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Original Research Article

Structure–Function Correlation Between Visual Field Parameters and Retinal Nerve Fiber Layer Thickness in Patients with Primary Glaucoma

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Abstract:

Background: Glaucoma is a chronic optic neuropathy that involves progressive changes to the retinal nerve fiber layer (RNFL) and resulting changes to the function of the visual field. Assessment of structural and functional changes is required for early diagnosis and monitoring of glaucoma. Optical Coherence Tomography (OCT) is an objective measure of RNFL thickness and Standard Automated Perimetry (SAP) is the gold standard measure of visual field defects. Knowing how these parameters are related is critical for glaucoma management.

Objectives: To assess the correlation between visual field parameters and retinal nerve fibre layer thickness in patients with primary glaucoma.

Methodology: This is an observational cross-sectional study which was carried out in the Department of Ophthalmology, Narayan Medical College and Hospital,Sasaram, Bihar in 24 months. 78 patients (156 eyes) with primary glaucoma were enrolled. All participants received complete ophthalmic examination, Standard Automated Perimetry with Humphrey Field Analyzer (HFA) and retinal nerve fiber layer (RNFL) assessment with Spectral-Domain Optical Coherence Tomography (SD-OCT). Visual field indices: Mean Deviation (MD), Pattern Standard Deviation (PSD), and Visual Field Index (VFI) were correlated with RNFL thickness measurements.

Results: The mean RNFL thickness was 76.39 ± 21.78 µm. A significant positive correlation was seen between the RNFL thickness and Mean Deviation ($\rho = 0.682$, $p < 0.001$) and Visual Field Index ($\rho = 0.658$, $p < 0.001$). Moderate negative correlation was observed between the thickness of RNFL and Pattern Standard Deviation ($\rho = -0.486$, $p < 0.001$). A progressive thinning of the RNFL was correlated with increasing severity of glaucoma, which suggests deteriorating structure and function.

Conclusion: The findings obtained from the study of thickness of the RNFL by SD-OCT demonstrated a good correlation with the results of visual field in primary glaucoma. Structural and functional assessment is an integrated approach that enhances the diagnosis, staging and monitoring of glaucoma, allowing for earlier identification of glaucoma progression and improved preservation of visual function.

Keywords: Primary Glaucoma, Retinal Nerve Fiber Layer, Optical Coherence Tomography, Standard Automated Perimetry, Visual Field Index, Mean Deviation, Structure–Function Correlation.

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Introduction

Glaucoma is a leading cause of permanent blindness globally and is a major public health problem in ophthalmology. Glaucoma is responsible for around 12% of blindness worldwide and affected more than 76 million people in 2020, with this number expected to increase to almost 111.8 million by 2040 due to population ageing and increasing life expectancy, especially in developing countries of Asia and Africa where access to eye-care services is still limited [1,2] , reports the World Health Organization (WHO).The disease is characterised by progressive degeneration of the retinal ganglion cells (RGCs) and their axons leading to recognisable structural alteration of the optic nerve head (ONH) and concomitant vision field deficit [3]. Permanent vision loss and blindness can result from untreated glaucoma and can have a serious impact on the quality of life of those affected.

While high intraocular pressure (IOP) is the most important modifiable risk factor for glaucoma, the disease process is complicated. Its pathophysiology has been attributed to several factors including vascular dysregulation, oxidative stress, neurodegeneration, hereditary susceptibility and biomechanical changes of the optic nerve head [4] . Moreover, disease development can occur in the presence of normal IOP, highlighting the complexity of glaucomatous optic neuropathy and the necessity of thorough diagnostic techniques [5] .

Patients with glaucoma are often asymptomatic until significant and irreversible damage has occurred, earning the disease the moniker of "silent thief of sight". Peripheral visual field loss is slow and is typically unrecognised by the patients [6]. Central vision is generally spared until the advanced stages of the disease. Therefore, early diagnosis and quick treatments are essential to prevent visual impairment and preserve visual function. However, a key issue in the management of glaucoma is the dissociation of structural damage and functional loss in the early stages of the disease.

