

EVALUATION OF OCT CHANGES IN MACULA IN PRIMARY OPEN ANGLE GLAUCOMA PATIENTS ATTENDING A TERTIARY CARE CENTRE

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ABSTRACT

Background: Macular ganglion cell analysis (GCA) has shown promise in early detection and diagnosis of primary open-angle glaucoma (POAG). It has been demonstrated that GCA serves as a sensitive indicator of glaucomatous damage. **Materials and Methods:** Total 100 patients were enrolled (50 POAG & 50 Control). All patients underwent a comprehensive assessment that included a history, clinical symptoms, ophthalmological evaluation, bruch's membrane opening (BMO) centered OCT scan of the retinal nerve fibre layer (RNFL), OCT Macula for ganglion cell layer (GCL) analysis, and visual fields (VF) by Humphrey field analyser. **Result:** Mean RNFL global volume (RNFL GV) in glaucoma group was 73.44 with SD of 16.23, whereas mean RNFL GV in control group was 98.28 with SD 8.37. Mean GCL GV in glaucoma group was 34.9 with SD of 9.81, whereas mean GCL GV in control group was 48.32 with SD 3.90. **Conclusion:** In the present study, both circumpapillary RNFL and macular GCL thickness were reduced in glaucoma group than in control group (p value < 0.05). The reduction in GCL thickness was consistent with reduction in RNFL thickness in all grades of glaucoma - early, moderate, severe glaucoma (all p value < 0.05).

INTRODUCTION

Globally, Glaucoma is one of the leading cause of irreversible blindness.^[1,2] In 2013, it was estimated that 64.3 million persons worldwide, were affected by primary open angle glaucoma (POAG) and primary angle closure glaucoma (PACG). By 2040, the global glaucoma population is expected to reach 111.8 million.^[3] It is characterized by structural alterations in optic nerve head (ONH) and retinal nerve fiber layer (RNFL) which are accompanied by a loss of functional visual field (VF). Elevated IOP triggers retinal ganglion cell (RGC) loss, whose axons project information to the visual cortex.^[4-6] Standard automated perimetry is regarded as gold standard for diagnosis and follow up of glaucoma, but 25 to 35 percent of RGCs must be lost before noticeable abnormalities in visual fields are detected.^[7,8] Peripapillary RNFL measurements by Optical Coherence Tomography (OCT) is a good parameter to detect glaucoma. However, this method analyses only the axonal component of RGCs, does not account for the cell bodies and dendrites, which are equally affected in glaucoma and are found in the ganglion cell layer (GCL) and the inner plexiform

layer (IPL) respectively.^[9] The only region of the eye where the GCL thickness is more than one cell layer is the macula, which can have up to seven layers of ganglion cell bodies. Consequently, the RNFL thickness increases with increasing distance from the disc, while the macular GCL is thicker than the circumpapillary area.^[10,11] Macular region comprises more than 50 percent of all retinal ganglion cells, along with 10% or fewer axons remaining in advanced glaucoma. Thus, it is an ideal portion to spot early ganglion cell loss alongside its changes over time because of high cell density.^[12-15]

Current research objective is to evaluate diagnostic ability of macular GCL thickness in evaluating retinal ganglion cell damage at different stages of glaucoma and correlating it with visual field changes.

MATERIALS AND METHODS

This has been analytical cross-sectional study done in Department of Ophthalmology in Southern Railway Headquarters Hospital, a tertiary care hospital at Chennai, Tamil Nadu, located in South India.

Inclusion Criteria

Study group included patients aged > 18 years and < 65 years diagnosed with primary open-angle glaucoma (POAG), IOP > 21 in untreated eye, open angles in gonioscopy, glaucomatous optic cup, glaucomatous visual field defects. Control group included adults aged >18 years and < 65 years of age with normal intraocular pressure, normal optic disc, normal visual fields, having no history of any eye disease.

Exclusion Criteria

Patients with primary angle closure glaucoma, ocular hypertension, normal tension glaucoma, glaucoma suspects, secondary glaucoma, non-glaucomatous secondary causes of raised intraocular pressure, patients with media opacity such as corneal opacity, dense cataracts, history of intraocular diseases, complicated intraocular surgery, co-existing retinal diseases that affects retinal thickness, neurological conditions or diseases affecting visual fields, patients on treatment affecting visual fields. OCT scan results with artifacts or poor signal strength, visual fields with low test reliability—fixation losses >20%, false positive error >20%, false negative error >20%, uncooperative patients and patients not willing to participate in the study had been excluded.

