OPEN AIMJ ORIGINAL ARTICLE

Neurosurgery

Endoscopic Endonasal Transsphenoidal Approach for Growth Hormone Secreting Pituitary Adenoma

Abdullatif Motawie Ahmed[1,*] M.B.B.ch., Adel Ragab Almelesy[1] MD., and Alazzazi Rabei Alazzazi [1] MD.

** Corresponding Author:*
Abdullatif Motawie Ahmed
abdellatifhantour@gmail.com

Received *for publication April 06, 2022;* ***Accepted*** *September 25, 2022;* ***Published online*** *September 25, 2022.*

doi: 10.21608/aimj.2022.131785.1905

Citation: *Abdullatif M. Adel R. and Alazzazi R. Joint Degeneration Cycle: Endoscopic Endonasal Transsphenoidal Approach for Growth Hormone Secreting Pituitary Adenoma. AIMJ. 2022; Vol.3-Issue9 : 158-164.*

[1]Department of Neurosurgery, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.

ABSTRACT

Background: The use of endoscopic endonasal trans-sphenoid surgery (EETS) as the first-line therapy for most pituitary adenomas is gaining popularity.

Aim of the work: The primary goal of this research was to see how transsphenoidal endoscopic technique for a growth hormone-secreting pituitary adenoma affected hormonal reduction in relation to surgical excision extent.

Patients and Methods: This prospective research was carried out at the Al Azhar University Hospitals' neurosurgery department (Al-Hussein and Bab El-Shaeria). This study was conducted on 15 cases with Growth hormone secreting pituitary adenoma that had undergone total or subtotal resection performed by endoscopic endonasal transsphenoidal surgery.

Result: there was highly statistically substantial (p-value < 0.001) decreased post-operative growth hormone (3.4 ± 1.2) when compared with pre-operative growth hormone (38.1 ± 29.8). Highly statistically significant (p-value < 0.001) decreased post-operative IGF-1 (242.3 ± 102.1) when compared with pre-operative IGF-1 (665 ± 253). No statistically significant difference (p-value > 0.05) between pre-operative and post-operative the following hormones (ACTH, cortisol, T3, T4, TSH, testosterone, FSH, LH and PRL, estradiol).

Conclusion: In individuals with acromegaly, the endoscopic endonasal transsphenoidal technique is an efficacious and secure treatment for adenomas. We discovered that using an endoscopic endonasal transsphenoidal technique reduced growth hormone and insulin-like growth factor-1 levels considerably.

Keywords: *Acromegaly; Growth Hormone secreting pituitary adenoma; Endoscopic endonasal surgery.*

Disclosure: *The authors have no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the authors.*
Authorship: *All authors have a substantial contribution to the article.*

INTRODUCTION

Pituitary neoplasms are benign tumors and mainly originate from adenohypophysis, classi¬fied differently according to their size or endo¬crine function. Pituitary microadenomas are defined as a group tumor of less than one cen¬timeter in diameter, correspondingly all the oth¬ers greater than acetimeter in diameter are called as pituitary macroadenomas.[1]

Except for prolactinoma, pituitary adenomas account for 10-22.5 percent of all primary intracranial tumors, and surgical excision is the first choice for treatment. [2]

Suppression of hormone hypersecretion, decrease of tumor bulk, maintenance of normal pituitary function, avoidance of long-term consequences from excess hormone secretion, and avoidance of tumor recurrence are all aims in the treating of those with pituitary lesions. [3]

The majority of pituitary adenomas occur in the anterior lobe of the pituitary gland and may be removed selectively with transsphenoidal adenomectomy, preserving pituitary function while eliminating the tumor. Some adenomas, on the other hand, develop inside the pituitary stalk and stay there. Other adenomas of the pituitary gland originate in the upper section of the anterior lobe and spread into the stalk. [4]

Acromegaly is a dangerous condition that, if left untreated, is linked to a higher likelihood of morbidity and death.

