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Comparison of ONH, GCC and RNFL with SDOCT in Normal, Pre-Perimetry and Glaucoma Patients

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Abstract: ***The purpose is to compare the ability of spectraldomain optical coherence tomography (SDOCT) retinal nerve fiber layer (RNFL), optic nervehead (ONH), and macular measurements (GCC) todetect glaucomatous damage. Methodology: This study was prospective, cross-sectional observational study.All patients went under the detailedglaucoma Workup.Patients were categorized in control group, pre-perimetry, Glaucoma with Normal visual field and Glaucoma with Visual field changes. Optic Nerve Head (ONH), RNFL parameters and Macular measurements (GCC) were tested by SDOCT. Results: Total 204 eyes of glaucoma patients were included with mean age M=57.55, SD=10.60. Oct ONH, Average RNFL and GCC analysis was done. Mean Average RNFL showed significant change between control (92.29±10.23) and glaucoma group(67.17±14.12)p<0.05.Average GCC+IPL in control group (80.15±6.51) and glaucoma patients(62.74±13.52)p<0.05. Diagnositic ability was tested in Average RNFL (0.80) and Average GCC (0.77) were found to be largest AUC curve. Conclusion: Our results have significant implications for the use of the SDOCT technology for diagnosing structural damage in eyes havingglaucoma.***

Keywords: ONH (Optic Nerve Head Analysis), Retinal Nerve fibre layer (RNFL), GCC (Ganglion cell complex), OCT, Glaucoma

1. Introduction

Glaucoma, a leading cause of irreversible blindness, can be prevented or stabilized the progression if identified early and managed it appropriately. In India, around 12 million people suffer from glaucoma, and 1.5 million are blind due to it, so making the third most common cause of blindness. More than 75% of glaucoma are undiagnosed, which perhaps represent the submerged portion of the iceberg phenomenon of the traditional disease explanations[1]

Glaucoma is achronic, progressive optic neuropathies that can lead to irreversible damage to retinal ganglion cells (RGC) and their axons with characteristic visual field defects. In the early stages the disease is largely asymptomatic and it is estimated that only half ofglaucoma patients are aware that they have the disease. The diagnosis of glaucoma is based on Visual field loss (VF) or the appearance of the disc, measurement of intraocular pressure or Retinal nerve fiber layer (RNFL) changes.Glaucomatous optic disc appearance was defined as vertical cup disc ratio >0.5, focal or diffuse thinning of the neuroretinal rim and asymmetry of the cup disc ratio ≥ 0.2 between two eyes. Quigley et al. reported that up to 40% to 50% of the RNFL could be lost before visual field defects are detected by conventional perimetry. The early detection of nerve fiber layer (NFL) changes is crucial for all patients with glaucoma. Thus RNFL assessment is an important parameter for preperimetric diagnosis of glaucoma [2].

Several previous studies have evaluated the accuracies of RNFL, ONH, and macula scans provided by SDOCT for glaucoma diagnosis. In the absence of clearly defined visual field losses, SDOCT could potentially be used to differentiate eyes with pre-perimetric glaucomatous damage from eyes that show suspicious optic disc appearances, but no structural damage [3]. Optical coherence tomography (OCT) can be used to quantify the morphological features of the ONH and the retinal nerve fiber layer (RNFL) thickness and is currently widely used because of its high image resolution and precise measurement. In this study, we evaluated the findings of OCT on the accuracy of glaucoma diagnosis in practice. [4]

2. Methodology

This study was prospective, cross-sectional observational study. Patients were included from 2018-2021 at rotary eye institute, Navsari. Institute Scientific review committee approved all protocols and methods described adhered to the tenets of the declaration of Helsinki. The study included 204 eyes. Patient age more than 40 were included with systemic history and family history of glaucoma were included. Patient whose clinical correlation was unable to estimate due to pathology were excluded from the study. Patient age less than 30 years were excluded from study. The comprehensive eye examination we describe below was followed for all glaucoma patients. Such a comprehensive eye examination comprises:

- Visual acuity and refraction, Visual acuity was checked with Snellen's letter chart and dot chart for illiterates.

Refractive error was first measured with autorefractometer and then the best corrected visual acuity was obtained by performing subjective refraction.