All patients underwent a comprehensive assessment that included a history, clinical symptoms and thorough ophthalmological evaluation that contained best corrected visual acuity by Snellen's chart alongside transformed to logarithm of minimal angle of resolution (log MAR) units for statistical analysis, slit lamp examination, Goldmann applanation tonometry, gonioscopy by Goldmann three mirror lens and 90D disc evaluation.

Visual field (VF) study was performed utilizing 24-2 SITA standard program in Humphrey field analyser. Glaucomatous damage severity was categorised according to Hodapp-Parrish-Anderson (HAP) criterion as early defect: MD (Mean Deviation) < -6 dB, Moderate defect: MD between -6 to -12 dB, Severe (Advanced) defect: MD > -12 dB.^[16]

OCT optic nerve head, RNFL thickness, macular GCC (ganglion cell complex) thickness were imaged by spectral domain OCT (SD-OCT). Spectralis Glaucoma Module combines the proprietary Anatomic Positioning System (APS) to locate 2 fixed anatomic landmarks, namely, fovea along with BMO (Bruch's membrane opening) center.^[17] Scanning protocols used were ONH RC (optic nerve head radial 24 & three circles), in which a BMO-centered RNFL's OCT scan is performed in circular pattern, circle unrolled alongside presented as horizontal OCT scan. RNFL's average thickness is computed along with displayed in a thickness profile which presents in a double hump configuration. The thickness across different sectors is displayed in a classification chart with colour coding as shown in [Figure 1].

To calculate macular ganglion cell thickness and asymmetry, a single posterior pole volume scan consisting of 61 OCT scan lines are taken across the

macula and segmented into individual retinal layers.^[18,19] The GCL deviation map report includes GCL thickness map, GCL thickness deviation map and macular GCL classification map. Retinal thickness across different sectors is displayed in classification chart with colour coding as shown in [Figure 2].

Statistical analysis: Mean as well as SD have been computed for continuous variables, percentage was computed for categorical variables. One-way ANOVA test has been utilized to compare severity within glaucoma group for data in normal distribution, along with Kruskal-Wallis test has been utilized to compare severity within glaucoma group for data which is not in normal distribution. Independent t-test has been utilized to compare glaucoma group and control group for data in normal distribution, along with Mann-Whitney U test has been utilized to compare glaucoma group and control group for data which is not in normal distribution. Pearson's correlation test has been utilized to correlate. Data entry has been accomplished in Microsoft Excel spreadsheet, alongside final analysis has been executed with SPSS (statistical package for social sciences) software version 20, along with p-value < 0.05 considered significant. Research adhered to Declaration of Helsinki alongside has been accepted by Institutional Ethics Committee.

RESULTS

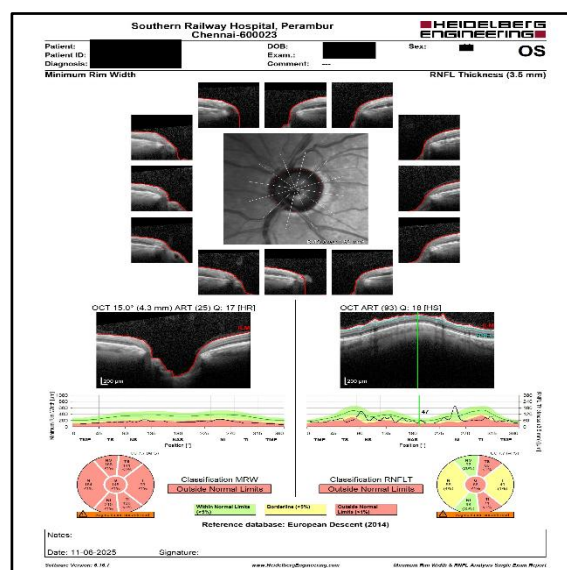


Figure 1: OCT circumpapillary RNFL analysis report

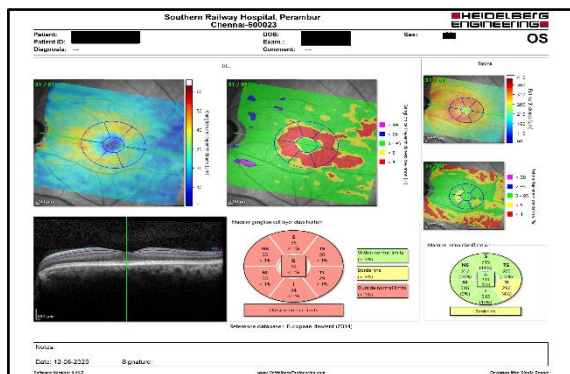


Figure 2: OCT macular ganglion cell layer and macular retinal thickness analysis report