Adenomas of the pituitary gland that secrete growth hormone (GH) cause acromegaly. GH hypersecretion may cause a variety of symptoms and indications, ranging from acral overgrowth and soft tissue edema to diabetes and heart failure. This presentation may include visual field abnormalities and headaches as a result of the growing tumor. [5]

During transsphenoidal pituitary surgery, neurosurgeons can now see obscure anatomical corners thanks to the use of endoscopes. [6]

Since 1997, one of the most considerable advances in the treatment of pituitary lesions has been the advancement of the endonasal endoscopic procedure for the resection of pituitary adenomas. The procedure has expanded around the globe and is currently the standard surgical treatment for sellar lesions in many neurosurgery facilities. [7]

The goal of the research was to see how an endoscopic transnasal transsphenoidal technique for a growth hormone-secreting pituitary adenoma affected hormonal decrease in relation to surgical excision extent.

PATIENTS AND METHODS

From September 2019 to August 2021, prospective study research was conducted on fifteen (15) patients who were operated on at the neurosurgery department at Al Azhar University Hospital "Al-Hussein" and "Bab El-Shaeria.". In this study, all Patients had been diagnosed as Growth Hormone secreting Pituitary lesion and underwent Endoscopic Endonasal Trans sphenoidal Procedure, assessed and evaluated as for preoperative, intraoperative, and postoperative. Neurological, endocrinological and radiological evaluations were assessed preoperatively as well as after surgery. This study covered all patients who had endoscopic endonasal transsphenoidal Procedure for Growth Hormone Pituitary Tumors. Before the trial, all patients completed an informed consent form.

The exclusion criteria: Patients with recurrent tumor, patients unfit for surgery, failure of pneumatization of sphenoid sinus and Patients with history of Radiotherapy .

Ethical considerations: All the necessary approvals for carrying out the research were obtained. An official approval for implementation of the study was obtained from Neurosurgery department before starting the study. The Ethical Committee of Al-Azhar University's Faculty of Medicine gave its approval to the research.

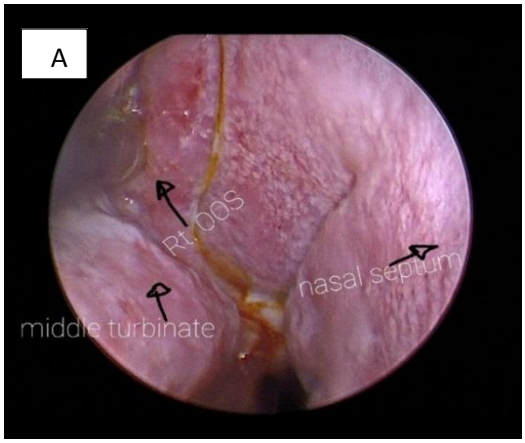
Methods

Preoperative Evaluation: All patients were submitted to the following items: Full history taking, Examination: included general, neurological examination and ophthalmological evaluation, Endocrinological assessment: (pre-operative hormonal profile) Lab. assessment (GH, IGF1, Prolactin, FSH, LH, ACTH, TSH, cortisone, T3, T4, and Testosterone, Estradiol). These hormonal assessments were repeated 3 months post operative during the follow up. Radiological assessment: Pre-operative MRI with contrast, CT sella and para nasal sinuses, Assessment of fitness for surgery by an anesthesiologist and all patients who included were fit. All patients were informed about the surgical techniques, the likelihood of failure, and the necessary after care. All patients signed a written permission form.

Surgical technique: Anesthesia, positioning and draping: To establish a normotensive state with a low pulse rate, general anesthesia with total intravenous anesthesia (TIVA) is used. Operative procedures: Nasal phase: The endoscope was placed into the nostril parallel to the MT, in line with the floor of the nasal canal, to see the choana first, then the anterior wall of the sphenoid. Sphenoidal phase : After palpating the sphenoid ostium using a blunt dissecting tool, it was opened. With angled punches, the front wall of the sphenoid was opened wide. To improve exposure, a tiny portion of the posterior nasal septum was removed. Sellar phase and removal of the tumor: A dissector was used to open the sella's floor, followed by Kerrison upcutting forceps. The size of the aperture is determined by the size of the sella and the distance between the two carotid arteries, but it should be big enough to allow for tool insertion and provide a clear view of the adenoma for removal. The pituitary gland was discovered by the neurosurgeon during surgery. The dura was incised in a linear or cruciate pattern in the midline. In individuals with macroadenomas, the superior and inferior intercavernous sinuses were generally squeezed and destroyed, rendering the dural incision bloodless.

