

Evaluation of Outcomes After Endoscopic Endonasal Surgery for Large and Giant Pituitary Macroadenoma: A Retrospective Review of 39 Consecutive Patients

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■ **BACKGROUND:** The endoscopic endonasal approach for pituitary neoplasms has shown similar efficacy compared with the microscopic approach. However, outcomes and complication rates with larger macroadenomas is not as well documented. This study addresses the efficacy and outcome of the fully endoscopic endonasal approach for large and giant pituitary adenomas.

■ **METHODS:** Endoscopic endonasal resection was performed in 39 patients with large (>3 cm) or giant (>4 cm) pituitary macroadenomas. Outcomes were assessed using formal visual examinations, endocrine status, and neurologic examinations. Statistical analyses of multiple variables were addressed for correlation to visual, endocrine, and neurologic outcomes.

■ **RESULTS:** Gross total resection of the pituitary macroadenoma was achieved in 22 of 39 (56.4%) patients based on postoperative magnetic resonance imaging. Higher Knosp grade was associated with near-total resection or subtotal resection ($P = 0.0004$). All patients had improved or stable visual symptoms. Time to diagnosis, preoperative visual deficit, and tumor size were not significant predictors of visual outcome. Of patients, 34 (87.1%) had a “good” endocrine outcome, whereas 5 did not. Among the 5 patients who did not have a good outcome, 1 had new hypopituitarism, and 4 required increased dosages of pharmacologic therapy. All patients with recurrent tumors had stable visual and good endocrine outcomes.

Postoperative cerebrospinal fluid leak occurred in 4 patients; lumbar drainage resolved the leak in 3, and reoperation was performed in 1 patient. There were no new cranial nerve deficits, new neurologic deficits, or mortality.

■ **CONCLUSIONS:** Endoscopic endonasal resection of large and giant pituitary macroadenomas is safe and efficient. Postoperative complications, including cerebrospinal fluid leak, are low. Surgical efficacy of the fully endoscopic endonasal approach for large and giant macroadenomas makes the technique a preferable option in this subset of patients.

INTRODUCTION

Pituitary adenomas account for 10%–15% of intracranial tumors (15, 42) with an age-adjusted prevalence of 16.7% in the general population (13). Patients with pituitary tumors often present with headaches (most common) and visual disturbances or various symptoms related to endocrine dysfunction (38). Although the treatment of functional (secretory) tumors, excluding most prolactinomas, requires gross total resection (GTR) for chemical remission (4, 29, 36), the treatment of larger tumors is more controversial. Giant pituitary adenomas, defined as tumors with a maximum diameter >4 cm, account for 5%–14% of adenomas that are treated surgically (12, 17, 18, 39). Although there are no established criteria for what constitutes a

Key words

- Endocrine outcomes
- Endoscopic endonasal surgery
- Giant macroadenoma
- Large macroadenoma
- Pituitary macroadenoma
- Skull base surgery
- Visual outcomes

Abbreviations and Acronyms

- CSF:** Cerebrospinal fluid
- DI:** Diabetes insipidus
- GH:** Growth hormone
- GTR:** Gross total resection
- HRT:** Hormone replacement therapy
- MRI:** Magnetic resonance imaging

NTR: Near-total resection

OGTT: Oral glucose tolerance test

STR: Subtotal resection

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“large” pituitary macroadenoma, some more recent series have defined these as >3 cm (21, 23, 34). Because of their predilection for suprasellar extension, large and giant macroadenomas most commonly manifest with long-standing visual disturbances and less frequently with other cranial nerve palsies, headache, or endocrine dysfunction (10, 14, 16, 34). Surgical decompression of the optic apparatus often results in immediate and long-term visual improvement (16, 23, 26, 33, 34, 43). However, for large adenomas, there is a risk of vascular injury or cranial nerve damage from resecting tumor grossly invading the cavernous sinus (22, 25). Because of this risk and the success of adjuvant radiotherapy in controlling residual disease (4, 32, 33), the goal of surgery is decompression and maximal resection without causing a new neurologic deficit.

Although technologic advancements in diagnostic imaging and microscopy have led to a preference of the less morbid transsphenoidal approach over purely transcranial surgery (41, 45), the narrow corridor of the microscopic transsphenoidal approach has limitations in visualizing the extrasellar extension frequently found in larger pituitary tumors. Open transcranial approaches, either primarily or in combination with the transsphenoidal approach, are sometimes required to achieve surgical goals (1, 22, 23, 45). However, microsurgical series of giant macroadenomas have shown a rate of GTR $<50\%$, with a high complication rate (17, 18, 26, 28).

