Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company’s public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Challenges, Learning Curve, and Safety of Endoscopic Endonasal Surgery of Sellar-Suprasellar Lesions in a Community Hospital

Mohamed A.R. Soliman¹,², Sydney Eaton², Elise Quint², Abdullah F. Alkhamees²,⁵, Saba Shahab², Avalon O’Connor², Erika Haberfellner², Jacob Im², Abdurrahim A. Elashaal³, Francis Ling⁴, Mustafa Elbreki⁴, Tommy Dang³, Dante J. Morassutti³, Abdalla Shamisa³

BACKGROUND AND OBJECTIVE: Endoscopic endonasal surgery (EES) for the management of sellar, suprasellar, and anterior skull base lesions is gaining popularity. Our aim was to analyze and present the clinical outcomes of EES for the management of these lesions in a community hospital setting.

METHODS: We retrospectively reviewed the charts of 56 patients with sellar, suprasellar, and anterior skull base lesions who underwent EES between 2010 and 2018.

RESULTS: There was male predominance (53.6%) with a mean age of 54.9 ± 13.7 years. Lesions were 45 pituitary adenomas, 5 meningiomas, 3 metastatic, 1 craniopharyngioma, 1 Rathke cyst, and 1 mucocele. Gross total excision was achieved in 57.1%, subtotal excision occurred in 37.5%, and decompression and biopsy were achieved in 5.4% patients. Postoperative vision normalized or improved in 27 patients (86.1%) and was stable in 4 patients (13.9%). Recovery of a preexisting hormonal deficit occurred in 13 (23.2%) patients, and a new hormonal deficit occurred in 9 patients (16.1%). The mean hospital stay was 6.1 ± 4.9 days. Postoperative complications included cerebrospinal fluid leak in 8 patients (14.3%), Four patients (7.1%) had meningitis. Diabetes insipidus was present in 19 patients (33.9%), and postoperative intracranial hematoma requiring evacuation was necessary in 2 patients (3.6%). The mean follow-up duration was 47.5 ± 25.8 months. Lesion progression or recurrence requiring redo surgery occurred in 5 patients (8.9%). Regarding the learning curve, the postoperative cerebrospinal fluid leak, meningitis, new hormonal deficits, and diabetes insipidus decreased in the second half of the patients.

CONCLUSIONS: EES provides an effective and safe surgical option with low morbidity and mortality for the treatment of sellar, suprasellar, and anterior skull base lesions in a community hospital setting.

INTRODUCTION

Endoscopic endonasal surgery (EES) has been gaining popularity over the past 2 decades as an atraumatic and a reliable approach for the management of sellar, suprasellar, and anterior cranial fossa lesions. Visual field defects, headaches, ophthalmoplegia, hypopituitarism, and hormone hypersecretion are common presentations of a pituitary adenoma, one of the most common sellar lesions.1-3 Microsurgical transsphenoidal approaches had been the gold standard for sellar and suprasellar procedures for decades before the introduction of EES into the neurosurgical field in the mid to late 1990s.4 The sellar and suprasellar EES technique was a translation from the field of otolaryngology, where it was initially used to replace the previous “open” method of sinus surgery.5 Microscopic transsphenoidal pituitary surgery had not evolved significantly since its introduction by Harvey Cushing in 1909, until the pioneering work of Hae-Dong Jho in 1997 at the University of Pittsburgh school of medicine.6 Jho et al6 demonstrated that endoscopic transsphenoidal approaches were possible for

Key words
- Clinical outcomes
- Community hospital
- Endoscopic endonasal surgery
- Olfactory groove
- Sellar
- Suprasellar
- Tuberculum sellae

Abbreviations and Acronyms
- CSF: Cerebrospinal fluid
- EES: Endoscopic endonasal surgery
- GTR: Gross total resection

From ¹Neurosurgery Department, Cairo University, Cairo, Egypt; ²Schulich School of Medicine and Dentistry, University of Western Ontario, London, Canada; ³Department of Neurosurgery and Ear, Nose and Throat Department, Windsor Regional Hospital, Western University, ON, Canada; and ⁴Neurosurgery Department, Qassim University, Qassim, Kingdom of Saudi Arabia
To whom correspondence should be addressed: Mohamed A.R. Soliman, M.D.
[E-mail: moh.ar.sol@kasralainy.edu.eg]
Citation: World Neurosurg. (2020) 138:e940-e954.
https://doi.org/10.1016/j.wneu.2020.04.028
Journal homepage: www.journals.elsevier.com/world-neurosurgery
Available online: www.sciencedirect.com
1878-8750/$ - see front matter © 2020 Elsevier Inc. All rights reserved.
pituitary surgery and could facilitate faster postoperative recovery compared with the gold standard microsurgical approach. EES has continued to gain favorability over conventional microsurgical transsphenoidal approaches for sellar-suprasellar lesions whatever the size and type of the tumor due to the panoramic view of the surgical field, easier mobility of surgical instruments, and better views of anatomic corners with angled lenses. 8–13

Endoscopic surgical approaches are associated with a learning curve, and for this reason many neurosurgeons have steered clear of attempting this newer technique. 11 However, current EES research has not focused on the specifics of this learning curve, the clinical and practical implications for a surgeon just beginning to practice EES, or the amount of experience required to become proficient. As well, neurosurgeons in favor of the traditional microscopic approach maintaining stereoscopic vision and direct instrument visualization throughout the procedure. Initially, there were concerns regarding instrument maneuverability in EES; however, technologic advances such as the binarial endoscopic approach have resolved early concerns. 14

Li et al 15 demonstrated that countries such as the United States, with high gross domestic products, tend to contribute more to the field of EES. With this in mind, it is understandable how only large, well-funded academic centers have been able to introduce EES successfully into their neurosurgery programs. 15

There is currently no research showing the adoption and success of EES in small, nonacademic community hospitals, yet a portion of patients with sellar and suprasellar lesions are seen by community neurosurgeons. In Ontario, wait times in 2018 exceeded 26 weeks for neurological patients to access surgery at a university-affiliated health science center. 16, 17 Knowledge regarding the feasibility of EES in smaller community hospitals may help increase access to evidence-based neurosurgical practices for patients with sellar and suprasellar lesions, especially after recent recommendations during the COVID-19 pandemic of fair allocation of medical resources among different types of hospitals. 18–20 The purpose of this study was to demonstrate that EES can be used successfully for the treatment of sellar, suprasellar, and anterior skull base lesions in a community hospital setting, as well as to demonstrate and quantify the steep learning curve associated with EES.

MATERIAL AND METHODS

STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were used to ensure the appropriate reporting of this observational study. 21

Data Acquisition

We retrospectively reviewed the charts of 56 patients with sellar, suprasellar, and anterior skull base lesions who underwent EES between 2010 and 2018 at Windsor Regional Hospital. Demographic and surgical characteristics were reviewed including patient age, sex, clinical picture, lesion size, extent of resection (according to postoperative MR), it was divided into gross total resection [GTR, absence of any tumor residual]; subtotal resection (<10% residual of the initial tumor size]; and biopsy), pathology, surgical complications, and clinical outcomes.

