Original articles

Retinal nerve fiber layer thickness in Indian eyes with optical coherence tomography

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Abstract

Introduction: Measuring the thickness of the retinal nerve fiber layer is a potential method of recognizing axon loss prior to the visual field abnormality.

Objective: To study normal individuals to quantify peripapillary retinal nerve fiber layer (RNFL) thickness in Asian Indian subjects.

Materials and methods: This was a prospective study of 150 normal subjects. Peripapillary RNFL was imaged with Optical Coherence Tomography (OCT3) and the thickness of the RNFL around the disc was determined in four quadrants with a 3.4 mm circle OCT scan. The influence of age and gender was evaluated on various parameters using unpaired t test, Pearson's correlation coefficient and ANOVA.

Results: The sample included 66 males and 84 females. The mean age of the study sample was 42.64 ± 13.63 years. The average RNFL thickness was 101.07 ± 10.13µm with the maximum thickness in the inferior quadrant (127.47±15.57) followed by the superior, nasal and temporal quadrants. The difference between the inferior and superior quadrants was statistically significant ($p < 0.001$). There was no significant difference in RNFL thickness between males and females. Negative correlation was found between age and average RNFL thickness, superior and temporal average (Pearson's correlation value = -0.262, - 0.209, -0.294 respectively and p = 0.02, 0.04, 0.001 respectively).

Conclusion: The present study provides additional data on the existing database of RNFL thickness in Asian Indians. It is also evident that RNFL thickness decreases with age but there is no relationship with gender.

Key-words: optical coherence tomography, retinal nerve fiber layer thickness, glaucoma

Introduction

Glaucoma is an optic neuropathy associated with accelerated apoptosis of retinal ganglion cells that manifests as increased cupping of the optic disc and thinning of the retinal nerve fiber layer (RNFL). The diagnosis of glaucoma is currently based on the appearance of optic disc, RNFL and standard achromatic perimetry (Budenz et al, 2007). 25-35% of retinal ganglion cells may be lost before an abnormality appears on visual field (VF) (Quigley et al, 1989, Mikelberg et al, 1995). It is well known now that pathologic changes of optic nerve head (ONH) precede visual field (VF) changes so measuring RNFL is a potential method of recognizing

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axon loss in advance of recognizing the VF abnormality (Quigley et al 1989). Many instruments like optical coherence tomography (OCT), confocal scanning laser ophthalmoscopy and scanning laser polarimetry have been developed for detecting structural damage before actual functional field loss develops. OCT works on the principle of low-coherence interferometry (Huang et al 1991) and generates in vivo high resolution cross-sectional images of RNFL. These values have been seen to be highly reproducible, quantitative and objective (Hee at al 1995). It is useful in diagnosis of glaucoma to study diffuse and localized thinning of RNFL (Bowd et al 2000, Zangwill et al 2000).

Stratus OCT3(Zeiss) normative database comprises data of mostly Caucasian population (63%) with just 3% subjects being of Asian origin (Patella 2003). So normal OCT database is required for different subsets of population as ethnic differences in RNFL thickness have been reported and the OCT normal database is commercially not available for Indian eyes

Materials and methods

It was a cross-sectional and observational study and subjects included were healthy patients presenting for routine eye check up or complaints of refractive error. The study was conducted in accordance with Declaration of Helsinki and the guidelines for good ethical clinical practice. The study was approved by our institute ethics committee. Informed consent was obtained from all patients. A complete ocular examination including visual acuity, refractive error, anterior and posterior segment examination, intraocular pressure (IOP) with Goldman applanation tonometry, Gonioscopy with Goldman single mirror was done to rule out any anterior and posterior segment pathology.

Patients included were those of more than 20 years of age, with visual acuity better than 20/40, refractive error less than ±4D, IOP less than 20mHg, a normal ONH with vertical CD ratio of less than or equal to 0.6 without asymmetry of more than 0.2. Patients excluded were those with history of ocular trauma, intraocular surgery/ laser, diabetes mellitus, family history of glaucoma, some ocular/neurological disease affecting ONH or causing RNFL thinning.

Visual field examination was done using Swedish Interactive Threshold Algorithm (SITA) standard 30-2, white on white Humphrey visual field. Subjects included were those with mean deviation (MD) and pattern standard deviation (PSD) on HFA within 95 % confidence interval and normal glaucoma hemi-field test. All were required to have reliable visual fields (less than 20 % fixation loss, less than 33% false positive and false negative errors).