The purely endoscopic endonasal approach has shown great promise in surgical management of pituitary tumors. Comparisons with microsurgical approaches have shown equivalent or superior outcomes with respect to length of stay, rate of resection, postoperative diabetes insipidus (DI), incidence of cerebrospinal fluid (CSF) leaks, and visual outcomes (2, 6-8, 19, 22, 23, 26, 35, 37). Studies including experiences with endoscopic resection of large and giant pituitary macroadenomas are less numerous (23, 26, 28). The purpose of our study is to validate further the appropriateness of the endoscopic endonasal approach for large and giant macroadenomas, with a specific focus on visual and endocrine outcomes and postoperative complications.

METHODS

After obtaining institutional review board approval, the medical records of 39 patients with large (>3.0 cm) or giant (>4 cm) pituitary macroadenomas that were surgically treated during the period 2009–2014 at Geisinger Medical Center and North Shore University Hospital were retrospectively analyzed (Figure 1). Indications for surgery included decreased visual acuity, visual field deficits, or cranial nerve palsies secondary to mass effect or invasion by the tumor. Prolactinomas were resected if they were refractory to medical therapy or if the patient was intolerant to medication.

Preoperative and postoperative magnetic resonance imaging (MRI) characteristics and visual and endocrine functions were reviewed. All surgeries were primarily performed by the lead neurosurgeon (A.D.) during this time period. Patients were followed during their hospital course to evaluate factors such as length of stay and complications including CSF leaks, DI, and other endocrine disturbances. All patients had postoperative follow-up (mean, 12 months) to assess symptomatic relief, complications, and postoperative morbidity.

All patients were seen by an experienced endocrinologist as an outpatient before and after surgery and as an inpatient for any complicated perioperative management. An endocrinopathy was defined as the presence of hypopituitarism or excess secretion from functional tumors. A good endocrine outcome was defined as 1) no new postoperative hypopituitarism, 2) stability of any previous hypopituitarism, or 3) chemical remission in functional adenomas. Chemical remission was based on the following criteria: for Cushing syndrome, a serum cortisol nadir of <2 $\mu\text{g/dL}$ or normal 24-hour urinary free cortisol test at 3 months; for growth hormone (GH)-secreting tumors, normalization of serum insulin-like growth factor, oral glucose tolerance test ≤ 0.4 ng/mL, or basal serum GH <2.5 ng/mL; and for prolactinomas, serum prolactin <15 ng/mL in male patients or <20 ng/mL in female patients. Patients with transient postoperative DI that resolved during the follow-up period were not considered to have a new endocrinopathy.

All patients received preoperative and postoperative formal visual acuity and visual field testing by a neuro-ophthalmologist. The presence of visual deficits, duration of deficits before surgery, and laterality of deficits were recorded. All patients received formal postoperative visual field examination within 6 weeks of the surgery. A patient was considered to have a “good” visual outcome if postoperative visual testing was unchanged or improved within this time period.

All patients underwent postoperative MRI within 48 hours of surgery. Multiple studies have confirmed the sensitivity of early postoperative MRI in detecting residual tumor and distinguishing postoperative changes from normal gland (40, 44). Postoperative MRI scans were read and interpreted by a neuroradiologist and reviewed by the primary neurosurgeon. The extent of tumor resection was documented comparing 1 or more of the postoperative MRI scans with the preoperative scans. Outcome was classified as GTR, near-total resection (NTR) with residual of $<10\%$, and subtotal resection (STR) with decompression but nodular tumor remnant. Follow-up MRI also looked for regrowth of residual tumor mass or recurrence of tumor.

Statistical analyses of multiple variables (age, sex, time to diagnosis, extent of visual or endocrine abnormality before treatment, tumor size, tumor location, extent of resection, and recurrent tumors) was addressed for correlation to visual, endocrine, and neurologic outcomes. Comparisons of categorical variables were carried out by χ^2 tests. Medians were presented for length of hospital stay owing to the skewness of the data, and Wilcoxon rank sum tests were used to assess their differences between groups. All statistical analyses were performed with SAS 9.3 (SAS Institute, Inc., Cary, North Carolina, USA).

Surgical Procedure

The operative technique used for these surgeries was a purely endoscopic endonasal approach. This technique has been well documented in the literature emphasizing a bimanual, 2-nostril technique for optimal safety and efficacy (8, 9, 33). For visualization, 0-degree and 30-degree 4-mm endoscopes (Karl Storz GmbH & Co., Tuttlingen, Germany) were used. Patients were registered to a frameless stereotactic navigation system (Stealth; Medtronic, Jacksonville, Florida, USA) to aid with intraoperative verification of anatomic structures. Lumbar drains were not routinely used before or after surgery.

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