International Journal Dental and Medical Sciences Research
Volume 7, Issue 6, Nov – Dec 2025 pp 161-167 www.ijdmsrjournal.com ISSN: 2582-6018

Comparative Analysis of Optical Coherence Tomography and Optical Coherence Tomography Angiography Changes at the Optic Disc and Macula in Glaucoma Suspects and Early Primary Open-Angle Glaucoma Patients

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Date of Submission: 05-12-2025 Date of Acceptance: 15-12-2025

ABSTRACT
Purpose: To compare the diagnostic performance of macular ganglion cell–inner plexiform layer (mGCIPL) and peripapillary retinal nerve fiber layer (pRNFL) thickness measured by optical coherence tomography (OCT) with macular and peripapillary perfusion changes detected by optical coherence tomography angiography (OCTA) in glaucoma suspects and patients with early primary open-angle glaucoma (POAG).
Methods: This cross-sectional prospective study included 75 participants (25 normal, 25 glaucoma suspects, and 25 early POAG). Spectral-domain OCT (TOPCON 3D OCT-1 MAESTRO-2) was used to assess average and sectoral mGCIPL and pRNFL thicknesses. OCTA was used to evaluate macular vessel density (VD), optic nerve head (ONH) perfusion, and flux index (FI). Statistical analyses included analysis of variance (ANOVA), Pearson's correlation, and area under the receiver operating characteristic (AUROC) curve calculations.
Results: Macular VD, ONH perfusion, and FI were significantly reduced in early POAG compared with normal eyes ($p < 0.001$). The strongest correlation was observed between ONH FI and average RNFL thickness in both glaucoma suspects ($r = 0.47$, $p < 0.01$) and early POAG ($r = 0.53$, $p < 0.01$). Among OCTA parameters, ONH perfusion was significantly lower in glaucomatous eyes than in suspects ($p < 0.001$). Average GCIPL (AUROC = 0.82) and macular VD (AUROC = 0.76) best differentiated glaucoma suspects from controls. Rim area (AUROC = 0.92) and ONH FI (AUROC = 0.81) were the most effective OCT and OCTA parameters, respectively, for distinguishing early POAG from normal eyes.
Conclusion: OCTA-derived vascular indices demonstrated strong correlations with structural changes at both the optic disc and macula. OCT parameters exhibited superior diagnostic accuracy compared to OCTA for early glaucoma, although vascular alterations occurred in the earliest disease stages, highlighting OCTA's value as a complementary diagnostic tool.

Keywords: Glaucoma, Optical Coherence Tomography, Optical Coherence Tomography Angiography, Macular Vessel Density, Optic Nerve Head Perfusion, Flux Index, Ganglion Cell Analysis, Retinal Nerve Fiber Layer.

I. INTRODUCTION

Glaucoma is a multifactorial, progressive optic neuropathy that causes irreversible damage to retinal ganglion cells (RGCs), leading to characteristic optic nerve head (ONH) changes and visual field (VF) defects. It remains the second leading cause of blindness globally and the most common cause of irreversible blindness. Early detection is critical, yet challenging, as structural and functional changes are often subtle in the initial stages.

The hallmark of glaucomatous neuropathy is loss of RGCs and subsequent thinning of the retinal nerve fiber layer (RNFL), which precedes measurable VF loss. Standard automated perimetry (SAP) remains the gold standard for functional assessment, but it often fails to detect damage until approximately 25–35% of RGCs are lost. This diagnostic lag underscores the importance of imaging modalities that can identify structural and vascular changes before functional loss occurs.

Optical coherence tomography (OCT) provides high-resolution, cross-sectional retinal imaging, allowing quantification of macular ganglion cell–inner plexiform layer (mGCIPL) and peripapillary RNFL thickness. These measurements have shown significant diagnostic utility for early glaucoma detection. However, glaucoma is increasingly recognized as a disease not only of mechanical and structural origin but also of vascular dysregulation, leading to ischemic damage of the optic nerve.

The advent of optical coherence tomography angiography (OCTA) has enabled non-invasive, depth-resolved visualization of retinal and

ONH microvasculature using motion contrast imaging. OCTA offers quantitative analysis of parameters such as vessel density (VD), perfusion density (PD), and flux index (FI). Several studies have demonstrated reduced macular and peripapillary VD in glaucomatous eyes, supporting the vascular component of disease pathogenesis.