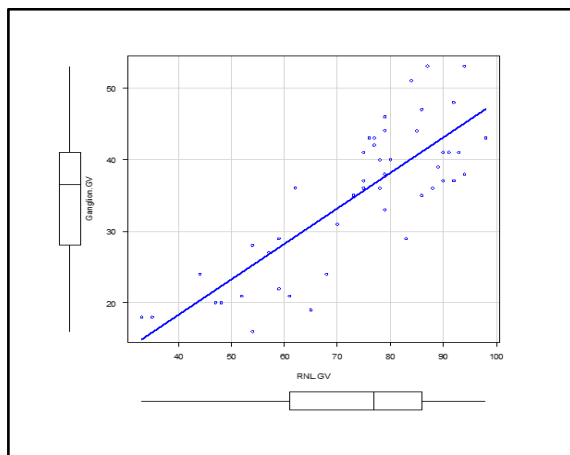


Figure 3: Scatter plot showing strong positive correlation for ganglion GV and RNFL GV in glaucoma group

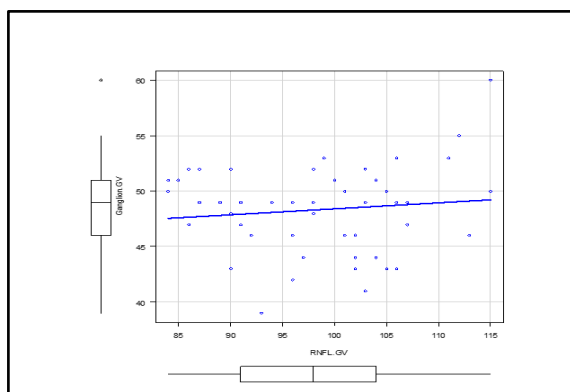


Figure 4: Scatter plot showing weak positive correlation for ganglion GV and RNFL GV in control group

About 100 participants had been included in study, out of which 50 participants had been in POAG group, along with 50 participants in control group. Participants mean age in glaucoma group has been 63.04 with SD of 11.32, majority of the participants 18/50 (36%) were seen in 61 to 70 years age group and age ranged from 33 to 86 years in glaucoma group, Mean age of participants in control group has been 54.06 having SD of 10.745, majority 20/50 (40%) were seen in 51 to 60 years age group and age ranged from 24 to 77 years in control group. Males were more common, about 39(78%) and 29(58%) in POAG & control groups, respectively. Both eyes are equally affected in the glaucoma group, whereas right eye preponderance (54%) is observed in control group. Patients in glaucoma group were regrouped by the severity of the defect noted in visual fields as mild glaucomatous defect in 22(44%), moderate glaucomatous defect in 18(36%) and severe glaucomatous defect in 10(20%).

Visual field analysis in the glaucoma group with different severities is shown in [Table 1]. Analysis of RNFL GV and GCL GV in different severities of glaucoma is shown in [Table 2]. By applying one way ANOVA test and comparing early, moderate, alongside severe glaucoma, there has been statistically significant difference for VFI, PSD, RNFL GV and Ganglion GV, with early group having greater mean value for VFI, RNFL GV and Ganglion GV and severe group having greater mean value for PSD. On applying Kruskal-Wallis' test and comparing early, moderate, alongside severe glaucoma, there has been statistically significant difference for Mean Deviation (p value< 0.001) as given in [Table 1].

By applying independent t-test and comparing glaucoma group as well as control group, statistically significant difference has been observed in visual field index and PSD. Control group has higher mean value than the glaucoma group in the visual field index, as illustrated in [Table 3].

There is strong positive correlation for ganglion GV as well as RNFL GV in glaucoma group with correlation coefficient r as 0.817, p value <0.05, as shown in [Figure 3], weak positive correlation for ganglion GV and RNFL GV in control group with correlation coefficient r as 0.114, p value 0.431 as shown in [Figure 4].

