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Postoperative Visual Outcomes and the Influence of Optic Nerve Status on Visual Acuity in Endoscopic Endonasal Surgery of Non-functioning Pituitary Macroadenoma Patients

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ABSTRACT

OBJECTIVE: To evaluate postoperative visual outcomes including visual acuity (VA) and visual field (VF), and the relationship of optic nerve status and postoperative VA improvement in non-functioning pituitary macroadenoma (NFPA) patients who underwent endoscopic endonasal surgery (EES).

METHODS: Data of NFPA patients with visual impairment who underwent EES with tumor removal were retrospectively reviewed from 2017 to 2021. The postoperative visual outcomes (at least 6 months after surgery), and the relationship between optic nerve status and postoperative VA improvement were analyzed. The extent of resection, postoperative complications, and mortality were evaluated.

RESULTS: Twenty-three patients were included in this study with 86.9% favorable vision after surgery. The VA and VF were separately analyzed. The postoperative VA showed 75.8% improved, 9% stable, and 15.2% worsened in preoperative VA impairment eyes. The optic nerve atrophy group had 65.3% improved, 13% stable, and 21.7% worsened VA. The normal optic nerve group had 52.9% improved, 35.4% stable, and 11.8% worsened VA. The p-value was 0.677 between the 2 groups. The postoperative VF examination showed 68.4% improved and 31.6% stable in VF defective eyes. The gross total resection of tumor provided more improvement of VA (72.2%) but not VF comparison with near-total and subtotal resection of tumor.

CONCLUSION: The EES in NFPAs is considered safe with a satisfactory visual improvement rate. Optic nerve atrophy tends to have a higher rate of postoperative VA deterioration.

KEYWORDS: endoscopic endonasal surgery, non-functioning pituitary adenoma, optic nerve atrophy, pituitary tumor, visual outcomes

INTRODUCTION

Pituitary adenoma is a common brain tumor[1]. Non-functioning pituitary macroadenomas (NFPAs) are defined by a tumor size greater than 10 millimeters; and they do not secrete abnormal pituitary hormones. The common presentations of patients with NFPAs are visual impairment, including decreasing visual acuity (VA) or

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visual field (VF) defects or both, headaches, hypopituitarism, and ophthalmoparesis[2]. The visual impairment the indication for surgery in NFPA. In the current literature regarding pituitary adenoma, the rate of postoperative visual improvement varied between 67.5% and 91%[1,3-7]. The predictive factors associated with visual improvement are duration of symptoms, severity of VF defect and VA, retinal nerve fiber layer thickness, size of tumor, and tumor extension[8]. The optic nerve atrophy or optic disc pallor as a predictive factor is still controversial due to a discrepancy in the results[9-10].

The common route of surgery is transsphenoidal route unless there are contraindications. The transsphenoidal surgery can be either performed by microscope or endoscope. Advancements in endoscopic surgical techniques and technology have enabled endoscopic endonasal surgery (EES) to provide a satisfactory tumor resection rate, postoperative visual improvement, and a low rate of complications, including postoperative meningitis and mortality[2-4,11-12]. The unique complications of EES are postoperative cerebrospinal fluid (CSF) leakage and nasal complications such as anosmia, epistaxis, sinusitis, and nasal crusting[13-15].

In this article, the authors aim to present the postoperative visual outcomes in NFPA patients, and the relationship between preoperative optic nerve status and postoperative VA improvement. We also provide the relationship of extent of resection and postoperative visual examination, complications, and mortality.

METHODS

Pituitary tumor data from the Faculty of Medicine, Vajira Hospital, Navamindradhiraj University were analyzed. The inclusion criteria were NFPA patients who underwent EES with tumor removal by 3 neurosurgeons from 2017 to 2021 due to visual impairments (decreased VA or VF or both) and patient's age more than 18 years old. Patients with pituitary adenoma without visual impairment, recurrent pituitary adenoma, and transcranial surgery were excluded from this study. Primary outcome was postoperative visual status compared with preoperative status. Patients were divided into 2 groups based on postoperative visual examination. The favorable vision group was defined as an improved or stable visual examination (VA or VF) at 6 months after surgery. The unfavorable vision group was defined as a worse visual examination (VA or VF) at 6 months after surgery. The visual assessments were performed by ophthalmologists before and after surgery and included VA, VF, and eye examination. The VA assessment was performed by using standard Snellen chart with pinhole occlude. At least 1 line improvement on Snellen chart was considered as VA improvement. If the VA was severe and unable to read the Snellen chart, the severity of VA was measured as blindness, light perception, hand motion detection, and finger counting. At least 1 step improvement of vision was considered as VA improvement. The VF was assessed by Goldmann perimetry. At least small part improvement of VF within the quarter of defect was considered as VF improvement. The patients with pale optic disc by eyeground examination were considered as the optic nerve atrophy group.

