Visual Outcomes after Endoscopic Pituitary Surgery in Patients Presenting with Preoperative Visual Deficits

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J Neurol Surg B 2017;78:461–465.

Abstract

Introduction Pituitary adenomas represent 15% of primary brain tumors. Visual disturbance is a common clinical manifestation of these neoplasms due, among other factors, to local mass effect on the optic system.

Objective To evaluate changes of the visual fields in patients undergoing endoscopic endonasal approach (EEA) for pituitary adenomas and to find predictive factors for successful visual field outcome.

Material and Methods This is a cross-sectional study. A review was conducted of medical records of consecutive patients with tumors of the sellar region undergoing EEA between January 2008 and December 2012 at the Skull Base Unit of Guillermo Grant Benavente Hospital, University of Concepción, Concepción, Chile, and who had undergone pre- and postoperative visual field evaluation.

Results A total of 35 patients, with a mean age of 50.2 years, fulfilled the inclusion criteria. All patients had objective visual field disturbances before the surgery. Following surgery, 25 patients (71.4%) had favorable outcomes, whereas 8 (22.8%) had no change and 2 (5.8%) had an unfavorable outcome. Complete tumor removal was associated with a better visual outcome than those obtained after a subtotal removal.

Discussion The EEA for pituitary tumors is particularly effective for visual field disturbances, with reported improvement rates ranging from 50 to 90%. Our series show similar results, with a 71.4% improvement of visual field disturbances.

Conclusion This study adds further evidence to the current belief that EEA for pituitary adenomas is a safe and effective technique to improve visual field alterations. Complete removal of the tumor during surgery seems to be a predictive factor for a good visual outcome.

Keywords

- pituitary
- endoscopic endonasal approach
- visual field
- optic nerve
- optic chiasm

received
March 17, 2017
accepted after revision
June 3, 2017
published online
July 19, 2017

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Stuttgart · New York

DOI <https://doi.org/10.1055/s-0037-1604169>.
ISSN 2193-6331.

Introduction

Pituitary adenomas are common intracranial neoplasms that represent approximately 15% of primary brain tumors.¹ Postmortem studies show a prevalence of up to 15% of undiagnosed pituitary adenomas in the general population.² Most of these tumors are intrasellar; however, they may extend to the suprasellar and parasellar regions and may even invade adjacent structures, such as the cavernous sinuses and the bone of the sella turcica and clivus. Therefore, despite their usually benign histology, one must consider local aggressiveness as a potential feature.³

Clinically, these tumors may be asymptomatic or may present with classic syndromes of hormone hypersecretion or hypopituitarism, and symptoms due to mass effect, such as headache or visual disturbances.⁴ Functional pituitary adenomas are characterized by the secretion of any hormone pertaining to the anterior pituitary gland. Those that produce prolactin, growth hormone, or adrenocorticotrophic hormone are most frequent.⁵ Nonfunctioning adenomas are those without any recognizable hormone production and may present clinically with vision loss or hypopituitarism.⁶

A broad spectrum of visual symptoms has been reported in the literature, ranging from no alteration to blindness.⁷ Visual impairment may comprise a decrease in visual acuity (41%), impaired color vision (56–71%), ocular movement alterations (8%), and visual field disturbances, the last one being the most common, with a reported prevalence from 37 to 96% in different studies.^{8–13} Visual impairment is primarily due to direct tumor compression on the optic nerve with subsequent nerve atrophy and devascularization.¹⁴ Potential mechanisms of axonal injury from a compressive lesion include direct disruption of conduction along the axon, impaired axoplasmic flow, demyelination with impaired signal conduction, and ischemia from compression or stretching of the blood supply of the chiasm by the tumor.¹⁵

Despite advances in radiation therapy and pharmacological treatment, surgery remains the first-line treatment, except for prolactinomas. The presence of visual abnormalities is one of the main indications for surgical resection and chiasmatic decompression.¹⁶