The excision of macroadenomas was carried out in stages. Before the upper aspect of the lesion was excised, the inferior and lateral pieces were eliminated. Sellar reconstruction: The goal of this procedure was to provide a watertight seal, eliminate dead space, and inhibit the chiasm from descending into the sellar cavity. Nonetheless, excessive packing must be avoided to avoid optic system compression. In rare situations, sellar packing was done using gel foam and fibrin glue.

Postoperative follows up: Antibiotics as a preventative measure Serial visual examination and monitoring of endocrine functions (post-operative hormonal profile) and metabolic state were part of the postoperative follow-up. The majority of patients were released on the second or third postoperative day, with frequent outpatient clinic follow-up (follow-up protocol: one week, one month, three months, six months), and home therapy maintained if necessary. On the second day following surgery, a follow-up MRI was performed. Every patient's case sheet was filled with the required information. The study's biggest flaw was the small number of instances it included. This research also had a brief follow-up procedure. The study's findings were obtained by statistical analysis of the gathered data.



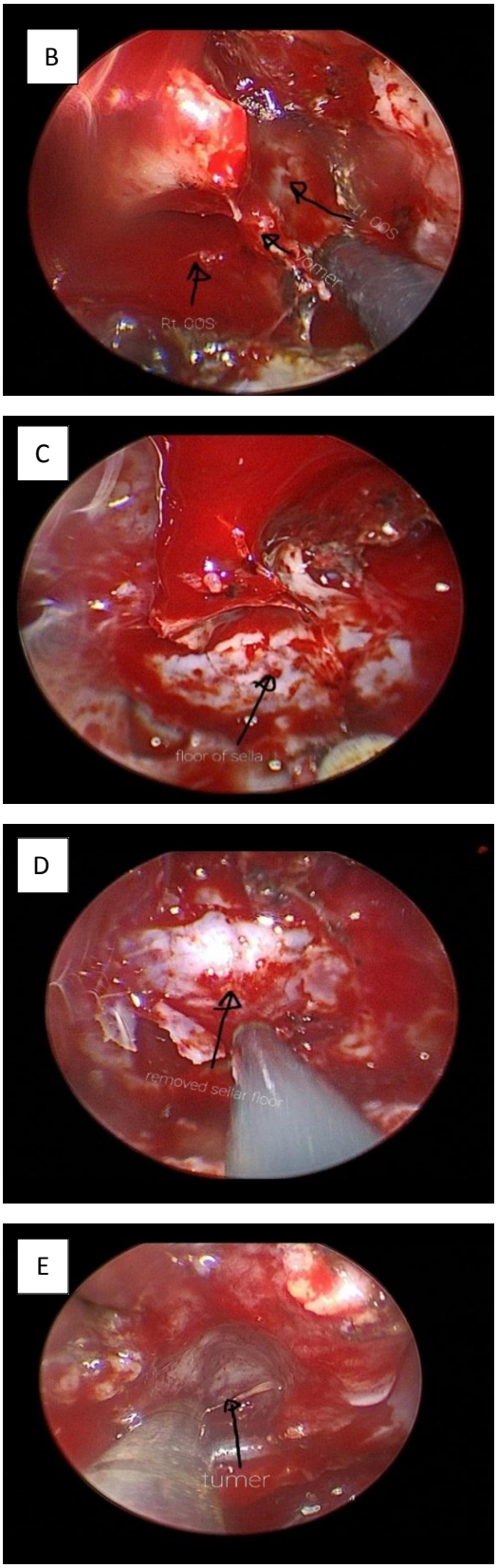


Fig. 1: various steps of the approach and tumor resection (a) nasal phase (b) sphenoidal phase (c) sellar phase (d) removal of sellar bone part (e) removal of pituitary tumor

RESULTS

Demografic Data:

Tabe (1) 15 patients were joined in this research, 8 males (53.3%) and 7 females (46.7%), between ages of 19 to 64 years the median age of all analyzed patients was 41.3 ± 16.07 years underwent endoscopic endonasal transsphenoidal surgery.

		Studied patients (N = 15)	
Age (years)	**Median ±SD**	41.3 ± 16.07	
	Min – Max	19 – 64	
Sex	**Male**	8	53.3%
	Female	7	46.7%

Table 1: Demographic characteristics of all patients included in the study

Clinical presentation:
Table (2) shows the description of clinical presentation in all studied patients. Acromegaly features was presented in 15 patients (100%), headache was presented in 11 patients (73.3%), menstrual irregularity was presented in 3 patients (20%) and visual impairment was presented in 10 patients (66.7%).