Surgical Technique

All surgeries were performed by 1 of the 4 neurosurgeons and 1 of the 2 otolaryngologists. They achieved binostril access using a 4-handed technique. A perioperative lumbar drain was not used generally except in 2 patients who developed postoperative cerebrospinal fluid (CSF) leak. All patients received intravenous cefazolin 30 minutes before surgery and another single dose 8 hours after surgery, which is similar to previously reported regimens. 20, 21 After the patient was generally anesthetized and endotracheally intubated, the area of the nose was prepared and draped in the usual sterile fashion. Next, the otolaryngologist lateralized the middle turbinates bilaterally, followed by harvesting a vascularized unilateral nasoseptal flap. In recurrent cases, the vascularized nasoseptal flap of the contralateral side of the previous approach was harvested. Depending on the location and extent of the tumor, the bony access was expanded from the sphenoid to include translacial and/or tranplanum exposure (extended endonasal) as needed. In the olfactory groove meningioma patient, the tumor was accessed through a transethmoid approach. The dura over the tumor was coagulated and opened in a cruciate fashion. The tumor excision/biopsy was carried out according to the pathology of the tumor. After excision/biopsy of the tumor, adequate hemostasis was achieved, followed by reconstruction of the skull base using a simple layer of Surgicel (Ethicon, Somerville, New Jersey, USA), a layer of Tisseel (Baxter Healthcare, Deerfield, Illinois, USA); a small layer of fat graft in the sinus, followed by of Tisseel (Baxter Healthcare, Deerfield, Illinois, USA); and finally a vascularized nasoseptal flap (added only in the second half of patients). In cases of intraoperative high-flow CSF leak and extended approaches, an additional layer of inlay and onlay fascia lata graft were used. Valsalva maneuver was done to confirm no CSF leakage. Medialization of the middle turbinates were done as the final stage of the procedure.

Learning Curve

For each surgeon, the patients were divided evenly into the first and second halves. The results of the first and second halves of each surgeon and the total number of patients were compared in terms of postoperative CSF leak, meningitis, new hormonal deficit, permanent diabetes insipidus, and visual improvement. We divided the outcomes according to surgeons to show the initial outcomes of neurosurgeons who received formal training on the endoscopic transsphenoid skull base surgeries and compare them with the other general neurosurgeons.

Literature Review

We compared our results with the recently published data discussing in detail the clinical outcomes of EES in pituitary adenoma resection (most of our patients were pituitary adenomas, and there is a paucity of studies describing the outcomes of sellar-suprasellar lesions in general) at academic centers in the past 5 years. Non-English language studies and studies describing the clinical outcome in a certain age group were excluded.
Statistical Analysis
Continuous variables were described as a mean ± standard deviation, whereas discrete variables were described as frequency (% of total). Continuous and discrete variables were analyzed via the Exact Fischer test and chi-square test. P value <0.05 was considered statistically significant. Data were analyzed using SPSS version 16.0 (IBM Inc).

RESULTS

Preoperative Characteristics
In our retrospective observational study, there were 56 patients, with male predominance (53.6%) and a mean age of 54.9 ± 13.7 (range, 27–82) years. The mean follow-up duration was 47.5 ± 25.8 months. All patients were undergoing a first-time resection of their lesion except there were 5 patients (8.9%) who had recurrent tumors treated with prior surgery (4 with previous microscopic transnasal transsphenoidal and 1 with a previous transcranial resection). Lesions included 45 pituitary adenomas (36 nonfunctioning, 3 prolactinomas, 3 gonadotrophin releasing hormone secreting, 2 adrenocorticotropic hormone secreting, and 1 growth hormone secreting), 5 meningiomas (4 tuberculum sellae and 1 olfactory groove), 3 metastatic lesions, 1 craniopharyngioma, 1 Rathke cyst, and 1 mucocele (Table 1). The mean size of the lesions was 2.76 ± 1.06 cm in the craniocaudal dimension, 2.15 ± 0.82 cm in the anteroposterior dimension, and 2.2 ± 0.81 cm in the transverse dimension (Figures 1 and 2). The patients with Knosp grades 3 and 4 were 35.5% of the pituitary adenoma patients. The tumor location, extension, and neurovascular relations of each case are reported in Table S1.

Clinical Presentation
The clinical presentation of patients in our study was heterogeneous. Patients presented with, in order of prevalence, headache, hormonal deficit, visual deficit, cranial nerve deficit, diplopia, and pituitary apoplexy. The majority of patients (42/56, 75%) presented with headache. A large proportion also presented with some form of hormonal deficit (31/56, 57.1%). These included panhypopituitarism, hypothyroidism, hypogonadism, hypoadrenalism, and hyperprolactinemia. Some patients experienced more than 1 hormonal deficit. The GnRH-secreting pituitary adenomas presented with mass effect rather than endocrine symptoms. Most (31 of 56) patients (55.4%) presented with a visual deficit. The most common visual deficit was bitemporal hemianopia (14/31, 45% of patients with visual field defects). Ten patients had cranial nerve deficits (17.9%), most commonly a third nerve palsy. Nine (16.1%) of 56 patients experienced diplopia. Eight (14.3%) of 56 patients had pituitary apoplexy. The majority of patients had a normal mental status; however, 12.5% presented with a disturbed level of consciousness (Table 2).

Perioperative Outcomes
Standard EES was done in 49 (87.5%) patients, and extended EES was done in 7 (12.5%) patients. GTR was achieved in 32 (57.1%) patients, subtotal excision in 21 (37.5%) patients, and decompression and biopsy in three (5.4%) patients. The reasons for not achieving GTR were cavernous sinus invasion in 13 (23.2%) patients, surgeon’s inexperience in 5 (8.9%) patients, and optic apparatus invasion/adherence in 2 (3.6%) patients. Finally, the initial aim of surgery was not GTR in four (7.1%) patients. None of the patients received adjuvant radiotherapy except the 3 metastatic lesions. There was no reported intraoperative complication. Postoperative vision normalized or improved in 27 (86.1%) patients or remained stable in 4 (13.9%) patients. There was no worsening of visual symptoms. Recovery of a preexisting hormonal deficit occurred in 13 (23.2%) patients, and a new hormonal deficit requiring hormonal replacement occurred in 9 (16.1%) patients. The mean hospital stay was 6.1 ± 4.9 days. Postoperative complications included postoperative CSF leak in 8 (14.3%) patients (3 [5.4%] of them were operated on by extended EES). Four (7.1%) patients had meningitis, diabetes insipidus was present in 19 (33.9%) patients (6 permanent and 13 transient), and postoperative intracranial hematomas required evacuation in 2 (3.6%) patients. Of the 8 patients who suffered a CSF leak, 3 resolved nonoperatively. One resolved by bed rest only, and 2 resolved with a lumbar drain. Five patients with postoperative CSF leak required surgical repair with Surgicel (Ethicon, Somerville, New Jersey, USA), Tisseel (Baxter Healthcare, Deerfield, Illinois, USA), fat graft, and fascia lata graft. Two of these patients required only 1 repair attempt, 1 required 2 attempts, and 2

| Parameter | Value |
|-----------|-------|
| Age (years) | Mean 54.9 Range 27–82 Standard deviation 13.7 |
| Sex | Male 30 (53.6) Female 26 (46.4) |
| Recurrent tumor | 5 (8.9) |
| Lesion type | Pituitary adenomas 45 (80.4) Nonfunctioning 36 (64.3) Prolactinoma 3 (5.4) Growth hormone secreting 1 (1.8) GnRH secreting 3 (5.4) ACTH secreting 2 (3.8) Meningioma 5 (8.9) Tuberculum sellae 4 (7.1) Olfactory groove 1 (1.8) Metastasis 3 (5.4) Craniopharyngioma 1 (1.8) Mucocele 1 (1.8) |

