• Clinical Research •

Relationship between retinal nerve fibre thickness, suprasellar extension and post-operative visual outcome in pituitary macroadenoma

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Abstract

● **AIM:** To evaluate the relationship between retinal nerve fibre layer (RNFL) thickness, suprasellar extension (SSE), tumour volume (TV) and visual outcome after pituitary adenoma surgery.

● **METHODS:** A prospective observational study was conducted in a tertiary teaching hospital which included patients with pituitary macroadenoma who required surgical resection between December 2015 to February 2020. Agreeable subjects underwent complete ocular examination, Humphrey visual field (HVF) and RNFL measurement using spectral domain optical coherence tomography preoperatively and 3-month postoperatively. Post-operative visual outcome was evaluated using both best-corrected visual acuity (BCVA, logMAR) and HVF mean deviation (MD). TV was estimated by multiplying the transverse, anteroposterior, and craniocaudal maximum diameter; and SSE by measuring tumour extension beyond the supraclinoid internal carotid artery from magnetic resonance imaging.

● **RESULTS:** Thirty-eight patients (18 males) were recruited. The mean age was 47.6±14.8y. The median and interquartile range (IQR) was 10.78 (6.45–16.94) cm^3 and 14.05 (4.99–22.90) mm for TV and SSE, respectively. While postoperative RNFL significantly reduced in all sectors, significant improvement was seen in median BCVA in logMAR (from 0.301 to 0.176, P<0.001) and MD of HVF (from -10.04 to -3.91, P<0.001). Pre-operative global RNFL was significantly correlated with post-operative logMAR (r=-0.303, P=0.015) and MD (r=0.510, P<0.001). Only SSE showed significant negative correlations with all RNFL sectors. Each 10 μm thicker pre-operative global RNFL was associated with 0.13 lower (better) postoperative logMAR (β=-0.013, P<0.001) and 0.83 dB higher (better) MD (β=0.083, P=0.008). Patients with normal RNFL had better post-operative MD [median (IQR)=-2.35 (-1.45, -5.94)] than with thinned RNFL [median (IQR)=-6.63 (-2.80, -8.77), P=0.009].

● **CONCLUSION:** SSE shows stronger association with RNFL thinning than TV, and thicker pre-operative RNFL predicted better post-operative visual outcomes.

● **KEYWORDS:** optical coherence tomography; pituitary macroadenoma; retinal nerve fibre layer; visual outcome; suprasellar extension

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INTRODUCTION

Pituitary adenoma comprises approximately 10%–15% of all primary intracranial neoplasms. The estimated prevalence was reported to be around 17% to 20%, although only a third manifests[1]. The size divides it into microadenoma (less than 10 mm) and macroadenoma (10 mm or more). Visual disturbances result from its proximity to the nerve fibres at the optic chiasm and tract. While all patients require endocrine evaluation for hormone hyper or hyposecretion, macroadenomas particularly require visual field evaluation[2].

While most patients achieve favourable outcomes with observation or a single treatment modality[3], surgical resection remains the treatment of choice in visually symptomatic pituitary tumours with chiasmal compression. Surgery is also a treatment of choice in secretory tumours which have failed medical therapy. Surgical resection provides prompt relief from mass effect and excess hormone secretion regardless of tumour size[4].

Visual outcome varies following pituitary tumour resection, partly affected by the compressive effect of the tumour on the retinal nerve fibre bundle. However, irreversible axonal loss will invariably result in non-recovery in patients with chiasmal compression[5]. The optical coherence tomography (OCT) provides an objective measurement of the retinal nerve fibre layer (RNFL) thickness. RNFL thinning was shown to be topographically related to location and severity of visual field defect in compressive optic neuropathies[5]. Several studies using the time-domain OCT have shown that measurement of the preoperative RNFL was useful in predicting the visual outcome after surgery[5-7]. The spectral-domain OCT (SD-OCT) provides higher resolution images with reduced speckle noise. In the more recent studies, SD-OCT has been used to analyse the retinal layers quantitatively in patients with pituitary adenoma compared to normal patients[8-10].

