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Original Article

Ophthalmology Section

Correlation of Retinal Nerve Fiber Layer Thickness and Axial Length on Fourier Domain Optical Coherence Tomography

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ABSTRACT

Introduction: The assessment of the peripapillary Retinal Nerve Fiber Layer (RNFL) thickness has been an important tool for evaluating and diagnosing glaucoma and its progression. Literature suggests that myopic eyes are at an increased risk for developing glaucoma. This study gives an insight into the relationship of RNFL thickness to the axial length in normal population.

Aim: To correlate the RNFL thickness and the axial length in normal individuals with Fourier domain Optical Coherence Tomography (OCT).

Materials and Methods: In the current study, 298 eyes of 149 normal individuals (10 years or older) with or without refractive error were recruited. The RNFL thickness was measured using Optovue (RTVue) three-dimensional Fourier domain OCT.

Results: We observed an inverse relationship between average RNFL thickness and increasing axial length(p=0.003). Maximum RNFL thickness was seen in the Infero-Temporal (IT) quadrant and minimum in the Supero-Nasal (SN) quadrant. RNFL thickness did not show any tendency to decline with age using the Pearsons correlation (r=0.07). Females had an increased RNFL thickness in the Supero-Temporal (ST) and Infero-Nasal (IN) quadrant (p-value 0.046 and 0.02) in comparison to males. There was a statistically significant thinning in Ganglion Cell Complex (GCC) with increasing axial length (p-value 0.000)

Conclusion: The current study suggests that the average RNFL thickness does not decrease with age. The RNFL and GCC thickness shows an inverse correlation with axial length of the eyeball hence observations have to be carefully interpreted in myopic eyes. Clinicians need to keep the anatomical variations in RNFL for better patient management.

Keywords: Best corrected visual acuity, Ganglion cell complex, Goldmann's applanation tonometer

INTRODUCTION

The Retinal Nerve Fiber Layer (RNFL) thickness analysis is an invaluable tool in the early diagnosis and periodic assessment of glaucoma and other optic neuropathies [1]. As it has been well recognized that myopes are at an increased risk of developing glaucoma and the clinical diagnosis can be challenging because of anatomical variations and sometimes an unusual optic disc appearance [2].

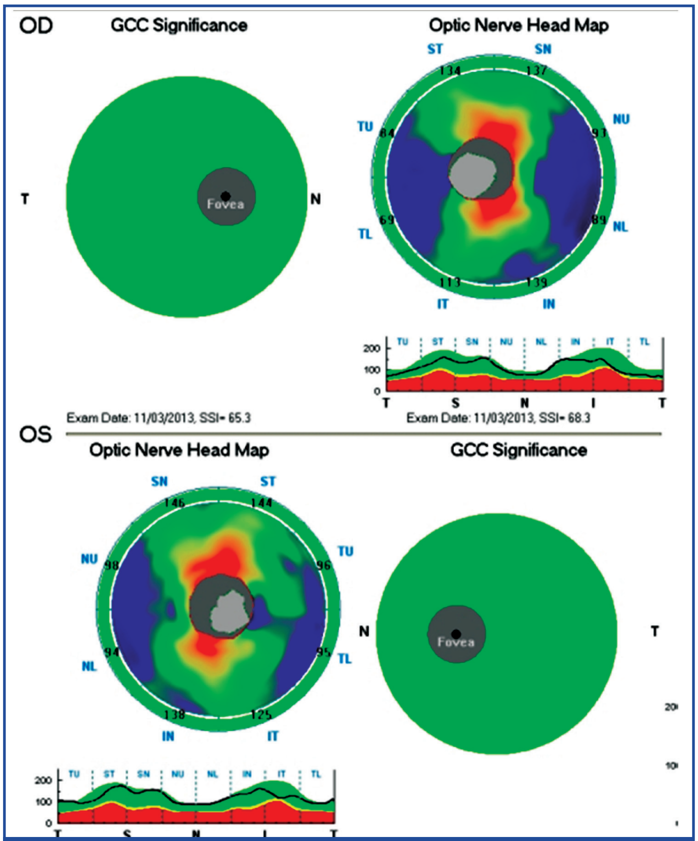
Optical Coherence Tomography (OCT) has emerged as new imaging device for the quantitative and objective assessment of RNFL thickness [3-10]. The assessment of RNFL thickness has been reported to be unreliable in myopic eyes with OCT in previous studies due to the variable topographic profiles seen in myopic eyes and has been classified to be outside normal limits for the nasal sector [2]. The RNFL thickness is also subject to variability with age, gender, race and ethnicity [3]. The Fourier domain OCT can eliminate this error as it takes into account sector by sector analysis of the RNFL thickness profile in each scan of the optic disc [11]. As there are only a few clinical studies [9,12,13], which have studied and analysed the RNFL thickness (mean varying from 101.07±10.13 to 111.75±4.83 µm) normal database available for the Indian population and its variation according to the axial length is in far a stretch, still in research. Acknowledging the various studies conducted in the past and each with varying results, the present study was aimed to study the correlation between thickness of RNFL and axial length of the eyeball by Fourier Domain OCT (RTVue-100, Optovue) in normal healthy subjects.

