was a male patient, 16 years old, presented with headache, blurring of vision, delayed puberty, absent secondary sexual characters, decreased pubic and axillary hair, history of cabergoline intake 5 months ago with no

improvement. Vision assessment: bilateral temporal hemianopia. The full hormonal profile showed increased serum prolactin level. MRI brain with contrast showed giant pituitary adenoma with the suprasellar extension [Hardy's classification stage c]. The endonasal endoscopic transsphenoidal approach is used for the excision of pituitary adenoma. Postoperative gross total resection, visual field improved, serum prolactin level decreased then normalized 2 months later by medical treatment [Figure 1]. The second patient was a male patient 57 years old who presented with bilateral vision diminution more at left eye and headache. Visual assessment: left eye temporal hemianopia, Visual acuity: Right 6/18, Left 6/36. Stable hormonal profile. MRI showed giant pituitary adenoma, Endonasal endoscopic transsphenoidal approach used for excision of pituitary adenoma postoperative vision improved MRI showed gross total resection [Figure 2]. The third case was a female patient 29 years old who presented with bilateral vision diminution more at left eye associated with headache and Acromegalic features. Visual acuity [VA]; Right eye counting fingers 60cm, Left eye: hand motion, Hormonal assessment: increased GH level. Postoperative vision improved, GH level decreased, and post-MRI showed subtotal excision with the right parasellar residual. GH level controlled by medications 3 months later, underwent Gamma knife radiosurgery for residual 6 months later [Figure 3].

Table [1]: Postoperative complication

	No.	%
Diabetes insipidus [DI]	3	20
CSF leak	2	13.3
Pnumocphalus	2	13.3
Meningitis	0	0
Vision deterioration	0	0
Death	1	6.6

Table [2]: Visual outcome

	Improved	Stationary
Diminution of vision	10	2
Field defect	8	2
6TH nerve palsy	1	0
3rd nerve palsy	0	1

Table [3]: Hormonal outcome

	Normalized	Decreased
Prolactin	2	3
GH	1	2
Total number of patients	3	5
%	37.5%	62.5%

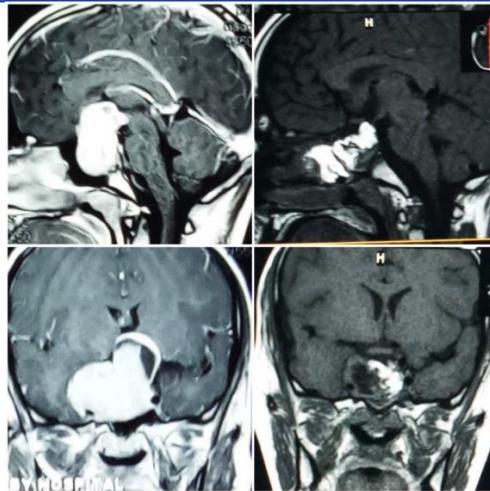


Figure [1]: Sagittal and coronal of MRI pre and postoperative showing complete tumor removal with fat graft within the sellar region

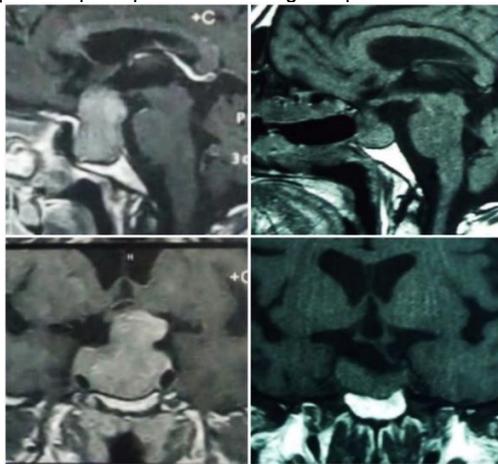


Figure [2]: Sagittal and Coronal MRI pre and postoperative showing gross total resection with fat graft within sellar space

