

Predictive value of retinal nerve fibre layer thickness for postoperative visual improvement in patients with pituitary macroadenoma

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To cite: Kurian DE, V R, Horo S, *et al*. Predictive value of retinal nerve fibre layer thickness for postoperative visual improvement in patients with pituitary macroadenoma. *BMJ Open Ophthalmology* 2022;**7**:e000964. doi:10.1136/bmjophth-2021-000964

A pilot of this study with a smaller number was presented as a poster titled 'Role of OCT – RNFL (Optical coherence tomography – Retinal nerve fibre layer) in determining visual prognosis in patients with pituitary macroadenoma undergoing surgical management' at the 76th Annual Conference of the All India Ophthalmological Society at Coimbatore, India held between 22 and 25 February 2018.

Received 14 January 2022
Accepted 11 June 2022



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ABSTRACT

Objective To determine the usefulness of retinal nerve fibre layer (RNFL) thickness and a reliable cut-off value that can predict postoperative visual function improvement in patients with pituitary macroadenoma.

Methods and Analysis This was a prospective observational study. Preoperative optical coherence tomography of the RNFL was performed in patients with pituitary macroadenoma. Postoperative visual function changes (acuity and visual fields) were identified using predefined criteria. Receiver operating characteristic curves were constructed for RNFL values to define the ideal cut-off value that predicted improvement. Other variables including preoperative visual acuity, mean deviation, visual field index and tumour volume were also analysed.

Results Twenty-nine eligible subjects (58 eyes) were recruited. The mean (\pm SD) age was 43.9 (\pm 12.85) years and 65.5% were male. The mean (\pm SE) follow-up duration was 20.8 (\pm 6.42) months. RNFL thickness was significantly thinner in eyes with visual dysfunction and optic disc pallor. Better preoperative logarithmic minimum angle of resolution (logMAR) visual acuity, higher RNFL thickness and smaller tumour volume were associated with postoperative visual field improvement on univariate analysis; however, only mean RNFL thickness had significant association on multivariate analysis. None of the preoperative variables showed significant association with improvement in visual acuity. The best cut-off of mean RNFL thickness for visual field improvement was estimated at 81 μ m with 73.1% sensitivity and 62.5% specificity.

Conclusion Preoperative RNFL thickness can be an objective predictor of visual field outcomes in patients undergoing surgery for pituitary macroadenomas, with moderate sensitivity and specificity. It is, however, not a good predictor of visual acuity outcome.

INTRODUCTION

Pituitary macroadenomas are of importance to the ophthalmologist as they compress the chiasma, causing visual defects.^{1–3} Trans-sphenoidal excision of these tumours is preferred to craniotomy for its lower complication rates.^{3–6} However, reliable and consistent predictions of visual outcome

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Most of the predictors of visual outcome following surgery for pituitary macroadenoma are subjective.
- ⇒ Preoperative optical coherence tomography- retinal nerve fibre layer (RNFL) thickness may help predict visual outcome, but objective cut- off parameters are ill defined.
- ⇒ It is unclear whether visual acuity and visual fields have the same predictors for improvement postoperatively.

WHAT THIS STUDY ADDS

- ⇒ A reasonable objective cut- off of preoperative RNFL thickness that predicted postoperative improvement in visual field was determined.
- ⇒ Potential for recovery of acuity might be unrelated to RNFL thickness.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Preoperative counselling of patients can be done objectively.
- ⇒ Factors that predict postoperative visual acuity need to be explored further.

following surgical decompression of pituitary macroadenomas can be difficult. Some studies have identified age of the patient, duration of symptoms, volume of the tumour, preoperative visual parameters and retinal nerve fibre layer (RNFL) thickness as predictors, whereas others have not been able to show statistical significance of these factors.^{1–5 7 8} Most predictors of visual outcomes are subjective, and some patients, including those with normal preoperative ocular vision, deteriorate following surgery. The reason for the inability to predict outcomes with any degree of accuracy is hypothesised to be a clinically imperceptible but irreversible damage to the retinal ganglion cell axons. Whether visual acuity and visual fields have the same predictors for improvement has not been adequately

explored. Although RNFL thickness has been investigated in recent studies as a predictive factor, cut-offs are not clearly defined. The lack of a well-defined cut-off for RNFL makes it difficult to counsel patients regarding visual recovery. This study evaluated the predictive value of RNFL thickness for improvement in visual fields and visual acuity.

