Comparison of endoscopic and microscopic removal of pituitary adenomas: single-surgeon experience and the learning curve

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Object. The endoscopic endonasal approach for resection of pituitary lesions is an effective surgical option for tumors of the sella turcica. In this study the authors compared outcomes after either purely endoscopic resection or traditional microscope-aided resection. They also attempted to determine the learning curve associated with a surgical team converting to endoscopic techniques.

Methods. Retrospective data were collected on patients who were surgically treated for a pituitary lesion at the Hospital of the University of Pennsylvania between July 2003 and May 2008. Age, sex, race, presenting symptoms, length of hospital stay, surgical approach, duration of surgery, tumor pathological features, gross-total resection (GTR) of tumor, recurrence of the lesion, and intraoperative and postoperative complications were noted. All procedures were performed by the same senior neurosurgeon, who was initially unfamiliar with the endoscopic endonasal approach.

Results. A total of 25 patients underwent microscopic resection and 25 patients underwent endoscopic resection performed by a single skull base team consisting of the same senior neurosurgeon and otorhinolaryngologist (M.S.G. and B.W.O.). In the microscopically treated cohort, there were 8 intra- or postoperative complications, 6 intraoperative CSF leaks, 17 (77%) of 22 patients had GTR on postoperative imaging, 5 patients underwent ≥ 2 operations, and 10 (59%) of 17 patients reported total symptom resolution at follow-up. The endoscopically treated group had 7 intra- or postoperative complications and 7 intraoperative CSF leaks. Of the patients who had pre- and postoperative imaging studies, 14 (66%) of 21 endoscopically treated patients had GTR; 4 patients had ≥ 2 operations, and 10 (66%) of 15 patients reported complete symptom resolution at follow-up. The first 9 patients who were treated endoscopically had a mean surgical time of 3.42 hours and a mean hospital stay of 4.67 days. The next 8 patients treated had a mean surgical time of 3.11 hours and a mean hospital stay of 3.13 days. The final 8 patients treated endoscopically had a mean surgical time of 2.22 hours and a mean hospital stay of 3.88 days. The difference in length of operation between the first 9 and the last 8 patients treated endoscopically was significantly different. There was a trend toward decreased CSF leaks and other complications from the first 2 groups compared with the third group.

Conclusions. In this subset of patients, the use of endoscopic endonasal resection results in a similar complication and symptom resolution rate compared with traditional techniques. The authors postulate that the learning curve for endoscopic resection can be ≤ 17 procedures. (DOI: 10.3171/FOC.2008.25.12.E10)

KEY WORDS • endoscopy • learning curve • microsurgery • outcome • pituitary adenoma

HALSTEAD¹⁰ and Hirsch¹⁴ introduced the transsphenoidal approach to pituitary lesions in the early 1900s. Cushing^{5,6} perfected and popularized the sublabial transeptal approach shortly thereafter, making modifications that reduced morbidity. In the 1960s, Hardy¹² introduced the operating microscope for visualization

Abbreviations used in this paper: ACTH = adrenocorticotrophic hormone; DI = diabetes insipidus; GH = growth hormone; GTR = gross-total resection; LOS = length of stay; SIADH = syndrome of inappropriate antidiuretic hormone.

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during transsphenoidal procedures, a technical advance that enabled safer extirpation of sellar lesions. Since that time, most skull base surgeons have been trained and are comfortable with the transsphenoidal approach aided by the operating microscope.¹⁶ With the evolution of endoscopic sinus surgery, many groups have advocated for the use of endoscopy for both transsphenoidal exposure of the sella turcica and resection of pituitary lesions. Although the sublabial microscopic approach is still the most common one to the sphenoid sinus, it is slowly being replaced by endonasal endoscopic approaches. In the mid 1990s, neurosurgeons began to use rigid endoscopes for resec-

FIG. 1. Representative endoscopic images. A: View of the patient through the endoscope as the device is being brought into the field. B: View after introduction of the endoscope into the left nasal cavity by using a single-operator, 1-nostril technique. Note the middle turbinate (mt) has been lateralized. C: After further advancement of the endoscope, the superior turbinate (st) can be identified. The face of the sphenoid sinus is in the center of the image. D: After opening the sphenoid ostia and drilling the anterior sphenoid face, the contents of the sphenoid sinus (ss) are evident. E: After further dissection and bone removal, the vertical sphenoid septum (*asterisk*) and the entire posterior wall of the sphenoid sinus can be visualized. F: The wall has been removed and the dura mater is evident. G: After a cruciate dural incision, the tumor can be resected. H: A 30° scope has been introduced, allowing the entire resection cavity to be inspected. The normal pituitary (pit) and descended diaphragma (d) can be visualized.

