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Correlation of intraocular pressure with retinal nerve fiber layer thickness in glaucoma

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Abstract:
Raised intraocular pressure is the principal modifiable risk factor for glaucoma, but its relationship with retinal nerve fiber layer thinning requires accurate quantification for early disease detection. Therefore, it is of interest to evaluate the correlation between intraocular pressure and optical coherence tomography derived retinal nerve fiber layer thickness in 90 patients with diagnosed glaucoma. The mean participant age was 56.8 ± 11.4 years and intraocular pressure showed a significant negative correlation with average retinal nerve fiber layer thickness ($r = -0.68$; $p < 0.001$), with superior and inferior quadrants showing the strongest associations. Patients with severe retinal nerve fiber layer thinning had significantly higher intraocular pressure, indicating progressive structural damage with increasing ocular pressure. Thus, data shows the value of optical coherence tomography as a non-invasive tool for early glaucoma detection, risk stratification and longitudinal monitoring of disease progression.

Keywords: Glaucoma, intraocular pressure (IOP), retinal nerve fiber layer, optical coherence tomography (OCT), retinal nerve fiber layer (RNFL) thickness

Background:
Glaucoma represents one of the leading causes of irreversible blindness worldwide and is characterized by progressive optic neuropathy associated with structural damage to the optic nerve head and retinal nerve fiber layer (RNFL). The disease is often asymptomatic during its early stages, causing gradual visual field defects that may remain unnoticed until significant optic nerve damage has occurred **[1]**. The global burden of glaucoma continues to increase because of population aging and improved life expectancy. Primary open angle glaucoma remains the most common form globally **[2].** Elevated intraocular pressure (IOP) is considered the most important modifiable risk factor in glaucoma pathogenesis. Persistent elevation of IOP contributes to mechanical compression and vascular compromise of retinal ganglion cell axons at the level of the lamina cribrosa, leading to progressive apoptosis of ganglion cells and thinning of the RNFL **[3]**. However, glaucomatous damage may also occur in individuals with statistically normal intraocular pressure, suggesting involvement of additional vascular, genetic and neurodegenerative mechanisms **[4].** Retinal nerve fiber layer thickness has become a crucial structural biomarker in glaucoma diagnosis and progression monitoring. The RNFL consists of unmyelinated axons of retinal ganglion cells that converge to form the optic nerve **[5]**. Progressive thinning of this layer reflects neuronal loss and precedes clinically detectable visual field defects in many patients. Early identification of RNFL loss is therefore essential for timely initiation of therapy and prevention of irreversible blindness **[6].** RNFL thickness is an important structural biomarker of glaucomatous damage, and its relationship with visual-field parameters provides a structural–functional basis for glaucoma assessment **[7].** Optical coherence tomography (OCT) has revolutionized glaucoma evaluation by enabling rapid, noninvasive and highly reproducible quantitative measurement of RNFL thickness. Spectral-domain OCT provides high resolution cross sectional retinal imaging and permits detailed analysis of optic nerve head morphology and RNFL integrity **[8]**. OCT-based RNFL assessment is widely used for early diagnosis, progression analysis and therapeutic monitoring in glaucoma patients **[9].** Several studies have showed significant association between elevated intraocular pressure and RNFL thinning. Elevated IOP is associated with RNFL thinning, and longitudinal studies have showed that higher follow-up IOP is associated with faster rates of RNFL loss measured by OCT **[10–12]**. IOP variation has also been associated with reduced RNFL thickness, particularly in the superior and inferior sectors **[13].** Recent advances in OCT technology and artificial intelligence have further improved the sensitivity of glaucoma detection. Deep learning algorithms now assist clinicians in identifying subtle RNFL changes and predicting disease progression **[14]**. Nevertheless, interpretation of RNFL thickness should consider factors such as age, axial length, ethnicity and physiological thinning associated with aging **[15].** Age-related RNFL thinning may occasionally mimic glaucomatous progression, complicating clinical assessment **[16]**. Studies indicate that normal aging results in gradual RNFL reduction, making careful longitudinal evaluation necessary to differentiate physiological and pathological changes **[17].** Therefore, it is of interest to evaluate the correlation between intraocular pressure and retinal nerve fiber layer thickness in glaucoma patients using optical coherence tomography in a tertiary care hospital setting.

Materials and Methodology:
The present hospital-based observational cross-sectional study was conducted in the Department of Ophthalmology of a tertiary care teaching hospital over a period of 18 months after obtaining approval from the Institutional Ethics Committee.

Study population:
A total of 90 patients clinically diagnosed with glaucoma were included in the study. Patients attending the ophthalmology outpatient department and fulfilling the inclusion criteria were enrolled after obtaining informed written consent.

