

Factors Affecting Visual Outcomes after Transsphenoidal Pituitary Adenectomy

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Abstract

Background: Pituitary tumours are considered to be about 10-15% of all brain tumours, of which 9% are the adenomas, which are classified by size and ability to secrete hormones or not. Most commonly non-functional pituitary adenomas and less commonly functional pituitary adenomas present with visual disturbances due to optic chiasm compression over time. The most commonly expressed visual field pattern is the bitemporal hemianopia.

Optic nerve damage resulting from compression by the adenoma caused by direct interruption of axonal conduction, impairment of axonal flow, demyelination and ischaemia. These are reversible at first but over time, they may be permanent.

This thesis aims for studying the different factors affecting the visual outcomes after endonasal transsphenoidal pituitary adenectomy and thereby deducing an array of prognostic factors to make a basic forecast of the postoperative visual outcomes.

Aim of Study: To determine the factors that could affect the prognosis of transsphenoidal pituitary adenectomy and its effect on the outcome of vision.

Patients and Methods: This is a prospective observational study of 15 cases of pituitary adenomas (secretory and non-secretory) treated via an endonasal transsphenoidal pituitary adenectomy at Kasr Al-Ainy University Hospitals and Nasser Institute Hospital. Preoperatively, all cases studied patients underwent evaluation by best-corrected visual acuity (BCVA), visual field by confrontation test, dilated fundus examination, slit-lamp bio microscopy and automated perimetry. Visual Impairment scoring (VIS), developed by the German Ophthalmological Society, was thereby assessed for all patients. All patients underwent endoscopic transsphenoidal pituitary adenectomy. Postoperative perimetry and postoperative visual acuity were done one month postoperatively to discern the outcome of this study. Visual impairment scoring was done again on all patients.

Results: This study comprised 15 cases, 8 males and 7 females, ages ranged from 22 to 61 years (mean age 41 years).

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Of the 15 cases, 13 cases were non-functioning tumours, 1 acromegalic patient and 1 Cushing's disease who were all operated upon by endoscopic endonasal transsphenoidal approach. Poorer postoperative visual outcomes were seen in patients with duration of symptoms >8ms, tumour vertical size >3cm, tumour volume >6.8cm³, sagittal optic chiasm displacement >22.5mm and coronal optic chiasm displacement >22mm.

Conclusion: In conclusion, different factors as duration of symptoms, tumour size, tumour volume and optic chiasm displacement inversely affect the visual outcome postoperatively as they increase in magnitude. The most significant of all was the optic chiasm displacement with a direct involvement in the affection of visual health, which makes it the most powerful prognostic factor with a higher degree of significance over the tumour dimensions (tumour vertical size and tumour volume).

Key Words: Pituitary adenoma – Visual field – Visual impairment – Visual recovery – Transsphenoidal pituitary adenectomy.

Introduction

PITUITARY tumours accounts for about 10-15% of all brain tumours, of which 9% are the adenomas, which are classified by its size and ability to hypersecrete the hormones or not [1].

Non-functioning pituitary adenomas (NFPAs) are benign tumours arising from the adenohypophyseal cells characterized by the absence of clinical evidence of hormonal hypersecretion. They usually present with the effects of local pressure such as visual disturbances. Patients with NFPA mainly present with decreased visual acuity, visual field defects and hypopituitarism, caused by mass effects of the tumour [2,3,4]. The typical visual field defect, bitemporal hemianopia, is due to the anatomical compression of the optic chiasm, which contains the crossing nasal fibers of each optic nerve [5-7].