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FIG. 2. Representative real-time images combined with views from the neuronavigation system (Visualization Technology, Inc.) In each image the coronal, sagittal, and axial planes visualized using the neuronavigation system are noted, with the *cross-hairs* demonstrating the location of the suction device. The real-time endoscopic image is shown in the *lower right corner* in each panel. A: Introduction of the scope into the nasal cavity. B: Location and visualization of the posterior septum. C: Suction within the resection cavity. D: Suction pointing to the right lateral wall.

tion of pituitary tumors.^{2,9,18} Since these initial reports, there have been several more case series describing the successful application of the endoscope to the resection of pituitary tumors.^{1,7,13,19–22,26,27,30–32} The endoscope has several potential advantages compared with traditional techniques.^{8,16} Endoscopy provides additional lighting and a superior field of vision. With the use of angled scopes, one can visualize critical anatomy such as the optic and carotid protuberances as well as the clival indentation, in addition to being able to assess extrasellar extension of pituitary lesions. In comparison with the sublabial ap-

proach, the endoscopic approach minimizes the risks of upper lip and incisor paresthesias.²⁹ In both sublabial and septal techniques, postoperative nasal packing often leads to discomfort, nasal cavity or septal injury, and sinusitis, all of which are avoided with most endonasal endoscopic techniques. However, endoscopic resection requires the surgeon to trade the binocular, handless microscope for the monocular, more technically challenging endoscope, a technology with which most neurosurgeons are not as familiar. There have been a number of case series directly comparing endoscopic and microscopic surgical results

by individual surgeons.^{3,11,15,23,29,33} We describe our experience in conversion of a cranial base surgery program from traditional methods to the entirely endoscopic method of approach and resection for pituitary lesions. We compare 2 patient cohorts that underwent resection by the same senior neurosurgeon and otorhinolaryngologist (M.S.G. and B.W.O.). The senior neurosurgeon was trained to perform the procedure by using traditional microscopic techniques and has many years of experience using this technology.

Methods

Patient Variables

Retrospective data were collected on patients who were surgically treated for pituitary adenomas at the Hospital of the University of Pennsylvania between July 2003 and May 2008. Age, sex, race, presenting symptoms, LOS, surgical approach, duration of surgery, tumor pathological findings, GTR of tumor, tumor recurrence, and intra- and postoperative complications were noted. The mean operative time was defined as the time-marked incision to the time-marked end of surgery time because these data were available from operating room records and were entered by the operating room staff for all patients. The tumor pathological type was determined by a board-certified pathologist using the appropriate immunostaining. Achievement of GTR was determined by neuroradiologists on MR images obtained postoperatively as part of routine care.

Surgical Technique

All patients were evaluated, diagnosed, and treated by a multidisciplinary team consisting of a senior neurosurgeon and a senior otorhinolaryngologist. The surgical technique used was consistent with those reported previously.^{4,16,17} A single-nostril, 1-operator technique was used (Fig. 1A). After entering the nostril, the middle turbinate was immediately visualized and lateralized (Fig. 1B), and then the sphenoid ostia was identified (Fig. 1C). The posterior nasal septum was injected and the middle turbinate was lateralized. Suction cautery was used to dissect the posterior nasal septum and mucosa off of the face of the sphenoid (Fig. 1D). A wide sphenoidotomy was created using forceps and punches. A drill was used to remove the rostrum of the sphenoid and the vertical sphenoid septa (Fig. 1E). The drill was used to open the anterior sellar floor (Fig. 1F), the dura mater was cauterized, and a cruciate incision was made within the dura (Fig. 1G). Following resection of the pituitary lesion, a 30 or 45° endoscope was used to assess the surgical site for residual disease or extrasellar extension (Fig. 1H). If a CSF leak was noted following the procedure, an abdominal fat graft was harvested and supplemented with fibrin glue. If no CSF leak was appreciated, gelatin sponges were partially placed over the sellar cavity. Postoperatively, no nasal splints or packs were placed. All cases were treated under imaging guidance by using the Visualization Technology, Inc. system. The image guidance system was registered,

