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Brijesh Patil[1], Anupama C Shetgar[2], and Divya Teja V[3]*

[1]MS, Professor, Department of Ophthalmology, S. Nijalingappa Medical College and HSK Hospital, Bagalkot, Karnataka, India
[2]MS, Associate Professor, Department of Ophthalmology, S. Nijalingappa Medical College and HSK Hospital, Bagalkot, Karnataka, India
[3]2nd DOMS, S. Nijalingappa, Medical College and HSK Hospital, Bagalkot, Karnataka, India

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***Corresponding author:** Divya Teja V, Doctor, 2nd DOMS, S. Nijalingappa Medical College and HSK Hospital, Room No: 46, PG Ladies hostel, Navanagar, Bagalkot-587102, Karnataka, India, Tel: 9441686800; E-mail: divyatejavemula@gmail.com

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Research Article

Evaluation of Retinal Nerve Fiber Layer Thickness using Spectral Domain-Optical Coherence Tomography in Glaucomatous, Ocular Hypertensive and Normal Eyes and its Correlation with Visual Fields

Abstract

Objective: The aim of the study was to correlate the findings of peripapillary retinal nerve fiber layer (RNFL) thickness calculated with optical coherence tomography(OCT) with visual field changes in glaucomatous, ocular hypertensive and normal eyes.

Materials and Methods: 30 normal, 30 ocular hypertensive and 30 glaucomatous eyes were included in the study. All underwent applanation tonometry, disc evaluation, octopus white on white (W/W) perimetry and OCT. Average and segmental RNFL thickness values were compared among all groups. A correlation was sought between global indices of perimetry and RNFL thickness in ocular hypertensive group.

Results: Of the 90 eyes (mean age: 51.20±9.23 years), the mean RNFL thickness was significantly less in ocular hypertensives 83.83±26.20μm; P< 0.001) and glaucomatous eyes (55.33±34.72 μm; P <0.001), than in normal (103.27±16.23 μm). Ocular hypertensives had thinner RNFL in the superior, inferior, nasal and temporal quadrants (P < 0.001) when compared to normal. The RNFL thickness could not be significantly correlated with global indices of visual fields in ocular hypertensives.

Conclusion: Optical coherence tomography is capable of detecting changes at the level of RNFL in ocular hypertensive eyes with normal appearance of discs and W/W perimetry fields.

Abbreviations

RNFL: Retinal Nerve Fiber Layer; OCT: Optical Coherence Tomography; ONH: Optic Nerve Head; SLP: Scanning Laser Polarimetry; HRT: Hiedelberg Retinal Tomography; CDR: Cup-Disc Ratio; BCVA: Best Corrected Visual Acuity; MD: Mean Defect

Introduction

Glaucoma is a group of many conditions sharing a final common pathway characterized by accelerated death of retinal ganglion cells and their retinal nerve fiber layer (RNFL) axons resulting in characteristic visual field defects and corresponding optic nerve head anatomical changes. The ability to detect structural loss is fundamental in the diagnosis and management of glaucoma. While glaucomatous structural damage can be assessed subjectively by clinically examining the optic nerve head (ONH) and peripapillary retinal nerve fibre layer (RNFL), the introduction of ocular imaging modalities into clinical management has allowed for supplemental objective and quantitative evaluation of ocular structure.

Optical coherence tomography (OCT), first described in 1991, is a noncontact, noninvasive imaging technique that can reveal layers of the retina by looking at the interference patterns of reflected laser light. Automated software segmentation algorithms are able to outline the retinal nerve fiber layer with much precision, which is relevant in glaucoma since this layer is thinned as ganglion cells are lost. OCT became widely popular in 2002 with the release of Stratus OCT, a time-domain technology (TD-OCT) that was well-studied and validated for use in glaucoma and retina and went on to become a standard structural imaging test. Only four years later, spectral-domain