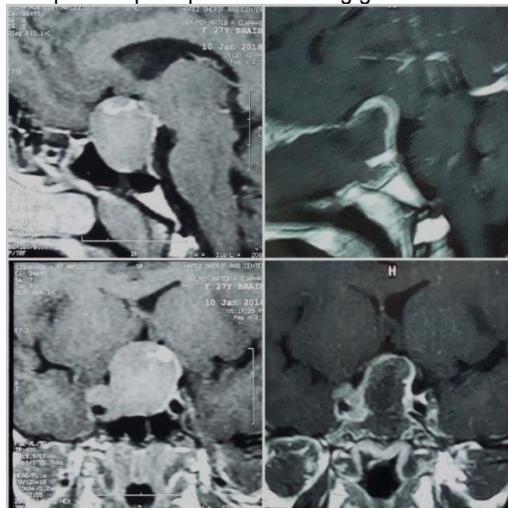


Figure [3]: Pre and postoperative MRI showed subtotal resection and Right parasellar cavernous residual of the tumor.

**DISCUSSION**

The present work presented the clinical experience and outcome of endoscopic transsphenoidal Surgery for Giant Pituitary Adenoma from a tertiary care hospital. Results showed that the giant pituitary tumors

were more frequent in males [60%], and the mean age was 40.7 years. Juraschka *et al.*<sup>[18]</sup> included 73 patients with older age [average age 54.5 years], and 68.5% were males. This study confirmed the male-sex predilection for giant pituitary tumors and reflected a wider range of ages that could be affected by the

tumor. Different selection criteria could be responsible for variation in patient age.

In the present study, visual symptoms were the most frequent presentations because 80% of patients with pituitary adenoma had a suprasellar extension with subsequent compression on the optic apparatus. Juraschka *et al.* [18] reported comparable distribution [57.5% had reduced visual acuity and/or 45.2% presented by visual field deficits. Forty-seven patients out of 73 patients [64.4%] were found to have endocrine dysfunction before surgery. Before surgery, 9.6% experienced ophthalmoplegia.

In the current work, the headache was the second frequent symptom in this study, and it was found in 73.3 % of the patients; the severity of headache ranged from mild to severe. Gondim *et al.*[9] reported that patients with pituitary macroadenoma usually present with a headache even without a demonstrable suprasellar extension. Small changes in the intrasellar pressure caused by macroadenoma within the confined sella are sufficient to stretch the diaphragm sellae with a resultant headache. The severity of the headache didn't correlate with the size of the adenoma or the presence of suprasellar extension.

MRI with intravenous contrast was done for all studied cases preoperative and postoperative for follow-up in our work. This is in line with Boxerman *et al.* [19], who stated that MR is the method of choice to imaging the pituitary gland and the parasellar area. Advanced MR techniques – MR diffusion, MR spectroscopy, and MR perfusion have been increasingly applied.

The main goals of surgery for pituitary giant adenomas are restoration or preservation of vision, preservation of pituitary function, recovery of neurological symptoms, and maximal safe tumor removal with the achievement of tumor control [10]. The current study revealed improvement of visual field defects in 80.0% and improved visual acuity among 83.3%. The basis for these favorable endoscopic results regarding visual improvement was attributed to better visualization of the suprasellar area, which was not limited by the tubular channel created by the nasal speculum. The gland-diaphragm distinction was easier and better visualized by 0° and angled endoscope, so the tumor was removed totally with subsequent decompression of the optic apparatus [20].

In the present study, there were no cases with postoperative visual deterioration. After endonasal endoscopic transsphenoidal surgery [EETS], the visual prognosis is usually excellent, with a significant improvement in most patients [62–80%]. Previous works showed a worsening after surgery in only a small percentage [<5%][18,21]. Besides, among the different approaches, EETS has proven to be much more effective than the microscopic transsphenoidal [MTS] or Transcranial [TC] approach to improve visual prognosis[22]. Current results agree with the study by Cappabianca and his colleagues [23], who compared the visual outcome between the microscopic and the endoscopic technique. They found that the average of visual improvement was reported between 56 % and 66% using a microscope and between 62% and 92% using an endoscope. Hofstetter *et al.* [24] in a prospective study about the endoscopic endonasal approach for pituitary adenoma in 71 patients documented improvement of vision in 80% of cases. Also, Paluzzi *et al.* [15] documented visual recovery in 81% of the 237 patients presenting with vision impairment.

