

Prognostic Utility of Optical Coherence Tomography for Long-Term Visual Recovery Following Pituitary Tumor Surgery



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- **PURPOSE:** To investigate the association between optical coherence tomography (OCT) parameters and long-term visual recovery following optic chiasm decompression surgery.
- **DESIGN:** Prospective cohort study.
- **METHODS:** Consecutive patients who underwent pituitary or parasellar tumor resection between January 2009 to December 2018 were recruited in a single-center, 2-year prospective, longitudinal cohort study. Best-corrected visual acuity, visual fields, and OCT retinal nerve fiber layer (RNFL) thickness, macular thickness and volume were assessed preoperatively, and at 6 weeks, 6 months, and 2 years postoperatively. Long-term visual field recovery and maintenance were defined as a mean deviation of > -3 at 24 months, and visual acuity recovery and maintenance were defined as a logarithm of minimal angle of resolution (logMAR) of 0 (Snellen 20/20) or better at 24 months.
- **RESULTS:** A total of 239 patients (129 men, 110 women; mean \pm SD age: 52 ± 16 years) were included. Multiple logistic regression analysis demonstrated that increased inferior RNFL thickness (per 10 μm) was associated with higher odds of long-term visual field recovery and maintenance (odds ratio [OR]: 1.26; 95% confidence interval [CI]: 1.12-1.41; $Q < 0.001$), and greater superior RNFL thickness (per 10 μm) was associated with higher odds of visual acuity recovery and maintenance (OR: 1.13; 95% CI: 1.03-1.27; $Q = 0.031$). A multivariable risk prediction model developed for long-term visual field recovery and maintenance that incorporated

age, preoperative visual function, and RNFL thickness demonstrated C-statistics of 0.83 (95% CI: 0.72-0.94).

- **CONCLUSION:** Preoperative RNFL thickness was associated with long-term visual recovery and maintenance following chiasmal decompression. The multivariable risk prediction model developed in the present study may assist with preoperative patient counseling and prognosis. (Am J Ophthalmol 2020;218:247-254. © 2020 Elsevier Inc. All rights reserved.)

PITUITARY TUMORS ACCOUNT FOR APPROXIMATELY 15% of primary intracranial lesions¹ and frequently cause visual impairment secondary to compression of the optic chiasm.² Although visual function can improve considerably following tumor resection and chiasmal decompression, the extent of recovery remains difficult to prognosticate.²⁻⁴ A number of clinical predictors for postoperative visual recovery have been extensively investigated, with varying degrees of prognostic ability being reported.²⁻⁴ Previous studies have demonstrated inconsistent results for the prognostic performance of age, symptom duration, tumor size, preoperative visual function, and optic atrophy.²⁻¹⁶

In recent years, there has been growing evidence of the prognostic ability of optical coherence tomography (OCT) measurements for visual recovery following pituitary tumor resection.^{2,17} OCT facilitates rapid, noninvasive, *in vivo* cross-sectional imaging of the retinal layers and offers a number of surrogate markers for retinal ganglion cell injury.^{2,17,18} In particular, the predictive ability of retinal nerve fibre layer (RNFL) thickness for postoperative visual function has been confirmed by numerous reports.^{3,10,17,19-26}

However, many of the earlier studies that investigated the prognostic ability of OCT parameters were limited by relatively modest sample sizes of <50 patients. The study follow-up periods were also generally <12 months, although there has been increasing recognition of the potential for delayed visual recovery that could occur beyond this time period.^{2,27} In addition, the predictive ability of OCT macular parameters has received less attention.^{22,23,28,29} Therefore, the purpose of this 2-year prospective longitudinal study was to investigate the prognostic ability of OCT parameters for long-term visual recovery and maintenance following pituitary tumor resection.

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METHODS

- PATIENTS:** This single-center, 2-year prospective, longitudinal cohort study followed the tenets of the Declaration of Helsinki and was prospectively approved by the institutional review board. Informed consent was obtained from participants after explanation of the nature and possible consequences of the study. Consecutive patients, aged 16 years or older, who underwent pituitary or parasellar tumor resection between January 2009 to December 2018, were recruited. Participants were eligible for inclusion following confirmation of magnetic resonance imaging (MRI) evidence of optic chiasm compression secondary to the pituitary or parasellar tumor and availability for 2-year postoperative follow-up. Exclusion criteria included previous anterior segment, posterior segment, or optic nerve disease other than compressive optic neuropathy (eg, glaucoma, cup disc ratio asymmetry of >0.2 , focal notching, or optic nerve hemorrhage), as well as spherical refractive error outside of the range of >5 diopter (D) or >2 D of astigmatism. In addition, patients with unreliable preoperative visual field testing, which was defined as $>25\%$ false positive, false negative, or fixation loss rate, were also excluded.