Structural damage to the retinal ganglion cells and their axons occurs before functional abnormalities can be detected with routine visual field testing, as established in a number of histological and clinical studies. It has been estimated that 30–50% of the retinal ganglion cells could be destroyed before the distinctive visual field abnormalities are observed on standard automated perimetry (SAP) [7]. This structural-functional separation emphasises the necessity of sensitive imaging technology that can detect early glaucomatous damage before the onset of permanent functional impairment.

The advent of Optical Coherence Tomography (OCT) and more specifically Spectral-Domain Optical Coherence Tomography (SD-OCT) has revolutionised the diagnosis and monitoring of glaucoma. OCT delivers non-invasive and reproducible cross-sectional imaging of the retinal structures with high resolution enabling accurate assessment of the retinal nerve fibre layer (RNFL) thickness. Thinning of the RNFL is thought to be one of the early structural signs of glaucomatous damage and has been found to precede clinically evident visual field abnormalities [8]. Therefore, SD-OCT peripapillary RNFL thickness measurement has become an important part of the glaucoma work-up to allow earlier detection of disease and more effective monitoring of progression.

Despite breakthroughs in structural imaging Standard Automated Perimetry (SAP) remains the gold standard for assessment of functional vision loss in glaucoma. Automated perimetry is most typically accomplished with the Humphrey Field Analyser (HFA) which permits quantitative evaluation of visual field defects and essential indices such as Mean Deviation (MD), Pattern Standard Deviation (PSD) and Visual Field Index (VFI). These indicators are frequently used for staging disease severity, for monitoring illness progression and for evaluation of therapy outcomes [9]. However, SAP is essentially subjective and may be affected by patient cooperation, weariness, learning effects, fixation losses and response variability. Such limits may restrict its sensitivity in detecting early glaucomatous damage when the visual field deficiencies are mild.

Contemporary glaucoma care increasingly focuses on a combined structure-function approach since glaucoma affects structural and functional components of the visual system concurrently. The correlation between the OCT-measured RNFL thickness and visual field characteristics determined by automated perimetry has been the subject of many studies. Many investigations have shown substantial associations between decreasing RNFL thickness and worsening visual field indices, supporting the hypothesis that structural and functional alterations evolve simultaneously throughout the course of the disease [10]. However, the strength of this correlation varies with the severity of the disease. In early glaucoma, structural measures are often more sensitive than functional testing, but in advanced disease a 'floor effect' in OCT measurements may limit further ability to identify progression, making visual field assessment more helpful [11].

Glaucoma seen in the clinical practice is mostly primary glaucoma which can be further classified into Primary Open-Angle Glaucoma (POAG) and Primary Angle-Closure Glaucoma (PACG). India has a very large burden of glaucoma and is anticipated to have around 18 million affected people by 2030, making it one of the countries most affected by glaucoma-related blindness. Indian studies in the past have showed substantial correlations between RNFL thickness and visual field metrics like as MD and PSD, emphasising the possible benefits of integrating structural and functional evaluations in the regular management of glaucoma [12]. However, regional studies are justified by the differences in demographic features, ocular anatomy, genetic variables and disease manifestation among various groups.

Recent investigations have provided further support for the evidence of a structure-function link in glaucoma. Chanekar et al. showed a good association between RNFL thickness obtained by SD-OCT and visual field indices, and emphasised the role of OCT in early diagnosis and follow-up of primary glaucoma [13]. Similarly, Chua et al. found that correction of RNFL measures for demographic and anatomical characteristics substantially enhanced structure–function concordance, highlighting the necessity for population-specific evaluation.

In the backdrop of expanding burden of glaucoma in India and the increasing relevance of incorporating structural and functional assessments in clinical practice, evaluating the link between visual field metrics and RNFL thickness is of great relevance. Building a robust structure–function relationship can enable earlier diagnosis, better tracking of disease progression and more informed treatment decisions. The present study was carried out in the Department of Ophthalmology, Narayan Medical College and Hospital, South Bihar to assess correlation of visual field parameters obtained by automated perimetry with retinal nerve fibre layer thickness as measured by SD-OCT in patients with primary glaucoma.

Methodology

Study Design: This study was carried out as an observational cross sectional study at the hospital level, to assess the structure–function relationship between the RNFL thickness in primary glaucoma patients using Optical Coherence Tomography (OCT) and the visual field parameters using Standard Automated Perimetry (SAP).