The prolactin hormone level normalized in 2 out of 5 patients [40%]. Growth hormone level normalized in 1 out of 3 [33.3%]. In a study performed by Jho[25] on 150 patients operated by endonasal endoscopic approach, among the 38 patients with prolactinoma, 25 patients [66%] normalized their postoperative prolactin level. Among the 13 patients with acromegaly, 11 patients [85%] had normalized postoperative IGF-1 levels. In the study of Cappabianca *et al.*[23], 160 patients were operated endoscopically, the normalization of prolactin hormone level was achieved in 77% of patients, improvement of acromegalic features with normalization of GH occurred in 78%. In a study performed by Dehdashti *et al.* [26], 34 patients had GH secreting tumors. After the endoscopic resection, 24 patients [71%] presented with biochemical cure with normalized GH and insulin-like growth factor-1 levels and adequate suppression to an oral glucose tolerance load. Six patients had no residual tumor evidence on MRI scanning and showed improvement in hormonal levels that did not fulfill the cure criteria. The remaining four patients with no remission after surgery had cavernous sinus involvement and were referred for radiation treatment. Endoscopic resection achieved gross tumor resection

with normalization of PRL levels and subsequent remission in 22 of 25 [88%] of these patients. The remaining three patients with persistently high PRL levels continued the dopamine-agonist therapy after surgery, and those with cavernous sinus involvement [2 patients] were referred for radiosurgery.

Regarding the radiological outcome in our study, the gross total resection [GTR] in 41.6% of patients with suprasellar extension, subtotal removal in 50% of patients, partial tumor resection in one patient 8.4%. For patients with Para sellar extension, the subtotal resection achieved in 66.6%, and partial resection in 33.3%, with no gross total resection achievement shown in this study in a patient with para sellar extension. The incomplete removal of the tumor was due to the tumor's fibrous nature and the presence of part of the tumor above and laterals to the carotid artery. The extent of tumor resection is guided by the parasellar extension of the tumor in MRI and its relation to the carotid artery. The most important factor in determining the degree of tumor resection was cavernous sinus invasions<sup>[27]</sup>. Dehdashti *et al.*<sup>[26]</sup> published a series of 200 patients, among which 98 patients had suprasellar extension without cavernous sinus involvement, and total gross removal was achieved in 96%. 18 patients had macroadenoma with cavernous sinus invasion [9%]. No attempt was made to remove the tumor's intra cavernous content radically.

Jho<sup>[25]</sup> published a series with 150 patients with pituitary adenomas operated by endonasal endoscopic approach; 90 cases were nonfunctioning, 71 were totally removed [79 %]. He reported that the endoscope resulted in a lower incidence of complications related to blind dissection and provided better accessibility through its angled lenses for complete tumor removal. Moreover, Cappabianca *et al.* <sup>[13]</sup> reported favorable results after a complete endoscopic approach for removing residual or recurrent pituitary tumors.

In Zada *et al.*<sup>[28]</sup> study, 109 patients had been operated on through the microscopic transsphenoidal approach; in patients with nonfunctioning pituitary adenomas, complete tumor removal was in 95% of noninvasive macroadenomas, 40% of invasive macroadenomas, and 33% of giant adenomas, respectively. The lower remission rates of tumor removal were associated with invasive and giant adenomas.