TABLE 1: Demographic and clinical data in 50 patients with pituitary adenomas*

Parameter	Microscopy Group	Endoscopy Group
total no. of patients	25	25
male (%)	16 (64)	15 (60)
female (%)	9 (36)	10 (40)
age in yrs (range)	50.8 (23–78)	47.9 (18–73)
mean FU in yrs (range)	0.74 (0.08–3.58)	0.41 (0.08–2.08)
no. of macroadenomas (%)	23 (92)	22 (88)
no. of microadenomas (%)	2 (8)	3 (12)
tumor type		
PRL-producing	0	3
GH-producing	1	1
ACTH-producing	1	2
TSH-producing	0	1
gonadotropin	3	6
null cell tumor	1	1
multiple hormone-producing	12	10
ND	7	1

* FU = follow-up; ND = undifferentiated, not characterized, or not hormone producing; PRL = prolactin; TSH = thyroid-stimulating hormone.

calibrated, and checked frequently throughout the procedure. The neuronavigation system allowed for the proper orientation of the endoscope at the beginning of the case (Fig. 2A), identification of the posterior septum (Fig. 2B), confirmation of the location within the tumor cavity (Fig. 2C), and confirmation of vital structures bordering the cavity (Fig. 2D).

Statistical Analysis

Microscopic and endoscopic resection outcomes were compared using a 1-tailed, equal-variance t-test. Items were considered statistically significant if the probability value was < 0.05. Statistical analyses were computed using Statistical Package for Social Sciences or SAS software.

Results

Patient Characteristics and Presentations

Fifty consecutive patients seen at the Center for Cranial Base Surgery at the University of Pennsylvania Medical Center were treated surgically for resection of their pituitary adenomas between July 2003 and May 2008 by a single skull base team consisting of the same senior neurosurgeon and otorhinolaryngologist (Table 1). The first 25 patients were treated with standard microscopy-assisted resection. In this group, the endoscope was used during the final 4 procedures to ease transition to endoscopic resection. The final 25 patients underwent fully endoscopic resection of their pituitary lesion. In addition to comparing microscopy-assisted and endoscopic resec-

FIG. 3. Representative MR images. Preoperative sagittal (A) and coronal (B) MR images demonstrating a 3-cm tumor in the sella turcica. Postoperative sagittal (C) and coronal (D) MR images demonstrating endoscopy-assisted GTR of the tumor with placement of a fat graft.

tion, the patients in the endoscopic group were divided into 3 temporal groups to compare their outcome with respect to oncological efficacy, complications, operating time, and LOS.

In the microscopy group, 7 patients presented with visual changes, 7 lesions were discovered incidentally, 6 patients reported headaches, 3 showed signs and symptoms of acromegaly, 1 had galactorrhea, 1 had signs of Cushing disease, and 1 patient presented with hypopituitarism. There were 25 patients who underwent endoscopic resection of their pituitary adenomas. One of these patients had undergone microscopic resection 2 years previously, and is thus in both groups. Ten patients reported vision problems (decreased peripheral vision and/or diplopia), 8 reported headaches, 4 presented with dysmenorrhea, 3 had galactorrhea, 3 reported syncope and/or dizziness, 2 presented with weight gain or loss, 2 exhibited signs of acromegaly, 2 were diagnosed incidentally, 1 reported decreased libido and sexual dysfunction, 1 presented with acute confusion, and 1 complained of hair loss.

Immunohistochemical and Pathological Findings

In the microscopically treated group, 12 specimens

stained positive for multiple hormones, 7 were not characterized, 3 stained positive for luteinizing hormone or follicle-stimulating hormone, 1 was a null cell adenoma, 1 was positive for ACTH, and 1 was positive for GH. In the endoscopically treated group, 1 specimen was not characterized, 6 stained positive for follicle-stimulating hormone or luteinizing hormone, 10 were positive for multiple hormones, 3 were positive for prolactin, 2 stained positive for ACTH, 1 was positive for GH, and 1 was a null cell tumor (Table 1).

Outcome and Complications

Postoperative assessment of resection was determined by comparing preoperative (Fig. 3A and B) and postoperative (Fig. 3C and D) MR images. In the microscopic resection group, GTR of the tumor was accomplished in 17 (77%) of 22 patients; GTR of the tumor was achieved in 14 (66%) of 21 patients who were assessed after undergoing endoscopic resection (Table 2).