Unlike recent studies that focus primarily on retinal structural parameters alone, our study uniquely integrates RNFL thickness with objective radiological metric, specifically suprasellar extension (SSE) and tumour volume (TV) to evaluate their relative influence on postoperative visual recovery. We aim to predict the post-operative visual outcome using the RNFL measured with the SD-OCT, and asses its correlation with SSE and TV following tumour resection in patients with pituitary macroadenoma. Recent evidence shows that preoperative RNFL thinning correlates strongly with postoperative visual outcomes in pituitary macroadenoma patients, reinforcing structural assessment as a predictive tool[11]. Based on previous reports of limited visual field improvement in patients with thinner postoperative RNFL[5-6,12], we hypothesise that a thinner preoperative RNFL in SD-OCT predicts a poorer postoperative visual outcome after surgery.

PARTICIPANTS AND METHODS

Ethical Approval This study was approved by the Research and Ethics Committee of Universiti Kebangsaan Malaysia (Approval No. UKM 1.5.3.5/244/FF-2016-005) and conformed to the tenets of the Helsinki Declaration. Informed consent was obtained from all patients.

This was a prospective observational study involving patients with treatment naïve pituitary macroadenoma (largest diameter >1 cm) who presented to the neurosurgery or ophthalmology departments from December 2015 to February 2020. Patients who did not undergo surgery, those with recurrent tumour, history of previous treatment, diabetics with severe non-proliferative or proliferative diabetic retinopathy; or had significant retinal anomalies such as those who had received panretinal photocoagulation treatment and macular oedema; patients with dense cataract, high myopia, and patients with other causes of optic neuropathy such as glaucoma, were excluded.

Patients were recruited based on convenient sampling. Best corrected visual acuity (BCVA) were assessed using the Snellen chart with pinhole and refraction where applicable. Visual acuity values were converted to logarithm of the minimum angle of resolution (logMAR) for ease of analysis. Vision of counting fingers, hand movements, perception of light and no perception of light were assigned logMAR of 2.10, 2.40, 2.70, and 3.00, respectively. A complete slit lamp biomicroscopy examination, Humphrey visual field (HVF) examination and RNFL measurements were also done a week prior and at 3mo after surgery.

RNFL thickness was measured with the SD-OCT Heidelberg Spectralis™ (Heidelberg Engineering, Heidelberg, Germany) by an experienced technician (Saiful Anwar A) using a circumpapillary 30°×30° field of view lens and segmented into 6 standard sectors: superotemporal, superonasal, inferotemporal, inferonasal, nasal, and temporal sectors. The global RNFL represents the average RNFL thickness. Automated visual field was carried out using the Swedish Interactive Threshold Algorithm 24-2 of the Humphrey Field Analyzer programme (Carl Zeiss Meditec, Inc). A size III stimulus was used for all patients. VF deficit was quantified using the mean deviation (MD) in decibel (dB)[5-6]. The reliability of the test was indicated by fixation loss of less than 20%, and false positive and negative rates of less than 33%. Only reliable tests were included in the analysis.

Magnetic resonance imaging (MRI) of the brain was studied to determine TV and SSE using axial and coronal cuts. The maximum tumour diameters were measured in transverse, anteroposterior and craniocaudal planes. TV was estimated by multiplying all three measurements. SSE was identified by measuring the superior extension of the pituitary lesion from the supraclinoid internal carotid artery as the landmark, which is located lateral to the optic chiasm. Tumour size was further categorised into small (>1 cm to ≤2 cm), large (>2 cm to ≤4 cm), and giant adenoma (>4 cm) according to their largest diameter.

All patients underwent surgical decompression of the tumour by an experienced neurosurgeon (Thanabalan J). Transsphenoidal tumour resection was used unless the tumour was too large which required a transcranial approach. The transsphenoidal approach involves partial middle and superior turbinectomies after the nose was packed with modified moffat ribbon gauze. Posterior ethmoidectomy and septectomy were

then performed to allow access to the anterior wall of the sphenoid sinus. The sphenoid rostrum was identified, drilled and opened to expose the sellar floor which was also drilled to allow entry into the sellar turcica using a Kerrison punch. The tumour was then identified and removed in piecemeal using curette and gentle suction. The transcranial tumour resection involves a reversed U-shaped incision made on the frontotemporal scalp followed by pterional craniotomy. Curvilinear durotomy was performed to expose the temporal lobe. Intracapsular tumour dissection was then performed and delivered in piece meal manner. Postoperatively, patients were monitored in the intensive care unit and treated as per post-operative protocol.