Study Area: This study has been done in the Department of Ophthalmology, Narayan Medical College and Hospital, Sasaram, Bihar, India

Study Duration: The study period has been conducted for 24 months starting from 16 March 2024 and ending on 16 March 2026.

Sample Size: Overall, 78 patients were enrolled in the study. The sample size was computed as:

$n = Z^2pq / m^2$

Where:

- n = Sample size
- Z = 1.96 at 95% confidence interval
- p = Prevalence of glaucoma (0.035)
- q = 1 – p
- m = Permissible error (0.05)

A sample size of 52 was calculated. With a design effect of 1.5, the new sample size was:

$n' = 1.5 \times 52 = 78$

Therefore, the subjects were selected through convenient sampling and the number of the subjects was 78.

Sample Population: The research population comprised the patients who attended Ophthalmology Out Patient Department with Primary Glaucoma in the age group of 40-70 years during the study period. It included newly diagnosed glaucoma cases as well as those who were previously diagnosed and treated for glaucoma.

Data Collection: Informed written consent was obtained for recruitment of eligible patients. Data on demographic information, medical history, ocular history, and family history of glaucoma were obtained in a pre-designed proforma. Clinical examination parameters, visual field parameters, and OCT measurements were obtained and recorded for analysis.

Inclusion Criteria

- Patients aged 40–70 years.
- Myopia less than –3.00 D.
- Hypermetropia < +3.00 D.
- Astigmatism less than +/- 2.00 D.
- Those patients who have been diagnosed with primary open angle glaucoma, primary angle closure glaucoma or normal tension glaucoma.
- Newly diagnosed or previously diagnosed glaucoma patient(s) who are being treated.
- Best corrected visual acuity (BCVA) 6/18 or better.
- Patients who are willing to give informed consent.

Exclusion Criteria

- Secondary glaucoma and juvenile glaucoma.
- Cataract, corneal opacity or vitreous hemorrhage obscuring the fundus exam.
- Retinal diseases or other optic nerve disorders.
- Medications and systemic diseases with a known effect on visual field or RNFL thickness.
- If the OCT signal strength is below 5, the results will not be displayed.
- Visual field tests that are unreliable due to false positives more than 33% or false negatives more than 33%.
- Patients who refuse or are not capable of good performance for OCT or perimetry.

Ethical Consideration: The study was done with approval from the Institutional Ethics Committee of Narayan Medical College and Hospital (IEC/2024/059). All participants gave written informed consent before taking part in the study. All patient information was kept confidential and all procedures followed the ethical guidelines of the Declaration of Helsinki.

Procedure: Patients were thoroughly evaluated by the ophthalmologist in all cases.

Clinical Evaluation

- Medical history, ophthalmological history and family history were taken.
- Visual acuity was assessed using a Snellen's chart.

- Objective and subjective refraction were carried out.
- Anterior segment analysis was done using slit lamp bio microscopy.
- The posterior segment examination was performed with the 90D lens.
- Gonioscopy was done to determine the type of glaucoma.
- Intraocular pressure (IOP) was measured by Goldmann applanation tonometry.
- Central corneal thickness (CCT) was measured using NIDEK NT-530P.

Optic Disc Assessment

Optic nerve head was examined for glaucomatous changes such as:

- Neuroretinal rim thinning.
- Optic disc hemorrhage.
- Focal notching.
- Rim excavation.
- Defects in the retinal nerve fiber layer.
- Asymmetry in cup-disc ratio > 0.2.

Visual Field Assessment: Standard Automated Perimetry was conducted on the ZEISS Humphrey Field Analyzer 3 with either 24-2 or 10-2 perimetry protocols. The following visual field parameters were taken:

- Mean Deviation (MD)
- Pattern Standard Deviation (PSD)
- Visual Field Index (VFI)
- Glaucoma Hemifield Test (GHT)

The visual field tests used in analysis were only reliable ones.

Optical Coherence Tomography: Peripapillary RNFL thickness was assessed on ZEISS High-Definition Cirrus OCT on the same day as the visual field test and superior, inferior, nasal and temporal quadrant RNFL measurements were documented.