OCT was done on all the subjects after pupillary dilatation by a single experienced observer and good quality OCT scans having signal strength more than 7 were included for analysis. Subject's approximate refractive error was set on machine and he was asked to fixate on an internal fixation target. Peripapillary RNFL was determined in four quadrants with Stratus OCT, using Fast RNFL scan which consists of 3 peripapillary scans each consisting of 256 test points measured along a circle having a diameter of 3.46mm centered on the optic disc. Measurements were than assessed using RNFL thickness average analysis protocol.

Statistics: Data was analyzed using SPSS11 software. Data of one eye that fulfilled all criteria was included in study. Independent variables were evaluated using unpaired t test. Pearson's correlation coefficient, Spearman's rank Correlation coefficient and ANOVA were used to determine the effect of age on RNFL measurements.

Results

Out of 162 subjects who volunteered to participate, 150 were included, out of which 66(44.0 %) were males and 84(56.0 %) females. Seven subjects of those excluded had unreliable visual fields, 3 were glaucoma suspects and 2 had visual acuity less than 20/40. Mean age of the study sample was 42.64±13.63yrs (Range 20-70). Age and sex distribution is shown in Table 1. No significant difference (p=0.24) in RNFL thickness was seen between males (99.92±8.97) and females (101.92±10.88).

The average ± SD RNFL thickness was 101.07±10.13µm with 95% confidence interval ranging from 99.39 to 102.75µm. The thickness in the inferior quadrant was maximum (127.47±15.57) followed by superior (125.77±16.52), nasal (83.56±17.35) and temporal (65.68±12.13) quadrant. The mean RNFL thickness in four quadrants and for all clock hours is shown in Table 2. Difference between inferior and superior quadrants was found to be statistically significant (p<0.001). Percentile levels at 95%, 5% and 1% for our study population is shown in table3.

Negative correlation was found between age and average RNFL thickness, superior and nasal average (Pearson's correlation value= -0.262, -0.209, -0.294 resp. and p=0.02, 0.04, 0.001 resp.). Average RNFL thickness declined by 2.0µm/decade (Range 0.47-3.49, p=0.02).

Table 1
Age and gender distribution

Age Group(years)	Males	Females
20-30	15(10%)	17(11.3%)
30-40	14(9.3%)	22(14.6%)
40-50	22(14.6%)	20(13.3%)
50-60	10(6.6%)	14(9.3%)
60-70	05(3.3%)	11(7.3%)
Total	66(44.0%)	84(56.0%)

Table 2
RNFL thickness changes with age (RNFL thickness mean± SD (um)

Parameter	20-30	30-40	40-50	50-60	60-70	P value
Average	104.28± 10.04	103.81 ± 9.65	99.69 ±11.05	98.99 ±6.84	95.90 ±10.47	0.021
Quadrant						
Inferior	127.96 ±19.21	127.83 ±16.98	127.80 ±15.37	127.08 ±10.44	125.23 ±13.31	0.987
Nasal	81.26 ±18.49	92.66 ±16.68	77.12 ±14.24	88.50 ±15.46	79.07 ±19.29	0.001
Superior	127.53 ±16.46	132.16 ±8.90	124.95 ±18.86	120.66 ±16.89	119.0 ±18.01	0.049
Temporal	68.13 ±15.58	68.16 ±9.98	65.70 ±13.14	59.95 ±7.84	64.76 ±7.92	0.093
Clock Hours						
1	139.10 ±22.24	136.64 ±13.93	127.49 ±27.58	126.95 ±23.79	125.43 ±27.73	0.129
2	126.73 ±20.51	125.71 ±14.53	117.03 ±30.78	122.90 ±18.87	109.57 ±27.29	0.124
3	107.17 ±17.95	108.50 ±21.03	96.78 ±21.32	106.60 ±23.09	94.71 ±25.98	0.073
4	66.43 ±14.59	76.07 ±18.70	61.65 ±15.29	70.55 ±15.60	73.00 ±30.42	0.024
5	79.10 ±16.26	82.18 ±23.62	73.70 ±17.72	81.60 ±21.00	85.29 ±35.68	0.384
6	114.93 ±23.72	108.79 ±28.36	113.73 ±26.48	116.75 ±18.96	107.36 ±25.57	0.714
7	145.10 ±29.69	137.54 ±29.64	143.46 ±24.33	143.75 ±14.02	129.29 ±25.20	0.324
8	127.60 ±30.58	128.79 ±16.47	124.24 ±31.28	123.25 ±16.93	125.36 ±29.89	0.937
9	75.30 ±24.31	66.82 ±12.55	66.24 ±15.42	61.90 ±12.64	65.86 ±17.18	0.079
10	54.30 ±9.92	53.75 ±10.95	51.89 ±13.61	49.05 ±9.23	47.79 ±9.23	0.260
11	79.80 ±22.12	80.75 ±13.05	78.57 ±18.90	74.10 ±15.46	72.07 ±13.88	0.470
12	125.80 ±24.80	131.43 ±18.90	123.57 ±25.94	116.90 ±19.75	117.07 ±17.18	0.169