Tumor characteristics were analyzed using magnetic resonance imaging (MRI) of the brain and pituitary gland by radiologist and neurosurgeon. The tumor diameter was measured in width*anteroposterior (AP)*height dimension, and tumor volume was calculated by using BrainLab Iplan software (BrainLab, Feldkirchen, Germany). Preoperatively, the rostro-caudal extensions were documented ventricularly (extended to lateral or third ventricle), subfrontal, sphenoid sinus, clivus and/or posterior fossa extension. The lateral extension was documented using the Knosp classification[12]. Postoperative extent of resection was evaluated using the latest postoperative MRI of the brain and

pituitary gland. Gross total resection (GTR) was defined as none of the tumor seen in the postoperative MRI; near-total resection (NTR) was defined as less than 10% of the residual tumor. More than 10% of postoperative residual tumor was defined as subtotal resection (STR).

Furthermore, patient characteristics, presenting symptoms, intraoperative and postoperative complications (intraoperative major vascular injury, blood loss, postoperative meningitis, diabetes insipidus and postoperative CSF leakage requiring surgical intervention) and mortality were recorded.

This study was approved by the Institutional Review Board of the Faculty of Medicine, Vajira Hospital. The certificate of approval number is 118/2565. Statistics were analyzed using SPSS statistics version 28.0.0.0. Data between the groups were compared using the Fisher's exact test and unpaired t-test as appropriate. P-value < 0.05 was considered as statistically significant.

RESULTS

Thirty-one NFPA patients were surgically treated using the endoscopic endonasal approach. Eight patients were excluded due to intact preoperative visual examination (both VA and VF). A total of 23 patients were included in this study. Patient demographics are shown in Table 1. The mean age was 53.7 years old. Twelve (52.2%) were male and 11 (47.8%) female. The most presenting symptom was visual impairment in 21 patients (91.3%). Three patients presented with symptoms of pituitary apoplexy. Other presentations were ophthalmoparesis due to cavernous sinus invasion, headaches, hypotension, and head injury with incidentally found pituitary tumor.

The tumor characteristics were classified using the Knosp classification, as shown in Table 2. There was no tumor classified Knosp 3b in this study. The rostro-caudal extension of a tumor: 11 tumors were extended into the clivus bone. The sphenoid sinus, third ventricle, subfrontal, corpus callosum, and posterior fossa extension were seen in 8, 8, 3, 1, and 1 tumor, respectively. Five of 23 NFPAs (21.7%) were giant pituitary adenomas with maximal tumor diameter greater than 40 mm.

Table 1 Patient demographics

Characteristics	Value
Number of patients	23
Mean age (years)	53.7 ± 11.3
Sex (n, (%))	
Male/Female	12 (52.2%) / 11 (47.8%)
Clinical presentation (n)	
Visual impairment	21 (91.3%)
Pituitary apoplexy	3 (13%)
Cavernous sinus syndrome	1 (4.3%)
Headache	2 (8.7%)
Hypotension	1 (4.3%)
Incidental finding	1 (4.3%)
Preoperative pituitary hormone deficiency (n)	17 (73.9%)
One axis	3 (13%)
Two axes	8 (34.8%)
Panhypopituitarism	6 (26.1%)

Abbreviation: n, number

Table 2 Tumor characteristics

Characteristics	Value
Tumor volume (mean, mL)	3.95 ± 0.75
Tumor diameter (mean, mm)	26.2 ± 10.3*22.6 ± 9.9*30.1 ± 15.4 (W*AP*H)
Knosp Classification (n, (%))	
Knosp 0	1 (4.3%)
Knosp 1	4 (17.4%)
Knosp 2	5 (21.7%)
Knosp 3a	10 (43.4%)
Knosp 3b	0 (0%)
Knosp 4	3 (13%)
Rostro-caudal extension (n)	
Subfrontal	3 (13%)
Third ventricle	8 (34.8%)
Corpus callosum	1 (4.3%)
Clivus	11 (47.8%)
Posterior fossa	1 (4.3%)
Sphenoid sinus	8 (34.8%)
Extent of resection (n, (%))	
GTR	11 (47.8%)
NTR	8 (34.8%)
STR	4 (17.4%)

Abbreviations: AP, anteroposterior; GTR, gross total resection; H, height; mL, millilitre; mm, millimeter; n, number; NTR, near-total resection; STR, subtotal resection; W, width
The tumor characteristics table provided the mean tumor volume (mL), the mean tumor diameter in W*AP*H dimension, the Knosp classification, the rostro-caudal extension of tumor, and extent of resection. The extent of resection composed of GTR (none of residual tumor), NTR (< 10% of residual tumor), and STR (> 10% of residual tumor).

