A Benchmark for Preservation of Normal Pituitary Function After Endoscopic Transsphenoidal Surgery for Pituitary Macroadenomas

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■ INTRODUCTION: **We report a contemporary consecutive series of 80 patients operated on for benign pituitary macroadenomas, followed endocrinologically for at least 3 months postoperatively. These patients were systematically evaluated preoperatively by high-resolution magnetic resonance imaging designed to detect the position of normal gland relative to the lesion. The rate of preservation of normal pituitary was critically analyzed using this strategy combined with endoscopic transsphenoidal resection.**

■ METHODS: **This is a retrospective review of 46 women and 34 men with mean postoperative follow-up of 14 months (range, 3–30 months). The lesions encountered consisted of 80 pituitary macroadenomas (55 nonfunctioning, 18 acromegaly, 5 prolactinoma, 1 Cushing, one thyroid-stimulating hormone). Pituitary endocrine status was determined preoperatively and at most recent follow-up, and categorized as normal or impaired, based on laboratory studies showing new hormone deficiency or the need for pituitary hormone replacement therapy.**

■ RESULTS: **Fifty-three patients (66.3%) had normal endocrine function preoperatively; 3 (5.7%) had loss of function postoperatively (1 transient). Twenty-seven patients (33.8%) had impaired function preoperatively; postoperatively 20 (74.1%) were unchanged, and 5 (18.5%) were worse; 2 (7.4%) recovered lost pituitary function. Of 80 patients undergoing resection, 5 (6.3%) had worsened pituitary function postoperatively. Patients with recurrent lesions ($n = 5$, 6.3%) and those presenting with pituitary tumor apoplexy ($n = 5$, 6.3%) were more likely to become further impaired. Other endocrine sequelae included 2 patients with permanent postoperative diabetes insipidus and 3 with transient symptomatic syndrome of inappropriate secretion of antidiuretic hormone.**

■ CONCLUSIONS: **The preservation and restoration of hormonal function are essential to assessing the outcome of surgery and to the patient's quality of life. Careful analysis of the anatomy of the pituitary lesions and their effect on the anatomy and physiology of the pituitary gland are crucial to success and allow modern technological advances to provide fewer complications of therapy and improved outcomes for our patients. The benchmarks provided in this article are a stimulus for even better results in the future as we take advantage of technical and conceptual advances and the benefits of multidisciplinary collaboration.**

INTRODUCTION

One of the major goals in pituitary surgery is the preservation or restoration of pituitary hormonal function that has been altered by the effects of the tumor. Likewise, one of the complications of pituitary surgery is the loss of pituitary function from either the anterior or the posterior lobe of the pituitary gland. Reports of preservation or restoration of pituitary function after surgery have been attempted over time.[1-22] Although there are several reviews of complications of pituitary surgery that include some aspects of postoperative hypopituitarism, they are rarely comprehensive, adequately inclusive, and appropriately followed over time. Few reflect current sophisticated neuroimaging and the use of modern surgical techniques such as

Key words
- Endoscopic transsphenoidal surgery
- Macroadenoma
- Pituitary function
- Pituitary surgery

Abbreviations and Acronyms
3D: Three-dimensional
MRI: Magnetic resonance imaging

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endoscopy. It is difficult to design a prospective controlled trial, because techniques and surgeon preferences change, and it is well recognized that analyses using historical controls are neither reliable nor useful. For those reasons, we present our analysis as a benchmark, with results that we hope will be surpassed in the future, as diagnostic and therapeutic capabilities continue to advance.

The desire to locate accurately the position and extent of normal pituitary adjacent to a pituitary tumor was a motivation for our previous article entitled "MRI validation of pituitary gland compression and distortion by typical sellar pathology."[23] We reasoned that if the location and extent of normal gland could be accurately determined preoperatively, the surgeon could more effectively preserve the gland and its function.

Many investigators have contended that endoscopic pituitary surgery is more precise in the removal of pituitary tumor and in the separation of tumor from normal gland.[24,25]

These advantages of superior visualization have not yet resulted in definitive studies showing superiority of the endoscope over previous microscopic surgical series.[26,27]

This article, therefore, is an attempt to provide the contributions of contemporary pathoanatomic imaging[23] and endoscopic surgery by an experienced team[24] that ideally result in less surgical damage to the pituitary gland and enhanced recovery of impaired pituitary function.

