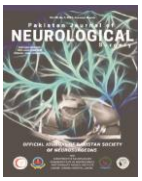

PAKISTAN JOURNAL OF NEUROLOGICAL SURGERY (QUARTERLY) – OFFICIAL JOURNAL OF PAKISTAN SOCIETY OF NEUROSURGEONS

Original Article (BRAIN)

Results of Resection of Giant Pituitary Adenomas through Endoscopic Endonasal Approach

Zubair Mustafa Khan, Hannan Tayyab, Syed Ahmad Faizan, Sumaira Kiran, Aqeel Butt, Asif Bashir[1]

Department of Neurosurgery, Unit-III, Punjab Institute of Neurosciences, Lahore

ABSTRACT

Background/Objective: A minimally invasive surgical method is in use to create endoscopic transsphenoidal surgery. Because of the intricate dissection of the sellar region, surgical treatment of large pituitary adenomas is challenging. The study focused to determine the frequency of complications after endonasal endoscopic transsphenoidal resection of giant pituitary macroadenomas.

Materials and Methods: A descriptive case series study was conducted at the Neurosurgical Department of Lahore General Hospital, Lahore. A total of 70 patients fulfilling the selection criteria were enrolled. Major vascular injury was noted when there is an injury to the internal carotid artery or cavernous sinus. After discharge, patients were followed-up in OPD for 3 months. After 3 months, patients were evaluated for CSF leak and vision. The presence of complications was recorded. During surgery, operative time was noted.

Results: Mean age of patients was 55.7 ± 6.5 years. 45.71% of patients were male while the remaining 54.29% of patients were female Total of 41.43% of patients had disease < 2 years, whereas the duration of surgery was ≤ 3 hours in 64.3% of patients. A total 15.71% had complications which included diabetes insipidus (8.57%), infections (5.71%), pituitary dysfunction (4.29%), CSF leak (2.8%) and vascular injury (1.43%). The mortality rate was 1.43%.

Conclusion: The complication rate after endonasal endoscopic transsphenoidal resection of giant pituitary macroadenomas was high.

Keywords: Endonasal Endoscopic, Transsphenoidal Resection, Pituitary Macroadenomas, Complications.

Corresponding Author: Zubair Mustafa Khan
Department of Neurosurgery, Unit-III
Punjab Institute of Neurosciences, Lahore
Email: drzmkhan_ns@hotmail.com

Date of Submission: 02-03-2022
Date of Revision: 29-03-2022
Date of Acceptance: 30-03-2022
Date of Online Publishing: 31-3-2022
Date of Print: 31-3-2022

DOI: 10.36552/pjns.v26i1.644

INTRODUCTION

As the average life expectancy rises, so will the medical treatment for older people with symptomatic pituitary adenoma.[1] Pituitary adenomas account for 10 – 12% of all intracranial

tumors.[2] Because of the intricate dissection of the sellar region, surgical treatment of large pituitary adenomas is challenging. The extent of tumor excision influences surgical therapy efficacy.[2] Except for prolactinoma, which responds well to pharmaceutical therapy, surgical excision is the first-line treatment for any pituitary adenoma. Endonasal transsphenoidal endoscopy eliminates the need for a sublabial or transseptal incision, any transsphenoidal retractor, and nasal packing. Hermann Schloffer pioneered the transsphenoidal technique for pituitary adenoma removal more than a century ago.[3] Endoscopic endonasal pituitary tumor surgery gives a clearer and more panoramic image, allowing the tumor, cavernous sinus, and arachnoid membrane boundaries to be distinguished.[4-7] In contrast, postoperative CSF leak and associated infectious problems have persisted and have become a frequent consequence.[8-9] Chone et al.[10] observed that surgery-related difficulties were recognized in 10% of cases. They found the commonest complication to be leakage of CSF (17%) followed by bleeding occurred (4%). The visual acuity improved in all cases, and pituitary dysfunction was not identified.[11] Another research found that 52.6 percent of people had CSF leaks, 10.5 percent had pituitary dysfunction, and 3.6 percent had vision degeneration.[3] Another research discovered CSF leak in 2.6 percent, pituitary malfunction in 3.6 percent, visual degeneration in 0.6 percent, and bleeding in 1.1 percent.[11]