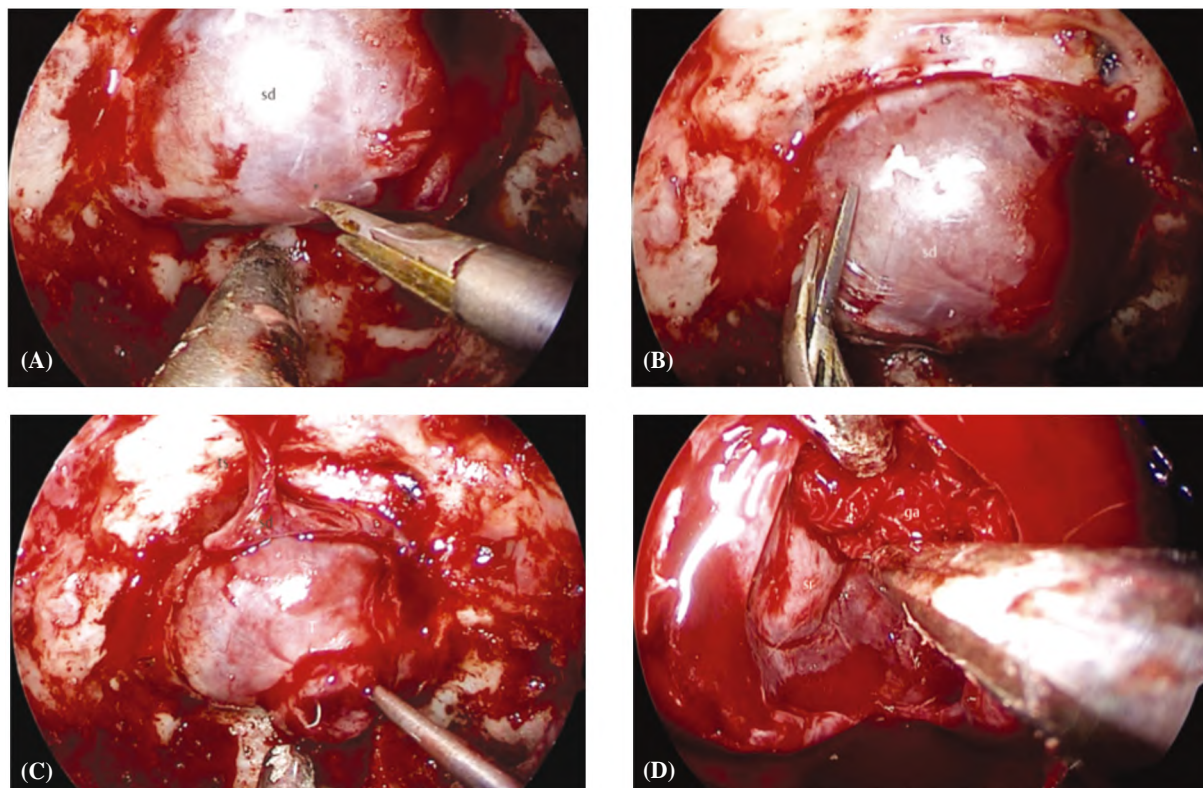


Fig. (1): (A): Incision over endosteal layer of dura using Cappabianca knife. sd: Endosteal layer of dura; *: Incision line. (B): Extension of dural incision using Kassam rotatable scissors. sd: Endosteal layer of dura; ts: Bone over tuberculum sellae; *: Line of extension of incision over endosteal layer of dura. (C): Exposure of tumor and the two-suction technique for excision of tumor. sd: Endosteal layer of dura; ts: Bone over tuberculum sellae; T: Tumor. (D): Q-tip technique for exposure of any residual tumor. ga: Gauze; sr: Sellar region.

Growth hormone secreting pituitary adenomas arise mainly from acidophilic cells (chromophobic and amphophilic cells may also be present). Prolactin secreting pituitary adenomas arise mainly from chromophobic or amphophilic cells. ACTH adenomas are usually basophilic or chromophobic. TSH-Producing Adenomas, Gonadotroph Adenomas and ACTH Cell Adenomas are rare and arise from chromophobic cells in the pituitary gland. Unlike non-functioning pituitary adenomas that cause pressure symptoms, secretory adenomas produce symptoms in accordance to the secreted tumour prior to the pressure symptoms [8].

Nevertheless, the visual field defect depends on the relation between the chiasm and the tumour. If the tumour is anterior to the optic chiasm or if the chiasm is post-fixed, conditions such as central scotoma, arcuate scotoma, and monocular visual constriction can be noted. If the tumour compresses the optic tracts or if the chiasm is pre-fixed, a homonymous hemianopia could be detected [9,10].

Transsphenoidal surgery is the treatment of choice, resulting in improvement of visual field defects in 75-100% of all patients [2,3,4]. Transsphenoidal surgery (TSS) is the procedure of choice

for their initial management [4,11]. Endoscopic transnasal transsphenoidal (ETNTS) approach was first described in 1992 and is standard approach for the resection of benign pituitary adenomas. The main neurological principle on which surgical decisions are based on, is the extent of deterioration of visual field [12].

Visual field testing is essential if there is suprasellar extension and the tumour reaches optic chiasm. Documentation of the visual fields will demonstrate if the tumour is causing visual impairment and provides a record which can be used to show the effects of surgery on the loss. Visual field defects, optic disc pallor, vision, loss of colour vision, oculomotor disturbances are seen in these patients [1].

Several studies reported improvement in the visual function after trans-sphenoidal surgery for pituitary adenomas, ranging from 56% to 90% [13], but there is much to consider about the curve of improvement and the different variables (gender, age, associated chronic diseases, tumor size and chronicity of the complaint) that may augment the results postoperatively.

Patients and Methods

The study was conducted on ongoing prospectively collected data of 15 cases in the Neurosurgery Department of Cairo University Hospitals and Nasser Institute Hospital admitted in the period between October 2020 and August 2021, suffering from pituitary adenoma. The study was carried out to study the factors affecting the visual outcomes after transsphenoidal pituitary adenectomy.

Study group selection:

The following criteria was placed and carried away to determine eligibility for this scientific research:

Population of study:

- Males and females.
- 18-70 years old.
- Chronic debilitating diseases that don't contradict case operability (e.g. Hypertension and diabetes mellitus).
- Doesn't include pregnant and breastfeeding women and children.

Inclusion criteria:

- Males and Females.
- 18-70 years old.
- Pituitary Adenoma (Secretory and Non-Secretory) patients complaining of visual disturbance.

Exclusion criteria:

- Patients with apopleptic pituitary adenomas.
- Patient with possible visual disturbances related to lesions or diseases other than pituitary adenomas.
- Patients with recurrent pituitary tumor.
- Pregnant and breastfeeding women.
- Children and teenagers under the age of 18 years old.

Statistical analysis:

Recorded data were analysed using the statistical package for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean \pm standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- The Comparison between groups with qualitative data was done by using Chi-square test and Fisher's exact test instead of Chi-square test only when the expected count in any cell less than 5.