Previous research has focused on either peripapillary or macular OCTA parameters, or compared glaucomatous eyes to healthy controls. However, few studies, particularly in the Indian population, have comprehensively evaluated both OCT structural changes (mGCIPL and RNFL) and OCTA vascular indices (macular and peripapillary) in glaucoma suspects and early POAG. Understanding these relationships could improve early diagnostic accuracy and help elucidate the pathophysiology of glaucoma.

This study therefore aimed to (1) assess structural changes using OCT and vascular alterations using OCTA at the optic disc and macula, (2) compare these parameters among glaucoma suspects, early POAG, and normal controls, and (3) determine which imaging biomarkers most effectively distinguish early glaucomatous eyes from normal eyes.

II. MATERIALS AND METHODS

Study Design and Ethical Approval: A hospital-based, observational cross-sectional study was conducted from January 1, 2024, to July 31, 2025, at a tertiary care medical college in Eastern Odisha. Written informed consent was obtained from all participants.

Participants: Seventy-five subjects were enrolled and categorized into three groups of 25 each: Normal controls, Glaucoma suspects, and Early POAG patients. All participants were over 40 years old with open angles on gonioscopy and refractive errors within ±5.0 D spherical and ±3.0 D cylindrical power.

Exclusion criteria: Patients with media opacities, prior intraocular surgery, secondary glaucoma, retinal or neurological diseases affecting VF, or systemic diseases influencing vascular density (except controlled hypertension/diabetes) were excluded.

Clinical Examination: All subjects underwent a comprehensive ophthalmic evaluation, including BCVA, IOP, slit-lamp biomicroscopy, fundus evaluation, CCT, and visual field testing with Humphrey Field Analyzer.

Imaging Protocol: OCT and OCTA imaging were performed using(TOPCON 3D OCT-1 MAESTRO-2). The Optic Disc Cube 200×200 and Macular Cube 200×200 protocols were used for pRNFL, rim area, CDR, and GCIPL measurements. OCTA macular (6×6 mm) and ONH (4.5×4.5 mm) scans provided VD, PD, and FI data. Images with signal strength ≥6 were included. Examiners were masked to patient diagnosis.

Diagnostic Criteria: Glaucoma suspects had IOP >21 mmHg or optic disc suspicion with normal VF. Early POAG required glaucomatous ONH and VF defects per Hodapp–Parrish–Anderson criteria. Normals had IOP ≤21 mmHg and normal ONH and VF.

Statistical Analysis: Data were analyzed using STATA 11.2. Continuous variables were expressed as mean ± SD. ANOVA, Pearson's correlation, and AUROC were used. $p < 0.05$ was considered significant.

III. RESULTS

Demographic and Baseline Characteristics: Seventy-five patients (39 eyes of early POAG, 46 eyes of suspects, and 39 eyes of controls) were analyzed. Age and sex distributions were comparable ($p > 0.05$). Mean baseline IOP was higher in early POAG (21.3 ± 3.07 mmHg) versus suspects (18.0 ± 2.97 mmHg) and controls (15.6 ± 2.23 mmHg) ($p < 0.001$). Family history of glaucoma was more frequent in glaucomatous eyes ($p = 0.005$). CCT differences were nonsignificant ($p = 0.64$).

OCT Parameters: Mean RNFL was 94.9 ± 8.0 µm in controls, 89.4 ± 7.4 µm in suspects, and 74.4 ± 12.7 µm in early POAG ($p < 0.001$). GCA values showed similar patterns. The strongest correlation was between RNFL and GCA thinning in inferior and temporal quadrants ($r = 0.64$, $p < 0.001$).

OCTA Parameters: Macular VD, ONH perfusion, and FI were significantly lower in glaucomatous eyes ($p < 0.001$). Macular VD and ONH FI were also reduced in suspects compared with controls ($p < 0.001$). ONH perfusion was lowest in POAG versus suspects ($p < 0.001$).

Correlation and Diagnostic Accuracy: ONH FI correlated strongly with average RNFL in suspects ($r = 0.47$, $p = 0.001$) and POAG ($r = 0.52$, $p = 0.001$). Macular VD correlated with average GCA ($r = 0.55$, $p < 0.001$). AUROC analysis showed GCA (0.82) and macular VD (0.76) best distinguished suspects vs controls; rim area (0.92) and ONH FI (0.81) best distinguished early POAG vs controls.

