Original Article

Comparison of Quadrantic Retinal Nerve Fiber Layer Thickness between Glaucoma Patients and Age Matched Controls

Nargis Nizam Ashraf¹, Nisar Ahmed Siyal², Muhammad Ibrahim³ Department of Ophthalmology, ¹⁻³Dow University of Health Sciences, Karachi

ABSTRACT

Purpose: To compare the quadrantic retinal nerve fiber layer thickness between the glaucoma patients and agematched controls.

Study Design: Descriptive observational study.

Place and Duration of study: Eye Department of Civil Hospital Karachi, from January 2018 to December 2020.

Methods: Two hundred and fifty eyes were included in this study. There were 128 eyes of the glaucoma patients and 122 eyes were age-matched controls. After complete ocular examination, all participants underwent optical coherence tomography and retinal nerve fiber layer thickness measurement in four quadrants. Prior quadrants were subsequently analyzed. Heidelberg 3-D optical coherence tomography 2017, Spec- TR- 04859 was used. Readings were saved on Excel sheet and analyzed on SPSS version 25. For descriptive statistics the mean and standard deviations were calculated for each quadrant and for inferential statistics the data was first checked for the normality. Comparison of the quadrants was done using non-parametric Paired Sample t-test (Wilcoxon signed rank test).

Results: Out of 250. Form which 128 (51%) eyes were those of glaucoma patients and 122 (49%) eyes were of non-glaucoma patients. The mean difference between the Glaucomatous and non-Glaucomatous eyes were statistically significant in all four quadrants (p > 0.05).

Conclusion: Glaucomatous eyes had reduced RNFL thickness in all quadrants. The thickness of the inferior quadrant was more as compared to the other quadrants in both glaucoma and control groups. Whereas the least thickness was that of the temporal quadrant.

Key Words: Retinal nerve fiber layer, Optical coherence tomography, Glaucoma.

How to Cite this Article: Ashraf NN, Siyal NA, Ibrahim M. Comparison of Quadrantic Retinal Nerve Fiber Layer Thickness between Glaucoma Patients and Age Matched Controls. Pak J Ophthalmol. 2021, **37 (3):** 274-277. Doi: 10.36351/pjo.v37i3.1199

Correspondence: Nargis Nizam Ashraf Eye Unit Dow University of Health Sciences Karachi Email: nargis.ashraf99@hotmail.com

Received: January 21, 2021 Accepted: May 3, 2021

INTRODUCTION

The main diagnostic tools used to examine and analyze optic nerve and retinal nerve fiber layer (RNFL) are disc photography, Confocal scanning laser ophthalmoscopy and Ocular coherence tomography.¹ It is possible to observe and analyze the objective and quantitative details of retinal layers with Spectral domain OCT. This is done by means of automated algorithms.² Delay in echo-time and quantity of reflected light are put to use through interferometry for

3 D analysis.³ Additional information is obtained with swept source (SS) OCT which has a much faster speed than conventional OCT and also has a longer wave length.⁴

The effect of age-related thinning of RNFL should be taken into account when assessing for glaucomatous changes.⁵ Literature shows that RNFL thinning was more prominent in the superior and inferior quadrants in patients with glaucoma.⁶ When the superior and inferior quadrants of the disc are involved there are more chances of profound visual field defects. This is explained by the arrangement of axons of ganglion cells in the disc. Nowadays ganglion cell complex is also taken into account and the ideal area is around the optic disc. It is here that the ganglion cells converge and exit from the eye.⁷

In this study, we compared the quadrantic thickness of RNFL between normal controls and glaucoma patients in a tertiary care hospital of Karachi.

METHODS

Patients with clinical findings of glaucoma were included in the study by convenient sampling technique. Patients with ocular diseases other than glaucoma were excluded. Sample size was calculated by open epi program and came out to be 250 eyes. Out of these, 128 eyes were those of glaucoma patients and 122 eyes were non-glaucomatous controls. After complete ocular examination including visual acuity, intraocular pressures, slit lamp examination and Fundoscopy, OCT was done for RNFL thickness. Thickness of all four quadrants; superior, inferior, nasal and temporal was documented.Heidelberg 3-D optical coherence tomography 2017, Spec-TR-04859 was used. The patients' pupils were dilated with Tropicamide eye drops. Statistical analysis was doneby SPSS version 25. Sample t-test was performed for comparison of data of normal subjects with that of glaucoma patients. Frequencies were checked and cross tabulation was done for descriptive analysis.