In 50 total procedures, there were no surgery-related or postoperative deaths or cerebral vascular accidents. In the microscopic resection group, intraoperative CSF leaks occurred in 6 patients (24%), whereas intraoperative

TABLE 2: Data on CSF leaks, complications, and outcomes in 50 patients who underwent microscopy- versus endoscopy-assisted tumor resection

Factor	No. w/ Microscopy (%)	No. w/ Endoscopy (%)
intraop CSF leak	6 (24)	7 (28)
patients w/ complications	8 (32)	7 (28)
postop CSF leak	1 (4)	3 (12)
lumbar drain	1 (4)	0
postop infection	1 (4)	0
postop DI	4 (16)	1 (4)
DI at FU	2 (8)	0
other*	3 (12)	3 (12)
reop	5 (20)	4 (16)
GTR†	17 of 22 (77)	14 of 21 (66)
total symptom resolution‡	10 of 17 (59)	10 of 15 (66)

* In the microscopic resection group, 1 patient had new visual field cut, 1 had encephalitis, and 1 had panhypopituitarism. In the endoscopic resection group, 1 patient had transient SIADH, 1 had postoperative seizures, and 1 had new right visual loss.

† Represents the percentage of patients for whom data were available.

CSF leaks occurred in 7 individuals (28%) undergoing endoscopic resection. This difference is not statistically significant. Of the 7 intraoperative CSF leaks in the endoscopic group, 4 occurred in the first 9 procedures, 3 occurred in the following 8 procedures, and none occurred in the final 8 procedures. The differences in intraoperative CSF leaks between the groups were not statistically significant. Postoperative CSF leaks occurred in only 1 patient (4%) in the microscopic resection group compared with 3 patients (12%) in the endoscopic group. The patient with the postoperative CSF leak in the microscopic group required surgical repair. Of the 3 patients with postoperative CSF leaks in the endoscopic group, 1 required surgical intervention and in 2 patients the leak resolved with conservative treatment. In the endoscopic postoperative CSF leaks, 2 were present in the first 9 procedures, both following intraoperative CSF leaks, and 1 was present in the last endoscopic procedure, in the absence of witnessed intraoperative CSF leakage.

The most common complication in the microscopic group was DI, which occurred in 4 patients (16%) postoperatively; however, at follow-up only 2 patients (8%) had DI. One patient who underwent endoscopic resection experienced DI postoperatively; no endoscopically treated patients had DI at follow-up. In the microscopic group, 1 patient exhibited panhypopituitarism, 1 patient had new visual field cut, and 1 patient had encephalitis that was treated conservatively, with full recovery. Finally, in the endoscopic group, 1 patient experienced seizures, another had transient SIADH, and 1 had new right visual loss.

Operative Data and LOS

Gross-total resection and complete symptom resolu-

TABLE 3: Operating time and LOS in 50 patients who underwent microscopy- and/or endoscopy-assisted tumor resection

Procedure	No. of Patients	Mean Op Time in Hrs (range)*	LOS in Days (range)
microscopic resection, all	29	4.41 (2.93–8.75)†	4.84 (3–9)†
microscopic + endoscopic resection	4	5.29 (4.5–7)	4.50 (3–6)
endoscopic resection	25	2.94 (1.52–4.12)†	3.92 (3–9)†
1st group	9	3.42 (2.93–4.12)†	4.67 (3–9)‡
2nd group	8	3.11 (1.73–4.08)	3.13 (3–7)
3rd group	8	2.22 (1.52–3)†	3.88 (3–5)‡

* The mean operating time was defined as the time-marked incision to the time-marked end of surgery from operating room records as entered by the operating room staff.

† Statistically significant ($p < 0.0001$ for comparison of microscopic to endoscopic resection groups; $p = 0.0001$ for comparison of operating times in 1st and 3rd endoscopic groups; $p = 0.03$ for comparison of LOS in microscopic and endoscopic groups; $p = 0.02$ for comparison of length of operation in microscopic and endoscopic groups).