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OCT (SD-OCT), a fourier-domain OCT, which improved upon TD-OCT by capturing more data in less time at a higher axial image resolution, around 5 µm is developed. OCT thus produces high-resolution cross-section images of the posterior pole of the eye, and can be useful in glaucoma diagnosis for its ability to study the diffuse and localized thinning of RNFL [1]. Some studies suggest that OCT may be superior to scanning laser polarimetry (SLP) and Heidelberg retinal tomography (HRT) for detecting a specific pattern of reduction in the average and focal RNFL thickness as well as the disc parameters [2,3]. Individuals with glaucoma are usually asymptomatic until late the disease processes and it is possible to either slow or prevent the progression of vision loss if detected early by adequate treatment. Therefore, a glaucoma screening tool for the general population is desirable.

White on White (W/W) perimetry is a generally accepted method for monitoring visual field damage in glaucoma patients and suspects. Glaucoma patients suffer a loss of about 40% of their retinal ganglion cells before this loss is picked up on W/W perimetry [4].

Aim

The aim of the study was to measure the RNFL thickness by OCT in eyes with glaucoma and in ocular hypertensives and to compare the results with that of age-matched normal eyes and to correlate the findings with global indices of visual fields in ocular hypertensives.

Materials and Methods

A total of 90 eyes (30 normal, 30 ocular hypertensive and 30 glaucomatous eyes) of individuals (age range 30 to 70 years) attending SNMC Eye OPD at Bagalkot, between October 2015 and October 2016 were enrolled in this cross-sectional observational study. The study was approved by the ethical committee of our Institute. Informed consent was taken from all study subjects. All subjects had open angles on gonioscopy with best corrected visual acuity (BCVA) of 20/40 or better with clear lens. Inclusion criteria were

a) **Normal eyes:** No history of ocular surgery or laser treatment, intraocular pressure (IOP) of 21mmHg or less, normal slit-lamp examination, cup disc (CD) ratio 0.2 to 0.4, symmetrical cupping and normal W/W perimetry.

b) **Ocular hypertension:** IOP greater than 21mmHg on a diurnal day curve before treatment on at least two separate occasions with normal visual fields and CD ratio of 0.2 to 0.4.

c) **Glaucoma:** IOP greater than 21mmHg and an abnormal W/W perimetry that fulfilled the minimum criteria for glaucomatous visual field defects, namely, a cluster of three or more non-edge points in a location typical for glaucoma, all of which were depressed on pattern deviation plot at P <5% level and one of which was depressed at P <1% level, ONH defects characteristic of glaucomatous excavation, notching, focal or diffuse atrophy of RNFL, vertical CD ratio more than 0.6 or disc asymmetry more than 0.2 between the two eyes.

Exclusion criteria for all subjects included a BCVA worse than 20/40, angle abnormalities on gonioscopy, any other intraocular eye diseases, diseases affecting visual fields (pituitary lesions, demyelinating diseases, diabetes mellitus, the acquired immunodeficiency syndrome) or secondary causes of IOP increase (pseudoexfoliation, corticosteroid use, iridocyclitis, trauma) and any pathological condition, including retinal, that could affect the visual fields.

A detailed medical and surgical history was elicited from the patients. Slit-lamp biomicroscopy, visual acuity testing with refraction, ONH examination, applanation tonometry, gonioscopy, octopus perimetry and OCT evaluation of RNFL was performed in all groups. W/W perimetry was performed with Octopus 300 with Dynamic G2 Strategy. A reliable test was defined as having fewer than 20% false-positive or false-negative scores and fewer than 33% fixation losses. Perimetry and OCT examinations were performed on the same day.

Optical coherence tomography was performed by using Optovue spectral Domain OCT. The results were analyzed with Version 4.0.1 software. A-scan data centered over the optic nerve in which a 3.4 mm diameter circle of RNFL data is extracted to create what is referred to as the TSNIT map (temporal, superior, nasal, inferior, temporal). It is displayed as a false colour scale with the thickness values referenced to a normative database. The numeric values for all parameters are shaded as white, green, yellow, or red, with the yellow and red representing, < 5% and < 1%, respectively compared to the normative database. The TSNIT map displays RNFL thickness values by quadrants and clock hours. Three circular scans were obtained from each test eye. All scans were performed by the same investigator. An internal fixation target was used in all scans, and the location of each scan on the retina was monitored on the built-in infrared-sensitive video camera.The best quality, properly aligned scan was chosen for analysis. Average RNFL thickness was calculated globally and separately for superior, inferior, temporal and nasal quadrants.