METHODS

A total of 80 patients with pituitary macroadenomas operated on between September 2011 and June 2013 were included in the study. This retrospective study design includes all patients from our previous study wherein contemporary magnetic resonance imaging (MRI) methods were compared for concordance with intraoperative localization of the normal pituitary gland in a series of 80 consecutive patients with pituitary macroadenomas operated on using the endoscopic transsphenoidal approach.[23]

All preoperative MRIs were obtained at our institution using a BrainLab protocol (BrainLab, Munich, Germany).

The magnets were 1.5 or 3.0 Tesla. All studies had a standard protocol that included pre- and postcontrast T1 sequences in coronal and sagittal planes at 3 mm thickness with 0 mm skip, which were used as the main set of images. Additional supporting sequences for all cases included sagittal T2-weighted volume acquisition using 0.4 mm thickness for 1.5 T and 1.0 mm thickness for 3.0 with coronal reformatted images, and axial postcontrast 1.4 mm volume acquisition with coronal and sagittal reformatted images. All studies had Magnevist (Bayer, Munich, Germany) intravenous contrast at 0.1 mm/kg body weight (0.2 mL/kg) with a maximum dose of 20 mL.

Patients from this group who were able to follow our standard postoperative protocol were analyzed with regard to preservation or loss of preoperative normal anterior and posterior pituitary function. This protocol consisted of a preoperative evaluation in our multidisciplinary pituitary clinic, taking advantage of the interactions among a pituitary neuroendocrinologist and our neurosurgical and neuroradiologic team. Preoperative pituitary hormonal function was determined in every case; the need for serum cortisol replacement and evaluation for syndrome of inappropriate secretion of antidiuretic hormone was systematically determined at 1 week postoperatively. Six weeks postoperatively a neuroendocrine visit evaluating all pituitary hormones was accomplished; the patients were evaluated again at 3 months, at which time a definitive postoperative MRI scan was obtained, and they were evaluated again at 1 year after surgery. This allowed us to obtain an excellent volume of robust endocrine data, which were used to test the hypothesis. The hypothesis was that precise neuroimaging recognition of the position and extent of normal gland combined with endoscopic transsphenoidal surgery in the hands of an experienced surgical team would lead to improved endocrine outcomes, possibly setting a new benchmark.

The demographics of the patients are given in Table 1. Fifty-five of these patients had clinically nonfunctioning tumors, and the remaining 25 had a variety of hyperfunctioning tumors with associated endocrine disorders. Categorization of the preoperative hormonal status after laboratory evaluations (fasting cortisol, thyroid-stimulating hormone, total T4, insulin-like growth factor 1, prolactin, total testosterone in men, follicle-stimulating hormone/luteinizing hormone in women), was as follows: normal or impaired. Staining for the α subunit of the glycoproteins is no longer a part of our routine evaluation. Categorization based on postoperative hormonal replacement status at the time of most recent follow-up was as follows: normal, impaired, transiently impaired, worse (addition of 1 or more new hormonal deficiencies), and improved over preoperatively (recovery of at least some hormonal function) (Table 2). Thyroid gland-related hypothyroidism (eg, Graves disease, Hashimoto thyroiditis) was not considered impairment pre- or postoperatively in this analysis. The mean follow-up was 14 months (range, 3–30 months). Preoperative visual loss was present in 21 patients. Five of these patients had presented with recurrent tumors after previous surgery, and 5 presented with pituitary tumor apoplexy.

We presented the endocrine data in a practical fashion from the standpoint of the patient (ie, whether new hormone replacement was needed or whether preoperative pituitary function was impaired or improved postoperatively). We have specific data for all of the hormone axes, concentrating on cortisol and thyroid replacement (Table 3).

All patients in this study had a minimally invasive endoscopic transsphenoidal approach. Most of the cases (64%) were treated using the three-dimensional (3D) endoscope.[24] The endoscope and microscope were used together in 3 cases. The intent to treat was with the endoscope in all cases. Our endoscopic experience began in 1998 and became primarily 3D in 2010. As we became more proficient with the 3D endoscope, it was used more often than the two-dimensional endoscope. Inability to use the 3D endoscope in the intraoperative MRI operating suite

Table 1. Demographics of 80 Patients with Pituitary Macroadenoma

Sex	Number (%)	Age (years) (mean, range)
Female	46 (57.5)	53.5 (16–84)
Male	34 (42.5)	53.0 (16–79)