‡ Not statistically significant ($p = 0.21$ for comparison of hospital stay in 1st and 3rd endoscopic groups).

tion was determined for each group. The mean follow-up times in years were 0.74 (range 0.08–3.58) and 0.41 (range 0.08–2.08) for the microscopic and endoscopic resection groups, respectively. In the microscopic group, GTR was achieved in 77% of patients (17 of 22) and complete symptom resolution occurred in 59% (10 of 17) (Table 2). In the endoscopic group, GTR was achieved in 66% of patients analyzed (14 of 21) and total symptom resolution occurred in 66% of patients (10 of 15). Each endoscopic subgroup was analyzed (early, middle, or late group) to evaluate if there was a change in the degree of resection or symptom resolution with time. In terms of GTR, the first group had GTR in 89% of patients (8 of 9), the middle group had GTR in 50% (3 of 6), and the last group had GTR in 50% (3 of 6). In terms of complete symptom resolution, the first group had complete resolution in 57% of eligible patients (4 of 7), the middle group had resolution in 83% (5 of 6), and the last group had resolution in 1 of 2 eligible patients (50%). With regard to GTR and symptom resolution, there did not appear to be an increase with time and the surgeon's experience with endoscopic treatment, although complete data were not available for all patients. Additionally, complete pre- and postoperative hormonal data were not available in enough patients to analyze this aspect in a meaningful manner.

The mean operative time was compared among the surgical groups (Table 3). The mean operative time was defined as the time-marked incision to the time-marked end of surgery as entered by the operating room staff because these data were available from operating room records for all patients. The mean operating time for the microscopic group was 4.41 hours (range 2.93–8.75 hours). The mean operating time for the last 4 microscopic resections, in which the neurosurgical team was beginning to

TABLE 4: Published studies comparing endoscopic and microscopic resection

Authors & Year	No. of Patients		% w/ GTR		Complication Rate*	
	Microscopic Resection	Endoscopic Resection	Microscopic Resection	Endoscopic Resection	Microscopic Resection	Endoscopic Resection
Jain et al., 2007	10	10	50	50	0.7	0.2
Neal et al., 2007	15	14	67	79	0.93	0.21
present study	25	25	77	66	0.32	0.28

* The complication rate was calculated as total number of complications/total number of patients. The complication rate for Neal et al. was calculated after removing data on intraoperative CSF leaks from complications. In the other studies cited as well as in this study, intraoperative CSF leakage is not considered a complication.

use the endoscope, was 5.29 hours (range 4.5–7 hours). The mean operating time for the endoscopic resection group was 2.94 hours (range 1.52–4.12 hours). The difference among the microscopic and endoscopic resection times was statistically significant ($p < 0.0001$). The mean operative time for the first 9 endoscopic procedures was 3.42 hours (range 2.93–4.12 hours). The mean operating times for the second and third group of 8 endoscopic procedures were 3.11 hours (range 1.73–4.08 hours) and 2.22 hours (range 1.52–3), respectively. There was a statistically significant difference in operating time among the first and third group ($p = 0.0001$), and when we compared the first and second group with the third group ($p = 0.0003$).

The LOS was compared among the surgical groups (Table 3). The average hospital stay for the microscopically treated group was 4.84 days (range of hospital stay 3–9 days). The average hospital stay for the endoscopic resection group was 3.92 days (range 3–9 days). There was a significant difference between the 2 groups ($p = 0.03$). On comparison of the endoscopic groups, the means for the 3 groups were 4.67 days for the first 9 patients treated (range 3–9 days), 3.13 days for the next 8 patients treated (range 3–7 days), and 3.88 days (range 3–5 days) for the final 8 patients treated. The duration of hospital stay between the first and third groups was not statistically significant ($p = 0.21$; 1-tailed, equal-variance t-test).

Discussion

With the introduction of any surgical technique, there are stringent criteria that must be met. This is especially important when an alternative technique has been shown to be efficacious. In a comparison of endoscopic with traditional microscopic resection, the primary concern is equal tumor extirpation, with similar rates of CSF leaks, complications, and reoperation rates. The proposed advantages of endoscopic resection, including better visualization, decreased incidence of nasal complications, decreased time of operation, and shorter hospital stay are only relevant in the face of equal oncological efficacy.