Table 1: Demographics details and examination of the three groups (normal controls, glaucoma suspects, and early glaucoma patients)

Parameter	Normal, n=25	Glaucoma suspects, n=25	Early glaucoma patients,n=25	P
Age (Mean±SD) (years)	50.1±8.9	47.6±7.9	50.9±5.8	0.25[a]
Sexratio(M:F)	15:10	16:9	18:7	0.86[b]
Patients with a family history of glaucoma	0(0%)	4(13.33%)	8(26.67%)	0.005[b]
Patients with hypertension	7(23.3%)	7(23.3%)	8(26.6%)	0.9[b]
Patients with diabetes mellitus	4(13.3%)	7(23.3%)	6(20%)	0.6[b]
Patients with hypothyroidism	1(3.3%)	3(10%)	1(3.3%)	0.61[b]
Number of antiglaucoma drugs(%)	30 (100%)	18 (60%)	16 (53.33%)	
0		12 (40%)	10 (33.33%)	
1			2(6.67%)	
2			2(6.67%)	
3				
BaselineIOP(mmHg) (Mean±SD)	15.64±2.23	18.02±2.97	21.3±3.07	<0.001[a]
CCT(μm) (Mean±SD)	537.0±24.29	537.28±36.82	531.61±28.67	0.64[a]
CDR(Mean±SD)	0.38±0.07	0.68±0.07	0.73±0.09	<0.001[a]

CCT=central corneal thickness, CDR=cup–disc ratio, F=female, IOP=intraocular pressure, M=male, SD=standard deviation. [a]One - way analysis of variance among the three groups. [b] Pearson's Chi - squared test

Table 2:Comparison of OCT and OCTA parameters among the three groups

Parameter	Normal (39 eyes)	Glaucoma suspects (46 eyes)	Early glaucoma (39 eyes)	pa	pb Normal versus early glaucoma	pb Normal versus suspects	pb Glaucoma suspects versus early glaucoma
AverageCDR	0.46±0.06	0.71±0.05	0.74±0.06	<0.001	**<0.001**	**<0.001**	0.10
Rimarea (mm^2)	1.43±0.24	1.17±0.19	0.92±0.25	<0.001	**<0.001**	**<0.001**	**<0.001**
Average RNFL(μm)	94.9±8.0	89.4±7.4	74.4±12.7	<0.001	**<0.001**	**0.02**	**<0.001**
RNFL superior(μm)	118.7±16.4	107.4±11.7	90.9±19.6	<0.001	**<0.001**	**0.005**	**<0.001**
RNFL inferior(μm)	122.3±15.8	113.8±20.5	90.0±22.7	<0.001	**<0.001**	0.15	**<0.001**
RNFL nasal (μm)	73.7±14.6	71.3±8.9	62.8±11.5	<0.001	**<0.001**	1.0	**0.004**
RNFL temporal(μm)	63.9±6.0	62.7±11.8	53.4±9.8	<0.001	**<0.001**	1.0	**<0.001**
GCA average(μm)	83.5±3.5	76.4±9.0	71.9±10.5	<0.001	**<0.001**	**<0.001**	**0.04**
GCA superior(μm)	83.1±3.4	76.5±9.3	73.3±9.8	<0.001	**<0.001**	**0.001**	0.23
GCA inferior(μm)	82.1±5.4	74.5±8.5	69.3±11.9	<0.001	**<0.001**	**<0.001**	**0.02**
GCA nasal(μm)	84.8±4.3	77.7±10.0	74.4±11.5	<0.001	**<0.001**	**0.002**	0.29
GCA temporal(μm)	82.9±4.4	76.3±9.6	70.6±9.9	<0.001	**<0.001**	**0.001**	**0.006**
Superficial macular VD(mm/mm^2)	15.64±1.87	12.75±3.25	12.48±3.51	<0.001	**<0.001**	**<0.001**	**1.000**
ONH perfusion(%)	44.33±1.0	44.02±1.58	42.69±1.95	<0.001	**<0.001**	1.0	**<0.001**
ONH fluxindex	0.44±0.03	0.41±0.03	0.39±0.043	<0.001	**<0.001**	**<0.001**	0.27

Significant P values are given in bold, CCT=central corneal thickness, GCA=ganglion cell analysis, OCT=optical coherence tomography,