The rationale of the present study was to investigate the incidence of problems following endonasal endoscopic transsphenoidal excision of big pituitary macroadenomas. As a result, we undertook this study to collect local data so that we could integrate the findings in the local community and recommend modifications in surgical methods if we discovered a significant risk of complication with endonasal endoscopic trans-sphenoidal excision of large pituitary macroadenomas. The purpose of this study was to determine the frequency of complications following endonasal endoscopic transsphenoidal resection of giant pituitary macroadenomas. Population-based research from 1992-to 2007, in Northern Finland, showed the normalized incidence rates per 100,000 people when all patients within a health care district were sent to a preset medical facility.[12] Adenomas are categorized based on their size and cell of origin. Microadenomas are lesions that are less than 1 cm in size, whereas macroadenomas are lesions that are bigger than 1 cm in size. Adenomas can develop from any kind of anterior pituitary cell and can cause increased secretion of the hormones generated by that cell as well as decreased production of other hormones due to compression of other cell types. Malignant tumors from within or around the sella, while others spread to this location. Germ cell tumors, sarcomas, chordomas, and lymphomas are examples of primary malignancies that form in the parasellar area. Pituitary carcinomas are uncommon, 1 – 2% of sellar masses are caused by metastases to the hypothalamus and pituitary gland, while others can be germ cell tumors, chordomas, or primary lymphomas.[14-15] In one study, the average survival time for 36 individuals was six months.[16] Several forms of cysts, including Rathke's cleft, arachnoid, and dermoid cysts, can arise in the sellar and/or suprasellar region.[17-19] The most prevalent is Rathke's cleft cysts, which are benign cysts formed from the remains of Rathke's pouch, the same structure from which craniopharyngiomas arise. Pituitary size increases with abscess formation or arteriovenous fistulas. When an arteriovenous fistula is closed, pituitary size returns to normal. Several kinds of hypophysitis can cause pituitary enlargement early in their course.[20-21]

It allows a wider field of view, which is useful in large tumors. The operative field is visualized on a high-definition screen. Because most endoscopes are monocular, the surgeon loses binocular vision and depth perception, although 3D endoscopes are under development. Although

marketed as relatively "noninvasive," the width of access required for successful manipulation of the endoscope and resection tools may require greater dissection in the nasal cavity itself, with partial resection of the turbinates and a wider opening in the face of the sphenoid. Most adenomas (65 – 70%) secrete an excess amount of hormone including prolactin, growth hormone (GH), corticotropin (ACTH), or thyroid-stimulating hormone (TSH). Transsphenoidal surgery is the mainstay of treatment for most kinds of pituitary adenomas and other sellar masses. Transsphenoidal surgery helps in reaching the sella in a non-invasive fashion by employing as the surgeon approaches the sinus through the nasal passages. Successful resection requires that the surgeon navigates to the sella, visualizes the tumor through a relatively narrow corridor, excises the tumor as much as possible, and minimizes damage to the surrounding structures, including the normal pituitary gland. Risks of surgery include hormonal deficiencies and iatrogenic injury to parasellar structures, as well as general surgical risks. All complications occur less frequently with more experienced surgeons and institutions. The rate of new postoperative hormonal deficiencies ranged from 7 to 20 percent in one large survey. Diabetes insipidus occurs transiently in approximately 10 to 20 percent of surgeries but permanently in only 2 to 7 percent. Potential damage to parasellar structures as a result of surgery includes CSF rhinorrhea, damage to an internal carotid artery, optic chiasma, or nerves.[22-23]

MATERIAL AND METHODS:

Study Design & Setting

A descriptive case series was performed at the Department of Neurosurgery, Lahore General Hospital, Lahore for six months from 25-01-2021 to 24-07-2021.