Post-operative visual outcome was defined as the combination of BCVA (logMAR) and visual field function (HVF, MD), and these measures were used to assess the relationship with RNFL thickness and SSE in patients with pituitary macroadenoma. All data were analysed using the Statistical Package for Social Sciences (SPSS, Version 23, IBM Corp. Armonk, NY). Data normality was assessed with the Kolmogorov-Smirnov test. Continuous data were expressed as mean±standard deviation and median and interquartile range (IQR) for normally distributed and skewed data respectively. Categorical variables were described as frequency (*n*) and percentages. Wilcoxon signed ranks test was used to analyse the changes in BCVA, MD, and RNFL thickness after pituitary surgery. Spearman correlation was used to determine the relationship of the tumour size with other study parameters.

The difference in global circumpapillary RNFL thickness based on the surgical approach (transcranial and transsphenoidal) was assessed using the Mann-Whitney *U* test. The differences in BCVA and MD between patients with normal and thinned global RNFL were analysed using Mann-Whitney *U* test. Kruskal-Wallis analysis of variance (ANOVA) test was used to analyse the difference in visual functions across the three categories of tumour size. Statistical significance was accepted when $P<0.05$.

RESULTS

Of the 62 patients identified, 17 were excluded as they did not undergo surgery. Forty-five patients who met the inclusion and exclusion criteria underwent either transsphenoidal or transcranial resection. Thirty-eight patients (76 eyes) completed the study, while 7 patients were lost to follow-up or were too ill to come for their postoperative assessment. Patients' demographics, median TV, and SSE are shown in Table 1.

Pre-operative median BCVA and MD were 0.301 (IQR=0.176–0.602) and -10.04 (IQR=-4.72 to -17.72), respectively. After surgical resection, there were significant improvements in both BCVA and MD at 3mo postoperatively. However, there was significant reduced RNFL thickness in all sectors. The changes of all the three parameters are summarised in Table 2. Sectoral analysis revealed that the horizontal sectors (temporal and nasal) exhibited greater thinning, with an average reduction of 3.25 μm, compared to the vertical sectors, which showed an average thinning of 2.25 μm.

Table 1 Patients' demographics and tumour size at baseline *n* (%)

Characteristics	Data
Age, y, mean±SD (range)	47.6±14.8 (22 to 71)
Sex	
Male	18 (47)
Female	20 (53)
Ethnicity	
Malay	21 (55)
Chinese	17 (45)
Surgical approach	
Transsphenoidal	32 (84)
Transcranial	6 (16)
Category of macroadenoma	
Small	9 (23.7)
Large	25 (65.8)
Giant	4 (10.5)
Tumour volume, cm^3, median (IQR)	10.78 (6.45–16.94)
Suprasellar extension, mm, median (IQR)	14.05 (4.99–22.90)

SD: Standard deviation; IQR: Interquartile range.

Correlations between pre-operative peripapillary RNFL thickness and post-operative visual function (BCVA and MD) were analysed and are shown in Table 3. There was a significant correlation between global RNFL thickness and post-operative BCVA (r=-0.303, P=0.015) and MD (r=0.510, P<0.001) at 3mo.

Simple linear regression was used to test if pre-operative global RNFL significantly predicted post-operative visual outcome. The fitted regression model for post-operative BCVA was BCVA=1.579−(0.013×pre-operative global RNFL thickness). The overall regression was statistically significant [R^2=0.230, F=18.47, P<0.001]. The fitted regression model for post-operative MD was MD=-13.475+(0.083×pre-operative global RNFL thickness). The overall regression was also statistically significant [R^2=0.139, F=7.60, P=0.008]. The pre-operative global RNFL thickness significantly predicted post-operative BCVA (β=-0.013, P<0.001) and MD (β=0.083, P=0.008). On average, every 10 μm thicker pre-operative global RNFL was associated with 0.13 lower (better) post-operative BCVA in logMAR and 0.83 dB higher (better) MD. The regression analyses are illustrated in Figure 1 (BCVA *vs* RNFL thickness) and Figure 2 (MD *vs* RNFL thickness), both showing the positive association between thicker pre-operative RNFL and better postoperative visual outcomes.