International Journal Dental and Medical Sciences Research
Volume 7, Issue 6, Nov – Dec 2025 pp 161-167 www.ijdmsrjournal.com ISSN: 2582-6018

OCTA=OCT angiography, ONH=optic nerve head, RNFL=retinal nerve fiber layer, VD=vessel density.[a]P- value among three groups assessed by one - way analysis of variance. [b]P- value for comparison between two groups assessed by post hoc analysis with Bonferroni method

IV. DISCUSSION

This study comprehensively evaluated OCT and OCTA parameters in glaucoma suspects and early POAG. Both pRNFL and mGCIPL thinning were evident in early glaucoma, confirming that structural damage occurs early. Inferotemporal and inferior sectors were most affected, consistent with previous findings.

Macular GCA thickness showed stronger correlation with VFI than RNFL or rim area, suggesting macular analysis may better reflect functional impairment. OCTA revealed macular VD and ONH FI reductions even in suspects, indicating that vascular compromise can precede structural loss. However, differences between suspects and early glaucoma were smaller, implying neuronal degeneration becomes dominant later.

Our findings align with earlier reports linking reduced peripapillary and macular VD to glaucoma. ONH FI correlated well with RNFL thickness, supporting the link between vascular and structural damage. Despite this, OCT parameters maintained higher diagnostic accuracy (AUROC 0.82–0.92) than OCTA (AUROC 0.76–0.81), consistent with studies by Hou, Chung, and Lu et al.

Variations among studies likely reflect differences in imaging devices, segmentation algorithms, ethnicity, and disease stage. Nevertheless, consistent vascular loss underscores glaucoma's vascular component.

Limitations include a modest sample size, cross-sectional design, and potential medication effects on perfusion. Future longitudinal studies with larger samples and higher OCT signal thresholds are needed.

Table 3: Pearson's correlation coefficient between ONHOCT, macular OCT and OCTA parameters in glaucoma suspects and early POAG eyes

Parameters	**Glaucoma suspects**		**Early POAG**	
	Correlation coefficient (r)[a]	**P**	**Correlation coefficient (r)[a]**	**P**
ONH perfusion with rim area	-0.07	0.62	0.11	0.49
ONHperfusionwithaverageRNFL	0.37	**0.01**	0.38	**0.02**
ONH flux index with rim area	0.14	0.36	0.38	**0.02**
ONH flux index with average RNFL	0.47	**0.001**	0.52	**0.001**
Macular VD with average GCA	0.19	0.20	0.55	**<0.001**
Macular VD with superior GCA	0.14	0.35	0.32	**0.04**
Macular VD with inferior GCA	0.21	0.14	0.58	**<0.001**
Macular VD with nasal GCA	0.22	0.12	0.44	**0.004**
Macular VD with temporal GCA	0.13	0.35	0.60	**<0.001**

Significant Pvalues are given in bold, GCA=ganglion cell analysis, OCT=optical coherence tomography, OCTA=OCT angiography, ONH=optic nerve head,

POAG=primary open angle glaucoma, RNFL=retinal nerve fiber layer, VD=vessel density.[a]Pearson's correlation

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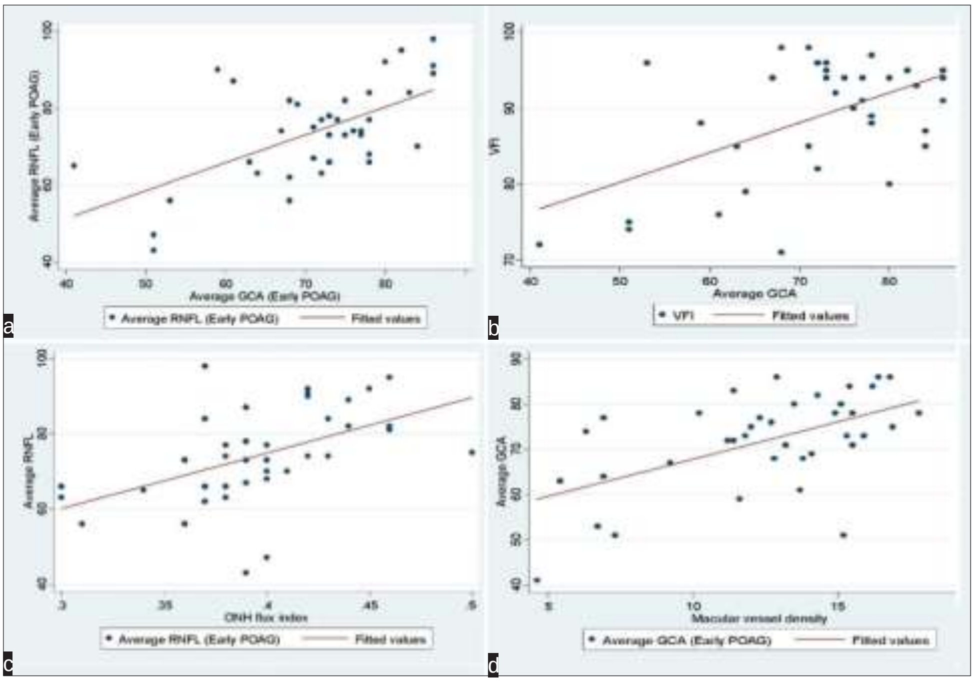
Volume 7, Issue 6, Nov – Dec 2025 pp 161-167 www.ijdmsrjournal.com ISSN: 2582-6018