The endoscopic endonasal approach (EEA) is widely accepted as a modality of surgery, as it has proven to be an effective technique in terms of tumor resection and improvement of hormonal disorders and visual defects, with a low surgical morbidity and low mortality rate in high-volume centers.¹⁷ The EEA is particularly effective to correct visual field disturbances, with reported improvement rates that range from 50 to 90%, and less effective for visual acuity, motor ocular involvement, and improving color vision.^{8–14}

Objective

The objective of this article is to evaluate changes in visual field of patients undergoing EEA surgery for pituitary adenomas at the Skull Base Unit of Guillermo Grant Benavente Hospital, University of Concepción, Concepción, Chile, from

2008 to 2012, and to found predictive factor for good visual field outcome.

Materials and Methods

This is a cross-sectional study. The authors reviewed the medical records of patients with tumors of the sellar region undergoing endonasal endoscopic surgery between January 1, 2008, and December 31, 2012, at the Skull Base Unit of the Guillermo Grant Benavente Hospital. Surgery was performed by a combined team of one neurosurgeon and one otolaryngologist - head and neck surgeon.

Surgical Technique

Patients are positioned supine on the operating table with the head in a neutral position elevated approximately 15 degrees. Povidone iodine solution is applied over the nose and upper lip, as well as into each naris. We use total intravenous anesthesia and 2 g of ceftriaxone as prophylactic antibiotic.

The nose is prepared with adrenaline (1:1,000) soaked patties to achieve mucosal decongestant and vasoconstriction. The septal mucosa is infiltrated with lidocaine 2% with epinephrine 1:100,000 in the donor site for the nasoseptal pedicled flap.

We routinely lateralize the middle and inferior turbinate by applying gentle pressure with a freer spatula and remove the superior turbinate. A nasoseptal flap is routinely harvested on the right side with its vascular pedicle containing the nasoseptal artery. Then, we performed a right sphenoidotomy. The posterior septum is disarticulated from the rostrum of the sphenoid bone, which is then removed to create a bilateral opening in the sphenoid sinus. The natural sphenoid ostium on the left is opened and widened so that there is communication with the previous sphenoidotomy on the right side, thus creating wide bilateral sphenoidotomies. The lateral margins of the sphenoidotomies are extended to the level of the medial pterygoid plates.

To optimize the available space, the endoscope is positioned superiorly at 12 o'clock position, with the suction in the 6-o'clock position in the right naris. Dissecting instruments can be introduced into the nasal cavity through the left naris.

The bony opening over the dura extends to the medial carotids. Bony septa are drilled flat as the median septum usually deviates laterally to overlies the carotid artery. The dural opening should allow as much intrasellar access laterally as possible. We use an X-shaped incision and create a single rectangular cavity of 3 × 3 mm within the sphenoid sinus.

As soon as the dura is opened, the tumor usually presents itself through the dural opening. Then, the tumor is biopsied and the samples are sent to histopathological studies. The tumor is debulked using ring curettes, staying in the inferior half of the tumor to avoid breaching the diaphragm. The capsule is held up with a small neurosurgical patty to allow full exploration of the sella. The medial cavernous sinus is examined with a Doppler probe to ensure we explored as far lateral as possible.

After tumor excision, we put gelatin sponges into the sella and then place the septal flap over the bony and dural defect and more gelatin sponges in the nasal cavity. If a cerebrospinal fluid leak is produced during surgery, we use a fat graft into the defect or fascia lata covered with the nasoseptal pedicled flap and gelatin sponges in the nasal cavity.

Patients

During that period, 89 patients with tumors of the sellar region were operated. Only 37 patients of them were included in the analysis after fulfilling our inclusion criteria (histologically proven pituitary adenoma and pre- and postoperative Goldmann visual field test). All visual field examinations were reviewed by a neuro-ophthalmologist and classified as favorable (if there was improvement in the postoperative test), unchanged, or unfavorable (if the visual field worsened). Two patients were excluded because they presented alterations of the visual field secondary to another cause (cataracts). Tumor extension using the Hardy¹⁸ classification of pituitary adenomas, which was subsequently modified by Wilson¹⁹ (►Table 1), and gross total resection were assessed by the senior authors.