Correlation analysis revealed both TV and SSE were significantly correlated with BCVA and MD. However, only SSE showed significant negative correlation with RNFL

Table 2 Changes in BCVA, MD and peripapillary RNFL thickness after surgical decompression of pituitary macroadenoma (*n*=76) median (IQR)

Parameters	Pre-operation	Post-operation (3mo)	Changes	*P*[a]
BCVA (logMAR)	0.301 (0.176–0.602)	0.176 (0–0.301)	-0.125	<0.001
MD of HVF	-10.04 (-4.72 to -17.72)	-3.91 (-1.75 to -7.64)	6.13	<0.001
Peripapillary RNFL thickness (μm)				
Superotemporal	135.00 (102.25–145.75)	133.50 (88.50–144.50)	-1.50	<0.001
Superonasal	93.50 (75.25–118.50)	91.00 (61.00–117.00)	-2.50	0.001
Inferotemporal	145.00 (124.00–162.25)	144.00 (103.25–162.25)	-1.00	0.001
Inferonasal	108.00 (75.25–124.25)	104.00 (64.75–122.00)	-4.00	0.001
Temporal	69.00 (45.00–82.00)	64.50 (39.00–80.00)	-4.50	<0.001
Nasal	58.50 (48.00–72.75)	56.50 (39.25–70.75)	-2.00	0.003
Global	91.00 (76.50–106.75)	90.00 (58.50–106.75)	-1.00	<0.001

[a]Wilcoxon Signed Rank test. Significant *P*-value<0.05. BCVA: Best corrected visual acuity; MD: Mean deviation; HVF: Humphrey visual field, RNFL: Retinal nerve fibre layer; IQR: Interquartile range; logMAR: Logarithm of the minimum angle of resolution.

Table 3 Correlations between preoperative RNFL and post-operative visual function (*n*=76)

Pre-operative peripapillary RNFL thickness	Post-operative BCVA		Post-operative MD of HVF	
	Correlation coefficient (*r*)	*P*[d]	Correlation coefficient (*r*)	*P*[d]
Superotemporal	-0.388	0.002	0.329	0.021
Superonasal	-0.276	0.027	0.508	<0.001
Inferotemporal	-0.263	0.036	0.277	0.054
Inferonasal	-0.156	0.218	0.323	0.023
Temporal	-0.249	0.047	0.410	0.003
Nasal	-0.230	0.067	0.429	0.002
Global	-0.303	0.015	0.510	<0.001

[d]Spearman's correlation test. Significant *P*-value<0.05. RNFL: Retinal nerve fibre layer; BCVA: Best corrected visual acuity; MD: Mean deviation; HVF: Humphrey visual field.

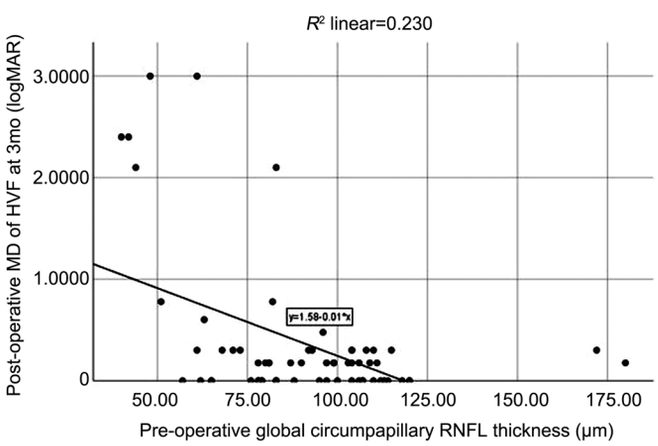

Figure 1 Simple scatter plot of post-operative BCVA in logMAR at 3mo by pre-operative global circumpapillary RNFL thickness BCVA: Best corrected visual acuity; logMAR: Logarithm of the minimum angle of resolution; RNFL: Retinal nerve fibre layer.

