Outcome of Endoscopic Transsphenoidal Surgery for Acromegaly

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■ OBJECTIVE: **Endoscopic transsphenoidal surgery has recently been introduced in pituitary surgery. We investigated outcomes and complications of endoscopic surgery in 2 referral centers in Korea.**

■ METHODS: **We enrolled 134 patients with acromegaly (microadenomas, n = 15; macroadenomas, n = 119) who underwent endoscopic transsphenoidal surgery at Seoul National University Hospital (n = 74) and Samsung Medical Center (n = 60) between January 2009 and March 2016. Remission was defined as having a normal insulin-like growth factor-1 and a suppressed growth hormone (GH) <1 ng/mL during an oral glucose tolerance test.**

■ RESULTS: **Remission was achieved in 73.1% of patients, including 13 of 15 microadenoma patients (86.7%) and 86 of 119 macroadenoma patients (72.3%). A multivariate analysis to determine a predictor of biochemical remission demonstrated that absence of cavernous sinus invasion and immediate postoperative GH levels <2.5 ng/dL were significant predictors of remission (adjusted odds ratio [OR], 5.14; 95% confidence interval [CI], 1.52–17.3 and OR, 9.60; 95% CI, 3.41–26.9, respectively). After surgery, normal pituitary function was maintained in 34 patients (25.4%). Sixty-four patients (47.7%) presented complete (n = 59, 44.0%) or incomplete (n = 5, 3.7%) recovery of pituitary function. Hypopituitarism persisted in 20 patients (14.9%) and worsened in 16 patients (11.9%). Postoperatively, transient diabetes insipidus was reported in 52 patients (38.8%) but only persisted in 2 patients (1.5%). Other postoperative complications were epistaxis (n = 2), cerebral fluid leakage (n = 4), infection (n = 1), and intracerebral hemorrhage (n = 1).**

■ CONCLUSIONS: **Endoscopic transsphenoidal surgery for acromegaly presented high remission rates and a low incidence of endocrine deficits and complications. Regardless of surgical techniques, invasive pituitary tumors were associated with poor outcome.**

INTRODUCTION

Patients with acromegaly have a considerable burden of complications, including cardiovascular diseases, respiratory complications, metabolic syndrome, malignancy, and musculoskeletal pain.[1] These factors contribute to increased mortality rates in patients with acromegaly. Therefore, treatment goals of acromegaly are to control growth hormone (GH) and insulin-like growth factor-1 (IGF-1) secretion, reduce tumor growth, and preserve pituitary hormone function.[2]

Surgical removal of GH-secreting pituitary adenomas is the primary therapy in most patients.[2] Transsphenoidal microscopic surgery has been the standard surgical approach in acromegalic patients. The surgical success rate of microscopic surgery has been reported at 67%–95% for microadenomas and 47%–68% for macroadenomas (overall, 42%–72%), based on large sample-sized data including up to 506 patients.[3-7] Recently,

Key words
- Acromegaly
- Endoscopic transsphenoidal surgery

Abbreviations and Acronyms
ACTH: Adrenocorticotropic hormone
CV: Coefficient of variation
ETS: Endoscopic transsphenoidal surgery
FSH: Follicle-stimulating hormone
GH: Growth hormone
IGF-1: Insulin-like growth factor-1
LH: Luteinizing hormone
MRI: Magnetic resonance imaging
SMC: Samsung Medical Center
SNUH: Seoul National University Hospital
TSH: Thyroid-stimulating hormone

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endoscopic transsphenoidal surgery (ETS) has been adopted for pituitary adenomas. When compared with a traditional microscopic approach, the endoscope provides a relatively wide view of the surgical site and enhances visualization of the lateral aspect of the cavernous sinus and suprasellar compartment of large tumors.[8,9] However, there is still no evidence that the endoscopic approach is superior to the microscopic approach in terms of efficacy or safety for pituitary adenoma surgery.[2,9-11] Favorable outcomes are largely dependent on the surgical skill and experience of the neurosurgeon. Single-surgeon treatment series can represent a personalized treatment outcome. Data from single-surgeon series have several limitations that result from the limited sample size and inconsistencies in data collection. In contrast, outcomes from registry data of surgeries performed by heterogeneous surgeons can provide a sufficient number of serial surgeries with broader applications of the results. This study represents the only comprehensive review of outcomes and complications after endoscopic pituitary surgery for acromegaly across a heterogeneous group of surgeons and patients. Here, we retrospectively investigated the initial surgical outcomes and complications of endoscopic pituitary surgery in the second largest data set of acromegaly patients from two referral centers, and elucidated which parameters affected biochemical remission.