In Komotar *et al.*<sup>[29]</sup> conducted a systematic review [1995–2010] to compare endonasal endoscopic transsphenoidal approach [EETS] with microscopic transsphenoidal [MTS] and open transcranial [TC] resection in giant pituitary adenomas. The EETS cohort had higher rates of gross total resection [47.2%] compared with the MTS [30.9%] and open TC [9.6%] cohorts. The EES cohort also showed an improved visual outcome [91.1%] compared with MT surgery [34.8%] and open TC [45.7%] cohorts, with lower morbidity and mortality. Given the size and extension of these tumors, the complete resections rate is low regardless of the approach. However, if we consider the near-total resection [>90%], the rate rises to 56%–84.6%.

The endoscope's better visualization allowed the surgeon to identify the carotid prominences, optic chiasm, normal pituitary gland from the tumor, and the diaphragm sella. Recognizing these structures during pituitary tumor removal was critical to avoid such complications, which had been reported in several microscopic series.

In the present study, CSF leakage was the commonest intraoperative problem present in 3 patients out of 15 [20%]. It was observed that the incidence of CSF leakage was more common in adenomas with suprasellar extensions due to excessive manipulations along the stretched diaphragm sellae, which led to arachnoid tear with resultant CSF leakage. In a study performed by Cappabianca *et al.* <sup>[23]</sup> on 160 patients, Sellar repair was done in 47 patients [27.6%]. In patients with an intraoperative CSF leak, proper packing of the sella with or without packing of the sphenoid sinus was performed. Postoperative CSF leak is one of the most important complications of pituitary surgery. The endoscopic surgery series variation is 1.2–6%<sup>[15]</sup>.

Repair techniques using different types of grafts and flaps and enhancing these techniques over time markedly affected the postoperative leak rate. Also, better visualization and better familiarity and experience with the endoscopic endonasal approach affected postoperative leak rate. Haddad *et al.* <sup>[30]</sup> presented the novel technique using a vascularized nasoseptal flap based on the sphenopalatine artery was a great turning point that caused a remarkable decrease of the postoperative CSF leak. Many centers worldwide have developed and tailored their repair

technique after endoscopic endonasal surgeries for the pituitary tumors and skull base lesions using the vascularized nasal septal mucosa flap as a final layer over the onlay graft [31].

In our study, a postoperative CSF leak occurred was reported in two patients [13.3%] operation. The treatment of these two patients' postoperative CSF leaks consisted of reoperation for sellar repair and sellar floor augmentation. In the study of Dehdashti *et al.* [26] the rate of CSF leakage after endoscopic surgery was 3.5%.

In the recent series about the outcome of endoscopic endonasal approach in 228 pituitary adenomas, Gondim *et al.* [13] reported that postoperative CSF leak was present in 3.1% of the patients in the first 150 cases of this series. The last 78 cases had no CSF leak. The absence of CSF leak in the last 78 cases is due to a vascularized nasal septal mucosa flap as a final layer over the onlay graft, followed by Foley catheter as a buttress that is removed in 48 hours.

Paluzzi *et al.* [15] reported in his endoscopic series on 555 pituitary patients that in spite of the fact that the rate of intra-operative CSF leak has remained similar before and after the use of the vascularized flap, the postoperative CSF leak rate has dramatically decreased from 11.5 to 2.9 % after the introduction of the nasoseptal flap.

In the present study, 3 patients [20%] had postoperative diabetes insipidus [DI] in the early postoperative period. It was a transient event for 3 weeks or less in all 3 patients. No permanent diabetes insipidus reported in our study. In Zada *et al.* [28] study, 109 patients had been operated on through the microscopic transsphenoidal approach, permanent diabetes insipidus [DI] was in 8% of cases

In this study, we had one case of pituitary adenoma mortality with huge suprasellar extension complicated intraoperative by CSF leak and excess bleeding. The patient developed disturbed conscious level 3rd day postoperative, the patient admitted to ICU all investigations were done including CT brain which showed interventricular hemorrhage for conservative treatment, more disturbed of conscious level happened on 5<sup>th</sup> day, CT brain follows up showed obstructed hydrocephalus, the patient underwent VP shunt 5<sup>th</sup> day postoperative; eventually, he died.