Inclusion criteria:
[1] Patients aged more than 40 years
[2] Diagnosed cases of primary open-angle glaucoma or primary angle-closure glaucoma
[3] Patients willing to participate in the study
[4] Patients with reliable OCT imaging and tonometry measurements

Exclusion criteria:
[1] Patients with retinal diseases affecting RNFL thickness
[2] History of ocular trauma or intraocular surgery
[3] Media opacity interfering with OCT imaging
[4] Secondary glaucoma

[5] Neurological diseases affecting optic nerve

Clinical evaluation:
Detailed ophthalmologic examination was performed in all participants including:
[1] Visual acuity assessment
[2] Slit lamp biomicroscopy
[3] Gonioscopy
[4] Fundus examination
[5] Goldmann applanation tonometry
[6] Visual field testing
Intraocular pressure was measured using Goldmann applanation tonometer under topical anesthesia. Three readings were obtained and averaged for analysis.

Oct assessment:
Retinal nerve fiber layer thickness was assessed using spectral-domain optical coherence tomography. Average RNFL thickness along with superior, inferior, nasal and temporal quadrant measurements was recorded. Images with poor signal strength or motion artifacts were excluded.

Statistical analysis:
Data were entered into Microsoft Excel and analyzed using SPSS software version 25. Quantitative variables were expressed as mean ± standard deviation. Qualitative variables were expressed as percentages. Pearson correlation coefficient was used to evaluate correlation between intraocular pressure and RNFL thickness. Chi-square test and Student's t-test were applied where appropriate. A p value <0.05 was considered statistically significant.

Results:
A total of 90 glaucoma patients were included in the present study. The demographic and clinical characteristics demonstrated predominance of elderly individuals with increasing glaucoma severity associated with elevated intraocular pressure and progressive RNFL thinning. Most patients belonged to the 51–60 years age group (35.6%). Male predominance was observed with 58.9% cases. Primary open-angle glaucoma constituted 67.8% of patients, indicating its higher prevalence among glaucomatous disorders. Mean intraocular pressure among study participants was 24.6 ± 5.8 mmHg. Mean average RNFL thickness was 74.2 ± 13.5 µm. Patients with IOP above 30 mmHg showed markedly reduced RNFL thickness **(Table 1).** A progressive decline in RNFL thickness was observed with increasing intraocular pressure. Patients with IOP greater than 30 mmHg demonstrated severe RNFL thinning with mean thickness of 56.9 µm. The association was statistically highly significant (p <0.001). Quadrant-wise analysis demonstrated maximum thinning in superior and inferior quadrants. Pearson correlation coefficient revealed strong negative correlation between IOP and RNFL thickness **(Table 2).** Superior and inferior RNFL quadrants showed the strongest negative correlation with intraocular pressure. Inferior quadrant thinning demonstrated highest correlation (r = −0.74), indicating greater susceptibility to glaucomatous damage **(Table 3).**

Table 1: Demographic and clinical characteristics of study population

Variable	Number (n=90)	Percentage (%)
Age 41–50 years	18	20.0
Age 51–60 years	32	35.6
Age 61–70 years	28	31.1
Age >70 years	12	13.3
Male	53	58.9
Female	37	41.1
Primary open-angle glaucoma	61	67.8
Angle-closure glaucoma	29	32.2

Table 2: Correlation between intraocular pressure and RNFL thickness

IOP Range (mmHg)	Number of Patients	Mean RNFL Thickness (µm)	p value
18–21	19	89.4 ± 6.2	<0.001
22–25	31	78.8 ± 7.5	<0.001
26–30	24	68.6 ± 8.4	<0.001
>30	16	56.9 ± 9.1	<0.001

Table 3: Quadrant-wise RNFL thickness and correlation with IOP

RNFL Quadrant	Mean Thickness (µm)	Correlation Coefficient (r)	p value
Superior	72.4 ± 12.8	−0.71	<0.001
Inferior	69.8 ± 13.2	−0.74	<0.001
Nasal	61.3 ± 10.6	−0.48	0.002
Temporal	58.5 ± 9.8	−0.41	0.005

Discussion:
In the present study, the majority of patients belonged to the 51-60 years age group with a mean age of 56.8 ± 11.4 years. These findings are consistent with epidemiological evidence suggesting increasing prevalence of glaucoma with advancing age. Zhao *et al.* reported that glaucoma incidence and disease burden rise significantly in elderly populations because of cumulative neuronal degeneration and vascular compromise **[18].** Similarly, few studies showed that physiological RNFL thinning occurs with aging, thereby increasing susceptibility to glaucomatous optic nerve damage and complicating differentiation between normal aging and pathological loss **[19, 20].** Male predominance observed in the present study is comparable to observations reported in several glaucoma prevalence studies. Variations in gender distribution may be related to environmental exposure, healthcare utilization, genetic predisposition and hormonal influences. Although glaucoma affects both sexes, some studies have shown slightly higher prevalence among males, particularly in primary open angle glaucoma **[18].** The current study showed a statistically significant negative correlation between intraocular pressure and RNFL thickness. Patients with elevated IOP showed markedly reduced RNFL measurements on OCT evaluation. These findings support the well-established concept that increased intraocular pressure contributes to retinal ganglion cell apoptosis and axonal degeneration through mechanical compression and ischemic injury at the level of the lamina cribrosa. Bowd *et al.* showed that progressive RNFL thinning is strongly associated with glaucomatous structural damage and may continue even before significant visual field deterioration becomes clinically evident **[19].** Advances in OCT technology