For descriptive statistics the mean and standard deviations were calculated for each quadrant and for inferential statistics the data was first checked for the normality and based on the p-values it was found that data is significantly deviated from the normal distribution (P < 0.05). Therefore, the Comparison of the quadrants was done using non-parametric Paired Sample t-test (Wilcoxon signed rank test).

RESULTS

The mean difference between the Glaucomatous and Non-Glaucomatous eyes are shown in table 1. Temporal quadrant was the thinnest in glaucomatous eyes while superior quadrant was thinnest in controls. Inferior quadrant was the thickest in both glaucomatous eyes as well as controls.

Table 1: Comparison of Total number of cases in term of quadrants.

Quadrants		Mean	p-value
Superior	Glaucomatous eye	56.5 ± 15.2	0.001
Quadrant	Control	126.1 ± 30.4	0.001
Inferior	Glaucomatous eye	57.8 ± 18	0.001
Quadrant	Control	131.2 ± 47.5	
Nasal	Glaucomatous eye	56.1 ± 16.9	0.001
Quadrant	Control	127.5 ± 39.2	
Temporal	Glaucomatous eye	55.7 ± 16.2	0.001
Quadrant	Control	127.1 ± 38.6	0.001

DISCUSSION

The technology of OCT is evolving. The spectral domain OCT has much higher scanning speed that is 25,000 A scans per second compared to time domain OCT. It produces a 3 D image of the retina.⁸ The advantage of OCT over other investigation techniques is that it is non-invasive, analyzes RNFL in all four quadrants. RNFL thickness varies under the influence of age, gender, axial length, optic disc size and refractive error.⁹ In our study we analyzed the retinal nerve fiber layer thickness in 4 quadrants. In a study by Kausar A and Akhtar N, the ISNT rule applied to the RNFL thickness.¹⁰ RNFL thickness is also being studied in cases of neurological diseases including Alzheimer and multiple sclerosis etc.¹¹⁻¹³ In a crosssectional study it was observed that retinal nerve fiber laver thickness diminished by 0.16 - 0.26 micrometer every year, indicating the effect of age on RNFL.¹⁴

The temporal and nasal quadrants were assessed by Hwang and Kim, especially the neuro-retinal rim on OCT.¹⁵ In our study when means were compared of normal and glaucoma patients, it was seen that the most decreased thickness was that of the temporal quadrant.

In another study, It was observed that about 6 years before onset of changes in fields, retinal nerve fiber layer thinning had started.¹⁶ The thickness of the retinal nerve fiber layer at the outset determines the course the disease. Another factor determining RNFL thickness is myopia. The greater the myopia the lesser

the thickness. In studies done in individuals with myopia, the average measurement of RNFL came out to be 107.49. In yet another research the average thickness came out to be 105 micrometers.¹⁷

In a study at Karachi, RNFL was of greatest thickness at the inferior pole.³ Most of the studies have concentrated on the parapapillary measurement of RNFL on OCT and on fundoscopy. However, other areas give useful information especially OCT of 6 by 6 mm square optic disc cube scan.¹⁸ In another study conducted in Spain on relation of RNFL defects to cardiovascular conditions, it was noted that atherosclerosis in right carotid artery led to decreased thickness of superior RNFL.¹⁹ Other conditions leading to superior quadrant changes are ocular ischemic syndrome, neovascular glaucoma and central retinal vein occlusion. When optical coherence tomography of cigarette smokers was done it was observed that thickness of nasal quadrant was decreased.12

Another way of assessing glaucomatous damage is analyzing retinal ganglion cells. The best area to study retinal ganglion cells is the macula, their greatest number being at this area. When the efficacy of analyzing retinal nerve fiber layer was compared to that of ganglion cells by Saha and Karti in their research, both were equally reliable.^{20,21} This was converse to what was observed by Kaushik and Kataria, they found retinal nerve fiber layer thickness to be a more reliable indicator of glaucoma progression than the retinal ganglion cell analysis.⁷ This could be because of the distribution of the different type of ganglion cells in the retina. Ganglion cells are analyzed at the macula, here P type of ganglion cells are in majority. For early diagnosis of glaucoma M type ganglion cell analysis is more reliable, which are not in the foveal region.