- MEASUREMENTS:** Best-corrected visual acuity, visual fields, and OCT parameters were assessed preoperatively, and then at 6 weeks, 6 months, and 2 years postoperatively. Best-corrected visual acuity was evaluated using a Snellen chart at 20 ft and converted to the logarithm of minimal angle of resolution (logMAR) scale for subsequent analysis. Automated perimetry for visual field assessment was performed using the 24-2 Swedish Interactive Threshold Algorithm on the Humphrey Field Analyzer II (Carl Zeiss Meditec, Jena, Thuringia, Germany), with a Goldmann size II stimulus on a 31.5 apostilb background; the mean deviation and pattern standard deviation measurements were recorded. Patients were able to repeat visual field testing up to 3 times preoperatively to obtain more reliable results, and the most reliable preoperative test results obtained were recorded. Quantitative OCT measurements, including RNFL thickness, and macular thickness and volume, were conducted using the Spectralis OCT machine (Heidelberg Engineering GmbH, Heidelberg, Germany) and analyzed using Heidelberg eye explorer software version 1.9.14.0. Long-term visual field recovery and maintenance was defined as a mean deviation >-3 at the 2-year postoperative follow-up visit,³ whereas long-term visual acuity recovery and maintenance was defined as a logMAR of 0 (Snellen visual acuity 20/20) or better at the 2-year postoperative follow-up visit.

- STATISTICAL ANALYSIS:** Statistical analysis was conducted using SPSS Statistics version 22.0 (IBM, Armonk,

TABLE 1. Demographic and Clinical Characteristics of Patients

Characteristics	Value
Age (y)	52 ± 16
Male sex	129 (54)
Pituitary tumor classification	
Pituitary adenoma	216 (90)
Rathke's cleft cyst	10 (4)
Craniopharyngioma	7 (3)
Astrocytoma	2 (0.8)
Epidermoid cyst	1 (0.4)
Metastatic undifferentiated carcinoma	1 (0.4)
Solitary fibrous tumor	1 (0.4)
Teratoma	1 (0.4)
Surgical approach	
Trans-sphenoidal	232 (97)
Craniotomy	7 (3)

Data are presented as mean ± SD or n (%).

NY) and MedCalc Statistical Software version 18.0 (Ostend, Belgium). Generalized estimating equation modeling was performed to account for within-subject intereye correlation, and false discovery rate adjustment of *P* values was applied and reported as *Q* values to account for multiple comparisons, when appropriate. Changes in visual function and OCT parameters during the study period were assessed using 1-way repeated measures analysis of variance, and *post hoc* pairwise multiplicity-adjusted Tukey's tests were conducted when significant trends were identified. The associations between preoperative OCT parameters and long-term visual field and acuity recovery and maintenance were assessed using multiple logistic regression that adjusted for confounding variables, including age, sex, and baseline mean deviation or visual acuity.

Patients were randomized into developmental (70%) and validation samples (30%) for the purposes of constructing and evaluating multivariable logit risk prediction models. A single randomly selected eye from each patient was incorporated, with no patients contributing to both the developmental and validation samples. Independent predictors ($P < .05$), which were identified using multiple logistic regression analysis of the developmental sample, were used to construct the multivariable logit risk prediction models. Discriminative performance in the validation sample was assessed using the concordance statistic (C-statistic) derived from the area under the receiver-operating characteristic (ROC) curve, and the Youden-optimal prognostic cutoff sensitivity, specificity, positive and negative predictive values were calculated. All tests were 2-tailed, and $P < .05$ or $Q < 0.05$ was considered significant.

TABLE 2. Visual Function and OCT Parameters of Patients During the Study Period.

Parameter	Preoperative		Postoperative		Q Value ^a
	Baseline	6 Weeks	6 Months	2 Year	
Visual fields (dB)					
Mean deviation	-5.0 ± 6.5	-3.0 ± 4.8	-2.4 ± 4.8	-2.3 ± 5.0	<0.001
Pattern standard deviation	5.2 ± 4.6	3.7 ± 3.5	3.4 ± 3.5	3.4 ± 3.5	<0.001
Best-corrected logMAR visual acuity	0.087 ± 0.267	0.081 ± 0.306	0.080 ± 0.356	0.078 ± 0.325	0.929
RNFL thickness (μm)					
Average	93 ± 21	90 ± 20	90 ± 21	88 ± 19	0.103
Superior	113 ± 27	112 ± 26	111 ± 29	109 ± 26	0.322
Inferior	121 ± 25	118 ± 24	118 ± 27	116 ± 24	0.103
Temporal	65 ± 23	62 ± 17	62 ± 20	62 ± 18	0.322
Nasal	71 ± 31	67 ± 32	67 ± 33	66 ± 27	0.322
Macular thickness (μm)					
Average	286 ± 35	287 ± 33	287 ± 34	283 ± 35	0.376
Foveal	216 ± 40	219 ± 37	216 ± 38	213 ± 41	0.376
Superior	287 ± 35	288 ± 36	284 ± 35	283 ± 37	0.322
Inferior	284 ± 35	286 ± 32	287 ± 32	282 ± 33	0.376
Temporal	277 ± 37	281 ± 34	280 ± 33	276 ± 35	0.322
Nasal	294 ± 37	294 ± 36	296 ± 35	292 ± 37	0.554
Macular volume (mm³)					
Total	7.61 ± 0.89	7.65 ± 0.88	7.66 ± 0.86	7.56 ± 0.89	0.376
Foveal	0.19 ± 0.04	0.20 ± 0.03	0.20 ± 0.05	0.19 ± 0.04	0.554
Superior	1.91 ± 0.23	1.91 ± 0.25	1.92 ± 0.23	1.89 ± 0.24	0.376
Inferior	1.88 ± 0.22	1.89 ± 0.21	1.89 ± 0.21	1.87 ± 0.22	0.322
Temporal	1.84 ± 0.25	1.86 ± 0.26	1.86 ± 0.27	1.83 ± 0.25	0.376
Nasal	1.98 ± 0.23	1.99 ± 0.22	1.99 ± 0.22	1.97 ± 0.24	0.554