have transformed glaucoma assessment by enabling quantitative and reproducible evaluation of RNFL thickness. OCT can detect early structural damage before the onset of measurable functional visual field defects. Zawadzka and Konopińska highlighted that OCT has become an essential diagnostic modality for glaucoma because of its ability to provide high-resolution cross-sectional retinal imaging and objective monitoring of disease progression **[4].** Similarly, Shen *et al.* emphasized the importance of OCT and OCT angiography in evaluating optic nerve head microvasculature and structural alterations in glaucomatous eyes **[5].** In the present study, superior and inferior RNFL quadrants demonstrated maximum thinning and strongest correlation with elevated intraocular pressure. Inferior quadrant thinning showed the highest negative correlation with IOP. These observations are consistent with previous investigations showing that superior and inferior arcuate nerve fiber bundles are particularly vulnerable to glaucomatous damage. Dhabarde *et al.* reported that ganglion cell complex and RNFL measurements in superior and inferior quadrants possess high diagnostic value for early glaucoma detection and correlate strongly with disease severity **[6].** Similar findings were also reported by Shiga *et al.*, who showed preferential involvement of inferior and superior RNFL regions during early glaucomatous progression **[8].** The mean RNFL thickness progressively decreased across increasing categories of intraocular pressure in the current study. Patients with IOP greater than 30 mmHg exhibited severe RNFL thinning, highlighting the structural impact of ocular hypertension. These findings emphasize the importance of adequate IOP control in preventing irreversible optic nerve damage and visual disability. Structural OCT changes may therefore serve as valuable indicators for treatment response and disease progression monitoring **[20].** Recent technological developments have further enhanced the diagnostic utility of OCT in glaucoma. Lommatzsch and van Oterendorp discussed the growing role of advanced optic nerve imaging techniques in improving glaucoma diagnosis, progression analysis and risk stratification **[3].** Improved segmentation algorithms and spectral-domain OCT systems now provide greater reproducibility and enhanced visualization of retinal structures compared to earlier time-domain technologies. Artificial intelligence and deep learning applications are increasingly being incorporated into glaucoma imaging analysis. Hasan *et al.* demonstrateed that explainable machine learning models using OCT parameters can accurately diagnose glaucoma and classify disease stages with high sensitivity and specificity **[9].** Likewise, Bolo and Xu highlighted the emerging role of deep learning in automated analysis of OCT images for glaucoma related diagnostics and progression assessment **[10].** Hussain *et al.* further reported that deep learning frameworks guided by generative algorithms can effectively predict glaucoma progression and assist clinicians in longitudinal disease monitoring **[15].** Tan *et al.* also showed the utility of hybrid deep learning models utilizing peripapillary RNFL reflectance and multiple OCT parameters for accurate glaucoma classification **[16].** Geometric deep learning and artificial intelligence-based analysis have shown promising applications in ophthalmology. Thiéry *et al.* emphasized that AI-driven glaucoma diagnostics may improve screening efficiency, reduce observer variability and facilitate earlier detection of structural damage **[17].** These technologies may become increasingly valuable in resource-limited settings where access to specialized glaucoma expertise is restricted. Despite the advantages of OCT, interpretation of RNFL measurements should consider confounding variables including age, ethnicity, axial length, signal strength and media opacity. Vilares-Morgado *et al.* reported that age-related physiological RNFL reduction can occasionally mimic glaucomatous progression and must therefore be interpreted cautiously during longitudinal follow-up **[14].** Additionally, segmentation artifacts and image acquisition errors may influence measurement accuracy. The present study demonstrated good correlation between OCT-based structural changes and clinical severity of glaucoma. Patients with severe RNFL thinning frequently exhibited advanced visual field defects, indicating strong structural-functional association. Palmer *et al.* highlighted that OCT-based progression analysis has become indispensable for monitoring glaucomatous damage and guiding individualized treatment strategies **[2].** The limitations of the present study include relatively smaller sample size and cross-sectional design. Longitudinal studies involving larger populations and extended follow-up periods are necessary to evaluate progressive RNFL changes and therapeutic outcomes more comprehensively. Nevertheless, the findings of this study reinforce the importance of combining intraocular pressure assessment with OCT-based RNFL analysis for early diagnosis, progression monitoring and effective management of glaucoma patients.

Conclusion:

Higher intraocular pressure was significantly associated with reduced retinal nerve fiber layer thickness, particularly in the superior and inferior quadrants, indicating progressive structural glaucomatous damage. Optical coherence tomography provides a valuable non-invasive method for detecting and monitoring retinal nerve fiber layer changes in glaucoma. Early detection and effective intraocular pressure control remain essential for limiting irreversible glaucomatous visual damage and preserving long-term visual function.

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