MATERIALS AND METHODS

This prospective study was conducted at the Department of Ophthalmology of a tertiary hospital in South India. Patients were recruited over 1 year from September 2015 to August 2016 and followed up over 4 years.

Patient material

After obtaining informed consent, the study included patients diagnosed with pituitary macroadenoma on MRI and planned for an endonasal endoscopic excision at the Department of Neurological Sciences. A complete ophthalmological evaluation was done, preoperatively and postoperatively. Patients with papilloedema, glaucoma, high myopia (>6 dioptres) and extensive retinal pathology were excluded, as were patients on cabergoline and those with prior pituitary surgery or radiation therapy. All patients who underwent resection of >90% of their tumour were included in the study as such resections are associated with good visual recovery.⁹ Pituitary apoplexy was not an exclusion criterion.

Tumour volume

Contrast-enhanced MRI of the brain was done using a Siemens MRI machine (either 1.5 Tesla or 3 Tesla). The volume of the tumour was calculated using the given formula based on Cavalieri's principle.¹⁰⁻¹²

Volume = $0.8 \pi abc$, where a, b and c are half the diameters in the three dimensions.

Ophthalmological assessment

The ophthalmological assessment included a complete history and ocular examination.

- ▶ *Visual acuity and fields:* visual acuity was measured using Snellen optotype self-illuminated vision drum under appropriate lighting conditions. Visual acuity was converted to logarithmic minimum angle of resolution (logMAR) equivalent values for statistical analysis.¹³ Visual field analysis was performed with the Humphrey Visual Field Analyzer (750i, V.5.0; Carl Zeiss Meditec), 30-2 program Swedish Interactive Threshold Algorithm (SITA standard) using a Goldmann size III stimulus against a 31.5 apostilb background. Quadrantanopia was defined based on either of the following criteria¹⁴:
 - Depression of thresholds by ≥ 5 dB in ≥ 3 contiguous points adjacent to the vertical meridian in the involved quadrant as compared with their mirror image points across the vertical meridian.
 - The pattern deviation plot showed ≥ 3 points adjacent to the vertical meridian in the involved

quadrant depressed to the 1% probability level with normal mirror image points across the vertical meridian.

For the diagnosis of hemianopia, the diagnostic criteria for quadrantanopia had to be applicable to both quadrants comprising the hemifield. All visual field analyses that did not show more than three contiguous points of depression in threshold by less than 5% of the age-matched population were considered normal. To quantify the visual field defect (VFD), mean deviation (MD) in decibels and visual field index (VFI) in percentage were used. Those who could not perform visual field analysis were excluded from the respective analysis.

- ▶ *Optical coherence tomography (OCT)-RNFL:* this was done using a DRI OCT Triton plus swept-source machine. This captures a 3.4 mm^2 area around the optic nerve head, and the nerve fibre layer thickness values of each quadrant, superior, nasal, inferior, temporal and average, were documented. Those with poor signal strength were excluded.

Visual outcome

Postoperative assessments were planned between 3 and 6 months following tumour resection; however, as most of our patients had to travel in from outside the state/country, follow-up duration varied among the subjects. Visual outcome was analysed separately for visual acuity and visual fields. Improvement in visual acuity was defined as any improvement in visual acuity compared with baseline. Visual field was documented as improved if there was improvement in MD by at least 5 dB or any improvement if the preoperative MD was within 5 dB; or an increase in VFI by at least 10% or any increase if the preoperative VFI was above 90%. A postoperative OCT-RNFL was not done. Only eyes with impairment in the visual acuity or field on preoperative assessment were included in the analysis of prognostic factors.

Statistical methods

- ▶ *Sample size calculation:* Danesh-Meyer *et al*¹⁵ observed that 97% of those with normal thickness (more than 97th percentile of normative data) compared with 72% of those with thin RNFL thickness (less than 97th percentile of normative data) showed significant improvement in visual acuity postoperatively. Based on this, the sample size calculated for our study was 58 eyes.
- ▶ *Predictive factors evaluated:* preoperative RNFL thickness (continuous variable) of each quadrant and the average were analysed. Other factors evaluated were with tumour volume (continuous variable), presence of optic disc pallor (yes/no), presence of field defect (yes/no), and visual parameters such as visual acuity (continuous variable), MD (continuous variable) and VFI (continuous variable).
- ▶ *Outcome measures:* data were summarised using mean with SD or median with IQR for continuous variable

depending on normality, and using frequency and percentage for categorical variables. Comparisons among groups were done by independent t-test and χ^2 test for continuous and categorical variables, respectively. Receiver operating characteristic (ROC) curves were constructed to define discrimination between two groups. All analyses were performed using STATA IC V.16.0 software.