		Studied patients (N = 15)	
Clinical presentation	Acromegaly features	15	100%
	Headache	11	73.3%
	menstrual irregularity	3	20%
	Visual impairment	10	66.7%

Table 2: Clinical presentation of all individuals investigated

Radiology:
Table (3) shows the description of pre-operative radiological examination in all studied patients. As regard volume, it was macro-adenoma in all studied patients (100%). As regard Cavernous Sinus Invasion, it was occurred in 6 patients (40%) of the studied patients. As regard extension, it was localized to Sella in 8 patients (53.3%) and Supra Sellar extension in 7 patients (46.7%).

		Studied patients (N = 15)	
Volume	Micro-adenoma	0	0%
	Macro-adenoma	15	100%
Cavernous Sinus Invasion	No	9	60%
	Yes	6	40%
Extension	Localized to Sella	8	53.3%
	Supra Sellar extension	7	46.7%

Table 3: Description of pre-operative radiological examination in all studied patients.

Surgical excision of the tumor:

Table (4) shows the description of surgical excision in all investigated patients. It was Total excision in 12 patients (80%) and Subtotal excision in 3 patients (20%).

		Studied patients (N = 15)	
Surgical excision	Total excision	12	80%
	Subtotal excision	3	20%

Table 4: Description of surgical excision in all investigated patients

Operative time and Hospital stay:
Table (5) shows the description of operative time & post-operative hospital stay in all studied patients. As regard operative time, the mean operative time of all studied patients was 165.2 ± 12.7 min with minimum operative time of 145 min and maximum operative time of 187 min. As regard post-operative hospital stay, the mean stay of all studied patients was 5.9 ± 0.8 days with minimum stay of 5 days and maximum stay of 7 days.

		Studied patients (N = 15)
Operative time (min)	Mean ±SD	165.2 ± 12.7
	Min – Max	145 – 187
Hospital stay (days)	Mean ±SD	5.9 ± 0.8
	Min – Max	5 – 7

Table 5: Description of operative time & post-operative hospital stay in all studied patients

Pre and post Hormonal profile:
Next table shows Highly statistically significant (p-value < 0.001) decreased post-operative growth hormone (3.4 ± 1.2) when compared with pre-operative growth hormone (38.1 ± 29.8). Highly statistical significant (p-value < 0.001) decreased post-operative IGF-1 (242.3 ± 102.1) when compared with pre-operative IGF-1 (665 ± 253). No statistical substantial variance (p-value > 0.05) between pre-operative and post-operative the following hormones (ACTH, cortisol, T3, T4, TSH, testosterone, E2, FSH, LH and PRL).

		Pre-op (N = 15)	Post-op (N = 15)	Stat. test
Growth hormone	Mean	38.1	3.4	T = 4.5
	±SD	29.8	1.2	
IGF-1	Mean	665.0	242.3	T = 6.0
	±SD	253.0	102.1	
ACTH (AM)	Mean	38.2	39.2	T = 0.26
	±SD	10.5	9.5	
ACTH (PM)	Mean	12.8	13.7	T = 0.27
	±SD	9.4	8.9	
Cortisol (AM)	Mean	6.3	6.2	T = 0.09
	±SD	4.3	3.7	
Cortisol (PM)	Mean	3.9	4.0	MW = 112.5
	±SD	2.3	2.5	
T3	Mean	3.0	3.1	T = 0.14
	±SD	0.6	0.7	
T4	Mean	0.9	1.0	T = 0.75
	±SD	0.4	0.4	
TSH	Mean	3.0	2.8	T = 0.73
	±SD	0.6	0.9	NS
Testosterone	Mean	8.0	23.9	MW = 99.5 0.595
	±SD	9.1	60.4	NS
E2	Mean	7.1	9.7	MW = 90.5 0.376
	±SD	24.0	24.5	NS
FSH	Mean	5.3	5.5	MW = 99.5 0.595
	±SD	6.5	5.3	NS
LH	Mean	3.6	3.5	T = 0.1 0.916
	±SD	2.7	2.8	NS
PRL	Mean	4.7	4.9	T = 0.24 0.806
	±SD	1.7	1.9	NS

Table 6: Comparison of pre-operative and post-operative hormonal profile in studied patients

T: independent sample T test.
HS: p-value < 0.001 highly substantial.
MW: Mann Whitney U test.
NS: p-value > 0.05 is non- substantial.