- Comparison between differences by time for non-parametric data using Wilcoxon Signed-Rank Sum test.
- Kruskal Wallis test: For multiple-group comparisons in non-parametric data & Mann Whitney U test: For two-group comparisons in non-parametric data.
- Spearman's rank correlation coefficient (r_s) was used to assess the degree of association between two sets of variables if one or both of them was skewed.
 - Value of " r " ranges from -1 to 0 = No linear correlation.
 - 1 = Perfect positive correlation.
 - -1 = Perfect negative correlation.
- Scatter plot: A graph in which the values of two variables are plotted along two axes, the pattern of the resulting points revealing correlation present.
- Receiver operating characteristic (ROC) curve analysis was used to find out the overall predictability of parameter in and to find out the best cut-off value with detection of sensitivity and specificity at this cut-off value.
 - o Sensitivity = $(\text{true +ve}) / [(\text{true +ve}) + (\text{false -ve})]$.
 - o Specificity = $(\text{true -ve}) / [(\text{true -ve}) + (\text{false +ve})]$.
 - o PPV = $(\text{true +ve}) / [(\text{true +ve}) + (\text{false +ve})]$.
 - o NPV = $(\text{true -ve}) / [(\text{true -ve}) + (\text{false -ve})]$.
 - o Accuracy = $(\text{TP} + \text{TN}) / [\text{TP} + \text{FP} + \text{TN} + \text{FN}]$.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p -value was considered significant as the following:
 - Probability (p -value)
 - p -value ≤ 0.05 was considered significant.
 - p -value ≤ 0.001 was considered as highly significant.
 - p -value > 0.05 was considered insignificant.

Results

The study was conducted on ongoing prospectively collected data of 15 cases in the Neurosurgery Department of Cairo University Hospitals and Nasser Institute Hospital admitted in the period between October 2020 and August 2021, suffering from pituitary adenoma. The study was carried out to study the factors affecting the visual outcomes after transsphenoidal pituitary adenectomy.

Age:

The age of the patients ranged from (22 to 61) years with a mean of 41.87 ± 13.07 SD.

Gender:

In our study, the gender distribution among 15 cases was 53.3% male (8 cases) to 46.7% female (7 cases).

Presenting symptoms:

There was a variety of presenting symptoms other than visual disturbances among the 15 cases of this study; 86.7% presented with headache (13 cases), 13.3% with none other than visual disturbances (2 cases), 13.3% with squint (2 cases), 6.7% with acromegalic features (1 case), 6.7% with cushionoid features (1 case) and no cases presented with milk production, menstrual irregularities and impotence.

Duration of symptoms:

The duration of symptoms in the group of patients studied ranged from (5 to 84) months with a mean of 29.60 ± 23.05 SD.

Duration of visual disturbances:

The duration of visual disturbances of each eye studied (30 eyes in total) in the group of patients observed ranged from (1 to 84) months with a mean of 17.50 ± 19.60 SD.

Tumor parameters:

The tumors studied (15 cases) had a vertical size ranging from (1.2 to 4.6) cm with a mean of 3.05 ± 1.08 SD. While the tumor volume ranged from (2.2116 to 21.6769) cm^3 with a mean of 10.60 ± 6.44 SD.

Optical chiasm displacement:

The highest optical chiasm displacement in the group of patients measured in the coronal MRI ranged from (0.3 to 3.5) centimetres with a mean of 2.02 ± 1.07 SD and in the sagittal MRI ranged from (0.5 to 3.45) centimetres with a mean of 2.02 ± 0.89 SD.

Visual field defect pattern:

There was a variety of visual field defect patterns among the 15 cases of this study; 40% presented with bilateral superotemporal quadrantanopia (6 cases), 33.3% with bitemporal hemianopia (2 cases), 13.3% with one temporal hemianopia and one superotemporal quadrantanopia (2 cases), 13.3% with one temporal hemianopia and one severe constriction (2 case) and no cases presented with unilateral superotemporal quadrantanopia, unilateral

temporal hemianopia, one temporal hemianopia and one superotemporal quadrantanopia, and enlarged blind spot.

Secretory:

In our study, 86.7% were non-secretory pituitary adenomas (13 cases) and 13.3% were secretory (2 cases).

Hormonal assay:

Pituitary hormone profile showed a variety of effects in this study; 46.7% showed normal hormonal profile (7 cases), 40% showed stalk effect (2 cases), 6.7% showed high ACTH and cortisol levels (1 case) and 6.7% showed high GH and IGF (1 case). No cases presented with hook effect and high prolactin levels.

Tumor size category:

Pituitary adenomas were subdivided into three magnitude categories in this study; 66.7% were large (2-4cm) pituitary macroadenomas (10 cases), 20% were giant (>4cm) pituitary macroadenomas (3 cases) and 13.3% were small (1-2cm) pituitary macroadenomas (2 cases).

Optic atrophy:

Amongst the 30 eyes studied, 46.7% had no optic disc atrophy (14 eyes), 30% had mild optic disc atrophy (9 eyes) and 23.3% had severe optic disc atrophy (7 eyes).

Preoperative and postoperative visual parameters:

After studying 30 eyes of 15 patients, preoperative visual perimetry mean deviation (MD) ranged from (0.78 to 33.54) with a mean of 14.41 ± 11.19 SD and postoperative visual perimetry mean deviation (MD) ranged from (0 to 32.04) with a mean of 10.94 ± 10.69 SD. The percentage postoperative perimetry morbidity ranged from (0 to 96%) with a mean of 10.94 ± 10.69 SD.

Preoperative visual acuity ranged from (0.02 to 1) with a mean of 0.55 ± 0.38 SD and postoperative visual acuity ranged from (0.02 to 1) with a mean of 0.62 ± 0.38 SD.

Preoperative visual field scoring ranged from (0 to 45) with a mean of 15.00 ± 10.72 SD and postoperative visual field scoring ranged from (0 to 26) with a mean of 9.27 ± 9.09 SD.

Preoperative visual impairment scoring ranged from (10 to 100) with a mean of 42.80 ± 33.45 SD and postoperative visual acuity ranged from (0 to 100) with a mean of 31.47 ± 32.03 SD.

Overall, there was an improvement in all visual parameters postoperatively.

Comparing preoperative and postoperative visual parameters:

Using the Wilcoxon Signed-Rank Sum test, the probability value of the visual parameters was derived with respect to the preoperative and postoperative data collected.

