Results of Resection of Giant Pituitary Adenomas through Endoscopic Endonasal Approach

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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.

INTRODUCTION

As the average life expectancy rises, so will the medical treatment for older people with symptomatic pituitary adenoma. Pituitary adenomas account for 10 – 12% of all intracranial
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. 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. In one study, the average survival time for 36 individuals was six months. Several forms of cysts, including Rathke’s cleft, arachnoid, and dermoid cysts, can arise in the sellar and/or suprasellar region. 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. 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

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 3 months, 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).

#### Gender Distribution

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

#### 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 1: Age (n = 70).

<table>
<thead>
<tr>
<th>Age (in Years)</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>16 – 45</td>
<td>24</td>
<td>34.29%</td>
</tr>
<tr>
<td>46 – 75</td>
<td>46</td>
<td>65.71%</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
<td>100</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>55.7 ± 6.5 years</td>
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</table>

### Table 2: Gender (n = 70).

<table>
<thead>
<tr>
<th>Gender</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>32</td>
<td>45.71%</td>
</tr>
<tr>
<td>Female</td>
<td>38</td>
<td>54.29%</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
<td>100.0</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Duration of Disease</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2 years</td>
<td>29</td>
<td>41.43%</td>
</tr>
<tr>
<td>&gt; 2 years</td>
<td>41</td>
<td>58.57%</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
<td>100.0</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.1 ± 0.2 years</td>
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### Table 4: Operative Time (n = 70).

<table>
<thead>
<tr>
<th>Operative Time</th>
<th>No. of Patients</th>
<th>%</th>
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<tr>
<td>≤ 3 hours</td>
<td>45</td>
<td>64.3%</td>
</tr>
<tr>
<td>&gt; 3 hours</td>
<td>25</td>
<td>35.7%</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
<td>100.0</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.7 ± 0.4 hours</td>
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### Table 5: Frequency of Complications (n = 70).

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. of Patients</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Total</td>
<td>11</td>
<td>15.71%</td>
</tr>
<tr>
<td>Post-op CSF leak</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td>Major Vascular Injury</td>
<td>1</td>
<td>1.43%</td>
</tr>
<tr>
<td>Visual Deterioration</td>
<td>2</td>
<td>2.86%</td>
</tr>
<tr>
<td>Pituitary Dysfunction</td>
<td>3</td>
<td>4.29%</td>
</tr>
<tr>
<td>Diabetes Insipidus</td>
<td>6</td>
<td>8.57%</td>
</tr>
<tr>
<td>Infection</td>
<td>4</td>
<td>5.71%</td>
</tr>
<tr>
<td>Mortality</td>
<td>1</td>
<td>1.43%</td>
</tr>
</tbody>
</table>
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.

**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%.

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%). Other complications they reported such as SIADH (4.1%) and worsening of headache (2.7%). Furthermore, epistaxis was noted in 2.7%, meningitis in 2.7%, and hydrocephalus in 2.7%. 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. 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%). 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.

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%). A meta-analysis conducted by Barker et al. 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%. In one study conducted in Belgium by De Witte et al., 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%. The death rate was 2.5% in this study which is comparable to the death rate (1.43%) in our study. Another study conducted by Charalampaki et al., 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. 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.

Postoperative risk of development of SIADH is managed with mild fluid restriction, 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. 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 (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. 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. 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.
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


Additional Information
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Human Subjects: Consent was obtained by all patients/participants in this study.
Conflicts of Interest:
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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

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Author’s Full Name</th>
<th>Intellectual Contribution to Paper in Terms of:</th>
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<tbody>
<tr>
<td>1</td>
<td>Zubair Mustafa Khan</td>
<td>Study Design, Methodology, and Paper Writing.</td>
</tr>
<tr>
<td>2</td>
<td>Hannan Tayyab</td>
<td>Data Calculation and Data Analysis.</td>
</tr>
<tr>
<td>3</td>
<td>Syed Ahmad Faizan</td>
<td>Interpretation of Results.</td>
</tr>
<tr>
<td>4</td>
<td>Sumaira Kiran</td>
<td>Statistical Analysis.</td>
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<td>Aqeel Natt</td>
<td>Literature Review.</td>
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<tr>
<td>6</td>
<td>Asif Bashir</td>
<td>Literature Review and Quality Insurer.</td>
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