Statistical analysis

The parameters compared were average RNFL thickness of the entire circumference of the optic disc and quadrant thickness consisting of superior (46 to 135 degrees), nasal (136 to 225 degrees), inferior (226 to 315 degrees) and temporal (316 to 345 degrees) quadrant areas between the three groups. Statistical significance is derived with Unpaired 't' test between the groups. Correlations between RNFL thickness and visual field parameters were assessed by correlation coefficients (Pearson's r).Data were reported as mean ± standard deviation (SD). A P value of less than 0.05 was considered statistically significant.

Results

Ninety eyes (30 normal, 30 ocular hypertensive and 30 glaucomatous) were enrolled. There was no difference between the groups with regard to gender, race and age. Mean age of the patients was 51.20±9.23years. The mean age of patients in the normal group is 53.16±7.2yrs, in ocular hypertensive group

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is 50.46 ±9.53yrs and glaucoma group is 52.76±11.23.The mean vertical CD ratio was 0.26, 0.36 and 0.74 in normal, ocular hypertensive and glaucomatous eyes respectively. The RNFL thickness was greatest in the superior and inferior quadrants and thinner in the nasal and temporal quadrants in the normal group. The RNFL profile demonstrated the "double hump" pattern.

Mean RNFL thickness was 55.33±34.72 µm in glaucomatous eyes, 83.83±26.20 µm in ocular hypertensives and 103.27±16.23 µm in normal (Figure 1).

Table 1, In the ocular hypertensive group, RNFL was thinner in the superior (107.40±35.39 µm), inferior (100.80±26.77 µm), nasal (67.10±19.26 µm) and temporal (58.30±24.99 µm) quadrants when compared to normals (P <0.001, unpaired 't' test). The RNFL was thinner in glaucomatous eyes in the superior (63.90±35.88 µm), inferior (57.10±34.70 µm), nasal (55.53±26.25 µm) and temporal (47.33±24.09 µm) quadrants when compared to normals (P<0.001). Mean defect (MD) of ocular hypertensive group is -2.32±1.37 with octopus perimetry. It is not statistically correlated with mean RNFL thickness of ocular hypertensive (r=+0.248, p=0.187, Pearson's r).

Discussion

Several instruments and techniques are used for the analysis of the optic nerve head, with the idea of detecting glaucomatous damage in its early stages, even before the functional field loss is detectable [5]. Optical coherence tomography (OCT) is a new optical technique for real-time, quantitative, objective, high-resolution measurements and cross-sectional imaging of the retina from which the RNFL is calculated [6]. OCT provides an assessment of the RNFL thickness by passing a near-infrared illumination (840 nm) beam into the eye and studying its reflectivity patterns by computer-assisted software. No reference plane is required to calculate RNFL thickness because OCT provides an absolute cross-sectional measurement of the retinal substructure, from which the RNFL thickness detectable visual field defects. Sommer et al. [7], in a 10-year follow-up study, reported that RNFL thinning is a sensitive indicator of the extent of glaucomatous damage and that RNFL loss precedes measurable ONH and visual field damage approximately six years before any detectable visual field defects. Thus, the possibility of detecting these defects in areas of physiological decreased visibility is enhanced when OCT, rather than a conventional method, is used.