RESULTS

Demographic details

A total of 45 patients were recruited but 16 patients were lost to follow-up, leaving 29 patients (58 eyes) included in the study. The demographic and clinical profiles of the patients are shown in [table 1](#). The mean age of the patients was 43.9 years (SD: 12.8) and majority were male (65.5%).

Preoperative visual function

The most common complaint was decrease in vision, reported by 72.4% of patients, followed by headache in 62.1%. Diplopia and perception of field defect were less commonly reported by patients. The mean preoperative logMAR vision in either eye was fairly good, as shown in [table 1](#) (0.26 and 0.36 in the right and left eye, respectively). Twenty-six eyes (44.8%) had a visual acuity of 6/6 and 43 eyes (74.1%) had a visual acuity of 6/12 and better. The proportion of eyes that had VFD on Humphrey field analyzer (HFA) was 72.4% (42 eyes), with temporal hemianopia being the most common pattern ([table 1](#)). The five who were classified as others under VFD in [table 1](#) were one with homonymous hemianopia, one with normal visual field in one eye and temporal hemianopia in the other, and three who could not perform HFA in one eye and temporal defect in the other eye. Of 58 eyes, 12 (20.7%) had a visual acuity of 6/6 but impaired visual fields, and 2 (3.44%) had normal fields but impaired vision. Of the 32 eyes (55.2%) with optic disc pallor, either temporal or total ([table 1](#)), 9 had normal visual acuity with temporal disc pallor alone. All eyes with total disc pallor had a reduction in visual acuity, and all eyes with any disc pallor, temporal or total, had some form of VFD.

Preoperative RNFL

The mean preoperative RNFL thickness (average) in our subjects was 89.02 μm (SD 25.63). The RNFL in the different quadrants was significantly thinner in eyes with visual dysfunction and disc pallor ([table 2](#)).

Postoperative visual outcome

The follow-up period varied between patients (range, 1–48 months; IQR: 5–24 months). There was a significant postoperative change in visual acuity, MD and VFI ([table 3](#)). Out of the 32 eyes (55.2%) that had a visual acuity of less than 6/6 preoperatively, 24 (75%) improved. Out of these, 16 eyes (50%) improved to 6/6, 5 eyes (15.6%) remained the same and 3 (9.4%) showed a drop in visual acuity. Of the 26 eyes with normal preoperative

Table 1 Demographic and clinical profile of patients (N=29)

Sex, n (%)	
Male	19 (65.5)
Female	10 (34.5)
Mean age (SD) in years	43.9 (12.8)
Presence of decrease in vision, n (%)	
Yes	21 (72.4)
No	8 (27.6)
Median (IQR) duration of visual complaints in months (n=21)	8 (3–12)
Symptom of field cut, n (%)	
Yes	4 (13.8)
No	25 (86.2)
Presence of diplopia, n (%)	
Yes	4 (13.8)
No	25 (86.2)
Mean tumour volume (\pm SE) in cubic centimetres	11.7 \pm 0.2
Mean logMAR VA in the right eye (SD)	0.3(0.3)
Mean logMAR in the left eye (SD)	0.4(0.4)
Visual field defects, n (%)	
No defect	8 (27.6)
Bilateral superior temporal quadrantanopia	3 (10.3)
Bitemporal hemianopia	12 (41.4)
Advanced depression	1 (3.4)
Others	5 (17.2)
Mean follow-up duration (\pm SE) in months	20.8 \pm 6.4
Disc pallor (%), n=58 eyes	
No pallor	26 (44.8)
Temporal pallor	23 (39.7)
Optic atrophy	9 (15.5)
Mean RNFL thickness in microns (SD), n=58 eyes	
Superior	115.1 (32.4)
Nasal	64.9 (22.6)
Inferior	118.7 (33.5)
Temporal RNFL	57.1 (20.6)
logMAR, logarithmic minimum angle of resolution; RNFL, retinal nerve fibre layer; VA, visual acuity.	

visual acuity, 1 had a drop in vision postoperatively while the rest remained at 6/6. Of the 42 eyes with VFD, 26 showed an improvement, but 2 of 16 eyes with normal preoperative visual fields deteriorated postoperatively. Thus, the rate of postoperative improvement for visual acuity was 75% and that for VFD was 61.9%.