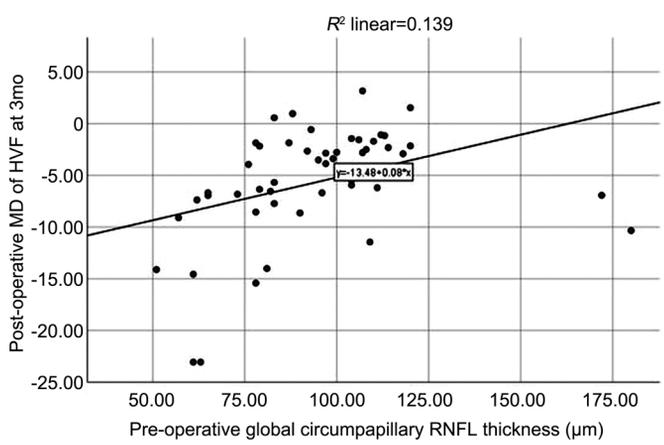

Figure 2 Simple scatter plot of post-operative mean deviation (MD) of Humphrey visual field (HVF) at 3mo by pre-operative global circumpapillary retinal nerve fibre layer (RNFL) thickness.

thickness in all sectors. TV did not show any correlation with RNFL thickness except for the nasal sector (*r*=-0.298, *P*=0.017). The correlation analysis is summarised in Table 4.

Of the 38 patients, 32 underwent transsphenoidal resection, while 6 patients underwent transcranial resection of the tumour. Both groups showed significant reduction in global RNFL thickness postoperatively. Median global RNFL thickness improved from 95.50 (IQR: 78.75–107.00) to 92.50 (IQR: 70.75–107.25) μm, *P*=0.001 in patients who underwent transsphenoidal surgery and from 78.00 (IQR: 48.75–103.75) to 54.00 (IQR: 41.25–103.75) μm, *P*=0.043 in patients who underwent transcranial surgery. The changes in global RNFL thickness are summarised in Table 5.

Table 6 summarised the changes of visual function according to RNFL thickness and tumour size. We found out that both

Table 4 Correlation between size of pituitary tumour and pre-operative BCVA, MD, and peripapillary RNFL thickness (*n*=76)

Pre-operative parameters	TV		SSE	
	Correlation coefficient (*r*)	*P*[d]	Correlation coefficient (*r*)	*P*[d]
BCVA (logMAR)	0.327	0.004	0.393	<0.001
MD of HVF	-0.514	<0.001	-0.540	<0.001
Peripapillary RNFL thickness (μm)				
Superotemporal	-0.063	0.619	-0.477	<0.001
Superonasal	-0.193	0.126	-0.600	<0.001
Inferotemporal	-0.179	0.157	-0.505	<0.001
Inferonasal	-0.170	0.180	-0.551	<0.001
Temporal	-0.088	0.490	-0.376	0.002
Nasal	-0.298	0.017	-0.591	<0.001
Global	-0.216	0.086	-0.629	<0.001

[d]Spearman's correlation test. Significant *P*-value<0.05. TV: Tumour volume; SSE: Suprasellar extension; BCVA: Best corrected visual acuity; MD: Mean deviation; HVF: Humphrey visual field; RNFL: Retinal nerve fibre layer; logMAR: Logarithm of the minimum angle of resolution.

Table 5 Global RNFL thickness changes in transsphenoidal and transcranial surgery median (IQR)

Type of surgery	Global RNFL thickness (μm)			
	Pre-operation	Post-operation	*P*[a]	Changes of RNFL thickness
Transsphenoidal (*n*=32)	95.50 (78.75–107.00)	92.50 (70.75–107.25)	0.001	-1.50 (-6.50 to 0.25)
Transcranial (*n*=6)	78.00 (48.75–103.75)	54.00 (41.25–103.75)	0.043	-0.50 (-21.25 to 0.00)
P[b]	0.073	0.058		0.452

[a]Wilcoxon Signed Rank test; [b]Mann-Whitney *U* test. Significant *P*-value<0.05. RNFL: Retinal nerve fibre layer; IQR: Interquartile range.

Table 6 Visual function changes according to RNFL thickness and tumour size median (IQR)