Case sample
male patient 50 years old presented with Acromegalic features, headache, chest pain of 4 years duration,Hormonal assay pre: GH(36.1 ng/ml) IGF1 (463 ng/ml),Hormonal assay post: GH(4.67 ng/ml) IGF1(130 ng/ml),Fundus examination: bilateral normal fundi,Operation:puree ndoscopic endonasal trans sphenoidal surgery.

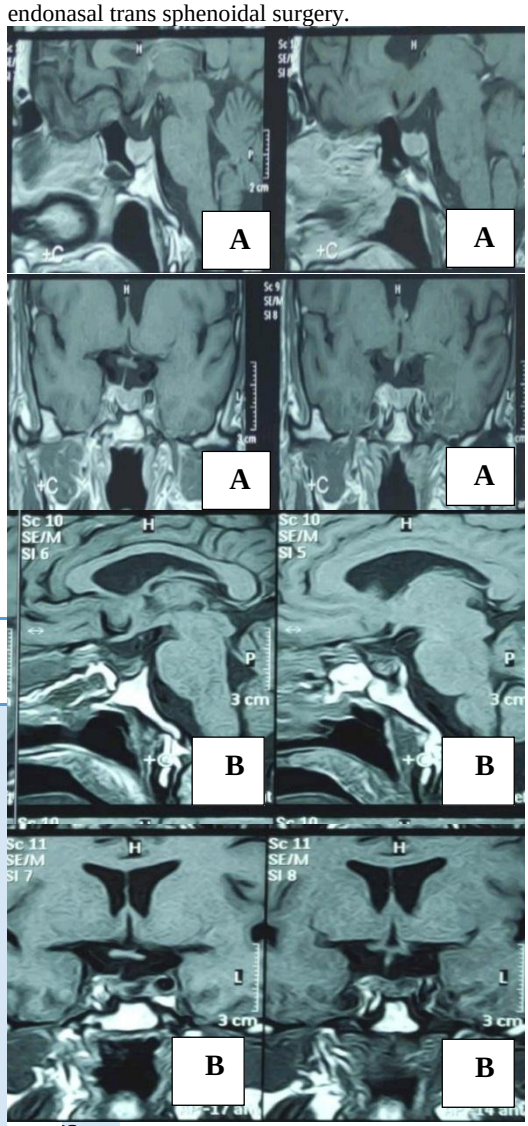


Fig. : (A) Preoperative, sagittal and coronal contrast-enhanced T1-weighted MR images of a case of GH

secreting pituitary adenoma (B) Postoperative sagittal and coronal T1-weighted MR images of a case of GH secreting pituitary adenoma after gross total Resection.

DISCUSSION

Surgical excision alone has been demonstrated to be beneficial in managing illness in up to 80% of patients with microadenomas and 50% of patients with macroadenomas, with up to 65% of patients experiencing long-term disease control. Surgery is often coupled with postoperative medicinal treatment, which may include somatostatin receptor ligands (SRL), GH-receptor antagonists, dopamine agonists (DA), and radiation in situations of resistant or persistent illness. [5]

ETPS is quickly supplanting both open transcranial and transsphenoidal microscope-based procedures for pituitary adenomas removal .

In terms of demographic data for all patients analyzed, our findings indicated that the median age of all patients was 41.3± 16.07 years, with a median age of 19 years and a maximum age of 64 years. In terms of gender, there were eight men (53.3%) and seven females (46.7%) among the patients investigated.

The current research, which was funded by Unal et al.,[8] sought to evaluate the outcomes of the transsphenoidal endoscopic technique for acromegaly and to identify predictors of remission. 73 individuals were involved in the trial, all of whom had surgery through the transsphenoidal endoscopic technique. There were 38 male (52.05%) and 35 female (50.75%) patients, with an average age of 49.3 years (range, 30–79 years).

Additionally, Aydin et al.,[9] conducted an endoscopic transsphenoidal procedure for acromegaly is being studied to see how effective it is. 106 individuals with acromegaly were included in the trial and underwent endoscopic endonasal transsphenoidal technique. There were 56 females (58.9 percent) and 39 males (41.1 percent), with an average age of 43.4 ±12.4 (range 16–79) years.