MATERIALS AND METHODS

The study was conducted in the Department of Ophthalmology, Himalayan Institute of Medical Sciences, Dehradun, over a period of 12 months from January 2012 to December 2012. This was an observational, non-randomized, prospective study and involved 149 (298 eyes) normal individuals, recruited from routine visits to the ophthalmology outpatient department at the institute. Written and informed consent was taken from the individuals before inclusion. The study was approved by the ethics committee.

The patients included in the study were all healthy individuals with or without refractive error and age of 10 years or above. The exclusion criteria included: best-corrected visual acuity less than 6/6, history of ocular trauma, history of intraocular or refractive surgery, neurological disorders, glaucoma or ocular hypertension, evidence of a reproducible visual-field defect, poor media clarity, amblyopia, any ocular disease, previous retinal laser treatment, any form of retinopathy and uncooperative patients. The patients were divided in 3 groups- Group I: Axial length <22.50 mm, Group II: Axial length 22.51 to 25.50 mm, Group III: Axial length >25.51 mm.

The clinical assessment of the patients included a complete ophthalmic and medical history according to a preset format. The ocular examination included Best Corrected Visual Acuity (BCVA) assessed using Snellen's chart, anterior segment evaluation using slit lamp biomicroscope, and fundus exam using +90D lens along with indirect ophthalmoscope (Heine Omega 200 bio binocular indirect Ophthalmoscope). Intraocular pressure was measured using Goldmann's Applanation tonometer, corneal curvature using manual keratometer (Bausch and Lomb, Rochester, NY) and, axial length using Ocuscan (Alcon laboratories). The RNFL thickness assessment, Ganglion Cell Complex (GCC) analysis and optic nerve head evaluation (ONH) was done using the Fourier domain Optovue RTVue OCT (Optovue, Inc., Fremont, CA). A single individual did the evaluation and image capturing after pupillary dilation using 1% tropicamide drops. RNFL thickness



[Table/Fig-1]: Optic Nerve Head scan.

Age Group (years)	Avg RNFL (μm)
10 – 19	108.58±8.55
20 – 29	104.95±9.89
30 – 39	105.85±8.61
40 – 49	108.18±10.33
50 – 59	107.51±11.13
60 – 70	108.20±10.99

[Table/Fig-2]: Average RNFL thickness in different age groups.

RNFL Quadrants	Male (n=198) eyes	Female (n=100) eyes	p-value
ST	124.36±18.85	129.09±20.17	0.046
IT	130.17±22.04	137.23±19.45	0.007
SN	117.46±20.11	116.7±23.12	0.770
IN	127.28±21.47	133.38±22.33	0.023
TU	83.07±14.01	86.15±14.71	0.079
TL	80.97±13.44	83.42±12.36	0.128
NU	90.44±15.88	90.78±13.29	0.854
NL	80.67±13.05	80.7±10.03	0.983

[Table/Fig-3]: Gender wise RNFL thickness in different quadrants.

RNFL quadrants	AL<22.5mm (n=100 eyes)	AL=22.5-25.5mm (n=100eyes)	AL>25.5mm (n=98eyes)	p-value
AvgRNFL	110.14±9.32	106.70±8.93	102.01±12.78	0.000
ST	133.32±14.63	126.90±18.46	111.94±24.28	0.000
IT	136.95±19.47	133.41±21.53	123.44±22.09	0.003
SN	124.25±25.0	117.27±19.68	103.75±15.82	0.000
IN	132.98±18.18	131.45±21.76	116.86±22.16	0.000
TU	85.48±15.61	84.43±14.17	80.82±12.67	0.211
TL	83.89±11.93	81.80±12.66	78.82±15.96	0.135
NU	92.76±13.17	90.16±13.43	89.10±22.14	0.381
NL	80.89±10.09	81.02±12.12	79±14.54	0.592

[Table/Fig-4]: RNFL in different quadrants in study groups.

was measured using the ONH protocol. This utilizes a 3.45 mm diameter circle centered around the optic nerve head and consists of 13 circular scans with diameter ranging from 1.3- 4.9 mm and 12 radial lines with 3.7 mm length. RNFL analysis was done in 8 sectors namely Superotemporal (ST), Superonasal (SN), Inferotemporal (IT), Inferonasal (IN), Nasal Upper (NU), Nasal Lower (NL), Temporal Upper (TU), and Temporal Lower (TL) [Table/Fig-1]. The GCC scan consists of 15 vertical lines scans which covers a 7 mm square region, and this is located 1 mm temporal to the centre of fovea.