Sample Size

The sample size of 70 cases was calculated with a 95% confidence level, 7% margin of error, and taking the expected percentage of surgery-related complications i.e., 10% after endonasal endoscopic trans-sphenoidal resection of giant pituitary macro-adenomas. Non Probability, the Consecutive sampling technique was considered.

Inclusion Criteria

Patients of age 16 – 75 years of both genders undergoing endonasal transsphenoidal resection of giant pituitary macro-adenomas were included.

Exclusion Criteria

Patients undergoing redo surgery or recurrent disease (on medical record), or those having a liver disease (ALT & AST > 40 IU, hepatitis B or C), renal dysfunction (creatinine e > 2.0 mg/d), and PT > 15 sec, APTT > 20 sec, INR > 2 were excluded from the study. Patients with h/o myocardial infarction, Ejection fraction < 50% on echocardiography, chest infection, pulmonary spasm, nasal infection, flu, common cold or tonsillitis, or apoplexy of pituitary adenomas (on clinical examination) were also not included in the study.

Data Collection Procedure

A total of 70 patients who met the screening criteria were recruited from the wards of the Department of Neurosurgery at Lahore General Hospital in Lahore. Demographic variables (name, age, gender, duration of diagnosis) were noted. All patients underwent surgery by a single surgical team under general anesthesia. During surgery, operative time was noted. The data was collected with informed consent from all patients or their attendants. Major vascular injury was noted when there is an injury to the internal carotid artery or cavernous sinus. After surgery, patients were shifted to post-surgical wards and

were followed up there for 3 days. After discharge, patients were followed-up in OPD for 3 months. After 3months, patients were evaluated for CSF leak and vision. If the patient develops clear watery discharge from the nose which increased in bending forward it was labeled as a CSF leak. If there is > 6/9 visual acuity obtained, then visual deterioration was labeled. The presence of complications was recorded. Patients with complications were managed as per hospital protocol. A predesigned proforma was used to collect information.

Statistical Analysis

All variables such as gender, duration of disease, operative time, and complication incidences were calculated in SPSS version 25.

RESULTS

A total of seventy patients participated in our study.

Age Distribution

In this study, 34.29% of patients were between the ages of 16 – 45 years, while 65.71% of patients were between the ages of 46 – 75 years. The mean age of patients was 55.7 ± 6.5 years **(Table 1)**.

Table 1: Age (n = 70).

Age (in Years)	No. of Patients	%
16 – 45	24	34.29%
46 – 75	46	65.71%
Total	**70**	**100**
Mean ± SD: 55.7 ± 6.5 years		

Gender Distribution

Regarding gender distribution, 45.71% of patients were male while the remaining 54.29% of patients were female **(Table 2)**.

Table 2: Gender (n = 70).

Gender	No. of Patients	%
Male	32	45.71%
Female	38	54.29%
Total	**70**	**100.0**

Table 3: Duration of Disease (n = 70).

Duration of Disease	No. of Patients	%
≤ 2 years	29	41.43%
> 2 years	41	58.57%
Total	**70**	**100.0**
Mean ± SD: 2.1 ± 0.2 years		

Duration of Disease & Surgery

With regards to the duration of disease, 41.43% of patients had a disease < 2 years, whereas 58.57% of patients had the disease for > 2 years. Duration of surgery was ≤ 3 hours in 64.3% of patients. On the other hand, 35.7% of patients had surgery duration of > 3 hours. With regards to the frequency of complications of the surgery, 15.71% had complications with the most common being diabetes insipidus i.e. 8.57% followed by infections and pituitary dysfunction i.e. 5.71% and 4.29% respectively. Visual deterioration was noted

Table 4: Operative Time (n = 70).