A wide range of intraoperative complications of the microscopic procedure was reported in many studies as diastases of the maxilla or fracture of the hard palate caused by overspreading of the speculum, fracture of the orbit, injury, or fracture of the cribriform plate. Also, optic and chiasmal injuries were reported in microsurgical trans-sphenoidal technique due to inability to determine normal gland from the tumor, and blind tumor dissection. None of these complications were encountered in our study. In Zada *et al.* [28] study, 109 patients were operated on through the microscopic transsphenoidal technique; the rate of surgical complications in this series was 3% for CSF leakage, 2% for meningitis, and 1% for carotid artery injury.

Comparative studies between microscopic and endoscopic transsphenoidal surgery regarding their complications were reported in different studies. Jho [25] compared between the endoscopic and microscopic transsphenoidal pituitary surgery, anterior pituitary insufficiency was found in 2.7% versus 19.4%, diabetes insipidus in 2.7% versus 17.8%, visual loss in 0% versus 1.8%, meningitis in 0% versus 1.5% and postoperative tumor hemorrhage in 2.7% versus 2.9%. However, CSF leakage incidence was higher in the endoscopic series, 6.7% versus 3.9%.

Anesthesia of the upper lip, saddle nose, nasal septum perforations, and anosmia caused by nasal septum dissection were late postoperative complications reported in different microscopic trans-sphenoidal surgeries; none of these complications reported in our study. In the study of 109 patients operated through the microscopic endonasal transsphenoidal approach, there was no need for sublabial incision or dissection of the nasal mucosa, so there were no nasoseptal perforations hematomas, or abscesses had been seen in this series, and only one patient required surgery for a postoperative mucocele. The questionnaire results showed serious complaints from patients concerning poor nasal airflow; nasal congestion, anosmia, facial pain, and upper lip numbness were the only 1 to 4% of patients [28].

Jho [25] studied 150 patients who were operated on endoscopically; he reported a lower rate of complications [one case of sinusitis, three cases with CSF leakage, seven cases had endocrine complications]. The basis for these lower complications rate was attributed to a wider overview inside the anatomy facilitated by the endoscope and the

decreased surgical trauma. In Cappabianca's study<sup>[23]</sup>, three patients complicated with sinusitis and mucocele of the sphenoid sinus among 146 patients were operated on by the endoscopic procedure, one out of three cases was symptomatic, and the other two patients had no symptoms; all were managed with medical treatment. This incidence [2.05%] was lower than that in most reports of complications of the microscopic transsphenoidal operation [1- 4%]. The reason for the decreased such complications and sinusitis, in particular, was the opening of the sphenoid ostium area, with respect to the osteomeatal complex, without using a transsphenoidal retractor. The best strategy for dealing with surgical complications was to avoid them. This depended on understanding the disease, the surgery, and the surgical techniques needed to obtain the optimal results.

Excellent results with minimal complications were not only dependent on the extent of tumor removal, but also other factors included a good view of the surgical target and adequate preservation of all structures around the lesion [pituitary gland and stalk, suprasellar cistern, cavernous sinus, and its contents].

Other studies performed by Cavallo *et al.*<sup>[32]</sup> reported that both endoscopy and microsurgery allowed effective transsphenoidal procedures that minimized functional and technical problems compared with those of the transcranial approach and its related brain retraction. The microscope had been essential in the development of a reliable procedure, with excellent-quality optical images, three dimensions, good depth of field, and comfortable surgical access because of the transsphenoidal retractor. The endoscope offered the opportunity for less intraoperative trauma and detailed inspection of the anatomy near the site of surgery, but it required a specific set of endoscopic skills that were acquired after a relatively long learning curve.

Conclusion: The minimally invasive Endoscopic endonasal transsphenoidal approach was found to be an effective and safe approach for the management of giant pituitary adenomas regarding resection rate, clinical outcome, and postoperative complications.

#### Financial and Non-financial Relationships and Activities of Interest

None

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