In our experience, we have found the oncological results to be similar between the 2 groups. In our study, we did find the percentage of GTR to be slightly less in the endoscopic group than the in microscopic group. This is not statistically significant and is probably secondary to

the small sample size. It is always the goal of resection, regardless of the technique, to provide a complete surgical cure. Also, it is important to note that GTR is a radiographic assessment in which preoperative imaging is essential, and may not be as conclusive as the name implies. In our series, the incidence of reoperation was the same. The follow-up hormonal data were not complete enough for us to comment specifically on the impact of the surgical technique on this variable. However, the number of patients with complete symptom resolution was slightly greater in the endoscopic cohort. It should be noted that the follow-up duration for endoscopically treated patients ranged from 1 month to 2 years, so in this subset of patients more follow-up is required. However, this follow-up is adequate for comparison of GTR with symptom resolution, as well as intraoperative and postoperative complications. It will be important to determine if the size and shape of the tumor affect the surgical cure rate of these tumors, and if such variables have an impact in different manners depending on the method used. These 2 questions may be answered with larger sample sizes that are prospectively followed for longer periods of time.

In both the endoscopic and microscopic resection groups, there were no operative or postoperative deaths or cerebral vascular accidents. Our results showed a trend over time toward a reduced percentage of total complications for patients undergoing endoscopic resection. Although there were more intraoperative and postoperative CSF leaks in the endoscopic group as a whole, this was not statistically significant. Furthermore, in the endoscopic group there were no instances of DI at follow-up. Whether the decreased incidence of DI is related to the better optics of the endoscope needs to be evaluated in a larger group of patients.

Several studies have compared microscopic with endoscopic resection (Table 4). Neal et al.²⁹ reported similar trends in complication rates, and overall the complication rate in these series was in the low range for both the microscopic and endoscopic resections. Interestingly, Neal et al. found a greater incidence of CSF leaks in the patients with microscopically resected tumors, which was a trend that we did not see. One would expect that with the advantages of angled and straight endoscopes there would be a decreased incidence of CSF leaks. Neal et al.

did report an increased rate of DI in their microscopic group, which is consistent with our data. They concluded that endoscopic resection has an acceptable risk of complication.

We found operative time to be less in the endoscopic group compared with the microscopic group by nearly half an hour. As the team became more experienced with the endoscopic method of excision, the operative time differences were > 2 hours (4.41 as opposed to 2.22 hours for microscopy group vs third group of endoscopically treated patients). The LOSs are significantly different between the microscopic and endoscopic groups, with the endoscopic group hospitalization ~ 1 day less. This difference in LOS may be understated where institutional protocols require observation for ~ 72 hours, despite the fact that most patients who undergo endoscopic resection can be discharged as early as postoperative Day 1.

It is important to note that, although endoscopes are being used by our group with equal efficacy, they should not necessarily replace microscopic dissection in all cases. Cho and Liao³ noted that, although the endoscope provided rapid access to the sphenoid sinus, it has problems such as less room for operative manipulation, clouding of the scope's lens with blood and moisture and more difficulty controlling bleeding. None of these problems were apparent in our experience, but should still be taken into consideration given specific patient characteristics.

In our endoscopic group, the incidence of complications was acceptable regardless of when the surgery was performed. There were more intraoperative CSF leaks in the first 2 groups assessed (4 [44%] of 9 patients and 3 [38%] of 8 patients) than in the final group (0%). It is important to note that in the final group there was 1 postoperative CSF leak without recognition of an intraoperative leak. As a result of our small sample, the differences among groups were not statistically significant. This implies that the transition from microscopic to endoscopic resection is safe, with no increased risk to the patients. In evaluating the learning curve of a senior neurosurgeon initially untrained in endoscopic methods, we found that surgical time decreased from the first 9 to the last 8 procedures performed. The difference in time between the first and third group was ~ 1 hour.

There is a significant amount of literature assessing the learning curve for a new surgical procedure. The learning curve can be defined as a time after which a procedure may be performed safely and with a plateau in efficiency, often characterized as "surgical operative time." Depending on the procedure and experience of the surgeon, the learning curve can be as few as ≤ 10 procedures, as in the case of minimally invasive total knee arthroplasty, or > 80 procedures for other types of surgery.^{24,35} Specifically in neurosurgery, Nowitzke²⁸ defined the learning curve of microendoscopic dissection at ~ 30 procedures, after which time the operative time and complications have stabilized. McLoughlin and Fourney²⁵ described the learning curve of the minimally invasive microdissection to be ~ 15 cases, suggesting that the 15-case difference may be related to Nowitzke's use of the endoscope, which is often unfamiliar to practicing neurosurgeons. Interestingly, Sonnenburg et al.³⁴ exam-

ined the learning curve in endoscopic pituitary surgery in their experience with 45 procedures performed. In dividing their procedures into groups of 15, they found no significant differences with respect to postoperative complications, concluding that there did not seem to be a significant learning curve for the transition from traditional methods to endoscopic resection. In comparison with our investigation, this study did not evaluate surgical times and had larger groups. Although our differences were not statistically significant, we found the number of CSF leaks trended down after the second group. Furthermore, we found significant differences with respect to operative times following the second group of patients. Therefore, we postulate that the significant part of the learning curve would be achieved following our second group, or after 17 endoscopic procedures. This number is only an estimate and could be affected by the familiarity of the team with the endoscopic equipment, the referral pattern as to the type and size of tumors, and surgical simulation or practice in cadavers prior to performing the surgical procedure.