Univariate analysis of the prognostic variables was performed for the 32 eyes with impaired visual acuity and 42 eyes with impaired visual field ([table 4](#)). There was no statistically significant difference in the prognostic variables between those eyes in which the visual acuity

Table 2 Preoperative visual function and fundus findings versus RNFL thickness in various quadrants (n=58 eyes)

	Inferior RNFL, μm	Superior RNFL, μm	Nasal RNFL, μm	Temporal RNFL, μm	Average RNFL, μm	P value
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Disc pallor						
Absent (n=26)	139.4 (21.4)	132.9 (19.1)	77.0 (18.1)	69.4 (14.8)	104.8 (15.3)	<0.001
Present (n=32)	101.8 (32.3)	100.6 (34.1)	55.0 (21.3)	47.2 (19.5)	76.2 (25.3)	
Visual acuity						
VA=6/6 (n=26)	129.1 (23.8)	127.3 (21.7)	74.5 (20.7)	64.9 (14.7)	99.1 (18.6)	0.04
VA <6/6 (n=32)	110.2 (37.9)	105.2 (36.5)	57.1 (21.4)	50.8 (22.7)	80.8 (27.8)	
VFD						
Absent (n=16)	141.3 (19.3)	134.8 (20.6)	80.3 (17.8)	71.7 (11.4)	107.2 (15.2)	0.004
Present (n=42)	110.0 (33.9)	107.5 (33.1)	59.0 (21.6)	51.6 (20.7)	82.1 (25.5)	

logMAR, logarithmic minimum angle of resolution; RNFL, retinal nerve fibre layer; VA, visual acuity; VFD, visual field defect.

did or did not improve. With respect to VFD, eyes that improved had significantly better preoperative visual acuity, thicker RNFL thicknesses (except in the temporal quadrant) and smaller tumour volume. Logistic regression performed on these variables shows that only RNFL thickness remained significantly associated with improvement in VFD, with OR of 1.1 for every 1 μm of average RNFL thickness ($p=0.006$) (table 5).

The ROC plotted for preoperative OCT-RNFL thickness determined that the average RNFL thickness of 81 μm predicted an improvement in VFD with 73.1% sensitivity and 62.5% specificity with (area under the curve (AUC) being 0.7).

DISCUSSION

Predicting visual outcome following surgery for pituitary macroadenomas, while useful in preoperative patient counselling, is difficult. Age of the patient, duration of symptoms, disc pallor, volume of the tumour and preoperative visual parameters are some of the documented predictors.^{1 2 5 7 8 15 16} However, deterioration of vision due to intraoperative and postoperative complications, although rare, is reported and cannot be predicted. In this unpredictable scenario, parameters other than preoperative visual function that might predict visual improvement in a simple yet consistent manner need to be explored. Although preoperative RNFL thickness

has been shown to correlate with severity of preoperative field defects,¹⁷ it has an unclear correlation with visual outcome. This formed the basis for our investigation.

RNFL thickness and preoperative visual function

Reductions in RNFL thickness and papillomacular bundle have been shown to correlate well with degree of temporal hemianopia and central field defects, respectively.¹⁷⁻²⁰ These correlations have been drawn by mapping optic nerve head sectors with the VFD values in the corresponding areas of the field map. Most studies have analysed visual field while correlations with visual acuity are scarce. Monteiro *et al*¹⁷ used segmented macular thickness and demonstrated that macular RNFL and ganglion cell layer correlated with visual field loss as well as band atrophy. The correlation was reportedly better than peripapillary RNFL. In our study, peripapillary RNFL was significantly thicker in all quadrants in those with normal visual acuity and normal visual field compared with those with impaired acuity and fields (table 2). Hence, RNFL may possibly be substituted for field analysis in those who are unable to perform field analysis due to reliability issues or severe visual impairment. We also found that RNFL was significantly thinner in those with disc pallor. This is useful, as early optic disc pallor is a rather subjective finding and has been found to be an inconsistent predictive factor of visual recovery.²¹

RNFL thickness and visual field following surgery

The preoperative visual parameters in our subjects were comparable with the findings of a meta-analysis²² including 19 studies that showed that eyes with normal RNFL had a greater likelihood of achieving approximately normal visual fields.^{15 21 23 24} Danesh-Meyer *et al*¹⁵ had determined that with similar severities of VFD the thicker RNFL group had better improvement in the postoperative visual field. Meyer *et al*,²⁵ in a later publication, reported a faster visual field recovery and a greater chance of improvement to normal fields in the group with

Table 3 Postoperative change in visual function

	Preoperative mean (SD)	Postoperative mean (SD)	P value
LogMAR visual acuity	0.4 (0.7)	0.3 (0.7)	<0.001
Mean deviation in (-) decibels	10.8 (7.4)	7.2 (5.4)	0.01
Visual field index in percentage	72.8 (25.7)	85.1 (18.2)	0.011

logMAR, logarithmic minimum angle of resolution.