Comparison between the preoperative and postoperative visual perimetry mean deviation is statistically highly significant $p < 0.001$.

Comparison between the preoperative and postoperative visual acuity is statistically highly significant $p < 0.001$.

Comparison between the preoperative and postoperative visual field scoring is statistically significant $p < 0.019$.

Comparison between the preoperative and postoperative visual acuity scoring is statistically significant $p < 0.004$.

Comparison between the preoperative and postoperative visual impairment scoring is statistically highly significant $p < 0.001$.

This means there is an improvement in the overall visual parameters postoperatively.

Association between visual field defect patterns and data variables:

Using the Kruskal Wallis test, the probability value of a significant relationship between the visual field defect patterns and the patients' data collected was derived.

Association between the visual field defect pattern and:

- The patient's age is statistically significant $p = 0.002$, which means younger age has higher rates of early diagnosis and smaller visual defects.
- The preoperative visual perimetry MD is statistically highly significant $p < 0.001$, which means an increase in field defect increases the preoperative visual perimetry MD.
- The postoperative visual perimetry MD is statistically highly significant $p < 0.001$, which means an increased field defect increases the postoperative visual perimetry MD.
- The percentage postoperative visual perimetry morbidity is statistically highly significant $p < 0.001$, which means an increased field defect increases the postoperative visual perimetry

morbidity owing to a better improvement with smaller visual defects.

- The preoperative visual acuity is statistically highly significant $p < 0.001$, which means increased field defect causes a direct decrease in preoperative visual acuity.
- The postoperative visual acuity is statistically highly significant $p < 0.001$, which means increased field defect causes a direct decrease in postoperative visual acuity.
- The preoperative visual impairment scoring is statistically significant $p = 0.007$, which means increased field defect causes a direct increase in preoperative VIS.
- The postoperative visual impairment scoring is statistically significant $p = 0.009$, which means increased field defect causes a direct decrease in postoperative VIS.

Association between hormonal assay with baseline demographics and characteristics:

Using the Kruskal Wallis test, the probability value of a significant relationship between the hormonal assay and the visual characteristics was derived.

Association between the hormonal assay and:

- The patient's age is statistically highly significant $p < 0.001$, which means that agitated hormonal profiles cause early diagnosis in younger subjects than others.
- The preoperative visual perimetry MD is statistically significant $p = 0.003$, which means the presence of secretory tumors causes early diagnosis leading to a lower preoperative visual perimetry MD.
- The postoperative visual perimetry MD is statistically significant $p = 0.006$, which means the presence of secretory tumors causes early diagnosis leading to a lower postoperative visual perimetry MD.
- The percentage postoperative visual perimetry morbidity is statistically significant $p = 0.007$. Early diagnosis due to the abnormal hormonal profile caused by the above mentioned factors causes lower rates of postoperative visual morbidity. This is an indirect relation between the percentage postoperative visual perimetry morbidity and the hormonal assay.
- The preoperative visual acuity is statistically significant $p = 0.004$, which means that patients with secretory pituitary adenomas have better preoperative visual acuity.

- The postoperative visual acuity is statistically significant $p=0.01$, which means that patients with secretory pituitary adenomas have better postoperative visual acuity.
- The preoperative visual impairment scoring is statistically significant $p=0.029$, which means that patients with secretory pituitary adenomas have better preoperative VIS.
- The postoperative visual impairment scoring is statistically significant $p=0.045$, which means that patients with secretory pituitary adenomas have better preoperative VIS.

Correlation between tumor vertical size and visual characteristics:

Using Spearman's rank correlation coefficient (rs), the probability value of a significant correlation between tumor vertical size (cm) and visual characteristics was derived.

Table (1): Demographic data distribution among study group.

Demographic data	Value
<i>Gender (N=15):</i>	
Female	7 (46.7%)
Male	8 (53.3%)
<i>Age (Years):</i>	
Range	22-61
Mean \pm SD	41.87 \pm 13.07

Table (2): Visual field defect pattern.

Visual field defect pattern	No.	Percentage
Unilateral SuperoTemporal Quadrianopia	0	0.0
Unilateral Temporal Hemianopia	0	0.0
Bilateral SuperoTemporal Quadrianopia	6	40.0
BiTemporal Hemianopia	5	33.3
One Temporal Hemianopia + One SuperoTemporal Quadrianopia	0	0.0
One Temporal Hemianopia + One Severe Constriction	2	13.3
Bilateral Severe Constriction	2	13.3
Enlarged Blind Spot	0	0.0

Table (3): Hormonal assay.

Hormonal assay	N°	Percentage
Normal	7	46.7
Stalk Effect	6	40.0
Hook Effect	0	0.0
High Protactin	0	0.0
High ACTH & Cortisol	1	6.7
High GH & IGF	1	6.7

Table (4): Pre and post operative visual parameters.

Pre & postoperative visual parameters	Range	Mean \pm SD
<i>Visual Perimetry MD (n=30):</i>		
Preoperative	0.78-33.54	14.41 \pm 11.19
Postoperative	0-32.04	10.94 \pm 10.69
Percentage Postoperative Perimetry Morbidity (%)	0-96	32.73 \pm 31.97
<i>Visual Acuity (n=30):</i>		
Preoperative	0.02-1	0.55 \pm 0.38
Postoperative	0.02-1	0.62 \pm 0.38
<i>Visual Field Scoring:</i>		
Preoperative	0-45	15.00 \pm 10.72
Postoperative	0-26	9.27 \pm 9.09
<i>Visual Acuity Scoring:</i>		
Preoperative	0-100	27.80 \pm 29.63
Postoperative	0-80	22.20 \pm 24.22
<i>Visual Impairment Scoring:</i>		
Preoperative	10-100	42.80 \pm 33.45
Postoperative	0-100	31.47 \pm 32.03