Additionally, Babu et al.,[10] sought to examine long-term remission rates in individuals with acromegaly after endoscopic transsphenoidal procedure and to connect these rates with genetic and radiographic indicators of disease aggressiveness. 58 individuals were recruited in the trial, all of whom underwent endoscopic endonasal transsphenoidal technique. 29 females and 29 men were present, ranging in age from 20 to 72 years (median 48.6 13.4 years).

In the current study regarding the pre-operative radiological examination in the studied patients we found that all studied patients (100%) had macro-adenoma. As regard Cavernous Sinus Invasion, it was occurred in 6 patients (40%) of the studied patients. As regard extension, it was localized to Sella in 8 patients (53.3%), and Supra Sellar extension in 7 patients (46.7%).

However, the study by Unal et al.,[8] reported that there were 57 macroadenomas (78%) and 16 microadenomas (22%) were surgically treated. The mean tumor volume was 2,073 mm3. Four patients had giant macroadenomas (>4>cm). Cavernous sinus invasion was detected in 32 (43.83%) of the 73 patients. Eighteen patients (24.6%) had a significant optic chiasm compression.

Also, the study by Aydin et al., [9] showed that Pituitary macroadenomas were found in 69 (72.6%) of the patients, with 12 (12.6%) of these being gigantic adenomas (4 cm). In 32 (33.6%) of the patients, suprasellar extension was seen. In 19 (20%) of the patients, preoperative sellar MRIs indicated Knosp Grade 3 or 4 cavernous sinus invasions.

As well, the study by Babu et al.,[10] reported that A total of 21 microadenomas and 37 macroadenomas were found. The tumor volume was 3.2 ±5.3 cc on average. There were 15 (25.8%) Knosp grade 0 tumors (entire tumor medial to the medial carotid tangent), 20 (34.4%) Knosp grade 1 cancers (cancer medial to the median carotid tangent), 12 (20.7%) Knosp grade 2 cancers (cancers medial to the lateral carotid tangent), 4 (6.8%) Knosp grade 3 cancers (cancers lateral to the (tumors encircling the carotid arteries).

Furthermore, Cardinal et al.,[11] reported that the median lesion diameter at presentation was 1.6 cm (IQR 1.1–2.3 cm); 10 lesions (19%) were microadenomas, and 42 (81%) were macroadenomas. On preoperative MRI, suprasellar extension was found in 18 patients (35%), infrasellar invasion in 40 patients (77%), and cavernous sinus invasion in seven patients (13 percent).

In the present study regarding clinical presentation in the studied patients, we found that acromegaly features were presented in 15 patients (100%), headache was presented in 11 patients (73.3%), menstrual irregularity was presented in 3 patients (20%) and visual impairment was presented in 10 patients (66.7%).

However, the study by Cardinal et al.,[11] reported that The majority of the patients (96%) had dysmorphic craniofacial traits, with 37 (71%) having larger rings or feet, 13 (25%) having skin tags, and 10 (19%) having excessive sweating. 25 (48 percent) of individuals with dysmorphic craniofacial traits had prognathism, 22 (42 percent) had frontal bossing, and 17 (32 percent) had macroglossia .

Also, Leopoldo et al.,[12] 23 acromegaly patients were recruited and underwent endoscopic transsphenoidal surgery. All of the patients had clinical indicators of acromegaly. Reduced visual acuity or visual fields, headaches, and bone and joint discomfort plagued around half of these individuals.

As well, Yano et al.,[13] enrolled Endoscopic transsphenoidal surgery was performed on 47 acromegalic individuals. Acromegalic characteristics were seen in 44 individuals (93.6%), and 13 patients

had visual impairments. One patient merely had a headache when he came in.

In relation to the description of surgical excision in all individuals investigated. In 12 cases (80%), entire excision was performed, while in three individuals, subtotal excision was performed (20 percent).

However, the study by Aydin et al.,[9] showed that there was subtotal excision in 76 patients (80%) and total excision in 19 patients (20%).

While, the study by Cardinal et al.,[11] reported that Sixty-six patients (69%) had gross-total resection (GTR; average maximum tumor diameter 1.47 cm), while sixteen patients (31%) had subtotal resection (STR; mean maximal tumor diameter 2.74 cm).

Regarding the operative characteristics, we found that the mean operative time of all studied patients was 165.2 ± 12.7 min with minimum operative time of 145 min and maximum operative time of 187 min. As regard post-operative hospital stay, the mean stay of all studied patients was 5.9 ± 0.8 days with minimum stay of 5 days and maximum stay of 7 days.