One of the important considerations we made in the transition to endoscopic resection was the integration of use of the endoscope in the final 4 microscopic procedures. Extra time spent during these procedures can make the entire team confident when the decision is made to undergo endoscopic excision. It is important for members of both the neurosurgery and otorhinolaryngology teams to be present throughout the entire procedure. The presence of the entire team enables the otorhinolaryngologist to troubleshoot endoscopic problems as they arise, because most otorhinolaryngologists are more familiar with the endoscope. It is also important to have the microscope available, with the team ready to convert to microscopic dissection if desired. Additionally, although nothing can replace a sound understanding of sellar anatomy, the use of neuronavigation can help to orient the surgeon and speed the learning curve. Thorough cooperation and understanding from everyone on the skull base team is needed for a smoother transition. We conclude that if these criteria are met, any skull base surgery program that is involved in resection of a sufficient volume of pituitary lesions is capable of conversion to the endoscopic method without increased morbidity to the patient and with an acceptable surgical learning curve.

Conclusions

Endoscopy represents a less invasive method of removing pituitary tumors, and when performed safely by a well-trained team may have few complications and an excellent outcome. Neurosurgeons can learn the technique quickly and without undue harm to their patients in as few as 17 surgical procedures. Further study is needed with more patients and longer follow-up to determine whether endoscopy is more efficacious than microscopic resection for certain tumor types or patient populations.

Disclaimer

The authors report no conflict of interest concerning the mate-

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rials or methods used in this study or the findings specified in this paper.