Twenty patients (86.9%) were in the favorable vision group and 3 patients (13.1%) were in the unfavorable vision group, as shown in Table 3. Moreover, 46 eyes were evaluated VA and VF, separately. Preoperatively, VA examination showed 33 impairments and 9 normal eyes (4 were missed). Twenty-five of the 33 (75.8%) impaired VA eyes were improved, 3 (9%) were stable, and 5 (15.2%) worsened, postoperatively. Of the 9 normal VA eyes, 7 (77.8%) were stable and 2 (22.2%) worsened, postoperatively. The preoperative VF examination showed 38 defective eyes and 8 normal eyes. Among the 38 defective eyes, 26 (68.4%) were improved and 12 (31.6%) were stable, postoperatively. Of the 8 normal VF eyes, 7 (87.5%) were stable and 1 (12.5%) worsened, postoperatively. The relationship between the extent of resection and postoperative visual examination were evaluated. Among the GTR group, the postoperative VA was 72.2% improved, 16.7% stable, and 11.1% worsened. The postoperative VF was 59% improved, 36.5% stable, and 4.5% worsened. Along with NTR and STR groups, the postoperative VA improvements was 50% in both, and the postoperative VF improvement was 50% in NTR group and 62.5% in STR group. The rest of results were shown in Table 3.

The preoperative optic disc examination was performed in 40 eyes: 23 optic discs were pale and 17 optic discs were normal. The pale optic disc group: 15 (65.3%) eyes were improved, 3 (13%) were stable, and 5 (21.7%) worsened in VA after surgery. The normal optic disc group: 9 (52.9%) eyes were improved, 6 (35.3%) were stable, and 2 (11.8%) worsened in VA after surgery, as shown in Table 4. The p-value was 0.677.

Eleven of 23 patients (47.8%) achieved GTR, 8 patients (34.8%) were NTR, and 4 patients

(17.4%) were STR. The factors associated with extent of resection were tumor extension, including cavernous sinus, corpus callosum, posterior fossa, and size of tumor. One of 5 (20%) giant pituitary adenomas achieved GTR. The 3 most common complications were meningitis (13%), CSF leakage (13%), and surgical site hematoma (13%). One patient (4.3%) had persistent CSF leakage and required surgical intervention. Complications and morbidity are shown in Table 5. There were no internal carotid artery injuries or mortalities.

Table 3 Visual outcomes

Visual outcome	Value (n, (%))		
Postoperative visual outcome (n = 23)			
Favorable vision	20 (86.9%)		
Unfavorable vision	3 (13.1%)		
	Postoperative visual examination		
	Improved	Stable	Worsened
Preoperative visual examination			
Visual acuity (total eyes = 46)			
33 Impaired VA	25 (75.8%)	3 (9%)	5 (15.2%)
9 Normal VA	-	7 (77.8%)	2 (22.2%)
4 Missing data			
Visual field (total eyes = 46)			
38 Impaired VF	26 (68.4%)	12 (31.6%)	0 (0%)
8 Normal VF	-	7 (87.5%)	1 (12.5%)
Extent of resection			
11 GTR (total eyes = 22)			
VA (18 eyes, 4 missing data)	13 (72.2%)	3 (16.7%)	2 (11.1%)
VF	13 (59%)	8 (36.5%)	1 (4.5%)
8 NTR (total eyes = 16)			
VA	8 (50%)	5 (31.3%)	3 (18.7%)
VF	8 (50%)	8 (50%)	0 (0%)
4 STR (total eyes = 8)			
VA	4 (50%)	2 (25%)	2 (25%)
VF	5 (62.5%)	3 (37.5%)	0 (0%)

Abbreviations: GTR, gross total resection; n, number; NTR, near-total resection; STR, subtotal resection; VA, visual acuity; VF, visual field
The missing data refers to patients whom preoperative VA data were not available.