Table 4 Univariate analysis of predictors of visual improvement in eyes with preoperative visual impairment

Preoperative variable	Visual acuity (n=32 eyes)			Visual field (n=42 eyes)		
	Improved (n=24, 75%)	Not improved (n=8, 25%)	P value	Improved (n=26, 61.9%)	Not improved (n=16, 38.1%)	P value
	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	
LogMAR visual acuity	0.3 (0.2–0.6)	0.8 (0.4–1.3)	0.08	0.2 (0.0–0.5)	0.45 (0.2–1.3)	0.04
MD in (–) decibels (SD)	16.7 (11.1–21.9)	14.3 (9.4–19.5)	0.7	11.4 (4.5–18.4)	16.6 (12.8–18.4)	0.34
VFI in percentage (SD)	51.5 (36–68.5)	62 (41.5–83.5)	0.7	68.5 (42.5–93)	54 (49–57)	0.56
Inferior RNFL in microns (SD)	117.5 (96.5–135.5)	93 (79.5–143.5)	0.5	121.5 (103–135)	98 (81–117)	0.03
Superior RNFL in microns (SD)	121 (92–131.5)	86.5 (73.5–120)	0.2	121.5 (109–133)	91.5 (70–125)	0.02
Nasal RNFL in microns (SD)	63 (46–75)	44.50 (39–67.5)	0.2	65.5 (55–79)	48 (39.5–60)	0.005
Temporal RNFL in microns (SD)	52 (35–60)	42.5 (29.5–90)	0.9	56.5 (43–67)	38 (26–55.5)	0.06
Average RNFL in microns (SD)	89.5 (63–97)	65.5 (58.5–105)	0.6	92.5 (75–108)	67 (57.5–91.5)	0.03
Tumour volume in cubic centimetres	12.5 (6.9–20.5)	13.7 (5.8–23.9)	0.9	6.9 (5.8–12.6)	20.5 (16.3–26.2)	0.001
Duration of symptoms in months	6 (5–10)	8.5 (5–12)	0.4	8 (3–10)	12 (5–18)	0.06

logMAR, logarithmic minimum angle of resolution; MD, mean deviation; RNFL, retinal nerve fibre layer; VFI, visual field index.

thicker RNFL at final follow-up (81% vs 37%, $p < 0.001$). When they plotted the RNFL of those who improved and those who did not against the degree of improvement, a rough RNFL cut-off of about 80 μm seemed to differentiate between the two groups. Our ROC analysis estimated the cut-off for improvement in visual fields as 81 μm (AUC 0.7), with 73.1% sensitivity and 62.5% specificity. Garcia *et al.*²⁶ in a retrospective study using time domain OCT reported nasal RNFL thickness of 68.50 μm as being predictive, but with poor sensitivity and specificity of 61% and 50%, respectively. Our study demonstrated an OR of about 1.1 for improvement in VFD for every 1 μm of mean RNFL thickness, which was in agreement with the OR of about 1.29 reported by Jacob *et al.*²⁴ In addition, they also did not find preoperative MD to be predictive of visual outcome as in our study. Although better preoperative

logMAR visual acuity and smaller tumour volume may be associated with better visual field outcome as seen in our univariate analysis, it did not show statistical significance in the multivariate analysis.

Danesh-Meyer *et al.*¹⁵ had divided their subjects into two groups based on RNFL thickness into normal and thin based on 97.5% of age-matched normative data, which is higher than the default of 95% used in routine practice. Nonetheless, 15% of those grouped into the thin RNFL group had normal preoperative visual fields. The concept of preperimetric compressive optic neuropathy was described based on these data. This was also explained in theory by Sun *et al.*²³ In the 15-month follow-up data published by Meyer *et al.*²⁵ both preoperative and postoperative RNFL thickness were thinner in patients who had VFD that improved to normal postoperatively compared with those with normal preoperative fields that remained normal. This suggests that RNFL thinning is a permanent structural change due to chronic compression and irreversible retrograde degeneration, even if there is potential for visual recovery. It may be slow and ongoing and can continue even for 3–6 months following visual field recovery.²⁷ On the other hand, not all eyes with significant VFD exhibit RNFL thinning. This could be due to the acuteness of compression, such as in pituitary apoplexy, and functional recovery could be attributed to restoration of axonal transport through decompression.^{25 28} Hence RNFL thickness is a significant investigative tool regardless of visual fields. The challenge is to identify retinal microstructure parameters that can differentiate between reversible and irreversible conduction block.²⁹