Correlation between the tumor vertical size (cm) and:

- The preoperative visual perimetry MD is statistically highly significant $p<0.001$. An increase in tumor vertical size increases preoperative visual perimetry MD.
- The postoperative visual perimetry MD is statistically significant $p=0.005$. An increase in tumor vertical size increases postoperative visual perimetry MD.
- The percentage postoperative visual perimetry morbidity is statistically significant $p=0.005$. An increase in tumor vertical size increases the percentage of postoperative visual perimetry morbidity.
- The preoperative visual acuity is statistically highly significant $p<0.001$. An increase in tumor vertical size decreases preoperative visual acuity.
- The postoperative visual acuity is statistically highly significant $p<0.001$. An increase in tumor vertical size decreases postoperative visual acuity.
- The preoperative visual impairment scoring is statistically significant $p=0.015$. An increase in tumor vertical size increases preoperative VIS.
- The postoperative visual impairment scoring is statistically significant $p=0.008$. An increase in tumor vertical size increases postoperative VIS.

Correlation between sagittal optical chiasm displacement and visual characteristics:

Using Spearman's rank correlation coefficient (rs), the probability value of a significant relationship between the sagittal optical chiasm displace-

ment and the visual characteristics was derived. Association between the sagittal optical chiasm displacement and:

- The preoperative visual perimetry MD is statistically highly significant $p < 0.001$. An increase in sagittal chiasm displacement increases preoperative visual perimetry MD.
- The postoperative visual perimetry MD is statistically highly significant $p < 0.001$. An increase in sagittal chiasm displacement increases postoperative visual perimetry MD.
- The percentage postoperative visual perimetry morbidity is statistically highly significant $p < 0.001$. An increase in sagittal chiasm displacement increases percentage postoperative visual perimetry morbidity.
- The preoperative visual acuity is statistically highly significant $p < 0.001$. An increase in sagittal chiasm displacement decreases preoperative visual acuity.
- The postoperative visual acuity is statistically highly significant $p < 0.001$. An increase in sagittal chiasm displacement decreases postoperative visual acuity.
- The preoperative visual impairment scoring is statistically significant $p = 0.022$. An increase in sagittal chiasm displacement increases preoperative VIS.
- The postoperative visual impairment scoring is statistically significant $p = 0.016$. An increase in sagittal chiasm displacement increases postoperative VIS.

Relation between impairment grades according to factors:

Using Fisher's exact test, the probability value of a significant relationship between the impairment grades (considering Grade 1 is of good prognosis and Grades 2-4 are of worse prognosis as a cut-off point) and different factors affecting the outcome was derived.

Table (5): Pre and post operative visual parameters.

Parameter	Preoperative	Postoperative	Wilcoxon signed-rank sum test			
			Mean Diff.	Change%	z-test	p-value
Visual Perimetry MD	14.41 ± 11.19	10.94 ± 9.69	-3.47	-24.10%	8.889	<0.001**
Visual Acuity	0.55 ± 0.38	0.62 ± 0.38	0.07	12.70%	-5.336	<0.001**
Visual Field Scoring	15.00 ± 10.72	9.27 ± 8.09	-5.73	-38.20%	2.653	0.019*
Visual Acuity Scoring	27.80 ± 24.63	22.20 ± 19.22	-5.6	-20.10%	3.437	0.004*
Visual Impairment Scoring	42.80 ± 33.45	31.47 ± 27.03	-11.33	-26.50%	5.759	<0.001**

Table (6): Correlation between variables and outcome.

Variables	Bilateral superotemporal quadrianopia		Bitemporal hemianopia		One temporal hemianopia + One severe constriction		Bilateral severe constriction		Kruskal wallis test	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	H-test	p-value
Age, Years	31.17B	8.03	46.40A	8.15	47.00A	16.17	57.50A	2.89	15.145	0.002*
Preoperative Visual Perimetry MD	4.03C	2.73	17.60B	7.40	21.35B	13.95	28.92A	5.44	19.224	<0.001**
Postoperative Visual Perimetry MD	1.46C	1.15	13.57B	7.89	16.90B	15.26	24.50A	5.99	18.482	<0.001**
% Postoperative Perimetry Morbidity	4.42D	3.45	40.60C	23.47	50.50B	46.05	73.25A	17.80	18.477	<0.001**
Preoperative Visual Acuity	0.92A	0.13	0.42B	0.29	0.34B	0.38	0.12D	0.14	18.799	<0.001**
Postoperative Visual Acuity	0.98A	0.06	0.50B	0.29	0.43B	0.48	0.17C	0.15	17.736	<0.001**
Preoperative Visual Impairment Scoring	12.00C	3.10	55.40B	24.58	46.50B	12.02	100.00A	0.00	11.990	0.007*
Postoperative Visual Impairment Scoring	1.67C	2.66	43.20B	23.18	40.00B	11.31	83.00A	24.04	11.546	0.009*

Association between the impairment grades and:

The visual field defect pattern is statistically significant $p < 0.008$. This means that as the visual field defect becomes more severe, the visual impairment grade increases.

- The hormonal assay is statistically significant $p < 0.026$. Secretory tumors had the upper hand in worse visual grading. Hence, as this causes a direct impact on the visual impairment grade increasing the latter.
- The tumor size category is statistically significant $p < 0.046$. A higher tumor size category causes an increase in the visual impairment grade.
- The level of optic atrophy is statistically highly significant $p < 0.001$. The level of optic atrophy increases causing an increase in the visual impairment grade and thereby increasing the post-operative visual morbidity.