Parameters	BCVA (logMAR)			MD of HVF		
	Pre-operation	Post-operation	*P*	Pre-operation	Post-operation	*P*[a]
Pre-operative global RNFL thickness (μm)						
Normal RNFL thickness (*n*=28)	0.176 (0.176–0.447)	0.088 (0–0.301)	0.001[a]	-4.88 (-2.75 to -8.91)	-2.35 (-1.45 to -5.94)	0.002
Thinned RNFL (*n*=48)	0.540 (0.207–1.477)	0.176 (0–0.433)	<0.001[a]	-13.97 (-9.36 to -19.22)	-6.63 (-2.80 to -8.77)	<0.001
P[b]	0.003	0.106		<0.001	0.009	
Tumour size						
>1 cm to ≤2 cm (small; *n*=9)	0.176 (0–0.345)	0.088 (0–0.176)	0.159[a]	-4.61 (-2.38 to -10.69)	-3.07 (-0.65 to -7.96)	0.005
>2 cm to ≤4 cm (large; *n*=25)	0.477 (0.301–0.702)	0.176 (0–0.301)	<0.001[a]	-10.38 (-6.09 to -18.57)	-3.91 (-1.78 to -6.94)	<0.001
>4cm (giant; *n*=4)	0.540 (0.176–1.825)	0.327 (0.044–2.244)	0.735[a]	-14.76 (-3.85 to -23.19)	-10.87 (-4.00 to 16.59)	0.463
P[c]	<0.001	<0.001		0.118	0.024	

[a]Wilcoxon Signed Rank test; [b]Mann-Whitney *U* test; [c]Kruskal Wallis test. Significant *P*-value <0.05. RNFL: Retinal nerve fibre layer; BCVA: Best corrected visual acuity; MD: Mean deviation; HVF: Humphrey visual field; IQR: Interquartile range; logMAR: Logarithm of the minimum angle of resolution.

normal and thinned RNFL groups had significant improvement of BCVA and MD after 3mo post-surgery. Patients with normal RNFL thickness had better post-operative BCVA [0.088 (0–0.301) *vs* 0.176 (0.00–0.433)] and MD [-2.35 (-1.45 to -5.94) *vs* -6.63 (-2.80 to -8.77)] than patients with thinned RNFL. However, the difference was only statistically significant for post-operative MD (*P*=0.009). Pituitary macroadenoma was also further divided into small, large, and giant macroadenoma based on the largest diameter of the lesions. Both median BCVA and MD significantly improved in patients with large pituitary mass [BCVA from 0.477 (IQR=0.301–0.702) to 0.176 (IQR=0–0.301), *P*<0.001 and MD from -10.38 (IQR=-6.09 to -18.57) to -3.91 (IQR=-1.78 to -6.94), *P*<0.001]. Small pituitary mass (>1 cm to ≤2 cm) only showed significant improvement in MD but not in BCVA at 3mo. However, there was no significant improvement in both BCVA and MD in patients with giant pituitary mass (>4 cm). Giant tumours were associated with worse BCVA and MD compared to small and large tumours with *P*-value of <0.001 and 0.024, respectively.

DISCUSSION

Pituitary adenoma, because of its close proximity to the optic chiasm, often causes progressive vision loss in one or both eyes, both with reduced vision and visual field defect[13]. Various pathophysiology for this was proposed including ischemic damage, demyelinating lesions, retrograde degeneration, and anterograde degeneration; manifested as the

thinning of the ganglion cell complex layer in the retina[14-15].

OCT is a non-invasive imaging technique that allows objective *in vivo* quantification of glaucomatous structural changes in the retina and optic nerve head[16]. OCT may detect early structural changes in optic nerve fibres even in absence of obvious visual field defects[17-18]. We analysed the RNFL thickness using SD-OCT to predict the visual outcome in patients with pituitary adenoma.

Our study subjects demonstrated post-operative progressive RNFL thinning in all sectors 3mo after pituitary surgery. On the contrary, some researchers found no change in RNFL thickness after pituitary surgery[8,19]. Both studies, however, have a relatively smaller sample size of 20 and 24 patients, respectively. The recovery of visual function after surgery has always been of interest. Beyond RNFL analysis, recent studies have highlighted the diagnostic and prognostic role of the ganglion cell complex in chiasmal compressive optic neuropathy[20]. Meanwhile, RNFL thickness was observed to continue decreasing until 3y after surgery[21]. This suggests that RNFL loss is not transient but a continuous process. Other postulated mechanisms for RNFL loss in pituitary macroadenoma other than from mechanical compression include iatrogenic thinning due to the proximity of pituitary mass with the optic chiasm, postoperative oedema, and compromised perineural microcirculation which is metabolically important to maintain nerve conduction and axonal transport[22]. Neuronal and axonal loss diminishes metabolic activity in the inner retinal layers, leading to reduced oxygen and blood demand and, consequently, regression of the superficial vessels[23].