Table 1: Visual Field Analysis: Visual field index, Mean Deviation, PSD, in Glaucoma Group with Different Severities

Description	Early (n22)	Moderate (n18)	Severe (n10)	p value
	Mean \pm SD	Mean \pm SD	Mean \pm SD	
Visual field index	89.59 \pm 4.113	71.94 \pm 12.712	51.90 \pm 10.236	<0.001*
Mean Deviation	-3.6718 \pm 1.1907	-9.0717 \pm 1.70918	-15.593 \pm 2.5467	<0.001*
PSD	4.9036 \pm 1.9105	10.453 \pm 1.83322	12.731 \pm 1.8571	<0.001+

*oneway ANOVA test, +Kruskal Wallis test

Table 2: Analysis of RNFL GV and Ganglion cell layer (GCL) GV in Different Severities of Glaucoma.

Description	Early (n22)	Moderate (n18)	Severe (n10)	p value
	Mean \pm SD	Mean \pm SD	Mean \pm SD	
RNFL GV	83.09 \pm 8.896	71.83 \pm 16.249	55.10 \pm 12.078	<0.001*
GCL GV	40.32 \pm 6.841	33.4 \pm 49.494	25.60 \pm 8.553	<0.001*

*one way ANOVA test

Table 3: Comparison of Visual Field index, PSD Among Glaucoma group with Control group

Description	Glaucoma Group (n=50)	Control Group(n=50)	p value
	Mean \pm SD	Mean \pm SD	
Visual field index	75.70 \pm 17.028	96.78 \pm 2.122	<0.001
PSD	8.4670 \pm 3.77155	2.8130 \pm 1.52828	<0.001

Table 4: Comparison of RNFL Thickness in Glaucoma and Control Groups

Description	Glaucoma Group (n=50)	Control Group(n=50)	p value
	Mean \pm SD	Mean \pm SD	
RNFL GV	73.44 \pm 16.239	98.28 \pm 8.376	<0.001
SN RNFL	85.76 \pm 27.684	114.70 \pm 23.784	<0.001
ST RNFL	94.18 \pm 28.381	126.76 \pm 20.641	<0.001
IN RNFL	82.56 \pm 25.852	113.52 \pm 18.749	<0.001
IT RNFL	95.86 \pm 42.094	142.10 \pm 21.662	<0.001
Nasal RNFL	64.90 \pm 15.504	85.04 \pm 11.207	<0.001
Temporal RNFL	53.56 \pm 12.487	67.12 \pm 8.322	<0.001

Table 5: Comparison of Ganglion cell Thickness in Glaucoma and Control Groups

Description	Glaucoma Group (n=50)	Control Group(n=50)	p value
	Mean \pm SD	Mean \pm SD	
Ganglion GV	34.90 \pm 9.817	48.32 \pm 3.904	<0.001
Ganglion Superior	36.76 \pm 11.087	49.62 \pm 3.927	<0.001
Ganglion Inferior	35.64 \pm 11.412	48.64 \pm 4.720	<0.001
SN Ganglion	37.80 \pm 9.961	49.04 \pm 4.066	<0.001
IN Ganglion	36.48 \pm 11.051	48.54 \pm 4.205	<0.001
ST Ganglion	31.86 \pm 9.906	44.82 \pm 4.588	<0.001
IT Ganglion	32.02 \pm 11.426	47.88 \pm 3.288	<0.001

DISCUSSION

GCL thickness is an advanced technique that helps in early diagnosis of glaucoma as it detects the loss of cell bodies at an earlier stage than other techniques, which measure only nerve fibre loss.^[20] Few studies had evaluated Ganglion cell analysis(GCA) for the diagnosis of pre-perimetric glaucoma and reported comparable diagnostic ability to that of RNFL parameters.^[21] Main objective of our study has been to assess ability of macular GCL thickness to diagnose glaucoma using OCT. In our study, we have compared the macular GCL thickness with circumpapillary RNFL thickness to discriminate glaucomatous (POAG) eyes from normal eyes. Both normal and glaucomatous patients were taken, and the patients with glaucoma had been divided into early, moderate, alongside severe stages of glaucoma according to Hodapp-Parrish-Anderson criteria, and the structural and functional measurements were assessed.^[16]

In our study, Mean age of participants in glaucoma group was 63.04 with 11.32 SD, along with mean age in control group was 54.06 with 10.745 SD. Studies conducted by Kim et al,^[22] showed that mean age in normal control subjects was 57.0 with SD 9.7years, along with in glaucoma patients, the mean age was 60.0 with SD 9.8years.

