

## ORIGINAL RESEARCH

# Correlation of Contributing Factors with Post- Endoscopic Trans-Sphenoid Surgery Clinical Outcomes of Patients with Pituitary Adenoma

Afsoun Seddighi<sup>1</sup>, Seyed Amin Nicksirat<sup>1</sup>, Amir Saied Seddighi<sup>1</sup>, Sally Mahmoudzadeh<sup>1</sup>, Yasaman Arjmand<sup>1</sup>, Anahid Nabavi<sup>2</sup>, Tohid Emami Meybodi<sup>1\*</sup>

1. Shohada Tajrish Comprehensive Neurosurgical Center of Excellence, Functional Neurosurgery Research Center of Shohada Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2. Semnan University of Medical Sciences and Health Services, Semnan, Iran.

Received: October 2019; Accepted: October 2019; Published online: December 2019

**Abstract:** **Introduction:** Pituitary adenomas are commonly benign, slow-growing tumors that arise from cells in the pituitary gland and consist of a common type of intracranial space-occupying lesions. Based on the functionality and size of the adenoma, both medical and surgical approaches have been described. In this study, the authors aim to determine the effects of contributing factors of patients with pituitary adenoma undergoing trans-sphenoidal endoscopic surgery to their postoperative clinical status. **Material and Methods:** From March 2015 to November 2016, 100 patients diagnosed with pituitary adenoma confirmed by Magnetic Resonance Imaging (MRI) underwent a trans-sphenoidal endoscopic approach in the department of Neurosurgery of Shohada Tajrish Hospital. Demographic data, as well as pre-defined relevant contributing factors regarding clinical status, were recorded. All patients underwent neuroimaging and neurological examination before surgery and were followed in the postoperative period by repeated neurological examination, imaging surveys, and histopathological studies. Statistical analysis was performed using SPSS program version 23. **Results:** This study consisted of 59 males and 41 females with a mean age of 45.2 (24-63 years). Visual field defect (48%) was the most frequent finding, while asymptomatic status (36%) was the second major clinical finding in the patients. Neuroimaging survey revealed small tumor size and low extension type in 39 and 40 patients, respectively. Following the trans-sphenoid surgical approach, intact adrenal, gonadal, and thyroid function was found in 92%, 92%, and 89% of the postoperative phase cases. In the postoperative period, visual field defects, need for re-operation, diabetes insipidus (DI), focal neurological deficits (FND), diplopia, post-operative hemorrhagic event, cerebrospinal fluid (CSF) leak and meningitis were observed in 15%, 6%, 5%, 4%, 3%, 3%, 2% and 1% respectively. Moreover, three patients expired in the postoperative period. Our statistical analysis identified the presence of headache (P-value 0.039), functional pituitary adenoma (P-value 0.031), abnormal adrenal gland function (P-value 0.028), abnormal thyroid function (P-value 0.003), and abnormal growth hormone (GH) levels (P-value 0.008) as the major relevant contributing factors in determining the clinical status such as radiological imaging studies of the pituitary region, and hormonal profiles of these groups of patients. **Conclusion:** In general, the current study revealed that headache, as well as the presence of functional pituitary adenoma and abnormal adrenal, thyroid, and growth hormone levels, are among the major contributing factors in the determination of the postoperative clinical status of patients diagnosed with pituitary adenomas underwent trans-sphenoid surgery.

**Keywords:** Clinical status; Postoperative; Pituitary adenoma; Trans-sphenoidal endoscopic surgery

**Cite this article as:** Seddighi A, Nicksirat S A, Seddighi A S, Mahmoudzadeh S, Arjmand Y, Nabavi A, Emami Meybodi T. Correlation of Contributing Factors with Post- Endoscopic Trans-Sphenoid Surgery Clinical Outcomes of Patients with Pituitary Adenoma. Mens Health J. 2019; 3(1): e18.