Table (7): Results summary.

Factors	Impairment Grades				Fisher's Exact	
	Grade 1 (n=7)		Grade 2-4 (n=8)		FE	p-value
	N°	%	N°	%		
<i>Gender:</i>						
Female	3	42.9	4	50.0	FE	0.782
Male	4	57.1	4	50.0		
<i>Visual Field Defect Pattern:</i>						
Bilateral SuperoTemporal Quadrianopia	6	85.7	0	0.0	11.786	0.008 *
BiTemporal Hemianopia	1	14.3	4	50.0		
One Temporal Hemianopia + One Severe Constriction	0	0.0	2	25.0		
Bilateral Severe Constriction	0	0.0	2	25.0		
<i>Hormonal Assay:</i>						
Normal	5	71.4	2	25.0	9.260	0.026*
Stalk Effect	0	0.0	6	75.0		
High ACTH & Cortisol	1	14.3	0	0.0		
High GH & IGF	1	14.3	0	0.0		
<i>Tumor Size Category:</i>						
Small Macroadenoma - 1-2cm	2	28.6	0	0.0	7.679	0.046*
Large Macroadenoma - 2-4cm	4	57.1	6	75.0		
Giant Macroadenoma - >4cm	1	14.3	2	25.0		
<i>Optic Atrophy:</i>						
None	Grade 1 (n=14) 13 92.9		Grade 2-4 (n=16) 1 6.3		22.825	<0.001 **
Mild	1 7.1		6 37.5			
Severe	0 0.0		9 56.3			

Discussion

Pituitary tumors accounts for about 10-15% of all brain tumors, of which 9% are the adenomas, which are classified by its size and ability to secrete hormones or not [1].

Nonfunctioning pituitary adenomas (NFPAs) are accounted to be benign tumors arising from the adenohypophy seal cells, known for their absence of clinical evidence of hormonal hypersecretion. They usually complain with symptoms of local pressure, as visual defects. Patients with NFPA mainly present with decreased visual acuity, visual field defects and hypopituitarism, caused by mass effects of the tumor [2,3,4]. The classic

visual field defect, bitemporal hemianopia, is caused by anatomical compression of optic chiasm, which encounters the crossing nasal fibers of each optic nerve [5].

Unlike non-functioning pituitary adenomas that cause pressure symptoms, secretory adenomas produce symptoms in accordance to the secreted tumor prior to the pressure symptoms [14].

Nevertheless, the visual field defects really depends on the relation between the chiasm and the tumor. In case of the tumor is being anterior to the optic chiasm or if the chiasm is post-fixed, defects such as central scotoma, arcuate scotoma, and monocular visual constriction could be detect-

ed. If the tumor compresses the optic tracts or the chiasm is pre-fixed chiasm, a homonymous hemianopia can be noticed [9,10,15].

When the optic chiasm is directly compressed, or its vascular supply is affected by a pituitary adenoma, retinal ganglion cell (RGC) axonal injury and visual defect will happen. The three main postulated pathological mechanisms are disturbance of conduction through the axon, impairment of flow and demyelination with impaired neurogenic signal conduction [6]. Visual field defects are the most common and usually the first symptom of visual disturbance due to compression of the crossing fibres in the optic chiasm by pituitary tumors. As the disease continues, the macular fibres can be affected and can cause other visual dysfunctions, such as VA damage, colour vision loss and optic disc pallor. However, VA deterioration, color vision loss, and optic disc pallor are associated with the degree of VF defect [13,16]. Therefore, VF defects are underlined in studies of the correlation between the retina and visual function.

Surgical is an important solution for pituitary adenoma and can make the visual function of patients better with visual complaints as per Schmalisch et al. and Mortini et al. [17,18].

Transsphenoidal surgery is the treatment of choice, resulting in improvement of visual field defects in 75-100% of all patients [2,3,4,11,13], but there is much to consider about the curve of improvement and the different variables (gender, age, associated chronic diseases, tumor size, tumor volume and chronicity of the complaint) that may augment the results postoperatively.

Secretory versus Non-secretory Pituitary Adenomas:

We found that macroadenomas and huge adenomas leading to visual deterioration are mostly non-functioning adenomas (97.8%). This result is consistent with previous studies; Gnanalingham et al. [19], Anderson et al. [20] and Miller et al. [21], and can be clarified by the absence of endocrine symptoms, which frequently result in a delay of the diagnosis since there are no vision complaints [20]. This description is consistent with what Monteiro et al. [22] have mentioned previously that non-functioning and prolactin-secreting adenomas are the most likely pituitary tumours associated with visual damage.

The results of this study show that different hormonal assays show a close relation to the visual outcome with $p=0.026$, which means that non-

secretory pituitary adenomas show higher grades of visual impairment when compared to secretory pituitary adenomas. 13.3% of the cases (2 out of 15 patients) had secretory macroadenomas. All of which had Grade 1 visual impairment score, a good prognostic factor. While 87% of the cases (13 out of 15 patients) had non-secretory macroadenomas; 5 of these cases (33.3% of all cases) had Grade 1 visual impairment score; a good prognostic factor, and 8 of these cases (53.3% of all cases) had Grade 2-4 visual impairment score; a poor prognostic factor. Early detection of secretory pituitary adenomas would prepare for early operative intervention with higher rates of visual improvement and lower degrees of postoperative visual field morbidity.

Visual impairment, optic atrophy and percentage of postoperative perimetry morbidity:

Gnanalingham et al.'s [19] findings revealed that better preoperative visual acuity and a smaller degree of diminishing in preoperative VF would have a better outcome on the visual consequence.