Statistical Analysis: The data was entered into computer software package MS Excel and analysed with using appropriate statistical software under the guidance of a qualified statistician. The data of continuous variables were expressed as mean ± standard deviation and categorical variables were presented as frequencies and percentages. Pearson's correlation coefficient or Spearman's rank correlation coefficient was used to evaluate the correlation between the visual field parameters (MD, PSD, VFI) and thickness of the RNFL measured by the OCT. A p value < 0.05 was used as the cut-off".

Result

The baseline demographic and clinical parameters of the study participants are given in table 1. 78 patients (156 eyes) were diagnosed with primary glaucoma and included in the study. The mean age of subjects was 56.68 ± 8.91 years, suggesting that glaucoma is more common in middle-aged and elderly people. There were 56.4% males and 43.6% females in the study population. The most common type of glaucoma was Primary Open Angle Glaucoma (POAG) (59.0%), followed by Primary Angle Closure Glaucoma (PACG) (30.8%) and Normal Tension Glaucoma (NTG) (10.2%).

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants (n = 78)

Variable	Value
Mean Age (years)	56.68 ± 8.91
Male, n (%)	44 (56.4%)
Female, n (%)	34 (43.6%)
POAG, n (%)	46 (59.0%)
PACG, n (%)	24 (30.8%)
NTG, n (%)	8 (10.2%)
Total Eyes Examined	156

Table 2 presents the clinical, visual field and OCT findings of the study eyes. The mean intraocular pressure was 24.59 ± 5.58 mmHg, and the mean central corneal thickness was 535.83 ± 34.61 µm. The mean vertical cup to disc ratio was 0.73 ± 0.11, indicating a significant glaucomatous optic nerve damage. Visual field assessment revealed a mean deviation (MD) of −10.21 ± 6.56 dB, pattern standard deviation (PSD) of 6.40 ± 3.07 dB, and visual field index (VFI) of 68.50 ± 23.11%. The mean thickness of the retinal nerve fiber layer (RNFL) obtained by OCT was 76.39 ± 21.78 µm.

Table 2: Clinical, Visual Field and OCT Characteristics of Study Eyes (n = 156)	
Parameter	**Mean ± SD**
Intraocular Pressure (mmHg)	24.59 ± 5.58
Central Corneal Thickness (µm)	535.83 ± 34.61
Vertical Cup-to-Disc Ratio	0.73 ± 0.11
Mean Deviation (MD, dB)	-10.21 ± 6.56
Pattern Standard Deviation (PSD, dB)	6.40 ± 3.07
Visual Field Index (VFI, %)	68.50 ± 23.11
Average RNFL Thickness (µm)	76.39 ± 21.78

As shown in Table 3, there are positive correlations between the average RNFL thickness and the MFIS values. There was a strong positive correlation between RNFL thickness and MD ($\rho = 0.682$, $p < 0.001$), which means that the higher the RNFL thickness, the better the visual field sensitivity. The same correlation was observed between RNFL thickness and visual field index ($\rho = 0.658$, $p < 0.001$). A moderate negative correlation was observed between RNFL thickness and pattern standard deviation ($\rho = -0.486$, $p < 0.001$), indicating that RNFL thinning was correlated with irregularity of visual field. The results demonstrate that there is a strong structure–function relationship in glaucoma.

Table 3: Correlation Between Average RNFL Thickness and Visual Field Parameters			
Correlation Pair	**Spearman's ρ**	**p-value**	**Interpretation**
Average RNFL vs MD	0.682	<0.001	Strong Positive
Average RNFL vs VFI	0.658	<0.001	Strong Positive
Average RNFL vs PSD	-0.486	<0.001	Moderate Negative

Table 4 shows the structure–function correlation as per glaucoma subtypes. The strongest correlation between RNFL thickness and mean deviation was observed in patients with POAG ($\rho = 0.712$, $p < 0.001$), followed by PACG ($\rho = 0.645$, $p < 0.001$) and NTG ($\rho = 0.598$, $p = 0.014$). The RNFL thickness was relatively lower and visual field loss was relatively more severe in POAG eyes than in PACG and NTG cases. However, noteworthy correlations were found in all glaucoma subgroups, reflecting the uniformity of the association of structural and functional damage, regardless of glaucoma type.