LogMAR = logarithm of the minimum angle of resolution; OCT = optical coherence tomography; RNFL = retinal nerve fiber layer.

Data are presented as mean ± SD.

^aOne-way repeated measures analysis of variance testing.

RESULTS

A TOTAL OF 462 EYES OF 239 PATIENTS (129 MEN, 110 women; mean ± SD age: 52 ± 16 years) were included in the analysis. Two hundred thirty-two (97%) patients underwent a trans-sphenoidal operative approach, and 216 (90%) patients presented with pituitary adenomas (Table 1).

Visual function and OCT parameters of patients during the study period are presented in Table 2 and Figure 1. Significant improvements in visual field mean deviation and pattern standard deviation were observed within 6 weeks following pituitary tumor resection (both $Q < 0.001$) (Table 3 and Figure 1), although no significant changes occurred between 6 weeks to 2 years (all $Q > 0.20$) (Table 3 and Figure 1). At the preoperative visit, 253 (55%) eyes exhibited a visual field mean deviation of > -3 dB, and 303 (66%) eyes exhibited a best-corrected logMAR visual acuity of 0 or better. At the 2-year postoperative follow-up visit, 331 (78%) eyes exhibited a visual field mean deviation of -3 dB, and 324 (76%) eyes exhibited a best-corrected logMAR visual acuity of 0 or better.

Multiple logistic regression results for long-term visual recovery and maintenance by OCT parameters are presented in Tables 4 and 5, and ROC curves are illustrated in Figure 2. Increased inferior RNFL thickness (per 10 μm) was associated with higher odds of improved long-term visual field recovery and maintenance (odds ratio: [OR]: 1.26; 95% confidence interval [CI]: 1.12-1.41; $Q < 0.001$), whereas greater superior RNFL thickness (per 10 μm) was associated with higher odds of visual acuity recovery and maintenance (OR: 1.13; 95% CI: 1.03-1.27; $Q = 0.031$). The association between average RNFL thickness and visual field recovery and maintenance was marginally significant (OR: 1.21; 95% CI: 1.06-1.39; $Q = 0.053$). No significant associations were observed between OCT macular parameters and long-term visual function (all $Q > 0.05$). Multivariable risk prediction models developed for long-term visual field and acuity recovery and maintenance, which incorporated independent predictors, including age, preoperative visual function, and RNFL thickness, demonstrated C-statistics of 0.83 (95% CI: 0.72-0.94) and 0.69 (95% CI: 0.55-0.84), respectively, in the validation sample (Table 5, Figure 2, and Supplemental Table S1).

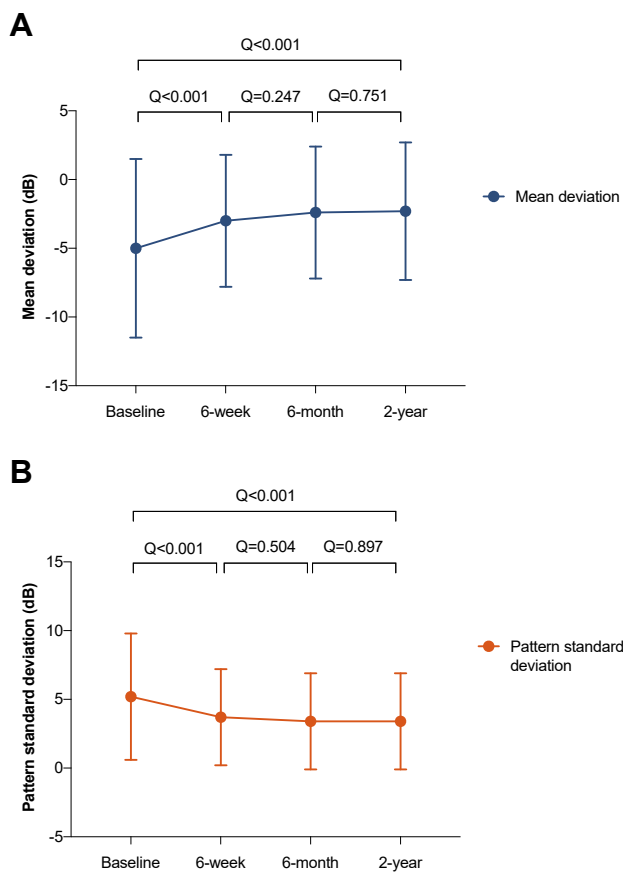


FIGURE 1. Visual Field During the Study Period Visual field (A) mean deviation and (B) pattern standard deviation during the study period. Points represent the mean visual field measurements, and error bars represent the SD.