Operative Time	No. of Patients	%
≤ 3 hours	45	64.3%
> 3 hours	25	35.7%
Total	**70**	**100.0**
Mean ± SD: 2.7 ± 0.4 hours		

Table 5: Frequency of Complications (n = 70).

Complications	No. of Patients	%
Total complications	11	15.71%
Post-op CSF leak	3	4%
Major Vascular Injury	1	1.43%
Visual Deterioration	2	2.86%
Pituitary Dysfunction	3	4.29%
Diabetes Insipidus	6	8.57%
Infection	4	5.71%
Mortality	1	1.43%

in 2.86%, post-operative CSF leak in 4%, and major vascular injury in 1.43%. The mortality rate was 1.43%. See **Tables 4 and 5**.

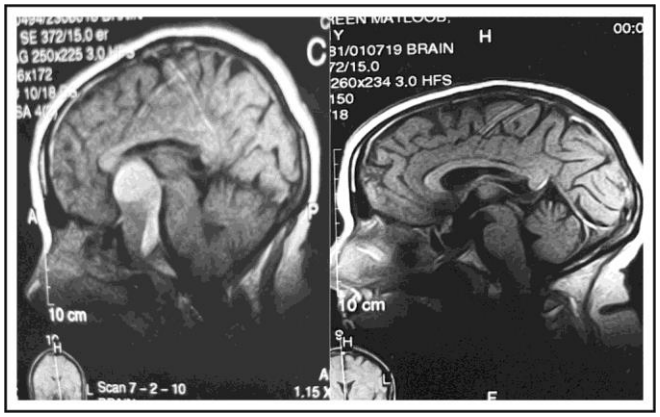

Figure 1: (Case 1). (a) Pre-op sagittal view MRI showing a pituitary adenoma (b) Post-op view after resection.

Figure 2: (Case 2). (a) Pre-op sagittal view MRI showing a pituitary adenoma (b) Post-op view after resection.

DISCUSSION

Transsphenoidal surgery is the mainstay of treatment for most kinds of pituitary adenomas and other sellar masses. This topic review covers the techniques, results, and complications of transsphenoidal surgery of pituitary adenomas and other sellar masses. Risks of surgery include hormonal deficiencies and damage to para-sellar structures, as well as general surgical risks. All complications occur less frequently with more experienced surgeons and institutions. Prolactinomas respond extremely well to pharmacological therapy. For tumors other than prolactinomas, the first-line therapy for all the pituitary adenomas is surgical resection. The strategy behind the use of endoscopy intransphenoidal surgery was a minimal invasion. With regards to the frequency of complications of the surgery, 15.71% of patients had complications of surgery. One study conducted in Toronto had a higher rate of complications in a patient with transsphenoidal surgery i.e., 37%.[24]

According to the results of our study, the most common complication was diabetes insipidus i.e., 8.57% followed by infections and pituitary dysfunction i.e., 5.71% and 4.29%, respectively. Visual deterioration was noted in 2.86%, post-operative CSF leak in 4%, and major vascular injury in 1.43%. In a similar study conducted in the USA, it was seen that the most common complication was sinusitis (14%) followed by CSF leak (10%).[24] Other complications they reported such as SIADH (4.1%) and worsening of headache (2.7%).[24] Furthermore, epistaxis was noted in 2.7%, meningitis in 2.7%, and hydrocephalus in 2.7%.[24] Another study conducted in Brazil involving the removal of macroadenoma using transsphenoidal endonasal endoscopic approach noted diabetes insipidus in 10% of patients and CSF leakage in 8% of patients.[25] In another study conducted in Spain, the most common complication was CSF leak (9%) followed by diabetes insipidus (3.3%) and transient SIADH (2.5%).[26] According to one study conducted in China, the postoperative complication rate after transsphenoidal endoscopic surgery was 20.1% which included mainly CSF leakage in 6.9%, nasal hemorrhage in 4.8%, and sphenoid sinusitis in 2.3% of patients.[27] Another similar study conducted in China has shown similar results. In this study, CSF leakage was noticed in 4% of patients, and diabetes insipidus in 3.1%.[28]