\* **Corresponding Author:** Amir Saied Seddighi; Address: Department of Neurosurgery, Shohada Tajrish Hospital, Tajrish Square, Tehran, Iran. Email:

a\_seddighi@sbmu.ac.ir, Tel: (+98)9122151591



## 1. Introduction

A pituitary adenoma is a common intracranial tumor with a 25% prevalence of people with a past or present diagnosis and an autopsy-found rate of 10 to 15% (1). The pituitary adenoma is reported to 94 per 100,000 subjects of the Iranian population (2). "The majority of pituitary adenoma cases remains undiagnosed until late neurological and metabolic symptoms which are related to the type of hormone with increased secretion such as hyperprolactinemia, acromegaly, Cushing's disease and hyperthyroidism (3)." some symptoms are related to the mass effect with parasellar and suprasellar extensions such as headache and visual disturbances (1, 3). Despite some pharmacological adventures and advanced radiotherapeutic treatments, surgical intervention remains the most effective treatment strategy (3-5). Trans-sphenoidal surgery is a safe choice in patients suffering from acromegaly and Cushing's disease without prolactinoma that provides acceptable results than accompanying medical comorbidities (4, 5). The endoscopic approach provides easier access to the sella turcica with less adverse effects such as nasal mucosal or septal injuries, sinusitis, intracranial nerve injuries, diabetes insipidus, rhinorrhea of cerebrospinal fluid (CSF), and meningitis (6-10). The authors aim to determine the effects of contributing factors of patients diagnosed with pituitary adenoma undergoing trans-sphenoidal endoscopic surgery concerning their postoperative clinical status, the primary clinical signs/symptoms at presentation, radiological imaging of the pituitary region, size of tumors, visual deficits, and hormonal profiles demonstrating relevant disordered secretion had to be available.

## 2. Material and Methods

A pituitary adenoma is a common intracranial tumor with a 25% prevalence of people with a past or present diagnosis and an autopsy-found rate of 10 to 15% (1). The pituitary adenoma is reported to 94 per 100,000 subjects of the Iranian population (2). "The majority of pituitary adenoma cases remains undiagnosed until late neurological and metabolic symptoms which are related to the type of hormone with increased secretion such as hyperprolactinemia, acromegaly, Cushing's disease and hyperthyroidism (3)." some symptoms are related to the mass effect with parasellar and suprasellar extensions such as headache and visual disturbances (1, 3). Despite some pharmacological adventures and advanced radiotherapeutic treatments, surgical intervention remains the most effective treatment strategy (3-5). Trans-sphenoidal surgery is a safe choice in patients suffering from acromegaly and Cushing's disease without prolactinoma that provides acceptable results than accompanying medical comorbidities (4, 5). The endoscopic approach provides easier access to the sella turcica with less adverse effects such as

nasal mucosal or septal injuries, sinusitis, intracranial nerve injuries, diabetes insipidus, rhinorrhea of cerebrospinal fluid (CSF), and meningitis (6-10). The authors aim to determine the effects of contributing factors of patients diagnosed with pituitary adenoma undergoing trans-sphenoidal endoscopic surgery concerning their postoperative clinical status, the primary clinical signs/symptoms at presentation, radiological imaging of the pituitary region, size of tumors, visual deficits, and hormonal profiles demonstrating relevant disordered secretion had to be available.

## 3. Results

In this study, males dominated the females' population as 59 versus 41 cases (59% versus 41%). Men ranged from 27 to 63 years with a mean age of 46.6 years, while female age ranged from 24 to 60 years with a mean age of 43.1 years. While 45% of patients were older than 40 years, patients had a mean age of 45.2 years. 36% of patients were asymptomatic and consisted of the second most frequent manifestation of pituitary adenoma following visual field defect with 48% prevalence/ other less frequent clinical symptoms are mentioned in Table 1. Our neuroimaging survey resulted in detecting small tumors and low extension type in 39 and 40 patients (40%), respectively. Preoperative hormonal assay revealed functional pituitary adenoma in 31%, defective gonadal function in 28%, defective thyroid function in 26%, intact thyroid function in 20%, non-functional pituitary adenoma in 12%, abnormal adrenal function in 11%, intact gonadal function in 8% and intact adrenal function in 6% of patients. Moreover, patients' hormonal and neurological status in the postoperative period is described in Table 2. Six cases underwent reoperation, and 3 of them passed away in the postoperative period. In addition, diabetes insipidus (DI), diplopia, post-operative hemorrhagic event, cerebrospinal fluid (CSF) leak and meningitis were observed in 5%, 3%, 3%, 2% and 1% respectively. Following trans-sphenoid endoscopic adenoma removal, postoperative MRI revealed no residual tumor in 89 cases (89%). In comparison, others were found to have a stable (non-progressive) residual tumor in 5 cases (5%), progressive tumor in 5 patients (5%), and recurrent one in 1 patient (1%) in the follow-up period. Statistical analysis of these data with adverse postoperative outcomes includes headache, functional pituitary adenoma, abnormal function of adrenal, thyroid(hypopituitarism), growth hormone(sensitivity decreases), and their correlation with associated contributing factors and conditions revealed statistically significant in Table 3.