DISCUSSION

THE RESULTS OF THIS STUDY DEMONSTRATED THAT PREOPERATIVE RNFL thickness was associated with long-term visual function. Greater inferior RNFL thickness was associated with higher odds of visual field recovery and maintenance, whereas increased superior RNFL thickness was associated with higher odds of visual acuity recovery and maintenance. Multivariable risk prediction models were then developed, incorporating independent predictors for visual recovery and maintenance, including age, preoperative visual function, and RNFL thickness. The risk prediction model for visual field recovery and maintenance exhibited moderate discriminative ability and could potentially assist with preoperative prognostication and patient counseling.

In agreement with the findings reported in earlier studies,^{3,10,17,19–26} preoperative RNFL thickness was associated with greater odds of visual recovery and maintenance following pituitary decompression in the present cohort. RNFL thickness provided an anatomical measurement of the structural integrity of the retinal

ganglion cell axons.^{2,17,30–36} Retrograde axonal degeneration resulting from chiasmal compression secondary to pituitary tumor enlargement could result in thinning of the RNFL and might indicate decreased reserve for visual recovery following decompression surgery.^{2,17,23,26,37–40} However, inferior RNFL thickness was a more robust predictor for visual field recovery and maintenance than average RNFL thickness in the present study, which contrasted with the findings of earlier studies.^{3,10,17,19–26} In addition, independent associations with visual acuity recovery and maintenance were limited to superior RNFL thickness in the present study. It is possible that the longer follow-up period of 2 years in the present prospective longitudinal study, as well as the multivariable analysis adjusted for confounding preoperative variables and multiple comparisons, might have contributed to this discrepancy. Nevertheless, our results might appear somewhat surprising, especially in the context of crossing nasal fibers of the optic chiasm, which arise predominantly from the nasal and temporal quadrants of the optic disc, whereas the maculopapillary bundle responsible for central visual acuity enters through the temporal sector.² However, diffuse thinning of the RNFL across all sectors was also reported to occur with chiasmal compression, even among patients with strict bitemporal hemianopic field loss. This is believed to infer the presence of crossing fibers that originate from the nasal hemiretina in all quadrants of the optic disc.^{2,23,26,38–40} Although a number of earlier studies reported that RNFL thinning was more prominent in the temporal and nasal quadrants with chiasmal compression,^{2,26,38–41} it was also hypothesized that the greater reduction in RNFL thickness in these quadrants might contribute to a more narrow range of measurements. This might compromise the discriminative ability to differentiate between patients who exhibited eventual visual recovery from those who did not.^{3,24} Inferior quadrant thickness was previously identified as the strongest OCT RNFL predictor of visual field recovery in 2 smaller cohorts,^{3,24} and these trends were consistent with the findings reported in the present study.

The present study did not identify macular thickness and volume measurements to be independently associated with long-term visual field and visual acuity recovery and maintenance, in contrast to the findings of earlier studies.^{22,23,28,29,42–45} It was possible that the contribution of non-retinal ganglion cell components, as well as the relatively more retrograde location of the macula,^{2,18} might partially explain the poorer overall discriminative ability of macular measurements in predicting long-term visual recovery and maintenance.

Advancing age was identified to be a negative predictor of long-term visual recovery and maintenance in both of the multivariable risk prediction models developed in the present study. These findings were consistent with a number of earlier studies^{6,24,46} and a recent meta-analysis that

TABLE 3. *Post-hoc* Pairwise Comparisons of Visual Function Parameters of Patients During the Study Period

Parameter	Comparison	Q-value ^a
Visual field mean deviation	Baseline vs 6 wks	< 0.001
	6-week vs 6 mos	0.247
	6-month vs 2 y	0.751
	Baseline vs 2 y	< 0.001
Visual field pattern standard deviation	Baseline vs 6 wks	< 0.001
	6-week vs 6 mos	0.504
	6-month vs 2 y	0.897
	Baseline vs 2 y	< 0.001

Bold values indicate statistically significant differences (Q < 0.05).

^a*Post-hoc* pairwise multiplicity-adjusted Tukey's test.

reported a weighted mean age difference of 12.32 years between patients who exhibited postoperative visual field improvement and those that did not.⁵ It was hypothesized that the lower neuronal density in the retina was associated

with aging, and that the decreased capacity for axonal remyelination, might contribute to a decreased reserve for visual recovery.^{2,47,48}

The longer follow-up period of 2 years in the present study was intended to investigate the potential for delayed long-term visual recovery. Interestingly, *post-hoc* analysis of visual field mean deviation and pattern standard deviation demonstrated that improvements occurred during the first 6 weeks postoperatively, and no significant changes were observed between 6 weeks to 2 years. These findings would suggest that most of visual recovery occurs in the early postoperative phase during the first 6 weeks.