- Refraction (Topcon KR-1)
- IOP measurement
- External examination and assessment of ocular motility,
- Examination of the pupil with special attention to the presence of a relative afferent pupillary defect,
- Slit-lampbiomicroscopy,
- Specular Microscopy (Topcon SP2000P)
- Gonioscopy to examine the angle of the eye,
- Dilated examination of the optic disc and retina and
- Optical Coherence Tomography (Structural Analysis-Zeiss Cirrus OCT)
- visual fields, automated perimetry is performed to detect functional defects in the visual field. (Zeiss Humphrey Visual Field Perimeter)

Clinical correlation was done between Cup Disc- Perimetry, Cup Disc-Neuro Retinal Rim thickness (NRRT), Cup Disc-Retinal Nerve Fibre layer Thicnkess (RNFL) and RNFL-Perimetry. Score was given as 0 means No correlation, 0.5 means partial correlation and 1 means complete correlation. All patients individual parameters were correlated and score was put. Patients were categorized in control group, pre-perimetry, Glaucoma with Normal visual field and Glaucoma with Visual field changes. Cirrus OCT used for understanding the five Optic Nerve Head (ONH),five RNFL parameters cube 200 x 200 scans and eight Macular measurements (GCC) cube 512 x 128 scans were taken with minimum signal strength of 7 was included in study. Areas under the receiver operating characteristic curves (AUC) were calculated to summarize diagnostic accuracies of the parameters. All data were analyzed with IBM spss 26.

3. Statistical Analysis

Statistical analysis was done using IBM SPSS softwareversion 26.Control, Pre-Perimetry, Glaucoma with Visual field and Glaucoma group analysis was doneby usingOne way ANOVA and to understand the diagnostics of instrument ROC curve was found for OCT instrument.

4. Results

Total 204 eyes of glaucoma patients were included with mean age M=57.55, SD=10.60. Out of 204, 146 eyes,87(60%) were males and 59(40%) were females in Glaucoma group, Out 204 eyes, 58(28%) Control Group, 15(7%) Pre-Perimetry Group, 44(22%) Glaucoma with Normal Visual field, 87(43%) were Glaucoma.

Table 1: Demographic and Clinical Characteristics in Control, Pre-perimetry, Glaucoma with Normal VF and Glacuoma group

Characteristics	Control Group	Pre-Perimetry Group	Glaucoma with Normal VF	Glaucoma	p-value
N	58	15	44	87	
Age	54.10±11.31	55.86±6.21	56.09±9.89	60.88±10.23	p<0.001
%Male	28%	7%	20%	45%	p=0.753
%Female	29%	8%	24%	39%	

Table 2: Mean±SD Values of ONH Parameters for Discriminating between Control, Pre-perimetry, Glaucoma with Normal VF and Glacuoma

OCT ONH Parameters	Control Group	Pre-Perimetry Group	Glaucoma with Normal VF	Glaucoma	p-value
N	58	15	44	87	
Avg VCD Ratio	0.63±0.16	0.69±0.08	0.57±0.15	0.77±0.09	p<0.05
Avg CD ratio	0.66±0.15	0.72±0.05	0.61±0.13	0.77±0.09	p<0.05
Cup volume	0.47±0.33	0.42±0.18	0.3±0.26	0.55±0.36	p=0.001
Rim Area	1.22±0.18	0.9±0.18	1.21±0.21	0.8±0.24	p<0.05
Disc Area	2.37±0.55	1.92±0.34	2.08±0.42	2.09±0.45	p<0.05

Table 3: AUC curve with cutoff values of ONH parameters measured with OCT

Test Result Variable(s)	Area	cut off	p-value
Average Vertical CD Ratio	0.69(0.04)	0.66-0.64	p<0.05
Average CD ratio	0.66(0.04)	0.70-0.67	p<0.05
Cup volume	0.54(0.04)	0.384-0.377	p=0.328
Rim Area	0.8(0.03)	1.13-1.15	p<0.05
Disc Area	0.64(0.04)	2.18-2.20	p=0.001