In our study, postoperative RNFL thinning was observed in all sectors, yet patients still demonstrated functional improvement in visual acuity and visual field. This structural-functional dissociation has also been explored in other studies, where circumpapillary and macular vessel density were shown to correlate with RNFL thickness, ganglion cell complex changes, and visual field defects[24]. Macular ganglion cell layer metric has also been shown to complement peripapillary RNFL measurements in predicting long-term visual recovery after decompression surgery[25]. Based on one of the studies, considerable reduced RNFL thickness was observed in all quadrants in patients with visual field defects (complete bitemporal hemianopia and concentric narrowing) in comparison with patients who had normal visual field (P<0.001)[26]. In our study, RNFL thinning was evident at 3-month follow-up, but earlier timepoints were not measured; therefore, the onset of thinning prior to 3mo cannot be determined. A longer follow up may show further progression of RNFL thickness after surgery.

However, while reduced RNFL thickness was seen, our findings showed a trend towards functional improvement of visual outcome with improved BCVA and MD following surgery agreeing with previous studies[10,21,27-29]. The improvement occurs in a continuous manner, overlapping between the early and late stages. Within the first few days after surgery, there is direct decompression of the retinal nerve fibres and increased conduction of sodium channels. After approximately 6mo, remyelination of the axons starts to take place, explaining the improved visual function after the mechanical blockage relief[27-28]. Recent evidence suggests that visual recovery following pituitary adenoma surgery is influenced not only by mechanical decompression but also by pre-existing retinal structural integrity and microvascular status, supporting the use of OCT-derived parameters as meaningful predictors of postoperative visual outcome[30].

Predictability of visual field recovery after optic chiasm decompression in pituitary macroadenoma underscores the value of incorporating objective structural markers, such as RNFL thickness, into preoperative assessment[31]. Studies looking at RNFL thickness measured with a time domain-OCT in predicting postoperative vision showed that a thinner preoperative RNFL resulted in reduced postoperative visual field recovery. A strong correlation between the RNFL thickness particularly in the nasal and temporal quadrants with the severity of visual field loss was documented[5-7]. Danesh-Meyer *et al*[29] showed that 77.6% of eyes with normal RNFL achieved a normal MD of greater than -2.0 compared to only 21.7% of those with thinned RNFL. When measured with an SD-OCT, we found no specific sector of the RNFL thickness correlated with the visual outcome except for global RNFL thickness. However, our sectoral analysis in Table 2 showed that the horizontal sectors (temporal and nasal) exhibited greater thinning compared to the vertical sectors, consistent with the characteristic “bow-tie” atrophy pattern seen in chiasmal compression. This provides quantitative support for the statement of preferential horizontal thinning.

When OCT shows a decrease in RNFL thickness, this must be considered an alarm sign even without impairment in visual field or visual acuity[26]. Patients with chiasmal compression have a greater degree of thinning in the nasal macula due to disruption of crossing fibres originating in the nasal retina[8]. We observed that a thicker preoperative global RNFL thickness resulted in better post-operative visual functions, including BCVA and MD, contradicting with Póczoš *et al*[32], who reported that preoperative RNFL thinning could not predict poor postoperative visual function recovery. We found that the global RNFL thickness was predictive of prognosticating the post-operative visual outcomes. We recommend performing the SD-OCT to measure the RNFL prior to pituitary surgery as this allows the operating surgeon to better prognosticate,

counsel on the possible postoperative outcome and decide the timing of surgery.

Transsphenoidal surgery is typically considered for prolactin-secreting tumors unresponsive to medical therapy, those with significant side effects from dopamine agonists, and those planning for pregnancy when the tumor exceeds 1 cm in size[33]. In our study, we found no statistically significant difference in global RNFL thickness between the transsphenoidal and transcranial groups. However, this could be attributed to the smaller sample size in the transcranial surgery group, which was only 6 patients (12 eyes). Although not statistically significant, patients in the transcranial surgery group had a thinner pre-operative global RNFL thickness compared to the transsphenoidal group. This is because most of the patients who underwent transcranial surgery were those with a larger pituitary mass. Interestingly, patients who had transcranial surgery were reported more likely to have progressive RNFL thinning at 3mo post-operatively than patients who underwent transsphenoidal surgery[34]. Meaningful visual field improvement was noticed following endoscopic transsphenoidal surgery for pituitary adenoma and have proposed predictive models incorporating preoperative clinical and radiological factors to estimate postoperative visual recovery[35]. In our cohort, the transcranial group consisted of only six patients, making the subgroup comparison underpowered and preliminary; larger studies are needed to confirm whether surgical approach independently influences RNFL changes.