Overall, the multivariable risk prediction models developed in the present study, which incorporated age, preoperative visual function, and RNFL thickness, demonstrated moderate discriminative abilities. The visual field recovery and maintenance prediction model demonstrated comparable discriminative ability with a previously developed nomogram that included MRI chiasmal compression grade but not age (C-statistics: 0.83 and 0.84, respectively).³ However, the discriminative ability of the visual acuity recovery and maintenance prediction model developed in

TABLE 4. Multiple Logistic Regression ORs for Long-Term Visual Recovery and Maintenance by OCT Parameters

Parameter	2-year Visual Field Recovery and Maintenance ^a		2-year Visual Acuity Recovery and Maintenance ^b	
	OR (95% CI)	Q-value	OR (95% CI)	Q-value
RNFL thickness (per 10 μm)				
Average	1.21 (1.06-1.39)	0.053	1.11 (1.01-1.24)	0.512
Superior	1.12 (1.01-1.24)	0.167	1.13 (1.03-1.27)	0.031
Inferior	1.26 (1.12-1.41)	< 0.001	1.05 (0.97-1.15)	0.512
Temporal	1.02 (0.92-1.14)	0.859	1.02 (0.93-1.12)	0.776
Nasal	1.14 (1.01-1.28)	0.167	1.07 (0.98-1.18)	0.512
Macular thickness (per 10 μm)				
Average	0.98 (0.91-1.05)	0.859	0.99 (0.94-1.04)	0.776
Foveal	0.94 (0.88-1.00)	0.167	0.97 (0.92-1.02)	0.512
Superior	0.98 (0.92-1.06)	0.859	0.98 (0.93-1.04)	0.776
Inferior	0.97 (0.91-1.06)	0.859	0.99 (0.92-1.04)	0.776
Temporal	0.97 (0.91-1.05)	0.859	1.00 (0.97-1.03)	0.776
Nasal	0.98 (0.93-1.04)	0.859	0.98 (0.93-1.04)	0.776
Macular volume (per 0.1 mm³)				
Total	1.00 (0.98-1.02)	0.943	0.99 (0.98-1.01)	0.512
Foveal	0.65 (0.35-1.21)	0.512	0.86 (0.55-1.33)	0.776
Superior	1.00 (0.91-1.09)	0.943	0.98 (0.90-1.07)	0.776
Inferior	1.01 (0.96-1.07)	0.859	0.94 (0.87-1.03)	0.512
Temporal	0.99 (0.90-1.09)	0.943	0.94 (0.86-1.03)	0.512
Nasal	1.00 (0.92-1.08)	0.943	0.98 (0.91-1.06)	0.917

CI = confidence interval; OR = odds ratio; RNFL = retinal nerve fiber layer.

Bold values indicate statistically significant differences (Q < 0.05).

^aGeneralized estimating equations (GEEs) multivariable logistic regression analysis accounting for intereye correlation, and adjusted for confounding variables, including age, sex, and baseline mean deviation.

^bGEEs multivariable logistic regression analysis accounting for intereye correlation, and adjusted for confounding variables, including age, sex, and baseline best-corrected visual acuity.

TABLE 5. Multiple Logistic Regression Modeling for Long-Term Visual Recovery and Maintenance Prognostication

Parameter	2-year Visual Field Recovery and Maintenance ^a		2-year Visual Acuity Recovery and Maintenance ^a	
	OR (95% CI)	P Value	OR (95% CI)	P value
Age (per 10 years)	0.85 (0.72-0.99)	.043	0.83 (0.71-0.98)	0.026
Baseline visual field mean deviation (per dB)	1.15 (1.07-1.24)	<.001	-	-
Baseline best-corrected visual acuity (per 0.1 logMAR unit)	-	-	0.89 (0.82-0.96)	0.007
Superior RNFL thickness (per 10 μm)	-	-	1.16 (1.03-1.33)	0.034
Inferior RNFL thickness (per 10 μm)	1.22 (1.06-1.52)	.001	-	-
Model summary^b				
Risk prediction equation	Log odds = -0.173 - (0.016 × age) + (0.129 × mean deviation) + (0.020 × inferior RNFL thickness)		Log odds = 0.467 - (0.018 × age) - (1.191 × logMAR visual acuity) + (0.014 × superior RNFL thickness)	
C-statistic (95% CI)	0.83 (0.72-0.94)		0.69 (0.55-0.84)	
Youden-optimal prognostic cut-off	>0.60		>0.70	
Sensitivity (95% CI)	85% (73%-92%)		74% (60%-85%)	
Specificity (95% CI)	67% (44%-84%)		58% (39%-76%)	
Positive predictive value (95% CI)	88% (79%-94%)		78% (68%-85%)	
Negative predictive value (95% CI)	60% (42%-75%)		54% (39%-68%)	
Positive likelihood ratio (95% CI)	2.55 (1.31-4.94)		1.79 (1.08-2.95)	
Negative likelihood ratio (95% CI)	0.23 (0.11-0.46)		0.44 (0.24-0.79)	

CI = 95% confidence interval; logMAR = logarithm of the minimum angle of resolution; OR = odds ratio; RNFL = retinal nerve fibre layer.