References

- Cappabianca P, Alfieri A, Thermes S, Buonamassa S, de Divitiis E: Instruments for endoscopic endonasal transsphenoidal surgery. **Neurosurgery** 45:392–396, 1999
- Carrau RL, Jho HD, Ko Y: Transnasal-transsphenoidal endoscopic surgery of the pituitary gland. **Laryngoscope** 106:914–918, 1996
- Cho DY, Liao WR: Comparison of endonasal endoscopic surgery and sublabial microsurgery for prolactinomas. **Surg Neurol** 58:371–376, 2002
- Ciric I, Mikhael M, Stafford T, Lawson L, Garces R: Transsphenoidal microsurgery of pituitary macroadenomas with long-term follow-up results. **J Neurosurg** 59:395–401, 1983
- Cushing H: Partial hypophysectomy for acromegaly. With remarks on the function of the hypophysis. **Ann Surg** 50:1002–1017, 1909
- Cushing H: Surgical experiences with pituitary disorders. **JAMA** 63:1515–1525, 1914
- Dew LA, Haller JR, Major S: Transnasal transsphenoidal hypophysectomy: choice of approach for the otolaryngologist. **Otolaryngol Head Neck Surg** 120:824–827, 1999
- Doglietto F, Prevedello DM, Jane JA Jr, Han J, Laws ER Jr: Brief history of endoscopic transsphenoidal surgery—from Philipp Bozzini to the First World Congress of Endoscopic Skull Base Surgery. **Neurosurg Focus** 19(6):E3, 2005
- Gamea A, Fathi M, el-Guindy A: The use of the rigid endoscope in trans-sphenoidal pituitary surgery. **J Laryngol Otol** 108:19–22, 1994
- Halstead A: Remarks on the operative treatment of tumors of the hypophysis. With the report of two cases operated on by an oronasal method. **Trans Am Surg Assoc** 28:73–93, 1910
- Har-El G: Endoscopic transnasal transsphenoidal pituitary surgery—comparison with the traditional sublabial transseptal approach. **Otolaryngol Clin North Am** 38:723–735, 2005
- Hardy J: Transsphenoidal microsurgery of the normal and pathological pituitary. **Clin Neurosurg** 16:185–217, 1969
- Heilman CB, Shucart WA, Rebeiz EE: Endoscopic sphenoidotomy approach to the sella. **Neurosurgery** 41:602–607, 1997
- Hirsch O: Endonasal method of removal of hypophyseal tumors. With a report of two successful cases. **JAMA** 5:772–774, 1910
- Jain AK, Gupta AK, Pathak A, Bhansali A, Bapuraj JR: Excision of pituitary adenomas: randomized comparison of surgical modalities. **Br J Neurosurg** 21:328–331, 2007
- Jane JA Jr, Han J, Prevedello DM, Jagannathan J, Dumont AS, Laws ER Jr: Perspectives on endoscopic transsphenoidal surgery. **Neurosurg Focus** 19(6):E2, 2005
- Jane JA Jr, Thapar K, Kaptain GJ, Maartens N, Laws ER Jr: Pituitary surgery: transsphenoidal approach. **Neurosurgery** 51:435–444, 2002
- Jankowski R, Auque J, Simon C, Marchal JC, Hepner H, Way-off M: Endoscopic pituitary tumor surgery. **Laryngoscope** 102:198–202, 1992
- Jho HD, Carrau RL: Endoscopic endonasal transsphenoidal surgery: experience with 50 patients. **J Neurosurg** 87:44–51, 1997
- Jho HD, Carrau RL: Endoscopy assisted transsphenoidal surgery for pituitary adenoma. Technical note. **Acta Neurochir (Wien)** 138:1416–1425, 1996
- Jho HD, Carrau RL, Ko Y, Daly MA: Endoscopic pituitary surgery: an early experience. **Surg Neurol** 47:213–223, 1997
- Kassam A, Snyderman CH, Mintz A, Gardner P, Carrau RL: Expanded endonasal approach: the rostrocaudal axis. Part II. Posterior clinoids to the foramen magnum. **Neurosurg Focus** 19(1):E4, 2005
- Koren I, Hadar T, Rappaport ZH, Yaniv E: Endoscopic transnasal transsphenoidal microsurgery versus the sublabial approach for the treatment of pituitary tumors: endonasal complications. **Laryngoscope** 109:1838–1840, 1999
- Lubowitz JH, Sahasrabudhe A, Appleby D: Minimally invasive surgery in total knee arthroplasty: the learning curve. **Orthopedics** 30:80–82, 2007
- McLoughlin GS, Fourny DR: The learning curve of minimally-invasive lumbar microdiscectomy. **Can J Neurol Sci** 35:75–78, 2008
- Moses RL, Keane WM, Andrews DW, Goel R, Simeone F: Endoscopic transseptal transsphenoidal hypophysectomy with three-dimensional intra-operative localization technology. **Laryngoscope** 109:509–512, 1999
- Nasseri SS, McCaffrey TV, Kasperbauer JL, Atkinson JL: A combined, minimally invasive transnasal approach to the sella turcica. **Am J Rhinol** 12:409–416, 1998
- Nowitzke AM: Assessment of the learning curve for lumbar microendoscopic discectomy. **Neurosurgery** 56:755–762, 2005
- Neal JG, Patel SJ, Kulbersh JS, Osguthorpe JD, Schlosser RJ: Comparison of techniques for transsphenoidal pituitary surgery. **Am J Rhinol** 21:203–206, 2007
- Rodziewicz GS, Kelley RT, Kellman RM, Smith MV: Transnasal endoscopic surgery of the pituitary gland: technical note. **Neurosurgery** 39:189–193, 1996
- Sethi DS, Pillay PK: Endoscopic management of lesions of the sella turcica. **J Laryngol Otol** 109:956–962, 1995
- Shah S, Har-El G: Diabetes insipidus after pituitary surgery: incidence after traditional versus endoscopic transsphenoidal approaches. **Am J Rhinol** 15:377–379, 2001
- Sheehan MT, Atkinson JL, Kasperbauer JL, Erickson BJ, Nippoldt TB: Preliminary comparison of the endoscopic transnasal vs the sublabial transseptal approach for clinically nonfunctioning pituitary macroadenomas. **Mayo Clin Proc** 74:661–670, 1999
- Sonnenburg RE, White D, Ewend MG, Senior B: The learning curve in minimally invasive pituitary surgery. **Am J Rhinol** 18:259–263, 2004
- Yung MW, Oates J, Vowler SL: The learning curve in stapes surgery and its implications to training. **Laryngoscope** 116:67–71, 2006

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