We used TV and SSE as our objective measurement of tumour size. Recent studies have highlighted optic chiasm morphometric parameters, including chiasmal volume and SSE distance as significant predictors of visual recovery[36-37]. Similarly, in our study, SSE demonstrated significant correlations across all RNFL sectors, whereas TV was only correlated with the nasal sector. This finding supports the view that SSE is a stronger and more consistent predictor of RNFL damage than overall TV. A large tumour could invade the sella and cavernous sinus without affecting the optic chiasm. By demonstrating that SSE shows stronger and more consistent correlations with RNFL thinning than TV, our findings provide clinically relevant insight into structural predictors of visual prognosis that are not captured by size metrics alone. This also supports the concept that the direction of tumour growth relative to the optic chiasm is more clinical meaningful than absolute tumour size. Advanced radiological approaches, such as delta-radiomics of the optic chiasm derived from serial MRI, have recently been shown to predict postoperative visual recovery in pituitary adenoma patients, highlighting the growing role of quantitative imaging biomarkers alongside conventional anatomical assessment[38-39]. A 2024 retrospective study of 142 patients showed that higher preoperative RNFL values and lower suprasellar TV were associated with better visual field MD and visual acuity recovery at 12mo after surgery, supporting the relevance of structural imaging markers in predicting functional outcome[40]. Other factors affecting visual outcome has also been reported, including age, duration of symptoms, type and size of tumour, pre-operative visual acuity, and visual field defect[38].

To further evaluate the effect of tumour size on the visual outcome of patients with pituitary adenoma, a subgroup analysis of the tumour size was done. We found both postoperative BCVA and MD improved significantly in large macroadenoma, consistent with other studies[26-27]. In our study, patients with small macroadenoma only had significant improvement in MD but not in BCVA, possibly because of good baseline BCVA in patients with small tumours. Patients with giant macroadenoma had the poorest visual function preoperatively which did not improve significantly after surgery, suggesting a poorer visual prognosis in these groups of patients. These results show the importance of early surgical intervention in patients with larger tumours to preserve their visual functions.

One of the limitations in our study is the short follow-up period of 3mo. This timeframe may not fully capture the long-term course of both structural and functional changes, as RNFL thinning and visual recovery may continue to evolve over 6–12mo or longer. Future studies with extended follow-up provide more comprehensive insights into these trajectories. Another important limitation is the apparent paradox between progressive RNFL thinning and improved visual function observed in our cohort. Possible mechanisms include Wallerian degeneration of damaged axons, delayed retrograde degeneration, surgical trauma, or ischemic changes affecting the optic pathways[5,21]. These factors may explain why structural decline can persist despite functional gains.

The comparison of RNFL changes between surgical approaches (transsphenoidal *vs* transcranial) should also be interpreted with caution. While our data suggested a trend toward greater RNFL thinning after transcranial surgery, the small number of patients in this subgroup (n=6) limits statistical reliability, and the differences may reflect baseline tumour size and surgical complexity rather than a true approach-related effect. Our study is also limited by a relatively small sample size and being conducted in a single tertiary centre. Subgroup analyses, such as those involving patients with giant adenomas or those undergoing transcranial surgery, are therefore underpowered, and conclusions from these groups should be regarded as exploratory rather than definitive. While TV was calculated by multiplying the diameters of three different dimensions, in reality tumors are not square. This method is a simplication,

and more accurate three-dimensional volumetric segmentation techniques such as region of interest-based volume should be considered in future research to improve precision. Future multicentre studies with longer follow-up and advanced volumetric segmentation techniques may further refine prognostic modelling.

While postoperative RNFL declines after surgery as opposed to visual functions, patients with thicker or normal RNFL were more likely to regain visual function, underscoring the prognostic value of preoperative RNFL thickness. Moreover, SSE showed stronger and more consistent correlations with RNFL thinning than TV, highlighting its importance as a structural predictor of visual outcome. These findings support the clinical utility of SD-OCT-based RNFL assessment in preoperative counselling which may aid surgical timing decisions and prognostication of patients undergoing pituitary adenoma resection.

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