^aMultivariable logistic regression analysis of developmental sample.

^bDiagnostic accuracy values of risk prediction models in validation sample.

the present study was relatively more modest (C-statistic, 0.69). Further research investigating clinical and imaging prognostic factors for visual acuity recovery and maintenance following pituitary tumor resection is required.

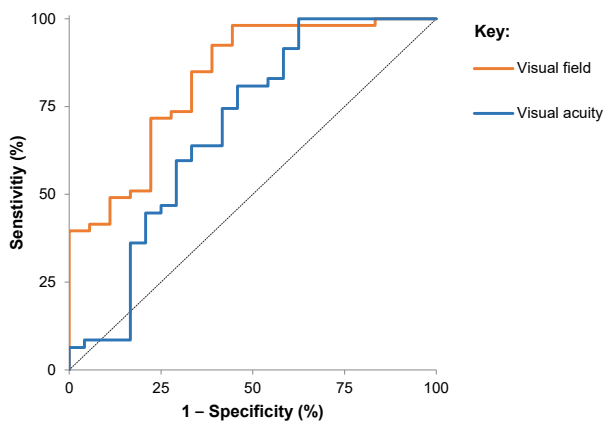


FIGURE 2. Receiver-Operating Characteristic Curves. Receiver-operating characteristic curves for the discriminative performance of the multivariable risk prediction models developed for long-term visual field and acuity recovery and maintenance.

This study had several limitations. The single-center setting had the potential to introduce selection bias, and external validation of the risk prediction model in future studies is required. The unavailability of data on the duration of symptoms before surgery was a study limitation. However, pituitary adenomas are a heterogeneous group of tumors, with variable clinical presentations that can be influenced by the presence of hormone secretion or mass effect, and even patients with the same histological tumor classification may present with different symptoms.² Moreover, pituitary tumors are often incidental findings.² Patients referred to our institution were usually tertiary referrals, and therefore, it was not possible to accurately determine the initial presentation or how long symptoms were present. Future studies are required to investigate whether the incorporation of symptom duration might further augment the prognostic performance of risk prediction models for long-term visual recovery and maintenance. In addition, craniopharyngiomas and astrocytomas were present in a small proportion of cases, whereas none of the patients presented with meningiomas. It remained unclear whether the study findings were generalizable to these rarer etiologies, and caution should be applied when applying the risk prediction models in the clinical setting.

The Spectralis OCT device used in the present study does not segment the ganglion cell complex (GCC), which is acknowledged to be a study limitation. A number of earlier reports suggested that GCC thickness might be more sensitive than RNFL measurements.^{22,23,28,29} Future studies are required to confirm the prognostic usefulness of OCT GCC measurements for long-term visual recovery following chiasmal decompression.

In conclusion, this prospective longitudinal study showed that preoperative RNFL thickness was associated with a 2-year postoperative visual field and acuity recovery and maintenance following pituitary tumor resection. The multivariable risk prediction model developed for visual field recovery and maintenance demonstrated moderate discriminative ability and might assist in providing tailored preoperative prognostication and patient counseling.