Therefore, the higher the incidence of visual impairment, the higher the probability of optic atrophy occurrence, which is proved by this study with a significant probability value ($p=0.013$). Henceforth, the percentage of postoperative perimetry morbidity would increase with higher grades of optic atrophy and degree of visual impairment. These correlations, too, had a highly significant probability value ($p<0.001$). This means that there is a weaker chance of visual acuity and visual field full recovery.

Visual field defects pattern:

Recent studies, Rivoal et al. [10], Monteiro et al. [22] and Levy et al. [12], have exposed a relationship between the size of pituitary adenoma and VF defects. These efforts clearly illustrated that patients with larger tumours be disposed to have VF abnormality, and that the severity of VF defects is faithfully related to tumour size [10,12,22].

This research is in accord with previous studies done on the effect of visual field defects on the postoperative visual outcome. There is a good significant probability value for that ($p=0.008$) which means as the visual field defect increases in size, the outcome becomes of poorer prognosis.

In our report, five patients presented with bitemporal hemianopia before transsphenoidal adenectomy (TSA). The tumour size ranged from 3.1cm (large macroadenoma) to 4.5cm (giant macroadenoma). This variation might be due to the position of the macroadenoma, the loss of optic nerve

elasticity and decreased optic nerve thickness with respect to age of the patients.

Tumour vertical size:

Pituitary adenomas are usually divided into microadenomas, macroadenomas, and giant adenomas according to their size [23,24,25]. The larger the pituitary adenoma is, the higher is the risk of optic chiasm or optic nerve affection [4,20,26]. In general, the size of macroadenomas range from 1 to 4cm. Smaller macroadenomas will not result in any visual impairment, while the larger tumors will usually cause severe visual incapacity.

Undeniably, vision can rapidly be better within minutes or days after tumour excision [6]. Among all surgical resection techniques, TSA is likely the most actual for providing rapid relief of visual symptoms in patients with a pituitary adenoma [25,27]. So, early surgical resection of the tumour should be considered for patients with a large or giant macroadenoma causing visual loss to save their vision.

Eda et al. [28] contended that the correlation between tumour size and the degree of visual field defect exists only when the optic chiasm is in a normal anatomical position. Thus, the prognosis for visual field recovery is not only related to tumour volume, but also to the complex interaction of such factors as the anatomical position of the optic chiasm, the anatomical position of the tumour, and the degree of upper expansion of the saddle.

The pattern and severity of VF defects depend on the relative location between the optic chiasm and the tumour, as well as the growth direction and size of the tumour according to studies done by Ho et al. [29] and Ogra et al. [30]. Larger tumours with superiorising growth increase the pressure on the chiasm, resulting in a more severe degree of visual loss [22].

Ho et al. [29] specified a cut-off point in the vertical size of the pituitary macroadenoma (2cm) which determined the postoperative visual outcome; adenomas smaller than 2cm would show no visual symptoms or minimal visual dysfunction would have better postoperative visual outcome than adenomas larger than 2cm.

This study clearly showed that pituitary adenomas less than 3cm usually have no or only a minimal effect on the visual apparatus with a highly significant probability value ($p < 0.001$). Thus, to accentuate which tumours are a threat the macroadenomas between 1 and 4cm were further subdivided into 2 groups : (1) "small macroadenomas" - tu-

mours with less than 2cm in size, and (2) "large macroadenomas" - tumours ranging from 2 to 4cm.

The level of discrepancy between this study and previous reports might be due to the narrow scope of this report (15 cases) and widening the range of the study would yield a more steadfast result.

Tumour volume with respect to direction of tumour extension:

Lee et al. [31] proved that there is a close correlation between visual field defects and 3-dimensional tumour volume which has a significantly positive correlation with visual field defects by Humphrey perimetry.

Larger bulk tumours will usually result in a higher risk of compression at the chiasm; however, this association is not found when tumour extension mainly occurs at the infra-sellar or para-sellar region instead of the suprasellar region. In fact, we found that if the adenoma grows in the upright-course, it would usually result in more severe visual damage. If the adenoma grows in the planecourse, it will usually cause less vision damage, but there is a greater chance of adenoma reappearance [32,33]. This is because horizontal growth of the adenoma may invade the cavernous sinus, which makes it difficult for the surgeon to remove the tumour totally. Therefore, only the vertical size of adenomas was inspected in this study.

Yu et al. [16] claimed that small preoperative tumour size was an independent factor in visual field recovery after transsphenoidal pituitary adenectomy, and in the present study, the correlation with tumour bulk was statistically highly significant ($p=0.003$) and a cut-off tumour volume of $<6.8\text{cm}^3$ for a good prognostic visual outcome.

Optic chiasm displacement:

Some of the previous studies have iscoursed the relation between the optic chiasm situation and visual loss. Ikeda and Yoshimoto [34] found that visual diminishing occurred when the displacement of the optic chiasm was more than 8mm above the reference line on the sagittal image and more than 13mm above on the coronal image on brain MRI. Monteiro et al. [22] have also shown that tumour exceeding 10mm above the sagittal standard line and 12mm above the coronal standard line had a significant effect on visual loss. The discoveries of these studies are similar to what was found in this study, which showed that significant visual impairment (VIS grade ≥ 2) occurred when the optic chiasm was moved by the tumor more than

11.2mm above the reference line on the sagittal view and more than 15.3mm on the coronal image.

Schmalisch et al. [17] stated that the degree of upper expansion of the saddle of the pituitary tumour (>8mm sagittal plane, >12mm coronal plane) had a strong link with the visual field defect pattern and degree of diminished visual acuity.

In this study, reports of highly significant relationship between optic chiasm displacement and visual impairment postoperatively where increase in optic chiasm displacement from its original anatomical point (>22.5mm sagittal plane, >22mm coronal plane) would lead to a poorer VIS grade (>2).