The study by Hofstetter et al.,[14] analyzed 24 endoscopic transsphenoidal surgeries and reported that the endoscopic transsphenoidal surgeries lasted a median of 182 minutes (range 104–326 minutes) and the mean hospital stay was 3.6 ± 1.8 days.

Also, the study by Shin et al.,[15] In this research of 53 patients, 42 (79.2%) had gross entire resection and 11 (20.8%) had near whole resection (90–99 percent resection). Subtotal resection was not performed on any of the patients. The study reported that the mean operative time was (3:42 hours, ranged from 1:28–8:10 hours) the mean hospital stay 3.6 (1–15) days.

Furthermore, Castaño-Leon et al.,[16] compared endoscopic transsphenoidal surgery (ETSS) with the microscopic sublabial trans-septal transsphenoidal surgery (MTSS) for pituitary adenomas. And found that the ETSS (150 min (IQR = 60)) had none significantly shorter operative time than MTSS (180 min (IQR = 30)) (p=.054). While the ETSS (6 day (IQR = 4)) had significantly shorter hospital stay than MTSS (8 day (IQR = 4)) (p<0.001).

As well, the study by Babu et al., 10 reported that the median length of stay was 2.24 days (range 1-4 days).

Highly statistically significant (p-value < 0.001) decreased post-operative IGF-1 (242.3 ± 102.1) when compared with pre-operative IGF-1 (665 ± 253). No statistically significant difference (p-value > 0.05) between pre-operative and post-operative the following hormones (ACTH, cortisol, T3, T4, TSH, testosterone, E2, FSH, LH and PRL).

Our results were supported by Unal et al.,[8] who reported that 29 (39.7%) of the 73 patients attained biochemical remission at the immediate postoperative period, and 16 additional patients (21.9%) were in remission based on their 3- month post-operative hormone levels. The results suggested that the mean GH IGF-1 levels were significantly improved postoperatively.

In agreement with our results the study by Aydin et al., 9 reported that The average preoperative GH level was 31.3± 21.2 ng/mL (range 2–76), while the average preoperative IGF-1 level was 657.3 ±333.7 ng/mL (range 238–1600). GH and IGF-1 levels were 1.8± 1.2 (range 0.1–10.3) ng/mL and 236.3 ±112.1 (range 84–755 ng/mL) at the final follow-up visit, respectively. At the postoperative 3rd month assessment, 63 (66.3%) patients had achieved early surgical remission.

Also, the study by Babu et al.,[10] reported that at three months following surgery, 40 patients (69%) satisfied biochemical remission requirements (based GH and IGF-1 values). IGF-1 levels in eighteen of the participants remained above normal. 3 months following surgery, IGF-1 levels varied from 0.4 to 4.1 times the upper limit of normal (mean 2.6 ±0.7). The duration of long-term follow-up varied from 38 to 98 months (mean 64 months; median 28.9 months). At the 6-month follow-up, 43 (97.7%) of the 44 patients in biochemical remission stayed in remission, giving a long-term remission rate of 74.1 percent.

In addition, Taghvaei et al.,[17] showed that the overall rate of remission was 71.4 percent, with gross total resection obtained in 45 out of 49 patients (91.8 percent).

CONCLUSION

In individuals with acromegaly, the endoscopic endonasal transsphenoidal technique is an efficacious and secure treatment for adenomas. We discovered that using an endoscopic endonasal transsphenoidal technique reduced growth hormone and insulin-like growth factor-1 levels considerably. To corroborate these findings, further research with a larger sample size and extended follow-up durations is required.

Conflict of interest : none

REFERENCES

1. Zhong A, Pu J, Ruan L, Jin J, Tan S, Wang F, et al. The complications of endoscopic transsphenoidal surgery for pituitary neoplasms. *Int J Clin Exp Med*, 2016; *9*(10), 20026-31.
2. Halvorsen H, Ramm-Pettersen J, Josefsen R, Rønning P, Reinlie S, Meling T, Berg-Johnsen J, Bollerslev J, Helseth E. Surgical complications after transsphenoidal microscopic and endoscopic surgery for pituitary adenoma: a consecutive series of 506 procedures. Acta neurochirurgica. 2014 Mar;156(3):441-9.
3. Bronstein MD, Paraiba DB, Jallad RS. Management of pituitary tumors in pregnancy. *Nature Reviews Endocrinology*, 2011; *7*(5), 301-10.
4. Nagata Y, Takeuchi K, Yamamoto T, Ishikawa T, Kawabata T, Shimoyama Y, et al. Peel-off resection of the pituitary gland for functional pituitary

adenomas: pathological significance and impact on pituitary function. *Pituitary*, 2019*; 22*(5), 507-13.