All values are number of patients (%) unless stated otherwise. GnRH, gonadotropin releasing hormone; ACTH, adrenocorticotropic hormone.
required 3 attempts to treat the CSF leak. There is no reported mortality during the first 30 days post surgery. Lesion progression or recurrence requiring redo surgery occurred in 5 (8.9%) patients; all of them were nonfunctioning pituitary adenomas (Table 3). We compared our results with the recently published data discussing in detail the clinical outcomes of EES in pituitary adenoma resection at academic centers in the past 5 years (Table 4).

Learning Curve
There was a higher rate of complications in earlier cases. When comparing the first half of operations to the latter half, the combined 4 neurosurgeons found a statistically significant (P < 0.05) decrease in postoperative CSF leak from 7/28 (25%) to 1/28 (3.6%) cases (Figure 3A). Combined rates of postoperative meningitis decreased from 3/28 (10.7%) to 1/28 (3.6%) cases (P = 0.3) (see Figure 3B). Combined rates of new hormonal deficits decreased from 6/28 (21.4%) to 3/28 (10.7%) (P = 0.28) (see Figure 3C). Combined rates of permanent postoperative diabetes insipidus decreased from 5/28 (17.9%) to 1/28 (3.6%) cases (P = 0.08) (see Figure 3D). As well, combined rates of visual improvement increased from 13/17 (76.5%) to 17/18 (94.4%) cases (P = 0.13) when comparing the early half of cases.

Figure 1. T1-weighted magnetic resonance imaging of the head with contrast of a 62-year-old female patient who presented with loss of smell sensation. (A) Preoperative axial view. (B) Preoperative coronal view. (C) Postoperative axial view. (D) Postoperative coronal view.
to the latter half (see Figure 3E). The least rate of complications was among the only neurosurgeon who did a formal endoscopic skull base fellowship (Table 5).

**DISCUSSION**

There is a growing trend toward fully endoscopic endonasal transsphenoidal surgery. Many studies show a similar if not greater efficacy of EES compared with the gold standard microsurgical techniques.²⁶⁴⁷⁴⁸ This is the first study to look for the outcomes of patients undergoing endoscopic transnasal sellar, suprasellar, and anterior cranial fossa lesion excisions in a community hospital setting. It has also been demonstrated that the transition to EES is hindered by its learning curve, although the details of this learning curve and its clinical implications have not been studied in detail.⁴⁹ Given the prevalence of sellar and suprasellar lesions, as well as the growing evidence for the efficacy of endoscopic endonasal transsphenoidal surgery,
understanding the dynamics of the learning curve, especially in the setting of a community hospital, may help increase adoption, surgical proficiency, and improve outcomes in the management of patients with these lesions in the future in all hospital settings (academic centers, community hospitals, and developing country hospitals). Other supportive specialties, such as neurointervention to back up any intraoperative vascular complications and neuroendocrine for managing any endocrine manifestations perioperatively should be present.

**Extent of Resection**

It is difficult to evaluate or compare the extent of resection when discussing the many different types of sellar and suprasellar lesions that may be approached and resected through endoscopic endonasal surgery. Certain lesions require an attempt for GTR, while others, such as metastatic lesions, have high levels of success when combined with adjuvant therapy. Definitions of GTR, subtotal resection, decompression, and/or biopsy are unique and can vary for each study. In a review of 16 studies of giant adenomas, Komotar et al. demonstrated that microscopic transsphenoidal cohort had a lower rate of total resection and worse visual outcome than the endoscopic group. Pituitary adenomas are the most frequently studied and managed endoscopically. A 2018 metanalysis of 50 studies by Almutairi et al. demonstrated a GTR rate for pituitary adenomas of 74%. For tumors invading the cavernous sinus, many authors noted a higher resection rate with an endoscope than a microscope, indicating the advantage of the panoramic and angled views of the medial wall of the cavernous sinus provided by endoscopes. In addition, endoscopic endonasal surgery has been reported to be a valid option for resection in recurrent adenomas. Graffeo et al. demonstrated in their metanalysis that current GTR rates are 89.7% for olfactory groove meningiomas, 79.9% for tubercula sella meningiomas, 59% for craniopharyngiomas, and 58.8% for clival chordomas. Our series showed that GTR was achieved in 62.2% of pituitary adenomas, 50% of tuberculum sellae meningiomas, olfactory groove meningioma and mucocoele patient, subtotal resection of the tumor in the craniopharyngioma patient, and decompression and biopsy of the tumors in all metastasis patients. The main reason for not achieving GTR in our series was the cavernous sinus invasion (23.1%). Due to the paucity of cases of olfactory groove meningiomas, metastasis, craniopharyngioma, mucocoele, and Rathke cyst, we could not compare our results with the literature for such pathologies.

### Perioperative Outcomes

Visual and postoperative outcomes in our study were consistent with the results shown in other studies. Of patients experiencing visual issues at the time of diagnosis, 86.1% of patients had vision improvement and only 13.9% had no change in vision. No patients had a worsening vision. Other studies have reported rates of vision improvement from as low as 23% to as high as 100%. In our study, no patients had vision worsening.

### Table 2. Clinical Presentation

| Parameter                  | Value         |
|----------------------------|---------------|
| Headache                   | 42/56 (75%)   |
| Hormonal deficit           | 32 (57.1%)    |
| Hypothyroidism             | 12/32 (37.5%) |
| Hypogonadism               | 11/32 (34.4%) |
| Panhypopituitarism         | 6/32 (18.8%)  |
| Hyperprolactinemia         | 5/32 (15.6%)  |
| Hypoadrenalinism           | 4/32 (12.5%)  |
| Cushing disease            | 3/32 (9.4%)   |
| Visual field deficit       | 31/56 (55.4%) |
| Bitemporal hemianopia      | 14/31 (45.2%) |
| Other deficits             | 17/31 (54.8%) |
| Cranial nerve deficit      | 10/56 (17.9%) |
| Third nerve palsy          | 3/10 (33.3%)  |
| Diplopia                   | 9/56 (16.1%)  |
| Pituitary apoplexy         | 8/56 (14.3%)  |
| Disturbed level of consciousness | 7/56 (12.5%) |

All values are number of patients (%) unless stated otherwise.