In our study, the mortality rate was 1.43%. In a similar study conducted in China, mortality was noted at 0.3%. One more study from China has

revealed the complication rate after transsphenoidal surgery as 14.4% which included mainly diabetes insipidus (7%), epistaxis (1.72%), and meningitis (1.03%).[29] A meta-analysis conducted by Barker et al,[30] revealed the overall complication rate after transsphenoidal surgery as 11.3% which mainly included diabetes insipidus (4.6%), anterior pituitary insufficiency (1.9%), and CSF leakage (1.3%). A similar study conducted in Italy has shown a complication rate of only 3.4% which included CSF leakage at 1.7% and hematoma in the tumor field at 1.7%.[31] In one study conducted in Belgium by De Witte et el., the complication rate was found to be 36.1%. They reported anterior lobe insufficiency in 19.8%, CSF leak in 6.2%, and diabetes insipidus in 4.9%.[32] The death rate was 2.5% in this study which is comparable to the death rate (1.43%) in our study.[33] Another study conducted by Charalampaki et al,[33] in Germany has shown the complication rate of 19.7% with diabetes insipidus as 5.9%. In a study conducted in China, researchers found temporary diabetes insipidus in 8.19% of patients and CSF leak in 1.75% of patients. It was further established in this study that the complication rate was relatively low among surgeons with several procedures>500. One similar study was conducted by Lopez et al,[34] in Ecuador. They revealed CSF leakage in 12.5% of patients, a hormonal deficit in 18.75%, and sella hematoma in 3.75%. One meta-analysis included two randomized and three prospective, nonrandomized trials, but the number of patients was too small to draw definitive conclusions about the comparative efficacy or risks of the two techniques.[35]

Postoperative risk of development of SIADH is managed with mild fluid restriction,[36-38,] and CSF rhinorrhea is observed and if leakage is suspected, the fluid should be tested for beta transferrin (tau protein). Sellar masses can be found incidentally on CT or MRI scans, causing the development of neurological symptoms by mass effect or through abnormal secretion of hormones from the pituitary gland. Visual impairment is the commonest symptom of pituitary adenomas. Most of these 80% are gonadotrophs.[39] Extension of tumor size cranially in the sellar region causes compression on the optic chiasma leading to visual impairment, especially in the temporal fields, however other patterns of visual loss can also occur. An unexplained visual loss should alarm a physician of a pituitary cause. Other neurologic symptoms that may cause a patient with a sellar mass to seek medical attention include headaches, diplopia, cerebrospinal fluid rhinorrhea, and Parinaud syndrome. Because few studies are prospective or randomized, comparisons of the two procedures (microscopic versus endoscopic approaches) are restricted. As a result, the comparison is based on reviews and meta-analyses of individual technique studies. Several meta-analyses have shown no clear difference between the two techniques for incomplete removal of the adenoma. The largest of these reviewed 38 papers, of which 24 reported endoscopic results in 2125 patients and 22 reported microscopic results in 3518 patients 40 (Ammirati et al). In Cushing's disease, a meta-analysis of 97 studies showed similar remission rates (approximately 80 percent) in microadenomas for both endoscopic and microscopic approaches, with a trend towards improved remission in macroadenomas with the endoscopic approach.[41] Some of these reviews report that the endoscopic approach showed decreased operating time, length of hospital stays, risk of diabetes insipidus, nasal complications, and pain and discomfort.[42-44] One meta-analysis included two randomized and three prospective, nonrandomized trials, but the number of patients was too small to draw definitive conclusions about the comparative efficacy or risks of the two techniques.[35]

CONCLUSION & RECOMMENDATIONS

It can be concluded from our study that despite clinical benefits like reduced operational time, hospital stay, diabetes insipidus, and remission of disease, the complication rate after endonasal endoscopic trans-sphenoidal resection of giant pituitary macro-adenomas was still high. To evaluate the results and complications of endoscopic pituitary surgery, more research with a long-term follow-up is needed.