5. Melmed S, Bronstein MD, Chanson P, Klibanski A, Casanueva FF, Wass JA, et al. A consensus statement on acromegaly therapeutic outcomes. *Nature Reviews Endocrinology*, 2018; 14(9), 552-61.
6. Cappabianca P, Frank G, Pasquini E, De Divitiis O, Calbucci F. (). Extended endoscopic endonasal transsphenoidal approaches to the suprasellar region, planum sphenoidale & clivus. In *Endoscopic endonasal transsphenoidal surgery*, 2003; 176-87.
7. Mortini P. Cons: Endoscopic endonasal transsphenoidal pituitary surgery is not superior to microscopic transsphenoidal surgery for pituitary adenomas. Endocrine, 2014; 47: 415-20.
8. Unal TC, Aydoseli A, Ozgen U, Dolas I, Sabanci PA, Aras Y, et al. A single-center experience of transsphenoidal endoscopic surgery for acromegaly in 73 patients: results and predictive factors for remission. British Journal of Neurosurgery, 2021; 1-6.
9. Aydin S, Ozoner B, Sahin S, Alizada O, Comunoglu N, Oz B, et al. A follow-up study on outcomes of endoscopic transsphenoidal approach for acromegaly. Clinical Neurology and Neurosurgery, 2020; 198, 106201.
10. Babu H, Ortega A, Nuno M, Dehghan A, Schweitzer A, Bonert HV, et al. Long-term endocrine outcomes following endoscopic endonasal transsphenoidal surgery for acromegaly and associated prognostic factors. Neurosurgery, 2017; 81(2), 357-66.
11. Cardinal T, Rutkowski MJ, Micko A, Shiroishi M, Liu CSJ, Wrobel B, et al. Impact of tumor characteristics and pre-and postoperative hormone levels on hormonal remission following endoscopic transsphenoidal surgery in patients with acromegaly. Neurosurgical focus, 2020; 48(6), E10.
12. Leopoldo C, Leopoldo FS, Santos AD, Veiga J, Lima JV, Scalissi NM, et al. Long term follow-up of growth hormone-secreting pituitary adenomas submitted to endoscopic endonasal surgery. Arquivos de neuro-psiquiatria, 2017; 75, 301-06.
13. Yano S, Shinojima N, Kawashima J, Kondo T, Hide, T. Intraoperative Scoring System to Predict Postoperative Remission in Endoscopic Endonasal Transsphenoidal Surgery for Growth Hormone–Secreting Pituitary Adenomas. World Neurosurgery, 2017; 105, 375-85.
14. Hofstetter CP, Mannaa RH, Mubita L, Anand VK, Kennedy JW, Dehdashti AR, et al. Endoscopic endonasal transsphenoidal surgery for growth hormone–secreting pituitary adenomas. Neurosurgical focus, 2010; 29(4), E6.
15. Shin SS, Tormenti MJ, Paluzzi A, Rothfus WE, Chang YF, Zainah H, et al. Endoscopic endonasal approach for growth hormone secreting pituitary adenomas: outcomes in 53 patients using 2010 consensus criteria for remission. Pituitary, 2013; 16(4), 435-44.
16. Castaño-Leon AM, Paredes I, Munarriz PM, Jiménez-Roldán L, Hilario A, Calatayud M,et al. Endoscopic transnasal trans-sphenoidal approach for pituitary adenomas: a comparison to the microscopic approach cohort by propensity score analysis. Neurosurgery, 2020; 86(3), 348-56.
17. Taghvaei M, Sadrehosseini SM, Miri SM, Zeinalizadeh M. Endoscopic transsphenoidal approach for surgical treatment of growth hormone secreting pituitary adenoma: endocrinological outcome in 49 patients based on 2010 consensus criteria for remission-preliminary results. Arch Neurosci. 2017 Jul 1;4(3):e14131.