### Table 3. Perioperative Outcomes

| Parameter                  | Value         |
|----------------------------|---------------|
| Excision                   |               |
| Gross total excision       | 31 (55.4%)    |
| Subtotal excision          | 22 (39.3%)    |
| Decompression and biopsy   | 3 (5.4%)      |
| Vision                     |               |
| Normal to improved         | 27 (86.1%)    |
| Remained stable            | 4 (13.9%)     |
| Worsened                   | 0             |
| Complications              |               |
| New hormone deficiency     | 9 (16.1%)     |
| Postoperative CSF leak     | 8 (14.3%)     |
| Meningitis                 | 4 (7.1%)      |
| Diabetes insipidus         |               |
| Transient                  | 13 (23.2%)    |
| Permanent                  | 6 (10.7%)     |
| Hematoma and evacuation    | 2 (3.6%)      |
| Vascular injury            | 0             |
| Nasal complications        | 0             |
| Other complications        | 0             |
| Lesion progression or recurrence | 5 (8.9%) |

All values are number of patients (%) unless stated otherwise.
| Study                  | Age (Years) | Sex (% male) | Macroadenoma (%) | GTR | Vision Normalized or Improved (%) | Vision Worsened (%) | New Hormonal Deficit (%) | Postoperative CSF Leak (%) | Postoperative Hematoma (%) | Meningitis (%) | Permanent DI (%) | 30-day Mortality (%) | Recurrence |
|------------------------|-------------|--------------|------------------|-----|-----------------------------------|---------------------|--------------------------|----------------------------|---------------------------|----------------|------------------|---------------------|------------|
| Chabot et al., 2015    | 56.3        | 64.1         | 100              | 85  | 79                                | 0                   | 12.8                     | 10.3                       | —                         | —              | 7.7              | 0                   | 0         |
| Marenco et al., 2015   | 72.4        | 44           | 100              | 65.4| 70.8                              | 0                   | 16                       | 4                          | —                         | —              | 4                | 4                   | 21.4       |
| Wang et al., 2015      | 40.3        | 44.3         | 79               | 91.7| 92                               | 0.43                | 1.3                      | 0.6                        | 0.69                      | 1.03           | 0.69             | —                   | —         |
| Akin et al., 2016      | 35.5        | 46.5         | 86.6             | -   | 100                               | 0                   | 18.2                     | 2.1                        | —                         | 2.8            | 0                | —                   | 3.5        |
| Guo-Dong et al., 2016  | 43.4        | 59           | -                | 73.1| 75                                | 0                   | 3                        | 1                          | 3                         | 0              | 1                | 0                   | —         |
| Jang et al., 2016      | 48.4        | 43.8         | 70.4             | 68.2| —                                 | —                   | —                        | 1.2                        | 1.8                       | 0.6            | 0.6              | 0.9                | 0.3        |
| Jones et al., 2016     | 62.3        | 96           | —                | 80  | 100                               | 0                   | 0                        | 4                          | 0                         | 0              | 0                | —                   | —         |
| Magro et al., 2016     | 57          | 57           | 100              | 59  | 86.6                              | 2.4                 | 13.7                     | 2.7                        | 2                         | 3.3            | 6.2              | 0.7                | —         |
| Qureshi et al., 2016   | 52.6        | 55.1         | 96.1             | 93.6| 96.5                              | 0                   | 10.8                     | 1.3                        | —                         | —              | 2.6              | —                   | —         |
| Yildirim et al., 2016  | 48.5        | 55           | 100              | 90  | 39.1                              | 0                   | 7.5                      | 1.8                        | —                         | —              | 1.3              | 0.6                | —         |
| Zhan et al., 2016      | 36.5        | 57.8         | 62.2             | 86.7| 92.7                              | 0                   | 11.1                     | 4.4                        | —                         | 0              | 0                | 0                   | —         |
| Beltrame et al., 2017  | 48.5        | 44           | 78.6             | 60  | 73.8                              | 3.2                 | 12.1                     | 2.1                        | 1.4                       | 1.4            | 3.2              | 0.7                | 2.9        |
| Gondim et al., 2017    | 54.9        | 69.2         | 100              | 79.5| 74.1                              | —                   | —                        | 0                          | —                         | 0              | 5.1              | 0                   | —         |
| Linsler et al., 2017   | 55.5        | 41.4         | 81.4             | 88  | —                                 | 0                   | 11                       | 0                          | 0                         | 0              | 1.4              | 0                   | 6         |
| Thawani et al., 2017   | 55.7        | 51.2         | 100              | 29.6| —                                 | 1.48                | —                        | 10.3                       | —                         | 1              | 4.4              | 1                   | —         |
| Zhang et al., 2017     | —           | 53.3         | 100              | 67.2| 37.2                              | 0.7                 | 3.5                      | 1.5                        | —                         | 2.9            | 0                | —                   | 16.7       |
| Zoli et al., 2017      | 52.4        | 62.7         | 100              | 80  | 85.5                              | 0                   | 20                       | 1.3                        | —                         | 0              | 5.3              | —                   | 4         |
worsened vision after surgery. This is consistent with results found by other researchers who generally saw a very low rate of worsened visual deficits after surgery, on the order of 0%–3.2%.22–33

The rate of recovery from hormonal deficits in our study is greater than that found by other researchers. Most of our patients (83.9%) showed stable or improved hormonal deficits. Pablo et al.43 and Castano-Leon42 found that hormonal deficits were stable or improved in 76.9% and 75.3% of patients, respectively. However, our rate of new deficits postoperatively seems to be in line with that of other researchers, at 16.1%. Rates of new deficits in other studies have ranged from 0% to 20%.22–36,39–43

Perioperative complications that we analyzed include the rates of hematoma requiring evacuation, diabetes insipidus, CSF leak, and meningitis. Our patients experienced a similar rate of postoperative hematoma when compared with previous studies described in the literature. In our literature review, the rate of this complication ranged from 0% to 3%.24,26–29,33,35,39,40,42,43 Two (3.6%) of our patients experienced this complication and required surgical evacuation of the hematoma. We did have a high rate of permanent diabetes insipidus postoperatively. Six (10.7%) of our patients experienced this complication, whereas the existing literature estimates this complication occurring in 0%–7.7% of cases.22,24–38,40–43