Comparing the degree of significance in the results of the optic chiasm displacement (sagittal and coronal) and the tumour measurements (vertical size and volume) proved that the optic chiasm displacement results are more significant. This means that it is a more reliable indicator as a prognostic factor to the worsening of the visual status of the patient preoperatively. The tumour could expand infra-sellar easier depending on the degree of pneumatization of the sphenoid sinus causing lesser degrees of optic chiasm displacement with an increase in the tumour vertical size. Similarly, the tumour volume could increase with parasellar and infrasellar extension without affecting the optic chiasm. While on the other hand, the optic nerve well-being is affected directly by the optic chiasm displacement from the normal optic chiasm site.

Conclusion:

Vision is one of the most important senses and its distortion suppresses the quality of life. Early intervention aids early and better recovery from visual acuity and visual field disturbances. This preserves optic nerve thickness, integrity, vasculature, and macular health, thereby, preserving the quality of life.

Early diagnosis might be impeded by different social and socioeconomic factors. People do not have information to protect themselves from ignoring an alarming symptom as such. This was observed in the age difference in cases with better prognosis who were younger in comparison to elder patients who had poorer prognosis of visual recovery.

As discussed previously a strong significance has been proven by different factors as duration of symptoms, tumour size, tumour volume and optic chiasm displacement on the degree of visual

recovery postoperatively. The most significant of all was the optic chiasm displacement with a direct involvement in the affection of visual health.

A more powerful prognostic factor; optic chiasm displacement, has been proved with a higher degree of significance over the tumour dimensions (tumour vertical size and tumour volume).

Thus, in conclusion, as these factors increase in magnitude, they inversely affect the visual outcome postoperatively.

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العوامل المؤثرة على النتائج البصرية بعد استئصال الغدة النخامية بالمنظار الجراحي

الخلفية: تمثل أورام الغدة النخامية حوالي ١٠-١٥٪ من جميع أورام الدماغ، منها ٩٪ أورام غدية حميدة وتقسم حسب حجمها وقدرتها على إفراز الهرمونات أولاً. معظم أورام الغدة النخامية غير الوظيفية وينسب أقل أورام الغدة النخامية الوظيفية تظهر مع اضطرابات بصرية بسبب الضغط على تصالب العصب البصري بمرور الوقت. نمط المجال البصري الأكثر شيوعاً هو العمى النصفى الصدغى.

يهدف هذا البحث: إلى دراسة العوامل المختلفة المؤثرة على النتائج البصرية بعد استئصال الغدة النخامية عبر الأنف والجيوب الأنفية الوتدية وبالتالي استنتاج مجموعة من العوامل التنبؤية لعمل توقع أساسى للنتائج البصرية بعد الجراحة.

الطريقة: هذه دراسة استطلاعية رصدية لـ ١٥ مريضاً من أورام الغدة النخامية (الإفرازية وغير الإفرازية) تم علاجهم عن طريق استئصال أورام الغدة النخامية عبر الأنف والجيوب الأنفية الوتدية فى مستشفيات جامعة القاهرة قصر العينى ومستشفى معهد ناصر. قبل الجراحة، خضع جميع المرضى للتقييم من خلال مقياس الحدة البصرية المصححة (BCVA)، ومجال الإبصار عن طريق اختبار المواجهة، وفحص قاع العين، والتنظير المجهرى الحيوى بالمصباح الشقى، والقياس الألى للمحيط البصرى. وبالتالي تم حساب نقاط الضعف البصرى (VIS)، الذى طورته الجمعية الألمانية لطب لعيون، لجميع المرضى. خضع جميع المرضى لعملية استئصال الأورام بالغدة النخامية عبر الجيوب الأنفية الوتدية بالمنظار. تم إجراء قياس محيط ما بعد الجراحة ووحدة البصر بعد العملية الجراحية بعد شهر واحد من الجراحة لتمييز نتيجة هذه الدراسة. تم إجراء تقييم ضعف البصر مرة أخرى على جميع المرضى.

النتائج: اشتملت هذه الدراسة على ١٥ حالة، ٨ ذكور و ٧ إناث، تراوحت الأعمار من ٢٢ إلى ٦١ سنة (متوسط العمل ٤١ سنة). من بين ١٥ حالة، كانت ١٣ حالة أوراماً غير وظيفية، ومريض واحد بورم مفرز لهرمون النمو، ومريض واحد بمرض كوشينغ. وتم إجراءهم جميعاً عن طريق استئصال الورم عبر الأنف والجيوب الأنفية الوتدية بالمنظار. شوهدت نتائج بصرية أضعف بعد الجراحة فى المرضى الذين كانت مدة الأعراض لديهم أكثر من ٨ شهور، طول الورم العامودى تخطى ٣سم، وحجم الورم أكثر من ٦.٨سم^٢، وتزحزح التصالب البصرى على المقاطع السهمية على الرنين أعلى من ٢٢.٥مم، وازاحة التصالب البصرى على المقاطع الإكليلي على الرنين أعلى من ٢٢مم.

الخلاصة: فى الختام، هناك عوامل مختلفة مثل مدة الأعراض وارتفاع الورم وحجم الورم ونسبة تزحزح التصالب البصرى تؤثر عكسياً على النتائج المرئية بعد الجراحة لأنها تزداد فى الحجم. أهم العوامل المؤثرة هو نسبة تزحزح التصالب البصرى مع المشاركة المباشرة فى التأثير على الصحة البصرية، مما يجعله أقوى عامل تنبؤى بدرجة أعلى للأهمية عن أبعاد الورم (الحجم الرأسى للورم وحجم الورم).