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Results and risk factors for recurrence following endoscopic endonasal transsphenoidal surgery for pituitary adenoma

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ABSTRACT

Background: Endoscopic endonasal (EE) transsphenoidal surgery is an important surgical approach to the treatment of sellar pathology, particularly for pituitary adenomas. Risk factors for the radiographic recurrence of pituitary adenomas resected using a purely endoscopic approach have not been established. This study investigates outcomes and identifies risk factors for recurrence following EE transsphenoidal surgery for pituitary adenoma.
Methods: We performed a retrospective review of 64 patients with pituitary adenomas undergoing EE surgery by a single, right-handed surgeon preferentially operating through the right nares. Post-operative MRI studies were utilized to monitor for residual disease or disease recurrence.
Results: Residual tumor was found in 31.2% of patients. Over a median follow-up period of 23.1 months (range 4–62.5), 4 (20%) of these patients showed recurrence. Two patients with inconclusive post-operative imaging had subsequent imaging consistent with recurrence, making the total recurrence in our series 9.4%. While no statistically significant effects of gender, age or history of previous treatment were seen, amenorrhea on presentation and maximum tumor diameter >10 mm were significant risk factors for radiographic recurrence ($p = 0.044$ and 0.005, respectively). No predominant side of residual tissue was identified in these tumors operated through the right nares.
Conclusions: Only 20% of patients with residual tumor developed recurrent disease over a median follow up of 23.1 months. This recurrence rate may be an important consideration in cases where gross total resection is not feasible. Preferentially operating from the right does not seem to influence the location of residual tumor.

1. Introduction

Transsphenoidal surgery is the preferred approach for a wide range of pathology involving the sella turcica, including the surgical treatment of pituitary adenomas. Since its introduction by Schloffer in 1906, transsphenoidal surgery has advanced significantly from the use of a headlight for visualization to the endoscopic techniques that are becoming common practice today [1]. These endoscopic techniques allow for excellent visualization of regional anatomy and extensive tumor resection.

Numerous studies have documented the success of the endoscopic endonasal (EE) approach to date [2–7]. Several direct comparisons to microscopic or transcranial approaches have demonstrated comparable, or superior, results with the EE approach [8–14]. However, the EE approach to the resection of pituitary adenomas does have its limitations, which include post-operative nasal complaints as well as risk for post-operative CSF leak [15]. Additionally, limitations inherent to surgical disease of the pituitary gland remain in the EE approach: these include subtotal resection, the recurrence of tumors post-operatively, and the risk for serious intra-operative complications [13].

Given the relatively recent implementation of EE transsphenoidal surgery for pituitary tumors, risk factors for residual or recurrent disease following this procedure have not been defined [16]. Additionally, tumor re-growth rates in patients with residual disease have not been well examined. To our knowledge, this is the first study directly examining risk factors for recurrence following

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a purely EE approach to pituitary pathology. We examined a series of 64 patients undergoing surgery by a single surgeon at our institution between 2006 and 2011. We report our results, including residual rates and recurrence rates, in an effort to define outcomes and identify risk factors for recurrence with this rapidly evolving neurosurgical approach to pituitary pathology.

2. Materials and methods

2.1. Patient demographics

This study was conducted in accordance with institutional policies. We reviewed a retrospectively collected database of patients with pathology-confirmed pituitary adenoma who underwent EE surgery at our institution by a single surgeon between April 2006 and June 2011. However, those with less than 4 months of follow-up time or those undergoing a biopsy procedure were excluded. Presenting symptoms, operative details, pathological diagnoses, post-operative outcomes, and post-operative complaints were all recorded. Data were collected by chart review.

2.1.1. Radiographic evaluation

Preoperative and postoperative MRI was performed on all patients. An MRI was done on post-operative day (POD) 1, approximately POD 90, and at varying intervals thereafter based on patient characteristics. All MRI reports were reviewed for the presence of post-operative residual and/or evidence of tumor growth. Residual disease was defined as characteristic tissue identified on POD 1 or POD 90 MRI, as reported by the radiologist at the time of the study. Recurrence was defined as interval tumor growth on MRI between tumor resection and the last follow-up imaging study. Radiographic recurrence was reported by the radiologist at the time of the study.