In terms of the other postoperative complications, our study showed increased rates of postoperative CSF leak and meningitis. Among our patients, 14.3% experienced postoperative CSF leak. In previous studies, the prevalence of postoperative CSF leak ranged from 0%–10.3%.22–43 Of these 8 patients, 3 resolved nonoperatively (1 with bed rest only and 2 with a lumbar drain). Five required surgical repair using Surgicel (Ethicon, Somerville, New Jersey, USA), Tisseel (Baxter Healthcare, Deerfield, Illinois, USA), fat graft, fascia lata graft, and vascularized nasoseptal flap. Two patients required only 1 repair, 1 patient required 2 repair attempts, and 2 patients required 3 attempts to successfully treat the CSF leak. Out of the 7 patients who were operated on by extended EES, 3 (42.9%) of them developed postoperative CSF leak. This constitutes 37.5% of the patients who developed postoperative CSF leak. However, the CSF leak rate has significantly dropped from 25% to 3.6% (P < 0.05) after using vascularized nasoseptal flaps and proper skull base reconstruction, especially in extended EES cases, and the results were comparable with similar studies.24,25,28,29,33,41–43

Of our patients, 7.1% experienced meningitis, whereas the prevalence of this in other studies generally ranged from 0%–4.1%. The 30-day mortality rate was 0%, and in the other studies it ranged from 0%–4%.22,23,26,27,31–36,41–43 Fewer studies have assessed the length of stay after EES; however, our patients’ length of stay appears to be on the high end of a range from 3–6 days.33,41–43 Our patients remained in the hospital for 6.1 ± 4.9 days. This may have been due to the relative unfamiliarity of our center with the procedure; the staff therefore may have wanted to observe patients for a longer duration of time. Finally, our recurrence rate was 8.9%, which is within the reported range from 2%–21.4%.24,25,32,33,43,47,48

Overall, our outcome results and complication rates were relatively higher than those of researchers in academic
centers. However, this postoperative complication rate showed a decrease from the first to second half of cases. Therefore this number is likely influenced by the fact that such a large proportion of our cases represented our community neurosurgeons beginning to perform these types of surgeries.
Learning Curve

Our study showed that rates of postoperative CSF leak, meningitis, new hormonal deficits, and permanent diabetes insipidus decreased from the first group of surgeries to the second group when all surgeons were analyzed together. However, only the incidence of postoperative CSF leak decreased significantly (7/28 in the first patient group, 1/28 in the second patient group, P < 0.05). This significant decrease is attributed to the use of vascularized nasoseptal flap in the second half of patients. Our small sample size may be the reason that the other complications did not reach statistical significance. However, this is consistent with other studies that have also not shown statistical significance for a decrease in complications. One study has even shown an increase in the complication rate, which was hypothesized to be due to increased surgeon confidence and aggressiveness in attempting GTR as surgeons gained experience with the procedure. Despite this, the decrease in complication rate is certainly clinically significant and reduces the burden on surgeons and patients when reintervention is necessary.

In terms of improvement in outcome, the visual improvement did better from the first half of the case series (13 of 17 patients) to the second (17 of 18 patients); however, this was not statistically significant (P = 0.13). When we divided the outcomes according to surgeons, we found that the initial outcomes of the neurosurgeon who received formal training on the endoscopic transphenoid skull base surgeries were better than the other general neurosurgeons. The rapid decrease in complications from the first to second series of cases, while not statistically significant, shows that the learning curve for EES is steep. This means that once our surgeons gained experience with the procedure, the complication rates decreased dramatically.

Challenges and Limitations

This study has several limitations. Firstly, this is a retrospective study with an extremely heterogeneous patient population in regard to pathologic diagnosis encompassing a variety of pituitary adenomas, tuberculum sellae and olfactory groove meningiomas, metastasis, craniopharyngioma, Rathke cyst, and a mucocele. The patient population was small with 56 cases, with each of surgeons A, B, C, and D completing 10, 21, 12, and 13 operations, respectively. All of these challenges were overcome. We think that there is a better outcome in terms of patient care when there is interspecialty teamwork among neurosurgeons, otolaryngologists, endocrinologists, ophthalmologist/optometrist, and neuro-interventionist. One challenge in regards to initiating the EES, especially in a community hospital setting where EES is relatively new, is that neurosurgeons do not have an abundance of previous experience with endoscopic nasal anatomy. Therefore if there were any intraoperative complications regarding nasal anatomy, an otolaryngologist would be called into the operating room without any prior notice. This was going to lead to increased levels of frustration, especially between neurosurgeons and otolaryngologists. The obvious solution was to increase teamwork and collaboration between the specialties. In this regard, 2 neurosurgeons and 2 otolaryngologists attended several cadaveric courses to learn this new technique together. Only 2 of the local otolaryngologists agreed to participate in the EES operations. This presented another challenge. If any of the postoperative patients presented to the emergency department after discharge, none of the uninvolved otolaryngologists would consider seeing these patients. The otolaryngologists had to better intercommunicate so that they were all comfortable seeing patients post EES presenting with purely nasal problems such as epistaxis. The neuronavigation billing code for remuneration also needed to be alternated between the neurosurgeons and otolaryngologists to better develop the working relationship between the specialties. Other challenges that arose included administrative issues, such as a
lack of funding for and a shortage of nasal instrument sets; the logistics of arranging an otolaryngologist and neurosurgeon to be available at the same time; and education of the neurosurgical operating room nursing staff in regards to otolaryngologic procedures. We overcame all these challenges.

The future direction is to train more neurosurgeons in EES techniques. Then it will be more feasible to perform these cases in a community hospital setting. In our case series, only 1 surgeon (D) had a previous fellowship training in endoscopic transsphenoidal surgery with better outcomes than other neurosurgeons. We hope that new trainees will be trained and confident in performing these surgeries in community hospitals.

**CONCLUSION**

Despite the fact that our overall complications are higher than those in the reported literature, the outcomes of the second half of patients after the surgeons gained experience were similar to those in academic centers. However, complex cases (e.g., anterior cranial fossa lesions and craniopharyngiomas) should be referred to an experienced surgeon, such as a well-trained endoscopic skull base surgeon in the same center or in an academic center. The learning curve for EES is steep and improves greatly and quickly with adequate practice. So, endoscopic endonasal resection of sellar, suprasellar, and anterior skull base lesions is safe, minimally invasive, and efficient in a community hospital setting, provided the presence of a multidisciplinary team such as neurointervention and neuroendocrinology. Extent of resection, visual, and postoperative outcomes after gaining experience are similar to those reported in larger academic centers. In the future, as time will allow for the progression of endoscopy instruments and increased surgeon experience, this approach should become first line for the treatment of sellar and suprasellar lesions in hospitals of all settings (academic centers, community hospitals, and developing country hospitals).

**ACKNOWLEDGMENTS**

Special thanks to Dr. Samer Elbaba and Dr. Melvin Field for encouraging us to write this manuscript.