Statistical Analysis

The analysis includes multiple variables: functioning versus nonfunctioning adenoma, primary surgery versus reoperation, prior radiotherapy, tumor extension, and the presence of postoperative residual tumor. Statistical analysis was performed using Fisher's exact test and chi-square test (EPI INFO 2000 software [Center for Disease Control and Prevention]). A statistically significant *p*-value was defined as <0.05.

Results

Thirty-five patients fulfilled our inclusion criteria of histologically proven pituitary adenoma with pre- and postoperative Goldmann visual field test. Of the 35 patients, 17 were men (48.5%) and 18 women (51.5%), with an average of 50.2 years of age (range: 26–75). Twenty-two (62.8%) patients had nonfunctioning adenomas and 13 (37.2%) had functioning adenomas. Twenty-nine (82.8%) cases were primary surgeries

Table 2 Clinical characteristics of our patients

	N (%)
Sex	
Male	17 (48.5)
Female	18 (51.5)
Age (mean)	
20–29	2 (5.7)
30–39	1 (2.8)
40–49	14 (40)
50–59	9 (25.7)
60–69	6 (17.2)
70–79	3 (8.6)
Histological type	
Nonfunctioning adenomas	22 (62.8)
Functioning adenomas	13 (37.2)
Prior surgeries	
Yes	6 (17.2)
No	29 (82.8)
Prior history of radiotherapy	
Yes	6 (17.2)
No	29 (82.8)

and 6 cases (17.2%) were reoperations. Six patients (7.2%) had a history of prior radiotherapy (►Table 2). As for the extension, 28 patients (80%) had suprasellar extension, 9 (25.7%) had compressing the optic chiasm, 7 (20%) had laterosellar extension with compromise of the cavernous sinus, and 6 (17.2%) had extended to the infrasellar region. All tumors were classified as macroadenomas (►Table 3).

All 35 patients (70 eyes) presented preoperative visual field abnormalities. After surgery, the visual field was

Table 1 Hardy classification (Modified by Wilson)

Stage	Grade
0: no suprasellar extension	I: sella is normal; tumor < 10 mm
A: extension to suprasellar cistern	II: sella is enlarged; tumor ≥ 10 mm
B: recesses of third ventricle obliterated	III: local perforation of sellar floor
C: third ventricle grossly displaced	IV: diffuse sellar floor destruction
D: intracranial	
E: into/beneath the cavernous sinus	

Table 3 Tumor stage and grade

Stage	N (%)
0	0
A	12 (32.4)
B	12 (32.4)
C	4 (10.8)
D	0
E	7 (19)
Grade	
I	0
II	31 (83.8)
III	3 (8.1)
IV	3 (8.1)

normalized in 17.2% of patients (6 cases) and improved in another 54.2% (19 cases); therefore, there was a favorable outcome in 71.4% of cases (25 patients). In 22.8% of cases (8), there was no change, and in 5.8% (2 cases), there was an unfavorable outcome.

Regarding the extension of the tumor, the patients with suprasellar extension had 56% of improvement, tumors compressing the optic chiasm or the ones with infrasellar extension had 67% of improvement, and tumors with laterosellar or multiple extensions had 83% of improvement. No statistical significance was found regarding tumor extension.

On bivariate analysis, the complete removal of the tumor was associated with a better visual outcome when compared with a subtotal removal ($p < 0.05$). The rest of the analyzed variables—history of previous radiotherapy, primary surgery or reoperation, functioning or nonfunctioning adenoma—showed no statistical significance ($p > 0.05$), but there was a tendency to present favorable outcomes in those patients with nonfunctioning adenoma (77% of improvement), primary surgery (75% of improvement), and no history of prior radiotherapy (► Table 4).