Table 5: AUC curve with cutoff values of RNFL parameters measured with OCT

Test Result Variable(s)	Area Under Curve (AUC)	Cutoff	p-value
Oct Average RNFL	0.8(0.03)	88.50-90.50	p<0.05
Superior RNFL	0.79(0.03)	109.50-111.50	p<0.05
Inferior RNFL	0.8(0.03)	110.50-112.50	p<0.05
Nasal RNFL	0.72(0.03)	71.50-73.50	p<0.05
Temporal RNFL	0.6(0.04)	56.50-58.50	p=0.026

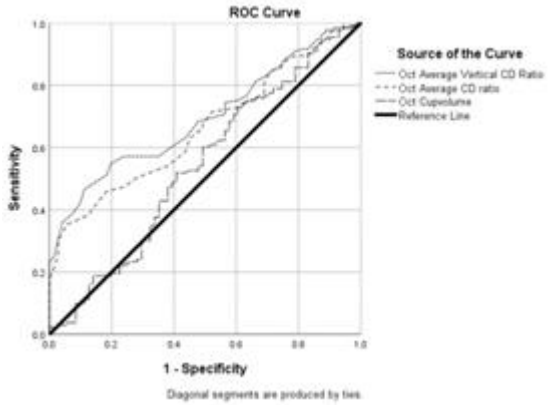

Figure 1: ROC curves for the ONH parameters with largest areas under the ROC curves: Oct Vertical Average CD Ratio

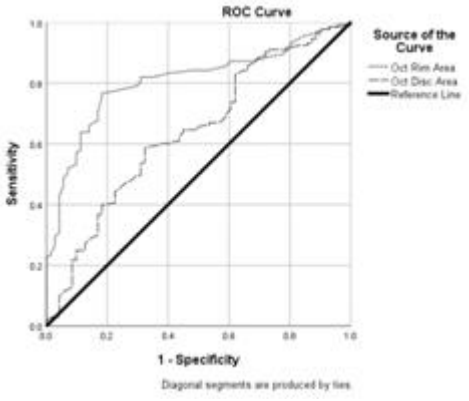

Figure 2: ROC curves for the ONH parameters with largest areas under the ROC curves: Oct Rim Area

Table 4: Mean±SD Values of RNFL Thickness (OCT) for Discriminating between Control, Pre-perimetry, Glaucoma with Normal VF and Glacuoma

RNFL(µm)	Control Group,	Pre-Perimetry	Glaucoma with Normal VF	Glaucoma	p-value
N	58	15	44	87	
Oct Average RNFL	92.29±10.23	79.8±8.84	89.38±10.43	67.17±14.12	p<0.05
Superior RNFL	115.26±17.42	100.33±13.58	111.18±20.78	78.14±24.07	p<0.05
Inferior RNFL	117.6±20.67	96.33±16.36	115.84±16.6	75.28±23.39	p<0.05
Nasal RNFL	76.59±11.89	68.13±11.68	70.75±11.94	61.36±11.86	p<0.05
Temporal RNFL	59.43±7.62	54.53±8.18	59.09±9.42	52.28±11.97	p<0.05

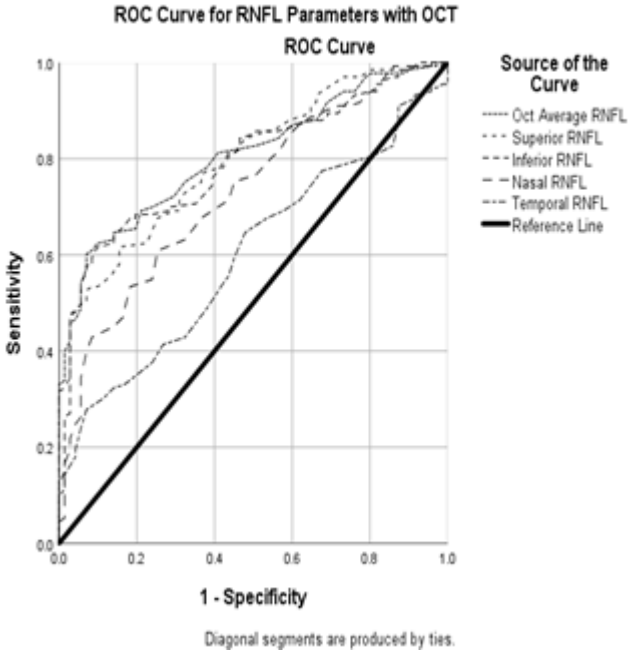

Figure 3: ROC curves for the Five RNFL parameters with largest areas under the ROC curves: average RNFL thickness, Superior and Inferior quadrant RNFL Thickness