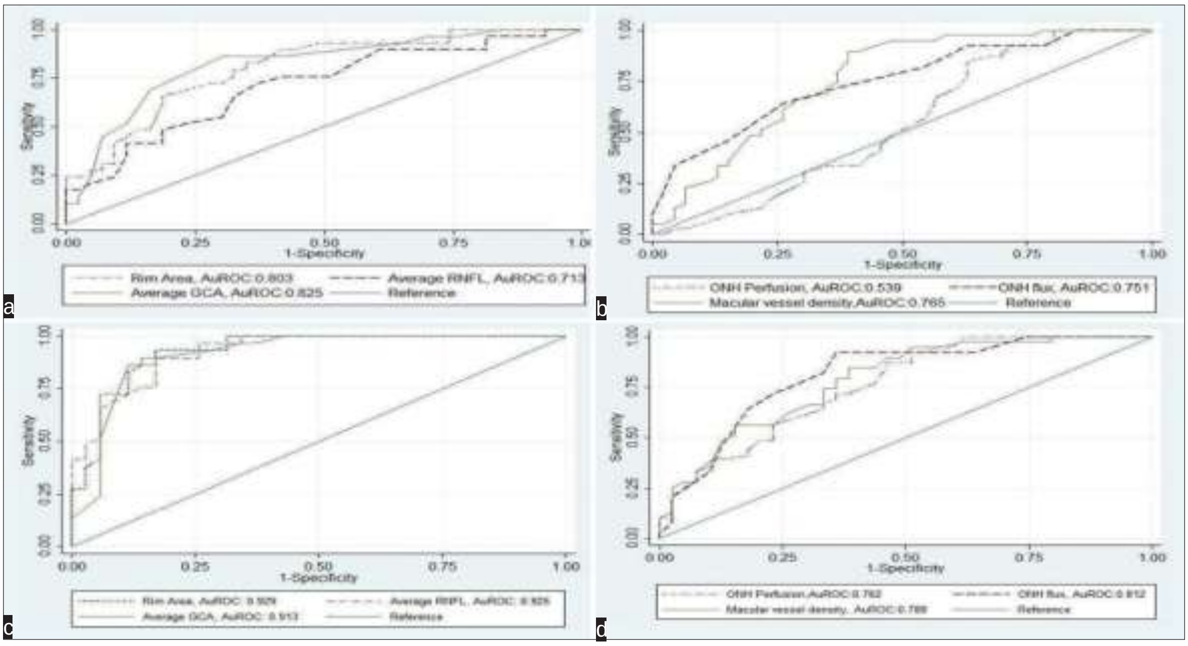


Figure 2: AUROC curves for parameters differentiating glaucoma suspects and normal subjects: (a) OCT and (b) OCTA. AUROC curves for parameters differentiating early POAG patients and normal subjects:(c)OCT (d)OCTA. AUROC=area under the receiver operating characteristic, OCT = optical coherence tomography; OCTA = OCT angiography, POAG = primary open angle glaucoma

V. CONCLUSION

OCTA parameters reveal early vascular alterations correlating with structural damage in glaucoma suspects and early POAG. Although OCT remains more accurate for diagnosis, OCTA enhances early detection by providing complementary vascular insights. Combining these modalities may improve early glaucoma management.

Financial Support and Sponsorship
Nil.

Conflicts of Interest
None declared.

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