RNFL thickness and visual acuity following surgery

Variable rates of improvement of visual outcome, from 44% to 93%, have been reported in the literature.^{1–5 7 8}

Table 5 Logistic regression analysis of prognostic variables

Preoperative variable	OR (SE)	P value	95% CI
For improvement in visual acuity			
Presence of disc pallor	1.5 (2.1)	0.7	0.11 to 21.5
Preoperative VFI	0.9 (0.02)	0.5	0.9 to 1.02
Average RNFL thickness	0.9 (0.03)	0.8	0.9 to 1.1
For improvement in visual field			
Presence of disc pallor	8.8 (11.3)	0.08	0.7 to 109.1
Average RNFL thickness	1.1 (0.02)	0.006*	0.01 to 1.1

* $P < 0.05$.
RNFL, retinal nerve fibre layer; VFI, visual field index.



The study by Danesh-Meyer *et al*¹⁵ reported improvement in visual acuity to more than 6/12 in 97% of eyes with thick RNFL and 72% of eyes with thin RNFL in 6 weeks ($p=0.02$). The mean preoperative RNFL thickness in their patients was $89.7\pm 20.1\ \mu\text{m}$, which was similar to our study ($89.02\ \mu\text{m}$, SD: 25.63). Meyer *et al*²⁵ later reported that improvement in visual acuity to 6/6 had evened out over 15 months between the thick and thin RNFL groups (73.4% vs 67.6%, $p=0.53$). In our study, 75% of the eyes showed an improvement in visual acuity, but there was no significant difference in the RNFL thickness between those who had improvement in acuity and those who did not. Additionally, we found that preoperative MD and VFI were worse in those with postoperative improvement in visual acuity compared with those without (table 4). Therefore, combining visual acuity and fields into a composite score to predict visual outcome in chiasmal compressions might not be prudent as they are probably independent physiological functions.

Arrangement of RNFL versus visual function

Jacob *et al*²⁴ have shown that temporal RNFL shows the maximum amount of thinning in patients with pituitary adenoma, which is also in keeping with the temporal pallor we often see in chiasmal compressions. However, they did not find temporal RNFL to be predictive of visual field improvement. Interestingly, we found that RNFL was significantly thicker in all quadrants, except the temporal in eyes that had improvement in visual fields compared with those that did not. It is likely that temporal RNFL, being mostly composed of papillomacular fibres, is more important for visual acuity than visual fields. Wang *et al*,³⁰ in a larger study, found inferior RNFL to be associated with higher odds of visual field recovery, superior RNFL to be associated with higher odds of visual acuity recovery, and that the visual improvement occurred in the first 6 weeks following surgery with no improvement thereafter. In our study, as there was no significant difference in RNFL thickness among those who had improvement in visual acuity versus those who did not, we further hypothesise that the potential for recovery of acuity might be unrelated to RNFL thickness and that other factors might be involved.

Alternative markers of visual function like RNFL thickness are all the more relevant in children where the former is unreliable. In a study by Parrozzani *et al*,³¹ the best RNFL cut-off that discriminated between normal and abnormal preoperative visual acuity in children with optic nerve glioma was $76.25\ \mu\text{m}$, which is close to the RNFL cut-off we have obtained in our study, although for predicting visual field outcome. This may suggest a possible range of RNFL thickness that could predict favourable visual outcome in tumours that affect the visual pathway. An ad-hoc analysis of a subset of 30 eyes of 15 patients, in whom data on postoperative RNFL thickness were available at 3–6 months, showed a postoperative decrease in average RNFL thickness compared with preoperative thickness by $2.37\ \mu\text{m}$ ($p<0.001$). This

suggests that RNFL thinning due to compression may be an ongoing process even after the compression is relieved; however, the sample is small to comment conclusively.