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REFERENCES

- Ostrom QT, Gittleman H, Truitt G, Boscia A, Kruchko C, Barnholtz-Sloan JS. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2011-2015. *Neuro Oncol* 2018;20(Suppl 4):iv1-iv86.
- Danesh-Meyer HV, Yoon JJ, Lawlor M, Savino PJ. Visual loss and recovery in chiasmal compression. *Prog Retin Eye Res* 2019;73:100765.
- Lee J, Kim SW, Kim DW, et al. Predictive model for recovery of visual field after surgery of pituitary adenoma. *J Neurooncol* 2016;130(1):155-164.
- Gnanalingham KK, Bhattacharjee S, Pennington R, Ng J, Mendoza N. The time course of visual field recovery following transphenoidal surgery for pituitary adenomas: predictive factors for a good outcome. *J Neurol Neurosurg Psychiatry* 2005; 76(3):415-419.
- Sun M, Zhang ZQ, Ma CY, Chen SH, Chen XJ. Predictive factors of visual function recovery after pituitary adenoma resection: a literature review and meta-analysis. *Int J Ophthalmol* 2017;10(11):1742-1750.
- Barzaghi LR, Medone M, Losa M, Bianchi S, Giovanelli M, Mortini P. Prognostic factors of visual field improvement after trans-sphenoidal approach for pituitary macroadenomas: review of the literature and analysis by quantitative method. *Neurosurg Rev* 2012;35(3):369-378. discussion 378-9.
- Anik I, Anik Y, Cabuk B, et al. Visual outcome of an endoscopic endonasal transsphenoidal approach in pituitary macroadenomas: quantitative assessment with diffusion tensor imaging early and long-term results. *World Neurosurg* 2018;112:e691-e701.
- Chohan MO, Levin AM, Singh R, et al. Three-dimensional volumetric measurements in defining endoscope-guided giant adenoma surgery outcomes. *Pituitary* 2016;19(3):311-321.
- Dutta P, Gyurmey T, Bansal R, et al. Visual outcome in 2000 eyes following microscopic transsphenoidal surgery for pituitary adenomas: protracted blindness should not be a deterrent. *Neurol India* 2016;64(6):1247-1253.
- Yoneoka Y, Hatase T, Watanabe N, et al. Early morphological recovery of the optic chiasm is associated with excellent visual outcome in patients with compressive chiasmal syndrome caused by pituitary tumors. *Neurol Res* 2015;37(1):1-8.
- Chabot JD, Chakraborty S, Imbarrato G, Dehdashti AR. Evaluation of outcomes after endoscopic endonasal surgery for large and giant pituitary macroadenoma: a retrospective review of 39 consecutive patients. *World Neurosurg* 2015; 84(4):978-988.
- Ho RW, Huang HM, Ho JT. The influence of pituitary adenoma size on vision and visual outcomes after trans-sphenoidal adenectomy: a report of 78 cases. *J Korean Neurosurg Soc* 2015;57(1):23-31.
- Prieto R, Pascual JM, Barrios L. Optic chiasm distortions caused by craniopharyngiomas: clinical and magnetic resonance imaging correlation and influence on visual outcome. *World Neurosurg* 2015;83(4):500-529.
- Yu FF, Chen LL, Su YH, Huo LH, Lin XX, Liao RD. Factors influencing improvement of visual field after trans-sphenoidal resection of pituitary macroadenomas: a retrospective cohort study. *Int J Ophthalmol* 2015;8(6):1224-1228.
- Jahangiri A, Lamborn KR, Blevins L, Kunwar S, Aghi MK. Factors associated with delay to pituitary adenoma diagnosis in patients with visual loss. *J Neurosurg* 2012;116(2):283-289.
- Monteiro ML, Zambon BK, Cunha LP. Predictive factors for the development of visual loss in patients with pituitary macroadenomas and for visual recovery after optic pathway decompression. *Can J Ophthalmol* 2010;45(4):404-408.
- Zhang J, Zhang S, Song Y, et al. Predictive value of preoperative retinal nerve fiber layer thickness for postoperative visual recovery in patients with chiasmal compression. *Oncotarget* 2017;8(35):59148-59155.
- Raz N, Bick AS, Klistorner A, et al. Physiological correlates and predictors of functional recovery after chiasmal decompression. *J Neuroophthalmol* 2015;35(4):348-352.
- Danesh-Meyer HV, Wong A, Papchenko T, et al. Optical coherence tomography predicts visual outcome for pituitary tumors. *J Clin Neurosci* 2015;22(7):1098-1104.
- Park HH, Oh MC, Kim EH, et al. Use of optical coherence tomography to predict visual outcome in parachiasmal meningioma. *J Neurosurg* 2015;123(6):1489-1499.
- Loo JL, Tian J, Miller NR, Subramanian PS. Use of optical coherence tomography in predicting post-treatment visual