Table 3
Distribution percentile of RNFL thickness in the study group

	100	95	5	1
1 o clock	187.00	174.00	88.50	79.20
2 o clock	183.00	158.00	85.00	39.70
3 o clock	158.00	139.00	66.50	56.50
4 o clock	157.00	102.00	43.00	34.70
5 o clock	172.00	112.50	49.00	38.50
6 o clock	178.00	160.00	76.00	65.60
7 o clock	200.00	185.00	100.00	72.10
8 o clock	179.00	165.50	88.50	54.00
9 o clock	173.00	95.00	45.00	37.10
10oclock	96.00	72.50	35.00	30.20
11oclock	134.00	119.50	53.00	40.80
12oclock	183.00	161.00	84.50	60.40
Average thickness	126.00	117.11	83.01	72.60

Discussion

The current study was done to determine the RNFL thickness in normal Indian population. The average RNFL thickness in our study was 101.07±10.13µm. It was comparable to previous studies done on Indian eyes (Ramakrishnan et al 2006, Sony et al 2004). Study done by Budenz et al (2007) on Caucasian eyes showed that they had mean RNFL values of 100.1±11.6µm which was significantly less than Asians (105.8±9.2). RNFL thickness in other Asian countries has also been seen to be on the higher side than Caucasians (Thai population= 109.3 ±10.5µm, Taiwanese= 108.7±9.4µm, Chinese=111.5 ±4.12) (Manassakorn et al, 2008; Peng et al, 2008; Luo et al, 1998). The normative reference values for RNFL thickness by Stratus OCT were developed in 2003 and comprised of 328 healthy subjects of various age, gender and ethnicities (Patella, 2003). 60% group in that database comprised of Caucasians with only 3% being Asians. So RNFL thickness has been seen to vary among ethnicities. The values of significant concern to us will be those that fall in the lower limits of the normal range and in the lower percentiles (fifth and first percentile). Asians with fifth percentile RNFL thickness in normative database may actually already have developed significant first percentile thinning.

Consistent with a previous study (Manassakorn et al, 2008) the RNFL thickness in our study followed the ISNT rule. Few studies (Budenz et al 2007, Sony et al, 2004) have found inferior thickness to be more than superior though the difference was not statistically significant. Another study (Ramakrisnan et al, 2006) reported the thickness of superior quadrant to be more than the inferior. RNFL thickness was not seen to correlate with gender similar to previous studies.

Age had significant negative correlation with average RNFL thickness which was comparable to earlier studies (Budenz et al, 2007; Sony et al, 2004) though few studies did not find any similar association (Ramakrisnan et al, 2006). RNFL thickness was found to decrease with age in Thai population (Manassakorn et al, 2008) at a rate of 2.3µm/ decade and in Caucasians (Budenz et al, 2007) at 2.0µm/decade. Our population also showed a decline of 2.0µm/decade. Cross- sectional studies of RNFL thickness using scanning laser polarimetry also have found a decrease in RNFL thickness with age (Chi et al, 1995; Poinoosawmy et al, 1997). Decrease in RNFL axons has also been demonstrated by histological analysis (Johnson et al, 1987).

Conclusion

Our study provides additional normative database of peripapillary RNFL thickness in Indians. RNFL thickness was found to decrease with age irrespective of gender. As RNFL measurement varies with the population used as a database, we need to be cautious while interpreting the data on Stratus OCT as commercially available normative data is not available for Indian eyes.

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