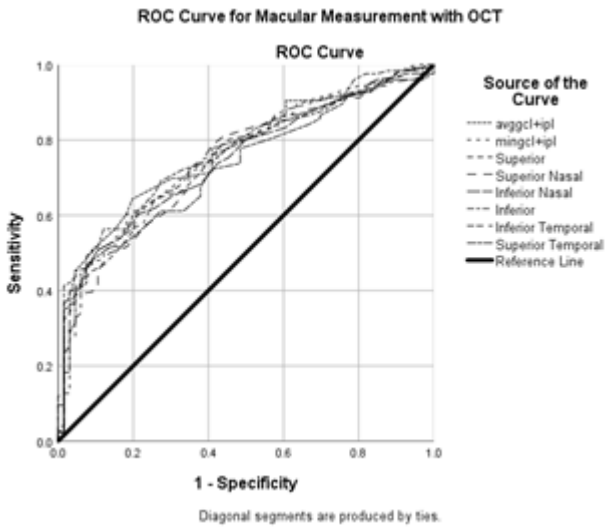

Figure 4: ROC curves for the Eight GCC parameters under the ROC curves

Table 5: Mean±SD Values of Macular Measurement Thickness (GCC) for Discriminating Between Control, Pre-perimetry, Glaucoma with Normal VF and Glacuoma

Macular Measurements(µm)	Control Group,	Pre-Perimetry	Glaucoma with Normal VF	Glaucoma	p-value
N	53	15	43	81	
GCC Superior	81.15±7.81	71.53±14.07	76±13	62.98±17.55	p<0.05
Superior Nasal	80.98±7.15	70.87±14.91	76.93±14.29	63.69±15.85	p<0.05
Inferior Nasal	80.11±6.96	67.93±14.68	77.28±14.05	62.52±14.33	p<0.05
GCC Inferior	77.81±7.14	67±12.37	74.86±13.19	60.23±13.03	p<0.05
Inferior Temporal	79.57±7.61	68.67±8.03	75.91±11.70	62.16±14.54	p<0.05
Superior Temporal	81±7.31	70.47±11.31	75.44±13.81	64.99±18.84	p<0.05
Average GCL +IPL	80.15±6.51	69.47±11.31	76.02±12.83	62.74±13.52	p<0.05
Min GCL+IPL	75.98±8.19	61.2±17.19	72.51±13.98	52.4±18.26	p<0.05

Table 6: AUC curve with cutoff values of GCC parameters measured with OC

Test Result Variable(s)	Area Under Curve (AUC)	Cutoff	p-value
Averag GCL+IPL	0.77(0.03)	76.50-78.50	p<0.05
Min GCL+IPL	0.76(0.04)	72.50-74.50	p<0.05
GCC Superior	0.75(0.04)	77.50-79.50	p<0.05
Superior Nasal	0.74(0.04)	77.50-79.50	p<0.05
Inferior Nasal	0.75(0.03)	77.50-79.50	p<0.05
GCC Inferior	0.77(0.03)	75.50-77.50	p<0.05
Inferior Temporal	0.76(0.03)	77.50-79.50	p<0.05
Superior Temporal	0.72(0.04)	78.50-80.50	p<0.05

5. Discussion

In this study we evaluated the SD-OCT features of ONH, RNFL and GCC classified as Normal, Pre‑Perimetric, Glaucoma with normal visual field and Glaucoma with visual field by glaucoma specialists. We studied the data values, of Oct classification and the deviation from normal thickness map provided by the machine of the RNFL and GCL+IPL maps. This Study focuses on Structural changes in glaucoma, functional parameters were checked and taken into consideration for diagnosing the condition. As shown table 1, Mean Cup disc ratio shows significant different in all groups with 0.77±0.09, 0.69±0.08 (p<0.05) in glaucoma and pre-perimetric glaucoma.