In our study, early glaucoma was more commonly seen in 44%, moderate glaucoma in 36% and advanced/severe glaucoma in 20%. Studies conducted by Gupta et al,^[23] showed that early glaucoma was seen in 44.15%, moderate glaucoma in 29.87 % and advanced glaucoma in 25.98 %, which was similar to our study.

The vision in LogMAR units in normal group was 0.1220, whereas in the glaucoma group it was 0.3020,

implying that vision in glaucoma group was significantly lower than control group. This is consistent with findings in study done by Chan et al,^[24] who evaluated the impact of visual acuity deterioration in patients with glaucoma and found significant deterioration of visual acuity in POAG patients.

In our study, VFI and MD were lower in glaucoma group than in normal participants and in glaucomatous group MD showed deterioration with advancement of the disease. The MD and PSD were similar to the previous study done by Gupta et al^[23], where the MD in the three groups was -3.55 ± 1.94 , -8.47 ± 1.85 , and -19.55 ± 6.02 dB, respectively. The PSD in the three groups was 2.86 ± 1.68 , 5.17 ± 3.38 , and 9.66 ± 3.09 dB, respectively.

In our study, RNFL thickness GV has been significantly lower in glaucoma group (73.44) compared to control group (98.28) & the RNFL GV thickness reduced with increased severity of glaucoma (In early glaucoma, 83.09; moderate glaucoma, 71.83; severe glaucoma, 55.10). Among the various sectors, the RNFL thickness was found to be higher in IT RNFL and ST RNFL sectors in the control group. Statistically significant reduction in RNFL thickness in all sectors has been found compared to control group, but maximum thinning was seen in the IT RNFL sector in our study. This is in accordance with a study conducted by Kim et al,^[22] using SD OCT, where they noted RNFL thickness is significantly reduced in all quadrants in glaucoma group than in healthy subjects.

In both superior as well as inferior quadrants, GCL thickness decreased in glaucomatous eyes relative to normal eyes was statistically significant. GCL GV thickness in the control group was 48.32, whereas in glaucoma group it was 34.90, which was significantly

lower than control group. There has been significant reduction in GCL thickness in all sectors in glaucoma group than control group; but maximum thinning in glaucoma group was seen in ST and IT sectors of ganglion cell thickness.

In a study by Moreno et al,^[25] they discovered that capacity of macular GC-IPL parameters to discriminate between normal eyes as well as glaucomatous eyes is high along with comparable to peripapillary RNFL as well as ONH parameters. Sevim et al,^[26] in their research, found that GCC, as well as RNFL thickness measured by OCT, showed high diagnostic ability in detecting glaucoma. In the present study, we found that diagnostic ability of macular GCL to differentiate between glaucomatous as well as normal eyes is high along with comparable to circum-papillary RNFL. Thus, macular ganglion cell thickness might be suitable alternative, objective or complementary measurement to peripapillary RNFL thickness along with visual field parameters in clinical evaluation and management of glaucoma.

Limitations of our study were that the statistical indices (MD, PSD) could occasionally be deceptive in cases of advanced glaucoma because of poor reliability as well as reproducibility in 24-2 visual field, evaluation of disease severity relies on MD (mean deviation) of visual fields, and there can be high test-retest variability. Our sample size is limited; we require a bigger sample size, and longitudinal studies would be appropriate for confirming the findings. We also were unable to evaluate diagnostic ability of Spectralis OCT's segmented algorithm to that of other OCT machines.

CONCLUSION

Ability of macular GCL to discriminate among normal as well as glaucomatous eyes is high along with comparable to that of circumpapillary RNFL. Its ability to detect early changes, monitor progression, and provide localized insights into ganglion cell health underscores its potential clinical value. As there is no single test or clinical finding which helps in making a definitive diagnosis of glaucoma, both macular GCL and circumpapillary RNFL thicknesses should be assessed along with visual fields to detect and evaluate the severity and also to monitor the progression of glaucoma.

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