Discussion

Adenomas with a suprasellar extension may compress the optic chiasm causing visual impairment, mainly visual field deficits, such as bitemporal hemianopia, which may be the first manifestation of these tumors. The tumors first compress the optic chiasm causing visual field defect (bitemporal hemianopia) and then, at a later stage, compromise the macular fibers decreasing visual acuity.²⁰ This study included 35 patients presenting with preoperative visual field deficits; thus, decompression of the anterior visual pathways was the main indication for surgery.²¹

Improvement in visual function has been postulated to occur in three stages: rapid recovery within minutes to a couple of days, delayed recovery over weeks to months, and late recovery over months to years. The initial improvement is thought to be the result of the removal of a physiological conduction block. Further improvement during a stage of delayed recovery seems to be the result of remyelination of the decompressed optic pathways.¹⁵

The EEA approach has been highly effective in improving visual defects in patients with tumors of the sellar region, with reported rates ranging from 50 to 90%.^{8–14} This study found favorable results in 71.4% of the patients: 54.2%

showed improvement and 17.2% of patients normalized their postoperative Goldmann visual field test. The only significant prognostic factor associated with a better outcome of the visual field was the complete removal of the tumor (as opposed to partial tumor removal). Although there were no statistically significant differences, there was a tendency to better visual outcomes in patients with nonfunctioning adenomas, primary surgery, and without prior history of radiotherapy. Age was not an influential factor.

Several studies have proposed predictive factors for the improvement of visual field alterations after surgical decompression of the optic chiasm. Barzaghi et al demonstrated that the presence of a good preoperative visual evaluation, low tumor volume, and young age are positive predictive factors for postoperative visual function, whereas sex and duration of symptoms were not.²² Jacob et al demonstrated the importance of the thickness of the fibers of the retina as a predictor in the improvement of the visual field alterations.²³ Moon et al reported similar results.²⁴ Lee et al reported the importance of visual acuity as a predictive factor in improving visual field disturbances, showing better visual results for patients with good preoperative visual acuity tests.²⁵ A recent study by Yu et al showed that the expression of K_i-67 and vascular endothelial growth factor (VEGF) in low amounts are associated with better visual outcomes after surgery compared with those patients with high expression of K_i-67 and VEGF.²⁶ These two markers had showed an important role in invasive pituitary adenomas.²⁷ They also reported as positive predictive factor the presence of a good preoperative visual function, low tumor volume, and young age.²⁶ Our second objective was to determine favorable variables in the outcome of the postoperative visual field, finding only complete resection of the tumor as a favorable factor; therefore, we try to achieve complete excision in all our patients.

The EEA has higher rates of gross total resection and improved visual outcome than the microscopic transsphenoidal and the transcranial approach in the treatment of sellar tumors.²⁸ In our institution, since 1998, we have used the EEA for the treatment of pituitary tumors. Initially, we took biopsies of sellar tumors using this technique. Subsequently, with the extended endoscopic approaches and the greater experience of the skull base unit, complete tumor resection was achieved with a low rate of complications and mortality, becoming the treatment of choice in our hospital. One important factor to consider in the successful outcome of the surgery is the experience of the surgical team to achieve complete removal of the tumor with a low complication rate.¹⁷

We decided to evaluate only the alterations of the visual field since this is the variable that most improved with the EEA.^{8–14,28} The limitations of our study are the small number of patients and incomplete follow-up, and also, we did not measured variations in visual acuity, ocular motility, and color vision after surgery. We also did not evaluate our patients with optical coherence tomography and did not consider the time between the appearance of the symptoms

Table 4 Bivariate analysis

Variable	p-Value
Tumor extension	0.054
Primary surgery vs. surgery for recurrence	0.053
Nonfunctioning vs. functioning adenoma	0.051
Prior radiotherapy vs. no radiotherapy	0.057
Total vs. partial resection	0.047

and the surgical resolution. Since 2013, our patients have undergone a stricter preoperative study and follow-up protocol, considering all the previously mentioned variables. This study constitutes our initial experience and is the first to be published by a skull base department in Chile.

Conclusion

The EEA for pituitary tumors is a safe and effective technique in improving visual field alterations, presenting a favorable outcome in 71.4% of our cases, which is within the range reported in the literature. Complete removal of the tumor during surgery is a predictive factor of a good visual outcome on these patients.

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