Table 4 Preoperative optic nerve status and postoperative visual acuity

	Postoperative VA (n, (%))		
	Improved VA	Stable VA	Worsened VA
Pale optic disc (n = 23)	15 (65.3%)	3 (13%)	5 (21.7%)
Normal optic disc (n = 17)	9 (52.9%)	6 (35.3%)	2 (11.8%)
P-value = 0.677			

Abbreviations: n, number; VA, visual acuity

Table 5 Postoperative complication

Complications	n (%)
Meningitis	3 (13%)
CSF leakage	1 (4.3%)
Surgical site hematoma	3 (13%)
Intracapsular hematoma	1 (4.3%)
Subarachnoid hemorrhage	2 (8.7%)
Ischemic stroke	1 (4.3%)
Internal carotid artery injury	0
Mortality	0
Endocrinological complication	
New pituitary hormone deficiency	4 (17.4%)
One axis	2 (8.7%)
Panhypopituitarism	2 (8.7%)
Diabetes insipidus	3 (13%)
Transient	2 (8.7%)
Permanent	1 (4.3%)

Abbreviations: CSF, cerebrospinal fluid; n, number

DISCUSSION

Visual impairment was the most common presentation in the NFPA patients. The primary goal of surgery was to improve vision (both VA and VF). Multiple factors were associated with postoperative visual improvement as stated in the aforementioned studies[8-10]. Preoperative pale optic disc or optic nerve atrophy are believed to be associated with the reduction of the visual improvement rate.

In this study, the favorable visual outcome was 86.9%, which is comparable with the other studies in the literature[3-5,11-12]. We analyzed separately the postoperative VA and VF. Specifically, the authors aimed to find the relationship between optic nerve status and postoperative VA improvement. We found that the pale optic disc group tended to have postoperative VA deterioration (21.7%) more than the normal optic disc group (11.8%), but statistical analysis showed no significance. The pale optic disc was an indicator of optic nerve atrophy and occurred in long-standing anterior visual pathway compression by pituitary adenoma. This factor risked the optic nerve injury during the surgery. The mobilization of tumor capsule might compress and injury the optic nerve around the optic canal or optic chiasm. Meanwhile, VA improvement in the pale optic disc group was satisfactory compared with the normal optic disc group (65.3% versus 52.9%). The rate of VA improvement in the normal optic disc group was lower than in the pale optic disc group, but the postoperative stable VA rate was 35.3% because there were normal VA patients in the normal optic disc group. In the meta-analysis, the pallor optic disc and preoperative visual status affected the postoperative visual function recovery[8,12]. In contrast, the VF improvement rate was 68.4%, and 31.6% had stable VF, which was the same as preoperative status. None of the VF defective eyes deteriorated after surgery in this study. The multiple factors documented in previous studies may explain the persistent postoperative VF defects[16-17], such as age, duration of symptoms, and the severity of VF defect, all of which were not included in this study.

Moreover, the authors evaluated the relationship between the extent of resection and the postoperative visual improvement. In the GTR group tended to have more improvement in VA while postoperative VA declination occurred the most in the STR group. This might be explained by optic nerves compression by the residual tumor.

Two of GTR group showed worsened postoperative VA, 1 patient was pituitary apoplexy. Attempting the GTR might risk the optic nerve injury during the tumor mobilization. In contrast, the postoperative VF examination was not different among each group. One VF in the GTR group was worsened postoperatively, this might be explained by tumor mobilization during the surgery.

The postoperative Subarachnoid hemorrhage (SAH) in this study occurred in 2 patients (8.7%). One patient required anticoagulant due to postoperative venous thrombosis. Another was attempting removal of tumor within cavernous sinus, the postoperative SAH extended from cavernous sinus bleeding and caused postoperative left cavernous sinus syndrome. None of postoperative SAH patients had worsened VA or VF.

The limitations regarding this study should be noted. This study is retrospective. Furthermore, only a small number of patients were included due to its selective inclusion criteria.

CONCLUSION

The EES of NFPAs is considered safe with a satisfactory visual improvement rate. Surgeons should be aware of the postoperative visual deterioration that can occur in patients with preoperative optic nerve atrophy or pale optic disc. However, surgical intervention remains advantageous treatment among the NFPA patients.

CONFLICT OF INTEREST

The authors have no conflict of interest in this study. They received no financial support.

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None

DATA AVAILABILITY STATEMENT

The data that support the clinical results of this study are not openly available due to the sensitivity of the data. They are, however, available from the corresponding author upon request.

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