Table 4: Structure–Function Correlation According to Glaucoma Type					
Glaucoma Type	**Eyes (n)**	**Mean RNFL (µm)**	**Mean MD (dB)**	**Spearman's ρ**	**p-value**
POAG	92	73.85 ± 20.56	-10.85 ± 6.52	0.712	<0.001
PACG	48	78.42 ± 22.18	-9.56 ± 6.18	0.645	<0.001
NTG	16	81.25 ± 19.84	-8.92 ± 5.96	0.598	0.014

Table 5 shows the distribution of severity of the disease by RNFL thickness. The proportion of eyes classified as early glaucoma, moderate glaucoma and severe glaucoma were 30.8%, 34.6% and 34.6%, respectively, based on the mean deviation of visual fields. There was a progressive thinning of the RNFL with worsening disease severity. The mean RNFL thickness was 98.46 ± 15.32 µm in early glaucoma, 74.28 ± 12.64 µm in moderate glaucoma and 54.36 ± 10.18 µm in severe glaucoma. There was a significant difference between the severity groups ($p < 0.001$), which represents a great deterioration of structure as a disease progresses.

Table 5: Distribution of Disease Severity and Average RNFL Thickness			
Severity Group	**Eyes (n)**	**Percentage (%)**	**Average RNFL Thickness (µm)**
Early (MD > −6 dB)	48	30.8	98.46 ± 15.32
Moderate (MD −6 to −12 dB)	54	34.6	74.28 ± 12.64
Severe (MD < −12 dB)	54	34.6	54.36 ± 10.18
ANOVA p-value	—	—	**<0.001**

The correlation between RNFL thickness with mean deviation in various stages of glaucoma severity is presented in Table 6. In all severity groups, significant positive correlations were noted. In early, moderate, and severe glaucoma, the correlation coefficient was 0.424, 0.512, and 0.486 respectively. The results of this study indicated that structural and functional changes are still highly correlated throughout the evolution of glaucoma. The strongest correlation was found in moderate disease, however, suggesting that the association between OCT measurements of RNFL and visual field loss may be most prominent in intermediate disease stages.

Table 6: Correlation Between Average RNFL Thickness and MD According to Disease Severity

Severity Group	Mean RNFL (µm)	Mean MD (dB)	Spearman's ρ	p-value
Early	98.46 ± 15.32	-3.2 ± 1.8	0.424	0.003
Moderate	74.28 ± 12.64	-8.5 ± 1.9	0.512	<0.001
Severe	54.36 ± 10.18	-18.5 ± 4.2	0.486	<0.001

Discussion

In the present investigation, 78 individuals (156 eyes) with primary glaucoma were analysed to determine the connection between structural changes detected by spectral-domain optical coherence tomography (SD-OCT) and functional impairment assessed by standard automated perimetry (SAP). The mean age of study population was 56.68 ± 8.91 years with majority of the patients in the older age categories. This finding is in agreement with earlier epidemiological studies which have demonstrated an increase in prevalence of glaucoma with age due to the progressive loss of retinal ganglion cells and optic nerve degeneration". The preponderance of males (56.4%) in the present study is consistent with the findings of George et al. and Tham et al. who showed a larger burden of primary open-angle glaucoma (POAG) among males in Asian communities [2,3].

The most prevalent form of glaucoma was POAG (59.0%), followed by primary angle-closure glaucoma (PACG) (30.8%) and normal-tension glaucoma (NTG) (10.2%). Similar patterns have been found in Indian research where POAG accounts for about 60–70% of glaucoma cases [14]. The mean intraocular pressure was 24.59 ± 5.58 mmHg and the mean vertical cup-to-disc ratio was 0.73 ± 0.11, suggesting substantial glaucomatous optic nerve injury. The results are in accordance with those of Weinreb et al. who reported increased intraocular pressure and cupping of the optic disc as the predominant clinical signs of glaucoma development [4].