REFERENCES

1. Gondim JA, Almeida JP, de Albuquerque LA, Gomes E, Schops M, Mota JI. Endoscopic endonasal transsphenoidal surgery in elderly patients with pituitary adenomas. Journal of Neurosurgery, 2015; 123 (1): 31-8.
2. Wang S, Lin Sa, Wei L, Zhao L, Huang Y. Analysis of operative efficacy for giant pituitary adenoma. BMC Surgery, 2014 2014/08/28; 14 (1): 59.
3. Rehman L, Rehman UL, Jabeen R, Rizvi R. Endoscopic Trans-Sphenoidal surgery; Efficacy and response in Pituitary Adenoma. Pak J Med Sci. 2018; 34 (2): 412-7.
4. Dhandapani S, Singh H, Negm HM, Cohen S, Anand VK, Schwartz TH. Cavernous sinus invasion in pituitary adenomas: a systematic review and pooled data meta-analysis of radiologic criteria and comparison of endoscopic and microscopic surgery. World Neurosurgery, 2016; 96: 36-46.
5. Elhadi AM, Hardesty DA, Zaidi HA, Kalani MYS, Nakaji P, White WL, et al. Evaluation of surgical freedom for microscopic and endoscopic transsphenoidal approaches to the sella. Operative Neurosurgery, 2015; 11 (1): 69-79.
6. Singh H, Essayed WI, Cohen-Gadol A, Zada G, Schwartz TH. Resection of pituitary tumors: endoscopic versus microscopic. Journal of Neuro-oncology, 2016; 130 (2): 309-17.
7. Zoli M, Milanese L, Bonfatti R, Sturiale C, Pasquini E, Frank G, et al. Cavernous sinus invasion by pituitary adenomas: role of endoscopic endonasal surgery. Journal of Neurosurgical Sciences, 2016; 60 (4): 485-94.
8. de Divitiis E, Laws ER, Giani U, Iuliano SL, de Divitiis O, Apuzzo ML. The current status of endoscopy in transsphenoidal surgery: an international survey. World Neurosurgery, 2015; 83 (4): 447-54.
9. Magro E, Graillon T, Lassave J, Castinetti F, Boissonneau S, Tabouret E, et al. Complications related to the endoscopic endonasal transsphenoidal approach for nonfunctioning pituitary macroadenomas in 300 consecutive patients. World Neurosurgery, 2016; 89: 442-53.
10. Chone CT, Sampaio MH, Sakano E, Paschoal JR, Garnes HM, Queiroz L, et al. Ressecção endoscópica transesfenoidal de adenomas de hipófise: avaliação preliminar de pacientes consecutivos. Brazilian Journal of Otorhinolaryngology, 2014; 80: 146-51.
11. Agam MS, Wedemeyer MA, Wrobel B, Weiss MH, Carmichael JD, Zada G. Complications associated with microscopic and endoscopic transsphenoidal pituitary surgery: experience of 1153 consecutive cases treated at a single tertiary care pituitary center. Journal of Neurosurgery, 2018; 130 (5): 1576-83.
12. Raappana A, Koivukangas J, Ebeling T, Pirilä T. Incidence of pituitary adenomas in Northern Finland in 1992-2007. J Clin Endocrinol Metab. 2010; 95: 4268.
13. Morita A, Meyer FB, Laws ER Jr. Symptomatic pituitary metastases. J Neurosurg. 1998; 89: 69.
14. Ragel BT, Couldwell WT. Pituitary carcinoma: a review of the literature. Neurosurg Focus, 2004; 16: E7.
15. Fassett DR, Couldwell WT. Metastases to the pituitary gland. Neurosurg Focus, 2004; 16: E8.
16. Morita A, Meyer FB, Laws ER Jr. Symptomatic pituitary metastases. J Neurosurg. 1998; 89: 69.
17. Trifanescu R, Ansorge O, Wass JA, Grossman AB, Karavitaki N. Rathke's cleft cysts. Clin Endocrinol (Oxf). 2012; 76: 151.
18. Culver SA, Grober Y, Ornan DA, Patrie JT, Oldfield EH, Jane JA Jr, et al. A Case for Conservative Management: Characterizing the Natural History of Radiographically Diagnosed Rathke Cleft Cysts. J Clin Endocrinol Metab. 2015; 100: 3943.
19. Al-Holou WN, Terman S, Kilburg C, Garton HJ, Muraszko KM, Maher CO. Prevalence and natural history of arachnoid cysts in adults. J Neurosurg. 2013; 118: 222.
20. Sato N, Putman CM, Chaloupka JC, Glenn BJ, Vinuela F, Sze G. Pituitary gland enlargement