Limitations and strengths of the study

The principal strength of this study is that it is prospective. While earlier studies included chiasmal lesions other than pituitary adenomas, including meningiomas and craniopharyngiomas, operated by various routes,^{21 32} we included only pituitary macroadenoma operated transphenoidally. We also used swept-source OCT, which has better resolution, takes faster scans per second and is more sensitive as compared with time domain OCT used in prior studies.^{33 34} A limitation was that most of our subjects were international patients; hence, the follow-up time was variable. Postoperative visual fields may have been performed better by patients due to the learning effect and this could bias the results. A prospective study with larger sample size might be able to determine a cut-off for RNFL thickness with better sensitivity and specificity. We also did not study the ganglion cell layer complex (GCC), which has been reported to show thinning earlier than RNFL in cases of chiasmal compression.^{35 36} However, the advantage of using GCC over RNFL to predict visual outcome is not clear. Further studies comparing both parameters might help understand this better.

CONCLUSION

Preoperative average RNFL thickness $>81\ \mu\text{m}$ can be used as an objective predictor of postoperative visual field improvement in patients with pituitary macroadenoma. It may be used as a fair guide for counselling patients preoperatively. Since preoperative RNFL thickness did not correlate with visual acuity outcome, objective predictors of improvement in visual acuity are unclear.

Contributors Concepts: DEK, RV, SH, AGC, KP, SK. Literature search: DEK, RV, SH, AGC, KP, SK. Planning: DEK, RV, SH, AGC, SK. Design: DEK, RV, SH, AGC, GM, SK. Conduct: DEK, RV, SH, AGC, KP, GM, SK. Reporting: DEK, RV, SH, AGC, KP, GM, SK. Data acquisition: DEK, RV, SH, AGC, SK. Data analysis: DEK, RV, KP. Statistical analysis: KP. Manuscript preparation: DEK, RV, GM, SK. Manuscript editing: DEK, RV, SH, AGC, KP, GM, SK. Manuscript review: DEK, RV, SH, AGC, KP, GM, SK. Guarantor: DEK, SK.

Funding This study was funded by Christian Medical College, Vellore (IRB no: 9570).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval This study involves human participants and was approved by the Institutional Review Board of Christian Medical College and Hospital Vellore (approval no: 9570; dated 5 August 2015). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data sharing not applicable as no datasets generated and/or analysed for this study.