Limitation of this study is that it is a single center study and sample size is small. All patients with glaucoma were included irrespective to the stage of disease.

CONCLUSION

When quadrantic analysis was done on OCT in our population, the difference was most in the inferior quadrant. This is different from studies done in other populations in which nasal and temporal quadrants were more affected. This needs to be assessed with further studies in our population.

Ethical Approval

The study was approved by the institutional review board/Ethical review board (**OSP-IRB/2021/001**).

Conflict of Interest

Authors declared no conflict of interest.

REFERENCES

- 1. Optic nerve and retinal nerve fiber imaging. Available from: https://eyewiki.aao.org/Optic_Nerve_and_Retinal __Nerve_Fiber_Imaging
- Mariottoni EB, Jammal AA, Urata CN, Berchuck SI, Thompson AC, Estrela T, et al. Quantification of Retinal Nerve Fibre Layer Thickness on Optical Coherence Tomography with a Deep Learning Segmentation-Free Approach. Sci Rep. 2020; 10 (1): 402. Doi: 10.1038/s41598-019-57196-y.
- 3. **Hashmani N, Hashmani S.** Three-dimensional mapping of peripapillary retinal layers using a spectral domain optical coherence tomography. Clin Ophthalmol. 2017; **11:** 2191-2198.
- 4. Hondur G, Göktaş E, Al-Aswad L, Tezel G. Agerelated changes in the peripheral retinal nerve fiber layer thickness. Clin Ophthalmol. 2018; **12:** 401-409. Doi: 10.2147/OPTH.S157429.
- 5. Jeong D, Sung KR, Jo YH, Yun SC. Age-Related Physiologic Thinning Rate of the Retinal Nerve Fiber Layer in Different Levels of Myopia. J Ophthalmol. 2020; 2020: 1873581. Doi: 10.1155/2020/1873581.
- Hood DC, Slobodnick A, Raza AS, de Moraes CG, Teng CC, Ritch R. Early glaucoma involves both deep local, and shallow widespread, retinal nerve fiber damage of the macular region. Invest Ophthalmol Vis Sci. 2014; 55 (2): 632-649. Doi: 10.1167/iovs.13-13130.
- Kaushik S, Kataria P, Jain V, Joshi G, Raj S, Pandav SS. Evaluation of macular ganglion cell analysis compared to retinal nerve fiber layer thickness for preperimetric glaucoma diagnosis. Indian J Ophthalmol. 2018; 66 (4): 511-516. Doi: 10.4103/ijo.IJO 1039 17.
- Sung KR, Kim JS, Wollstein G, Folio L, Kook MS, Schuman JS. Imaging of the retinal nerve fibre layer with spectral domain optical coherence tomography for glaucoma diagnosis. Br J Ophthalmol. 2011; 95 (7): 909-914. Doi: 10.1136/bjo.2010.186924. Epub 2010 Oct 28. PMID: 21030413; PMCID: PMC3421150.
- Tatham AJ, Medeiros FA. Detecting Structural Progression in Glaucoma with Optical Coherence Tomography. Ophthalmology, 2017; 124 (12S): S57-S65. Doi: 10.1016/j.ophtha.2017.07.015.