- outcome in anterior visual pathway meningiomas. *Br J Ophthalmol* 2013;97(11):1455–1458.
22. Moon CH, Hwang SC, Kim BT, Ohn YH, Park TK. Visual prognostic value of optical coherence tomography and photopic negative response in chiasmal compression. *Invest Ophthalmol Vis Sci* 2011;52(11):8527–8533.
 23. Moon CH, Hwang SC, Ohn YH, Park TK. The time course of visual field recovery and changes of retinal ganglion cells after optic chiasmal decompression. *Invest Ophthalmol Vis Sci* 2011; 52(11):7966–7973.
 24. Jacob M, Raverot G, Jouanneau E, et al. Predicting visual outcome after treatment of pituitary adenomas with optical coherence tomography. *Am J Ophthalmol* 2009;147(1): 64–70.e2.
 25. Danesh-Meyer HV, Papchenko T, Savino PJ, Law A, Evans J, Gamble GD. In vivo retinal nerve fiber layer thickness measured by optical coherence tomography predicts visual recovery after surgery for parachiasmal tumors. *Invest Ophthalmol Vis Sci* 2008;49(5):1879–1885.
 26. Danesh-Meyer HV, Carroll SC, Foroosan R, et al. Relationship between retinal nerve fiber layer and visual field sensitivity as measured by optical coherence tomography in chiasmal compression. *Invest Ophthalmol Vis Sci* 2006; 47(11):4827–4835.
 27. Kerrison JB, Lynn MJ, Baer CA, Newman SA, Bioussé V, Newman NJ. Stages of improvement in visual fields after pituitary tumor resection. *Am J Ophthalmol* 2000;130(6): 813–820.
 28. Tieger MG, Hedges TR 3rd, Ho J, et al. Ganglion cell complex loss in chiasmal compression by brain tumors. *J Neuroophthalmol* 2017;37(1):7–12.
 29. Ohkubo S, Higashide T, Takeda H, Murotani E, Hayashi Y, Sugiyama K. Relationship between macular ganglion cell complex parameters and visual field parameters after tumor resection in chiasmal compression. *Jpn J Ophthalmol* 2012; 56(1):68–75.
 30. Costa-Cunha LV, Cunha LP, Malta RF, Monteiro ML. Comparison of Fourier-domain and time-domain optical coherence tomography in the detection of band atrophy of the optic nerve. *Am J Ophthalmol* 2009;147(1):56–63.e2.
 31. de Araujo RB, Oyamada MK, Zacharias LC, Cunha LP, Preti RC, Monteiro MLR. Morphological and functional inner and outer retinal layer abnormalities in eyes with permanent temporal hemianopia from chiasmal compression. *Front Neurol* 2017;8:619.
 32. Monteiro ML, Moura FC. Comparison of the GDx VCC scanning laser polarimeter and the stratus optical coherence tomograph in the detection of band atrophy of the optic nerve. *Eye (Lond)* 2008;22(5):641–648.
 33. Monteiro ML, Cunha LP, Vessani RM. Comparison of retinal nerve fiber layer measurements using Stratus OCT fast and regular scan protocols in eyes with band atrophy of the optic nerve and normal controls. *Arq Bras Oftalmol* 2008;71(4):534–539.
 34. Monteiro ML, Cunha LP, Costa-Cunha LV, Maia OO Jr, Oyamada MK. Relationship between optical coherence tomography, pattern electroretinogram and automated perimetry in eyes with temporal hemianopia from chiasmal compression. *Invest Ophthalmol Vis Sci* 2009;50(8):3535–3541.
 35. Monteiro ML, Hokazono K, Cunha LP, Oyamada MK. Correlation between multifocal pattern electroretinography and Fourier-domain OCT in eyes with temporal hemianopia from chiasmal compression. *Graefes Arch Clin Exp Ophthalmol* 2013;251(3):903–915.
 36. Sousa RM, Oyamada MK, Cunha LP, Monteiro MLR. Multifocal visual evoked potential in eyes with temporal hemianopia from chiasmal compression: correlation with standard automated perimetry and OCT findings. *Invest Ophthalmol Vis Sci* 2017;58(11):4436–4449.
 37. Zhang X, Sun P, Wang J, Wang Q, Song SK. Diffusion tensor imaging detects retinal ganglion cell axon damage in the mouse model of optic nerve crush. *Invest Ophthalmol Vis Sci* 2011;52(9):7001–7006.
 38. Kanamori A, Nakamura M, Matsui N, et al. Optical coherence tomography detects characteristic retinal nerve fiber layer thickness corresponding to band atrophy of the optic discs. *Ophthalmology* 2004;111(12):2278–2283.
 39. Monteiro ML, Leal BC, Rosa AA, Bronstein MD. Optical coherence tomography analysis of axonal loss in band atrophy of the optic nerve. *Br J Ophthalmol* 2004;88(7):896–899.
 40. Monteiro ML, Medeiros FA, Ostroscki MR. Quantitative analysis of axonal loss in band atrophy of the optic nerve using scanning laser polarimetry. *Br J Ophthalmol* 2003;87(1): 32–37.
 41. Leal BC, Moura FC, Monteiro ML. Retinal nerve fiber layer loss documented by Stratus OCT in patients with pituitary adenoma: case report. *Arq Bras Oftalmol* 2006;69(2):251–254.
 42. Moura FC, Medeiros FA, Monteiro ML. Evaluation of macular thickness measurements for detection of band atrophy of the optic nerve using optical coherence tomography. *Ophthalmology* 2007;114(1):175–181.
 43. Monteiro ML, Hokazono K, Fernandes DB, et al. Evaluation of inner retinal layers in eyes with temporal hemianopic visual loss from chiasmal compression using optical coherence tomography. *Invest Ophthalmol Vis Sci* 2014;55(5): 3328–3336.
 44. Monteiro ML, Costa-Cunha LV, Cunha LP, Malta RF. Correlation between macular and retinal nerve fibre layer Fourier-domain OCT measurements and visual field loss in chiasmal compression. *Eye (Lond)* 2010;24(8):1382–1390.
 45. Moura FC, Costa-Cunha LV, Malta RF, Monteiro ML. Relationship between visual field sensitivity loss and quadrantic macular thickness measured with Stratus-Optical coherence tomography in patients with chiasmal syndrome. *Arq Bras Oftalmol* 2010;73(5):409–413.
 46. Rivoal O, Brezin AP, Feldman-Billard S, Luton JP. Goldmann perimetry in acromegaly: a survey of 307 cases from 1951 through 1996. *Ophthalmology* 2000;107(5):991–997.
 47. Franklin RJ, Zhao C, Sim FJ. Ageing and CNS remyelination. *Neuroreport* 2002;13(7):923–928.
 48. Wei Y, Jiang H, Shi Y, et al. age-related alterations in the retinal microvasculature, microcirculation, and microstructure. *Invest Ophthalmol Vis Sci* 2017;58(9):3804–3817.