2.2. Surgical technique

The right nares was preferentially entered by this right-handed surgeon. After application of topical cocaine to the nasal mucosa, the mucosa of the middle turbinates was infiltrated with a mixture of 1% lidocaine and epinephrine (1:100,000). The sphenoid ostia were identified bilaterally and enlarged by removal of bone. A tissue shaver was used to resect the posterior third of the nasal septum. Using a highspeed drill and curettes, the anterior wall of the sella was opened. We attempted to resect microadenomas en bloc, whereas macroadenomas were decompressed internally first by removing the inferior portion of the tumor, followed by resection of the lateral portions. The dura mater was opened medial to the internal carotid artery in cases of cavernous sinus (CS) invasion. Brainlab neuronavigation was used for all cases. Skull base defects were closed in a multilayered fashion, as described previously [17].

2.3. Statistical evaluation

Fisher Exact Test was performed to determine significant risk factors for recurrence. Significance was defined as $p < 0.05$. Kaplan–Meier survival analysis was performed on patients with recurrence. Statistical analyses were performed using MedCalc for Windows, version 12.2.1 (MedCalc Software, Mariakerke, Belgium).

3. Results

Our cohort of patients consisted of 64 individuals who underwent a purely EE transsphenoidal resection of pituitary adenomas by a single surgeon at our institution between April 2006 and June 2011 (Table 1). The median age of patients in this study was 46 years, and female patients made up 62.5% of the cohort. The mean follow-up time was 24.3 months in this study (median 23.1, range 4.0–62.5). Headache and visual deficits were the most common complaints on initial patient evaluation, occurring in 43.8% and 39.1% of patients, respectively. Visual deficits included decreased visual acuity and decreased peripheral vision. The majority of lesions had a maximum diameter greater than 10 mm (78.1%). Surgical outcomes and complications are reported (Table 2).

Residual disease was reported by the radiologist evaluating the post-operative and 3-month follow-up MRI. Gross total resection (GTR) was achieved in 68.7% of patients. Residual tumor, classified as intracavernous or extracavernous based on MRI findings, was intracavernous in 14.1% of cases. However, only 4 of these patients (20%) showed evidence of radiologic recurrence during the follow-up period. Two additional patients who had post-operative imaging that was inconclusive for residual disease versus normal pituitary gland had recurrence, making a total of 6 patients (9.4%) with recurrence in our series. Three out of these 6 patients subsequently required surgical revision with repeat EE surgery and three patients received stereotactic radiosurgery. The decision for stereotactic radiosurgery on these three patients was based on patient

Table 1
Patient characteristics.

Number of patients	64
Age (years)	
Mean ± SD	46.7 ± 16.7
Median (range)	46 (12–81)
Sex	
Male	24 (37.5%)
Female	40 (62.5%)
Follow-up time (months)	
Mean	24.3
Median (range)	23.1 (4.0–62.5)
Presenting symptoms	
Headaches	28 (43.8%)
Visual deficits	25 (39.1%)
Amenorrhea	10 (15.6%)
Incidental	11 (17.2%)
Galactorrhea	13 (20.3%)
Decreased libido	5 (7.8%)
Diplopia	6 (9.4%)
Acromegaly	3 (4.7%)
Apoplexy	1 (1.6%)
Seizure	1 (1.6%)
Prior surgery	
Yes	4 (6.3 %)
No	60 (93.8%)
Maximum diameter (mm)	
Mean	18.9
Median (range)	19 (8–40)
Maximum diameter > 10 mm	
Yes	50 (78.1%)
No	9 (14.1%)

Table 2
Surgical outcomes.

Outcome	# patients (%)
Post-operative CSF leak	4 (4.1%)
Diabetes insipidus	2 (3.1%)
Panhypopituitarism	3 (4.7%)
Wound infection	1 (1.6%)
New visual field deficits	0
Improvement in presenting visual deficits	23/25 (92%)
Residual	
Yes	20 (31.3%)
- Within CS	9 (14.1%)
- Outside CS	11 (17.2%)
No residual (GTR)	44 (68.7%)
Surgical revision	7 (10.9%)
Adjuvant stereotactic radiosurgery	7 (10.9%)
Recurrence	6 (9.4%)