Functional examination revealed a mean deviation (MD) of 10.21 6.56 dB, pattern standard deviation (PSD) of 6.40 3.07 dB and visual field index (VFI) of 68.50 23.11%, suggestive of moderate to advanced visual field loss in a significant percentage of eyes. Hood and Raza have also reported similar MD values and shown that progressive retinal ganglion cell loss correlates well with deteriorating vision field indices [9]. The significant incidence of aberrant visual field findings in this study further supports the efficacy of SAP as the gold standard for functional evaluation in glaucoma.

OCT structural examination showed a mean average RNFL thickness of 76.39 ± 21.78 µm. Inferior and superior quadrants were thinned more than nasal and temporal quadrants, which is the normal pattern of glaucomatous damage. Quigley et al. showed a similar preferential involvement of the superior and inferior arcuate nerve fibre bundles due to their higher susceptibility to mechanical and vascular stress [15]. The considerable loss of RNFL thickness found in the present investigation compared with normative age-matched values underscores the relevance of OCT in detecting structural damage prior to the onset of substantial functional loss.

The main conclusion of the present investigation was the strong structure-function link between RNFL thickness and visual field parameters. Average RNFL thickness had a high positive connection with MD ($\rho = 0.682$, $p < 0.001$) and VFI ($\rho = 0.658$, $p < 0.001$), but a moderate negative correlation with PSD ($\rho = -0.486$, $p < 0.001$). These results concur with the findings of Rao et al., who found substantial associations between OCT-derived RNFL measures and visual field sensitivity in glaucomatous eyes [12]. However, the correlation coefficients found in the present study were slightly higher than those reported by Rao et al. Possibly due to inclusion of patients across a wider spectrum of disease severity, this increases the measurable dynamic range of both structural and functional parameters.

The connection between RNFL thickness and MD was highest in POAG ($\rho = 0.712$) followed by PACG ($\rho = 0.645$) and NTG ($\rho = 0.598$) in the analysis by subtype of glaucoma. These data indicate a somewhat predictable link between structural and functional deterioration in POAG. Similar results have been published by Chanekar et al. who showed that RNFL measures are very effective in monitoring glaucomatous development and detection of early optic nerve injury [13]. The substantial association even in NTG underlines the relevance of OCT based structural assessment in individuals who may not present with excessive IOP.

Analysis of disease severity showed increased RNFL thinning with increasing severity of glaucoma. The mean RNFL thickness was 98.46 ± 15.32 µm in early glaucoma, 74.28 ± 12.64 µm in intermediate glaucoma and 54.36 ± 10.18 µm in severe glaucoma ($p < 0.001$). These results are very comparable to the work of Bhat et al who demonstrated a progressive RNFL loss of about 25–44% with increasing severity of glaucoma. The highest structure-function link was seen in moderate glaucoma (ρ = 0.512), with somewhat lower correlations in early and severe illness. This observation is consistent with the concept of the "floor effect" by Medeiros et al., where in advanced glaucoma the RNFL measures tend to reach a residual baseline level, weakening the strength of structure-function relations [16].

In conclusion, the present investigation confirms a substantial and clinically important connection between the OCT-derived RNFL thickness and visual field measures in primary glaucoma. The results support the complimentary importance of structural and functional assessment in the diagnosis and monitoring of glaucoma. OCT allows for objective assessment of axonal loss. The SAP assesses the functional repercussions of such damage. The combination of both modalities may help in earlier diagnosis, better staging and better monitoring of disease progression in individuals with glaucoma.

Conclusion

This study showed structure–function correlation between the thickness of retinal nerve fiber layer (RNFL) evaluated with SD-OCT and visual field (VF) parameters in primary glaucoma patients in a significant and clinically relevant manner. Average RNFL thickness was strongly correlated with mean deviation (ρ = 0.682) and visual field index (ρ = 0.658) and moderately correlated with pattern standard deviation (ρ = −0.486), suggesting a strong link between structural damage and functional loss in the visual field. Progressive RNFL thinning was identified with increasing glaucoma severity and significant relationships were maintained throughout all glaucoma types and stages. These results illustrate the complementary role of OCT and VFT in the diagnosis, staging and follow-up management of primary glaucoma. Generally, integration of structural and functional assessments can help to detect glaucomatous damage at earlier stages, determine the rate of glaucoma progression more accurately and enable better clinical decision making to preserve visual function and prevent irreversible blindness.

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