## 4. Discussion

In this study, the authors assessed the clinical outcomes and adverse effects following trans-sphenoidal endoscopic

adenoma resection to detect potential correlations between these factors and adverse postoperative outcomes. The majority of pituitary adenomas are benign and manifest as hormonal over secretion or neurological and visual defects secondary to mass effects to the surrounding neuro-structures. Cushing's disease, hyperprolactinemia, and acromegaly are among hypersecretory conditions, whereas the local mass effect on the pituitary's microscopic structures will cause hypopituitarism. (11) Although medical therapy is beneficial in prolactin-secreting pituitary adenomas (prolactinomas), trans-sphenoid surgical resection remains the standard gold treatment of these tumors. The addition of novel technologies such as endoscopic probes enhanced surgical accuracy and improved the extent of tumor resection. (12) Greenfield et al. demonstrated that endoscopic surgery is a minimally-invasive beneficial method in pituitary adenoma cases, as was established in our study. (13) Also, de Divitiis et al. assessed ten patients who underwent endoscopic trans-sphenoidal surgical approach for pituitary adenoma with complete and partial success in 70% and 20%, respectively. (14) They reported a 20% rate for CSF rhinorrhea and also showed a 10% mortality rate. However, in our study, only three patients (three percent) died. Laufer et al. in the United States assessed ten patients under endoscopic trans-sphenoidal surgery for pituitary adenoma and found a 90% success rate. (15) However, only one case with CSF rhinorrhea was seen, and diabetes insipidus was present in 60%, persistent in five cases. Importantly, this complication was seen in five cases in our study (5%), and only one case was persistent. Cappabianca et al. assessed 33 patients under endoscopic trans-sphenoidal surgery for pituitary adenoma, and only three patients had side effects, including CSF leak, bacterial meningitis, and seizure each one in one patient. Our results were relatively similar. (16) Also, Dehdashti et al. demonstrated that adverse effects and hospital stay are low in patients under trans-sphenoidal surgery and our study. (17)

## 5. Conclusion

In general, it may be concluded that related factors for the clinical status of patients with pituitary adenoma under trans-sphenoidal endoscopic surgery are headache, Functional pituitary adenoma, Abnormal adrenal function, Abnormal thyroid function, and Abnormal GH. However, further studies with larger sample size and comparison with other surgical modalities for pituitary adenoma would develop different results.

## 6. Appendix

### 6.1. Acknowledgements

None.

### 6.2. Author contribution

All the authors have the same contribution.

### 6.3. Funding/Support

None.

### 6.4. Conflict of interest

No conflict of interest.

## References

- Daly AF, Rixhon M, Adam C, Dempegioti A, Tichomirowa MA, Beckers A. High prevalence of pituitary adenomas: a cross-sectional study in the province of Liege, Belgium. *The Journal of Clinical Endocrinology & Metabolism*. 2006;91(12):4769-75.
- Mehrazin M, Rahmat H, Yavari P. Epidemiology of primary intracranial tumors in Iran, 1978-2003. *Asian Pacific Journal of Cancer Prevention*. 2006;7(2):283.
- Luque-Ramírez M, Paramo C, da Costa CV, García-Mayor R. Cost of management of invasive growth hormone-secreting macroadenoma. *Journal of endocrinological investigation*. 2007;30(7):541-5.
- Okamoto Y, Okamoto F, Hiraoka T, Yamada S, Oshika T. Vision-related quality of life in patients with pituitary adenoma. *American journal of ophthalmology*. 2008;146(2):318-22. e1.
- Buchfelder M. Management of aggressive pituitary adenomas: current treatment strategies. *Pituitary*. 2009;12(3):256-60.
- Winn HR. *Youmans neurological surgery*: Elsevier/Saunders; 2011.
- Hoyts W. (1988) *Clinical neuroophthalmology*. 5th ed 1988.
- Mindermann T, Wilson CB. Age-related and gender-related occurrence of pituitary adenomas. *Clinical Endocrinology*. 1994;41(3):359-64.
- Escobar A. Hypophysis tumors. *Revista Mexicana de Neurociencia*. 2006;7(6):586-91.
- Kreutzer J, Vance M, Lopes M, Laws Jr E. Surgical management of GH-secreting pituitary adenomas: an outcome study using modern remission criteria. *The Journal of Clinical Endocrinology & Metabolism*. 2001;86(9):4072-7.
- Jane Jr JA, Catalino MP, Laws Jr ER. Surgical treatment of pituitary adenomas. *Endotext [Internet]: MDText. com, Inc.*; 2019.
- Seltzer J, Wedemeyer MA, Bonney PA, Carmichael JD, Weiss M, Zada G. Outcomes following transsphenoidal surgical management of incidental pituitary adenomas: a series of 52 patients over a 17-year period. *Journal of Neurosurgery*. 2018;130(5):1584-92.