secondary to dural arteriovenous fistula in the cavernous sinus: appearance at MR imaging. Radiology, 1997; 203: 263.
21. Jankowski R, Auque J, Simon C, Marchal JC, Hepner H, Wayoff M. Endoscopic pituitary tumor surgery. Laryngoscope, 1992; 102: 198.
22. Ciric I, Ragin A, Baumgartner C, Pierce D. Complications of transsphenoidal surgery: results of a national survey, review of the literature, and personal experience. Neurosurgery, 1997; 40: 225.
23. Nemergut EC, Zuo Z, Jane JA Jr, Laws ER Jr. Predictors of diabetes insipidus after transsphenoidal surgery: a review of 881 patients. J Neurosurg. 2005; 103: 448.
24. Juraschka K, Khan OH, Godoy BL, Eric Monsalves, Kilian A, Krischek B, et al. Endoscopic endonasal transsphenoidal approach to large and giant pituitary adenomas: institutional experience and predictors of extent of resection. J Neurosurg. 2014; 121: 75–83.
25. Gondim JA, Almeida JP, Albuquerque LA, Gomes EF, Shops M. Giant pituitary adenomas: surgical outcomes of 50 cases operated on by the endonasal endoscopic approach. World Neurosurg. 2014; 82 (1-2): e281-90.
26. Orales J, Halperin I, Hanzu F, Mora M, Alobid I, De Notaris M, et al. Cirugía endoscópica endonasal en tumores de hipófisis. Resultados en una serie de 121 casos operados en un mismo centro y por un mismo neurocirujano. Endocrinol Nutr. 2014; 61: 410–6.
27. Cheng Y, Xue F, Wang TY, et al. Analyses and treatments of postoperative nasal complications after endonasal transsphenoidal resection of pituitary neoplasms. Medicine, 2017; 96 (15): e6614.
28. ZhongA, Pu J, Ruan L, Jin K, 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.
29. Wang F, Zhou T, Wei S, Meng X, Zhang J, Hou Y, et al. Endoscopic endonasal transsphenoidal surgery of 1,166 pituitary adenomas. Surg Endosc. 2015; 29: 1270–80.
30. Barker FG 2nd, Klibanski A, Swearingen B. Transsphenoidal surgery for pituitary tumors in the United States, 1996-2000: mortality, morbidity, and the effects of hospital and surgeon volume. J Clin Endocrinol Metab. 2003; 88: 4709.
31. Cavallo LM, Solari D, Tasiou A, Esposito F, de Angelis M, D'Enza AI, Cappabianca P. Endoscopic endonasal transsphenoidal removal of recurrent and regrowing pituitary adenomas: experience on a 59-patient series. World Neurosurg. 2013; 80: 342–350.
32. De Witte O, Carlot S, Devuyst F, Choufani G, Hassid S. Minimally invasive endoscopic unilateral transsphenoidal surgery for pituitary adenomas. B-ENT. 2011; 12: 27.
33. Charalampaki P, Ayyad A, Kockro RA, Perneczky A. Surgical complications after endoscopic transsphenoidal pituitary surgery. J Clin Neurosci. 2009; 16: 786–9.
34. Lopez S, Jervis M, Santilla F, Jimenez G,Astudillo MA, Cardenas F, et al. Endoscopic endonasal approach for pituitary adenomas: Results from multidisciplinary management. Interdisc Neurosur. 2021; 25: 101136.
35. Bastos RV, Silva CM, Tagliarini JV,Zanini MA, Romero FR, Boguszewski CL, et al. Endoscopic versus microscopic transsphenoidal surgery in the treatment of pituitary tumors: systematic review and meta-analysis of randomized and non-randomized controlled trials. Arch Endocrinol Metab. 2016; 60: 411.
36. Winograd D, Staggers KA, Sebastian S,Takashima M, Yoshor D, Samson SL. An Effective and Practical Fluid Restriction Protocol to Decrease the Risk of Hyponatremia and Readmissions After Transsphenoidal Surgery. Neurosurgery, 2020; 87: 761.
37. Matsuyama J, Ikeda H, Sato S, Yamamoto K, Ohashi G, Watanabe K. Early water intake restriction to prevent inappropriate antidiuretic hormone secretion following transsphenoidal surgery: low BMI predicts postoperative SIADH. Eur J Endocrinol. 2014; 171: 711.
38. Burke WT, Cote DJ, Iuliano SI, Zaidi HA, Laws ER. A practical method for prevention of readmission for symptomatic hyponatremia following transsphenoidal surgery. Pituitary, 2018; 21: 25.
39. Snyder PJ. Gonadotroph adenomas. In: The Pituitary, 2nd, Melmed S (Ed), Blackwell Science Inc., Malden, MA. 2002: p.575.