Over the past few years, SD-OCT has become more popular, due to its remarkable advantages in the diagnosis.With the development of SDOCT, it is possible to image and measureGCC. In glaucomatous eyes, reduction in macular thickness is more significant, and loss of GCC is the main reason. Therefore, it becomes more important to measure GCC than macular thickness. In present study, we demonstrated that SD-OCT RNFL and GCC with cirrus OCT.Eight different GCC and IPL (inner plexiform layer) measurement were shown significant different in groups as shown in Table 5. Average GCC+IPL shows thining in glaucoma62.74±13.52, whereas Control group 80.15±6.51 and pre-peimetry 79.8±8.84. Average RNFL comparision was shown in Table 4, Shows a significant thining in the glaucoma patients having (67.17±14.12) thickness, whereas control group (92.29±10.23) and (79.8±8.84). RNFL thickness is decreased is pre-perimetry much than glaucoma with normal visual field. Patient with pre-perimetryneeds to be tested every 6 to 8 months to see both structural and functional changes.Similar study suggest GCC Measure with RT-vue OCT in pre-perimetry was 83.6± 7.2 and control was 91.2 ±6.6. Average RNFL was 86.0 ± 7.6, 99.5 ± 8.2.[3]Khanal et al in 2014 suggested mean (95% CI) RNFL thickness decreased significantly from normal, 109.8 m (106.7-112.9), and GS, 102.0 m(98.57-105.6 m).Similar studies conducted by Satya Prakash, Vinai, Arun Kumar, Shivangi, Kamaljeet and Jagriti on Comparison of Retinal Nerve Fibre Layer Thickness by SD- OCT in POAG,NTG and Glaucoma Suspect.

Diagnositic accuracies was measured by conducting ROC curve and determine the Area Under curve(AUC). In this study All OCT parameters ROC curve is estimated as shown in Figure 1 to 4. The ROC curve was found as shown in Table 3,5 and 6. Where Average Vertical CD ratio shows 0.69 AUC, with cut-off (0.66-0.64,p<0.05), Average RNFL shows 0.80 AUC, with cut-off (88.50-90.50,p<0.05) and Average GCL+IPL shows 0.77 AUC, with cut-off(76.50-78.50,p<0.05). Renato Lisboa et.al study, AUC curve was found in Cupdisc ratio, Average RNFL and GCC was 0.74,0.89 (0.03), 0.79 (0.04) which similar with current study. Structural and functional changes both were included as clinical correlation with instrument finding correlation.If the instrument fails to differentiate patients with clearly defined disease versus clinical correlation those without any suspicious findings of damage, were excluded from the study. The AUCs reported in our study were considerably similar than the ones reported in previous studies that evaluated the diagnostic ability of SDOCT in glaucoma.

RNFL measurements performed significantly better than optic disc measurements and GCC in our study. This finding indicates that in the presence of suspicious optic disc appearance, RNFL assessment seems to be more useful than optic disc topographic measurements to establish the diagnosis.Moreover, previous studies clarifies inperformance of the GCC protocol is that the current algorithmavailable on the RTVue SDOCT does not differentiate theganglion cell layer from the RNFL and internal limitingmembrane whereas Cirrus OCT measured with GCC+IPL thickness.Further studies should evaluate theability of thescanning SDOCT areas to detect progressivedamage in glaucoma with pre-perimetry and glaucoma with normal visual field. Our Study suggest to diagnose glaucoma clinical practice and expertise should take into consideration based on diagnositicabilty of the instrument should not be diagnosed irrespective of having better sensitivity and specificity.

Current study limitation, few numbers of patient were identified in pre-perimetry glaucoma and glaucoma with normal visual field having higher RNFL thickness compared to pre-perimetry both categories of patient needs to assess their progression. Another limitation of our study is that stereophotographic evaluation of the optic disc was not taken into consideration, clinical disc analysis was done by glaucoma experts which may create imperfect interobserver agreement. Studies of Glaucoma suggest diagnosing should be made on basis of Clinical structural correlation with diagnostics ability instrument.

6. Conclusion

The results of this study demonstrated thatSDOCT RNFL measurements performed significantly betterthan ONH and macular measurements in detecting Preperimetric glaucomatous damage. Our results have significant implications for the use of the SDOCT technology fordiagnosing structural damage in eyes havingglaucoma.

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