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REFERENCES

- Sullivan LJ, O'Day J, McNeill P. Visual outcomes of pituitary adenoma surgery. St. Vincent's Hospital 1968-1987. *J Clin Neuroophthalmol* 1991;11:262-7.
- Cohen AR, Cooper PR, Kupersmith MJ, et al. Visual recovery after transsphenoidal removal of pituitary adenomas. *Neurosurgery* 1985;17:446-52.
- Grković D, Bedov T. [Outcome of visual acuity after surgical removal of pituitary adenomas]. *Srp Arh Celok Lek* 2013;141:296-303.
- Dhasmana R, Nagpal RC, Sharma R, et al. Visual fields at presentation and after trans-sphenoidal resection of pituitary adenomas. *J Ophthalmic Vis Res* 2011;6:187-91.
- Yu F-F, Chen L-L, Su Y-H, et al. Factors influencing improvement of visual field after trans-sphenoidal resection of pituitary macroadenomas: a retrospective cohort study. *Int J Ophthalmol* 2015;8:1224-8.
- Goshtasbi K, Lehrich BM, Abouzari M, et al. Endoscopic versus nonendoscopic surgery for resection of pituitary adenomas: a national database study. *J Neurosurg* 2020;134:1-9.
- Monteiro MLR, 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;45:404-8.
- Dutta P, Gyurmei 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;64:1247.
- Müslüman AM, Cansever T, Yilmaz A, et al. Surgical results of large and giant pituitary adenomas with special consideration of ophthalmologic outcomes. *World Neurosurg* 2011;76:141-8.
- Sonmez OF, Odaci E, Bas O, et al. A stereological study of MRI and the Cavalieri principle combined for diagnosis and monitoring of brain tumor volume. *J Clin Neurosci* 2010;17:1499-502.
- Roberts N, Puddephat MJ, McNulty V. The benefit of stereology for quantitative radiology. *Br J Radiol* 2000;73:679-97.
- Lee JP, Park IW, Chung YS. The volume of tumor mass and visual field defect in patients with pituitary macroadenoma. *Korean J Ophthalmol* 2011;25:37-41.
- Holladay JT. Proper method for calculating average visual acuity. *J Refract Surg* 1997;13:388-91.
- Thomas R, Shenoy K, Seshadri MS, et al. Visual field defects in non-functioning pituitary adenomas. *Indian J Ophthalmol* 2002;50:127.
- Danesh-Meyer HV, Papchenko T, Savino PJ, et al. In vivo retinal nerve fiber layer thickness measured by optical coherence tomography predicts visual recovery after surgery for parasellar tumors. *Invest Ophthalmol Vis Sci* 2008;49:1879-85.
- Peter M, De Tribolet N. Visual outcome after transsphenoidal surgery for pituitary adenomas. *Br J Neurosurg* 1995;9:151-8.
- Monteiro MLR, 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;55:3328-36.
- Jeong AR, Kim E-Y, Kim NR. Preferential ganglion cell loss in the nasal Hemiretina in patients with pituitary tumor. *J Neuroophthalmol* 2016;36:152-5.
- Monteiro MLR, Costa-Cunha LVF, Cunha LP, et al. Correlation between macular and retinal nerve fibre layer Fourier-domain OCT measurements and visual field loss in chiasmal compression. *Eye* 2010;24:1382-90.
- Danesh-Meyer HV, Carroll SC, Foroozan 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;47:4827-35.
- Moon CH, Hwang SC, Kim B-T, et al. Visual prognostic value of optical coherence tomography and photopic negative response in chiasmal compression. *Invest Ophthalmol Vis Sci* 2011;52:8527-33.
- Amin MR, Nath HD, Hossain MA, et al. Early post-operative visual outcome in patient with pituitary adenoma. *Bangladesh Journal of Neuroscience* 2013;28:108-15.
- Sun M, Zhang Z-Q, Ma C-Y, et al. Predictive factors of visual function recovery after pituitary adenoma resection: a literature review and meta-analysis. *Int J Ophthalmol* 2017;10:1742-50.
- Jacob M, Raverot G, Jouanneau E, et al. Predicting visual outcome after treatment of pituitary adenomas with optical coherence tomography. *Am J Ophthalmol* 2009;147:64-70.
- Danesh-Meyer HV, Wong A, Papchenko T, et al. Optical coherence tomography predicts visual outcome for pituitary tumors. *J Clin Neurosci* 2015;22:1098-104.
- Garcia T, Sanchez S, Litre CF, et al. Prognostic value of retinal nerve fiber layer thickness for postoperative peripheral visual field recovery in optic chiasm compression. *J Neurosurg* 2014;121:165-9.
- Moon CH, Hwang SC, Ohn Y-H, et al. The time course of visual field recovery and changes of retinal ganglion cells after optic chiasmal decompression. *Invest Ophthalmol Vis Sci* 2011;52:7966-73.
- Al-Louzi O, Prasad S, Mallery RM. Utility of optical coherence tomography in the evaluation of sellar and parasellar mass lesions. *Curr Opin Endocrinol Diabetes Obes* 2018;25:274-84.
- Danesh-Meyer HV, Yoon JJ, Lawlor M. Visual loss and recovery in chiasmal compression, progress in retinal and eye research. *Prog Retin Eye Res* 2019;73:100765.
- Wang MTM, King J, Symons RCA, et al. Prognostic utility of optical coherence tomography for long-term visual recovery following pituitary tumor surgery. *Am J Ophthalmol* 2020;218:247-54.
- Parozzani R, Miglionico G, Leonardi F, et al. Correlation of peripapillary retinal nerve fibre layer thickness with visual acuity in paediatric patients affected by optic pathway glioma. *Acta Ophthalmol* 2018;96:e1004-9.
- Suri A, Narang KS, Sharma BS, et al. Visual outcome after surgery in patients with suprasellar tumors and preoperative blindness. *J Neurosurg* 2008;108:19-25.
- Lange AP, Sadjadi R, Saeedi J, et al. Time-Domain and spectral-domain optical coherence tomography of retinal nerve fiber layer in MS patients and healthy controls. *J Ophthalmol* 2012;2012:564627:7
- Leung D, Dul MW, Comer G. The development of a reference database with one-micron wavelength swept-source OCT dRI OCT Triton. *Invest Ophthalmol Vis Sci* 2018;59:1523
- Sun M, Zhang Z, Ma C, et al. Quantitative analysis of retinal layers on three-dimensional spectral-domain optical coherence tomography for pituitary adenoma. *PLoS One* 2017;12:e0179532.
- Cennamo G, Auriemma RS, Cardone D, et al. Evaluation of the retinal nerve fibre layer and ganglion cell complex thickness in pituitary macroadenomas without optic chiasmal compression. *Eye* 2015;29:797-802.