13. Greenfield J, Leng L, Chaudhry U, Brown S, Anand V, Souweidane M, et al. Combined simultaneous endoscopic transsphenoidal and endoscopic transventricular resection of a giant pituitary macroadenoma. *Minimally Invasive Neurosurgery*. 2008;51(05):306-9.
14. De Divitiis E, Cappabianca P, Cavallo LM, Esposito F, De Divitiis O, Messina A. Extended endoscopic transsphenoidal approach for extrasellar craniopharyngiomas. *Operative Neurosurgery*. 2007;61(suppl\_5):ONS219-ONS28.
15. Laufer I, Anand VK, Schwartz TH. Endoscopic, endonasal extended transsphenoidal, transplanum transtuberulum approach for resection of suprasellar lesions. *Journal of neurosurgery*. 2007;106(3):400-6.
16. Cappabianca P, Cavallo L, Esposito F, De Divitiis O, Messina A, De Divitiis E. Extended endoscopic endonasal approach to the midline skull base: the evolving role of transsphenoidal surgery. *Advances and technical standards in neurosurgery*: Springer; 2008. p. 151-99.
17. Dehdashti AR, Ganna A, Karabatsou K, Gentili F. Pure endoscopic endonasal approach for pituitary adenomas: early surgical results in 200 patients and comparison with previous microsurgical series. *Neurosurgery*. 2008;62(5):1006-17.

**Table 1:** The frequency of clinical manifestation in patients diagnosed with pituitary adenoma.

| Clinical manifestation     | Yes (exhibited) | No (not-exhibited) |
|----------------------------|-----------------|--------------------|
| Headache                   | 18              | 82                 |
| Apoplexia                  | 25              | 75                 |
| Visual defect              | 48              | 52                 |
| Rhinorrhea                 | 25              | 75                 |
| Acromegaly                 | 26              | 74                 |
| Congenital abnormality     | 29              | 71                 |
| Seizure                    | 25              | 75                 |
| Body Mass Index (BMI) > 30 | 28              | 72                 |
| Hypopituitarism            | 16              | 84                 |
| No symptoms                | 36              | 64                 |

**Table 2:** Postoperative patients' status.

| Postoperative evaluation | Yes | No |
|--------------------------|-----|----|
| Normal adrenal function  | 92  | 8  |
| Normal gonadal function  | 92  | 8  |
| Normal thyroid function  | 89  | 11 |
| Prolactin (normal range) | 88  | 12 |
| GH* (normal range)       | 86  | 14 |
| Visual defect            | 15  | 85 |
| Neurological defect      | 4   | 96 |
| Reoperation              | 6   | 94 |
| Mortality                | 3   | 97 |

\*Growth Hormone

**Table 3:** Contributing factors for postoperative adverse outcome in pituitary adenoma patients who underwent trans-sphenoid endoscopic resection.

| Factor/condition             | P-Value |
|------------------------------|---------|
| Headache                     | 0.039   |
| Functional pituitary adenoma | 0.031   |
| Abnormal adrenal function    | 0.028   |
| Abnormal thyroid function    | 0.003   |
| Abnormal GH                  | 0.008   |