STATISTICAL ANALYSIS

The data was analysed using the Microsoft Excel (2010) and SPSS version 17(Chicago, Illinois). These results have been presented in the form of percentage and proportions using descriptive statistical methods. The statistical relationship between the variables was established using Pearson's correlation, Student t-test, one-way ANOVA and post-hoc test.

RESULTS

The study included 298 eyes of 149 healthy patients. They were age matched and normal in distribution of males and females. There was an overall male preponderance in all groups. The number of males and females were 99 (66.5%) and 50 (33.5%) respectively, with male to female ratio of 1.9:1.

Average (Avg) RNFL Thickness According to Age

[Table/Fig-2] shows the average RNFL thickness in different age groups. No statistically significant correlation was observed using Pearson's correlation (r=0.07) between the different age groups and RNFL thickness.

Gender Wise RNFL Thickness

The RNFL was studied in 8 quadrants. [Table/Fig-3] shows that the maximum RNFL thickness was noted in the IT quadrant both in males and females. Females had a statistically significant thicker RNFL in ST and IN quadrant (p-value 0.046 and 0.02) in comparison to males.

Axial Length and RNFL

The RNFL was studied in three different groups according to axial length. The mean spherical equivalent in group 1(n=50) was +2.5±0.75, in group II (n=50) was +1.0±0.75 and Group III(n=49) was -4.0± 0.5 diopters. The mean RNFL in Group with axial length < 22.50 mm was 110.14±9.32μm, 106.70±8.93 μm in the group with axial length 22.51 – 25.50mm and 102.01±12.78 μm in the group with axial length >25.51mm. [Table/Fig-4] shows RNFL thickness in different quadrants. The RNFL thickness was maximum in the IT quadrant (p=0.003) in all three groups and minimum in lower temporal quadrant (p-value=0.381), which is not statistically significant. Statistically thicker RNFL was noted in IT, ST, IN and SN quadrants in the study group.

Axial Length and Ganglion Cell Complex (GCC)

The GCC thickness decreased as axial length increased in the three groups. It was 97.95 ±6.37μm in Group I, followed by group II 95.34±7.28 μm and 91.49±8.30 μm in Group III. The decrease in GCC thickness was statistically significant (p-value 0.000).

DISCUSSION

Debates are still open as to which factors affect the measurement of RNFL thickness with OCT in normal subjects. These factors include age, optic disc size, race and axial length. It is highly likely that these factors affect the RNFL thickness differently and hence affect the diagnosis and monitoring in diseased conditions [3].

In the current study it was observed that there was no significant decline of RNFL thickness with age and similar results were reported by Pakravan M et al., and Vernon SA et al., [4,5]. It has been reported in literature, that a large variation (7×10^5 to 1.4×10^6 fibers) exists for the retinal ganglion cell complex in the normal population, which further complicates the analysis [4]. Contradictory results were observed by Kusuhura AN et al., and Mansoori T et al., and it was attributed that decline in the RNFL thickness with increasing age was due to probable loss of large number of axons with increasing age [3,8].

In this current study the maximum RNFL thickness was observed in the IT quadrant and minimum in the NL quadrant in both males and females. The females had a statistically significant thicker RNFL in the ST and IT quadrants (p-value 0.046 and 0.02) in comparison to males. In the studies conducted by Mansoori T et al., and others so far, no relation of RNFL thickness with gender has been established [8-10].

In the present study, the average RNFL showed statistically significant thinning with the increasing axial length. Kusuhara AN et al., observed the average RNFL thickness (100.5±11.6 μm) to decrease with increasing axial length with a regression coefficient of -0.002 [3]. In the current study, RNFL was studied in eight sectors. Thinning of RNFL was statistically significant in superior and inferior sectors temporally and nasally with the increasing axial length from 22.50 mm to >25.51 mm. Similar findings have also reported by Kusuhura AN et al., and Sowmya V et al., [3,13]. However, in the current study, the RNFL was normal in horizontal sectors which is in contrast to study by Sowmya et al., where thinning was present in all quadrants.

The OCT measures all the eyes at a fixed angular distance from the geometric centre of the optic disc. Since OCT measures a fixed circular scan of 3.4 mm therefore, the RNFL thickness in a myopic eye is measured thinner than intended. The RNFL thickness was found to be maximum in the inferior quadrant followed by superior, nasal and temporal quadrants and was in accordance with ISNT rule and similar results have been observed [8-10]. In a study conducted by Ramakrishnan R et al., contradictory results were observed with maximum RNFL thickness in the superior followed by inferior, nasal and temporal quadrants [12].