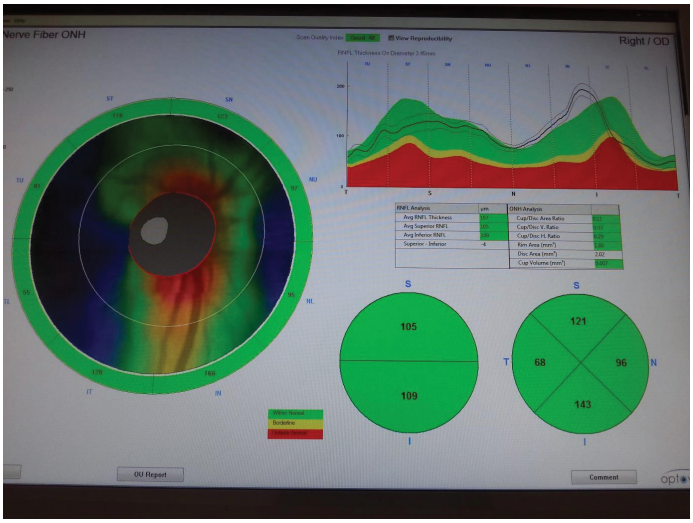

Figure 1: OCT image showing RNFL thickness in a normal eye with "Double Hump" pattern.

Table 1: Optical coherence tomography RNFL measurements in normal, ocular hypertensive and glaucomatous eyes.

	Normal eyes(A)	Ocular Hypertensive eyes(B)	Statistical analysis(A) Vs (B)	Glaucomatous eyes(C)	Statistical analysis(A) Vs (C)
Mean RNFL	103.27±16.23	83.83±26.20	P <0.001	55.33±34.72	P <0.001
Superior	115.17±16.60	107.40±35.39	P <0.001	63.90±35.88	P <0.001
Inferior	119.10±14.90	100.80±26.77	P <0.001	57.10±34.70	P <0.001
Nasal	84.53±14.66	67.10±19.26	P <0.001	55.53±26.25	P <0.001
Temporal	74.93±16.26	58.30±24.99	P <0.001	47.33±24.09	P <0.001

In our study, the mean thickness of the RNFL in glaucomatous patients and in ocular hypertensive patients was significantly less than in normal. Hoh et al. [8], reported that the mean RNFL thickness measured with OCT was significantly less in glaucomatous eyes (56.9±21.5 mm) than in ocular hypertensive (83.70±16.57 mm) and normal (90.86±14.17 mm) eyes; although RNFL thickness tended to be greater in normal than in ocular hypertensive eyes, this difference was not statistically significant.

Guedes et al. [9], reported that the inferior RNFL was the only parameter in which a statistically significant difference was observed between normal subjects and glaucoma suspect groups. Pieroth et al. [10], reported a specificity of 81% and sensitivity of 65% in detecting focal defects solely through statistical analysis of OCT measurements and also noted that focal RNFL defects are located in the inferotemporal and superotemporal regions of the RNFL. Soliman and associates [11], reported a significant correlation (correlation coefficient r = 0.557) between average RNFL thickness and mean deviation on W/W perimetry. Parisi et al. [12], and Zangwill et al. [13], have also reported a significant correlation between average RNFL thickness and MD. Kanamori et al. [14], showed that the highest correlation coefficient in all parameters was 0.729 at the average RNFL thickness, suggesting that average RNFL thickness was most useful for monitoring glaucoma. Localized RNFL defects can be clinically detected if more than 50% of the thickness of RNFL is lost. Therefore ocular hypertensive patients may have an impaired function of ganglion cells despite clinically normal-looking RNFL [15-19].

Andrew [20], in his study reported eyes with visible RNFL defects had a mean estimated retinal ganglion cell count of 657172 cells versus 968883 cells in healthy eyes(p<.001).Study concluded that although visible localized RNFL defects are often considered an early sign of glaucoma, it indicates that they are likely to be associated with large neuronal loss.

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Conclusion

Optical coherence tomography is capable of detecting pre perimetric changes at the level of peri papillary retinal nerve fiber layer in ocular hypertensive eyes with normal appearance of discs and normal visual fields. Examination of ONH and its surrounding RNFL is considered essential in the early diagnosis as well as monitoring of glaucoma.

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