40. Ammirati M, Wei L, Ciric I. Short-term outcome of endoscopic versus microscopic pituitary adenoma surgery: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry, 2013; 84: 843.
41. Broersen LHA, Biermasz NR, van Furth WR,de Vries F, Verstegen MJT, Dekkers OM, et al. Endoscopic vs. microscopic transsphenoidal surgery for Cushing's disease: a systematic review and meta-analysis. Pituitary, 2018; 21: 524.
42. Goudakos JK, Markou KD, Georgalas C. Endoscopic versus microscopic trans-sphenoidal pituitary surgery: a systematic review and meta-analysis. Clin Otolaryngol. 2011; 36: 212.
43. Rotenberg B, Tam S, Ryu WH, Duggal N. Microscopic versus endoscopic pituitary surgery: a systematic review. Laryngoscope, 2010; 120: 1292.
44. Strychowsky J, Nayan S, Reddy K, Farrokhyar F, Sommer D. Purely endoscopic transsphenoidal surgery versus traditional microsurgery for resection of pituitary adenomas: a systematic review. J Otolaryngol Head Neck Surg. 2011; 40: 175.

Additional Information

Disclosures: Authors report no conflict of interest.
Ethical Review Board Approval: The study was conformed to the ethical review board requirements.
Human Subjects: Consent was obtained by all patients/participants in this study.
Conflicts of Interest:
In compliance with the ICMJE uniform disclosure form, all authors declare the following:
Financial Relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.
Other Relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

AUTHOR CONTRIBUTIONS

Sr. No.	Author's Full Name	Intellectual Contribution to Paper in Terms of;
1	Zubair Mustafa Khan	Study Design, Methodology, and Paper Writing.
2	Hannan Tayyab	Data Calculation and Data Analysis.
3	Syed Ahmad Faizan	Interpretation of Results.
4	Sumaira Kiran	Statistical Analysis.
5	Aqeel Natt	Literature Review.
6	Asif Bashir	Literature Review and Quality Insurer.