MATERIALS AND METHODS

Study Subjects

We retrospectively included 134 acromegalic patients who underwent ETS at Seoul National University Hospital (SNUH) (n = 74) and Samsung Medical Center (SMC) (n = 60) between January 2009 and March 2016, consecutively. All patients were followed-up within at least 6 months after surgery. We excluded patients lost to follow-up (n = 5), patients with a lack of magnetic resonance imaging (MRI) or biochemical data (n = 7), and patients with the previous surgery in another hospital (n = 3). The surgical procedures were performed by 5 neurosurgeons (1 from SNUH, and 4 surgeons from SMC), and all data were retrieved from medical records and imaging studies. The study was approved by the institutional review board of each institution (numbers 1503-040-654 and SMC 011-02).

Study subjects underwent neuro-ophthalmologic and endocrinologic evaluations before and after surgery. Visual acuity and Goldmann perimetry testing were performed in patients with macroadenomas or microadenomas abutting the optic chiasms. Decreased visual acuity or visual field defects were considered visual deficits.

All pituitary adenomas were visible on preoperative MRI. Dynamic MRIs of the sella turcica and parasellar region were performed in the sagittal and coronal planes, both before and after administration of gadolinium contrast. The tumor size was presented as maximal tumor diameter based on MRI. Pituitary adenomas of <10 mm in maximal diameter were designated as microadenomas, whereas adenomas ≥10 mm in maximal diameter were defined as macroadenomas. Macroadenomas were categorized into 3 groups: 10–20, 20–30, and >30 mm. The lateral extension of the tumor was graded with the modified Knosp grading system based on coronal T1-weighted contrasted imaging, and only the complete encasement of internal carotid artery was regarded as grade 4.[12]

Hormone assessment was performed in all patients pre- and postoperatively. Biochemical remission was defined by demonstration of suppressed serum GH levels <1 ng/mL after a 75-g oral glucose load, and plasma IGF-1 levels within the normal range for age at approximately 12 weeks.[2] GH levels were measured by an immunoradiometric assay kit (Izotop, Budapest, Hungary). The intra-assay coefficients of variation (CVs) were 1.5%–3.5%, and the interassay CVs were 2.5%–3.3%. IGF-1 levels were measured by an immunoradiometric assay kit (Beckman Coulter, Brea, California, USA). The intra-assay CVs were ≤5.6%, and the interassay CVs were ≤8.3%. The lowest detectable levels of GH and IGF-1 were 0.02 and 4.55 ng/mL. The World Health Organization international standards for GH (98/574) and IGF-I (91/554) measurement were used. IGF-1 levels were presented as times of upper limit of normal. Immediate postoperative GH levels were measured in the early morning of postoperative day 1 or 2.

Hypopituitarism was assessed in all patients pre- and postoperatively, except the GH–IGF-1 axis. Luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol or total testosterone, prolactin, free T4, thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), and serum cortisol levels were measured by radioimmunoassay and immunoradiometric assay between 8 and 10 AM. ACTH deficiency was defined as peak cortisol levels ≤18 μg/dL after a short Synacthen test, or in cases where dynamic testing was not available, a low morning cortisol level (<5 μg/dL) with a low to normal ACTH level (10–65 pg/mL). TSH deficiency was defined according to a low free T4 level (<0.70 ng/dL) under a low to normal TSH level (reference range, 0.4–4.1 μIU/mL). Normal menopause was defined by FSH >30 mIU/mL and estradiol <50 pg/mL in hypopituitary patients. Premenopausal women with FSH/LH sufficiency were considered to have no menstrual disorders. In men, low testosterone levels under a low to normal FSH/LH level indicated a need to assess central hypogonadism. In patients with water diuresis and polydipsia, diabetes insipidus was considered. We defined transient (<1 month) or permanent (≥3 months) postoperative diabetes insipidus based on the usage of desmopressin because the management protocols of postoperative diuresis were different between the 2 institutions. Endocrinologic outcomes were classified as the following: 1) normal: no pituitary hormone deficiency before and after ETS; 2) normalized hypopituitarism: hypopituitarism recovered completely after ETS; 3) improved hypopituitarism: hypopituitarism resolved, but incompletely; 4) persistent hypopituitarism: the number of deficient axes of pituitary hormone did not change after ETS; and 5) worsened hypopituitarism: the number of deficient axes of pituitary hormone worsened after ETS.[13]

Surgical Procedures

The surgical procedures performed in this study aligned with those detailed in the current literature.[14,15] All surgical procedures were initiated though the binostril pure endonasal or transseptal routes, under the view of an endoscope, and all turbinates were preserved without posterior septectomy. We preferred to halt the bleeding from the nasal mucosa with hemostatic material, and tried to avoid coagulation to prevent postoperative synechiae and preserve mucosal function. The bony sella opening was performed enough to identify the superior intercavernous sinus and bilateral cavernous sinus. We attempted to find the pseudocapsule of the