- 10. Kausar A, Akhtar N, Afzal F, Ali K. Effect of refractive errors/axial length on peripapillary retinal nerve fibre layer thickness (RNFL) measured by Topcon SD-OCT. J Pak Med Assoc. 2018; 68 (7): 1054-1059.
- 11. Martinez-Lapiscina EH, Arnow S, Wilson JA, Saidha S, Preiningerova JL, Oberwahrenbrock T, et al. Retinal thickness measured with optical coherence tomography and risk of disability worsening in multiple sclerosis: a cohort study. Lancet Neurol. 2016; 15 (6): 574-584.

Doi: 10.1016/S1474-4422(16)00068-5. .

- Larrosa JM, Garcia-Martin E, Bambo MP, Pinilla J, Polo V, Otin S, et al. Potential new diagnostic tool for Alzheimer's disease using a linear discriminant function for Fourier domain optical coherence tomography. Invest Ophthalmol Vis Sci. 2014; 55 (5): 3043-3051. DOI: 10.1167/iovs.13-13629.
- 13. Young JB, Godara P, Williams V, Summerfelt P, Connor TB, Tarima S, et al. Assessing Retinal Structure in Patients with Parkinson's Disease. J Neurol Neurophysiol. 2019; 10 (1): 485. Doi: 10.4172/2155-9562.1000485.
- 14. Hirasawa H, Tomidokoro A, Araie M, Konno S, Saito H, Iwase A, et al. Peripapillary retinal nerve fiber layer thickness determined by spectral-domain optical coherence tomography in ophthalmologically normal eyes. Arch Ophthalmol. 2010; **128** (11): 1420-1426. Doi: 10.1001/archophthalmol.2010.244.
- Hwang YH, Kim YY. Glaucoma diagnostic ability of quadrant and clock-hour neuroretinal rim assessment using cirrus HD optical coherence tomography. Invest Ophthalmol Vis Sci. 2012; 53 (4): 2226-2234. Doi: 10.1167/iovs.11-8689.
- 16. Banitt MR, Ventura LM, Feuer WJ, Savatovsky E, Luna G, Shif O, et al. Progressive loss of retinal ganglion cell function precedes structural loss by several years in glaucoma suspects. Invest Ophthalmol Vis Sci. 2013 Mar; 54 (3): 2346-2352. Doi: 10.1167/iovs.12-11026.

- 17. Murugan C, Golodza BZ, Pillay k, Mthembu BN, Singh P, Maseko KS, et al. Retinal nerve fibre layer thickness of black and Indian myopic students at the University of KwaZulu-Natal. Afr Vision Eye Health, 2015; 74: 24.
- Zhang X, Dastiridou A, Francis BA, Tan O, Varma R, Greenfield DS, et al. Advanced Imaging for Glaucoma Study Group. Baseline Fourier-Domain Optical Coherence Tomography Structural Risk Factors for Visual Field Progression in the Advanced Imaging for Glaucoma Study. Am J Ophthalmol. 2016; 172: 94-103. Doi: 10.1016/j.ajo.2016.09.015.
- Wang D, Li Y, Zhou Y, Jin C, Zhao Q, Wang A, et al. Asymptomatic carotid artery stenosis and retinal nerve fiber layer thickness. A community-based, observational study. PLoS One. 2017; 12 (5): e0177277. Doi: 10.1371/journal.pone.0177277.
- 20. Saha M, Bandyopadhyay S, Das D, Ghosh S. Comparative analysis of macular and peripapillary retinal nerve fiber layer thickness in normal, glaucoma suspect and glaucomatous eyes by optical coherence tomography. Nepal J ophthalmol. 2016: 8: 110-118.
- Karti O, Yuksel B, Uzunel UD, Karahan E, Zengin MO, Kusbeci T. The assessment of optical coherence tomographic parameters in subjects with a positive family history of glaucoma. Clin Exp Optom. 2017; 100 (6): 663-667. Doi: 10.1111/cxo.12523.

Authors' Designation and Contribution

Nargis Nizam Ashraf; Assistant Professor: Concepts, Design, Literature search, Manuscript preparation, Manuscript editing, Manuscript review.

Nisar Ahmed Siyal; Associate Professor: *Concepts, Design, Manuscript review.*

Muhammad Ibrahim; Technologist: Data acquisition, Manuscript review.

···☆···