**REFERENCES**

1. Pal A, Leaver L, Wass J. Pituitary adenomas. BMJ. 2019;365:l2901.
2. Adams C, Burke CW. Current modes of treatment of pituitary tumors. Br J Neurosurg. 1993;7:123-127.
3. Stammberger H. Endoscopic endonasal surgery—concepts in treatment of recurring rhinosinusitis. Part II. Surgical technique. Otolaryngol Head Neck Surg. 1986;94(1):15-18.
4. Liu JK, Cohen-Gadol AA, Laws J, et al. Harvey Pituitary Surgery: An Early Experience. 1993;7:123-127.
5. Jho H-D, Carrau RL, Ko Y, Daly MA. Endoscopic pituitary surgery: an early experience. Surg Neurol. 1997;47:213-222.
6. Cappabianca P, Cavallino LM, 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. Adv Ther. 2008;25(15):193-199.
7. Cappabianca P, Cavallino LM, Solari D, De Divitiis O, Chiarantoni M, Esposito F. Size does not matter. The intrigue of giant adenomas: a true surgical challenge. Acta Neurochirurg. 2014:135; 2217-2220.
8. Cavallino LM, Solari D, Esposito F, Villa A, Mininni G, Cappabianca P. The role of the endoscopic endonasal route in the management of craniopharyngiomas. World Neurosurg. 2014;81(suppl 6):S32-S40.
9. de Divitiis E, Cappabianca P, Cavallino LM. Endoscopic transphenoidal approach: adaptability of the procedure to different sellar lesions. Neurosurg. 2002;51:699-705.
10. Di Maio S, Cavallino LM, Esposito F, Stangia V, Correro OV, Cappabianca P. Extended endoscopic endonasal approach for selected pituitary adenomas: early experience. J Neurosurg. 2011;114(4):55-1.
11. Hiroshi N. Recent evaluation of endoscopic transnasal surgery for treatment of pituitary adenomas. Neurol Med Chirirg. 2017;57(suppl 2):153-158.
12. Magill ST, Morshed RA, Lucas C-HG, et al. Tuberculm sellae meningiomas: grading scale to assess surgical outcomes using the transcranial versus transphenoidal approach. Neurosurg Focus. 2018;44:E5.
13. Solari D, Cavallino LM, De Angelis M, et al. Advances in trans-sphenoidal pituitary surgery. Panminerva Med. 2012;54:271-276.
14. Elldai AM, Hardesty DA, Zaidi HA, et al. Evaluation of surgical freedom for microscopic and endoscopic transphenoidal approaches to the sella. Neurosurg. 2013;61(suppl 2):69.
15. Li L, Ma X, Pandey S, Fan A, Deng X, Cui D. Bibliometric analysis of journals in the field of endoscopic endonasal surgery for pituitary adenomas. J Craniofac Surg. 2018;29:e83-87.
16. Barra B. Writing Your Turn. Vancouver, Canada: Fraser Institute; 2016.
17. Tepper J, Jaigobin C, Wang C. Health Human Resources for Neurosurgical Services in Ontario. Toronto, Canada: Institute for Clinical Evaluative Sciences; 2009.
18. Emanuel EJ, Persaud G, Upshur R, et al. Fair allocation of scarce medical resources in the time of Covid-19 [E-pub ahead of print]. N Engl J Med. 2020;382;1056-1067. https://doi.org/10.1056/NEJMsb2005114, accessed March 23, 2020.
19. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg. 2014;12: 1495-1499.
20. Moldovan ID, Agbi C, Kiby S, Alkherayer F. A systematic review of prophylactic antibiotic use in endoscopic transsphenoidal surgery for pituitary lesions. World Neurosurg. 2019;120:406-414.
21. Somma T, Marzolo AE, Esposito F, et al. Efficacy of ultra-short single agent regimen antibiotic cheemo-prophylaxis in reducing the risk of meningitis in patients undergoing endoscopic endonasal transphenoidal surgery. Clin Neurol Neurosurg. 2015;139:206-209.
endoscopic endonasal surgery for large and giant pituitary macroadenomas: a retrospective review of 39 consecutive patients. World Neurosurg. 2015;84:978-988.

23. Mareno HA, Zymbarg ST, Santos R de P, Ramalho CO. Surgical treatment of nonfunctioning pituitary macroadenomas by the endoscopic endonasal approach in the elderly. Arq Neuropsiquiat. 2015;73:764.

24. Wang FY, Zhou T, Wei SR, et al. Endoscopic endonasal transsphenoidal surgery of 1,166 pituitary adenomas. Surg Endosc. 2015;29:1270-1280.

25. Akin S, Iskay L, Soydemiroglu F, Yucel T, Guzlel A, Berker M. Reasons and results of endoscopic surgery for prolactinomas: 142 surgical cases. Acta Neurochir. 2016;158:93-94.

26. Guo-Dong H, Tao J, Ji-Hu Y, et al. Endoscopic versus microscopic transsphenoidal surgery for pituitary tumors. J Clin Neurol. 2016;12:638-655.

27. Jang JH, Kim KH, Lee YM, Kim JS, Kim YZ. Surgical results of pure endoscopic endonasal transsphenoidal surgery for 331 pituitary adenomas: a 15-year experience from a single institution. World Neurosurg. 2016;96:454-455.

28. Jones M, Johans S, Ziegler A, et al. Outcomes of patients undergoing endoscopic endonasal skull base surgery at a VA hospital. JAMA Surg. 2016;151:e163-1188.

29. Megro E, Grassi L, Lasave J, et al. Complications related to the endoscopic endonasal transsphenoidal approach for nonfunctioning pituitary macroadenomas in 300 consecutive patients. World Neurosurg. 2016;89:442-453.

30. Qureshi T, Chaud F, Fogl L, Dasgupta M, Straus D, Byrne RW. Learning curve for the transsphenoidal endonasal approach to pituitary tumors. Br J Neurosurg. 2016;30:637-642.

31. Yildirim AE, Sahinoglu M, Eksi I, et al. Nonfunctioning pituitary adenomas are really clinically nonfunctioning? Clinical and endocrinological symptoms and outcomes with endoscopic endonasal treatment. World Neurosurg. 2016;82:185-192.

32. Zhan R, Li X, Huang Y, et al. Endoscopic transnasal trans-sphenoidal approach for apoplectic pituitary tumor: surgical outcomes and complications in 45 patients. J Neurol Surg B Skull Base. 2016;77:54-60.

33. Beltrame S, Toscano M, Goldschmidt E, et al. Endoscopic treatment of 140 pituitary tumors: results and complications. Neuroendocrinology. 2017;12:207-74.

34. Gonlìm JA, de Albuquerque LAF, Almeida JP, et al. Endoscopic endonasal surgery for pituitary adenoma: 16 years of experience in a specialized pituitary center. World Neurosurg. 2017;108:137-142.

35. Limler S, Hero-Gross R, Friesenhahn-Ochs R, Sharif S, Lammert F, Ortel I. Preservation of hormonal function by identifying pituitary gland at endoscopic surgery. J Clin Neurol. 2017;43:240-246.

36. Thawani JP, Ramayya AG, Pisapia JM, Abdullah KG, Lee J-YK, Grady MS. Operative strategies to minimize complications following resection of pituitary macroadenomas. J Neurol Surg B Skull Base. 2017:178;185-190.

37. Zhang H, Wang F, Zhou T, et al. Analysis of 137 patients who underwent endoscopic transsphenoidal pituitary adenoma resection under high-field intraoperative magnetic resonance imaging navigation. World Neurosurg. 2017;104:802-812.