The average GCC showed statistically significant thinning with the increasing axial length in the three groups. Kim NR et al noted an average GCC of 93.87±7.76 μm and observed no significant statistical correlation between axial length and average GCC [11]. Recent studies have focused on study of GCC for early detection of glaucoma. The ganglion cells have the maximum density at the macula and it is suggested that study of this layer at macula could be early predictor of glaucoma. However, the current study shows that the GCC is also reduced with increasing axial length [14].

The current study highlights that the RNFL and GCC are affected by increasing axial length suggesting that the changes occur both at RNFL layer as well as inner retina in the study population. It also shows that age does not affect RNFL thickness in our region. A larger study sample is needed to further evaluate this.

LIMITATION

The limitation of the study was that, it was a non randomized study and included subjects belonging to the northern India only.

CONCLUSION

The current study shows that the RNFL and GCC thickness decreases with the increasing axial length in normal subjects. The assessment of RNFL and GCC thickness can be the mainstay in the early diagnosis and management of various optic neuropathies and thus an in-depth analysis is required to formulate diagnostic values of RNFL thickness. Clinicians need to keep in mind the axial length, race, gender, and ethnicity of patients before interpreting the results.

REFERENCES

[1] Ganekal S. Ganglion cell complex scan in the early prediction of glaucoma. *Nepalese Journal of Ophthalmology*. 2012;4(2):236-41.
[2] Kim MJ, Lee EJ, Kim TW. Peripapillary retinal nerve fibre layer thickness profile in subjects with myopia measured using the Stratus optical coherence tomography. *British Journal of Ophthalmology*. 2010;94(1):115-20.
[3] Nagai-Kusuhara A, Nakamura M, Fujioka M, Tatsumi Y, Negi A. Association of retinal nerve fibre layer thickness measured by confocal scanning laser ophthalmoscopy and optical coherence tomography with disc size and axial length. *British Journal of Ophthalmology*. 2008;92(2):186-90.
[4] Pakravan M, Aramesh S, Yazdani S, Yaseri M, Sedigh-Rahimabadi M. Peripapillary retinal nerve fiber layer thickness measurement by three-dimensional optical coherence tomography in a normal population. *Journal of Ophthalmic & Vision research*. 2009;4(4):220.
[5] Vernon SA, Rotchford AP, Negi A, Ryatt S, Tattersal C. Peripapillary retinal nerve fibre layer thickness in highly myopic Caucasians as measured by Stratus optical coherence tomography. *British Journal of Ophthalmology*. 2008;92(8):1076-80.
[6] Garas A, Vargha P, Hollo G. Diagnostic accuracy of nerve fibre layer, macular thickness and optic disc measurements made with the RTVue-100 optical coherence tomograph to detect glaucoma. *Eye*. 2011;25(1):57-65.
[7] Lee JY, Hwang YH, Lee SM, Kim YY. Age and retinal nerve fiber layer thickness measured by spectral domain optical coherence tomography. *Korean Journal of Ophthalmology*. 2012;26(3):163-68.
[8] Mansoori T, Viswanath K, Balakrishna N. Quantification of retinal nerve fibre layer thickness using spectral domain optical coherence tomography in normal Indian population. *Indian J Ophthalmol*. 2012;60(6):555-58.
[9] Malik A, Singh M, Arya SK, Sood S, Ichhpujani P. Retinal nerve fiber layer thickness in Indian eyes with optical coherence tomography. *Nepalese Journal of Ophthalmology*. 2012;4(1):59-63.
[10] Budenz DL, Anderson DR, Varma R, Schuman J, Cantor L, Savell J, et al. Determinants of normal retinal nerve fiber layer thickness measured by Stratus OCT. *Ophthalmology*. 2007;114(6):1046-52.
[11] Kim NR, Lee ES, Seong GJ, Kang SY, Kim JH, Hong S, et al. Comparing the ganglion cell complex and retinal nerve fibre layer measurements by Fourier domain OCT to detect glaucoma in high myopia. *British Journal of Ophthalmology*. 2010:bjo-2010.
[12] Ramakrishnan R, Mittal S, Ambatkar S, Kader MA. Retinal nerve fibre layer thickness measurements in normal Indian population by optical coherence tomography. *Indian Journal of Ophthalmology*. 2006;54(1):11.
[13] Sowmya V, Venkataramanan VR, Prasad V. Effect of Refractive Status and Axial Length on Peripapillary Retinal Nerve Fibre Layer Thickness: An Analysis Using 3D OCT. *Journal of Clinical and Diagnostic Research*: *JCDR*. 2015;9(9):NC01.
[14] Harwerth R.S.C.-D.L., Shen F., Smith E.L, 3rd, Crawford M.L. Ganglion cell losses underlying visual field defects from experimental glaucoma. *Invest Ophthalmol Vis Sci*. 1999;40:2242–50.

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