38. Zoli M, Milanese L, Faustini-Fustini M, et al. Endoscopic endonasal surgery for pituitary apoplexy: evidence on a 75-case series from a tertiary care center. World Neurosurg. 2017;106:331-338.

39. Hajdari S, Kellner G, Mayer A, Rosahl S, Gerlach R. Endoscopic endonasal surgery for removal of pituitary adenomas: a surgical case series of treatment results using different 2- and 3-dimensional visualization systems. World Neurosurg. 2018;119:e190-196.

40. López-García R, Abarca-Óliva J, Monjas-Cánovas I, Peño Alfonso AM, Moreno López P, Gras-Albert J. Endoscopic endonasal surgery in pituitary adenomas: surgical results in a series of 86 consecutive patients. Neuroendocrinology. 2018;129:106-119.

41. Taghaviri M, Sadrehosseini SM, Azadkia JR, Nakjhani M, Zeinalizadeh M. Endoscopic endonasal approach to the growth hormone-secreting pituitary adenomas: endocrinologic outcome in 68 patients. World Neurosurg. 2018;117:e239-e268.

42. Castaño-Leon AM, Paredes I, Munarriz PM, et al. Endoscopic transnasal trans-sphenoidal approach for pituitary adenomas: a comparison to the microscopic approach cohort by propensity score analysis. Neurosurgery. 2020;86:348-356.

43. Pablo A, Sofia B, Maximiliano T, et al. Endoscopic versus microscopic pituitary adenoma surgery: a single-center study. Neurol India. 2020;68:101-107.

44. Delhadihi AR, Ganna A, Karabasos K, Gentili F. Pure endoscopic endonasal approach for pituitary adenomas: early surgical results in 200 patients and comparison with previous microsurgical series. Neurosurgery. 2008;62:1006-1011.

45. Kenan K, Ihsan A, Dilek O, Burak C, Guzkân K, Savas C. The learning curve in endoscopic pituitary surgery and our experience. Neurosurgery. 2008;62:305-307.

46. Komotar RJ, Starke RM, Raper DM, Anand VK, Schwartz TH. Endoscopic endonasal compared versus microscopic transsphenoidal surgery for pituitary adenomas: a single-center study. Neurosurg Rev. 2016;39:1186-1187.

47. Almutairi R, Muskens I, Cote D, et al. Gross total resection of pituitary adenomas after endoscopic transnasal trans-sphenoidal approach for nonfunctioning pituitary adenomas. J Clin Neurosci. 2016;23:470-472.

48. Sarkanen J, Kharasch A, Reber L, et al. Endoscopic transnasal trans-sphenoidal surgery of 1,166 pituitary adenomas. World Neurosurg. 2019;127:985-990.

49. Cavallino LM, Solari D, Somma T, Cappabianca P. The 3F (fat, flap, and flash) technique for skull base reconstruction after endoscopic endonasal suprasellar approach. World Neurosurg. 2019;126:439-445.

50. Cavallino LM, Messina A, Espizito F, et al. Skull base reconstruction in the extended endoscopic transsphenoidal approach for suprasellar lesions. J Neurosurg. 2007;107:713-720.

51. Lofr ease G, Vigo V, Rigante M, et al. Learning curve of endoscopic pituitary surgery: experience of a neurosurgery/ENT collaboration. J Clin Neurosci. 2018;47:299-303.

52. Shou X, Shen M, Zhang Q, et al. Endoscopic endonasal pituitary adenomas surgery: the surgical experience of 178 consecutive patients and learning curve of two neurosurgeons. BMC Neurology. 2016;16:47.

Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. This work was previously shared as an oral presentation, International Federation of Neuroendoscopy Congress, 23 November, 2019, Orlando, Florida, United States (No sponsoring society).

Revised 27 March 2020; accepted 4 April 2020
Citation: World Neurosurg. (2020) 138:e940-e954.
https://doi.org/10.1016/j.wneu.2020.04.028
Journal homepage: www.journals.elsevier.com/world-neurosurgery
Available online: www.sciencedirect.com
1878-8750/$ - see front matter © 2020 Elsevier Inc. All rights reserved.
**Table S1. Tumor Type, Location, Extension, Neurovascular Relation, Type of Surgery, and Extent of Resection of 56 Patients**

| Case Number | Tumor Type             | Location          | Extension                     | Optic Chiasm | Vascular Relation                  | Surgery          | Extent of Resection |
|-------------|------------------------|-------------------|-------------------------------|--------------|------------------------------------|------------------|---------------------|
| 1           | Pituitary adenoma      | Sellar-suprasellar| Bilateral cavernous sinus     | Compressed   | Bilateral mass effect on carotid   | Standard         | GTR                 |
| 2           | Prolactinoma           | Sellar            | -                             | -            | -                                  | Standard         | GTR                 |
| 3           | Nonfunctioning pituitary adenoma | Sellar-suprasellar | Bilateral cavernous sinus     | Invasion     | Rt. encased Lt. mass effect        | Standard         | GTR                 |
| 4           | Nonfunctioning pituitary adenoma | Sellar-suprasellar | Bilateral cavernous sinus     | Compressed   | Rt. encased Lt. mass effect        | Standard         | GTR                 |
| 5           | Nonfunctioning pituitary adenoma | Sellar-suprasellar | Right cavernous sinus         | Compressed   | Rt. encased                       | Standard         | GTR                 |
| 6           | Nonfunctioning pituitary adenoma | Sellar            | -                             | -            | -                                  | Standard         | GTR                 |
| 7           | Olfactory groove       | Olfactory groove  | -                             | -            | -                                  | Extended GTR     |                     |
| 8           | Tuberculum sellae      | Suprasellar       | -                             | -            | -                                  | Standard GTR     |                     |
| 9           | Nonfunctioning pituitary adenoma | Sellar-suprasellar | Bilateral cavernous sinus     | Compressed   | Bilaterally around the carotid     | Standard         | GTR                 |
| 10          | Nonfunctioning pituitary adenoma | Sellar-suprasellar | -                             | Compressed   | -                                  | Standard         | GTR                 |
| 11          | Pituitary adenoma      | Sellar-suprasellar| Bilateral cavernous sinus     | Compressed   | Bilaterally around the carotid     | Standard         | GTR                 |
| 12          | Pituitary adenoma      | Sellar            | -                             | -            | -                                  | Standard         | GTR                 |
| 13          | Nonfunctioning pituitary adenoma | Sellar-suprasellar | -                             | Compressed   | -                                  | Standard         | GTR                 |
| 14          | Nonfunctioning pituitary adenoma | Sellar-suprasellar | Bilateral cavernous sinus, supraclinoid | Compressed | Bilaterally around the carotid     | Standard         | GTR                 |
| 15          | Pituitary adenoma      | Sellar-suprasellar| Bilateral cavernous sinus, left temporal lobe | - | Bilaterally around the carotid     | Standard         | GTR                 |
| 16          | Nonfunctioning pituitary adenoma | Sellar-suprasellar | Bilateral cavernous Sinus     | -           | Bilateral mass effect on carotid   | Standard         | GTR                 |
| 17          | Nonfunctioning pituitary adenoma | Sellar-suprasellar | Left cavernous sinus          | Compressed   | Lt. encased                       | Standard         | GTR                 |
| 18          | Prolactinoma           | Sellar            | -                             | -            | -                                  | Standard STR     |                     |
| 19          | Metastasis             | Suprasellar       | -                             | -            | -                                  | Standard STR     | Decompression and biopsy |
| 20          | Tuberculum sellae      | Sellar-suprasellar | -                             | Compressed   | -                                  | Standard STR     |                     |
| 21          | Tuberculum sellae      | Sellar-suprasellar | Frontal lobe                  | -            | -                                  | Extended         | GTR                 |
Table S1. Continued

| Case Number | Tumor Type                        | Location           | Extension                      | Optic Chiasm  | Vascular Relation                      | Surgery   | Extent of Resection |
|-------------|-----------------------------------|--------------------|--------------------------------|---------------|----------------------------------------|-----------|--------------------|
| 22          | Mucocele                           | Sellar             |                                |               |                                        | Standard  | GTR                |
| 23          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar | Bilateral cavernous sinus      | Compressed    | Rt. encased and left around the carotid but not totally encased | Standard  | STR                |
| 24          | Pituitary adenoma (GnRH)           | Sellar-suprasellar | Bilateral cavernous sinus      | Compressed    | Bilaterally around the carotid          | Standard  | STR                |
| 25          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar | Left cavernous sinus           | Compressed    | Lt. around the carotid                 | Standard  | STR                |
| 26          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar | Bilateral cavernous sinus      | Compressed    | Bilaterally around the carotid          | Standard  | STR                |
| 27          | Rathke cyst                        | Sellar-suprasellar |                                | Compressed    |                                        | Standard  | STR                |
| 28          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar | Rt. cavernous sinus            | Compressed    | Rt. around the carotid                 | Standard  | STR                |
| 29          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar | Bilateral cavernous sinus      | Compressed    | Bilaterally around the carotid          | Standard  | STR                |
| 30          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar |                                | Compressed    |                                        | Standard  | STR                |
| 31          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar | Rt. cavernous sinus            | Compressed    | Rt. encased                            | Standard  | STR                |
| 32          | Tuberculum sellae meningioma       | Sellar-suprasellar | Hypothalamus, orbital apex, left suprachiasmatic, frontal lobe | Compressed    | Lt. suprachiasmatic carotid artery encased | Extended  | STR                |
| 33          | Nonfunctioning pituitary adenoma   | Sellar             |                                |               |                                        | Standard  | GTR                |
| 34          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar |                                | Compressed    |                                        | Standard  | GTR                |
| 35          | Nonfunctioning pituitary adenoma   | Sellar             |                                |               |                                        | Standard  | GTR                |
| 36          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar |                                | Compressed    |                                        | Standard  | GTR                |
| 37          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar |                                | Compressed    |                                        | Standard  | STR                |
| 38          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar | Bilateral cavernous sinus      | Compressed    | Bilaterally around the carotid          | Standard  | STR                |
| 39          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar |                                | Compressed    |                                        | Standard  | STR                |
| 40          | Prolactinoma                       | Sellar-suprasellar | Bilateral cavernous sinus, frontal lobe | Compressed    | Bilaterally around the carotid          | Standard  | STR                |
| 41          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar |                                | Compressed    |                                        | Standard  | STR                |
| 42          | Pituitary adenoma (GH)             | Sellar             |                                |               |                                        | Standard  | GTR                |
| 43          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar | Bilateral cavernous sinus      | Compressed    | Bilaterally encased                    | Standard  | STR                |
| 44          | Nonfunctioning pituitary adenoma   | Sellar-suprasellar |                                | Compressed    |                                        | Standard  | GTR                |

All values are number of affected patients/total number of patients (%). 
GnRH, gonadotropin releasing hormone; GTR, gross total resection; ACTH, adrenocorticotropic hormone; STR, subtotal resection; GH, growth hormone.
Table S1. Continued

| Case Number | Tumor Type                        | Location                  | Extension                                                                 | Optic Chiasm         | Vascular Relation | Surgery                      | Extent of Resection |
|-------------|-----------------------------------|---------------------------|---------------------------------------------------------------------------|----------------------|-------------------|------------------------------|---------------------|
| 45          | Nonfunctioning pituitary adenoma  | Sellar                    | —                           | —                    | —                 | Standard GTR                | GTR                 |
| 46          | Nonfunctioning pituitary adenoma  | Sellar                    | Bilateral cavernous sinus, hypothalamus, bilateral temporal lobes          | Compressed           | Lt. encased        | Extended STR                 | STR                 |
| 47          | Nonfunctioning pituitary adenoma  | Sellar, suprasellar, infrasellar | Compressed                   |                       |                   | Standard GTR                | GTR                 |
| 48          | Nonfunctioning pituitary adenoma  | Sellar, suprasellar       | Bilateral cavernous sinus    | Compressed           | Bilaterally around the carotid | Standard GTR                | STR                 |
| 49          | Nonfunctioning pituitary adenoma  | Sellar, suprasellar       | Bilateral cavernous sinus    | Compressed           | Bilaterally mass effect  | Standard GTR                | GTR                 |
| 50          | Nonfunctioning pituitary adenoma  | Sellar, suprasellar       | —                           | Compressed           | —                 | Standard GTR                | GTR                 |
| 51          | Nonfunctioning pituitary adenoma  | Sellar, suprasellar       | Bilateral cavernous sinus, frontal lobe                                  | Compressed           | Bilaterally around the carotid | Standard GTR                | GTR                 |
| 52          | Nonfunctioning pituitary adenoma  | Sellar                    | —                           | —                    | —                 | Standard GTR                | GTR                 |
| 53          | Nonfunctioning pituitary adenoma  | Sellar, clival, infrasellar | Bilateral cavernous sinus, Rt. Meckel cave and prepontine cistern         | Invasion             | Encased bilateral   | Extended STR                 | STR                 |
| 54          | Metastasis                         | Sellar, infrasellar       | Bilateral cavernous sinus, Meckel cave                                    | —                    | Bilaterally around the carotid | Standard Decompression and biopsy |                     |
| 55          | Metastasis                         | Sellar, suprasellar       | Bilateral cavernous sinus, hypothalamus                                   | Compressed           | Bilaterally around the carotid | Standard Decompression and biopsy |                     |
| 56          | Craniopharyngioma                  | Sellar, suprasellar       | Hypothalamus                  | Invasion             | —                 | Extended STR                 | STR                 |

All values are number of affected patients/total number of patients (%).
GnRH, gonadotropin releasing hormone; GTR, gross total resection; ACTH, adrenocorticotropic hormone; STR, subtotal resection; GH, growth hormone.